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FINAL REPORT

Testing Facility Study No. 20248897

A GLP Intramuscular Combined Developmental and Perinatal/Postnatal Reproductive Toxicity Study of mRNA-1273 in Rats

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QUALITY ASSURANCE STATEMENT

Study Number: 20248897

This Study has been audited by Quality Assurance in accordance with the applicable Good Laboratory Practice regulations. Reports were submitted in accordance with SOPs as follows:

QA INSPECTION DATES

		Dates Findings Submitted to:	
Date(s) of Audit	**Phase(s) Audited**	**Study Director**	**Study Director Management**
18-Jun-2020	Final Protocol	18-Jun-2020	18-Jun-2020
18-Jun-2020	Final Protocol	18-Jun-2020	18-Jun-2020
30-Jun-2020	Dose Administration	30-Jun-2020	30-Jun-2020
01-Jul-2020	Protocol Amendment 01	01-Jul-2020	01-Jul-2020
24-Jul-2020	Protocol Amendment 02	24-Jul-2020	24-Jul-2020
30-Jul-2020	Dose Preparation	31-Jul-2020	31-Jul-2020
10-Aug-2020	Blood Collection	10-Aug-2020	10-Aug-2020
18-Aug-2020	Protocol Amendment 03	18-Aug-2020	18-Aug-2020
03-Sep-2020 09-Sep-2020	Littering/Culling	09-Sep-2020	09-Sep-2020
28-Sep-2020	Data Review - Technical Operations	28-Sep-2020	28-Sep-2020
28-Sep-2020	Data Review - Formulations	29-Sep-2020	29-Sep-2020
28-Sep-2020	Report Tables	28-Sep-2020	28-Sep-2020
27-Oct-2020 - 29-Oct-2020 02-Nov-2020 - 06-Nov-2020 09-Nov-2020	Data Review - Technical Operations	09-Nov-2020	09-Nov-2020
27-Oct-2020 - 29-Oct-2020 02-Nov-2020 - 06-Nov-2020 09-Nov-2020	Data Review - Necropsy	09-Nov-2020	09-Nov-2020
27-Oct-2020 - 29-Oct-2020 02-Nov-2020 - 06-Nov-2020 09-Nov-2020	Report Tables	09-Nov-2020	09-Nov-2020
29-Oct-2020	Data Review - Fetal Evaluations	09-Nov-2020	09-Nov-2020
09-Nov-2020 - 10-Nov-2020	Report - Materials and Methods	10-Nov-2020	10-Nov-2020
19-Nov-2020	Protocol Amendment 04	19-Nov-2020	19-Nov-2020
19-Nov-2020	Report - Results	19-Nov-2020	19-Nov-2020
08-Dec-2020	Report - Results	08-Dec-2020	08-Dec-2020
08-Dec-2020	Final Report	08-Dec-2020	08-Dec-2020

QUALITY ASSURANCE STATEMENT - Study Number: 20248897

QA INSPECTION DATES

Date(s) of Audit	Phase(s) Audited	Dates Findings Submitted to: Study Director	Study Director Management

In addition to the above-mentioned audits, process-based and/or routine facility inspections were also conducted during the course of this study. Inspection findings, if any, specific to this study were reported by Quality Assurance to the Study Director and Management and listed as a Phase Audit on this Quality Assurance Statement.

The Quality Assurance Statements for the work conducted at the Test Sites were reviewed and are included in the appropriate section of this report.

The Final Report has been reviewed to assure that it accurately describes the materials and methods, and that the reported results accurately reflect the raw data.

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(b) (6)

COMPLIANCE STATEMENT AND REPORT APPROVAL

The study was performed in accordance with the U.S. Department of Health and Human Services, Food and Drug Administration, United States Code of Federal Regulations, Title 21, Part 58: Good Laboratory Practice for Nonclinical Laboratory Studies and as accepted by Regulatory Authorities throughout the European Union (OECD Principles of Good Laboratory Practice), Japan (MHLW), and other countries that are signatories to the OECD Mutual Acceptance of Data Agreement.

The portion of this study conducted in Canada was performed in accordance with the OECD Principles of Good Laboratory Practice and as accepted by Regulatory Authorities throughout the European Union, United States of America (FDA), Japan (MHLW), and other countries that are signatories to the OECD Mutual Acceptance of Data Agreement.

Exceptions from the above regulations are listed below.

- Characterization of the Test and Control articles was performed by the Sponsor at a laboratory that follows FDA Good Manufacturing Practice (GMP) regulations. This exception had no adverse impact on the study because the analyses were performed by the Sponsor according to established SOPs, controls, and approved test methodologies that ensured the validity of the results.
- Stability testing of the supplied Test and Control articles was performed by the Sponsor at a laboratory that follows FDA GMP regulations. This exception had no adverse impact on the study because the analyses were performed by the Sponsor according to established SOPs, controls, and approved test methodologies that ensured the validity of the results.
- The antibody analysis was not in compliance with Good Laboratory Practice (GLP) regulations. This analysis was performed using established SOPs, controls, approved test methodologies, and good scientific practices. This exception had no adverse impact on the study because these analyses were performed using established Standard Operating Procedures (SOPs), controls, approved test methodologies, and good scientific practices.

This study was conducted in accordance with the procedures described herein. All deviations authorized/acknowledged by the Study Director are documented in the Study Records. The report represents an accurate and complete record of the results obtained.

There were no deviations from the above regulations that affected the overall integrity of the study or the interpretation of the study results and conclusions.

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(b) (6)

1. RESPONSIBLE PERSONNEL

1.1. Testing Facility

Study Director (b) (6)

Address as cited for the Testing Facility

Management Contact and Scientific Reviewer (b) (6)

Address as cited for the Testing Facility

General Manager (b) (6)

Associate Director, Operations

1.2. Principal Investigators (PI) at a Testing Facility-designated Test Site

Analytical Chemistry (b) (6)

Charles River Laboratories Montreal ULC
Senneville Site (CR-SEN)
22022 Transcanadienne
Senneville, QC H9X 3R3
Canada

1.3. PIs at a Sponsor-designated Test Site

Antibody Analysis (b) (6)

Integrated Biotherapeutics, Inc.
4 Research Court, Suite 300
Rockville, MD 20850
United States

2. SUMMARY

The objective of this study was to assess the potential effects of mRNA-1273, a vaccine development candidate against SARS-CoV-2 infection, when administered intramuscularly on Study Days 1 and 15 (28 and 14 days prior to mating, respectively) and Gestation Days 1 and 13 on fertility and pre and postnatal development in the pregnant and lactating female Sprague Dawley CD (Crl:CD[SD]) rat.

The study design was as follows:

Text Table 1
Experimental Design

Group No.	Test Material	Dose Level (µg/dose)	Dose Concentration (mg/mL)	Dose Volume (µL/dose)	No. of Females	
					Cohort 1 (Cesaearan-Sectioning Phase)	Cohort 2 (Natural Delivery Phase)
1	Control Article	0	0	200	22	22
2	mRNA-1273	100	0.5	200	22	22

A total of 88 female Crl:CD(SD) Sprague Dawley rats were randomly assigned to two dose groups of 44 rats per group. Additionally, each dose group consisted of two cohorts, 22 rats in each of Cohort 1 (Caesarean-Sectioning Phase) and Cohort 2 (Natural Delivery Phase). F0 generation female rats were administered mRNA-1273 or control article (20 mM Tris, 8.7% Sucrose, pH 7.5) formulations once daily via intramuscular injection on Study Day (SD) 1 (28 days prior to mating) and SD 15 (14 days prior to mating) and on Gestation Days (GD) 1 and 13. Study Day 1 was defined as the first day of dose administration. The dose volume was 200 µL/dose, injected into the quadriceps, alternating hindlimbs on each dosing occasion. All F0 female rats assigned to Cohort 1 were euthanized on GD 21 for Caesarean-sectioning and fetal examinations. All F0 generation females assigned to Cohort 2 were allowed to deliver their litters naturally. On Lactation Day 4 (LD 4), F1 generation naturally-delivered pups were culled, and litters were reduced to eight pups each (when possible) for continuation on study. All surviving F0 female rats with remaining pups assigned to Cohort 2 were euthanized after completion of the 21-Day postpartum period.

Robust IgG response to S2P antigen was observed in both the F0 and F1generation rats following immunization of F0 rats with mRNA-1273. In the F0 rats, peak titer of 442,138 AU/mL was reached on GD13. Titers subsequently plateaued at parturition (GD 21) and stayed relatively constant through LD 21. High IgG antibodies to S2P were also observed in GD 21 fetuses and LD 21 pups indicating strong transfer of antibodies from mother to fetus and from mother to pups.

In the F0 generation, there were no mRNA-1273-related mortalities, changes in body weight, body weight gain, food consumption, macroscopic observations, estrous cycling during precohabitation, mating and fertility, ovarian/uterine examinations or on any natural delivery or litter observation parameters.

mRNA-1273-related clinical signs observed in the F0 rats included transient thin fur cover, swollen hindlimbs and limited usage of the hindlimb during the premating, gestation and/or lactation phases of the study, with the most observations observed following administration on GD 13. These observations were not considered adverse as they did not significantly impair the

animal's mobility, access to food, ability to thrive, and only thin fur cover was still present during the lactation phase and was resolved by LD 18.

In the F1 generation, there were no mRNA-1273-related mortalities, clinical observations, changes in body weight, gross pathology, external or visceral malformations or variations, skeletal malformations, and mean number of ossification sites per fetus per litter.

mRNA-1273-related common skeletal variations consisting of wavy ribs and increase nodules were observed. Wavy ribs appeared in 6 fetuses in 4 litters for a fetal prevalence of 4.03% and a litter prevalence of 18.2%. Rib nodules appeared in 5 of those 6 fetuses. The fetal and litter incidence of wavy ribs exceeded the range observed historically at the Testing Facility (see Appendix 40, Historical Control Data) and the fetal and litter incidence of rib nodules was within the range. These findings were not considered adverse because there was no effect on pup growth and viability in the delivered litters, wavy ribs and rib nodules are known to resolve postnatally without medical intervention and these findings were observed without any other indicators of developmental toxicity.

Maternal administration of mRNA-1273 on SD 1 (28 days prior to mating), SD 15 (14 days prior to mating), GD 1 and GD 13 did not have any adverse effects on the F0 or F1 generations. mRNA-1273-related, non-adverse effects were limited to increase in the number of fetuses with common skeletal variations of 1 or more rib nodules and 1 or more wavy ribs with no effect on the viability and growth on the F1 generation pups.

3. INTRODUCTION

The objective of this study was to assess the potential effects of mRNA-1273, a vaccine development candidate against SARS-CoV-2 infection, when administered intramuscularly on Study Days 1 and 15 (28 and 14 days prior to mating, respectively) and Gestation Days 1 and 13 on fertility and pre and postnatal development in the pregnant and lactating female Sprague Dawley CD (Crl:CD[SD]) rat.

The design of this study was based on the study objective, the overall product development strategy for the test article, and ICH and FDA guidelines.[1,2,3]

The deviations, the last amended protocol, and protocol are presented in Appendix 1.

Study Initiation Date: 16 Jun 2020

Initiation of Dosing: 30 Jun 2020

Completion of In-life: 14 Sep 2020

4. MATERIALS AND METHODS

4.1. Test and Control Articles

4.2. Test and Control Article Characterization

The Sponsor provided to the Testing Facility documentation of the identity, strength, purity, composition, and stability for the test and control article. A Summary of Analysis was provided to the Testing Facility and is presented in Appendix 2. The Sponsor also provided information concerning the regulatory standard that was followed for these evaluations.

The Sponsor has appropriate documentation on file concerning the method of synthesis, fabrication or derivation of the test and control articles, and this information is available to the appropriate regulatory agencies should it be requested.

4.2.1. Test Article

	Test Article
Identification:	mRNA-1273 LNP Solution
Batch/Lot No.:	DH-03026
Expiration:	18 Nov 2020
Physical Description:	White to off-white dispersion; essentially free of visible particles.
Supplied Stock Concentration:	0.76 mg/mL
Correction Factor:	None
Storage Conditions (temperature set to maintain):	Ultrafrozen -60°C to -90°C

4.2.2. Control Article

	Control Article (Dilution Buffer)
Identification:	20 mM Tris, 8.7% Sucrose, pH 7.5
Batch/Lot No.:	DH-03026.2
Expiration Date:	18 Nov 2020
Physical Description:	Clear colorless solution free from visible particulates
Storage Conditions (temperature set to maintain):	Ultrafrozen -60°C to -90°C

4.3. Reserve Samples

For each batch (lot) of test article and control article, a reserve sample was collected and maintained under the appropriate storage conditions by the Testing Facility.

