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September 22, 1992

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U.S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

Attn: Section 8(e) Coordinator (CAP Agreement)

Re: CAP Agreement Identification No. 8ECAP-0110

Dear Sir or Madam:

Union Carbide Corporation ("Union Carbide") herewith submits the following report pursuant to the terms of the TSCA §8(e) Compliance Audit Program and Union Carbide's CAP Agreement dated August 14, 1991 (8ECAP-0110). This report describes a reproductive toxicology study with diethylene glycol butyl ether (CASRn 112-34-5).

"Fertility and General Reproductive Performance of Diethylene Glycol Butyl Ether in Rats", IRDC, DRD No. BSBTS-796S2 (191-900), January 10, 1984 (Test Article: B0547-01).

A complete summary of this report is attached.

Previous TSCA Section 8(e) or "FYI" Submission(s) related to this substance are:

(None)

Previous PMN submissions related to this substance are: (None)

B0547-01

RECEIVED 1/31/95

This information is submitted in light of EPA's current guidance. Union Carbide does not necessarily agree that this information reasonably supports the conclusion that the subject chemical presents a substantial risk of injury to health or the environment.

In the attached report the term "CONFIDENTIAL" may appear. This precautionary statement was for internal use at the time of issuance of the report. Confidentiality is hereby waived for purposes of the needs of the Agency in assessing health and safety information. The Agency is advised, however, that the publication rights to the contained information are the property of Union Carbide.

Yours truly,

William C. Kuryla, Ph.D.
Associate Director
Product Safety
(203/794-5230)

WCK/cr
Attachment (3 copies of cover letter, summary, and report)

# SUMMARY

FERTILITY AND GENERAL REPRODUCTIVE
PERFORMANCE OF DIETHYLENE GLYCOL BUTYL ETHER IN RATS

Detailed Study Report
January 10, 1984

# SUMMARY

2.

International Research
and Development Corporation
MATTAWAN, MICHIGAN, U.S.A. 49071 TELEPHONE (616) 668-3336

| | |
|---|---|
| SPONSOR: | The Procter and Gamble Company |
| TEST ARTICLE (TSIN): | B0547-01 |
| SUBJECT: | Study of Fertility and General Reproductive Performance in Rats |
| DRD NO.: | BSBTS-796S2 |
| DATE OF SUBMISSION: | January 10, 1984 |

RECEIVED BY
JAN 16 1984
OPERATIONS SECTION

191-900

"credence through research"

# SUMMARY



## II. SYNOPSIS

Charles River COBS® CD® male and female rats were used to determine the effects of B0547-01 on fertility and general reproductive performance. This study was comprised of six treated groups and one control group containing 25 males and 25 females each. The test article was administered orally by gavage to the males only in three groups beginning 60 days prior to mating and continuing until sacrifice; the females in these groups were not treated. In three other groups, the females only were dosed beginning 14 days prior to mating and continuing until sacrifice or weaning; male rats in these groups were not treated. Within each group, the treated animals were mated with their untreated counterparts. All treated animals received the test article orally by gavage at dosage levels of either 250, 500 or 1000 mg/kg/day as a single daily dose at a constant volume of 5 ml/kg. Both males and females in the control group received the vehicle only, deionized water, at a volume of 5 ml/kg on a comparable regimen and were similarly mated.

Approximately one-half of the mated females in each group underwent a uterine examination on gestation day 13 while the remaining females were allowed to deliver.

Among the groups of treated male rats, one rat died at the 500 mg/kg/day level and three rats died at the 1000 mg/kg/day level. Survival was 100% among males in the control and 250 mg/kg/day groups. These deaths occurred without apparent cause between study weeks 5 and 10 and no consistent pattern of antemortem or postmortem observations were evident. Among the treated female rats, two females died at the 250 mg/kg/day level, one was sacrificed *in extremis* at the 500 mg/kg/day level and three rats died at the 1000 mg/kg/day level. One untreated female in the male high dose group died. Survival was 100% among control females. Death or sacrifice *in extremis* among females occurred between

# SUMMARY



study weeks 6 and 11 and no definite treatment related trends on external or necropsy observations were evident. With the exception of one low-dose female that died as the result of an intubation error, the cause of death could not be determined for any of the females that died. However, the postmortem findings from several animals were not inconsistent with aspiration pneumonitis. The only effect on appearance or behavior attributable to treatment with B0547-01 was a slight excess salivation among female rats dosed at 1000 mg/kg/day.

The mean weekly body weights of male rats dosed at the 1000 mg/kg/day level were slightly reduced during all treated study weeks. No effects on body weights were present among males dosed at 250 or 500 mg/kg/day or among females at any dosage level. Similarly, no meaningful effects were evident in maternal female body weights during gestation or lactation in any study group.

The only definite test article effect observed during the litter portion of this study was a reduction in mean pup body weights during the latter stages of lactation among the offspring of females dosed at the 1000 mg/kg/day level.

Analyses of reproductive data suggested that treatment with B0547-01 may have reduced the mean numbers of uterine implantations in both groups dosed at the 1000 mg/kg/day level (male and females). These findings were indicated by reductions in viable litter size at parturition and total implantations observed during weaning uterine examination. However, a similar effect was not evident at 13-day uterine examination wherein the mean numbers of implantations were comparable in all treated groups to concurrent and historical control values. A definite treatment effect was dubious.

No other effects attributable to treatment were present in either the parturition, litter or uterine examination data.

# SUMMARY

In conclusion, at a dose level of 1000 mg/kg/day, treatment with B0547-01 to female Charles River COBS® CD® rats caused a reduction in mean pup body weight during lactation and may have reduced mean uterine implantations. Treatment to male Charles River COBS® CD® rats at 1000 mg/kg/day may also have resulted in a reduction in uterine implantations in females to which they were mated, however a clear effect was not evident.

B0547-01 had no effects on fertility or reproductive performance in either male or female rats at dosage levels of 500 mg/kg/day and less.

50-2-57

Attachment 3

B-8

↓ implantation
↓ litter/fetal wts
at highest
dose only

FERTILITY AND GENERAL REPRODUCTIVE
PERFORMANCE OF DIETHYLENE GLYCOL BUTYL ETHER IN RATS

Detailed Study Report
January 10, 1984

Dan Briggs P&G

International Research
and Development Corporation
MATTAWAN, MICHIGAN, U.S.A. 49071 TELEPHONE (616) 668-3336

SPONSOR: The Procter and Gamble Company

TEST ARTICLE (TSIN): B0547-01

SUBJECT: Study of Fertility and General Reproductive Performance in Rats

DRD NO.: BSBTS-796S2

DATE OF SUBMISSION: January 10, 1984

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## I. QUALITY ASSURANCE STATEMENT

Study Title: Study of Fertility and General Reproductive Performance in Rats

Test Article: B0547-01

The conduct of this study has been subjected to periodic inspections. The dates of inspection and the dates that findings were reported to management and the Study Director are listed in Appendix A.

This report has been reviewed by the International Research and Development Corporation Quality Assurance Department in accordance with the United States Food and Drug Administration's Good Laboratory Practice Regulations of June 20, 1979.

Approved And Submitted By: [redacted] 1/10/84

Director of Quality Assurance Date

## II. SYNOPSIS

Charles River COBS® CD® male and female rats were used to determine the effects of B0547-01 on fertility and general reproductive performance. This study was comprised of six treated groups and one control group containing 25 males and 25 females each. The test article was administered orally by gavage to the males only in three groups beginning 60 days prior to mating and continuing until sacrifice; the females in these groups were not treated. In three other groups, the females only were dosed beginning 14 days prior to mating and continuing until sacrifice or weaning; male rats in these groups were not treated. Within each group, the treated animals were mated with their untreated counterparts. All treated animals received the test article orally by gavage at dosage levels of either 250, 500 or 1000 mg/kg/day as a single daily dose at a constant volume of 5 ml/kg. Both males and females in the control group received the vehicle only, deionized water, at a volume of 5 ml/kg on a comparable regimen and were similarly mated.

Approximately one-half of the mated females in each group underwent a uterine examination on gestation day 13 while the remaining females were allowed to deliver.

Among the groups of treated male rats, one rat died at the 500 mg/kg/day level and three rats died at the 1000 mg/kg/day level. Survival was 100% among males in the control and 250 mg/kg/day groups. These deaths occurred without apparent cause between study weeks 5 and 10 and no consistent pattern of antemortem or postmortem observations were evident. Among the treated female rats, two females died at the 250 mg/kg/day level, one was sacrificed *in extremis* at the 500 mg/kg/day level and three rats died at the 1000 mg/kg/day level. One untreated female in the male high dose group died. Survival was 100% among control females. Death or sacrifice *in extremis* among females occurred between

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The only definite test article effect observed during the litter portion of this study was a reduction in mean pup body weights during the latter stages of lactation among the offspring of females dosed at the 1000 mg/kg/day level.

Analyses of reproductive data suggested that treatment with B0547-01 may have reduced the mean numbers of uterine implantations in both groups dosed at the 1000 mg/kg/day level (male and females). These findings were indicated by reductions in viable litter size at parturition and total implantations observed during weaning uterine examination. However, a similar effect was not evident at 13-day uterine examination wherein the mean numbers of implantations were comparable in all treated groups to concurrent and historical control values. A definite treatment effect was dubious.

No other effects attributable to treatment were present in either the parturition, litter or uterine examination data.

In conclusion, at a dose level of 1000 mg/kg/day, treatment with B0547-01 to female Charles River COBS® CD® rats caused a reduction in mean pup body weight during lactation and may have reduced mean uterine implantations. Treatment to male Charles River COBS® CD® rats at 1000 mg/kg/day may also have resulted in a reduction in uterine implantations in females to which they were mated, however a clear effect was not evident.

B0547-01 had no effects on fertility or reproductive performance in either male or female rats at dosage levels of 500 mg/kg/day and less.

## III. INTRODUCTION

### A. OBJECTIVE

The objective of the study was to establish the effect of the test article on fertility, parturition, neonatal viability, growth of the newborn and reproductive performance in rats. This study design utilized treatment of both sexes.

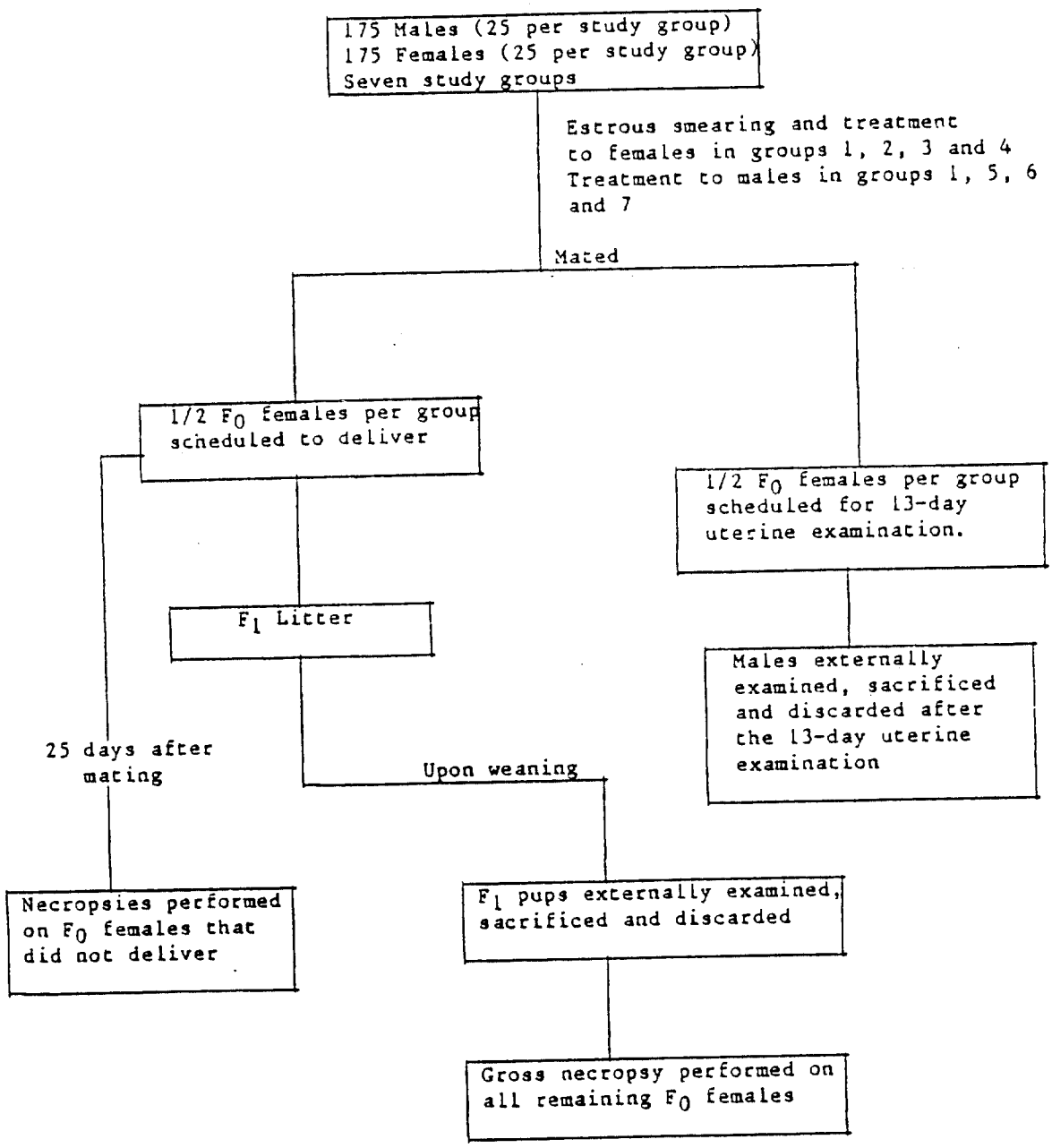
### B. STUDY DESIGN

This study was comprised of seven study groups containing 25 parental males and 25 parental females each. The test article, B0547-01, was administered to either the males or females in each treated group. In groups 2, 3 and 4, only female rats were treated and in groups 5, 6 and 7 only male rats were treated. The parental rats within each group ($F_0$ generation) were mated (treated with untreated) to produce the next ($F_1$) generation. For comparitive purposes, male and female $F_0$ control rats (group 1) both received the vehicle, deionized water. A diagramatic representation of the study design is presented in Figure 1.

FIGURE 1.

Study of Fertility and General Reproductive Performance in Rats

STUDY DESIGN




191-900

C. TEST ARTICLE IDENTIFICATION

The test article utilized on this study was received in five shipments from the Procter and Gamble Company, Cincinnati, Ohio. The first test article allotment was received on December 2, 1982 as indicated below:

| Label | Description |
|---|---|
| TEST SUBST. (TSIN) B0547-01 | clear liquid |
| DIV. REQUEST DOC. (DRD) BSBTS-796 | |
| DATE REC'D (OPER. SECTION) | |
| TYPE OF TEST TERATOLOGY | |
| GROSS WT. (INC. LID, CONT., LABEL) 1209.6 g. | |
| *TARE WT. 353.1 g. NET WT. 856.0 g. | |
| STORAGE CONDITIONS ROOM TEMP. | |
| EXPIRATION DATE NK | |
| HAZARD None | |
| D.O.T. HAZARD NON-HAZARDOUS | |
| RETURN TO DIVISIONAL TOXICOLOGIST WHEN TEST IS COMPLETED | |

*CONTAINER, LID, LABEL

Additional shipments of the test article were received on December 30, 1982, January 26, 1983, March 9, 1983 and May 12, 1983. Specific label information for each of these shipments is stored in the IRDC archives and is available upon Sponsor request.

D. VEHICLE CONTROL ARTICLE IDENTIFICATION

The vehicle control article used in this study was deionized water.

## IV. METHODS AND PROCEDURES

This study was conducted in accordance with the protocol as approved by the Sponsor and in compliance with the Standard Operating Procedures of International Research and Development Corporation (IRDC). Procedures pertinent to this study are described herein.

### A. EXPERIMENTAL DESIGN

#### 1. Animals

The animals utilized on this study, Charles River COBS® CD® rats, were received in two shipments from the Charles River Breeding Laboratories, Inc., Portage, Michigan. The first shipment of 210, 28-day old male rats was received on February 23, 1983 and the second shipment of 210, virgin 70-day old female rats was received on March 31, 1983.

All rats were acclimated for a minimum of 15 days prior to placement on study.

From animal aquisition until sacrifice, the rats were provided with a basal laboratory diet of Purina® Certified Rodent Chow® #5002 and tap water available ad libitum and carefully observed for changes in appearance and behavior.

The basal laboratory diet, Purina® Certified Rodent Chow® #5002, was analyzed by the manufacturer for the presence of pesticides, heavy metals and aflatoxins. Each diet lot used was recorded. The drinking water at IRDC is analyzed quarterly for the presence of pesticides, heavy metals and coliforms. The results of these analyses are stored in the International Research and Development Corporation Archives at Mattawan, Michigan and are available upon request.

Throughout the study, all animals were housed in an environmentally controlled room. Temperature ranged between 20° and 24° C, humidity was maintained between 20% and 70% and fluorescent lighting provided illumination 12 hours per day. Temperature was below the range specified by

the study protocol (21°-25° C) on two days and was inadvertently not recorded on six days. Humidity was below the specified range (35% to 65%) on 12 occasions and exceeded the range twice. All rats were individually housed, except during mating, gestation and lactation in suspended wire-mesh cages.

Each rat was identified by cage, group and individually by a Monel® metal ear tag bearing its animal number. The individual animal number plus the IRDC study number comprised a unique identification number for each animal. At study initiation (study week 0), male rats were 43 days of age and weighed from 165 to 215 grams. Females placed on study during week 6 were 91 days of age and weighed from 216 to 267 grams. At the time of placement on study, the body weights of 11 male rats slightly exceeded the protocol specified limit (210 grams) and the body weights of five females were slightly less than the limit (220 grams).

The study initiated with the randomization of $F_0$ males on March 9, 1983 and terminated with the last parental female sacrifice on July 6, 1983.

2. Organization of Test Groups

At the end of the acclimation period, all animals were weighed and subjected to a detailed physical examination. Animals considered suitable for study were randomly assigned to one control group and six treatment groups each containing 25 males and 25 females by the following computer-generated system. Animal numbers and corresponding body weights were entered onto magnetic tape which was used as the data source for the randomization procedure. Mean body weights and standard deviations were calculated by sex and a computer-generated edit developed a listing of those animals whose body weights were within $\pm$ 1.6 (males) or $\pm$ 1.5 (females) standard deviations of the mean. From the qualifying animals, the randomization procedure selected and assigned the required number of

animals. Bartlett's test for homogeneity of variances was applied to the groups. If the groups were judged to be heterogeneous, new randomizations were generated until homogeneity was established. The following table illustrates the $F_0$ group arrangement.

Animal and Treatment Designation

| Group Number | Number of Males | Number of Females | Sex Dosed | Dosage Level mg/kg/day |
|---|---|---|---|---|
| 1 | 25 | 25 | males and females | 0 (Control) |
| 2 | 25 | 25 | females only | 250 |
| 3 | 25 | 25 | females only | 500 |
| 4 | 25 | 25 | females only | 1000 |
| 5 | 25 | 25 | males only | 250 |
| 6 | 25 | 25 | males only | 500 |
| 7 | 25 | 25 | males only | 1000 |

3. Mating

For females in groups 1, 2, 3 and 4, vaginal smears were conducted daily to establish estrus cycles beginning 10 days prior to test article administration. Smearing continued until evidence of mating was found or until the end of the mating period.

In both phases, each male was housed with one female of the same strain and source in plastic cages with wood chip (Beta Chip®) bedding for mating. The occurrence of copulation was determined by daily inspection for a copulatory plug or by vaginal inspection for sperm. The day that evidence of mating was detected was designated day 0 of gestation and the female was placed in an individual plastic cage.

Any female failing to show evidence of copulation after an initial 10-day period was remated for an additional five days with a male of proven fertility selected from the same group. At the end of the second mating period, all nonbred females were transferred to individual plastic cages containing bedding until sacrifice.

B. TEST ARTICLE ADMINISTRATION

The selected route of administration was oral since this has historically been the route of choice for administering a known quantity of test substance.

The appropriate amount of B0547-01 for each group was weighed daily into a graduated mixing cylinder and a sufficient quantity of the vehicle, deionized water, was added to yield the necessary volume of prepared test material. The cylinder was shaken by hand to ensure dissolution and the contents dispensed into a capped glass container.

The test article was prepared at concentrations to permit the administration of dose levels of 250, 500 and 1000 mg/kg/day at a constant dosage volume of 5 ml/kg.

The test article was administered orally by gavage as a single daily dose. The males in groups 5, 6 and 7 were dosed beginning 60 days prior to mating and continued until sacrifice. Males in groups 2, 3 and 4 were not dosed. Test article administration to females in groups 2, 3 and 4 began 14 days prior to mating and continued through weaning of the pups or until gestation day 13 sacrifice. Females in groups 5, 6 and 7 were not dosed. Nonbred females were dosed until sacrifice. Both males and females in the control group received the vehicle only on comparable regimens at a volume of 5 ml/kg. Individual dosages were based on the most recently recorded body weights.

Males receiving the test article were mated with the untreated females from the same group and females receiving the test article were mated with the corresponding untreated males. Males and females both receiving the control substance were mated.

C. $F_0$ PARENTAL OBSERVATIONS

1. Appearance and Behavior

From receipt until sacrifice both male and female rats were observed twice daily for mortality and overt changes in appearance and

behavior. During treatment males and females were observed weekly in detail for clinical signs of toxicity. Untreated animals in both phases also received a detailed weekly examination.

2. Body Weights

Individual male (treated and untreated) body weights were recorded weekly from randomization until sacrifice. Individual female body weights (treated and untreated) were recorded weekly until evidence of copulation was observed or until sacrifice. Those dams selected for 13-day uterine examination were weighed on gestation days 0, 7 and 13 and the remaining dams, those allowed to deliver, were weighed on gestation days 0, 7, 13 and 20 and on lactation days 0, 7, 14 and 21.

D. $F_0$ GESTATION DAY 13 UTERINE EXAMINATION OBSERVATIONS

On gestation day 13, approximately one-half of the mated females from each group were selected for uterine examination by the following method and sacrificed by carbon dioxide inhalation. Within each dosage group, each dam was assigned a consecutive placement number beginning with the number one. Of the females with evidence of copulation on any given day, one-half were selected by use of a table of random numbers for uterine examination. The remaining females were allowed to deliver. This process was continued daily until all females that evidenced mating had been assigned.

Immediately following sacrifice, a uterine examination was performed on each female. The number and location of viable and nonviable embryos, early resorptions, the total number of implantations and corpora lutea were recorded. Each implantation site, including resorptions, was consecutively numbered from the left uterine horn to the right uterine horn. The abdominal and thoracic cavities and organs of the dams were examined for grossly evident morphological changes and the carcasses discarded.

Uteri from females that appeared nongravid were opened and placed in 10% ammonium sulfide solution for confirmation of pregnancy[1].

E. DISPOSITION OF MALES

At the completion of the 13-day uterine examinations, all $F_0$ treated and untreated males were examined externally, sacrificed and discarded.

F. $F_0$ PARTURITION AND $F_1$ LITTER OBSERVATIONS

The remaining $F_0$ females from each group were allowed to deliver. During the period of expected parturition, the $F_0$ females were observed twice daily for newborn litters. Lactation day 0 was designated as the day the entire litter was found and delivery was judged complete. The duration of gestation was calculated and any difficulties occurring at parturition were recorded. On lactation day 0, the litters were examined for litter size, stillbirths, live births and any gross anomalies. Throughout lactation, the dams were observed daily for behavioral abnormalities in nesting and nursing. On lactation day 4, litter size was reduced to 10 pups, of equal sex whenever possible, by use of a random numbers table. The culled pups were externally examined and discarded. Pups were weighed individually on lactation days 0, 4, 7 and 14 and individually by sex on lactation day 21. All pups were observed daily for overt signs of toxicity, changes in appearance, behavior and mortality. Intact pups found dead during the lactation period were examined for anomalies, necropsied and discarded. The heart was dissected by a method similar to one described by Staples[2].

On lactation day 21, all dams were examined, sacrificed, necropsied and the number of uterine implantation sites recorded. At weaning, all surviving pups were examined externally and sacrificed. If abnormalities were present, the pups were subjected to a gross necropsy. Pups that appeared normal were discarded.

On the 25th day after separation from the male, a gross necropsy was performed on all females where evidence of mating was found but failed to

deliver. On the 25th day after termination of mating, this procedure was performed on all females where no evidence of mating was observed and which did not deliver. Any condition which would have prevented pregnancy was recorded. Uteri from females that appeared nongravid were opened and placed in 10% ammonium sulfide solution for confirmation of pregnancy[1].

G. STATISTICAL ANALYSIS

All statistical analyses compared the treatment groups to the control group with a level of significance at $p<0.05$. All means were accompanied by standard deviations.

1. Gestation Day 13 Uterine Examination Data

Mean postimplantation loss was compared by the Mann-Whitney U-test, as described by Siegel[3] and Weil[4], to judge significance of differences. The mean numbers of corpora lutea, total implantations and viable embryos were compared by analysis of variance (one-way classification), Bartlett's test for homogeneity of variance and the appropriate t-test (for equal and unequal variances) as described by Steel and Torrie[5], using Dunnett's[6] multiple comparison tables to judge significance of differences.

2. Litter Data

The male and female fertility indices were compared using the Chi-square test criterion with Yates' correction for 2 x 2 contingency tables and/or Fisher's exact probability test as described by Siegel[3] to judge significance of differences. Pup survival indices on lactation day 4, 7, 14 and 21, and lactation indices (viable pups on lactation day 21 versus viable retained pups on lactation day 4) were compared by the Mann-Whitney U-test as described by Siegel[3] and Weil[4] to judge significance of differences.

Mean numbers of live pups per litter at birth and mean pup body weights recorded on lactation days 0, 4, 7, 14 and 21 were compared by

analysis of variance (one-way classification), Bartlett's test for homogeneity of variances and the appropriate t-test (for equal and unequal variances), as described by Steel and Torrie[5] using Dunnett's[6] multiple comparison tables to judge significance of differences.

H. DATA RETENTION

All preservable specimens, raw data, a sample of the test article and copies of the final report are retained in the International Research and Development Corporation Archives in Mattawan, Michigan.

V. RESULTS

A. PARENTAL OBSERVATIONS

1. Appearance and Behavior

A summary of estrous cycle observations is presented in Table 1 and individual data are presented in Table 2.

No mortality was observed among the parental male rats in groups 1, 2, 3, 4 or 5. One treated male rat in group 6 and three treated male rats in group 7 died on study between study weeks 5 and 10. Following is a review of parental male mortality: animal #30942 dosed at the intermediate level (500 mg/kg/day) died during study week 10. This animal previously (approximately one month) had observations of red/brown colored urine and brown stained and matted ventral haircoat but showed no visible external abnormalities at the time of death. Postmortem observations disclosed black material in the stomach, white spots on both kidneys, purulent material in one kidney, reddish brown fluid and reddened mucosa in the urinary bladder, distended ureters and stones in the left kidney and ureter, and in the urinary bladder. The kidneys of this animal were preserved in 10% neutral buffered formalin but at the discretion of the Study Director, were not examined histopathologically. The specific cause of death could not be determined. Among the males dosed with 1000 mg/kg/day of the test article, animal #30961 died during study week 8. Necropsy disclosed a frothy red fluid in the trachea, congested lungs and red fluid in the thoracic cavity. Animal #30965 died during study week 7 with no internal abnormalities and animal #30982 died during week 5 with congestion in the azygous lobe of the lungs, reddened lining and red fluid in the trachea and white friable material in the urinary bladder. All of the group 7 males that died showed no abnormal clinical signs prior to death and the specific cause of death could not be determined. However, the aforementioned pulmonary findings were not inconsistent with technique-related aspiration of test article.

Among the parental female rats, no mortality occurred in groups 1, 5 and 6. A total of six females died on study: two, three and one in

groups 2, 4 and 7, respectively. One additional female rat in group 3 was sacrificed in extremis. Following is an itemization of parental female mortality: In group 2, animal #31015 died with no visible anormalities during study week 8. Postmortem examination revealed congested lungs, reddish clear fluid in the thoracic cavity and a 1 cm tear in the esophagus. The cause of death was determined to be intubation error. Animal #31029 (group 2) died during study week 11 with hair loss on the forelimbs. Necropsy disclosed congested lungs. In group 3, female #31034 had numerous clinical observations including wet matted anogenital haircoat, loss of righting reflex, dyspnea, hypoactivity, apparent hypothermia and emaciated and moribund appearance. This animal was sacrificed in extremis during week 11 and appeared normal internally. In group 4, animal #'s 31074 and 31082 both died with no visible abnormalities during study week 8. The former animal was normal internally while the latter had congested lungs and a small amount of green mucoid material in the intestines. Animal from the same group died during study week 9 and also had no external clinical observations and congested lungs. In group 7, untreated female #31138 died with no apparent abnormalities during week 6. Necropsy revealed red fluid and material (presumably blood) in the lungs and thoracic cavity; congested lungs, bronchi and thymus, and severe clotting around the anterior heart and great vessels. With the exception of the group 2 female previously mentioned, the cause of death could not be determined for any of the females that died on study. However, the aforementioned pulmonary findings were not inconsistent with technique-related aspiration of test article.

Administration of B0547-01 had no effect on the appearance or behavior of male rats at any dosage level. Some of the observations noted occasionally in one or more study groups included hair loss on the forelimbs, hindlimbs, ventral abdominal and inguinal regions; red or black material around the eyes; scabbing on the head, neck, shoulders and forelimbs; anogenital matting; excess salivation, and respiratory rales.

No abnormalities attributable to the test article were noted in the estrous cycling of females treated at 250, 500 or 1000 mg/kg/day. Occasional observations of prolonged periods of estrous and diestrous were observed in all study groups including the control group.

The only apparent test article effect in females dosed with B0547-01 was excess salivation in the 1000 mg/kg/day group (group 4). Additional observations of hair loss on the forelimbs, ventral abdomen and ventral thorax, respiratory rales and dry black or red material around the nose occurred randomly among the study groups.

No abnormal postmortem observations were recorded for any treated female at either the gestation day 13 or lactation day 21 (weaning) uterine examinations. Untreated females in groups 1, 5, 6 and 7 had no meaningful necropsy observations.

A total of four female rats failed to deliver 25 days after separation from males and were sacrificed: one each in groups 2, 3, 4 and 5. Upon necropsy, all rats appeared normal internally and all but one (group 4) were nongravid.

2. Body Weights

Summaries of weekly group mean male and female body weights prior to mating are presented in Tables 3 and 5, respectively. Individual values are presented in Tables 4 and 6. A summary of group mean maternal body weight change during gestation and lactation is presented in Table 7 and individual values are presented in Table 8.

Administration of B0547-01 at the level of 1000 mg/kg/day caused a slight body weight depression in male rats throughout the measured study interval. These data did not indicate a cumulative toxic effect but rather a consistent body weight differential between the group 7 high dose

and control group animals. This difference fluctuated between 2.9% (study week 3) and 7.3% (week 9) and averaged about 4.9%. No effects on male body weight attributable to treatment with B0547-01 were evident in groups 5 or 6. Body weights in groups 2, 3 and 4 were similarly comparable to those in the control group.

Mean weekly body weights of treated females in groups 2, 3 and 4 did not indicate a test article effect at any dosage level. Fluctuations in these values, relative to those in the control group, were present in group 3 during study week 10 and group 4 during study week 12. However, these means and the corresponding control means were based on only one or two animals each, thus negating any valid comparisons between the groups. Weekly mean body weights of the untreated females in study groups 5, 6 and 7 exceeded the control values during all study weeks measured.

Mean maternal body weight gains of females treated with B0547-01 at levels of 250, 500 and 1000 mg/kg/day were comparable to respective control values during all intervals of gestation and over the entire gestation period. Slight depressions in maternal body weight gain were present in group 3 during the first interval of lactation, days 0 to 7, and over the entire lactation period, days 0 to 21. However, similar data were not existent in group 4 and the values were considered random in origin. No other abnormalities in body weight gain were present in groups 2, 3 or 4 during any interval of lactation (lactation days 0 to 7, 7 to 14 or 14 to 21) or over the entire lactation period (days 0 to 21).

Mean maternal body weight gains of females in group 7 were slightly depressed relative to control values from gestation days 13 to 20 and 0 to 20 and from lactation days 0 to 7. However, because these females were not treated and because the values were within the normal range of variability for this species, no relation to the test article was assumed. The remaining body weight values for this group and for

groups 5 and 6 throughout gestation and lactation were all comparable to respective control group values.

3. 13-Day Uterine Examination Observations

A summary of group mean maternal 13-day uterine examination observations is presented in Table 9 and individual values are presented in Table 10. A summary of historical control values is presented in Appendix B.

When administered to female rats at dosage levels of 250, 500 and 1000 mg/kg/day, the test article had no effect on any of the 13-day uterine examination parameters assessed on this study. The mean values of corpora lutea, total implantations, postimplantation losses and viable embryos were all comparable in groups 2, 3 and 4 to group 1 control values.

Among the untreated females mated to male rats treated with the test article, a slight increase in mean postimplantation loss was noted at the highest dosage level (group 7). This value lacked statistical significance and similar findings were not noted in groups 5 or 6.

No biologically meaningful or statistically significant differences were noted in the mean numbers of corpora lutea, total implantations or viable embryos in groups 5, 6 or 7 when compared to respective group 1 control values.

4. Parturition and $F_1$ Litter Observations

A summary of gestation and lactation data is presented in Table 11. Individual data are presented in Table 12 and a summary of historical control data is presented in Appendix B.

The fertility indices of females dosed at the 250 and 500 mg/kg/day levels (groups 2 and 3) were reduced relative to the control value. However, both data were within the range of the historical control and similar findings were not noted in group 4. Further, the

reduced pregnancy success rate present among the untreated males in groups 2 and 3 may have contributed to the decrease in female fertility: no relation to treatment with B0547-01 was assumed. The pregnancy rates of females in groups 5, 6 and 7 were not notably different relative to the control value.

Administration of the test article to male rats had no meaningful effects on male fertility at any dosage level. A slight reduction in male fertility was noted in group 6 (500 mg/kg/day). However, this value was within the range of variability for this species and a similar finding did not occur at the high dose level. The group 6 value was considered due to biological variation.

The mean gestation length was comparable in all dosage groups (treated and untreated females) to the control group. No differences attributable to treatment were evident in any study group, when compared to control values, regarding the mean numbers of stillborn pups. Mean viable litter size (live born pups) was slightly reduced in groups 4 and 7 when compared to the control group. A similar effect did not occur in groups 2, 3, 5 and 6.

Oral administration of B0547-01 to either male or female parental rats had no effect on the survival of ensuing offspring on days 0, 7, 14 or 21 of lactation. Slight depressions in pup survival were noted in groups 3 and 4 on lactation days 0 and/or 4. However, all values were within historical ranges and no consistent patterns indicative of a treatment effect were evident.

The mean body weight of $F_1$ pups on days 0 and 4 of lactation were not meaningfully different in study groups 2 through 7 when compared to group 1 values. Slight to moderate reductions in mean pup weight were evident in the highest female dosage group (group 4) on lactation days 7, 14 and 21 (male and female pups). The day 7 value was below the range

of the historical control and the day 14 value was statistically significant at $p<0.05$. Slight depressions in pup weight were also present in groups 2 and 3. However, the differences from respective control values were minor and no relation to treatment was assumed.

No biologically meaningful abnormalities in mean pup body weight were evident in groups 5, 6 or 7 during any measured interval of lactation. The day 21 female body weight in group 7 was significantly higher ($p<0.05$) than the control value but no treatment effect was suggested.

Observations at birth and throughout lactation failed to disclose any abnormalities in parturition or in parental nesting and nursing behavior in any study group. There were no notable trends regarding abnormal appearance or behavior of $F_1$ pups during lactation in any study group. One or two pups each in groups 1 and 4 appeared bluish on lactation day 0. A total of 18 $F_1$ pups that died during lactation were necropsied: two each in groups 1 and 4, three each in groups 2 and 6 and four each in groups 3 and 5. No internal abnormalities were present in any of these pups.

5. Uterine Examination Observations at Weaning

A summary of group mean maternal uterine examination observations at weaning and post weaning is presented in Table 13. Individual data are presented in Table 14 and a summary of historical control values is presented in Appendix B.

Moderate reductions in the mean numbers of implantation sites with corresponding reductions in the mean numbers of delivered pups were present in the two groups dosed at the 1000 mg/kg/day level (groups 4 and 7). These data indicate a possible test article effect on ovulation, fertilization and/or nidation in group 4 or on spermatogenesis, fertilization and/or nidation in group 7. The mean numbers of remaining implantation sites (implantations not corresponding to delivered pups) were comparable in all treated groups to the control group; no discernable effects on embryonic or fetal development were evident.

VI. SIGNATURES

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## VII. DISCUSSION AND CONCLUSION

Survival was 100% in groups 1 and 5. One male in group 6 and three males in group 7 died with no external abnormalities and of no apparent cause between study weeks 5 and 10. Postmortem observations noted among these animals included lesions and stones in the kidneys and in the associated organs of the urinary tract, fluid in and reddening of the trachea and congested lungs.

Two females in group 2, three females in group 4 and one female in group 7 died on study from weeks 6 to 11. One additional group 3 female with numerous clinical abnormalities was sacrificed in extremis during study week 11. No internal abnormalities were evident upon necropsy of this animal. Postmortem examination of the females that died on study disclosed occasional observations of congested lungs, fluid in the thoracic cavity, mucoid material in the intestines and red clotted material (presumably blood) around the cardiopulmonary organs. One female in group 2 had a 1 cm tear in the esophagus and presumably died as the result of intubation error. The cause of death could not be determined for the remaining animals. However, the postmortem findings from several animals were not inconsistent with aspiration pneumonitis.

No changes in appearance or behavior were evident in any group of male rats treated with B0547-01. Observations such as hair loss and/or scabbing (limbs, shoulders, inguinal and abdominal regions), red or black material around the eyes, matted haircoat, and excess salivation were noted occasionally in one or more study groups. Females responded to treatment with B0547-01 with slight increases in excess salivation in group 4 (1000 mg/kg/day) only. No other meaningful abnormalities in appearance or behavior were evident among treated females. Necropsy observations of treated females were comparable in all dosage groups to the control group.

A slight depression in weekly male body weight was present throughout the measured period in the 1000 mg/kg/day group (group 7) only. No effects on male body weight were evident in groups 2 through 6. Treatment with B0547-01 had no definite influence on weekly female body weights at any dosage level. Slight depressions were present in groups 3 and 4 during study weeks 10 and 12, respectively. However, mating and mortality had reduced the sample size in each group to only two rats each, thus valid comparisons could not be made. Analysis of mean maternal body weight data failed to disclose a definite treatment effect on maternal body weight gain in any study group. Slight depressions in body weight gain were noted in group 3 from lactation days 0 to 7 and 0 to 21 and in group 7 from gestation days 13 to 20, 0 to 20 and lactation days 0 to 7. The fluctuations present in the former group were not replicated at the next highest dose level and were considered of random occurrence. The depressions present in the latter group were not large enough to be considered meaningful.

Treatment with B0547-01 to either male or female rats at dosage levels from 250 to 1000 mg/kg/day had no meaningful effects on any of the uterine examination parameters. A slight increase in postimplantation loss occurred in group 7. However, this value represented treated males only, lacked statistical significance and was within historical control ranges. Further, concurring data were not present at weaning uterine examination; no relation to treatment was assumed. The mean postimplantation loss in the remaining groups and the mean numbers of corpora lutea, total implantations and viable fetuses were uniform in all study groups.

No meaningful differences indicative of a test article effect on either male or female fertility were present in the treated groups when compared to the control group. Slight variations were noted in some of the groups but were considered due to biological variation. The mean

gestation length and mean numbers of stillborn pups were uniform in all study groups including the control group. Slight reductions in the mean numbers of liveborn pups were present in both groups dosed at the 1000 mg/kg/day level (groups 4 and 7). These findings were substantiated by observations of reduced total implantations at the lactation day 21 (weaning) uterine examination. No effects on liveborn litter size were noted in any group dosed at 250 or 500 mg/kg/day.

Pup survival indices during lactation were not meaningfully different in the treated groups relative to concurrent and historical control values.

The mean body weights of pups born from females dosed at 1000 mg/kg/day were moderately reduced on lactation days 7, 14 and 21 (pups of both sex). The day 7 value was outside the range of the historical control and the day 14 value was statistically significant at $p<0.05$. Pup weight values were also slightly reduced in this group on lactation days 0 and 4 but the differences were not large enough to be considered meaningful. No other effects on mean pup body weights attributable to treatment were present in any other dosage group during the measured intervals of lactation.

Analysis of the lactation day 21 (weaning) uterine examination data indicated that reductions in total implantations present in groups 4 and 7 resulted in the decrease in live pups noted at parturition. These findings suggest a possible test article effect on the processes leading to and including nidation, i.e., spermatogenesis, ovulation and fertilization. However, because no influences on corpora lutea or total implantations or viable embryos were evident in the gestation day-13 uterine examination data, the effects of treatment with B0547-01, if any, were dubious.

The mean numbers of implantation sites not corresponding to delivered pups were comparable in all dosage groups to the control group. No effects on embryonic or fetal development were observed.

In conclusion, treatment with B0547-01 to female Charles River COBS® CD® rats at 1000 mg/kg/day probably reduced the body weights of offspring from days 4 to 21 of lactation and may have depressed the mean number of implantations by an effect on ovulation, fertilization or implantation. Treatment of male Charles River COBS® CD® rats at the same dosage level may also have influenced spermatogenesis, fertilization or nidation as evidenced by a reduction in total implantations. However, a definite treatment related effect was dubious. Treatment with B0547-01 to either male or female rats had no effects on fertility or reproductive performance at dose levels of 250 or 500 mg/kg/day.

To the best of my knowledge, there were no significant deviations from the Good Laboratory Practice Regulations which affected the quality and integrity of the study. This study was conducted in conformance with the Good Laboratory Practice Regulations. This report accurately reflects the raw data obtained during the performance of the study.

[redacted] 11/6/84
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TABLE 1. Analysis of Estrous Cycle Observations

| Finding In Period | 0 (Control) (1) | | 80547-01 mg/kg/day (Group Number)[a] 250 (2) | | 500 (3) | | 1000 (4) | |
|---|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | No. | % |
| Untreated Premating Period | | | | | | | | |
| Long Diestrous | 3 | 12.0 | 6 | 24.0 | 4 | 16.0 | 2 | 8.0 |
| Long Estrous | 2 | 8.0 | 2 | 8.0 | 2 | 8.0 | 0 | 0.0 |
| Long Post-estrous | 1 | 4.0 | 1 | 4.0 | 0 | 0.0 | 0 | 0.0 |
| Irregular Cycle | 0 | 0.0 | 1 | 4.0 | 0 | 0.0 | 0 | 0.0 |
| Treated Premating Period | | | | | | | | |
| Long Diestrous | 10 | 40.0 | 11 | 44.0 | 6 | 24.0 | 5 | 20.0 |
| Long Estrous | 2 | 8.0 | 2 | 8.0 | 2 | 8.0 | 1 | 4.2 |
| Long Post-estrous | 1 | 4.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Irregular Cycle | 2 | 8.0 | 2 | 8.0 | 0 | 0.0 | 1 | 4.2 |
| Mating Period | | | | | | | | |
| Long Diestrous | 2 | 8.0 | 2 | 8.3 | 2 | 8.0 | 3 | 13.0 |
| Long Estrous | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Long Post-estrous | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Irregular Cycle | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |

[a]Only females dosed
Long Diestrous - Diestrous greater than 5 consecutive days
Long Estrous - Estrous greater than 1 day
Long Post-estrous - Post-estrous greater than 1 day
Irregular Cycle - Other deviations from normal estrous cycle i.e. Post-Post-E, E-DI-E, Post-DI-Post, E-Pro-Post
Pro - Proestrous
DI - Diestrous
E - Estrous

TABLE 2. Daily Estrous Cycle Observations

| Group Number, Dosage Level, Female Number | Day of Estrous Smearing Prior to Treatment | | | | | | | | | | Day of Estrous Smearing During Treatment, Prior to Mating | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
| (1), 0 mg/kg/day (Control): | | | | | | | | | | | | | | | | | | | | | | | | | |
| 30984 | DI | DI | DI | DI | E | Post | DI | DI | DI | DI | DI | DI | DI | DI | Pro | Post | DI | DI | DI | E | E | DI | DI | DI | Pro |
| 30985 | DI | DI | Post | DI | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | DI | DI | DI | DI | E | DI | DI | DI | Post | DI |
| 30986 | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI |
| 30987 | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | DI | DI | DI | DI |
| 30988 | DI | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E |
| 30989 | DI | DI | DI | E | DI | DI | DI | DI | DI | DI | E | Post | DI | DI | DI | DI | DI | DI | E | Post | DI | DI | Pro | Post | DI |
| 30990 | DI | DI | DI | E | Post | DI | DI | E | DI | DI | DI | DI | DI | DI | DI | E | Post | DI | DI | DI | Pro | DI | DI | Post | DI |
| 30991 | Post | DI | DI | DI | E | DI | DI | E | E | DI | DI | DI | Post | DI | DI | DI | DI | DI | DI | DI | E | DI | DI | DI | DI |
| 30992 | DI | DI | DI | Pro | E | DI | DI | E | DI | DI | DI | DI | DI | Pro | E | DI | DI | DI | Pro | E | DI | DI | DI | Pro | E |
| 30993 | Pro | Post | DI | DI | DI | E | Post | DI | DI | DI | E | E | DI | DI | DI | Post | Post | E | DI | DI | DI | Pro | E | DI | DI |
| 30994 | DI | DI | DI | E | DI | DI | DI | DI | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | Pro | Post | DI |
| 30995 | E | Post | DI | DI | DI | E | E | DI | DI | E | Post | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI |
| 30996 | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI |
| 30997 | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E |
| 30998 | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | Pro | Post | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E |
| 30999 | E | DI | DI | DI | Pro | E | DI | DI | DI | E | Post | DI | DI | DI | DI | DI | DI | DI | E | DI | DI | DI | E | DI | DI |
| 31000 | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | DI | DI | DI | E | DI | DI | DI | Pro | Post | DI |
| 31001 | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | DI | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E |
| 31002 | E | DI | DI | DI | DI | E | DI | DI | DI | DI | DI | DI | DI | DI | DI | Pro | Post | DI | DI | DI | Pro | E | DI | DI | DI |
| 31003 | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI |
| 31004 | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | Pro | E |
| 31005 | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | Pro | DI | DI | DI | E | DI | DI | DI | E | DI | DI |
| 31006 | E | Post | DI | DI | DI | Pro | E | DI | DI | DI | DI | E | Post | DI | DI | DI | DI | DI | E | DI | E | DI | DI | DI | Pro |
| 31007 | DI | DI | DI | DI | E | Post | Post | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | Pro | E | DI | DI | DI | E | DI |
| 31008 | DI | DI | DI | E | DI | DI | DI | DI | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | Pro | E | DI |

DI - Diestrous
E - Estrous
Post - Post-estrous
Pro - Proestrous

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TABLE 2. Cont.

Daily Estrous Cycle Observations

| Group Number, Dosage Level, Female Number | Day of Estrous Smearing During Mating | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
| (1), 0 mg/kg/day (Control): | | | | | | | | | | | | | | | |
| 30984 | a | | | | | | | | | | | | | | |
| 30985 | DI | Pro | a | | | | | | | | | | | | |
| 30986 | a | | | | | | | | | | | | | | |
| 30987 | a | | | | | | | | | | | | | | |
| 30988 | DI | DI | DI | a | | | | | | | | | | | |
| 30989 | DI | DI | a | | | | | | | | | | | | |
| 30990 | DI | DI | a | | | | | | | | | | | | |
| 30991 | DI | DI | DI | a | | | | | | | | | | | |
| 30992 | DI | DI | DI | DI | a | | | | | | | | | | |
| 30993 | DI | E | a | | | | | | | | | | | | |
| 30994 | DI | DI | a | | | | | | | | | | | | |
| 30995 | DI | a | | | | | | | | | | | | | |
| 30996 | DI | DI | a | | | | | | | | | | | | |
| 30997 | DI | DI | Pro | a | | | | | | | | | | | |
| 30998 | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI | a |
| 30999 | DI | a | | | | | | | | | | | | | |
| 31000 | DI | DI | a | | | | | | | | | | | | |
| 31001 | DI | DI | DI | a | | | | | | | | | | | |
| 31002 | Pro | a | | | | | | | | | | | | | |
| 31003 | a | | | | | | | | | | | | | | |
| 31004 | DI | DI | DI | Pro | DI | DI | DI | DI | DI | DI | Di | DI | DI | DI | DI[b] |
| 31005 | DI | a | | | | | | | | | | | | | |
| 31006 | E | Post | DI | DI | DI | a | | | | | | | | | |
| 31007 | DI | DI | a | | | | | | | | | | | | |
| 31008 | DI | DI | a | | | | | | | | | | | | |

DI - Diestrus
E - Estrus
Post - Post-Estrus
Pro - Proestrus
[a]Evidence of copulation
[b]No evidence of copulation, mating complete, estrous smearing discontinued

TABLE 2. Cont.

Daily Estrous Cycle Observations

| Group Number, Test Article, Dosage Level, Female Number | Day of Estrous Smearing Prior to Treatment | | | | | | | | | | Day of Estrous Smearing During Treatment, Prior to Mating | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
| (2), B0547-01, 250 mg/kg/day: | | | | | | | | | | | | | | | | | | | | | | | | | |
| 31009 | DI | DI | DI | E | Post | DI | DI | E | DI | DI | DI | E | DI | DI | DI | Pro | DI | DI | DI | E | DI | DI | Pro | E | DI |
| 31010 | DI | DI | Pro | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | Post |
| 31011 | DI | Pro | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI |
| 31012 | DI | E | DI | DI | DI | DI | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | Pro | DI | DI | DI | DI | DI | DI | DI |
| 31013 | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | DI | Post | DI | Post | DI | DI | DI | Pro | E | DI | DI | Pro | E | DI |
| 31014 | DI | DI | DI | E | DI | DI | DI | Pro | DI | DI | DI | Pro | DI | DI | DI | DI | DI | DI | DI | E | DI | DI | DI | E | DI |
| 31015 | Pro | E | DI | DI | DI | DI | E | DI | DI | DI | DI | DI | DI | DI | Pro | DI | DI | DI | DI | DI | E | E | DI | DI | Died |
| 31016 | DI | DI | DI | Pro | E | DI | DI | DI | E | DI | DI | DI | DI | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E |
| 31017 | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | DI | DI | DI | DI | E | DI |
| 31018 | DI | E | DI | DI | DI | DI | DI | DI | DI | DI | DI | E | DI | DI | DI | DI | Pro | DI | DI | DI | E | DI | DI | DI | E |
| 31019 | E | E | Post | Post | Post | DI | DI | DI | E | DI | DI | DI | Pro | E | DI | DI | DI | Pro | E | Post | DI | DI | Pro | DI | DI |
| 31020 | DI | DI | E | DI | DI | DI | DI | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | DI | DI | DI | DI | E | DI | DI |
| 31021 | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | DI | Post | DI | DI | DI | DI | DI | E | Post | DI | E | Pro | Post | DI |
| 31022 | DI | DI | DI | E | E | DI | DI | DI | Pro | Post | DI | DI | DI | E | Post | DI | DI | DI | E | DI | DI | DI | Pro | Post | DI |
| 31023 | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI |
| 31024 | DI | DI | DI | E | DI | DI | DI | DI | DI | DI | DI | Pro | DI | DI | DI | DI | DI | DI | E | E | DI | DI | DI | E | DI |
| 31025 | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI |
| 31026 | DI | DI | DI | DI | DI | DI | E | DI | E | DI | DI | DI | DI | Pro | DI | DI | DI | DI | Pro | DI | DI | DI | DI | DI | DI |
| 31027 | DI | E | DI | DI | E | Post | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI |
| 31028 | DI | E | DI | DI | Pro | E | DI | DI | DI | E | Post | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI |
| 31029 | E | DI | DI | DI | E | Post | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | Pro | E |
| 31030 | Pro | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | DI | DI | DI | DI |
| 31031 | DI | DI | DI | DI | DI | E | Post | DI | DI | DI | E | DI | DI | DI | E | Post | DI | DI | DI | DI | DI | DI | DI | DI | DI |
| 31032 | DI | DI | DI | E | DI | DI | DI | DI | DI | DI | Pro | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI | E | DI |
| 31033 | Post | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | Post | DI | DI | E | DI | DI | DI | Pro |

DI - Diestrous
E - Estrous
Post - Post-estrous
Pro - Proestrous

TABLE 2. Cont.