4.4. Test and Control Article Inventory and Disposition

Records of the receipt, distribution, storage, and disposition of test materials were maintained. With the exception of reserve samples, all unused Sponsor-supplied bulk control article was discarded and unused Sponsor-supplied bulk test article was returned to the Sponsor.

4.5. Dose Formulation and Analysis

4.5.1. Preparation of Control Article

Dose formulations were performed under a biological safety cabinet using aseptic procedures.

The control article, 20 mM Tris, 8.7% Sucrose, pH 7.5, was administered as received. The bulk control article was removed from the freezer and allowed to thaw at room temperature for no more than 1 hour before dose formulation preparation. The storage of control article dose formulations at room temperature did not exceed 4 hours from the time of preparation to the time of dose administration. The formulation was not vortexed or sonicated but was gently swirled to ensure even mixing during formulation. Thawed control article vials were used only on the day of dose formulation preparation once thawed and were not used on subsequent dosing days.

Detailed preparation procedures (i.e., Formulation Batch Records [FBR]) were maintained in the raw data.

Any residual volumes were retained and were discarded prior to study finalization upon Sponsor and Study Director authorization.

4.5.2. Preparation of Test Article Formulations

Dose formulation preparations were performed under a biological safety cabinet using aseptic procedures.

The bulk test article stock was removed from the freezer and allowed to thaw at room temperature for at least 30 minutes (no more than 1 hour) before dose formulation preparation. The test article dosing formulations were prepared by diluting the bulk test article with the control article as necessary to the target concentration for administration and were not filtered. The storage of test article dosing formulations at room temperature did not exceed 4 hours from the time of preparation to the time of dose administration. The formulation was not vortexed or sonicated but was gently inverted 20 times to ensure even mixing during formulation. Stock vials were used only on the day of dose formulation preparation once thawed and were not used on subsequent dosing days.

Detailed preparation procedures (i.e., FBR) were maintained in the raw data.

Any residual volumes were retained and were discarded prior to study finalization upon Sponsor and Study Director authorization.

4.5.3. Sample Collection and Analysis

Dose formulation samples were collected for analysis as indicated in Text Table 2.

Text Table 2
Dose Formulation Sample Collection Schedule

Interval	Concentration	Sampling From
First Preparation: Day 1	Group 1: 5 x 0.5 mL (middle)	Preparation vessel
	Group 2: 5 x 0.5 mL (top, middle, bottom)[a]	
Approximate Middle Preparation: GD 1	Groups 1 and 2: 5 x 0.5 mL (middle)	Preparation vessel
Last Preparation: GD 13	Groups 1 and 2: 5 x 0.5 mL (middle)	Preparation vessel

[a] The homogeneity results obtained from the top, middle, and bottom preparations were averaged and utilized as the concentration results.

All samples to be analyzed were shipped (on dry ice) to Charles River Laboratories Montreal, on the date prepared, when possible. Upon receipt at the analytical laboratory, the samples were stored under ultrafrozen conditions at -60°C to -90°C.

4.5.3.1. Analytical Method

Analyses described below were performed under Test Site Study Number 2100930 by Ion-Exchange High Performance Liquid Chromotography (IEX-HPLC) using a validated analytical procedure (CR-SEN validation study 2100933).

4.5.3.2. Concentration and Homogeneity Analysis

Sample Allocation: Duplicate for analysis, triplicate for backup for Groups 1 and 2. The backup samples were discarded prior to report finalization.

Storage Conditions: Temperature set to maintain -60°C to -90°C. Samples were placed into autoclaved amber glass vials.

Acceptance Criteria: For concentration, the criteria for acceptability was mean sample concentration results within or equal to ± 15% of theoretical concentration. Each individual sample concentration result was within or equal to ± 20%.

For homogeneity, the criteria for acceptability was relative standard deviation (RSD) of concentrations of ≤ 5% for each group.

4.5.3.3. Stability Analysis

The documentation to support the stability of the test article in the control when prepared and stored under the same conditions at concentrations bracketing that used in the present study is on file with the Sponsor.

4.6. Test System

4.6.1. Receipt

A total of 93 timed-mated female Crl:CD(SD) Sprague Dawley rats were received in filtered cartons by truck from Charles River Laboratories, Inc., Raleigh, NC. The body weight range for

female rats was 217 g to 269 g at the initiation of dose administration. The females were approximately 74 days old at the initiation of dose administration.

4.6.2. Justification for Test System and Number of Animals

The test system was selected because: 1) this strain of rat has been demonstrated to be sensitive to reproductive and developmental toxins and has been widely used throughout industry for reproductive and developmental toxicity evaluations; 2) historical data and experience exist at the Testing Facility; and 3) the Test Article is pharmacologically active/immunogenic in the species and strain.

The number of animals chosen for this study is the smallest number considered necessary to provide the minimum number of pregnancies recommended by the applicable guidelines.

4.6.3. Animal Identification

Method: A subcutaneously implanted electronic identification chip.

4.6.4. Environmental Acclimation

After receipt at the Testing Facility, the F0 generation rats were acclimated for at least 7 days prior to initiation of dosing.

4.6.5. Selection, Assignment, Replacement, and Disposition of Animals

The disposition of all animals was documented in the study records.

4.6.5.1. F0 Generation

Female rats were selected for study on the basis of physical condition and body weights recorded during acclimation. Female rats were assigned to groups using a computer-based randomization procedure based on body weights recorded during the acclimation period.

Rats in poor health or at extremes of body weight range were not assigned to groups.

Eighty-eight (88) female rats were assigned to 2 dose groups, 44 rats per group. Additionally, each dose group consisted of two cohorts, 22 rats in each of Cohorts 1 and 2 as described in Text Table 3. Rats were assigned to cohorts following cohabitation.

Text Table 3
Selection and Assignment of Rats

Group No.	Cohort 1 (Caesarean– Sectioning Phase)	Cohort 2 (Natural Delivery Phase)
1	22	22
2	22	22

4.6.5.2. F1 Generation

Day 0 of lactation (postpartum) is defined as the day the delivery of the litter appeared to be completed. If the litter was observed to be completed at the morning viability check, Day 0 of lactation (postpartum) was defined as the previous day. Day 1 of lactation (postpartum) is defined as the first day on which all pups in a litter were individually weighed and clinical observations were recorded. On Day 0/1 of lactation (postpartum) all pups in a litter were sexed.

On Lactation Day 4 (LD 4) a randomization program was used to select F1 generation pups to be culled, and litters were reduced to eight pups each (when possible). Whenever possible, the same number of male and female pups per litter were continued on study.

4.7. Husbandry

All cage sizes and housing conditions were in compliance with the *Guide for the Care and Use of Laboratory Animals.*[4]

4.7.1. Housing

Caging: Polycarbonate cages containing appropriate bedding.

F0 generation rats were co-housed in solid-bottomed cages by dose group (no more than 2 per cage) until cohabitation. During the cohabitation period, one breeder male rat and one female rat were pair housed in the breeder male rat's solid-bottomed cage. After cohabitation, female rats were individually housed until the day of scheduled euthanasia (Cohort 1) or until parturition (Cohort 2), at which time, each dam and delivered litter were housed in a common nesting box during the postpartum period. The male breeder rats were returned to co-housing with their previous same box mates.

Control group animals were housed on a separate rack from the Test Article-treated animals.

4.7.2. Environmental Conditions

Target temperatures of 68°F to 79°F (20°C to 26°C) with a relative target humidity of 30% to 70% were targeted; actual relative humidity ranged as high as 82%. A 12-hour light/12-hour dark cycle was maintained. The study room was independently supplied with a minimum of 10 changes of fresh air per hour that had been passed through 99.97% HEPA filters.

4.7.3. Bedding

Type: Bed-o'Cobs®

Frequency: Changed as often as necessary to keep the animals dry and clean.

Analysis: Results of analysis for environmental contaminants are on file at the Testing Facility. It is considered that there are no known contaminants in the bedding that would interfere with the objectives of the study.

4.7.4. Food

Diet: Certified Rodent Diet® #5002 (PMI® Nutrition International)

Type: Pellets

Frequency: *Ad libitum*, except during designated procedures

Analysis: Results of analysis for nutritional components and environmental contaminants are on file at the Testing Facility. It is considered that there are no known contaminants in the feed that would interfere with the objectives of the study.

4.7.5. Water

Type: All water was from a local source and passed through a reverse osmosis membrane before use. Chlorine was added to the processed water as a bacteriostat; processed water was expected to contain no more than 1.2 ppm chlorine at the time of analysis.

Frequency/Ration: Available *ad libitum* from an automatic watering access system and/or individual water bottles attached to the nesting boxes (except during designated procedures).

Analysis: Periodic analysis of the water is performed, and results of these analyses are on file at the Testing Facility. It is considered that there are no known contaminants in the water that could interfere with the outcome of the study.

4.7.6. Animal Enrichment

Type/Frequency: For psychological/environmental enrichment, animals were socially housed and were provided with Crink-l'Nest™, stainless steel resting lofts, and a chewing item such as *ad libitum* pelleted rodent feed, except when interrupted by study procedures/activities.

Analysis: There are no known contaminants in the animal enrichment that would interfere with the objectives of the study.

4.7.7. Veterinary Care

Veterinary care was available throughout the course of the study, and rats were examined by the veterinary staff as warranted by clinical signs or other changes. All veterinary examinations and recommended therapeutic treatments were documented in the study records and reviewed by the Study Director. Food supplementation included provision of moistened food pellets daily (uneaten food discarded daily) for appetite stimulation for F0 generation rat 5542 (Group 1). None of the medical examinations and/or food supplementation had an adverse impact on the integrity of the study data or on the interpretation of the study results.

4.8. Experimental Design

Text Table 4
Experimental Design – F0 Generation

Group No.	Test Material	Dose Level (µg/dose)	Dose Concentration (mg/mL)	Dose Volume (µL/dose)	Assigned Rat Numbers	
					Cohort 1 (Caesarean-Sectioning Phase)	Cohort 2 (Natural Delivery Phase)
1	Control Article	0	0	200	5501-5513, 5515-5519, 5521-5523, 5528	5514, 5520, 5524-5527, 5529, 5530-5544
2	mRNA-1273	100	0.5	200	5545-5550, 5552, 5554-5557, 5559-5561, 5563-5570	5551, 5553, 5558, 5562, 5571-5588

4.8.1. Administration of Test and Control Articles

4.8.1.1. F0 Generation

Dose Route: Intramuscular injection into the quadriceps; alternating hindlimbs on each dosing occasion.

Frequency: Once on each day of dose administration

Duration: Premating Period: Study Day (SD) 1 (28 days prior to mating) and SD 15 (14 days prior to mating). Study Day 1 is defined as the first day of dose administration.

Gestation Period: GDs 1 and 13.

Special Procedures: The initiation of dose administration occurred at approximately the same time each day, when possible.

- Under no circumstances were the dosing formulations subjected to vortexing or vigorous shaking to avoid disruption of the test article. Before withdrawing a dose formulation into syringes, the dose formulation container was gently swirled to achieve homogeneity and this step was documented.
- The control article was maintained on a separate cart from the test article during dose procedures and was transported in a separate carrier. Only the control article was in the study room during dose administration of Group 1.
- Dose procedures for the control article group were completed before dosing for Group 2 was initiated.
- Dose administration was conducted in sequence from Group 1 to 2, to minimize any potential risk of test article cross-contamination. Personal Protective Equipment (PPE) used for dosing was changed between groups.
- The control article was removed from the study room before dosing for Group 2 was initiated.

4.8.1.2. F1 Generation

F1 generation pups were not directly given the test article or control article formulations but may have been exposed during maternal gestation (*in utero* exposure) or via maternal milk during the lactation period.

4.8.2. Justification of Route and Dose Levels

The intramuscular route of exposure was selected because this is the intended route of human exposure.

The dose level for this study (100 µg/dose) was chosen to approximate the human clinical dose.

4.9. In-life Procedures, Observations, and Measurements - F0 Generation

For deviations, see Appendix 1.

Text Table 5
General In-life Assessments – F0 Generation Females

Parameter	Frequency (minimum required)	Comments
Viability	• At least twice daily	-
Clinical Observations: General	• At least once weekly during the acclimation period • Daily before each dose was administered and daily on non-dosing days • Daily during the postdose period (including the day of scheduled euthanasia).	-
Clinical Observations: Postdose Observations	• 6 hours following dose administration.	-
Maternal Observations:	• Daily during the postpartum period (Cohort 2).	Maternal behavior was recorded.
Individual Body Weights	• On the day after arrival and at least once weekly during acclimation. • On SDs, 1,8, 15, 22, and 28 and on GDs 0, 1, 6, 10, 13, 15, 18, 21, and 25 (if necessary). • LD 1, 4, 7, 10, 14, 18 and 21 (Cohort 2)	-
Food Consumption	• Once weekly during the dose period until cohabitation. • On GDs 0, 1, 6, 10, 13, 15, 18, 21, and 25 (if necessary). • On LDs 1, 4, 7, 10 and 14 (Cohort 2)	Food consumption values were recorded. During cohabitation, when two rats occupied the same nesting box with one food jar, replenishment of the food jars was documented. Individual values were not recorded or tabulated. Food consumption was not tabulated after Day 14 postpartum, when it was expected that pups began to consume maternal food.
Estrous Cycle Evaluations	Samples were collected from females for 14 consecutive days before initiation of the cohabitation period and then until spermatozoa were observed in a smear of the vaginal contents and/or a copulatory plug was observed *in situ* during the cohabitation period.	Estrous cycles were evaluated by examining the vaginal cytology of samples obtained by vaginal lavage.

Parameter	Frequency (minimum required)	Comments
Reproductive Capacity	Within each dose group, rats were assigned to cohabitation (i.e., pairing), one breeder male per one female. The cohabitation period consisted of a maximum of 7 days. Females observed with spermatozoa in a smear of the vaginal contents and/or a copulatory plug observed *in situ* were considered to be at GD 0 and assigned to individual housing. Females not mated after completion of the 7-day cohabitation period were considered to be at GD 0 on the last day of cohabitation, assigned to individual housing (i.e., solid bottom or wire-bottom cages) and were euthanized 25 days after the end of the cohabitation period (for rats that did not deliver a litter). Rats were assigned to either Cohort 1 or 2 following cohabitation.	-
Natural Delivery Observations	Female rats were evaluated for: • Adverse clinical signs observed • Duration of Gestation (GD 0 to the time the first pup was observed) • Litter Size (defined as all pups delivered) • Pup Viability at Birth	-

4.10. In-life Procedures, Observations, and Measurements – F1 Generation

The in-life procedures, observations, and measurements listed below were performed for all F1 generation litters, with the litter as the unit of measure.

Text Table 6
General In-life Assessments – F0 Generation Females

Parameter	Frequency (minimum required)	Comments
Viability	Litters were observed for dead pups at least twice daily and the pups in each litter were counted at least once daily during the preweaning period.	-
Clinical Observations: General Appearance	At least once daily.	-
Individual Body Weights	Day 1, 4, 7, 10, 14, 18, and 21 postpartum.	-

4.11. Laboratory Evaluations – Antibody Evaluations

For deviations, see Appendix 1.

4.11.1. Maternal Samples (Cohorts 1 and 2)

Samples were collected according to Text Table 7.

Text Table 7
Antibody Sample Collection

Group Nos.	Cohort	Time Points					
		SD 1[a]	SD 15[a]	GD 1[a]	GD 13[a]	GD 21[b]	LD 21[b]
1-2	1	X	X	X	X	X	-
1-2	2	X	X	X	X	-	X

Method/Comments:	Jugular vein (SD 1, 15, GD 1, 13 in-life blood collections) or via the vena cava while under isoflurane/oxygen anesthesia (GD 21 and LD 21 terminal blood collections).
Target Volume (mL):	1.0 mL
Anticoagulant:	None, in SST
Special Requirements:	None
Processing:	Serum

X = Sample collected; - = Not applicable, SST = serum separator tube
[a] Sample collected prior to dose administration.
[b] Terminal blood sample collection.

4.11.2. Fetal Samples (Cohort 1)

On GD 21, pooled fetal blood was collected via decapitation from at least the first 5 fetuses assigned to visceral examination, to achieve target volume (more were used if deemed necessary and documented in the raw data). In cases where there were not enough viable fetuses assigned to visceral examinations, the carotid blood collection route was utilized from fetuses assigned to skeletal examination.

Target Volume: 1.0 mL pooled per litter

Anticoagulant: None/Serum separator tube

4.11.3. Pup Samples (Cohort 2)

On the day of scheduled euthanasia (LD 21), blood was collected from 2 pups per litter (1 male and 1 female, when possible) via the inferior vena cava while under isofluorane/oxygen anesthesia.

Target Volume: 1.0 mL pooled per litter

Anticoagulant: None/Serum separator tube

4.11.4. Antibody Analysis Sample Processing

Text Table 8
Antibody Sample Processing

Centrifugation	Aliquot 1 Volume	Aliquot 2 Volume	Storage Conditions
1800 g for 10 minutes Approximately 4°C	At least 240 µL (serum)	Remaining (serum)	-70°C

The blood samples were mixed gently and were centrifuged as soon as practical following an at least 20 minute clot time (not exceeding 1 hour). Blood samples were centrifuged for 10 minutes at 1800 g in refrigerated centrifuge (4°C). The resultant serum was separated into two aliquots as described in Text Table 8, transferred to uniquely labeled clear polypropylene tubes, and frozen immediately over dry ice until stored in a freezer set to maintain -70°C.

The first set of samples (aliquot 1/occasion) was shipped on dry ice with a temperature monitor to the Test Site for antibody analysis after the end of the treatment period. The second set of samples (aliquot 2/occasion) were maintained at the Testing Facility as back up samples. The Test Site for antibody analysis and the Sponsor Representative were notified before shipment of the samples. Samples were stored at the Test Site in a freezer set to maintain -80°C until analysis.

4.11.5. Antibody Sample Analysis

For deviations, see Appendix 1.

The samples were analyzed for antibodies produced as a result of mRNA-1273 administration using a qualified analytical procedure (BS-3857).

Antibody responses to SARS-CoV2 S protein were evaluated using optimized indirect ELISA assay.

In brief, 96-well microtiter plates were coated with SARS-CoV2 Spike protein (S2P) and incubated overnight. 5-Step serial dilutions of rat or pup sera were added, and the bound antibody detected with HRP-conjugated goat anti-rat IgG (KPL), followed by incubation with TMB substrate (KPL). The absorbance measured at OD650nm.

Antibody titers were calculated as “Antibody Units/mL” based on the four-parameter logistic curve fit (4PL) of a hyperimmune rat standard curve using a using VersaMax™ software (Molecular devices Inc.).

The residual aliquot 1 samples were archived at the Test Site. The aliquot 2 samples were archived at the Testing Facility.

4.12. Terminal Procedures – F0 Generation

For deviations, see Appendix 1.

Terminal procedures are summarized in Text Table 9 and Text Table 10.

Text Table 9
Terminal Procedures – F0 Generation Female Rats – Cohort 1

Group No.	Scheduled Euthanasia Day	Necropsy Procedures				Histology Processing and Microscopic Evaluation
		Ovarian/ Uterine Examination	Necropsy	Tissue Collection[a]	Organ Weights	
1	GD 21	X	X	X	X[b]	-
2						
Unscheduled Deaths		-	-	-	-	-

X = Procedure conducted; - = Not applicable; GD = Gestation Day.
[a] See Text Table 11 (Tissue Collection and Preservation) for tissues retained for possible future evaluation.
[b] The gravid uterus and the placentae were weighed for all rats that survived to scheduled euthanasia. For deviations, see Appendix 1.

Text Table 10
Terminal Procedures – F0 Generation Female Rats – Cohort 2

Group No.	Scheduled Euthanasia Day	Necropsy Procedures				Histology Processing and Microscopic Evaluation
		Ovarian/ Uterine Examination	Necropsy	Tissue Collection[a]	Organ Weights	
1	LD 21	X	X	X	-	-
2						
Unscheduled Deaths		-	-	-	-	-
Dams that did Not Deliver	GD 25	X	X	X	-	-
Dams with No Surviving Pups	b	X	X	X	-	-

X = Procedure conducted; - = Not applicable; GD = Gestation Day; LD = Lactation Day.
[a] See Text Table 11 (Tissue Collection and Preservation) for tissues retained for possible future evaluation.
[b] On the day the observation was made.

4.12.1. Method of Euthanasia

The GD 25 females, the dams with no confirmed date of mating and the F0 generation dams with no surviving pups were euthanized by carbon dioxide asphyxiation.

All other rats were euthanized via exsanguination following blood sample collection from the inferior vena cava while under isoflurane/oxygen anesthesia.

All live fetuses selected for Cohort 1 blood collection were euthanized by decapitation. All other fetuses were euthanized by an intraperitoneal injection of sodium pentobarbital (390 mg/mL).

4.12.2. Scheduled Euthanasia

4.12.2.1. Cohort 1

On GD 21, female rats assigned to Cohort 1 were euthanized, blood samples were collected as described in Section 4.11 (Laboratory Evaluations - Antibody Evaluations), and rats were examined for ovarian and uterine contents (Section 4.12.2.3, Ovarian and Uterine Examinations)

and gross lesions (Section 4.12.3, Necropsy) (including examination of the injection site). See Section 4.12.4 (Tissue Collection and Preservation) for tissues retained for possible future evaluation.

4.12.2.2. Cohort 2

After completion of the 21-Day postpartum period, female rats assigned to Cohort 2 were euthanized, blood samples were collected as described in Section 4.11 (Laboratory Evaluations - Antibody Evaluations), and rats were examined for gross lesions (including examination of the injection site). One dam with no surviving pups was euthanized after the last pup was found dead or missing, presumed cannibalized.

The rats were examined as described in Section 4.12.2.3 (Ovarian and Uterine Examinations) and Section 4.12.3 (Necropsy). See Section 4.12.4 (Tissue Collection and Preservation) for tissues retained for possible future evaluation.

Females that did not mate after the completion of the 7-day cohabitation period were euthanized 25 days after the end of the cohabitation period (females that did not deliver a litter) or continued on study (females that delivered) at the discretion of the Study Director. If euthanized, rats were examined for gross lesions (including examination of the injection site). The rats were examined as described in Section 4.12.2.3 (Ovarian and Uterine Examinations) and Section 4.12.3 (Necropsy). See Section 4.12.4 (Tissue Collection and Preservation) for tissues retained for possible future evaluation.

4.12.2.3. Ovarian and Uterine Examinations

For deviations, see Appendix 1.

4.12.2.3.1. Cohort 1

The reproductive tract was dissected from the abdominal cavity. The gravid uterus was weighed. The uterus was opened and the contents were examined. The fetuses were removed from the uterus and placed in individual containers. Each placenta was weighed.

The ovaries and uterus were examined for number and distribution of corpora lutea, implantation sites, placentae (size, color, or shape), live and dead fetuses, and early and late resorptions.

Uteri of apparently nonpregnant rats were examined while being pressed between glass plates to confirm the absence of implantation sites and were retained in 10% neutral buffered formalin and were archived.

4.12.2.3.2. Cohort 2

The reproductive tract was dissected from the abdominal cavity. The number and distribution of implantation sites were recorded.

Uteri of apparently nonpregnant rats were examined while being pressed between glass plates to confirm the absence of implantation sites. Uteri and ovaries of apparently nonpregnant rats were retained in 10% neutral buffered formalin and were archived.

4.12.3. Necropsy

A gross necropsy of the thoracic, abdominal and pelvic viscera was performed for each scheduled euthanized rat.

Images were generated for illustration of or consultation on gross observations. Generation of such images were documented. Images and associated documentation were retained and were archived.

4.12.4. Tissue Collection and Preservation

Representative samples of the tissues identified in Text Table 11 were collected from all F0 generation rats and preserved in 10% neutral buffered formalin, unless otherwise indicated. Unless specifically cited, all other tissues were discarded.

A table of random units was used to select one control group rat from which all tissues examined at necropsy were retained, in order to provide control tissues for any possible future evaluations of gross lesions.

Text Table 11
Tissue Collection and Preservation - F0 Generation Scheduled Euthanasia

Tissue	Weighed	Collected	Comment
Administration site	-	X	All scheduled euthanized rats.
Gravid Uterus	X	-	All pregnant rats at scheduled euthanasia
Gross lesions	-	X	All scheduled euthanized rats.
Placentae	X	-	All pregnant rats at scheduled euthanasia.

X = Procedure conducted

4.13. Terminal Procedures – F1 Generation (Cohort 2)

For deviations, see Appendix 1.

4.13.1. Method of Euthanasia

F1 generation pups assigned to Cohort 2 blood collections were euthanized via exsanguination following blood sample collections.

All other F1 generation pups were euthanized by an intraperitoneal injection of sodium pentobarbital (390 mg/mL) (pups ≤ 14 days of age) or by carbon dioxide asphyxiation (pups ≥15 days of age).