Daily Estrous Cycle Observations

| Group Number, Test Article, Dosage Level, Female Number | Day of Estrous Smearing During Mating | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
| (2), B0547-01, 250 mg/kg/day Cont.: | | | | | | | | | | | | | | | |
| 31009 | DI | DI | a | | | | | | | | | | | | |
| 31010 | DI | DI | DI | Post | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI[b] |
| 31011 | DI | a | | | | | | | | | | | | | |
| 31012 | a | | | | | | | | | | | | | | |
| 31013 | DI | DI | E | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI[b] |
| 31014 | DI | DI | a | | | | | | | | | | | | |
| 31015 | Died | | | | | | | | | | | | | | |
| 31016 | DI | DI | DI | a | | | | | | | | | | | |
| 31017 | DI | DI | a | | | | | | | | | | | | |
| 31018 | DI | DI | Pro | a | | | | | | | | | | | |
| 31019 | a | | | | | | | | | | | | | | |
| 31020 | DI | a | | | | | | | | | | | | | |
| 31021 | a | | | | | | | | | | | | | | |
| 31022 | DI | DI | a | | | | | | | | | | | | |
| 31023 | DI | a | | | | | | | | | | | | | |
| 31024 | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E[b] |
| 31025 | DI | a | | | | | | | | | | | | | |
| 31026 | DI | DI | Post | a | | | | | | | | | | | |
| 31027 | a | | | | | | | | | | | | | | |
| 31028 | a | | | | | | | | | | | | | | |
| 31029 | DI | DI | a | | | | | | | | | | | | |
| 31030 | a | | | | | | | | | | | | | | |
| 31031 | DI | a | | | | | | | | | | | | | |
| 31032 | DI | DI | a | | | | | | | | | | | | |
| 31033 | DI | DI | Pro | a | | | | | | | | | | | |

DI - Diestrus
E - Estrus
Post - Post-Estrus
Pro - Proestrus

TABLE 2. Cont.

Daily Estrous Cycle Observations

| Group Number, Test Article, Dosage Level, Female Number | Day of Estrous Smearing Prior to Treatment | | | | | | | | | | Day of Estrous Smearing During Treatment, Prior to Mating | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
| (3), B0547-01, 500 mg/kg/day: | | | | | | | | | | | | | | | | | | | | | | | | | |
| 31034 | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI |
| 31035 | DI | DI | DI | E | Post | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | Pro | E |
| 31036 | E | DI | DI | DI | Pro | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | Pro | Post | DI | DI | DI | DI | DI | DI | DI |
| 31037 | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | Pro | E | DI |
| 31038 | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | Pro | E |
| 31039 | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E |
| 31040 | Post | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | DI | DI | DI | DI | E | DI | DI | DI | E |
| 31041 | DI | DI | DI | DI | E | DI | DI | DI | DI | E | DI | DI | DI | E | E | DI | DI | DI | E | E | DI | DI | DI | E | Post |
| 31042 | DI | DI | E | Post | DI | DI | DI | DI | DI | DI | E | Post | DI | DI | E | Post | DI | DI | E | DI | DI | DI | E | DI | DI |
| 31043 | DI | DI | E | DI | DI | DI | DI | DI | DI | DI | E | DI | DI | DI | DI | DI | DI | DI | E | DI | DI | DI | E | DI | DI |
| 31044 | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | Post | DI | DI | E | DI | DI | DI | E |
| 31045 | DI | DI | E | DI | DI | DI | E | DI | DI | Pro | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI |
| 31046 | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI |
| 31047 | DI | DI | E | Post | DI | DI | DI | DI | DI | DI | DI | E | Post | DI | DI | Pro | E | DI | DI | DI | Pro | E | DI | DI | DI |
| 31048 | DI | Pro | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI |
| 31049 | E | DI | DI | DI | DI | E | DI | DI | DI | DI | E | DI | DI | DI | DI | DI | DI | DI | E | DI | DI | DI | E | DI | DI |
| 31050 | DI | E | DI | DI | DI | E | DI | DI | DI | Pro | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI |
| 31051 | E | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | Pro | DI | DI | DI | DI | DI | DI | DI |
| 31052 | DI | DI | E | DI | DI | DI | DI | DI | DI | Pro | E | DI | DI | Pro | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI |
| 31053 | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | DI | DI | DI | Pro | E | DI | DI | DI | Post | DI | DI |
| 31054 | DI | DI | DI | E | Post | DI | DI | DI | DI | E | DI | DI | DI | E | E | DI | DI | DI | DI | E | DI | DI | DI | Pro | DI |
| 31055 | Post | DI | DI | DI | E | DI | DI | E | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | Pro | E |
| 31056 | DI | DI | DI | DI | Pro | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI |
| 31057 | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E |
| 31058 | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI |

DI - Diestrous
E - Estrous
Post - Post-estrous
Pro - Proestrous

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TABLE 2. Cont.

Daily Estrous Cycle Observations

| Group Number, Test Article, Dosage Level, Female Number | Day of Estrous Smearing During Mating | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
| (3), B0547-01, 500 mg/kg/day Cont.: | | | | | | | | | | | | | | | |
| 31034 | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI | Sacrificed | | | |
| 31035 | DI | DI | DI | a | | | | | | | | | | | |
| 31036 | a | | | | | | | | | | | | | | |
| 31037 | DI | DI | a | | | | | | | | | | | | |
| 31038 | DI | DI | Pro | a | | | | | | | | | | | |
| 31039 | DI | DI | DI | a | | | | | | | | | | | |
| 31040 | DI | DI | Pro | a | | | | | | | | | | | |
| 31041 | DI | DI | DI | E | DI | DI | DI | a | | | | | | | |
| 31042 | DI | a | | | | | | | | | | | | | |
| 31043 | DI | a | | | | | | | | | | | | | |
| 31044 | DI | DI | DI | a | | | | | | | | | | | |
| 31045 | Pro | a | | | | | | | | | | | | | |
| 31046 | a | | | | | | | | | | | | | | |
| 31047 | a | | | | | | | | | | | | | | |
| 31048 | DI | Pro | Post | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI | Pro | E[b] |
| 31049 | a | | | | | | | | | | | | | | |
| 31050 | a | | | | | | | | | | | | | | |
| 31051 | a | | | | | | | | | | | | | | |
| 31052 | DI | a | | | | | | | | | | | | | |
| 31053 | DI | a | | | | | | | | | | | | | |
| 31054 | DI | DI | DI | a | | | | | | | | | | | |
| 31055 | DI | DI | DI | a | | | | | | | | | | | |
| 31056 | DI | DI | a | | | | | | | | | | | | |
| 31057 | DI | DI | DI | a | | | | | | | | | | | |
| 31058 | DI | DI | a | | | | | | | | | | | | |

DI - Diestrus
E - Estrus
Post - Post-Estrus
Pro - Proestrus
[a]Evidence of copulation
[b]No evidence of copulation, mating complete, estrous smearing discontinued

TABLE 2. Cont.

Daily Estrous Cycle Observations

| Group Number, Test Article, Dosage Level, Female Number | Day of Estrous Smearing Prior to Treatment | | | | | | | | | | Day of Estrous Smearing During Treatment, Prior to Mating | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
| (4), B0547-01, 1000 mg/kg/day: | | | | | | | | | | | | | | | | | | | | | | | | | |
| 31059 | DI | E | DI | DI | E | Post | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI |
| 31060 | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | DI | E | DI | DI | Pro | E | Post | DI | DI | DI | E | DI | DI | DI |
| 31061 | E | DI | DI | DI | E | DI | DI | DI | DI | DI | DI | E | E | DI | E | DI | E | Post | DI | DI | E | DI | DI | Pro | E |
| 31062 | DI | DI | DI | E | DI | DI | DI | E | Post | DI | DI | DI | E | Post | DI | DI | DI | DI | E | DI | DI | DI | DI | E | DI |
| 31063 | DI | E | DI | DI | DI | E | DI | DI | DI | E | Post | DI | DI | E | Post | DI | DI | DI | E | Post | DI | DI | E | DI | DI |
| 31064 | DI | DI | E | DI | DI | DI | E | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI | E | DI | DI | DI | DI | DI | DI |
| 31065 | Post | DI | DI | DI | E | DI | DI | DI | Post | DI | DI | Pro | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E |
| 31066 | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | Pro | E |
| 31067 | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E |
| 31068 | DI | DI | E | Post | DI | DI | DI | Pro | DI | DI | DI | E | Post | DI | DI | DI | DI | E | DI | DI | DI | DI | E | DI | DI |
| 31069 | DI | E | DI | DI | DI | Pro | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | DI | E | Post | DI | DI | Pro | E |
| 31070 | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI |
| 31071 | E | DI | DI | DI | E | Post | DI | DI | DI | E | DI | DI | DI | E | Post | DI | DI | DI | E | Post | DI | DI | DI | E | Post |
| 31072 | DI | DI | DI | E | DI | DI | DI | DI | DI | DI | Pro | E | Post | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E |
| 31073 | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | Pro | E |
| 31074 | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | Died |
| 31075 | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI |
| 31076 | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | DI | DI | DI | DI | E | DI | DI |
| 31077 | DI | DI | DI | E | DI | DI | DI | DI | DI | DI | Pro | E | DI | DI | DI | E | Post | DI | DI | DI | DI | DI | DI | DI | E |
| 31078 | DI | DI | E | DI | DI | Pro | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI |
| 31079 | DI | DI | E | DI | DI | DI | E | DI | DI | DI | Pro | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | Post | DI | DI |
| 31080 | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | DI | DI | DI | DI | E | DI | DI | DI | E |
| 31081 | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | Pro | E | Post | DI | DI | DI | Post | DI | DI | E | DI | DI |
| 31082 | E | Post | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | Post | DI | DI | Pro | Post | Died | | | | | |
| 31083 | DI | E | DI | DI | DI | E | DI | DI | DI | E | Post | DI | DI | E | DI | DI | DI | E | DI | DI | DI | E | DI | DI | DI |

DI - Diestrous
E - Estrous
Post - Post-estrous
Pro - Proestrous

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TABLE 2. Cont. Daily Estrous Cycle Observations

| Group Number, Test Article, Dosage Level, Female Number | Day of Estrous Smearing During Mating | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
| (4), B0547-01, 1000 mg/kg/day Cont.: | | | | | | | | | | | | | | | |
| 31059 | a | | | | | | | | | | | | | | |
| 31060 | a | | | | | | | | | | | | | | |
| 31061 | DI | DI | DI | a | | | | | | | | | | | |
| 31062 | DI | Pro | a | | | | | | | | | | | | |
| 31063 | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI | a | | | |
| 31064 | a | | | | | | | | | | | | | | |
| 31065 | a | | | | | | | | | | | | | | |
| 31066 | DI | a | | | | | | | | | | | | | |
| 31067 | DI | DI | DI | a | | | | | | | | | | | |
| 31068 | DI | Pro | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI[b] |
| 31069 | DI | DI | DI | Post | a | | | | | | | | | | |
| 31070 | DI | a | | | | | | | | | | | | | |
| 31071 | DI | DI | DI | a | | | | | | | | | | | |
| 31072 | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI | DI[b] |
| 31073 | DI | DI | Post | a | | | | | | | | | | | |
| 31074 | Died | | | | | | | | | | | | | | |
| 31075 | DI | a | | | | | | | | | | | | | |
| 31076 | DI | a | | | | | | | | | | | | | |
| 31077 | DI | DI | DI | a | | | | | | | | | | | |
| 31078 | DI | a | | | | | | | | | | | | | |
| 31079 | DI | a | | | | | | | | | | | | | |
| 31080 | DI | DI | DI | a | | | | | | | | | | | |
| 31081 | DI | a | | | | | | | | | | | | | |
| 31082 | Died | | | | | | | | | | | | | | |
| 31083 | a | | | | | | | | | | | | | | |

DI - Diestrus
E - Estrus
Post - Post-Estrus
Pro - Proestrus
[a]Evidence of copulation
[b]No evidence of copulation, mating complete, estrous smearing discontinued

TABLE 3.

MALES: Summary of Weekly Group Mean Body Weights

| | 0 mg/kg/day (Control) (1) | | | B0547-01 mg/kg/day (group number) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | 250FD (2) | | | 500FD (3) | | | 1000FD (4) | | |
| Study Week | Mean Body Weight (g) | Standard Deviation (±) | N | Mean Body Weight (g) | Standard Deviation (±) | N | Mean Body Weight (g) | Standard Deviation (±) | N | Mean Body Weight (g) | Standard Deviation (±) | N |
| 0 | 191 | 11.7 | 25 | 191 | 15.4 | 25 | 184 | 10.7 | 25 | 194 | 15.4 | 25 |
| 1 | 250 | 16.8 | 25 | 253 | 18.8 | 25 | 244 | 13.7 | 25 | 253 | 27.1 | 25 |
| 2 | 300 | 21.6 | 25 | 304 | 25.8 | 25 | 291 | 17.3 | 25 | 302 | 25.9 | 25 |
| 3 | 339 | 25.7 | 25 | 347 | 29.1 | 25 | 331 | 21.3 | 25 | 343 | 29.9 | 25 |
| 4 | 376 | 29.9 | 25 | 385 | 33.0 | 25 | 365 | 25.6 | 25 | 378 | 33.5 | 25 |
| 5 | 406 | 33.6 | 25 | 417 | 38.6 | 25 | 393 | 27.6 | 25 | 406 | 37.8 | 25 |
| 6 | 431 | 37.9 | 25 | 443 | 42.3 | 25 | 417 | 30.8 | 25 | 429 | 40.3 | 25 |
| 7 | 448 | 40.6 | 25 | 461 | 46.4 | 25 | 438 | 35.0 | 25 | 448 | 44.0 | 25 |
| 8 | 469 | 43.0 | 25 | 481 | 50.8 | 25 | 457 | 36.5 | 25 | 468 | 47.9 | 25 |
| 9 | 468 | 44.2 | 25 | 479 | 50.8 | 25 | 456 | 35.8 | 25 | 463 | 45.7 | 25 |
| 10 | 484 | 47.3 | 25 | 495 | 51.5 | 25 | 474 | 35.0 | 25 | 486 | 44.4 | 25 |
| 11 | 498 | 51.5 | 25 | 509 | 52.6 | 25 | 488 | 36.9 | 25 | 495 | 46.9 | 25 |
| 12 | 499 | 47.3 | 25 | 521 | 56.8 | 25 | 496 | 37.9 | 25 | 501 | 50.3 | 25 |

N - Number of animals utilized in calculation of means, remaining males died
FD - Only females dosed

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TABLE 3. Cont.

MALES: Summary of Weekly Group Mean Body Weights

B0547-01 mg/kg/day (group number)

| Study Week | 250MD (5) Mean Body Weight (g) | 250MD (5) Standard Deviation (±) | 250MD (5) N | 500MD (6) Mean Body Weight (g) | 500MD (6) Standard Deviation (±) | 500MD (6) N | 1000MD (7) Mean Body Weight (g) | 1000MD (7) Standard Deviation (±) | 1000MD (7) N |
|---|---|---|---|---|---|---|---|---|---|
| 0 | 187 | 11.4 | 25 | 195 | 11.7 | 25 | 188 | 13.8 | 25 |
| 1 | 246 | 16.4 | 25 | 256 | 14.2 | 25 | 240 | 18.3 | 25 |
| 2 | 294 | 17.8 | 25 | 307 | 18.1 | 25 | 289 | 21.4 | 25 |
| 3 | 333 | 22.5 | 25 | 349 | 22.5 | 25 | 329 | 27.0 | 25 |
| 4 | 370 | 25.8 | 25 | 384 | 29.6 | 25 | 362 | 29.4 | 25 |
| 5 | 401 | 27.7 | 25 | 410 | 34.4 | 25 | 383 | 36.9 | 24 |
| 6 | 428 | 29.8 | 25 | 434 | 41.0 | 25 | 408 | 39.3 | 24 |
| 7 | 448 | 33.0 | 25 | 453 | 42.7 | 25 | 427 | 43.0 | 24 |
| 8 | 470 | 36.0 | 25 | 473 | 45.8 | 25 | 440 | 47.9 | 22 |
| 9 | 467 | 37.1 | 25 | 470 | 46.4 | 25 | 434 | 47.7 | 22 |
| 10 | 486 | 36.5 | 25 | 493 | 49.3 | 24 | 460 | 49.6 | 22 |
| 11 | 501 | 38.5 | 25 | 505 | 52.1 | 24 | 471 | 50.8 | 22 |
| 12 | 510 | 41.0 | 25 | 509 | 53.9 | 24 | 474 | 51.9 | 22 |

N - Number of animals utilized in calculation of means, remaining males died
MD - Only males dosed

191-900

TABLE 4. Individual Weekly Male Body Weights

| Group Number, Test Article, Dosage Level, Male Number | Study Week 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| (1), 0 mg/kg/day (Control): | | | | | | | | | | | | | |
| 30809 | 179 | 227 | 276 | 312 | 343 | 373 | 396 | 418 | 435 | 435 | 449 | 454 | 453 |
| 30810 | 205 | 266 | 319 | 359 | 400 | 432 | 469 | 501 | 526 | 517 | 547 | 552 | 554 |
| 30811 | 188 | 244 | 292 | 339 | 375 | 408 | 431 | 452 | 475 | 467 | 484 | 482 | 500 |
| 30812 | 184 | 234 | 286 | 324 | 365 | 388 | 412 | 424 | 437 | 445 | 460 | 466 | 475 |
| 30813 | 189 | 249 | 307 | 341 | 380 | 413 | 437 | 459 | 482 | 494 | 503 | 517 | 532 |
| 30814 | 208 | 267 | 319 | 358 | 398 | 428 | 457 | 478 | 504 | 497 | 519 | 537 | 538 |
| 30815 | 211 | 278 | 330 | 374 | 416 | 441 | 468 | 484 | 513 | 518 | 526 | 550 | 555 |
| 30816 | 188 | 256 | 314 | 361 | 401 | 437 | 457 | 473 | 488 | 495 | 494 | 508 | 504 |
| 30817 | 192 | 244 | 284 | 302 | 329 | 350 | 372 | 381 | 403 | 400 | 424 | 442 | 444 |
| 30818 | 196 | 248 | 292 | 324 | 354 | 380 | 398 | 408 | 425 | 423 | 432 | 415 | 437 |
| 30819 | 195 | 265 | 323 | 375 | 413 | 450 | 478 | 500 | 515 | 520 | 544 | 562 | 471 |
| 30820 | 190 | 248 | 306 | 345 | 377 | 412 | 437 | 456 | 475 | 469 | 483 | 501 | 520 |
| 30821 | 207 | 260 | 305 | 340 | 378 | 409 | 439 | 457 | 468 | 466 | 482 | 494 | 506 |
| 30822 | 184 | 251 | 311 | 358 | 410 | 443 | 470 | 491 | 516 | 518 | 540 | 568 | 576 |
| 30823 | 180 | 224 | 251 | 301 | 337 | 365 | 387 | 404 | 428 | 417 | 426 | 453 | 460 |
| 30824 | 189 | 252 | 307 | 349 | 393 | 422 | 450 | 465 | 482 | 485 | 492 | 503 | 522 |
| 30825 | 190 | 246 | 299 | 343 | 377 | 414 | 448 | 466 | 488 | 500 | 527 | 541 | 557 |
| 30826 | 210 | 274 | 328 | 374 | 419 | 457 | 487 | 497 | 525 | 522 | 534 | 556 | 560 |
| 30827 | 193 | 255 | 311 | 344 | 384 | 420 | 448 | 464 | 485 | 487 | 511 | 533 | 542 |
| 30828 | 170 | 223 | 262 | 297 | 331 | 351 | 369 | 393 | 413 | 402 | 418 | 426 | 427 |
| 30829 | 172 | 228 | 277 | 324 | 355 | 391 | 412 | 428 | 440 | 452 | 453 | 466 | 472 |
| 30830 | 211 | 278 | 333 | 376 | 412 | 446 | 480 | 505 | 535 | 529 | 557 | 578 | 503 |
| 30831 | 184 | 242 | 289 | 326 | 352 | 380 | 396 | 398 | 415 | 420 | 429 | 450 | 465 |
| 30832 | 181 | 223 | 260 | 288 | 317 | 337 | 351 | 364 | 381 | 377 | 388 | 396 | 399 |
| 30833 | 189 | 261 | 313 | 353 | 387 | 415 | 429 | 442 | 462 | 454 | 474 | 489 | 500 |
| (2), 80547-01, 250 mg/kg/day: | | | | | | | | | | | | | |
| 30834 | 198 | 256 | 315 | 352 | 381 | 409 | 437 | 458 | 487 | 470 | 486 | 497 | 487 |
| 30835 | 204 | 269 | 328 | 375 | 422 | 460 | 486 | 491 | 525 | 527 | 516 | 554 | 569 |
| 30836 | 165 | 222 | 270 | 319 | 355 | 380 | 408 | 425 | 445 | 440 | 456 | 466 | 470 |
| 30837 | 165 | 215 | 260 | 285 | 316 | 333 | 351 | 363 | 381 | 386 | 389 | 393 | 400 |
| 30838 | 182 | 249 | 294 | 330 | 368 | 394 | 422 | 437 | 459 | 460 | 471 | 489 | 497 |
| 30839 | 203 | 278 | 338 | 377 | 421 | 458 | 483 | 510 | 541 | 524 | 535 | 549 | 557 |
| 30840 | 195 | 265 | 319 | 364 | 403 | 434 | 468 | 483 | 492 | 495 | 507 | 523 | 526 |
| 30841 | 191 | 267 | 331 | 380 | 437 | 482 | 518 | 550 | 583 | 571 | 594 | 627 | 648 |
| 30842 | 200 | 266 | 324 | 399 | 435 | 480 | 524 | 553 | 582 | 580 | 618 | 608 | 641 |
| 30843 | 197 | 271 | 337 | 382 | 433 | 473 | 509 | 527 | 550 | 563 | 571 | 576 | 594 |
| 30844 | 196 | 261 | 316 | 361 | 400 | 430 | 451 | 470 | 495 | 498 | 518 | 534 | 544 |
| 30845 | 201 | 265 | 325 | 368 | 405 | 435 | 459 | 481 | 496 | 505 | 521 | 537 | 541 |
| 30846 | 178 | 246 | 293 | 329 | 372 | 397 | 433 | 447 | 467 | 453 | 465 | 468 | 500 |
| 30847 | 214 | 258 | 305 | 342 | 370 | 388 | 405 | 417 | 426 | 417 | 440 | 456 | 460 |
| 30848 | 165 | 221 | 236 | 291 | 330 | 371 | 390 | 420 | 440 | 440 | 468 | 474 | 480 |
| 30849 | 206 | 265 | 317 | 356 | 396 | 422 | 455 | 476 | 503 | 497 | 509 | 519 | 542 |
| 30850 | 166 | 218 | 269 | 308 | 336 | 372 | 443 | 404 | 425 | 416 | 441 | 463 | 479 |
| 30851 | 205 | 274 | 321 | 356 | 392 | 421 | 414 | 455 | 467 | 478 | 486 | 494 | 507 |
| 30852 | 174 | 248 | 298 | 334 | 364 | 390 | 465 | 434 | 439 | 441 | 467 | 473 | 479 |
| 30853 | 185 | 246 | 304 | 350 | 400 | 439 | 422 | 480 | 503 | 515 | 532 | 548 | 556 |
| 30854 | 205 | 236 | 280 | 326 | 367 | 407 | 423 | 444 | 460 | 444 | 467 | 477 | 484 |
| 30855 | 199 | 265 | 323 | 375 | 414 | 462 | 483 | 513 | 530 | 519 | 533 | 556 | 560 |
| 30856 | 191 | 253 | 304 | 332 | 364 | 386 | 400 | 416 | 426 | 431 | 448 | 466 | 469 |
| 30857 | 178 | 236 | 284 | 318 | 358 | 379 | 404 | 421 | 442 | 442 | 455 | 477 | 490 |
| 30858 | 213 | 269 | 312 | 355 | 389 | 415 | 427 | 448 | 461 | 461 | 486 | 505 | 540 |

TABLE 4. Cont. Individual Weekly Male Body Weights

| Group Number, Test Article, Dosage Level, Male Number | Study Week 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| (3), B0547-01, 500 mg/kg/day: | | | | | | | | | | | | | |
| 30859 | 195 | 262 | 314 | 357 | 388 | 416 | 430 | 463 | 480 | 477 | 482 | 470 | 494 |
| 30860 | 193 | 252 | 307 | 343 | 384 | 413 | 441 | 457 | 490 | 482 | 499 | 495 | 515 |
| 30861 | 188 | 253 | 305 | 353 | 400 | 438 | 472 | 505 | 532 | 511 | 533 | 542 | 542 |
| 30862 | 181 | 236 | 277 | 315 | 342 | 373 | 398 | 419 | 429 | 435 | 455 | 475 | 480 |
| 30863 | 177 | 237 | 286 | 332 | 364 | 402 | 429 | 459 | 490 | 500 | 519 | 537 | 553 |
| 30864 | 201 | 268 | 322 | 360 | 408 | 433 | 458 | 485 | 489 | 489 | 508 | 529 | 537 |
| 30865 | 200 | 260 | 312 | 347 | 388 | 417 | 437 | 452 | 445 | 451 | 468 | 492 | 503 |
| 30866 | 167 | 228 | 266 | 303 | 347 | 368 | 395 | 417 | 434 | 444 | 467 | 482 | 488 |
| 30867 | 168 | 215 | 260 | 290 | 319 | 340 | 360 | 373 | 392 | 389 | 417 | 429 | 436 |
| 30868 | 191 | 257 | 318 | 364 | 403 | 438 | 470 | 492 | 514 | 513 | 532 | 554 | 556 |
| 30869 | 174 | 226 | 272 | 304 | 329 | 364 | 379 | 389 | 407 | 403 | 410 | 424 | 431 |
| 30870 | 177 | 233 | 282 | 317 | 350 | 376 | 399 | 424 | 444 | 436 | 471 | 486 | 490 |
| 30871 | 195 | 248 | 288 | 319 | 349 | 370 | 388 | 402 | 417 | 417 | 434 | 444 | 454 |
| 30872 | 178 | 247 | 295 | 340 | 379 | 410 | 440 | 470 | 493 | 494 | 514 | 534 | 540 |
| 30873 | 196 | 258 | 306 | 355 | 389 | 418 | 446 | 464 | 478 | 471 | 475 | 500 | 490 |
| 30874 | 186 | 246 | 292 | 337 | 374 | 383 | 421 | 454 | 469 | 464 | 485 | 500 | 509 |
| 30875 | 176 | 242 | 290 | 326 | 350 | 370 | 381 | 417 | 447 | 445 | 467 | 479 | 475 |
| 30876 | 177 | 239 | 293 | 347 | 388 | 418 | 443 | 464 | 484 | 498 | 500 | 517 | 534 |
| 30877 | 184 | 247 | 290 | 333 | 369 | 389 | 418 | 435 | 454 | 450 | 468 | 472 | 482 |
| 30878 | 196 | 248 | 284 | 311 | 342 | 366 | 381 | 387 | 402 | 398 | 411 | 422 | 433 |
| 30879 | 170 | 227 | 265 | 294 | 321 | 350 | 371 | 388 | 403 | 401 | 423 | 435 | 431 |
| 30880 | 185 | 248 | 299 | 346 | 381 | 410 | 432 | 458 | 479 | 469 | 490 | 513 | 525 |
| 30881 | 177 | 221 | 266 | 307 | 342 | 378 | 403 | 421 | 445 | 449 | 475 | 488 | 504 |
| 30882 | 199 | 258 | 301 | 340 | 370 | 401 | 422 | 443 | 460 | 463 | 477 | 497 | 506 |
| 30883 | 172 | 234 | 283 | 329 | 354 | 379 | 407 | 420 | 443 | 445 | 467 | 483 | 496 |
| (4), B0547-01, 1000 mg/kg/day: | | | | | | | | | | | | | |
| 30884 | 196 | 255 | 298 | 332 | 360 | 393 | 418 | 429 | 447 | 448 | 464 | 470 | 479 |
| 30885 | 168 | 162 | 234 | 277 | 315 | 341 | 360 | 372 | 387 | 385 | 406 | 417 | 421 |
| 30886 | 180 | 247 | 309 | 366 | 414 | 458 | 487 | 519 | 551 | 550 | 573 | 575 | 587 |
| 30887 | 191 | 265 | 327 | 381 | 419 | 458 | 482 | 502 | 527 | 482 | 520 | 545 | 556 |
| 30888 | 215 | 287 | 341 | 388 | 431 | 468 | 503 | 524 | 553 | 549 | 559 | 567 | 586 |
| 30889 | 165 | 204 | 247 | 278 | 311 | 338 | 361 | 374 | 391 | 395 | 411 | 420 | 430 |
| 30890 | 186 | 247 | 290 | 332 | 363 | 376 | 415 | 440 | 456 | 453 | 476 | 491 | 503 |
| 30891 | 171 | 231 | 286 | 324 | 353 | 412 | 390 | 413 | 433 | 433 | 446 | 498 | 479 |
| 30892 | 190 | 255 | 300 | 342 | 384 | 376 | 433 | 463 | 484 | 474 | 498 | 509 | 527 |
| 30893 | 200 | 254 | 293 | 326 | 354 | 366 | 392 | 412 | 421 | 423 | 436 | 449 | 454 |
| 30894 | 198 | 252 | 286 | 315 | 348 | 372 | 385 | 401 | 424 | 420 | 433 | 438 | 445 |
| 30895 | 168 | 227 | 275 | 311 | 340 | 368 | 397 | 412 | 430 | 428 | 443 | 450 | 453 |
| 30896 | 206 | 274 | 330 | 373 | 407 | 429 | 449 | 468 | 486 | 470 | 496 | 501 | 503 |
| 30897 | 210 | 276 | 329 | 369 | 409 | 428 | 460 | 478 | 490 | 488 | 521 | 534 | 560 |
| 30898 | 186 | 246 | 291 | 328 | 352 | 441 | 387 | 398 | 424 | 426 | 436 | 444 | 439 |
| 30899 | 178 | 234 | 279 | 318 | 346 | 377 | 399 | 418 | 444 | 442 | 461 | 465 | 455 |
| 30900 | 215 | 274 | 318 | 350 | 384 | 376 | 421 | 435 | 439 | 431 | 450 | 457 | 459 |
| 30901 | 215 | 285 | 329 | 373 | 403 | 404 | 448 | 465 | 488 | 472 | 492 | 501 | 505 |
| 30902 | 190 | 254 | 299 | 342 | 378 | 421 | 426 | 446 | 458 | 455 | 470 | 483 | 496 |
| 30903 | 214 | 278 | 322 | 368 | 400 | 401 | 451 | 462 | 484 | 483 | 495 | 518 | 523 |
| 30904 | 200 | 264 | 305 | 336 | 372 | 425 | 422 | 441 | 454 | 454 | 479 | 496 | 509 |
| 30905 | 197 | 256 | 304 | 344 | 381 | 406 | 430 | 457 | 470 | 474 | 488 | 499 | 513 |
| 30906 | 199 | 265 | 316 | 359 | 391 | 416 | 438 | 452 | 471 | 461 | 478 | 498 | 494 |
| 30907 | 199 | 266 | 314 | 364 | 410 | 436 | 463 | 489 | 514 | 528 | 548 | 555 | 568 |
| 30908 | 204 | 275 | 332 | 381 | 430 | 472 | 504 | 535 | 566 | 561 | 568 | 584 | 577 |

TABLE 4. Cont. Individual Weekly Male Body Weights

| Group Number, Test Article, Dosage Level, Male Number | Study Week 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| (5), 80547-01, 250 mg/kg/day: | | | | | | | | | | | | | |
| 30909 | 195 | 256 | 306 | 348 | 398 | 425 | 456 | 490 | 508 | 513 | 531 | 552 | 565 |
| 30910 | 196 | 262 | 313 | 362 | 394 | 422 | 453 | 467 | 488 | 480 | 503 | 509 | 506 |
| 30911 | 174 | 277 | 290 | 333 | 379 | 415 | 437 | 453 | 468 | 468 | 484 | 501 | 511 |
| 30912 | 180 | 237 | 287 | 320 | 358 | 389 | 414 | 431 | 447 | 448 | 470 | 485 | 496 |
| 30913 | 174 | 227 | 271 | 304 | 338 | 364 | 398 | 411 | 439 | 433 | 446 | 455 | 473 |
| 30914 | 197 | 261 | 323 | 368 | 419 | 450 | 478 | 500 | 530 | 522 | 542 | 571 | 579 |
| 30915 | 177 | 236 | 283 | 323 | 356 | 392 | 423 | 441 | 468 | 467 | 476 | 487 | 482 |
| 30916 | 179 | 227 | 276 | 311 | 337 | 367 | 383 | 406 | 418 | 412 | 429 | 439 | 448 |
| 30917 | 165 | 213 | 263 | 290 | 332 | 363 | 386 | 415 | 437 | 434 | 457 | 469 | 482 |
| 30918 | 194 | 262 | 311 | 358 | 400 | 433 | 465 | 485 | 515 | 500 | 512 | 530 | 540 |
| 30919 | 200 | 251 | 294 | 338 | 379 | 409 | 436 | 452 | 480 | 480 | 488 | 501 | 529 |
| 30920 | 195 | 263 | 320 | 366 | 410 | 448 | 476 | 510 | 541 | 540 | 555 | 563 | 574 |
| 30921 | 193 | 260 | 318 | 361 | 389 | 428 | 459 | 482 | 506 | 517 | 534 | 548 | 567 |
| 30922 | 181 | 243 | 292 | 338 | 374 | 409 | 427 | 462 | 478 | 486 | 511 | 530 | 545 |
| 30923 | 181 | 234 | 273 | 304 | 335 | 363 | 387 | 406 | 431 | 428 | 455 | 471 | 472 |
| 30924 | 196 | 262 | 320 | 369 | 413 | 450 | 483 | 513 | 541 | 538 | 559 | 573 | 586 |
| 30925 | 199 | 258 | 303 | 344 | 374 | 411 | 433 | 451 | 475 | 472 | 489 | 505 | 503 |
| 30926 | 180 | 227 | 275 | 313 | 342 | 371 | 395 | 410 | 440 | 438 | 467 | 486 | 498 |
| 30927 | 198 | 256 | 301 | 335 | 368 | 393 | 412 | 431 | 440 | 436 | 450 | 461 | 464 |
| 30928 | 174 | 228 | 277 | 311 | 346 | 373 | 399 | 414 | 432 | 424 | 434 | 448 | 452 |
| 30929 | 192 | 253 | 295 | 326 | 362 | 386 | 414 | 430 | 453 | 445 | 468 | 481 | 485 |
| 30930 | 203 | 252 | 297 | 335 | 367 | 389 | 415 | 429 | 441 | 435 | 460 | 466 | 471 |
| 30931 | 199 | 253 | 306 | 339 | 344 | 399 | 423 | 444 | 452 | 463 | 481 | 481 | 436 |
| 30932 | 168 | 225 | 272 | 309 | 365 | 381 | 408 | 427 | 445 | 436 | 467 | 501 | 507 |
| 30933 | 177 | 230 | 280 | 326 | 368 | 399 | 431 | 450 | 469 | 469 | 491 | 504 | 516 |
| (6), 80547-01, 500 mg/kg/day: | | | | | | | | | | | | | |
| 30934 | 184 | 237 | 278 | 317 | 340 | 358 | 379 | 388 | 409 | 405 | 434 | 428 | 443 |
| 30935 | 207 | 265 | 314 | 362 | 400 | 434 | 459 | 475 | 496 | 492 | 502 | 517 | 529 |
| 30936 | 190 | 254 | 307 | 345 | 376 | 401 | 420 | 428 | 456 | 456 | 496 | 501 | 509 |
| 30937 | 188 | 256 | 313 | 362 | 395 | 421 | 450 | 476 | 493 | 483 | 517 | 530 | 525 |
| 30938 | 174 | 229 | 285 | 322 | 360 | 391 | 399 | 437 | 457 | 458 | 472 | 478 | 484 |
| 30939 | 200 | 255 | 295 | 332 | 369 | 397 | 391 | 440 | 449 | 457 | 476 | 489 | 493 |
| 30940 | 187 | 253 | 304 | 354 | 382 | 416 | 459 | 478 | 504 | 494 | 524 | 542 | 557 |
| 30941 | 189 | 251 | 298 | 351 | 386 | 415 | 443 | 456 | 483 | 477 | 493 | 497 | 497 |
| 30942 | 182 | 244 | 295 | 332 | 360 | 352 | 362 | 395 | 421 | 421 | Died | | |
| 30943 | 209 | 265 | 316 | 340 | 372 | 400 | 418 | 439 | 453 | 455 | 475 | 488 | 495 |
| 30944 | 215 | 293 | 351 | 400 | 453 | 477 | 519 | 550 | 582 | 582 | 607 | 630 | 625 |
| 30945 | 178 | 245 | 306 | 359 | 407 | 440 | 462 | 493 | 509 | 504 | 541 | 559 | 577 |
| 30946 | 200 | 261 | 316 | 362 | 409 | 439 | 469 | 489 | 507 | 520 | 531 | 557 | 557 |
| 30947 | 199 | 253 | 293 | 330 | 353 | 377 | 391 | 398 | 411 | 403 | 396 | 421 | 426 |
| 30948 | 203 | 263 | 311 | 351 | 375 | 399 | 426 | 442 | 466 | 459 | 468 | 486 | 489 |
| 30949 | 214 | 256 | 324 | 362 | 398 | 427 | 452 | 461 | 469 | 470 | 484 | 488 | 490 |
| 30950 | 201 | 270 | 330 | 378 | 430 | 461 | 495 | 515 | 543 | 552 | 573 | 589 | 593 |
| 30951 | 206 | 268 | 318 | 365 | 398 | 432 | 453 | 460 | 481 | 482 | 499 | 508 | 513 |
| 30952 | 184 | 244 | 295 | 335 | 370 | 396 | 421 | 439 | 455 | 444 | 479 | 493 | 505 |
| 30953 | 185 | 241 | 285 | 319 | 344 | 372 | 401 | 399 | 416 | 410 | 433 | 449 | 448 |
| 30954 | 206 | 269 | 320 | 363 | 404 | 438 | 460 | 481 | 496 | 482 | 505 | 509 | 518 |
| 30955 | 190 | 251 | 296 | 337 | 376 | 392 | 419 | 436 | 452 | 459 | 478 | 491 | 483 |
| 30956 | 208 | 283 | 339 | 389 | 435 | 469 | 504 | 518 | 548 | 540 | 560 | 574 | 582 |
| 30957 | 183 | 250 | 299 | 344 | 379 | 403 | 435 | 451 | 475 | 456 | 472 | 482 | 469 |
| 30958 | 198 | 243 | 278 | 307 | 331 | 349 | 367 | 379 | 391 | 395 | 407 | 414 | 400 |

TABLE 4. Cont.

Individual Weekly Male Body Weights

| Group Number, Test Article, Dosage Level, Male Number | Study Week 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| (7), B0547-01, 1000 mg/kg/day: | | | | | | | | | | | | | |
| 30959 | 177 | 228 | 273 | 307 | 328 | 355 | 377 | 388 | 406 | 404 | 410 | 431 | 439 |
| 30960 | 170 | 217 | 274 | 311 | 347 | 372 | 408 | 423 | 402 | 375 | 427 | 451 | 456 |
| 30961 | 171 | 220 | 258 | 296 | 330 | 357 | 391 | 406 | Died | | | | |
| 30962 | 176 | 230 | 279 | 328 | 365 | 391 | 424 | 442 | 466 | 469 | 493 | 505 | 511 |
| 30963 | 209 | 278 | 349 | 398 | 444 | 476 | 510 | 539 | 565 | 559 | 594 | 616 | 613 |
| 30964 | 205 | 248 | 290 | 323 | 355 | 360 | 387 | 389 | 400 | 394 | 416 | 419 | 392 |
| 30965 | 206 | 259 | 306 | 343 | 368 | 387 | 411 | Died | | | | | |
| 30966 | 180 | 236 | 285 | 326 | 356 | 357 | 377 | 401 | 413 | 403 | 442 | 467 | 474 |
| 30967 | 180 | 238 | 285 | 319 | 346 | 355 | 372 | 388 | 395 | 390 | 410 | 420 | 425 |
| 30968 | 172 | 226 | 263 | 291 | 327 | 351 | 379 | 396 | 402 | 396 | 417 | 424 | 435 |
| 30969 | 205 | 242 | 306 | 350 | 388 | 417 | 433 | 448 | 457 | 454 | 476 | 492 | 487 |
| 30970 | 187 | 230 | 275 | 308 | 331 | 348 | 372 | 388 | 384 | 390 | 402 | 408 | 414 |
| 30971 | 169 | 215 | 273 | 316 | 319 | 364 | 394 | 415 | 425 | 419 | 445 | 450 | 456 |
| 30972 | 198 | 262 | 299 | 342 | 371 | 395 | 426 | 441 | 451 | 434 | 474 | 487 | 486 |
| 30973 | 185 | 219 | 253 | 276 | 294 | 314 | 332 | 352 | 364 | 358 | 365 | 397 | 397 |
| 30974 | 176 | 240 | 289 | 327 | 350 | 373 | 403 | 430 | 446 | 442 | 459 | 460 | 473 |
| 30975 | 176 | 207 | 268 | 301 | 343 | 369 | 402 | 428 | 453 | 450 | 481 | 477 | 496 |
| 30976 | 186 | 244 | 295 | 337 | 375 | 411 | 436 | 463 | 487 | 480 | 514 | 526 | 516 |
| 30977 | 194 | 234 | 282 | 316 | 339 | 361 | 372 | 394 | 399 | 406 | 432 | 434 | 433 |
| 30978 | 194 | 252 | 299 | 345 | 379 | 404 | 429 | 444 | 456 | 457 | 473 | 485 | 483 |
| 30979 | 201 | 263 | 325 | 376 | 420 | 469 | 500 | 526 | 530 | 520 | 542 | 546 | 559 |
| 30980 | 181 | 243 | 293 | 331 | 360 | 387 | 406 | 429 | 446 | 443 | 465 | 476 | 486 |
| 30981 | 213 | 276 | 308 | 353 | 372 | 401 | 421 | 433 | 448 | 442 | 466 | 474 | 468 |
| 30982 | 195 | 245 | 305 | 352 | 369 | Died | | | | | | | |
| 30983 | 203 | 238 | 300 | 349 | 382 | 406 | 433 | 455 | 478 | 466 | 501 | 511 | 520 |

TABLE 5. FEMALES: Summary of Weekly Group Mean Body Weights

| | 0 mg/kg/day (Control) (1) | | | B0547-01 mg/kg/day (group number) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | 250FD (2) | | | 500FD (3) | | | 1000FD (4) | | |
| Study Week | Mean Body Weight (g) | Standard Deviation (±) | N | Mean Body Weight (g) | Standard Deviation (±) | N | Mean Body Weight (g) | Standard Deviation (±) | N | Mean Body Weight (g) | Standard Deviation (±) | N |
| 6 | 237 | 14.1 | 25 | 239 | 10.6 | 25 | 241 | 11.6 | 25 | 242 | 12.1 | 25 |
| 7 | 249 | 16.8 | 25 | 250 | 10.5 | 25 | 252 | 15.0 | 25 | 248 | 15.9 | 25 |
| 8 | 256 | 19.1 | 25 | 257 | 13.2 | 25 | 259 | 15.8 | 25 | 258 | 13.0 | 24 |
| 9[a] | 262 | 13.1 | 8 | 270 | 13.2 | 7 | 263 | 31.6 | 11 | 265 | 14.8 | 10 |
| 10 | 293 | 17.7 | 2 | 297 | 35.2 | 3 | 235 | 145.0 | 2 | 292 | 7.5 | 3 |
| 11 | 294 | - | 1 | 309 | 36.3 | 3 | 342 | - | 1 | 297 | 13.4 | 2 |
| 12 | 373 | - | 1 | 372 | 91.2 | 3 | 373 | - | 1 | 348 | 77.1 | 2 |
| 13 | | | | 298 | - | 1 | 409 | - | 1 | 293 | - | 1 |
| 14 | | | | 307 | - | 1 | | | | 296 | - | 1 |

a - Mating initiated
N - Number of animals utilized in calculation of means, remaining females either died or had evidence of copulation.
FD - Only females dosed
- Not applicable

TABLE 5. Cont.

FEMALES: Summary of Weekly Group Mean Body Weights

B0547-01 mg/kg/day (group number)

| Study Week | 250MD (5) Mean Body Weight (g) | 250MD (5) Standard Deviation (±) | 250MD (5) N | 500MD (6) Mean Body Weight (g) | 500MD (6) Standard Deviation (±) | 500MD (6) N | 1000MD (7) Mean Body Weight (g) | 1000MD (7) Standard Deviation (±) | 1000MD (7) N |
|---|---|---|---|---|---|---|---|---|---|
| 6 | 242 | 10.4 | 25 | 241 | 8.6 | 25 | 239 | 14.1 | 25 |
| 7 | 256 | 12.9 | 25 | 254 | 15.4 | 25 | 253 | 14.7 | 24 |
| 8 | 267 | 16.2 | 25 | 264 | 12.2 | 25 | 265 | 16.4 | 24 |
| 9[a] | 278 | 10.2 | 9 | 272 | 14.8 | 7 | 271 | 16.3 | 6 |
| 10 | | | | 307 | 0.0 | 2 | | | |
| 11 | | | | 315 | 26.9 | 2 | | | |
| 12 | | | | 308 | - | 1 | | | |
| 13 | | | | | | | | | |
| 14 | | | | | | | | | |

a - Mating initiated
N - Number of animals utilized in calculation of means, remaining males died or had evidence of copulation
MD - Only males dosed
- Not applicable

191-900

TABLE 6. Individual Weekly Female Body Weights

| Group Number, Test Article, Dosage Level, Female Number | Study Week 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 |
|---|---|---|---|---|---|---|---|---|---|
| (1), 0 mg/kg/day (Control): | | | | | | | | | |
| 30984 | 267 | 287 | 304 | a | | | | | |
| 30985 | 221 | 230 | 239 | a | | | | | |
| 30986 | 216 | 221 | 231 | a | | | | | |
| 30987 | 223 | 229 | 240 | a | | | | | |
| 30988 | 221 | 235 | 238 | 254 | a | | | | |
| 30989 | 250 | 263 | 269 | a | | | | | |
| 30990 | 235 | 250 | 258 | a | | | | | |
| 30991 | 236 | 251 | 252 | 263 | a | | | | |
| 30992 | 251 | 264 | 273 | 280 | a | | | | |
| 30993 | 223 | 236 | 245 | a | | | | | |
| 30994 | 247 | 263 | 276 | a | | | | | |
| 30995 | 240 | 255 | 266 | a | | | | | |
| 30996 | 256 | 264 | 277 | a | | | | | |
| 30997 | 223 | 230 | 234 | 246 | a | | | | |
| 30998 | 242 | 245 | 252 | 270 | 305 | a | | | |
| 30999 | 241 | 254 | 274 | a | | | | | |
| 31000 | 218 | 228 | 233 | a | | | | | |
| 31001 | 238 | 246 | 234 | 247 | a | | | | |
| 31002 | 231 | 252 | 258 | a | | | | | |
| 31003 | 229 | 236 | 243 | a | | | | | |
| 31004 | 238 | 250 | 254 | 255 | 280 | 294 | 373 | b | |
| 31005 | 221 | 235 | 248 | a | | | | | |
| 31006 | 253 | 266 | 268 | 277 | a | | | | |
| 31007 | 235 | 246 | 250 | a | | | | | |
| 31008 | 259 | 281 | 290 | a | | | | | |
| (2), B0547-01, 250 mg/kg/day: | | | | | | | | | |
| 31009 | 229 | 243 | 255 | a | | | | | |
| 31010 | 239 | 255 | 255 | 257 | 271 | 296 | 355 | b | |
| 31011 | 230 | 242 | 253 | a | | | | | |
| 31012 | 262 | 272 | 285 | a | | | | | |
| 31013 | 266 | 278 | 290 | 294 | 337 | 350 | 471 | b | |
| 31014 | 239 | 252 | 255 | a | | | | | |
| 31015 | 232 | 239 | 240 | Died | | | | | |
| 31016 | 247 | 258 | 266 | 275 | a | | | | |
| 31017 | 228 | 243 | 250 | a | | | | | |
| 31018 | 244 | 260 | 262 | 268 | a | | | | |
| 31019 | 225 | 238 | 245 | a | | | | | |
| 31020 | 235 | 244 | 248 | a | | | | | |
| 31021 | 234 | 245 | 261 | a | | | | | |
| 31022 | 250 | 253 | 273 | a | | | | | |
| 31023 | 234 | 249 | 260 | a | | | | | |
| 31024 | 244 | 261 | 265 | 261 | 283 | 281 | 291 | 298 | 307[c] |
| 31025 | 228 | 235 | 247 | a | | | | | |
| 31026 | 248 | 258 | 266 | 275 | a | | | | |
| 31027 | 225 | 236 | 245 | a | | | | | |
| 31028 | 239 | 248 | 269 | a | | | | | |
| 31029 | 239 | 247 | 243 | a | | | | | |
| 31030 | 243 | 249 | 249 | a | | | | | |
| 31031 | 246 | 256 | 238 | a | | | | | |
| 31032 | 228 | 245 | 251 | a | | | | | |
| 31033 | 240 | 248 | 245 | 257 | a | | | | |

[a]Evidence of mating observed, weekly weights not required
[b]No evidence of copulation, dam delivered, see gestation and lactation body weights (Table 8
[c]No evidence of copulation, females sacrificed 25 days following seperation from male