4.13.2. Unscheduled Deaths

4.13.2.1. Days 0 to 21 Postpartum

Pups that were found dead during delivery or at the completion of littering (Days 0 or 1 postpartum) were evaluated for vital status at birth. The lungs were removed and immersed in water. Pups with lungs that sank were identified as stillborn; pups with lungs that floated were identified as liveborn and to have died shortly after birth. Pups (whole animal) were preserved in 10% neutral buffered formalin for possible future evaluation.

Pups that died (Days 1 to 21 postpartum) or were euthanized (Days 0 to 21 postpartum) before scheduled termination were examined for gross lesions and the cause of death or condition as soon as possible after the observation was made. Pups euthanized on Days 0 to 4 postpartum or found on Days 1 to 4 postpartum were preserved in 10% neutral buffered formalin (whole animal) for possible future evaluation. For the one pup found dead (5544-5) on PND 5, the whole animal was fixed in 10% NBF (except for the eyes/optic nerve/harderian gland and testes which were retained in Davidson's and Modified Davidson's fixative, respectively).

4.13.3. Scheduled Euthanasia

Pups culled on Day 4 postpartum were examined for gross lesions as described in Section 4.13.4 (Necropsy). Necropsy included a single cross-section of the head at the level of the frontal-parietal suture and examination of the cross-sectioned brain for apparent hydrocephaly.

On Day 21 postpartum, F1 generation rats were euthanized and examined for gross lesions (Section 4.13.4, Necropsy). Necropsy included a single cross-section of the head at the level of the frontal-parietal suture and examination of the cross-sectioned brain for apparent hydrocephaly. See Section 4.13.5 (Tissue Collection and Preservation) for tissues retained for possible future evaluation.

4.13.4. Necropsy

A gross necropsy of the thoracic, abdominal and pelvic viscera was performed for each animal.

Images were generated for illustration of or consultation on gross observations. Generation of such images were documented. Images and associated documentation were retained and were archived.

4.13.5. Tissue Collection and Preservation

Representative samples of the tissues identified in Text Table 12 were collected and preserved in 10% neutral buffered formalin, unless otherwise indicated. Unless specifically cited, all other tissues were discarded.

A table of random units was used to select one F1 generation control group rat of each sex from which all tissues examined at necropsy were retained, in order to provide control tissues for any possible histopathological evaluations of gross lesions.

Text Table 12
Tissue Collection and Preservation – F1 Generation Scheduled Euthanasia

Tissue	Collected	Comment
Gross Lesions	X	All scheduled euthanized animals.

5. FETAL EXAMINATIONS – COHORT 1

Representative photographs of external, visceral and skeletal abnormalities were taken at the discretion of the Study Director or designee for illustration of, or consultation on, observations. Photographs will not be included in the report but were retained as electronic images and archived with the raw data. Abnormalities were classified as malformations, variations, and incidental.

Examination	Procedure
Conceptuses *in utero*	Examined for external, visceral, and/or skeletal abnormalities to the extent possible.
Late Resorptions	Examined for external abnormalities to the extent possible, and discarded without further examination
Body Weights	Recorded for each live fetus.
External	All fetuses were examined for sex and for external abnormalities.
Visceral	Approximately one-half of the fetuses in each litter were examined for visceral abnormalities by using a modification of the microdissection technique of Staples.[5] Each fetus was fixed in Bouin's solution and the heads were subsequently examined by free-hand sectioning;[6] head sections with abnormal findings were stored in alcohol. All other head sections were discarded. The decapitated carcasses were not retained.
Skeletal	The remaining fetuses (approximately one-half of the fetuses in each litter) were examined for skeletal abnormalities after staining with alizarin red S.[7] Following examination, skeletal preparations were retained in glycerin with thymol added as a preservative.

6. STATISTICAL ANALYSIS

Any data collected during the predose period were not tabulated or summarized, unless applicable to analyses in the proceeding sections. Litter values were used, where appropriate.

Clinical and necropsy observations data were summarized but no inferential statistical analysis was performed.

Numerical data collected on scheduled occasions were summarized and statistically analyzed as indicated below according to sex and occasion or by litter.

6.1. Descriptive Statistical Analyses

Means, standard deviations (or % coefficient of variation or standard error, when deemed appropriate), ratio, percentages, numbers, and/or incidences were reported as appropriate by dataset.

6.2. Constructed Variables

The following parental indices and litter calculations were included, where applicable:

Female Mating Index = $\frac{\text{Number of Females with Evidence of Mating (or no confirmed mating date and pregnant)}}{\text{Number of Females Paired}}$

Female Fertility Index = $\frac{\text{Number of Pregnant Females}}{\text{Number of Females with Evidence of Mating (or no confirmed mating date and pregnant)}}$

Female Pregnancy Index = $\frac{\text{Number of Pregnant Females}}{\text{Number of Females Paired}}$

Pre-Implantation Loss = $\frac{\text{Number of Corpora Lutea – Number of Implants}}{\text{Number of Corpora Lutea}} \times 100$

Post-Implantation Loss = $\frac{\text{Number of Implants – Number of Live Fetuses}}{\text{Number of Implants}} \times 100$

Sex Ratio (% males) = $\frac{\text{Number Male Fetuses}}{\text{Total Number of Fetuses}} \times 100$

Litter % of Fetuses with Abnormalities = $\frac{\text{Number of Fetuses in Litter with a given Finding}}{\text{Number of Fetuses in Litter Examined}} \times 100$

The following natural delivery/reproductive parameters were included, as appropriate:

- Gestation Length: The gestation length was calculated from GD 0 to the day the first pup was observed.
- Female Pregnancy Index: $\frac{\text{Number of Pregnant Females}}{\text{Number of Females Paired}}$
- Gestation Index: Percentage of pregnancies that resulted in birth of live litters

  $\frac{\text{Number of Animals with Live Offspring}}{\text{Number of Animals Pregnant}} \times 100$
- Live Birth Index: Percentage of pups born alive.

  $\frac{\text{Number of Live Newborn Pups}}{\text{Number of Newborn Pups}} \times 100$
- Viability Index: Percentage of pups born that survived 4 days postpartum

  $\frac{\text{Number of Live Pups on Day 4 Postpartum}}{\text{Number of Live Newborn Pups}} \times 100$
- Lactation Index: Percentage of pups that survived 21 days postpartum

  $\frac{\text{Number of Live Pups on Day 21 Postpartum}}{\text{Number of Live Pups on Day 4 (postculling) Postpartum}} \times 100$

- Post-Implantation Loss/Litter $\frac{\text{Number of Implants – Total Newborn Pups}}{\text{Number of Implants}} \times 100$

- Sex Ratio (% males) Percentage of male pups per litter

  $\frac{\text{Number of Live Male Pups}}{\text{Total Number of Live Pups}} \times 100$

6.3. Inferential Statistical Methods

All statistical tests were conducted at the 5% significance level. All pairwise comparisons were conducted using two sided tests and were reported at the 1% and 5% levels, unless otherwise noted.

Analyses were conducted and pairwise comparisons of interest were carried out as listed below:

F0 Generation/Litters (Preweaning)		
Group 2	vs.	Group 1

Analyses were performed according to the matrix below when possible but excluded any group with less than 3 observations.

Text Table 13
Statistical Matrix Statistical Matrix

Variables for Inferential Analysis	Statistical Method		
	Parametric/ Non-Parametric	**Non-Parametric**	**Incidence**
General Data			
Body Weight[a]	X	-	-
Body Weight Gains[a]	X	-	-
Food Consumption[a]	X	-	-
Parental Indices and Mortality	-	-	X
Gravid Uterine Weight and Corrected Maternal Body Weights[a]	X	-	-
Natural Delivery and Litter Data			
Natural Delivery and Litter Observations (Proportional) (e.g. Pregnant, Females with Liveborn, Gestation Index, Female with Liveborn)	-	-	X
Natural Delivery and Litter Observations (Count) (e.g. Gestation Length, Live Pups, Implantation Sites)	-	X	-
Litter Observations (Continuous) (e.g. Sex Ratio - Males, Mean Litter Bodyweights)	X	-	-
Live Birth Index	-	X	-
Estrous Cycling, Mating and Fertility			
Number of Estrous Cycles and Mean Cycle Length	-	X	-
Pregnancy, Mating and Fertility Indices	-	-	X
Precoital Interval[b]	-	X	-
Caesarean-section Late Gestation[d]			
Ovarian and Uterine Examinations[b]	-	X	-
Litter Observations (Litter Means)[b, d]	X		-
Litter % of Fetuses with Gross/External/Visceral/Skeletal Abnormalities[e]	-	X	-
Mean Fetal Ossification Sites[e]	-	X	-

[a] Excludes animals not pregnant from the gestation phase summarization and statistical analysis.
[b] Excludes animals with no confirmed mating date from summarization and statistical analysis.
[c] Excludes animals euthanized preterminally from summarization and statistical analysis.
[d] Presented for males, females and sexes combined; live fetuses only.
[e] Presented for sexes combined; live fetuses only.

6.4. Parametric/Non-parametric

Levene's test was used to assess the homogeneity of group variances. The groups were compared using a Dunnett's test if Levene's test was not significant or Dunn's test if it was significant.

6.5. Non-Parametric

Datasets were compared using a Dunn's test.

6.6. Incidence

A Fisher's exact test was used to conduct pairwise group comparisons of interest.

7. COMPUTERIZED SYSTEMS

Critical computerized systems used in the study are listed below or presented in the appropriate Phase Report.

Text Table 14
Critical Computerized Systems

System Name	Description of Data Collected and/or Analyzed
(b) (4)	Test material receipt, accountability, formulation activities, in-life (e.g., clinical observations, body weights, food consumption), and/or postmortem (e.g., pathology, ovarian and uterine contents, and fetal parameters)
	Temperature, humidity and light cycle times
	Deviations
	Reporting
	Collection of Part 11 compliant signatures

8. RETENTION OF RECORDS, SAMPLES, AND SPECIMENS

All study-specific raw data, documentation, samples, and specimens from this study generated at the Testing Facility were archived at the Testing Facility by no later than the date of final report issue. At least one year after issue of the draft report, the Sponsor will be contacted.

Electronic records and data generated by the Testing Facility were archived at the Charles River Laboratories facility location in Wilmington, MA by no later than the date of final report issue.

All study-specific raw data, documentation and the Final Report generated from the Analytical Chemistry phase were archived per the final phase report.

All study-specific documentation generated from the Antibody Analysis phase were archived at the Test Site and are maintained electronically on the server for at least 5 years.

9. RESULTS

9.1. Dose Formulation Analyses

(Appendix 3)

No mRNA-1273 was identified in the control article formulation.

All mRNA-1273 samples analyzed had mean concentrations within or equal to the acceptance criteria of ± 15% (individual values within or equal to ± 20%) of their theoretical concentrations. The RSD of concentrations for all samples in each group analyzed was within the acceptance criteria of ≤ 5%. All formulations were acceptable for use on study.

9.2. F0 Generation

9.2.1. Mortality

(Appendix 4, Appendix 5, and Appendix 6)

There was no mRNA-1273-related mortality in the study.

There was a single early death in the control group during the course of this study. One rat (No. 5520) administered the control article was euthanized on LD 3 due to no surviving pups. This rat was administered 4 doses of the control article and delivered 13 live pups on GD 21. There were no adverse clinical observations or body weight changes observed prior to euthanasia. The rat was not observed nursing the pups during the first two days following delivery. All pups were observed cold to touch on Day 1 postpartum. On Day 2 postpartum, 6 pups were found dead, 6 pups were missing (presumed cannibalized) and 1 pup was observed with moderate dehydration and cold to touch. On Day 3 postpartum, the last pup was missing and presumed cannibalized. The death of the pups is related to the lack of maternal care for this litter. There were no macroscopic changes observed at the maternal gross necropsy examination. All other rats were euthanized at the scheduled termination interval.

9.2.2. Maternal Clinical Observations

(Table 1, Table 2, Table 3, Appendix 7, Appendix 8, and Appendix 9)

The rats administered mRNA-1273 were observed with thin fur cover, swollen hindlimbs and limited usage of the hindlimb during the premating, gestation and/or lactation phases of the study, with the most observations observed following administration on GD 13. These observations are considered related to the administration of mRNA-1273 but were not considered adverse as these effects can be expected following test article administration. Limited usage of the hindlimb was observed from GD 13-15 and swollen hindlimb was observed from GD 13-20 in rats administered mRNA-1273. Only thin fur cover was still present during the lactation phase and was resolved by LD 18.

The other observations were few in number, sporadic in nature and/or are consistent with this Test System.

9.2.3. Maternal Body Weights and Body Weight Gains

(Figure 1, Figure 2, Figure 3, Table 4, Table 5, Table 6, Table 7, Table 8, Table 9 Appendix 10, Appendix 11, Appendix 12, Appendix 13, Appendix 14, and Appendix 15)

There were no mRNA-1273-related body weights or body weight gain changes throughout the study.