TABLE 6. Cont. Individual Weekly Female Body Weights

| Group Number, Test Article, Dosage Level, Female Number | Study Week 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 |
|---|---|---|---|---|---|---|---|---|---|
| (3), B0547-01, 500 mg/kg/day: | | | | | | | | | |
| 31034 | 222 | 218 | 241 | 178 | 132 | d | | | |
| 31035 | 247 | 260 | 256 | 271 | a | | | | |
| 31036 | 253 | 264 | 273 | a | | | | | |
| 31037 | 240 | 250 | 256 | a | | | | | |
| 31038 | 251 | 263 | 269 | 282 | a | | | | |
| 31039 | 246 | 253 | 268 | 274 | a | | | | |
| 31040 | 227 | 235 | 239 | 252 | a | | | | |
| 31041 | 233 | 250 | 253 | 254 | a | | | | |
| 31042 | 250 | 253 | 266 | a | | | | | |
| 31043 | 249 | 263 | 269 | a | | | | | |
| 31044 | 238 | 238 | 234 | 265 | a | | | | |
| 31045 | 227 | 240 | 247 | a | | | | | |
| 31046 | 223 | 229 | 226 | a | | | | | |
| 31047 | 261 | 277 | 276 | a | | | | | |
| 31048 | 262 | 286 | 299 | 301 | 337 | 342 | 373 | 409 | b |
| 31049 | 239 | 247 | 256 | a | | | | | |
| 31050 | 236 | 247 | 258 | a | | | | | |
| 31051 | 243 | 253 | 258 | a | | | | | |
| 31052 | 225 | 236 | 244 | a | | | | | |
| 31053 | 230 | 250 | 261 | a | | | | | |
| 31054 | 243 | 250 | 252 | 259 | a | | | | |
| 31055 | 252 | 263 | 273 | 285 | a | | | | |
| 31056 | 234 | 243 | 258 | a | | | | | |
| 31057 | 252 | 261 | 267 | 271 | a | | | | |
| 31058 | 251 | 268 | 278 | a | | | | | |
| (4), B0547-01, 1000 mg/kg/day: | | | | | | | | | |
| 31059 | 227 | 221 | 240 | a | | | | | |
| 31060 | 233 | 218 | 246 | a | | | | | |
| 31061 | 251 | 263 | 250 | 255 | a | | | | |
| 31062 | 243 | 259 | 249 | a | | | | | |
| 31063 | 246 | 245 | 258 | 249 | 292 | a | | | |
| 31064 | 233 | 261 | 274 | a | | | | | |
| 31065 | 252 | 259 | 259 | a | | | | | |
| 31066 | 248 | 257 | 266 | a | | | | | |
| 31067 | 258 | 256 | 267 | 292 | a | | | | |
| 31068 | 251 | 260 | 272 | 261 | 285 | 306 | 402 | b | |
| 31069 | 229 | 237 | 240 | 244 | a | | | | |
| 31070 | 221 | 230 | 234 | a | | | | | |
| 31071 | 236 | 240 | 253 | 258 | a | | | | |
| 31072 | 233 | 222 | 245 | 266 | 300 | 287 | 293 | 293 | 296[c] |
| 31073 | 225 | 226 | 240 | 267 | a | | | | |
| 31074 | 252 | 246 | 255 | Died | | | | | |
| 31075 | 246 | 262 | 270 | a | | | | | |
| 31076 | 222 | 241 | 247 | a | | | | | |
| 31077 | 252 | 264 | 273 | 272 | a | | | | |
| 31078 | 243 | 253 | 260 | a | | | | | |
| 31079 | 246 | 258 | 267 | a | | | | | |
| 31080 | 266 | 270 | 278 | 283 | a | | | | |
| 31081 | 245 | 267 | 273 | a | | | | | |
| 31082 | 229 | 233 | Died | | | | | | |
| 31083 | 255 | 258 | 264 | a | | | | | |

[a]Evidence of mating observed, weekly weights not required
[b]No evidence of copulation, dam delivered, see gestation and lactation bodyweights (Table 8)
[c]No evidence of copulation, female sacrificed 25 days following separation from male
[d]Sacrificed *in extremis*

TABLE 6. Cont. Individual Weekly Female Body Weights

| Group Number, Test Article, Dosage Level, Female Number | Study Week 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 |
|---|---|---|---|---|---|---|---|---|---|
| (5), 80547-01, 250 mg/kg/day: | | | | | | | | | |
| 31084 | 234 | 249 | 256 | a | | | | | |
| 31085 | 219 | 231 | 242 | a | | | | | |
| 31086 | 241 | 251 | 259 | a | | | | | |
| 31087 | 238 | 252 | 262 | a | | | | | |
| 31088 | 245 | 266 | 284 | 282 | a | | | | |
| 31089 | 248 | 268 | 280 | a | | | | | |
| 31090 | 250 | 264 | 278 | a | | | | | |
| 31091 | 256 | 264 | 272 | 284 | a | | | | |
| 31092 | 245 | 262 | 289 | a | | | | | |
| 31093 | 243 | 259 | 263 | 278 | a | | | | |
| 31094 | 223 | 236 | 247 | a | | | | | |
| 31095 | 243 | 265 | 276 | 278 | a | | | | |
| 31096 | 236 | 246 | 252 | 261 | a | | | | |
| 31097 | 253 | 267 | 280 | a | | | | | |
| 31098 | 241 | 255 | 273 | a | | | | | |
| 31099 | 242 | 256 | 267 | a | | | | | |
| 31100 | 247 | 265 | 268 | 276 | a | | | | |
| 31101 | 261 | 281 | 299 | a | | | | | |
| 31102 | 238 | 254 | 270 | a | | | | | |
| 31103 | 257 | 278 | 292 | 298 | a | | | | |
| 31104 | 241 | 255 | 274 | 280 | a | | | | |
| 31105 | 242 | 253 | 247 | 269 | a | | | | |
| 31106 | 229 | 233 | 242 | a | | | | | |
| 31107 | 224 | 235 | 240 | a | | | | | |
| 31108 | 245 | 258 | 269 | a | | | | | |
| (6), 80547-01, 500 mg/kg/day: | | | | | | | | | |
| 31109 | 231 | 239 | 250 | a | | | | | |
| 31110 | 244 | 260 | 268 | 282 | a | | | | |
| 31111 | 226 | 239 | 255 | a | | | | | |
| 31112 | 254 | 266 | 271 | a | | | | | |
| 31113 | 242 | 254 | 263 | a | | | | | |
| 31114 | 236 | 253 | 264 | a | | | | | |
| 31115 | 241 | 260 | 271 | a | | | | | |
| 31116 | 239 | 254 | 258 | 273 | a | | | | |
| 31117 | 232 | 242 | 249 | 248 | a | | | | |
| 31118 | 240 | 253 | 269 | a | | | | | |
| 31119 | 229 | 240 | 252 | a | | | | | |
| 31120 | 242 | 264 | 275 | a | | | | | |
| 31121 | 232 | 246 | 253 | a | | | | | |
| 31122 | 250 | 258 | 277 | a | | | | | |
| 31123 | 252 | 265 | 276 | 277 | a | | | | |
| 31124 | 228 | 272 | 258 | a | | | | | |
| 31125 | 255 | 273 | 283 | a | | | | | |
| 31126 | 238 | 245 | 260 | 255 | a | | | | |
| 31127 | 247 | 263 | 273 | 287 | 307 | 296 | 308 | 363 | b |
| 31128 | 236 | 240 | 250 | a | | | | | |
| 31129 | 251 | 273 | 277 | a | | | | | |
| 31130 | 244 | 249 | 264 | a | | | | | |
| 31131 | 230 | 204 | 235 | a | | | | | |
| 31132 | 249 | 264 | 268 | 282 | 307 | 334 | b | | |
| 31133 | 251 | 272 | 286 | a | | | | | |

[a]Evidence of mating observed, weekly weights not required
[b]No evidence of copulation, dam delivered, see gestation and lactation in body weights (Table 8)

TABLE 6. Cont. Individual Weekly Female Body Weights

| Group Number, Test Article, Dosage Level, Female Number | Study Week 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 |
|---|---|---|---|---|---|---|---|---|---|
| (7), 80547-01, 1000 mg/kg/day: | | | | | | | | | |
| 31134 | 229 | 241 | 249 | 254 | a | | | | |
| 31135 | 242 | 252 | 257 | 257 | a | | | | |
| 31136 | 236 | 249 | 259 | 258 | a | | | | |
| 31137 | 253 | 272 | 274 | a | | | | | |
| 31138 | 234 | Died | | | | | | | |
| 31139 | 228 | 240 | 247 | a | | | | | |
| 31140 | 218 | 229 | 236 | a | | | | | |
| 31141 | 248 | 261 | 275 | a | | | | | |
| 31142 | 226 | 237 | 248 | a | | | | | |
| 31143 | 219 | 239 | 254 | a | | | | | |
| 31144 | 221 | 234 | 250 | a | | | | | |
| 31145 | 258 | 273 | 285 | 288 | a | | | | |
| 31146 | 251 | 262 | 269 | 279 | a | | | | |
| 31147 | 255 | 269 | 285 | 289 | a | | | | |
| 31148 | 258 | 274 | 291 | a | | | | | |
| 31149 | 251 | 263 | 280 | a | | | | | |
| 31150 | 229 | 244 | 260 | a | | | | | |
| 31151 | 223 | 242 | 249 | a | | | | | |
| 31152 | 243 | 255 | 267 | a | | | | | |
| 31153 | 221 | 237 | 252 | a | | | | | |
| 31154 | 247 | 262 | 290 | a | | | | | |
| 31155 | 251 | 261 | 280 | a | | | | | |
| 31156 | 225 | 240 | 252 | a | | | | | |
| 31157 | 254 | 272 | 291 | a | | | | | |
| 31158 | 256 | 273 | 263 | a | | | | | |

[a]Evidence of mating observed, weekly weights not required

TABLE 7. Summary of Group Mean Maternal Body Weights and Body Weight Changes During Gestation and Lactation

| | Group Mean Maternal Body Weights (grams) B0547-01 mg/kg/day (group number) | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 0 (Control) (1) | | $250^{FD}$ (2) | | $500^{FD}$ (3) | | $1000^{FD}$ (4) | | $250^{MD}$ (5) | | $500^{MD}$ (6) | | $1000^{MD}$ (7) | |
| | Mean | ±S.D. | Mean | ±S.D. | Mean | ±S.D. | Mean | ±S.D. | Mean | ±S.D. | Mean | ±S.D. | Mean | ±S.D. |
| **Day of Gestation** | | | | | | | | | | | | | | |
| 0 | 267 | 19.1 | 265 | 10.1 | 265 | 16.4 | 259 | 19.4 | 276 | 17.1 | 270 | 16.0 | 271 | 17.2 |
| 7 | 297 | 17.8 | 294 | 13.2 | 296 | 16.4 | 288 | 18.5 | 306 | 17.0 | 303 | 13.5 | 301 | 19.1 |
| 13 | 321 | 20.3 | 317 | 16.5 | 316 | 15.7 | 309 | 19.9 | 329 | 19.1 | 323 | 15.6 | 324 | 20.1 |
| 20 | 392 | 21.1 | 388 | 27.6 | 389 | 20.9 | 384 | 35.4 | 393 | 23.4 | 394 | 22.8 | 393 | 25.0 |
| **Day of Lactation** | | | | | | | | | | | | | | |
| 0 | 304 | 20.8 | 305 | 22.2 | 316 | 27.4 | 299 | 31.3 | 304 | 23.9 | 307 | 12.7 | 310 | 16.8 |
| 7 | 326 | 20.5 | 323 | 15.9 | 326 | 20.8 | 319 | 24.0 | 324 | 20.5 | 329 | 17.7 | 324 | 14.1 |
| 14 | 348 | 24.1 | 343 | 23.2 | 344 | 16.0 | 339 | 28.6 | 342 | 16.7 | 351 | 10.3 | 341 | 18.5 |
| 21 | 326 | 22.2 | 330 | 18.3 | 331 | 11.5 | 336 | 28.6 | 331 | 13.6 | 328 | 28.0 | 329 | 14.9 |
| | Group Mean Maternal Body Weight Change (grams)[a] | | | | | | | | | | | | | |
| **Days of Gestation** | | | | | | | | | | | | | | |
| 0 to 7 | 30 | 6.3 | 28 | 6.5 | 32 | 10.3 | 29 | 10.0 | 30 | 7.9 | 33 | 7.6 | 29 | 8.4 |
| 7 to 13 | 23 | 6.7 | 24 | 6.3 | 20 | 10.0 | 21 | 7.5 | 23 | 7.5 | 20 | 5.1 | 23 | 3.9 |
| 13 to 20 | 72 | 6.5 | 73 | 16.2 | 76 | 14.7 | 73 | 15.6 | 70 | 16.5 | 73 | 11.2 | 65 | 17.3 |
| 0 to 20 | 124 | 9.8 | 124 | 20.1 | 123 | 19.0 | 126 | 25.5 | 123 | 22.3 | 125 | 15.5 | 118 | 20.1 |
| **Days of Lactation** | | | | | | | | | | | | | | |
| 0 to 7 | 22 | 10.8 | 18 | 10.0 | 10 | 9.9 | 20 | 15.6 | 20 | 15.3 | 22 | 11.8 | 14 | 11.8 |
| 7 to 14 | 22 | 9.0 | 20 | 9.1 | 18 | 12.0 | 20 | 10.0 | 17 | 9.6 | 23 | 12.4 | 18 | 12.2 |
| 14 to 21 | -23 | 10.6 | -13 | 8.9 | -13 | 10.1 | -3 | 11.8 | -10 | 15.1 | -23 | 25.9 | -12 | 15.9 |
| 0 to 21 | 21 | 12.3 | 25 | 8.0 | 15 | 22.7 | 37 | 16.3 | 27 | 21.4 | 22 | 25.4 | 20 | 20.2 |

[a]Values represent the mean of the individual changes in maternal body weight for these intervals

MD - Only males dosed

FD - Only females dosed

S.D. - Standard deviation

191-900

TABLE 8. Individual and Group Mean Maternal Body Weights During Gestation and Lactation

| Group Number, Test Article, Dosage Level, Dam Number | Actual Body Weight (grams) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Day of Gestation | | | | Day of Lactation | | | |
| | 0 | 7 | 13 | 20 | 0 | 7 | 14 | 21 |
| (1), 0 mg/kg/day (Control): | | | | | | | | |
| 30984 | 305 | 328 | 347 | a | | | | |
| 30985 | 250 | 285 | 308 | 384 | 284 | 311 | 332 | 311 |
| 30986 | 235 | 266 | 298 | 361 | 286 | 303 | 331 | 325 |
| 30987 | 244 | 281 | 308 | a | | | | |
| 30988 | 260 | 293 | 320 | a | | | | |
| 30989 | 277 | 317 | 345 | a | | | | |
| 30990 | 267 | 295 | 321 | 399 | 320 | 342 | 360 | 330 |
| 30991 | 262 | 281 | 302 | 373 | 296 | 307 | 324 | 321 |
| 30992 | 290 | 324 | 353 | 415 | 333 | 349 | 370 | 337 |
| 30993 | 252 | 286 | 298 | a | | | | |
| 30994 | 285 | 306 | 330 | a | | | | |
| 30995 | 275 | 302 | 327 | 396 | 304 | 340 | 352 | 331 |
| 30996 | 290 | 303 | 325 | 396 | 308 | 320 | 350 | 336 |
| 30997 | 250 | 283 | 310 | 386 | 279 | 312 | 336 | 297 |
| 30998 | 294 | 325 | 347 | 420 | 325 | 366 | 391 | 372 |
| 30999 | 282 | 314 | 336 | a | | | | |
| 31000 | 241 | 268 | 272 | a | | | | |
| 31001 | 257 | 290 | 313 | a | | | | |
| 31002 | 268 | 301 | 331 | a | | | | |
| 31003 | 247 | 281 | 299 | 376 | 297 | 310 | 336 | 310 |
| 31004 | b | | | | 299 | 320 | 332 | 310 |
| 31005 | 253 | 283 | 302 | 366 | 282 | 311 | 322 | 297 |
| 31006 | 273 | 298 | 322 | a | | | | |
| 31007 | 264 | 302 | 340 | a | | | | |
| 31008 | 292 | 323 | 343 | 426 | 345 | 350 | 394 | 359 |
| Mean | 267 | 297 | 321 | 392 | 304 | 326 | 348 | 326 |
| ±S.D. | 19.1 | 17.8 | 20.3 | 21.1 | 20.8 | 20.5 | 24.1 | 22.2 |
| (2), B0547-01, 250 mg/kg/day: | | | | | | | | |
| 31009 | 261 | 294 | 307 | a | | | | |
| 31010 | b | | | | 277 | 306 | 319 | 310 |
| 31011 | 269 | 300 | 320 | a | | | | |
| 31012 | 282 | 318 | 347 | 432 | 318 | 335 | 352 | 330 |
| 31013 | b | | | | 336 | 356 | 390 | 361 |
| 31014 | 263 | 296 | 322 | a | | | | |
| 31015 | Died | | | | | | | |
| 31016 | 275 | 297 | 336 | a | | | | |
| 31017 | 264 | 291 | 314 | 350 | 297 | 317 | 322 | 325 |
| 31018 | 269 | 311 | 335 | a | | | | |
| 31019 | 250 | 271 | 294 | a | | | | |
| 31020 | 258 | 278 | 303 | 381 | 285 | 310 | 333 | 316 |
| 31021[d] | 263 | 270 | 271 | a | | | | |
| 31022 | 283 | 306 | 328 | a | | | | |
| 31023 | 269 | 303 | 327 | 414 | 322 | 338 | 367 | 349 |
| 31024 | b | | | | c | | | |
| 31025 | 257 | 290 | 308 | a | | | | |
| 31026 | 273 | 300 | 324 | 412 | 325 | 326 | 357 | 345 |
| 31027 | 245 | 272 | 283 | 363 | 278 | 305 | 321 | 303 |
| 31028 | 274 | 298 | 322 | a | | | | |
| 31029[d] | 264 | 272 | Died gestation day 11 | | | | | |
| 31030 | 257 | 274 | 298 | 367 | 283 | 311 | 326 | 323 |
| 31031[d] | 257 | 284 | 285 | a | | | | |
| 31032 | 267 | 299 | 332 | 401 | 330 | 330 | 357 | 347 |
| 31033 | 262 | 288 | 310 | 375 | 301 | 315 | 328 | 319 |
| Mean | 265 | 294 | 317 | 388 | 305 | 323 | 343 | 330 |
| ±S.D. | 10.1 | 13.2 | 16.5 | 27.6 | 22.2 | 15.9 | 23.2 | 18.3 |

[a]Sacrificed for 13-day uterine examination
[b]No evidence of copulation
[c]Did not deliver, sacrificed 25 days following termination of mating (nongravid), not included in calculation of mean
[d]Nongravid, not included in calculation of mean

 S.D. - Standard deviation

TABLE 8. Cont.

Individual and Group Mean Maternal Body Weights During Gestation and Lactation



| Group Number, Test Article, Dosage Level, Dam Number | Actual Body Weight (grams) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Day of Gestation | | | | Day of Lactation | | | |
| | 0 | 7 | 13 | 20 | 0 | 7 | 14 | 21 |
| (3), 80547-01, 500 mg/kg/day: | | | | | | | | |
| 31034 | Sacrificed | | | | | | | |
| 31035 | 280 | 307 | 319 | 405 | 333 | 336 | 351 | 332 |
| 31036 | 271 | 288 | 311 | 359 | 329 | 341 | 345 | 332 |
| 31037 | 265 | 287 | 308 | 386 | 302 | 308 | 338 | 330 |
| 31038 | 286 | 315 | 323 | 307 | c | | | |
| 31039 | 283 | 319 | 321 | 396 | 316 | 331 | 343 | 324 |
| 31040 | 255 | 287 | 317 | 390 | 319 | 336 | 338 | 323 |
| 31041 | 270 | 291 | 319 | a | | | | |
| 31042 | 272 | 297 | 320 | 399 | 304 | 328 | 360 | 350 |
| 31043[d] | 284 | 311 | 316 | a | | | | |
| 31044 | 256 | 306 | 338 | a | | | | |
| 31045 | 255 | 313 | 305 | a | | | | |
| 31046 | 225 | 264 | 281 | 352 | 268 | 284 | 306 | 315 |
| 31047 | 273 | 293 | 316 | a | | | | |
| 31048 | b | | | | 380 | 366 | 368 | 349 |
| 31049[d] | 250 | 265 | 261 | a | | | | |
| 31050 | 256 | 290 | 308 | 399 | 308 | 320 | 350 | 318 |
| 31051 | 252 | 278 | 295 | a | | | | |
| 31052 | 240 | 273 | 297 | a | | | | |
| 31053 | 269 | 301 | 322 | 421 | 311 | 319 | 351 | 340 |
| 31054[d] | 265 | 285 | 283 | a | | | | |
| 31055 | 296 | 334 | 348 | a | | | | |
| 31056 | 254 | 293 | 324 | a | | | | |
| 31057 | 277 | 308 | 337 | a | | | | |
| 31058 | 277 | 302 | 318 | 378 | 302 | 316 | 335 | 326 |
| Mean | 265 | 296 | 316 | 389 | 316 | 326 | 344 | 331 |
| ±S.D. | 16.4 | 16.4 | 15.7 | 20.9 | 27.4 | 20.8 | 16.0 | 11. |
| (4), 80547-01, 1000 mg/kg/day: | | | | | | | | |
| 31059 | 236 | 271 | 283 | a | | | | |
| 31060[e] | 252 | Died | | | | | | |
| 31061 | 263 | 280 | 290 | 332 | 265 | 288 | 294 | 313 |
| 31062 | 270 | 303 | 319 | a | | | | |
| 31063 | 280 | 303 | 328 | a | | | | |
| 31064 | 258 | 291 | 288 | a | | | | |
| 31065 | 244 | 270 | 287 | a | | | | |
| 31066[d] | 261 | 266 | 274 | a | | | | |
| 31067 | 288 | 333 | 340 | 440 | 376 | 368 | 399 | 395 |
| 31068 | b | | | | 284 | 332 | 344 | 350 |
| 31069 | 249 | 269 | 288 | 355 | 278 | 313 | 323 | 323 |
| 31070 | 228 | 267 | 290 | 364 | 280 | 297 | 311 | 290 |
| 31071 | 267 | 295 | 313 | a | | | | |
| 31072 | b | | | | f | | | |
| 31073 | 262 | 285 | 311 | a | | | | |
| 31074 | Died | | | | | | | |
| 31075 | 259 | 281 | 303 | 376 | 294 | 297 | 333 | 317 |
| 31076 | 241 | 275 | 299 | a | | | | |
| 31077 | 280 | 311 | 338 | a | | | | |
| 31078 | 224 | 269 | 297 | 367 | 297 | 311 | 333 | 334 |
| 31079 | 270 | 277 | 304 | a | | | | |
| 31080 | 293 | 314 | 345 | 432 | 324 | 342 | 359 | 358 |
| 31081 | 247 | 288 | 314 | 387 | 292 | 315 | 340 | 339 |
| 31082 | Died | | | | | | | |
| 31083 | 267 | 301 | 330 | 400 | 298 | 324 | 353 | 337 |
| Mean | 259 | 288 | 309 | 384 | 299 | 319 | 339 | 336 |
| ±S.D. | 19.4 | 18.5 | 19.9 | 35.4 | 31.3 | 24.0 | 28.6 | 28.6 |

[a]Sacrificed for 13-day uterine examination
[b]No evidence of copulation
[c]Did not deliver, sacrificed 25 days following termination of mating (nongravid), not included in calculation of mean
[d]Nongravid, not included in calculation of mean
[e]Dam died gestation day 3, pregnancy status unknown, not included in calculation of means
[f]Did not deliver, sacrificed 25 days following termination of mating (gravid)

S.D. - Standard deviation

TABLE 8. Cont.

Individual and Group Mean Maternal Body Weights During Gestation and Lactation



| Group Number, Test Article, Dosage Level, Dam Number | Actual Body Weight (grams) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Day of Gestation | | | | Day of Lactation | | | |
| | 0 | 7 | 13 | 20 | 0 | 7 | 14 | 21 |
| (5), 80547-01, 250 mg/kg/day: | | | | | | | | |
| 31084 | 267 | 303 | 317 | a | | | | |
| 31085 | 250 | 277 | 302 | 367 | 276 | 305 | 322 | 322 |
| 31086 | 250 | 290 | 315 | 371 | 310 | 320 | 346 | 342 |
| 31087 | 269 | 302 | 322 | a | | | | |
| 31088 | 285 | 306 | 341 | a | | | | |
| 31089 | 288 | 304 | 326 | a | | | | |
| 31090 | 279 | 315 | 341 | a | | | | |
| 31091 | 286 | 316 | 331 | a | | | | |
| 31092 | 293 | 320 | 347 | 430 | 339 | 352 | 366 | 366 |
| 31093 | 282 | 314 | 334 | a | | | | |
| 31094 | 245 | 274 | 300 | 377 | 270 | 304 | 322 | 329 |
| 31095 | 282 | 302 | 315 | a | | | | |
| 31096 | 266 | 281 | 312 | 383 | 287 | 301 | 330 | 334 |
| 31097 | 280 | 310 | 335 | a | | | | |
| 31098 | 269 | 311 | 334 | a | | | | |
| 31099[d] | 270 | 314 | 311 | a | | | | |
| 31100 | 283 | 315 | 340 | 396 | 337 | 348 | 350 | 331 |
| 31101 | 305 | 322 | 329 | 370 | 326 | 340 | 360 | 331 |
| 31102 | 276 | 307 | 322 | 425 | 304 | 355 | 361 | 326 |
| 31103 | 309 | 349 | 383 | a | | | | |
| 31104 | 283 | 321 | 360 | 422 | 313 | 312 | 332 | 314 |
| 31105 | 272 | 307 | 328 | 399 | 305 | 314 | 346 | 322 |
| 31106 | 243 | 280 | 300 | 380 | 280 | 315 | 322 | 327 |
| 31107 | 245 | 255 | 263 | 263 | c | | | |
| 31108 | 277 | 304 | 327 | a | | | | |
| Mean | 276 | 306 | 329 | 393 | 304 | 324 | 342 | 331 |
| ±S.D. | 17.1 | 17.0 | 19.1 | 23.4 | 23.9 | 20.5 | 16.7 | 13.6 |
| (6), 80547-01, 500 mg/kg/day: | | | | | | | | |
| 31109 | 248 | 285 | 301 | a | | | | |
| 31110[d] | 290 | 325 | 335 | a | | | | |
| 31111 | 255 | 291 | 304 | a | | | | |
| 31112 | 282 | 308 | 321 | a | | | | |
| 31113 | 264 | 301 | 326 | a | | | | |
| 31114 | 278 | 306 | 325 | 408 | 314 | 365 | 363 | 356 |
| 31115 | 274 | 303 | 323 | 406 | 308 | 329 | 362 | 327 |
| 31116 | 276 | 315 | 340 | a | | | | |
| 31117 | 254 | 286 | 300 | 358 | 288 | 306 | 337 | 316 |
| 31118 | 272 | 300 | 325 | a | | | | |
| 31119[d] | 258 | 285 | 291 | a | | | | |
| 31120 | 277 | 316 | 331 | 400 | 315 | 320 | 344 | 320 |
| 31121 | 250 | 297 | 307 | 378 | 302 | 322 | 335 | 330 |
| 31122 | 271 | 302 | 328 | a | | | | |
| 31123 | 290 | 308 | 333 | 402 | 319 | 330 | 364 | 356 |
| 31124 | 263 | 306 | 323 | 399 | 295 | 314 | 350 | 247 |
| 31125 | 301 | 332 | 353 | 437 | 327 | 353 | 363 | 342 |
| 31126 | 254 | 295 | 311 | a | | | | |
| 31127 | b | | | | 315 | 340 | 349 | 317 |
| 31128 | 260 | 290 | 307 | 359 | 291 | 311 | 342 | 329 |
| 31129 | 294 | 313 | 333 | a | | | | |
| 31130 | 265 | 290 | 314 | 386 | 296 | 310 | 347 | 338 |
| 31131 | 247 | 286 | 312 | 400 | 295 | 334 | 353 | 344 |
| 31132 | b | | | | 320 | 342 | 360 | 347 |
| 31133 | 293 | 332 | 357 | a | | | | |
| Mean | 270 | 303 | 323 | 394 | 307 | 329 | 351 | 328 |
| ±S.D. | 16.0 | 13.5 | 15.6 | 22.8 | 12.7 | 17.7 | 10.3 | 28.0 |

[a]Sacrificed for 13-day uterine examination
[b]No evidence of copulation
[c]Did not deliver, sacrificed 25 days following termination of mating (nongravid), not included in calculation of mean
[d]Nongravid, not included in calculation of mean

S.D. - Standard deviation

TABLE 8. Cont.

Individual and Group Mean Maternal Body Weights During Gestation and Lactation

| Group Number, Test Article, Dosage Level, Dam Number | Actual Body Weight (grams) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Day of Gestation | | | | Day of Lactation | | | |
| | 0 | 7 | 13 | 20 | 0 | 7 | 14 | 21 |
| (7), 80547-01, 1000 mg/kg/day: | | | | | | | | |
| 31134 | 263 | 281 | 304 | 367 | 296 | 315 | 325 | 316 |
| 31135 | 271 | 301 | 323 | a | | | | |
| 31136 | 276 | 279 | 303 | a | | | | |
| 31137 | 280 | 312 | 330 | a | | | | |
| 31138 | Died | | | | | | | |
| 31139 | 250 | 292 | 320 | a | | | | |
| 31140 | 237 | 259 | 280 | a | | | | |
| 31141 | 280 | 314 | 335 | 403 | 299 | 321 | 363 | 337 |
| 31142 | 248 | 281 | 308 | a | | | | |
| 31143 | 262 | 288 | 304 | 389 | 294 | 304 | 327 | 338 |
| 31144 | 254 | 296 | 317 | 406 | 300 | 315 | 340 | 306 |
| 31145 | 297 | 334 | 363 | a | | | | |
| 31146 | 286 | 314 | 342 | 400 | 331 | 328 | 353 | 346 |
| 31147 | 288 | 313 | 339 | 398 | 293 | 332 | 339 | 342 |
| 31148 | 291 | 322 | 349 | 430 | 319 | 343 | 374 | 340 |
| 31149 | 283 | 311 | 333 | 404 | 307 | 322 | 340 | 325 |
| 31150 | 264 | 305 | 327 | 378 | 329 | 330 | 343 | 312 |
| 31151 | 253 | 275 | 298 | a | | | | |
| 31152 | 268 | 300 | 322 | a | | | | |
| 31153 | 254 | 282 | 308 | 347 | 292 | 297 | 303 | 310 |
| 31154 | 293 | 327 | 349 | 428 | 340 | 342 | 336 | 329 |
| 31155 | 286 | 314 | 329 | 365 | 315 | 333 | 352 | 348 |
| 31156 | 254 | 283 | 304 | a | | | | |
| 31157 | 293 | 316 | 341 | a | | | | |
| 31158 | 284 | 319 | 349 | a | | | | |
| Mean | 271 | 301 | 324 | 393 | 310 | 324 | 341 | 329 |
| ±S.D. | 17.2 | 19.1 | 20.2 | 25.0 | 16.8 | 14.1 | 18.5 | 14.9 |

[a]Sacrificed for 13-day uterine examination
S.D. - Standard deviation

TABLE 9. Summary of Group Mean Maternal and Fetal Observations at 13-Day Uterine Examination

| | B0547-01 mg/kg/day (group number) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 0 (Control) (1) | | | 250FD (2) | | | 500FD (3) | | | 1000FD (4) | | |
| | No. | % | ±S.D. | No. | % | ±S.D. | No. | % | ±S.D. | No. | % | ±S.D. |
| Animals scheduled for uterine examination: | 12 | - | - | 11 | - | - | 12 | - | - | 11 | - | - |
| Animals that were gravid: | 12 | - | - | 9 | - | - | 9 | - | - | 10 | - | - |
| Animals examined at uterine examination: | 12 | - | - | 11 | - | - | 12 | - | - | 11 | - | - |
| Nongravid: | 0 | - | - | 2 | - | - | 3 | - | - | 1 | - | - |
| Gravid: | 12 | - | - | 9 | - | - | 9 | - | - | 10 | - | - |
| Dams with resorptions only: | 0 | - | - | 0 | - | - | 0 | - | - | 0 | - | - |
| Dams with viable embryos: | 12 | - | - | 9 | - | - | 9 | - | - | 10 | - | - |
| Viable embryos/dam: | 13.5 | - | 3.32 | 13.9 | - | 1.45 | 14.1 | - | 2.62 | 13.6 | - | 0.52 |
| Postimplantation loss/dam: | 0.8 | - | 0.75 | 1.2 | - | 1.48 | 0.3 | - | 0.50 | 0.8 | - | 0.79 |
| Total implantations/dam: | 14.3 | - | 3.57 | 15.1 | - | 1.45 | 14.4 | - | 2.79 | 14.4 | - | 1.17 |
| Corpora lutea/dam: | 16.1 | - | 3.03 | 16.6 | - | 1.88 | 15.3 | - | 2.35 | 15.7 | - | 2.06 |
| Group mean preimplantation loss (%)[a]: | - | 11.4 | - | - | 8.7 | - | - | 5.8 | - | - | 8.3 | - |
| Group mean postimplantation loss (%)[b]: | - | 5.3 | - | - | 8.1 | - | - | 2.3 | - | - | 5.6 | - |

Values from the treated groups, specified to be tested in the report, did not differ significantly from the control group; $p>0.05$.

[a] $\frac{\text{Total No. Corpora Lutea} - \text{Total No. Implantations}}{\text{Total No. Corpora Lutea}} \times 100 = \text{Group mean preimplantation loss (\%)}$

[b] $\frac{\text{Total No. Implantations} - \text{Total No. Viable Fetuses}}{\text{Total No. Implantations}} \times 100 = \text{Group mean postimplantation loss (\%)}$

FD - Only females dosed
S.D. - Standard deviation
- Not applicable

191-900

TABLE 9. Cont. Summary of Group Mean Maternal and Fetal Observations at 13-Day Uterine Examination

| | B0547-01 mg/kg/day (group number) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 250[MD] (5) | | | 500[MD] (6) | | | 1000[MD] (7) | | |
| | No. | % | ±S.D. | No. | % | ±S.D. | No. | % | ±S.D. |
| Animals scheduled for uterine examination: | 13 | - | - | 12 | - | - | 12 | - | - |
| Animals that were gravid: | 12 | - | - | 10 | - | - | 12 | - | - |
| Animals examined at uterine examination: | 13 | - | - | 12 | - | - | 12 | - | - |
| Nongravid: | 1 | - | - | 2 | - | - | 0 | - | - |
| Gravid: | 12 | - | - | 10 | - | - | 12 | - | - |
| Dams with resorptions only: | 0 | - | - | 0 | - | - | 0 | - | - |
| Dams with viable embryos: | 12 | - | - | 10 | - | - | 12 | - | - |
| Viable embryos/dam: | 14.4 | - | 2.84 | 13.7 | - | 3.20 | 13.6 | - | 2.87 |
| Postimplantation loss/dam: | 0.7 | - | 0.78 | 0.6 | - | 1.00 | 1.5 | - | 1.51 |
| Total implantations/dam: | 15.1 | - | 2.91 | 14.3 | - | 3.33 | 15.1 | - | 2.61 |
| Corpora lutea/dam: | 16.4 | - | 1.62 | 15.8 | - | 2.20 | 15.8 | - | 2.14 |
| Group mean preimplantation loss (%)[a]: | - | 8.1 | - | - | 9.5 | - | - | 4.2 | - |
| Group mean postimplantation loss (%)[b]: | - | 4.4 | - | - | 4.2 | - | - | 9.9 | - |

[a] $\frac{\text{Total No. Corpora Lutea} - \text{Total No. Implantations}}{\text{Total No. Corpora Lutea}} \times 100 = \text{Group mean preimplantation loss (\%)}$

[b] $\frac{\text{Total No. Implantations} - \text{Total No. Viable Fetuses}}{\text{Total No. Implantations}} \times 100 = \text{Group mean postimplantation loss (\%)}$

MD - Only males dosed
S.D. - Standard deviation
- Not applicable

191-900

TABLE 10. Individual and Group Mean Maternal Observations at 13-Day Uterine Examination

| Group Number, Dosage Level, Dam Number | First Male Used | Second Male Used | Embryos Viable | Embryos Nonviable | Early Resorptions | Post-implantation Loss | Total Implantations | Corpora Lutea |
|---|---|---|---|---|---|---|---|---|
| (1), 0 mg/kg/day (Control): | | | | | | | | |
| 30984 | 30809 | - | 16 | 0 | 2 | 2 | 18 | 20 |
| 30987 | 30812 | - | 12 | 0 | 1 | 1 | 13 | 14 |
| 30988 | 30813 | - | 14 | 0 | 1 | 1 | 15 | 15 |
| 30989 | 30814 | - | 18 | 0 | 0 | 0 | 18 | 21 |
| 30993 | 30818 | - | 15 | 0 | 1 | 1 | 16 | 17 |
| 30994 | 30819 | - | 14 | 0 | 2 | 2 | 16 | 19 |
| 30999 | 30824 | - | 12 | 0 | 1 | 1 | 13 | 13 |
| 31000 | 30825 | - | 15 | 0 | 1 | 1 | 16 | 17 |
| 31001 | 30826 | - | 6 | 0 | 0 | 0 | 6 | 13 |
| 31002 | 30827 | - | 15 | 0 | 0 | 0 | 15 | 17 |
| 31006 | 30831 | - | 9 | 0 | 0 | 0 | 9 | 11 |
| 31007 | 30832 | - | 16 | 0 | 0 | 0 | 16 | 16 |
| Total | - | - | 162 | 0 | 9 | 9 | 171 | 193 |
| Mean | - | - | 13.5 | 0.0 | 0.8 | 0.8 | 14.3 | 16.1 |
| ±S.D. | - | - | 3.32 | 0.00 | 0.75 | 0.75 | 3.57 | 3.03 |

S.D. - Standard deviation
- Not applicable

TABLE 10. Cont. Individual and Group Mean Maternal Observations at 13-Day Uterine Examination

| Group Number, Test Article, Dosage Level, Dam Number | First Male Used | Second Male Used | Embryos | | Early Resorptions | Post-implantation Loss | Total Implantations | Corpora Lutea |
|---|---|---|---|---|---|---|---|---|
| | | | Viable | Nonviable | | | | |
| (2), B0547-01, 250 mg/kg/day: | | | | | | | | |
| 31009 | 30834 | - | 12 | 0 | 4 | 4 | 16 | 17 |
| 31011 | 30836 | - | 14 | 0 | 0 | 0 | 14 | 15 |
| 31014 | 30839 | - | 14 | 0 | 1 | 1 | 15 | 15 |
| 31016 | 30841 | - | 12 | 0 | 0 | 0 | 12 | 15 |
| 31018 | 30843 | - | 16 | 0 | 0 | 0 | 16 | 20 |
| 31019 | 30844 | - | 16 | 0 | 0 | 0 | 16 | 17 |
| 31021 | 30846 | - | Nongravid | | | | | |
| 31022 | 30847 | - | 14 | 0 | 3 | 3 | 17 | 19 |
| 31025 | 30850 | - | 14 | 0 | 1 | 1 | 15 | 15 |
| 31028 | 30853 | - | 13 | 0 | 2 | 2 | 15 | 16 |
| 31031 | 30856 | - | Nongravid | | | | | |
| Total | - | - | 125 | 0 | 11 | 11 | 136 | 149 |
| Mean | - | - | 13.9 | 0.0 | 1.2 | 1.2 | 15.1 | 16.6 |
| ±S.D. | - | - | 1.45 | 0.00 | 1.48 | 1.48 | 1.45 | 1.88 |

S.D. - Standard deviation
- Not applicable

TABLE 10. Cont. Individual and Group Mean Maternal Observations at 13-Day Uterine Examination

| Group Number, Test Article, Dosage Level, Dam Number | First Male Used | Second Male Used | Embryos Viable | Embryos Nonviable | Early Resorptions | Post-implantation Loss | Total Implantations | Corpora Lutea |
|---|---|---|---|---|---|---|---|---|
| (3), B0547-01, 500 mg/kg/day: | | | | | | | | |
| 31041 | 30866 | - | 15 | 0 | 0 | 0 | 15 | 16 |
| 31043 | 30868 | - | Nongravid | | | | | |
| 31044 | 30869 | - | 16 | 0 | 0 | 0 | 16 | 16 |
| 31045 | 30870 | - | 15 | 0 | 0 | 0 | 15 | 15 |
| 31047 | 30872 | - | 11 | 0 | 1 | 1 | 12 | 13 |
| 31049 | 30874 | - | Nongravid | | | | | |
| 31051 | 30876 | - | 12 | 0 | 0 | 0 | 12 | 12 |
| 31052 | 30877 | - | 16 | 0 | 1 | 1 | 17 | 17 |
| 31054 | 30879 | - | Nongravid | | | | | |
| 31055 | 30880 | - | 10 | 0 | 0 | 0 | 10 | 15 |
| 31056 | 30881 | - | 18 | 0 | 1 | 1 | 19 | 20 |
| 31057 | 30882 | - | 14 | 0 | 0 | 0 | 14 | 14 |
| Total | - | - | 127 | 0 | 3 | 3 | 130 | 138 |
| Mean | - | - | 14.1 | 0.0 | 0.3 | 0.3 | 14.4 | 15.3 |
| ±S.D. | - | - | 2.62 | 0.00 | 0.50 | 0.50 | 2.79 | 2.35 |

S.D. - Standard deviation
- Not applicable

TABLE 10. Cont. Individual and Group Mean Maternal Observations at 13-Day Uterine Examination

| Group Number, Test Article, Dosage Level, Dam Number | First Male Used | Second Male Used | Embryos Viable | Embryos Nonviable | Early Resorptions | Post-implantation Loss | Total Implantations | Corpora Lutea |
|---|---|---|---|---|---|---|---|---|
| (4), B0547-01, 1000 mg/kg/day: | | | | | | | | |
| 31059 | 30884 | - | 14 | 0 | 1 | 1 | 15 | 15 |
| 31062 | 30887 | - | 14 | 0 | 1 | 1 | 15 | 19 |
| 31063 | 30888 | 30884 | 14 | 0 | 2 | 2 | 16 | 16 |
| 31064 | 30889 | - | 13 | 0 | 0 | 0 | 13 | 14 |
| 31065 | 30890 | - | 13 | 0 | 0 | 0 | 13 | 13 |
| 31066 | 30891 | - | Nongravid | | | | | |
| 31071 | 30896 | - | 13 | 0 | 0 | 0 | 13 | 19 |
| 31073 | 30898 | - | 14 | 0 | 0 | 0 | 14 | 14 |
| 31076 | 30901 | - | 14 | 0 | 1 | 1 | 15 | 15 |
| 31077 | 30902 | - | 14 | 0 | 2 | 2 | 16 | 17 |
| 31079 | 30904 | - | 13 | 0 | 1 | 1 | 14 | 15 |
| Total | - | - | 136 | 0 | 8 | 8 | 144 | 157 |
| Mean | - | - | 13.6 | 0.0 | 0.8 | 0.8 | 14.4 | 15.7 |
| ±S.D. | - | - | 0.52 | 0.00 | 0.79 | 0.79 | 1.17 | 2.06 |

S.D. - Standard deviation
- Not applicable

TABLE 10. Cont. Individual and Group Mean Maternal Observations at 13-Day Uterine Examination

| Group Number, Test Article, Dosage Level, Dam Number | First Male Used | Second Male Used | Embryos Viable | Embryos Nonviable | Early Resorptions | Post-implantation Loss | Total Implantations | Corpora Lutea |
|---|---|---|---|---|---|---|---|---|
| (5), B0547-01, 250 mg/kg/day: | | | | | | | | |
| 31084 | 30909 | - | 13 | 0 | 1 | 1 | 14 | 18 |
| 31087 | 30912 | - | 13 | 0 | 2 | 2 | 15 | 15 |
| 31088 | 30913 | - | 15 | 0 | 0 | 0 | 15 | 15 |
| 31089 | 30914 | - | 16 | 0 | 0 | 0 | 16 | 18 |
| 31090 | 30915 | - | 15 | 0 | 2 | 2 | 17 | 17 |
| 31091 | 30916 | - | 16 | 0 | 0 | 0 | 16 | 16 |
| 31093 | 30918 | - | 16 | 0 | 1 | 1 | 17 | 18 |
| 31095 | 30920 | - | 7 | 0 | 0 | 0 | 7 | 15 |
| 31097 | 30922 | - | 14 | 0 | 0 | 0 | 14 | 14 |
| 31098 | 30923 | - | 15 | 0 | 1 | 1 | 16 | 17 |
| 31099 | 30924 | - | Nongravid | | | | | |
| 31103 | 30928 | - | 19 | 0 | 0 | 0 | 19 | 19 |
| 31108 | 30933 | - | 14 | 0 | 1 | 1 | 15 | 15 |
| Total | - | - | 173 | 0 | 8 | 8 | 181 | 197 |
| Mean | - | - | 14.4 | 0.0 | 0.7 | 0.7 | 15.1 | 16.4 |
| ±S.D. | - | - | 2.84 | 0.00 | 0.78 | 0.78 | 2.91 | 1.62 |

S.D. - Standard deviation
- Not applicable

TABLE 10. Cont. Individual and Group Mean Maternal Observations at 13-Day Uterine Examination

| Group Number, Test Article, Dosage Level, Dam Number | First Male Used | Second Male Used | Embryos Viable | Embryos Nonviable | Early Resorptions | Post-implantation Loss | Total Implantations | Corpora Lutea |
|---|---|---|---|---|---|---|---|---|
| (6), B0547-01, 500 mg/kg/day: | | | | | | | | |
| 31109 | 30934 | - | 11 | 0 | 1 | 1 | 12 | 12 |
| 31110 | 30935 | - | Nongravid | | | | | |
| 31111 | 30936 | - | 14 | 0 | 0 | 0 | 14 | 14 |
| 31112 | 30937 | - | 17 | 0 | 0 | 0 | 17 | 17 |
| 31113 | 30938 | - | 14 | 0 | 0 | 0 | 14 | 19 |
| 31116 | 30941 | - | 15 | 0 | 0 | 0 | 15 | 17 |
| 31118 | 30943 | - | 15 | 0 | 1 | 1 | 16 | 17 |
| 31119 | 30944 | - | Nongravid | | | | | |
| 31122 | 30947 | - | 17 | 0 | 0 | 0 | 17 | 17 |
| 31126 | 30951 | - | 14 | 0 | 3 | 3 | 17 | 17 |
| 31129 | 30954 | - | 14 | 0 | 1 | 1 | 15 | 15 |
| 31133 | 30958 | - | 6 | 0 | 0 | 0 | 6 | 13 |
| Total | - | - | 137 | 0 | 6 | 6 | 143 | 158 |
| Mean | - | - | 13.7 | 0.0 | 0.6 | 0.6 | 14.3 | 15.8 |
| ±S.D. | - | - | 3.20 | 0.00 | 1.00 | 1.00 | 3.33 | 2.20 |

S.D. - Standard deviation
- Not applicable

TABLE 10. Cont. Individual and Group Mean Maternal Observations at 13-Day Uterine Examination

| Group Number, Test Article, Dosage Level, Dam Number | First Male Used | Second Male Used | Embryos Viable | Embryos Nonviable | Early Resorptions | Post-implantation Loss | Total Implantations | Corpora Lutea |
|---|---|---|---|---|---|---|---|---|
| (7), B0547-01, 1000 mg/kg/day: | | | | | | | | |
| 31135 | 30960 | - | 9 | 0 | 1 | 1 | 10 | 15 |
| 31136 | 30962 | - | 8 | 0 | 5 | 5 | 13 | 14 |
| 31137 | 30962 | - | 17 | 0 | 0 | 0 | 17 | 17 |
| 31139 | 30964 | - | 15 | 0 | 3 | 3 | 18 | 18 |
| 31140 | 30963 | - | 12 | 0 | 0 | 0 | 12 | 12 |
| 31142 | 30967 | - | 15 | 0 | 2 | 2 | 17 | 17 |
| 31145 | 30970 | - | 17 | 0 | 0 | 0 | 17 | 17 |
| 31151 | 30976 | - | 15 | 0 | 1 | 1 | 16 | 17 |
| 31152 | 30977 | - | 12 | 0 | 1 | 1 | 13 | 13 |
| 31156 | 30981 | - | 15 | 0 | 1 | 1 | 16 | 16 |
| 31157 | 30964 | - | 15 | 0 | 3 | 3 | 18 | 19 |
| 31158 | 30983 | - | 13 | 0 | 1 | 1 | 14 | 14 |
| Total | - | - | 163 | 0 | 18 | 18 | 181 | 189 |
| Mean | - | - | 13.6 | 0.0 | 1.5 | 1.5 | 15.1 | 15.8 |
| ±S.D. | - | - | 2.87 | 0.00 | 1.51 | 1.51 | 2.61 | 2.14 |

S.D. - Standard deviation
- Not applicable

TABLE 11.

$F_0$ Summary of Gestation and Lactation Data

| Group Number, Test Article, Dosage Level, (mg/kg/day) | Fertility/Pregnancy Indices[a] Gravid Females Total Females Mated | % | Fertile Males Total Males Mated | % | Mean Gestation Length (days ±S.D.) | | Mean No. Dead Pups at Day 0 (±S.D.) | | Mean No. Live Pups at Day 0 (±S.D.) | |
|---|---|---|---|---|---|---|---|---|---|---|
| (1), 0 (Control) | 25/25 | 100.0 | 24/25 | 96.0 | 21.8 | 0.58 | 0.0 | 0.00 | 13.6 | 1.66 |
| (2), B0547-01, 250[FD] | 20/24 | 83.3 | 20/24 | 83.3 | 21.4 | 0.53 | 0.2 | 0.40 | 13.1 | 3.18 |
| (3), B0547-01, 500[FD] | 20/24 | 83.3 | 19/24 | 79.2 | 21.8 | 0.42 | 0.2 | 0.60 | 13.2 | 3.40 |
| (4), B0547-01, 1000[FD] | 21/22 | 95.5 | 20/21 | 95.2 | 22.1 | 0.60 | 0.3 | 0.48 | 12.3 | 1.89 |
| (5), B0547-01, 250[MD] | 23/25 | 92.0 | 23/25 | 92.0 | 22.0 | 0.45 | 0.3 | 0.47 | 13.2 | 3.57 |
| (6), B0547-01, 500[MD] | 23/25 | 92.0 | 22/25 | 88.0 | 21.9 | 0.30 | 0.2 | 0.60 | 14.0 | 1.87 |
| (7), B0547-01, 1000[MD] | 24/24 | 100.0 | 22/22 | 100.0 | 21.9 | 0.79 | 0.1 | 0.29 | 12.2 | 3.83 |

[a]Fertility and pregnancy indices include animals scheduled to deliver and the animals scheduled for day 13 uterine examination
[FD]Only females dosed
[MD]Only males dosed

TABLE 11. Cont.

$F_0$ Summary of Gestation and Lactation Data

| Group Number, Test Article, Dosage Level, (mg/kg/day) | Pup Survival Index (Lactation Days) 0: No. Live Pups at Day 0 / Total Born | % | 4: No. Live Pups at Day 4 B.R. / No. Live Pups at Day 0 | % | 7: No. Live Pups at Day 7 / No. Live Pups at Day 4 A.R. | % | 14: No. Live Pups at Day 14 / No. Live Pups at Day 7 | % | 21: No. Live Pups at Day 21 / No. Live Pups at Day 14 | % |
|---|---|---|---|---|---|---|---|---|---|---|
| (1), 0 (Control) | 177/177 | 100.0 | 174/177 | 98.3 | 130/130 | 100.0 | 130/130 | 100.0 | 130/130 | 100.0 |
| (2), B0547-01, 250[FD] | 144/146 | 98.6 | 140/144 | 97.2 | 105/105 | 100.0 | 105/105 | 100.0 | 105/105 | 100.0 |
| (3), B0547-01, 500[FD] | 145/147 | 98.6 | 139/145 | 95.8 | 104/104 | 100.0 | 104/104 | 100.0 | 104/104 | 100.0 |
| (4), B0547-01, 1000[FD] | 123/126 | 97.6 | 119/123 | 96.7 | 99/99 | 100.0 | 99/99 | 100.0 | 99/99 | 100.0 |
| (5), B0547-01, 250[MD] | 145/148 | 98.0 | 141/145 | 97.2 | 103/104 | 99.0 | 103/103 | 100.0 | 103/103 | 100.0 |
| (6), B0547-01, 500[MD] | 182/185 | 98.4 | 179/182 | 98.4 | 130/130 | 100.0 | 130/130 | 100.0 | 130/130 | 100.0 |
| (7), B0547-01, 1000[MD] | 146/147 | 99.3 | 144/146 | 98.6 | 106/106 | 100.0 | 106/106 | 100.0 | 106/106 | 100.0 |

B.R. - Before Reduction
A.R. - After Reduction
[FD]Only females dosed
[MD]Only males dosed

TABLE 11. Cont.