Two instances of statistically-significant increases in body weight gains were observed in the mRNA-1273 group, as compared to controls; however, the differences were not considered related to mRNA-1273 since the increases were only observed in a single isolated interval in the gestation and lactation phases and there were no significant differences in body weights or any trends that would indicate a test article effect.

9.2.4. Maternal Food Consumption

(Table 10, Table 11, Table 12, Appendix 16, Appendix 17, and Appendix 18)

There were no mRNA-1273-related changes in food consumption throughout the study.

There were scattered instances of statistically-significant increases or decreases in food consumption in the group administered mRNA-1273, however, these changes were not consistent with body weight changes and did not have an overall effect on the rats, in comparison with the group administered the control article.

9.2.5. Estrous Cycling

(Table 13, Appendix 19, and Appendix 20)

There were no mRNA-1273-related changes in estrous cycling during precohabitation.

Although the mean number of cycle lengths was statistically-significantly higher in the mRNA-1273 group as compared to the control group, this was not considered mRNA-1273-related because there were no statistically significant differences in the number of cycles, mating or fertility parameters were not impacted, and this difference represented normal biological variations for the number of animals being evaluated.

9.2.6. Mating and Fertility

(Table 14, Table 15, Appendix 21, and Appendix 22)

There were no mRNA-1273-related effects on mating and fertility in the rats assigned to the Caesarean-section and natural delivery phases.

Forty-four (44) female rats in each of the control and mRNA-1273 groups were paired with male breeders and 42 and 39 females in the control and mRNA-1273 groups, respectively, had mating confirmed. The pre-coital interval was 2.2 days in the control group and 2.1 days in the mRNA-1273 group. There were no rats in either group that were pregnant with no confirmed mating. Mating occurred in 95.5% of the rats in the control group and 88.6% of the rats in the mRNA-1273 group. There were 41 and 37 pregnant rats in the control and mRNA-1273 groups, respectively. The female fertility index was 97.6% and 94.9% in the control and mRNA-1273 groups, respectively. The female pregnancy index (number of rats mating/number of rats in the group) was 93.2% and 84.1% in the control and mRNA-1273 groups, respectively.

9.2.7. Ovarian and Uterine Observations and Litter Observations

(Table 16, Table 17, Appendix 23, Appendix 24, Appendix 25, and Appendix 26)

There were no mRNA-1273-related effects on ovarian/uterine examination or litter parameters. In the surviving rats assigned to ovarian/uterine and litter examinations on GD 21, pregnancy occurred in 21 (95.5%) rats in the control group and 22 (100.0%) rats in the mRNA-1273 group.

The litter averages for corpora lutea, implantations, percentage of pre-implantation loss, litter sizes, live fetuses, early and late resorptions, percentage of post-implantation loss, percentage of rats with any resorptions, percentage of resorbed conceptuses per litter, percentage of rats with all conceptuses resorbed, percentage of live male fetuses, percentage of rats with viable fetuses, fetal body weights (total, male, and female), gravid uterine weights and corrected maternal body weights were comparable between the dose groups and did not significantly differ. No rat had a litter consisting of only resorbed conceptuses. There were no dead fetuses. All placentae appeared normal and the mean litter placental weights were comparable between the dose groups and did not significantly differ.

9.2.8. Maternal Gross Pathology Observations

(Table 20, Table 21, Table 22, Appendix 28, Appendix 29, and Appendix 30)

There were no mRNA-1273-related maternal gross findings.

9.2.9. Fetal Examinations

(Table 18, Table 19, Appendix 26, and Appendix 27)

Fetal observations were defined as: 1) malformations (irreversible changes that occur at low incidences in this species and strain); or 2) variations (common findings in this species and strain and reversible delays or accelerations in development). Litter means were calculated for specific fetal ossification sites as part of the evaluation of the degree of fetal ossification.

Fetal evaluations were based on 278 and 308 live, GD 21 Caesarean-delivered fetuses in 21 and 22 litters in control and mRNA-1273 dose groups, respectively. Each fetus was examined for external abnormalities. Of these fetuses, 134 and 150 fetuses were examined for visceral abnormalities and 144 and 158 fetuses were examined for skeletal abnormalities and fetal ossification site averages in the control and mRNA-1273 dose groups, respectively.

9.2.9.1. External Abnormalities

There were no mRNA-1273-related malformations or variations in the control or mRNA-1273 groups at fetal external examination.

Fetal external examination revealed one fetus in the control group with a protruding tongue, absent anus and misshapen genital tubercle.

9.2.9.2. Visceral Examination

There were no mRNA-1273-related malformations or variations in the control or mRNA-1273 groups at the visceral examination.

All soft tissue abnormalities that occurred on study were considered to be unrelated to administration of mRNA-1273 because the abnormality occurred in a single fetus on study or in each group and/or the litter incidence, the most relevant parameter, was within the range of

historical control data for the Testing Facility (see Appendix 40, Historical Control Data). These abnormalities consisted of an absent innominate artery, absent caudate process lobe of the lung, moderate or severe dilation of the left or bilateral ureters and moderate dilation of the lateral ventricles of the brain.

9.2.9.3. Skeletal Examination

There were no mRNA-1273-related skeletal malformations observed. mRNA-1273-related variations were observed at skeletal examination. There was a statistically significant increase in the number of fetuses in the mRNA-1273 group that had common skeletal variations of 1 or more nodules on the ribs and 1 or more wavy ribs, as compared with controls. Wavy ribs appeared in 6 fetuses in 4 litters for a fetal prevalence of 4.03% and a litter prevalence of 18.2%. Rib nodules appeared in 5 of those 6 fetuses. The fetal and litter incidence of wavy ribs exceeded the range observed historically at the Testing Facility (see Appendix 40, Historical Control Data) and the fetal and litter incidence of rib nodules was within the range. These findings were not considered adverse because there was no effect on pup growth and viability in the delivered litters, wavy ribs and rib nodules are known to resolve postnatally without medical intervention and these findings were observed without any other indicators of developmental toxicity.

All other skeletal abnormalities were considered to be unrelated to maternal administration of mRNA-1273 because: 1) the findings occurred at a low incidence; 2) the number of fetuses/litter affected was similar to the control group; and/or 3) the litter and fetal incidences were within the historical range of the Testing Facility (see Appendix 40, Historical Control Data).

9.2.9.4. Fetal Ossification Site Averages

(Table 19 and Appendix 27)

There were no mRNA-1273-related effects on the mean number of ossification sites per fetus per litter.

The average numbers of ossification sites per fetus for the hyoid, vertebrae (cervical, thoracic, lumbar, sacral, and caudal), ribs, sternum (manubrium, sternal centers, and xiphoid), forelimbs (carpals, metacarpals, and phalanges), hindlimbs (tarsals, metatarsals, and phalanges) in the mRNA-1273 group were comparable to the control group.

9.3. Natural Delivery and Litter Observations (F1 Generation Pups)

(Table 23, Table 24, Table 26, Appendix 31, Appendix 32, and Appendix 34)

There were no mRNA-1273-related effects on any natural delivery or litter observation parameters.

The numbers of rats delivering litters, the duration of gestation, averages for implantation sites per delivered litter, gestation index (number of dams with one or more liveborn pups/number of pregnant rats), litter sizes, viability and lactation indices and percentage of live male pups per litter were comparable between groups. Pregnancy occurred in 20 (90.9%) and 15 (68.2%) of the 22 and 22 rats assigned to the natural delivery phase in the control and mRNA-1273 dose groups, respectively. There were 20 and 15 rats that delivered a litter with 1 or more liveborn pups available for evaluation in the two respective dose groups.

9.3.1. Mortality (F1 Generation Pups)

(Table 28, Appendix 37 and Appendix 38)

There were no mortalities in the F1 generation pups attributed to maternal treatment with mRNA-1273.

There were 18 and 5 found dead or stillborn pups in the control and mRNA-1273 dose groups, respectively.

9.3.2. Clinical Observations (F1 Generation Pups)

(Table 25 and Appendix 33)

There were no effects on postpartum maternal care of offspring and no clinical observations in the F1 generation pups attributed to maternal treatment with mRNA-1273.

All clinical observations during the course of the study were considered unrelated to administration of mRNA-1273 because: 1) the observation only occurred in one pup; 2) the observations was only observed in a single litter; 3) the observation was observed at an increased incidence in the control group; and/or 4) the observation is common in this species and strain of laboratory animal. The clinical signs observed included a skin scab, dehydration, cold to touch, red discharge, ungroomed fur, no milk band present and pale, purple or black discolored skin.

9.3.3. Pup Body Weights

(Table 27, Appendix 35, and Appendix 36)

There were no mRNA-1273-related changes in mean pup body weights.

There were scattered instances of statistically-significant increases in mean pup body weights observed in the mRNA-1273 group as compared to controls, that are not considered related to the administration of mRNA-1273 since only increases were observed and were limited to female pups and combined sexes at two intervals.

9.3.4. Gross Pathology (F1 Generation Pups)

(Table 28 and Appendix 38)

There were no necropsy observations in any of the F1 generation pups attributed to maternal administration of mRNA-1273.

Among the pups that were found dead or stillborn and necropsied, there was 1 pup in the control group with moderate brain dilation. At scheduled euthanasia, 1 pup in the mRNA-1273 dose group was observed with bilateral, small, minimal renal papilla and another pup from the same litter was observed with left, small, moderate renal papilla. These findings were not considered related to mRNA-1273 because the observations occurred only in 2 pups from a single litter. All other pups in this litter and all other litters appeared normal at the gross necropsy examination.

9.3.5. Antibody Analysis Evaluations

(Appendix 39)

Robust IgG response to S2P antigen was observed in both the F0 and F1generation rats following immunization of F0 rats with mRNA-1273. In the F0 rats, peak titer of 442,138 AU/mL was reached on GD 13. Titers subsequently plateaued at parturition (GD 21) and stayed relatively constant through LD 21. High IgG antibodies to S2P were also observed in

GD 21 fetuses and LD 21 pups indicating strong transfer of antibodies from mother to fetus and from mother to pups.

Four maternal samples (Animal No's. 5506, 5509, 5515 and 5543) from Group 1 (Control) exhibited signals above the limit of detection, across timepoints SD 1, SD 15, GD 1 and GD 13. The elevated signals appeared to be inherent to these four rats, since the re-tested data were consistent with the original data.

10. CONCLUSION

In conclusion, maternal administration of mRNA-1273 on SD 1 (28 days prior to mating), SD 15 (14 days prior to mating), GD 1 and GD 13 did not have any adverse effects on the F0 or F1 generations. mRNA-1273-related, non-adverse effects were limited to an increase in the number of fetuses with common skeletal variations of 1 or more rib nodules and 1 or more wavy ribs with no effect on the viability and growth on the F1 generation pups.

11. REFERENCES

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3. Food and Drug Administration (FDA). Guidance for Industry: Considerations for developmental toxicity studies for preventative and therapeutic vaccines for infectious disease indications, CBER Division of Vaccines and related products (February 2006).
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5. Staples RE. Detection of visceral alterations in mammalian fetuses. *Teratology* 1974;9(3):A37-A38.
6. Wilson JG. Methods for administering agents and detecting malformations in experimental animals. In: Wilson JG, Warkany J, editors. *Teratology: principles and techniques*. Chicago (IL): University of Chicago Press; 1965. p. 262-77.
7. Staples RE, Schnell VL. Refinements in rapid clearing technic in the KOH-alizarin red S method for fetal bone. *Stain Technol* 1964;39:61-3.