$F_0$ Summary of Gestation and Lactation Data

| Group Number, Test Article, Dosage Level, (mg/kg/day) | Group Mean Body Weight (grams) of Live Pups During Lactation (Lactation Days) | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | | 4 B.R. | | 4 A.R. | | 7 | | 14 | | 21 | | | |
| | | | | | | | | | | | Male | | Female | |
| | Mean | ±S.D. | Mean | ±S.D. | Mean | ±S.D. | Mean | ±S.D. | Mean | ±S.D. | Mean | ±S.D. | Mean | ±S.D. |
| (1), 0 (Control) | 6.0 | 0.62 | 9.6 | 1.33 | 9.6 | 1.28 | 14.7 | 1.84 | 29.9 | 2.50 | 49.4 | 4.47 | 46.9 | 3.28 |
| (2), B0547-01, 250[FD] | 6.0 | 0.55 | 9.4 | 1.24 | 9.4 | 1.26 | 14.7 | 1.15 | 29.8 | 1.04 | 49.4 | 2.92 | 48.0 | 3.11 |
| (3), B0547-01, 500[FD] | 6.0 | 0.42 | 9.5 | 1.33 | 9.5 | 1.36 | 14.9 | 1.95 | 29.5 | 2.80 | 49.0 | 4.92 | 45.8 | 3.93 |
| (4), B0547-01, 1000[FD] | 5.9 | 0.41 | 9.3 | 0.51 | 9.3 | 0.55 | 13.8 | 0.73 | 27.5* | 1.88 | 46.4 | 2.77 | 44.7 | 2.92 |
| (5), B0547-01, 250[MD] | 6.3 | 0.50 | 10.0 | 1.03 | 10.0 | 0.99 | 15.6 | 1.15 | 31.0 | 2.09 | 50.6 | 2.93 | 49.6 | 2.96 |
| (6), B0547-01, 500[MD] | 6.1 | 0.34 | 9.3 | 0.73 | 9.4 | 0.71 | 14.7 | 1.03 | 29.8 | 2.14 | 50.5 | 2.91 | 47.5 | 3.25 |
| (7), B0547-01, 1000[MD] | 6.5 | 0.75 | 10.2 | 1.90 | 10.3 | 1.86 | 15.9 | 2.37 | 32.0 | 3.96 | 53.1 | 5.82 | 51.0* | 6.00 |

B.R. - Before reduction
A.R. - After reduction
[FD]Only females dosed
[MD]Only males dosed
*Significantly different from control group; $p<0.05$

TABLE 12.

$F_1$ Individual Litter Data

| Group Number, Test Article, Dosage Level, Dam Number | First Male Used | Second Male Used | Gestation Length (Days) | No. Pups Dead on Day 0 | Number Live Pups on Lactation Day 0 | 4 Reduction Before | 4 Reduction After | 7 | 14 | 21 Male | 21 Female | Mean Weight (grams) of Live Pups on Lactation Day 0 | 4 Reduction Before | 4 Reduction After | 7 | 14 | 21 Male | 21 Female |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| (1), 0 mg/kg/day (Control): | | | | | | | | | | | | | | | | | | |
| 30985 | 30810 | - | 22 | 0 | 14 | 14 | 10 | 10 | 10 | 5 | 5 | 5.9 | 9.5 | 9.6 | 14.0 | 27.1 | 46.8 | 44.0 |
| 30986 | 30811 | - | 22 | 0 | 11 | 11 | 10 | 10 | 10 | 5 | 5 | 6.2 | 10.4 | 10.4 | 15.8 | 31.4 | 50.5 | 49.2 |
| 30990 | 30815 | - | 21 | 0 | 15 | 15 | 10 | 10 | 10 | 5 | 5 | 5.2 | 8.1 | 8.3 | 12.9 | 29.2 | 45.7 | 46.8 |
| 30991 | 30816 | - | 21 | 0 | 14 | 13 | 10 | 10 | 10 | 4 | 6 | 5.4 | 8.1 | 8.3 | 12.5 | 26.4 | 42.5 | 42.1 |
| 30992 | 30817 | - | 23 | 0 | 11 | 11 | 10 | 10 | 10 | 5 | 5 | 7.2 | 12.8 | 12.7 | 19.1 | 34.9 | 59.4 | 54.1 |
| 30995 | 30820 | - | 22 | 0 | 13 | 13 | 10 | 10 | 10 | 4 | 6 | 5.8 | 9.8 | 9.9 | 15.6 | 31.9 | 53.0 | 50.3 |
| 30996 | 30821 | - | 22 | 0 | 14 | 14 | 10 | 10 | 10 | 5 | 5 | 5.9 | 9.3 | 9.2 | 13.9 | 27.9 | 47.3 | 44.1 |
| 30997 | 30822 | - | 22 | 0 | 16 | 16 | 10 | 10 | 10 | 5 | 5 | 5.6 | 8.7 | 8.6 | 14.4 | 29.6 | 52.0 | 45.5 |
| 30998 | 30823 | 30809 | 22 | 0 | 16 | 16 | 10 | 10 | 10 | 5 | 5 | 5.6 | 8.5 | 8.5 | 12.8 | 28.1 | 47.6 | 44.1 |
| 31003 | 30828 | - | 21 | 0 | 15 | 14 | 10 | 10 | 10 | 5 | 5 | 5.3 | 8.1 | 8.1 | 13.0 | 28.2 | 45.7 | 45.5 |
| 31004 | 30829[a] | 30810 | b | 0 | 12 | 11 | 10 | 10 | 10 | 4 | 6 | 6.8 | 10.4 | 10.5 | 15.4 | 29.4 | 46.2 | 46.9 |
| 31005 | 30830 | - | 22 | 0 | 13 | 13 | 10 | 10 | 10 | 5 | 5 | 6.4 | 10.3 | 10.1 | 16.0 | 32.6 | 52.8 | 46.8 |
| 31008 | 30833 | - | 22 | 0 | 13 | 13 | 10 | 10 | 10 | 5 | 5 | 6.7 | 10.2 | 10.2 | 15.9 | 32.2 | 52.1 | 49.9 |
| Total | - | - | - | 0 | 177 | 174 | 130 | 130 | 130 | 130 | | - | - | - | - | - | - | - |
| Mean | - | - | 21.8 | 0.0 | 13.6 | 13.4 | 10.0 | 10.0 | 10.0 | 10.0 | | 6.0 | 9.6 | 9.6 | 14.7 | 29.9 | 49.4 | 46.9 |
| ±S.D. | - | - | 0.58 | 0.00 | 1.66 | 1.71 | 0.00 | 0.00 | 0.0 | 0.00 | | 0.62 | 1.33 | 1.28 | 1.84 | 2.50 | 4.47 | 3.20 |
| (2), B0547-01, 250 mg/kg/day: | | | | | | | | | | | | | | | | | | |
| 31010 | 30835[a] | 30834 | b | 1 | 9 | 9 | 9 | 9 | 9 | 6 | 3 | 6.6 | 10.7 | 10.7 | 15.7 | 30.6 | 48.4 | 47.7 |
| 31012 | 30837 | - | 22 | 0 | 15 | 15 | 10 | 10 | 10 | 5 | 5 | 6.0 | 9.2 | 9.1 | 14.6 | 28.9 | 48.6 | 45.0 |
| 31013 | 30838[a] | 30836 | b | 1 | 17 | 16 | 10 | 10 | 10 | 6 | 4 | 6.0 | 8.7 | 8.6 | 14.5 | 30.1 | 53.2 | 50.1 |
| 31015 | - | - | Died | | | | | | | | | | | | | | | |
| 31017 | 30842 | - | 22 | 0 | 6 | 6 | 6 | 6 | 6 | 5 | 1 | 7.1 | 12.0 | 12.0 | 16.8 | 31.2 | 52.3 | 53.2 |
| 31020 | 30845 | - | 21 | 0 | 14 | 14 | 10 | 10 | 10 | 5 | 5 | 5.9 | 8.7 | 8.6 | 14.1 | 29.2 | 49.3 | 47.1 |
| 31023 | 30848 | - | 21 | 0 | 13 | 13 | 10 | 10 | 10 | 5 | 5 | 6.1 | 8.4 | 8.4 | 13.7 | 29.0 | 44.4 | 46.0 |
| 31024 | 30849 | 30837 | Did not deliver | | | | | | | | | | | | | | | |
| 31026 | 30851 | - | 21 | 0 | 16 | 16 | 10 | 10 | 10 | 5 | 5 | 5.6 | 8.1 | 8.1 | 13.6 | 29.3 | 46.0 | 44.2 |
| 31027 | 30852 | - | 22 | 0 | 14 | 14 | 10 | 10 | 10 | 5 | 5 | 5.6 | 9.8 | 9.8 | 15.6 | 30.4 | 50.7 | 49.2 |
| 31029 | 30854 | - | Died - nongravid | | | | | | | | | | | | | | | |
| 31030 | 30855 | - | 22 | 0 | 12 | 12 | 10 | 10 | 10 | 4 | 6 | 6.6 | 10.8 | 10.9 | 16.2 | 31.4 | 53.9 | 53.3 |
| 31032 | 30857 | - | 21 | 0 | 13 | 13 | 10 | 10 | 10 | 5 | 5 | 5.5 | 8.9 | 9.0 | 13.5 | 28.2 | 48.2 | 45.5 |
| 31033 | 30858 | - | 21 | 0 | 15 | 12 | 10 | 10 | 10 | 5 | 5 | 5.3 | 8.5 | 8.5 | 13.8 | 29.0 | 48.5 | 45.9 |
| Total | - | - | - | 2 | 144 | 140 | 105 | 105 | 105 | 105 | | - | - | - | - | - | - | - |
| Mean | - | - | 21.4 | 0.2 | 13.1 | 12.7 | 9.5 | 9.5 | 9.5 | 9.5 | | 6.0 | 9.4 | 9.4 | 14.7 | 29.8 | 49.4 | 48.0 |
| ±S.D. | - | - | 0.53 | 0.40 | 3.18 | 3.00 | 1.21 | 1.21 | 1.21 | 1.21 | | 0.55 | 1.24 | 1.26 | 1.15 | 1.04 | 2.92 | 3.11 |

[a]Pregnancy attributed to this male
[b]No evidence of copulation
S.D. - Standard deviation
- Not applicable

TABLE 12. Cont.

$F_1$ Individual Litter Data

| Group Number, Test Article, Dosage Level, Dam Number | First Male Used | Second Male Used | Gestation Length (Days) | No. Pups Dead on Day 0 | Number Live Pups on Lactation Day 0 | 4 Reduction Before | 4 Reduction After | 7 | 14 | 21 Male | 21 Female | Mean Weight (grams) of Live Pups on Lactation Day 0 | 4 Reduction Before | 4 Reduction After | 7 | 14 | 21 Male | 21 Femal |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| (3), 80547-01, 500 mg/kg/day: | | | | | | | | | | | | | | | | | | |
| 31034 | 30859 | 30860 | Sacrificed | | | | | | | | | | | | | | | |
| 31035 | 30860 | - | 21 | 2 | 13 | 13 | 10 | 10 | 10 | 5 | 5 | 6.0 | 9.9 | 9.9 | 16.1 | 31.1 | 52.9 | 48.3 |
| 31036 | 30861 | - | 22 | 0 | 4 | 4 | 4 | 4 | 4 | 2 | 2 | 6.7 | 12.5 | 12.5 | 18.7 | 34.9 | 55.7 | 52.1 |
| 31037 | 30862 | - | 22 | 0 | 16 | 14 | 10 | 10 | 10 | 4 | 6 | 5.9 | 7.6 | 7.5 | 12.0 | 25.9 | 45.6 | 40.2 |
| 31038 | 30863 | - | Did not deliver | | | | | | | | | | | | | | | |
| 31039 | 30864 | - | 22 | 0 | 13 | 13 | 10 | 10 | 10 | 5 | 5 | 6.2 | 9.4 | 9.4 | 15.0 | 29.1 | 47.8 | 45.4 |
| 31040 | 30865 | - | 22 | 0 | 14 | 14 | 10 | 10 | 10 | 5 | 5 | 6.1 | 9.6 | 9.9 | 15.8 | 30.4 | 52.5 | 47.4 |
| 31042 | 30867 | - | 22 | 0 | 13 | 13 | 10 | 10 | 10 | 5 | 5 | 5.9 | 9.8 | 9.9 | 15.4 | 31.8 | 52.6 | 43.7 |
| 31046 | 30871 | - | 22 | 0 | 15 | 14 | 10 | 10 | 10 | 5 | 5 | 5.7 | 8.6 | 8.6 | 13.2 | 26.8 | 42.4 | 43.9 |
| 31048 | 30873 | 30861 | b | 0 | 13 | 12 | 10 | 10 | 10 | 4 | 6 | 5.1 | 8.6 | 8.6 | 13.4 | 28.2 | 43.4 | 44.7 |
| 31050 | 30875 | - | 22 | 0 | 15 | 13 | 10 | 10 | 10 | 5 | 5 | 5.9 | 10.6 | 10.7 | 16.8 | 32.2 | 55.6 | 52.2 |
| 31053 | 30878 | - | 21 | 0 | 17 | 17 | 10 | 10 | 10 | 5 | 5 | 5.6 | 8.1 | 8.1 | 13.2 | 27.1 | 45.8 | 40.9 |
| 31058 | 30883 | - | 22 | 0 | 12 | 12 | 10 | 10 | 10 | 5 | 5 | 6.4 | 9.5 | 9.5 | 13.9 | 27.2 | 45.1 | 45.2 |
| Total | - | - | - | 2 | 145 | 139 | 104 | 104 | 104 | 104 | | - | - | - | - | - | - | - |
| Mean | - | - | 21.8 | 0.2 | 13.2 | 12.6 | 9.5 | 9.5 | 9.5 | 9.5 | | 6.0 | 9.5 | 9.5 | 14.9 | 29.5 | 49.0 | 45.8 |
| ±S.D. | - | - | 0.42 | 0.60 | 3.40 | 3.17 | 1.81 | 1.81 | 1.81 | 1.81 | | 0.42 | 1.33 | 1.36 | 1.95 | 2.80 | 4.92 | 3.93 |
| (4), 80547-01, 1000 mg/kg/day: | | | | | | | | | | | | | | | | | | |
| 31060 | 30885 | - | Died | | | | | | | | | | | | | | | |
| 31061 | 30886 | - | 23 | 0 | 10 | 10 | 10 | 10 | 10 | 7 | 3 | 6.2 | 9.6 | 9.6 | 14.0 | 27.5 | 47.1 | 44.6 |
| 31067 | 30892 | - | 22 | 0 | 13 | 13 | 10 | 10 | 10 | 5 | 5 | 6.4 | 9.5 | 9.5 | 14.4 | 28.9 | 49.4 | 45.4 |
| 31068 | 30893[a] | 30885 | b | 0 | 16 | 15 | 10 | 10 | 10 | 5 | 5 | 5.5 | 8.2 | 8.1 | 13.4 | 29.2 | 47.3 | 48.8 |
| 31069 | 30894 | - | 22 | 0 | 13 | 13 | 10 | 10 | 10 | 5 | 5 | 5.4 | 9.1 | 9.0 | 13.2 | 26.8 | 45.0 | 42.9 |
| 31070 | 30895 | - | 22 | 1 | 11 | 9 | 9 | 9 | 9 | 5 | 4 | 5.7 | 9.2 | 9.2 | 12.7 | 25.4 | 41.7 | 41.6 |
| 31072 | 30897 | 30886 | Did not deliver (gravid) | | | | | | | | | | | | | | | |
| 31074 | - | - | Died | | | | | | | | | | | | | | | |
| 31075 | 30900 | - | 22 | 0 | 12 | 12 | 10 | 10 | 10 | 5 | 5 | 6.2 | 10.0 | 10.1 | 14.7 | 27.9 | 49.6 | 46.6 |
| 31078 | 30903 | - | 21 | 0 | 10 | 10 | 10 | 10 | 10 | 4 | 6 | 5.5 | 9.0 | 9.0 | 13.6 | 27.3 | 43.2 | 41.6 |
| 31080 | 30905 | - | 22 | 1 | 14 | 13 | 10 | 10 | 10 | 5 | 5 | 6.3 | 9.7 | 9.5 | 15.1 | 30.3 | 49.8 | 49.7 |
| 31081 | 30906 | - | 22 | 0 | 13 | 13 | 10 | 10 | 10 | 5 | 5 | 5.7 | 9.1 | 8.9 | 13.7 | 28.0 | 45.6 | 43.9 |
| 31082 | - | - | Died | | | | | | | | | | | | | | | |
| 31083 | 30908 | - | 23 | 1 | 11 | 11 | 10 | 10 | 10 | 4 | 6 | 6.4 | 9.7 | 9.7 | 13.4 | 23.8 | 45.0 | 41.9 |
| Total | - | - | - | 3 | 123 | 119 | 99 | 99 | 99 | 99 | | - | - | - | - | - | - | - |
| Mean | - | - | 22.1 | 0.3 | 12.3 | 11.9 | 9.9 | 9.9 | 9.9 | 9.9 | | 5.9 | 9.3 | 9.3 | 13.8 | 27.5* | 46.4 | 44.7 |
| ±S.D. | - | - | 0.60 | 0.48 | 1.89 | 1.85 | 0.32 | 0.32 | 0.32 | 0.32 | | 0.41 | 0.51 | 0.55 | 0.73 | 1.88 | 2.77 | 2.92 |

*Significantly different from control; $p<0.05$
[a]Pregnancy attributed to this male
[b]No evidence of copulation
S.D. - Standard deviation
- Not applicable

TABLE 12. Cont.

$F_1$ Individual Litter Data

| Group Number, Test Article, Dosage Level, Dam Number | First Male Used | Second Male Used | Gestation Length (Days) | No. Pups Dead on Day 0 | Number Live Pups on Lactation Day 0 | 4 Reduction Before | 4 Reduction After | 7 | 14 | 21 Male | 21 Female | Mean Weight (grams) of Live Pups on Lactation Day 0 | 4 Reduction Before | 4 Reduction After | 7 | 14 | 21 Male | 21 Female |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| (5), B0547-01, 250 mg/kg/day: | | | | | | | | | | | | | | | | | | |
| 31085 | 30910 | - | 22 | 1 | 13 | 12 | 10 | 10 | 10 | 5 | 5 | 6.0 | 10.0 | 10.1 | 15.1 | 29.4 | 48.6 | 45.8 |
| 31086 | 30911 | - | 22 | 0 | 9 | 9 | 9 | 9 | 9 | 2 | 7 | 6.4 | 10.7 | 10.7 | 15.6 | 30.5 | 53.2 | 51.1 |
| 31092 | 30917 | - | 22 | 0 | 14 | 14 | 10 | 10 | 10 | 5 | 5 | 6.5 | 10.2 | 10.2 | 16.8 | 32.5 | 53.3 | 50.4 |
| 31094 | 30919 | - | 22 | 0 | 13 | 13 | 10 | 10 | 10 | 5 | 5 | 7.2 | 10.7 | 10.7 | 16.1 | 30.9 | 50.0 | 50.3 |
| 31096 | 30921 | - | 22 | 0 | 14 | 14 | 10 | 10 | 10 | 5 | 5 | 6.2 | 9.5 | 9.4 | 15.5 | 31.4 | 50.6 | 51.2 |
| 31100 | 30925 | - | 21 | 0 | 12 | 12 | 10 | 10 | 10 | 5 | 5 | 5.8 | 9.6 | 9.6 | 15.1 | 30.9 | 50.8 | 48.4 |
| 31101 | 30926 | - | 22 | 0 | 5 | 5 | 5 | 5 | 5 | 3 | 2 | 7.0 | 12.3 | 12.3 | 18.1 | 35.2 | 54.5 | 53.4 |
| 31102 | 30927 | - | 22 | 0 | 16 | 16 | 10 | 10 | 10 | 5 | 5 | 6.3 | 9.6 | 9.5 | 15.1 | 31.1 | 51.6 | 47.7 |
| 31104 | 30929 | - | 23 | 0 | 17 | 17 | 10 | 10 | 10 | 5 | 5 | 6.5 | 9.9 | 9.9 | 15.9 | 31.8 | 51.6 | 54.0 |
| 31105 | 30930 | - | 22 | 1 | 15 | 13 | 10 | 9 | 9 | 1 | 8 | 5.8 | 8.8 | 9.0 | 13.6 | 26.5 | 43.8 | 44.3 |
| 31106 | 30931 | - | 22 | 1 | 17 | 16 | 10 | 10 | 10 | 5 | 5 | 5.6 | 8.5 | 8.7 | 15.0 | 30.8 | 48.6 | 49.4 |
| 31107 | 30932 | - | Did not deliver | | | | | | | | | | | | | | | |
| Total | - | - | - | 3 | 145 | 141 | 104 | 103 | 103 | 103 | | - | - | - | - | - | - | - |
| Mean | - | - | 22.0 | 0.3 | 13.2 | 12.8 | 9.5 | 9.4 | 9.4 | 9.4 | | 6.3 | 10.0 | 10.0 | 15.6 | 31.0 | 50.6 | 49.6 |
| ±S.D. | - | - | 0.45 | 0.47 | 3.57 | 3.43 | 1.51 | 1.50 | 1.50 | 1.50 | | 0.50 | 1.03 | 0.99 | 1.15 | 2.09 | 2.93 | 2.96 |
| (6), B0547-01, 500 mg/kg/day: | | | | | | | | | | | | | | | | | | |
| 31114 | 30939 | - | 22 | 0 | 14 | 14 | 10 | 10 | 10 | 5 | 5 | 6.3 | 9.6 | 9.5 | 14.1 | 32.0 | 51.6 | 50.8 |
| 31115 | 30940 | - | 22 | 2 | 12 | 12 | 10 | 10 | 10 | 6 | 4 | 6.6 | 10.8 | 10.9 | 16.6 | 32.5 | 53.6 | 50.3 |
| 31117 | 30942 | - | 22 | 0 | 11 | 11 | 10 | 10 | 10 | 5 | 5 | 6.2 | 9.4 | 9.4 | 14.6 | 30.4 | 49.1 | 47.4 |
| 31120 | 30945 | - | 21 | 0 | 15 | 15 | 10 | 10 | 10 | 5 | 5 | 5.5 | 8.2 | 8.4 | 13.4 | 28.7 | 45.2 | 43.6 |
| 31121 | 30946 | - | 22 | 0 | 14 | 13 | 10 | 10 | 10 | 5 | 5 | 6.4 | 8.7 | 8.7 | 12.7 | 25.8 | 45.8 | 42.0 |
| 31123 | 30948 | - | 22 | 0 | 14 | 12 | 10 | 10 | 10 | 5 | 5 | 6.2 | 8.9 | 8.9 | 14.6 | 29.1 | 49.4 | 48.2 |
| 31124 | 30949 | - | 22 | 0 | 16 | 16 | 10 | 10 | 10 | 5 | 5 | 5.6 | 8.6 | 8.8 | 14.4 | 28.8 | 50.0 | 46.9 |
| 31125 | 30950 | - | 22 | 0 | 17 | 17 | 10 | 10 | 10 | 5 | 5 | 6.1 | 9.3 | 9.3 | 15.8 | 31.9 | 54.6 | 51.0 |
| 31127 | 30952 | 30934 | b | 0 | 15 | 15 | 10 | 10 | 10 | 5 | 5 | 6.0 | 9.4 | 9.2 | 14.3 | 27.1 | 48.7 | 42.1 |
| 31128 | 30953 | - | 22 | 1 | 11 | 11 | 10 | 10 | 10 | 1 | 9 | 6.2 | 9.9 | 9.9 | 15.2 | 29.3 | 53.3 | 48.6 |
| 31130 | 30955 | - | 22 | 0 | 14 | 14 | 10 | 10 | 10 | 5 | 5 | 5.5 | 8.9 | 8.9 | 14.5 | 28.1 | 50.3 | 46.3 |
| 31131 | 30956 | - | 22 | 0 | 16 | 16 | 10 | 10 | 10 | 5 | 5 | 6.0 | 9.0 | 9.3 | 14.5 | 30.8 | 50.8 | 48.8 |
| 31132 | 30957[a] | 30935 | b | 0 | 13 | 13 | 10 | 10 | 10 | 5 | 5 | 6.3 | 10.4 | 10.5 | 15.8 | 32.6 | 53.5 | 51.5 |
| Total | - | - | - | 3 | 182 | 179 | 130 | 130 | 130 | 130 | | - | - | - | - | - | - | - |
| Mean | - | - | 21.9 | 0.2 | 14.0 | 13.8 | 10.0 | 10.0 | 10.0 | 10.0 | | 6.1 | 9.3 | 9.4 | 14.7 | 29.8 | 50.5 | 47.5 |
| ±S.D. | - | - | 0.30 | 0.60 | 1.87 | 1.96 | 0.00 | 0.00 | 0.00 | 0.00 | | 0.34 | 0.73 | 0.71 | 1.03 | 2.14 | 2.91 | 3.25 |

[a]Pregnancy attributed to this male
[b]No evidence of copulation
S.D. - Standard deviation
- Not applicable

TABLE 12. Cont.

$F_1$ Individual Litter Data

| Group Number, Test Article, Dosage Level, Dam Number | First Male Used | Second Male Used | Gestation Length (Days) | No. Pups Dead on Day 0 | Number Live Pups on Lactation Day 0 | 4 Reduction Before | 4 Reduction After | 7 | 14 | 21 Male | 21 Female | Mean Weight (grams) of Live Pups on Lactation Day 0 | 4 Reduction Before | 4 Reduction After | 7 | 14 | 21 Male | 21 Female |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| (7), B0547-01, 1000 mg/kg/day: | | | | | | | | | | | | | | | | | | |
| 31134 | 30959 | - | 21 | 0 | 15 | 15 | 10 | 10 | 10 | 5 | 5 | 5.3[c] | 8.1 | 8.2 | 13.0 | 28.6 | 49.1 | 44.8 |
| 31138 | - | - | Died | | | | | | | | | | | | | | | |
| 31141 | 30966 | - | 22 | 0 | 15 | 15 | 10 | 10 | 10 | 5 | 5 | 5.7 | 8.7 | 8.8 | 14.1 | 29.7 | 50.2 | 47.7 |
| 31143 | 30968 | - | 21 | 0 | 15 | 15 | 10 | 10 | 10 | 4 | 6 | 5.7 | 8.0 | 8.1 | 13.3 | 28.2 | 43.8 | 42.8 |
| 31144 | 30969 | - | 21 | 0 | 15 | 15 | 10 | 10 | 10 | 5 | 5 | 6.2 | 10.0 | 10.0 | 16.5 | 30.9 | 51.2 | 50.7 |
| 31146 | 30971 | - | 21 | 0 | 13 | 13 | 10 | 10 | 10 | 5 | 5 | 5.5 | 8.2 | 8.3 | 12.6 | 26.3 | 47.5 | 46.3 |
| 31147 | 30972 | - | 23 | 0 | 15 | 15 | 10 | 10 | 10 | 5 | 5 | 6.8 | 8.8 | 8.8 | 16.6 | 32.5 | 52.8 | 51.4 |
| 31148 | 30973 | - | 23 | 0 | 14 | 14 | 10 | 10 | 10 | 6 | 4 | 7.1 | 11.6 | 11.6 | 18.6 | 33.4 | 53.4 | 52.3 |
| 31149 | 30974 | - | 22 | 1 | 13 | 13 | 10 | 10 | 10 | 3 | 7 | 6.6 | 10.4 | 10.6 | 14.8 | 32.2 | 54.9 | 51.0 |
| 31150 | 30975 | - | 23 | 0 | 6 | 6 | 6 | 6 | 6 | 3 | 3 | 7.5 | 13.4 | 13.4 | 18.7 | 37.7 | 62.8 | 62.3 |
| 31153 | 30978 | - | 22 | 0 | 5 | 5 | 5 | 5 | 5 | 1 | 4 | 7.2 | 12.5 | 12.5 | 18.7 | 37.6 | 63.3 | 56.9 |
| 31154 | 30979 | - | 22 | 0 | 13 | 13 | 10 | 10 | 10 | 5 | 5 | 6.7 | 10.5 | 10.6 | 15.7 | 29.0 | 50.4 | 46.1 |
| 31155 | 30980 | - | 22 | 0 | 7 | 5 | 5 | 5 | 5 | 2 | 3 | 7.2 | 12.3 | 12.3 | 18.6 | 37.7 | 57.4 | 59.3 |
| Total | - | - | - | 1 | 146 | 144 | 106 | 106 | 106 | 106 | | - | - | - | - | - | - | - |
| Mean | - | - | 21.9 | 0.1 | 12.2 | 12.0 | 8.8 | 8.8 | 8.8 | 8.8 | | 6.5 | 10.2 | 10.3 | 15.9 | 32.0 | 53.1 | 51.0* |
| ±S.D. | - | - | 0.79 | 0.29 | 3.83 | 4.11 | 2.12 | 2.12 | 2.12 | 2.12 | | 0.75 | 1.90 | 1.86 | 2.37 | 3.96 | 5.82 | 6.00 |

[c]Body weight does not represent total number of pups
*Statistically different from control; $p<0.05$
S.D. - Standard deviation
- Not applicable

TABLE 13. Summary of Group Mean Maternal Uterine Observations at Weaning

| Group Number, Test Article, Dosage Level, (mg/kg/day) | No. of Implantation Sites | | No. of Pups Delivered | | No. of Remaining Sites[a] | |
|---|---|---|---|---|---|---|
| | Mean | (±)S.D. | Mean | (±)S.D. | Mean | (±)S.D. |
| (1), 0 (Control) | 15.0 | 1.29 | 13.6 | 1.66 | 1.4 | 1.45 |
| (2), B0547-01, 250[FD] | 14.0 | 3.46 | 13.3 | 3.20 | 0.7 | 1.01 |
| (3), B0547-01, 500[FD] | 14.3 | 3.61 | 13.4 | 3.44 | 0.9 | 1.04 |
| (4), B0547-01, 1000[FD] | 12.5 | 4.34 | 11.5 | 4.20 | 1.0 | 1.26 |
| (5), B0547-01, 250[MD] | 14.5 | 3.36 | 13.5 | 3.75 | 1.1 | 0.94 |
| (6), B0547-01, 500[MD] | 15.5 | 1.61 | 14.2 | 1.64 | 1.2 | 1.17 |
| (7), B0547-01, 1000[MD] | 12.5 | 4.27 | 12.3 | 3.86 | 0.5 | 0.69 |

[a] - Implantation sites not corresponding to delivered pups; values represent postimplantation loss and/or complete cannibalization
FD - Only females dosed
MD - Only males dosed
S.D. - Standard deviation

TABLE 14. Individual and Group Mean Maternal Observations at Weaning

| Group Number, Test Article, Dosage Level, Dam Number | Total Implantation Sites | No. of Pups Delivered | Resorp Site |
|---|---|---|---|
| (1), 0 mg/kg/day (Control): | | | |
| 30985 | 16 | 14 | |
| 30986 | 13 | 11 | |
| 30990 | 16 | 15 | |
| 30991 | 16 | 14 | |
| 30992 | 14 | 11 | |
| 30995 | 14 | 13 | |
| 30996 | 15 | 14 | |
| 30997 | 16 | 16 | |
| 30998 | 16 | 16 | |
| 31003 | 15 | 15 | |
| 31004 | 17 | 12 | |
| 31005 | 13 | 13 | |
| 31008 | 14 | 13 | |
| Mean | 15.0 | 13.6 | |
| ±S.D. | 1.29 | 1.66 | |
| (2), B0347-01, 250 mg/kg/day: | | | |
| 31010 | 10 | 10 | |
| 31012 | 16 | 15 | |
| 31013 | 18 | 18 | |
| 31017 | 6 | 6 | |
| 31020 | 15 | 14 | |
| 31023 | 13 | 13 | |
| 31024 | Did not deliver (nongravid) | | |
| 31026 | 16 | 16 | |
| 31027 | 14 | 14 | |
| 31029 | Died | | |
| 31030 | 13 | 12 | |
| 31032 | 16 | 13 | |
| 31033 | 17 | 15 | |
| Mean | 14.0 | 13.3 | |
| ±S.D. | 3.46 | 3.20 | |
| (3), B0547-01, 500 mg/kg/day: | | | |
| 31034[b] | Sacrificed | | |
| 31035 | 15 | 15 | |
| 31036 | 4 | 4 | |
| 31037 | 16 | 16 | |
| 31038 | Did not deliver (nongravid) | | |
| 31039 | 15 | 13 | |
| 31040 | 15 | 14 | |
| 31042 | 14 | 13 | |
| 31046 | 15 | 15 | |
| 31048 | 16 | 13 | |
| 31050 | 17 | 15 | |
| 31053 | 17 | 17 | |
| 31058 | 13 | 12 | |
| Mean | 14.3 | 13.4 | |
| ±S.D. | 3.61 | 3.44 | |

[a] Implantation sites not corresponding to delivered pups; values repres postimplantation loss and/or complete cannibalization

[b] Sacrificed *in extremis*, no evidence of copulation, unable to determin pregnancy status

S.D. - Standard deviation

TABLE 14. Cont. Individual and Group Mean Maternal Observations at Weaning

| Group Number, Test Article, Dosage Level, Dam Number | Total Implantation Sites | No. of Pups Delivered | Remaini Sites[a] |
|---|---|---|---|
| (4), B0547-01, 1000 mg/kg/day: | | | |
| 31060[c] | Died | | |
| 31061 | 10 | 10 | 0 |
| 31067 | 15 | 13 | 2 |
| 31068 | 16 | 16 | 0 |
| 31069 | 15 | 13 | 2 |
| 31070 | 13 | 12 | 1 |
| 31072[d] | 1 | 0 | 1 |
| 31074 | Died | | |
| 31075 | 13 | 12 | 1 |
| 31078 | 10 | 10 | 0 |
| 31080 | 15 | 15 | 0 |
| 31081 | 13 | 13 | 0 |
| 31082 | Died | | |
| 31083 | 16 | 12 | 4 |
| Mean | 12.5 | 11.5 | 1.0 |
| ±S.D. | 4.34 | 4.20 | 1.2 |
| (5), B0547-01, 250 mg/kg/day: | | | |
| 31085 | 14 | 14 | 0 |
| 31086 | 11 | 9 | 2 |
| 31092 | 16 | 14 | 2 |
| 31094 | 14 | 13 | 1 |
| 31096 | 14 | 14 | 0 |
| 31100 | 14 | 12 | 2 |
| 31101 | 7 | 5 | 2 |
| 31102 | 17 | 16 | 1 |
| 31104 | 19 | 17 | 2 |
| 31105 | 16 | 16 | 0 |
| 31106 | 18 | 18 | 0 |
| 31107 | Did not deliver (nongravid) | | |
| Mean | 14.5 | 13.5 | 1. |
| ±S.D. | 3.36 | 3.75 | 0. |
| (6), B0547-01, 500 mg/kg/day: | | | |
| 31114 | 15 | 14 | 1 |
| 31115 | 17 | 14 | 3 |
| 31117 | 12 | 11 | 1 |
| 31120 | 15 | 15 | 0 |
| 31121 | 15 | 14 | 1 |
| 31123 | 15 | 14 | 1 |
| 31124 | 16 | 16 | 0 |
| 31125 | 18 | 17 | 1 |
| 31127 | 16 | 15 | 1 |
| 31128 | 16 | 12 | 4 |
| 31130 | 16 | 14 | 2 |
| 31131 | 17 | 16 | 1 |
| 31132 | 13 | 13 | 0 |
| Mean | 15.5 | 14.2 | 1 |
| ±S.D. | 1.61 | 1.64 | 1 |

[a] Implantation sites not corresponding to delivered pups; values
postimplantation loss and/or complete cannibalization
[b] Sacrificed in extremis, no evidence of copulation, unable to
pregnancy status
[c] Died gestation day 3; unable to determine pregnancy status
[d] Did not deliver, sacrificed 25 days after separation from mal

S.D. - Standard deviation

TABLE 14. Cont. Individual and Group Mean Maternal Observations at Weaning

| Group Number, Test Article, Dosage Level, Dam Number | Total Implantation Sites | No. of Pups Delivered | Remaining Sites[a] |
|---|---|---|---|
| (7), 80547-01, 1000 mg/kg/day: | | | |
| 31134 | 14[e] | 15 | - |
| 31141 | 16 | 15 | 1 |
| 31143 | 15 | 15 | 0 |
| 31144 | 15 | 15 | 0 |
| 31146 | 14 | 13 | 1 |
| 31147 | 15 | 15 | 0 |
| 31148 | 16 | 14 | 2 |
| 31149 | 15 | 14 | 1 |
| 31150 | 6 | 6 | 0 |
| 31153 | 5 | 5 | 0 |
| 31154 | 14 | 13 | 1 |
| 31155 | 7 | 7 | 0 |
| Mean | 12.5 | 12.3 | 0.5 |
| ±S.D. | 4.27 | 3.86 | 0.69 |

[a]Implantation sites not corresponding to delivered pups; values repre postimplantation loss and/or complete cannibalization
[e]Pups delivered exceeds total implantation sites, value excluded from calculation of mean
S.D. - Standard deviation
- Not applicable

APPENDIX A

Quality Assurance Inspections

Quality Assurance Inspections

| Dates of Inspections | Dates of Reports to Management and to Study Director |
|---|---|
| 3/10/83 | 5/12/83 |
| 3/14/83 | 5/26/83 |
| 3/17/83 | 8/22/83 |
| 3/18/83 | 8/24/83 |
| 5/09/83 | 11/07/83 |
| 5/10/83 | 11/22/83 |
| 5/18/83 | |
| 5/19/83 | |
| 5/23/83 | |
| 5/24/83 | |
| 5/25/83 | |
| 6/01/83 | |
| 6/21/83 | |
| 8/19/83 | |
| 11/07/83 | |
| 11/22/83 | |

# APPENDIX B

## Historical Control Data

## Summary of Maternal and Fetal Observations at Cesarean Section

| | |
|---|---|
| No. of animals in the historical control: | 1758 |
| No. of animals that died: | 1 |
| No. of animals that delivered: | 6 |
| No. of animals examined at Cesarean section: | 1751 |
| No. nongravid: | 164 |
| No. gravid: | 1587 |
| No. of dams with resorptions only: | 8 |
| No. of dams with live fetuses: | 1579 |
| No. of live fetuses/dam: | 13.3[10.5-15.7] |
| No. of postimplantation losses/dam: | 0.8[0.3-1.6] |
| No. of implantations/dam: | 14.2[11.6-16.3] |
| No. of corpora lutea/dam: | 16.0[13.7-19.7] |
| Fetal sex ratio: Male:Female | 10756:10430 |
| Mean fetal body weight (g): | 3.6[3.4-4.2] |

[ ] - Range of means

IRDC REPRODUCTIVE HISTORICAL CONTROL DATA
Charles River CORS® CD® Rats

| Sex, (When Applicable) Reproductive/Litter Parameter | | Number | Value | Range |
|---|---|---|---|---|
| **MALE** | | | | |
| Fertility Index | Fertile Males / Total Males Mated | 407 / 432 | 94.2% | (80.0% - 100.0%) |
| **FEMALE** | | | | |
| Fertility Index | No. of Females Pregnant / No. of Females Mated | 926 / 1027 | 90.2% | (62.1% - 100.0%) |
| Gestation Length (Days) | Total No. of Days / No. of Pregnant Dams | 16325 / 745 | 21.9 | (21.6 - 22.4) |
| No. Implantation Sites at Weaning/Dam | Total No. of Implantation Sites / No. of Pregnant Dams | 1064 / 73 | 14.6 | (14.0 - 14.9) |
| Postimplantation Loss/Dam | No. of Implantation Sites at Weaning- Total No. Pups at Birth / No. of Implantation Sites | 1064-989 / 1064 | 7.0% | (3.3% - 8.3%) |
| **LITTER SIZE** | | | | |
| Viable Pups/Litter at Day 0 | Total No. of Viable Pups / No. of Pregnant Dams | 10832 / 860 | 12.6 | (10.1 - 15.0) |
| Stillborn Pups/Litter | Total No. of Stillborn Pups / No. of Pregnant Dams | 208 / 860 | 0.2 | (0.0 - 1.4) |
| **PUP SEX DISTRIBUTION AT WEANING** | Total No. of Males: Total No. of Females | Total No. of Males: Total No. of Females 4451:4466 | %Male:%Female 49.9:50.1 | %Male:%Female - %Male%Female (40.7:44.1 - 55.9:59.3) |
| **PUP SURVIVAL AT BIRTH** | | | | |
| Gestation Survival Index | Total No. of Viable Pups at Birth / Total No. of Pups Born | 10594 / 10791 | 98.2% | (89.3% - 100.0%) |
| **PUP SURVIVAL INDICES THROUGH WEANING** | | | | |
| Lactation Day 4 (Before Reduction) | Total No. of Viable Pups on Day 4 (B.R.) / Total No. of Viable Pups on Day 0 | 5909 / 6013 | 98.3% | (95.7% - 100.0%) |
| Lactation Day 4 (No Reduction of Litter Size) | Total No. of Viable Pups on Day 4 / Total No. of Viable Pups on Day 0 | 3398 / 3438 | 98.8% | (95.3% - 100.0%) |
| Lactation Day 12 | Total No. of Viable Pups on Day 12 / Total No. of Viable Pups on Day 4 (N.R.) | 2768 / 2784 | 99.4% | (98.4% - 100.0%) |

IRDC REPRODUCTIVE HISTORICAL CONTROL DATA
Charles River CORS® CD® Rats

| Sex, (When Applicable) Reproductive/Litter Parameter | | Number | Value | Range |
|---|---|---|---|---|
| Lactation Day 14 | Total No. of Viable Pups on Day 14 / Total No. of Viable Pups on Day 4 (AR), 5 (AR) or 7 | 4898 / 4923 | 99.5% | (97.0% - 100.0%) |
| Lactation Day 21 | Total No. of Viable Pups on Day 21 / Total No. of Viable Pups on Day 12 or 14 | 8310 / 8347 | 99.6% | (97.1% - 100.0%) |
| PUP BODY WEIGHT (g) AT BIRTH | | | | |
| Male | Total Viable Male Pup Weight at Birth / Total No. of Viable Male Pups | 1272.0 / 191 | 6.6 g | (6.4 g - 7.1 g) |
| Female | Total Viable Female Pup Weight at Birth / Total No. of Viable Female Pups | 1197.9 / 192 | 6.2 g | (6.1 g - 6.8 g) |
| Litter Weight (Males and Females) | Total Mean Viable Litter Weight at Birth / Total No. of Litters | 2669.8 / 415 | 6.4 g | (5.6 g - 7.4 g) |
| PUP BODY WEIGHT (g) THROUGH WEANING | | | | |
| Lactation Day 4 (Before Reduction) Litter Weight (Males and Females) | Total Mean Viable Litter Weight on Day 4 (B.R.) / Total No. of Litters on Day 4 (B.R.) | 4974.6 / 485 | 10.3 g | (9.2 g - 11.3 g) |
| Lactation Day 4 (After Reduction) | | | | |
| Litter Weight (Males and Females) | Total Mean Viable Litter Weight on Day 4 (A.R.) / Total No. of Litters on Day 4 (A.R.) | 3557.7 / 350 | 10.2 g | (9.2 g - 11.2 g) |
| Lactation Day 4 (No Reduction of (Litter Size) | | | | |
| Male | Total Viable Male Pup Weight on Day 4 / Total No. Viable Male Pups on Day 4 | 2092 / 196 | 10.7 g | (9.2 g - 11.8 g) |
| Female | Total Viable Female Pup Weight on Day 4 / Total No. Viable Female Pups on Day 4 | 1975.8 / 196 | 10.1 g | (9.7 g - 11.5 g) |
| Litter Weight (Males and Females) | Total Mean Viable Litter Weight on Day 4 / Total No. of Litters on Day 4 | 644.6 / 61 | 10.6 g | (9.7 g - 11.5 g) |
| Lactation Day 7 | | | | |
| Male | Total Viable Male Pup Weight on Day 7 / Total No. Viable Male Pups on Day 7 | 738.9 / 47 | 15.7 g | (15.6 g - 15.8 g) |
| Female | Total Viable Female Pup Weight on Day 7 / Total No. Viable Female Pups on Day 7 | 704.6 / 47 | 15.0 g | (15.0 g - 15.0 g) |
| Litter Weight (Males and Females) | Total Mean Viable Litter Weight on Day 7 / Total No. Litters on Day 7 | 1840.3 / 124 | 14.8 g | (14.2 g - 15.9 g) |
| Lactation Day 12 | | | | |
| Male | Total Viable Male Pup Weight on Day 12 / Total No. Viable Male Pups on Day 12 | 3714.8 / 151 | 24.6 g | (22.3 g - 28.2 g) |
| Female | Total Viable Female Pup Weight on Day 12 / Total No. Viable Female Pups on Day 12 | 3553 / 151 | 23.5 g | (22.1 g - 27.3 g) |
| Litter Weight (Males and Females) | Total Mean Viable Litter Weight on Day 12 / Total No. Litters on Day 12 | 1459.0 / 61 | 23.9 g | (22.0 g - 25.6 g) |

IRDC REPRODUCTIVE HISTORICAL CONTROL DATA
Charles River CORS® CD® Rats

| Sex, (When Applicable) Reproductive/Litter Parameter | | Number | Value | Range |
|---|---|---|---|---|
| Lactation Day 14 | | | | |
| Male | Total Viable Male Pup Weight on Day 14 / Total No. Viable Male Pups on Day 14 | 1030.4 / 47 | 27.7 g | (27.4 g - 28.0 g) |
| Female | Total Viable Female Pup Weight on Day 14 / Total No. Viable Female Pups on Day 14 | 126.5 / 47 | 26.9 g | (26.7 g - 27.1 g) |
| Litter | Total Mean Viable Litter Weight on Day 14 / Total No. Litters on Day 14 | 10333.2 / 353 | 29.3 g | (26.9 g - 34.3 g) |
| Lactation Day 21 | | | | |
| Male | Total Viable Male Pup Weight on Day 21 / Total No. Viable Male Pups on Day 21 | 38738 / 848 | 45.7 g | (39.1 g - 54.7 g) |
| Female | Total Viable Female Pup Weight on Day 21 / Total No. Viable Female Pups on Day 21 | 37503 / 851 | 44.1 g | (37.5 g - 52.6 g) |

The historical control data compiled includes study data from the interval of April 17, 1977 to September 29, 1980 (20 studies)

# APPENDIX C

## Personnel Involved in the Study

The following list of people were responsible for the supervision of various phases of this study:

| | |
|---|---|
| [redacted] | Unit Supervisor, Test Material Control |
| [redacted] | Group Supervisor, Reproduction and Teratology |
| [redacted] | Unit Supervisor, Reproduction and Teratology |
| [redacted] | Group Supervisor, Test Material Control |
| [redacted] | Report Writer, Reproduction and Teratology |
| [redacted] | Assistant Director, Toxicology Division and Director of Reproduction and Teratology, Study Director |
| [redacted] | Unit Supervisor, Reproduction and Teratology |
| [redacted] | Assistant to the Director, Reproduction and Teratology |
| [redacted] | Director of Laboratory Services |

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

William C. Kuryla, Ph.D.
Associate Director, Product Safety
Union Carbide Corporation
39 Old Ridgebury Road
Danbury, Connecticut 06817-0001

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MAR 30 1995

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., 8EHQ-00-0000) assigned by EPA to your submission(s). Please cite the assigned 8(e) number when submitting follow-up or supplemental information and refer to the reverse side of this page for "EPA Information Requests".

All TSCA 8(e) submissions are placed in the public files unless confidentiality is claimed according to the procedures outlined in Part X of EPA's TSCA §8(e) policy statement (43 FR 11110, March 16, 1978). Confidential submissions received pursuant to the TSCA §8(e) Compliance Audit Program (CAP) should already contain information supporting confidentiality claims. This information is required and should be submitted if not done so previously. To substantiate claims, submit responses to the questions in the enclosure "Support Information for Confidentiality Claims". This same enclosure is used to support confidentiality claims for non-CAP submissions.

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EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Sincerely,

Terry R. O'Bryan

Terry R. O'Bryan
Risk Analysis Branch

Enclosure 12459A

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# Triage of 8(e) Submissions

Date sent to triage: _____

NON-CAP CAP

Submission number: 12459A

TSCA Inventory: Y N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX SBTOX SEN w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX CTOX EPI RTOX GTOX

STOX/ONCO CTOX/ONCO IMMUNO CYTO NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

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**Notes:**

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CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ- 0992 - 12459 SEQ. A

TYPE: (INT.) SUPP FLWP

SUBMITTER NAME: Union Carbide Corporation

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0639) REFER TO CHEMICAL SCREENING
(0678) CAP NOTICE

VOLUNTARY ACTIONS:
(0401) NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKERS/OTHERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

SUB. DATE: 09/22/92 OTS DATE: 09/29/92 CSRAD DATE: 01/31/95

CHEMICAL NAME:

CAS#
112-34-5

| INFORMATION TYPE: | | P F C |
|---|---|---|
| 0201 | ONCO (HUMAN) | 01 02 04 |
| 0202 | ONCO (ANIMAL) | 01 02 04 |
| 0203 | CELL TRANS (IN VITRO) | 01 02 04 |
| 0204 | MUTA (IN VITRO) | 01 02 04 |
| 0205 | MUTA (IN VIVO) | 01 02 04 |
| 0206 | REPRO/TERATO (HUMAN) | 01 02 04 |
| (0207) | REPRO/TERATO (ANIMAL) | 01 (02) 04 |
| 0208 | NEURO (HUMAN) | 01 02 04 |
| 0209 | NEURO (ANIMAL) | 01 02 04 |
| 0210 | ACUTE TOX. (HUMAN) | 01 02 04 |
| 0211 | CHR. TOX. (HUMAN) | 01 02 04 |
| 0212 | ACUTE TOX. (ANIMAL) | 01 02 04 |
| 0213 | SUB ACUTE TOX (ANIMAL) | 01 02 04 |
| 0214 | SUB CHRONIC TOX (ANIMAL) | 01 02 04 |
| 0215 | CHRONIC TOX (ANIMAL) | 01 02 04 |

| INFORMATION TYPE: | | P F C |
|---|---|---|
| 0216 | EPI/CLIN | 01 02 04 |
| 0217 | HUMAN EXPOS (PROD CONTAM) | 01 02 04 |
| 0218 | HUMAN EXPOS (ACCIDENTAL) | 01 02 04 |
| 0219 | HUMAN EXPOS (MONITORING) | 01 02 04 |
| 0220 | ECO/AQUA TOX | 01 02 04 |
| 0221 | ENV. OCCC/REL/FATE | 01 02 04 |
| 0222 | EMER INCI OF ENV CONTAM | 01 02 04 |
| 0223 | RESPONSE REQEST DELAY | 01 02 04 |
| 0224 | PROD/COMP/CHEM ID | 01 02 04 |
| 0225 | REPORTING RATIONALE | 01 02 04 |
| 0226 | CONFIDENTIAL | 01 02 04 |
| 0227 | ALLERG (HUMAN) | 01 02 04 |
| 0228 | ALLERG (ANIMAL) | 01 02 04 |
| 0239 | METAB/PHARMACO (ANIMAL) | 01 02 04 |
| 0240 | METAB/PHARMACO (HUMAN) | 01 02 04 |

| INFORMATION TYPE: | | P F C |
|---|---|---|
| 0241 | IMMUNO (ANIMAL) | 01 02 04 |
| 0242 | IMMUNO (HUMAN) | 01 02 04 |
| (0243) | CHEM/PHYS PROP | 01 02 04 |
| 0244 | CLASTO (IN VITRO) | 01 02 04 |
| 0245 | CLASTO (ANIMAL) | 01 02 04 |
| 0246 | CLASTO (HUMAN) | 01 02 04 |
| 0247 | DNA DAM/REPAIR | 01 02 04 |
| 0248 | PROD/USE/PROC | 01 02 04 |
| 0251 | MSDS | 01 02 04 |
| 0299 | OTHER | 01 02 04 |

[redacted]

| TRIAGE DATA: | NON-CBI INVENTORY | ONGOING REVIEW | SPECIES | TOXICOLOGICAL CONCERN: | USE: | PRODUCTION: |
|---|---|---|---|---|---|---|
| | (YES) | YES (DROP/REFER) | RAT | (LOW) | | |
| CAS SR | NO | NO (CONTINUE) | | MED | | |
| | DE MINIMIS | REFER | | HIGH | | |

COMMENTS: oral gavage, multigen feed reproduction: 1) treated males mated with untreated females 2) treated females mated with untreated males

treated males 1000 mg/kg - 3/25 died, reduced BW gain, reduced implantations
500 mg/kg - 1/25 died
250 mg/kg - no effects

treated females 1000 mg/kg - 5/25 died, reduced implantation, reduced pup weight
500 mg/kg - 4/25 died
250 mg/kg - 2/25 died

[N.B. uncertain if deaths due to gavage errors]