Figure 1

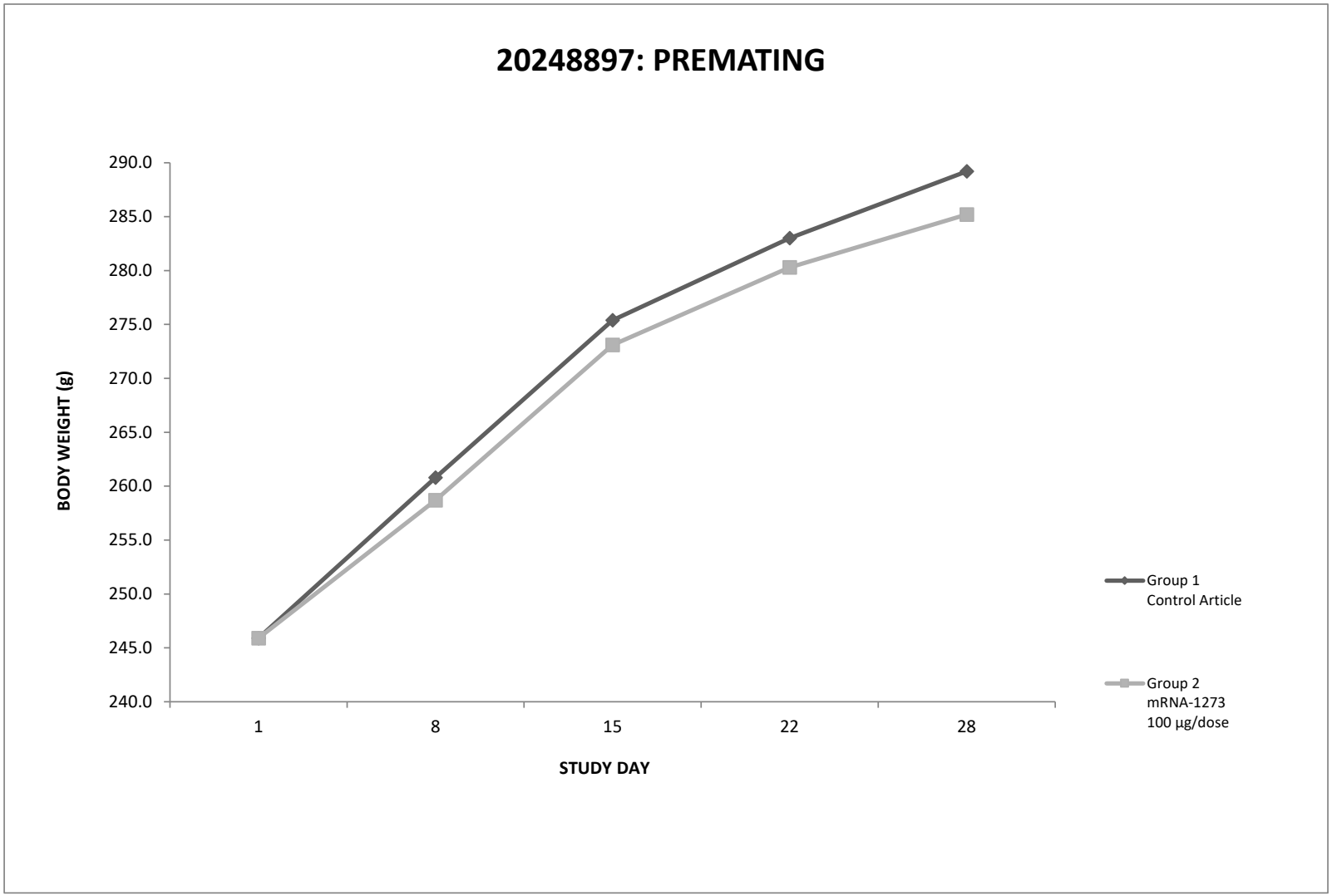

20248897: PREMATING
BODY WEIGHT (g)
290.0
285.0
280.0
275.0
270.0
265.0
260.0
255.0
250.0
245.0
240.0
1
8
15
22
28
STUDY DAY
Group 1
Control Article
Group 2
mRNA-1273
100 µg/dose

Figure 2

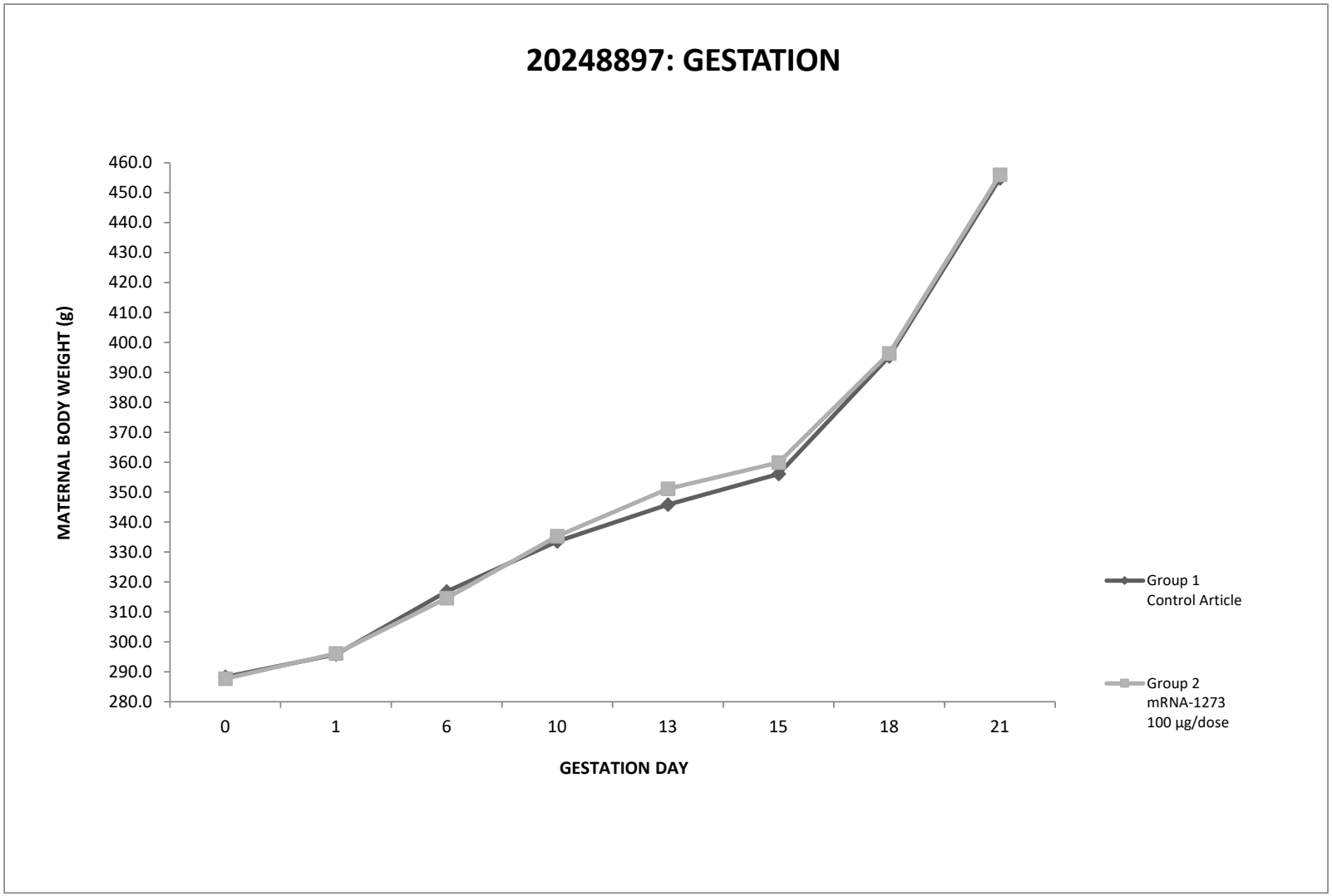
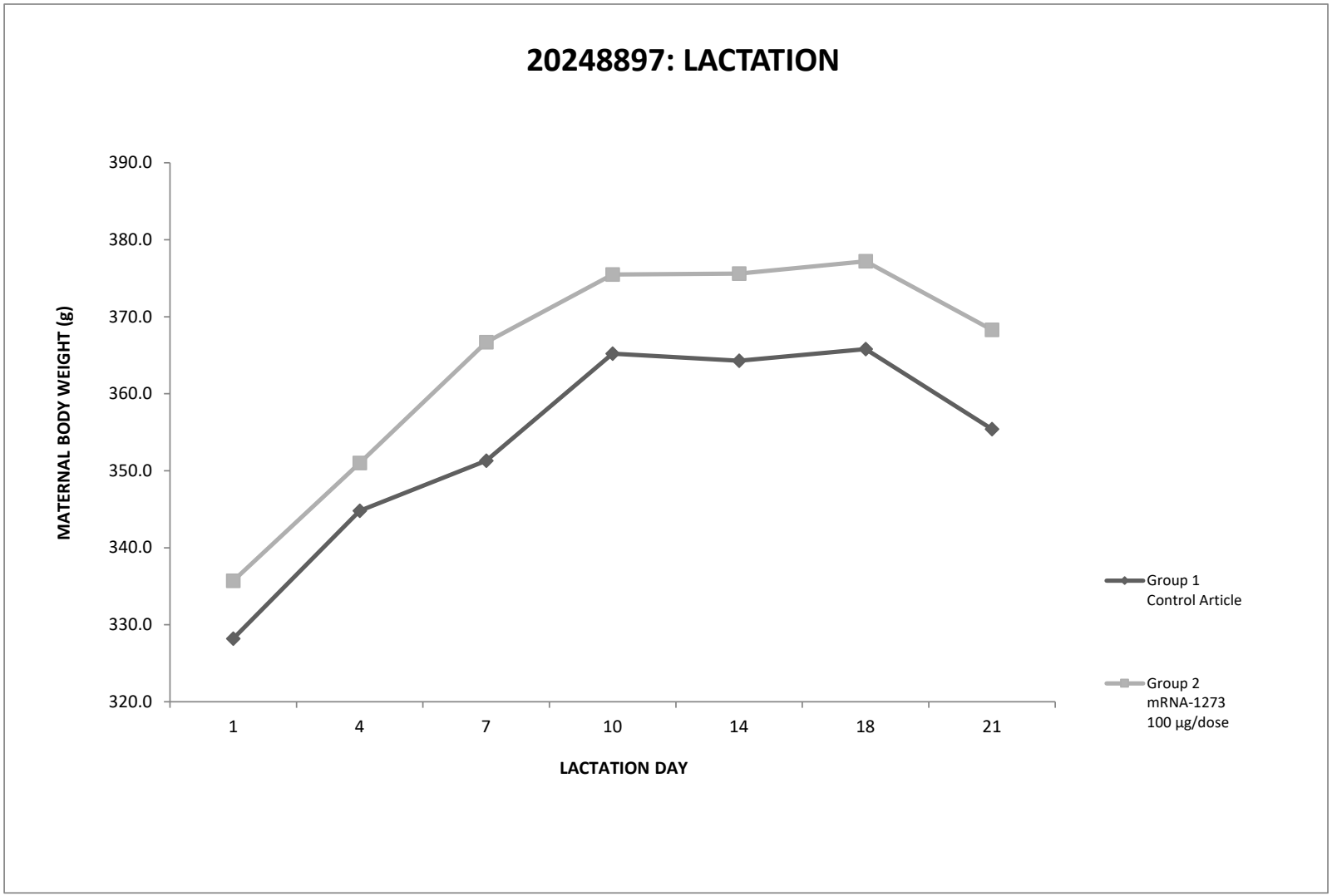

20248897: GESTATION
MATERNAL BODY WEIGHT (g)
460.0
450.0
440.0
430.0
420.0
410.0
400.0
390.0
380.0
370.0
360.0
350.0
340.0
330.0
320.0
310.0
300.0
290.0
280.0
0
1
6
10
13
15
18
21
GESTATION DAY
Group 1
Control Article
Group 2
mRNA-1273
100 µg/dose

Figure 3


20248897: LACTATION
MATERNAL BODY WEIGHT (g)
390.0
380.0
370.0
360.0
350.0
340.0
330.0
320.0
1
4
7
10
14
18
21
LACTATION DAY
Group 1
Control Article
Group 2
mRNA-1273
100 µg/dose

20248897

Summary Tables Explanation Page

All Day(s) referenced throughout the outputs generated are Study Day, Gestation Day, or Lactation Day

Abbreviations consistent throughout the Summary Tables

Note: All of the abbreviations listed on these pages may not be applicable to this report.

Abbreviation	Description
%Diff G1 or % Diff	% Difference from Group 1
(g)	Grams
N	Number of values included in analysis
(M),(F),(both)	Male, Female, Both Male and Female fetuses
(Litter A)	First Litter

All weights are collected and reported in grams.

Dosing Information

Dosing information is abbreviated on various data outputs; the following represents the dosing information for this study:

Group No.	Test Material	Dose Level (µg/dose)	Dose Concentration (mg/mL)	Dose Volume (µL/dose)
1	Control Article	0	0	200
2	mRNA-1273	100	0.5	200

Summarization of females not pregnant is restricted to Maternal Performance, Clinical Observations, and Gross Pathology in Cohort 1 and Clinical Observations and Gross Pathology after the cohabitation period in Cohort 2.

Summary of Clinical and Maternal Observations

Abbreviation	Description	Abbreviation	Description
-	A dash is entered when there are no observations in a group	First to Last Seen	Days listed may not be inclusive

Note: Only animals with findings are presented on this table.

Summary of Body Weights and Body Weight Gains

Abbreviation	Description
-	Not calculable, not scheduled to be performed, animal was an early death or less descriptive statistics chosen for output than lines needed for Report Headings

Summary of Gravid Uterine Weights and Corrected Maternal Body Weights

Abbreviation	Description	Abbreviation	Description
Corrected BW	Terminal body weight – gravid uterine weight	Corrected BWG (0-TBW)	(Terminal body weight - gravid uterine weight) - Day 0 body weight

Summary of Food Consumption

Abbreviation	Description	Abbreviation	Description
.	Not calculable or less descriptive statistics chosen for output than lines needed for Report Headings	Cons	Consumption

Summary of Estrous Cycling

The Number of Cycles are summarized based on the following:

Start of cycle is E:

- If consecutive E's exist, start of the cycle is defined as the first E
- If the first value in the reporting period is E, it is ignored as a cycle start
- Last E or assumed E (as indicated below) is ignored as a cycle start (it is however used to calculate cycle length of the last full cycle)

Start of a cycle for Assumed E:

- If P is followed by M (i.e. E is missing), start of cycle is taken as the P immediately before the M
- If P is followed by D (i.e. E & M are missing), start of cycle is taken as the P immediately before the D

Mean cycle length = the sum of the number of days in each complete cycle/the number of complete cycles

Summary of Maternal Performance and Mortality

Abbreviation	Description	Abbreviation	Description
Fem	Female	N+ve	Count Positives

Includes all Cohort 1 animals that survived to scheduled euthanasia, as well as any animals found dead, unscheduled euthanized, aborted or delivered.

Summary of Ovarian and Uterine Examinations and Litter Observations

Abbreviation	Description	Abbreviation	Description
Pre-implantation Loss (%)	Percentage of Preimplantation Loss [(Number of Corpora Lutea – Number of Implantations)/Number of Corpora Lutea] x 100	Post-implantation Loss (%)	Percentage of Postimplantation Loss [(Number of Implantations – Number of Live Fetuses)/Number of Implantations] x 100
Live Male Fetus/Litter (%)	Percentage of Live Male fetuses (Number of Male Fetuses/Number of Fetuses) x 100	-	Not calculable

Note: Total Fetuses and Live Male Fetuses % include only litters with at least 1 sexed fetus.

Summary of Fetal Abnormalities

Included only for evaluation sets that have at least 1 fetus with any abnormality.

Number of Fetuses Examined - Includes only live fetuses examined from litters euthanized as scheduled for that examination
Number of Fetuses Evaluated - Includes all fetuses (live and dead) evaluated from litters euthanized as scheduled for all examinations
Number of Litters Examined - Includes only litters euthanized as scheduled with at least 1 live fetus for that examination
Number of Litters Evaluated - Includes all litters euthanized as scheduled with at least 1 fetus for all examinations
Litter % of Fetuses - Mean Litter Percentage of fetal findings were calculated by finding per fetal examination and/or by classification.

Summary of Natural Delivery Observations

Abbreviation	Description	Abbreviation	Description
-	Not calculable	N+ve	Count Positives
Live Male Pups/ Litter (%) Birth	Percentage of Live Male pups (Number of Male Pups/Number of Pups) x 100 at Birth	Stillborn Pups/Litter	Percentage of stillborn pups (Number of Stillborn Pups/Number of Newborn Pups) x 100
Gestation Index	Percentage of pregnancies that result in birth of live litters (Number of Animals with Live Offspring/ Number of Animals Pregnant) x 100	Live Birth Index (%)	Percentage of pups born alive. Number of Liveborn Pups on Day 1 Postpartum/ Number of Newborn Pups) x 100
Post-implantation Loss (%)	Percentage of Postimplantation Loss [(Number of Implantations – Number of Live pups)/Number of Implantations] x 100		

Summary of Litter Observation

Abbreviation	Description	Abbreviation	Description
Live Male Pups/Litter (%) - 21	Percentage of Live Male pups (Number of Male Pups/Number of Pups) x 100 on Day 21	N+ve	Count Positives
Lactation Index	Percentage of pups that survive 21 days Postpartum (Number of Live Pups on Day 21/ Number of Live Pups on Day 4 Postpartum) x 100	Viability Index	Percentage of pups born that survive 4 days postpartum (Number of Live Pups on Day 4 Postpartum/ Number of Liveborn Pups on Day 1 Postpartum) x 100

Summary of Pup Gross Pathology

Included only for evaluation sets that have at least 1 pup with any abnormality.

Number of Pups Examined - Pup Necropsy - Includes only pups examined from litters euthanized as scheduled (terminal euthanasia), and at least 1 pup with a finding.
Pup Necropsy - Unscheduled - Includes only pups examined with a removal other than terminal euthanasia and at least 1 pup with a finding.

Number of Litters Examined- Includes number of litters with at least 1 pup examined for Pup Necropsy or Pup Necropsy -Unscheduled for that examination set.

Table 1

Summary of Clinical Observations: Premating

20248897

Observation Type: All Types From Day 1 (Start Date (A)) to -1 (Mating)	Female 0 ug/dose Group 1	 100 ug/dose Group 2
Fur, Thin Cover		
Number of Animals Affected	1	9
Number of Times Recorded	6	108
% of Affected Animals	2	20
First to Last seen	24 - 29	24 - 60
Skin, Scab		
Number of Animals Affected	1	1
Number of Times Recorded	4	7
% of Affected Animals	2	2
First to Last seen	28 - 31	19 - 25
Swollen Hindlimb		
Number of Animals Affected	0	5
Number of Times Recorded	0	18
% of Affected Animals	0	11
First to Last seen	-	48 - 55
Discharge, Red		
Number of Animals Affected	0	1
Number of Times Recorded	0	3
% of Affected Animals	0	2
First to Last seen	-	15 - 17

Table 2

Summary of Clinical Observations: Gestation

20248897

Observation Type: All Types Sex: Female From Day 0 (Mating (A)) to 0 (Littering)	0 ug/dose Group 1	100 ug/dose Group 2
Limited Usage, Hindlimb		
Number of Animals Affected	0	20
Number of Times Recorded	0	28
% of Affected Animals	0	51
First to Last seen	-	13 - 15
Hunched Posture		
Number of Animals Affected	1	0
Number of Times Recorded	6	0
% of Affected Animals	2	0
First to Last seen	6 - 11	-
Fur, Loss		
Number of Animals Affected	1	0
Number of Times Recorded	6	0
% of Affected Animals	2	0
First to Last seen	15 - 20	-
Fur, Thin Cover		
Number of Animals Affected	0	16
Number of Times Recorded	0	110
% of Affected Animals	0	41
First to Last seen	-	0 - 25
Skin, Scab		
Number of Animals Affected	2	0
Number of Times Recorded	7	0
% of Affected Animals	5	0
First to Last seen	0 - 15	-
Thin		
Number of Animals Affected	1	0
Number of Times Recorded	9	0

Table 2

Summary of Clinical Observations: Gestation

20248897

Observation Type: All Types Sex: Female From Day 0 (Mating (A)) to 0 (Littering)	0 ug/dose Group 1	100 ug/dose Group 2
Thin (Continued...)		
% of Affected Animals	2	0
First to Last seen	7 - 14	-
Swollen Hindlimb		
Number of Animals Affected	0	39
Number of Times Recorded	0	136
% of Affected Animals	0	100
First to Last seen	-	13 - 20
Discharge, Red		
Number of Animals Affected	0	1
Number of Times Recorded	0	1
% of Affected Animals	0	3
First to Last seen	-	0 - 0
Discharge, Mucoid		
Number of Animals Affected	0	1
Number of Times Recorded	0	1
% of Affected Animals	0	3
First to Last seen	-	0 - 0

Table 3

Summary of Clinical Observations: Lactation

20248897

Observation Type: All Types Sex: Female From Day 1 (Littering (A)) to 21 (Littering)	0 ug/dose Group 1	100 ug/dose Group 2
Fur, Thin Cover		
Number of Animals Affected	1	4
Number of Times Recorded	9	63
% of Affected Animals	5	27
First to Last seen	7 - 15	1 - 18

Table 4
Summary of Body Weights: Premating

20248897
Bodyweight (g)

Sex: Female		Day(s) Relative to Start Date				
		1	8	15	22	28
0	Mean	245.9	260.8	275.4	283.0	289.2
ug/dose	SD	9.8	10.7	12.2	13.8	15.0
	N	44	44	44	44	44
Group 1		-	-	-	-	-
100	Mean	245.9	258.7	273.1	280.3	285.2
ug/dose	SD	11.1	12.5	13.7	13.7	16.8
	N	44	44	44	44	44
Group 2	%Diff	0.0	-0.8	-0.8	-1.0	-1.4

Anova & Dunnett

Table 5
Summary of Body Weight Gains (g): Premating

20248897
Bodyweight Gain (Interval)

Sex: Female		Day(s) Relative to Start Date			
		1 → 8	8 → 15	15 → 22	22 → 28
0	Mean	14.9	14.6	7.6	6.2
ug/dose	SD	4.3	5.3	5.5	7.9
	N	44	44	44	44
Group 1		-	-	-	-
100	Mean	12.8	14.5	7.2	4.9
ug/dose	SD	6.5	7.0	5.1	9.2
	N	44	44	44	44
Group 2		-	-	-	-

Anova & Dunnett

Table 6
Summary of Body Weights: Gestation

20248897
Bodyweight (g)

Sex: Female		Day(s) Relative to Mating (Litter: A)			
		0 [G]	1 [G1]	6 [G1]	10 [G1]
0	Mean	288.3	295.8	316.8	333.5
ug/dose	SD	11.4	13.3	20.6	17.9
	N	41	41	41	41
Group 1		-	-	-	-
100	Mean	287.7	296.1	314.6	335.3
ug/dose	SD	17.2	15.2	17.3	18.7
	N	37	37	37	37
Group 2	%Diff	-0.2	0.1	-0.7	0.6

[G] - Kruskal-Wallis & Dunn
[G1] - Anova & Dunnett

Table 6
Summary of Body Weights: Gestation

20248897
Bodyweight (g)

Sex: Female		Day(s) Relative to Mating (Litter: A)			
		13	15	18	21
0	Mean	345.8	356.1	395.3	454.8
ug/dose	SD	16.7	16.7	19.8	24.7
	N	41	41	41	40
Group 1		-	-	-	-
100	Mean	351.1	359.9	396.3	456.0
ug/dose	SD	21.3	21.4	25.2	28.3
	N	37	37	37	35
Group 2	%Diff	1.5	1.1	0.2	0.3

Anova & Dunnett

Table 7
Summary of Body Weight Gains (g): Gestation

20248897
Bodyweight Gain (Interval)

Sex: Female		Day(s) Relative to Mating (Litter: A)						
		0 → 1	1 → 6	6 → 10	10 → 13	13 → 15	15 → 18	18 → 21
0	Mean	7.5	21.0	16.6	12.3	10.3	39.2	59.1
ug/dose	SD	5.4	12.5	9.5	7.9	4.6	7.6	9.0
	N	41	41	41	41	41	41	40
Group 1		-	-	-	-	-	-	-
100	Mean	8.4	18.5	20.7*	15.7	8.9	36.4	59.0
ug/dose	SD	5.5	6.2	7.3	8.1	4.8	8.6	10.1
	N	37	37	37	37	37	37	35
Group 2		-	-	-	-	-	-	-

Anova & Dunnett: * = $p \leq 0.05$

Table 8
Summary of Body Weights: Lactation

20248897
Bodyweight (g)

Sex: Female		Day(s) Relative to Littering (Litter: A)			
		1 [G]	3 [I]	4 [G]	7 [G1]
0	Mean	328.2	-	344.8	351.3
ug/dose	SD	21.3	-	22.3	17.7
	N	20	0	19	19
Group 1		-	-	-	-
100	Mean	335.7	-	351.0	366.7
ug/dose	SD	28.2	-	26.3	28.6
	N	15	-	15	15
Group 2	%Diff	2.3	-	1.8	4.4

[G] - Anova & Dunnett
[I] - n - Inappropriate for statistics
[G1] - Kruskal-Wallis & Dunn

Table 8
Summary of Body Weights: Lactation

20248897
Bodyweight (g)

Sex: Female		Day(s) Relative to Littering (Litter: A)			
		10	14	18	21
0	Mean	365.2	364.3	365.8	355.4
ug/dose	SD	16.1	17.1	15.0	15.3
	N	19	19	19	19
Group 1		-	-	-	-
100	Mean	375.5	375.6	377.2	368.3
ug/dose	SD	30.3	34.4	32.8	25.3
	N	15	15	15	15
Group 2	%Diff	2.8	3.1	3.1	3.6

Kruskal-Wallis & Dunn

Table 9
Summary of Body Weight Gains (g): Lactation

20248897
Bodyweight Gain (Interval)

Sex: Female		Day(s) Relative to Littering (Litter: A)					
		1 → 4	4 → 7	7 → 10	10 → 14	14 → 18	18 → 21
0	Mean	17.0	6.5	13.9	-0.9	1.5	-10.4
ug/dose	SD	11.5	8.5	13.2	13.0	13.1	7.9
	N	19	19	19	19	19	19
Group 1		-	-	-	-	-	-
100	Mean	15.3	15.7**	8.7	0.1	1.6	-8.9
ug/dose	SD	7.7	10.2	8.6	14.0	11.8	13.1
	N	15	15	15	15	15	15
Group 2		-	-	-	-	-	-

Anova & Dunnett: ** = $p \leq 0.01$

Table 10
Summary of Food Consumption: Premating

20248897
Daily Food Cons Per Animal (g)

Sex: Female		Day(s) Relative to Animal Start Date			
		1 → 8	8 → 15	15 → 22	22 → 28
0	Mean	19.4	19.1	18.1	17.6
ug/dose	SD	1.1	1.2	1.1	1.5
	N	22	22	22	22
Group 1		-	-	-	-
100	Mean	18.9	19.5	17.4	18.3
ug/dose	SD	1.7	2.2	1.7	1.3
	N	22	22	22	22
Group 2	%Diff	-2.8	2.3	-3.6	4.1

Anova & Dunnett

Table 11
Summary of Food Consumption: Gestation

20248897
Food Mean Daily Consumption (g/animal/day)

Sex: Female		Day(s) Relative to Mating (Litter: A)						
		0 → 1	1 → 6	6 → 10	10 → 13	13 → 15	15 → 18	18 → 21
0	Mean	22.83	20.81	23.23	24.21	24.54	25.57	27.18
ug/dose	SD	4.36	2.42	2.25	2.55	2.55	2.45	2.69
	N	41	40	41	41	41	41	38
Group 1		.	.	.	.	.	.	.
100	Mean	24.78	19.63*	24.21	26.27**	21.00**	26.25	28.82*
ug/dose	SD	4.62	2.01	2.57	2.53	2.35	2.94	3.31
	N	36	37	37	37	37	37	35
Group 2	%Diff	8.54	-5.68	4.21	8.50	-14.41	2.67	6.01

Anova & Dunnett: * = $p \leq 0.05$; ** = $p \leq 0.01$

Table 12
Summary of Food Consumption: Lactation

20248897
Food Mean Daily Consumption (g/animal/day)

Sex: Female		Day(s) Relative to Littering (Litter: A)			
		1 → 4	4 → 7	7 → 10	10 → 14
0	Mean	34.98	42.65	54.09	61.89
ug/dose	SD	4.92	5.90	6.85	6.07
	N	19	18	15	16
Group 1		.	.	.	.
100	Mean	37.13	47.20*	57.33	67.25
ug/dose	SD	5.74	5.95	4.68	7.86
	N	15	15	8	8
Group 2	%Diff	6.15	10.67	6.00	8.66

Anova & Dunnett: * = $p \leq 0.05$

Table 13
Summary of Estrous Cycling: Precohabitation

20248897

Sex: Female Day(s) Relative to Pairing (Litter: A)		0 ug/dose Group 1	100 ug/dose Group 2
Group Size - Females		44	44
Number of Cycles d-13→d0 [k]	Mean	2.1	2.0
	SD	0.5	0.5
	N	44	43
	%Diff	-	-5.4
Mean of Cycle Lengths (Days) d-13→d0	Mean	4.28	4.53**
	SD	1.31	1.04
	N	44	43
	%Diff	-	5.67

[k] - Dunn: ** = $p \leq 0.01$

Table 14

Summary of Reproductive Performance

20248897

Sex: Female Day(s) Relative to Pairing (Litter: A)		0 ug/dose Group 1	100 ug/dose Group 2
Group Size - Females		44	44
Paired - Females	N+ve	44	44
Mated Females	N+ve	42	39
Pregnant	N+ve	41	37
Pre-coital Interval (Days) [k]	Mean	2.2	2.1
	SD	1.4	1.1
	N	42	39
	%Diff	-	-4.9
Pregnant No Confirmed Mating [f]	N+ve	0	0
Confirmed Mating Days 1-7 [f]	N+ve	42	39
	%	100.0	100.0
Female Mating Index [f]	%	95.5	88.6
	ProA	42/44	39/44
Female Fertility Index [f]	%	97.6	94.9
	ProA	41/42	37/39
Female Pregnancy Index [f]	%	93.2	84.1
	ProA	41/44	37/44

[k] - Kruskal-Wallis & Dunn
[f] - Fisher's Exact

Table 15

Summary of Maternal Performance and Mortality

20248897

Sex: Female Day(s) Relative to Mating (Litter: A)		0 ug/dose Group 1	100 ug/dose Group 2
Group Size - Females		22	22
Number of Females Pregnant [f]	N+ve	21	22
	%	95.5	100.0
Female with Live Fetuses [f]	N+ve	21	22
	%	100.0	100.0
Female with Resorptions [f]	N+ve	6	9
	%	28.6	40.9
Female with all Nonviable [f]	N+ve	0	0
	%	0.0	0.0
Terminal Euthanasia [f]	N+ve	22	22
	%	100.0	100.0
Unscheduled Death/Euthanasia [f]	N+ve	0	0
	%	0.0	0.0
Found Dead [f]	N+ve	0	0
	%	0.0	0.0
Unscheduled Euthanasia [f]	N+ve	0	0
	%	0.0	0.0
Aborted [f]	N+ve	0	0
	%	0.0	0.0
Delivered [f]	N+ve	0	0
	%	0.0	0.0

[f] - Fisher's Exact

Table 16

Summary of Ovarian and Uterine Examinations and Litter Observations

20248897

Sex: Female Day(s) Relative to Mating (Litter: A)		0 ug/dose Group 1	100 ug/dose Group 2
Female with Live Fetuses [f]	N+ve	21	22
	%	100.0	100.0
Number of Corpora Lutea [k]	Mean	15.8	16.1
	SD	2.4	2.0
	N	21	22
	%Diff	-	2.1
Number of Implantations [k]	Mean	13.7	14.5
	SD	2.4	2.1
	N	21	22
	%Diff	-	6.1
Pre-implantation Loss (%) [k]	Mean	12.82	9.44
	SD	12.53	10.98
	N	21	22
	%Diff	-	-26.36
Total Number of Resorptions [k]	Mean	0.5	0.5
	SD	0.9	0.7
	N	21	22
	%Diff	-	14.5
Number of Early Resorptions [k]	Mean	0.4	0.5
	SD	0.8	0.7
	N	21	22
	%Diff	-	27.3
Number of Late Resorptions [k]	Mean	0.0	0.0
	SD	0.2	0.0
	N	21	22
	%Diff	-	-100.0
Total Number of Fetuses [k]	Mean	13.2	14.0
	SD	2.7	2.1
	N	21	22
	%Diff	-	5.8
Number of Live Fetuses [k]	Mean	13.2	14.0
	SD	2.7	2.1
	N	21	22
	%Diff	-	5.8

[f] - Fisher's Exact
[k] - Kruskal-Wallis & Dunn

Table 16

Summary of Ovarian and Uterine Examinations and Litter Observations

20248897

Sex: Female Day(s) Relative to Mating (Litter: A)		0 ug/dose Group 1	100 ug/dose Group 2
Number of Live Male Fetuses [k]	Mean	6.5	6.9
	SD	2.3	2.5
	N	21	22
	%Diff	-	6.7
Number of Live Female Fetuses [k]	Mean	6.8	7.1
	SD	2.0	1.9
	N	21	22
	%Diff	-	4.9
Number of Dead Fetuses [k]	Mean	0.0	0.0
	SD	0.0	0.0
	N	21	22
	%Diff	-	-
Post-implantation Loss (%) [k]	Mean	3.94	3.81
	SD	7.06	5.13
	N	21	22
	%Diff	-	-3.22
Live Male Fetus/Litter (%) [k]	Mean	48.37	48.78
	SD	12.58	13.59
	N	21	22
	%Diff	-	0.86
Mean Fetal Weight all (g) [G]	Mean	5.793	5.779
	SD	0.283	0.319
	N	21	22
	%Diff	-	-0.231
Mean Fetal Weight males (g) [G]	Mean	5.949	5.924
	SD	0.324	0.328
	N	21	22
	%Diff	-	-0.428
Mean Fetal Weight females (g) [G]	Mean	5.642	5.629
	SD	0.293	0.332
	N	21	22
	%Diff	-	-0.230

[k] - Kruskal-Wallis & Dunn
[G] - Anova & Dunnett

Table 16

Summary of Ovarian and Uterine Examinations and Litter Observations

20248897

Sex: Female Day(s) Relative to Mating (Litter: A)		0 ug/dose Group 1	100 ug/dose Group 2
Live Mean Placental Weight (g) [G]	Mean	0.567	0.594
	SD	0.044	0.067
	N	21	22
	%Diff	-	4.779

[G] - Anova & Dunnett

Table 17

Summary of Gravid Uterine Weights and Corrected Body Weights: Gestation

20248897

Sex: Female Day(s) Relative to Mating (Litter: A)		0 ug/dose Group 1	100 ug/dose Group 2
Bodyweight on Day 0 (g) [G]	Mean	287.0	287.3
	SD	11.1	18.7
	N	21	22
	%Diff	-	0.1
Terminal Body Weight (g) [G1]	Mean	455.2	455.5
	SD	27.4	29.2
	N	21	22
	%Diff	-	0.1
Gravid Uterus Weight (g) [G1]	Mean	100.01	106.70
	SD	17.85	15.21
	N	21	21
	%Diff	-	6.68
Corrected Bodyweight (g) [G1]	Mean	355.2	348.8
	SD	18.4	21.8
	N	21	21
	%Diff	-	-1.8
Corrected BWG (0-TBW) (g) [G1]	Mean	68.2	62.0
	SD	13.7	10.9
	N	21	21
	%Diff	-	-9.0

[G] - Kruskal-Wallis & Dunn
[G1] - Anova & Dunnett

Table 18

Summary of Fetal Abnormalities by Classification

20248897

Exam Type: External	0 ug/dose Group 1	100 ug/dose Group 2
Number of Fetuses Examined:	278	308
Number of Fetuses Evaluated:	278	308
Number of Litters Examined:	21	22
Number of Litters Evaluated:	21	22
Malformation		
Number of Fetuses	1	0
Litter % of Fetuses [k]	0.28	0.00
Number of Litters	1	0
All classifications		
Number of Fetuses	1	0
Litter % of Fetuses [k]	0.28	0.00
Number of Litters	1	0

[k] - Kruskal-Wallis & Dunn

Table 18

Summary of Fetal Abnormalities by Classification

20248897

Exam Type: Fixed Head	0 ug/dose Group 1	100 ug/dose Group 2
Number of Fetuses Examined:	134	150
Number of Fetuses Evaluated:	278	308
Number of Litters Examined:	21	22
Number of Litters Evaluated:	21	22
Variation		
Number of Fetuses	1	1
Litter % of Fetuses [k]	0.60	0.76
Number of Litters	1	1
All classifications		
Number of Fetuses	1	1
Litter % of Fetuses [k]	0.60	0.76
Number of Litters	1	1

[k] - Kruskal-Wallis & Dunn

Table 18

Summary of Fetal Abnormalities by Classification

20248897

Exam Type: FreshVisBody	0 ug/dose Group 1	100 ug/dose Group 2
Number of Fetuses Examined:	134	150
Number of Fetuses Evaluated:	278	308
Number of Litters Examined:	21	22
Number of Litters Evaluated:	21	22
Variation		
Number of Fetuses	2	1
Litter % of Fetuses [k]	1.55	0.65
Number of Litters	2	1
Malformation		
Number of Fetuses	1	0
Litter % of Fetuses [k]	0.60	0.00
Number of Litters	1	0
All classifications		
Number of Fetuses	2	1
Litter % of Fetuses [k]	1.55	0.65
Number of Litters	2	1

[k] - Kruskal-Wallis & Dunn

Table 18

Summary of Fetal Abnormalities by Classification

20248897

Exam Type: Skeletal	0 ug/dose Group 1	100 ug/dose Group 2
Number of Fetuses Examined:	144	158
Number of Fetuses Evaluated:	278	308
Number of Litters Examined:	21	22
Number of Litters Evaluated:	21	22
Variation		
Number of Fetuses	22	27
Litter % of Fetuses [k]	16.50	17.90
Number of Litters	12	12
All classifications		
Number of Fetuses	22	27
Litter % of Fetuses [k]	16.50	17.90
Number of Litters	12	12

[k] - Kruskal-Wallis & Dunn

Table 18

Summary of Fetal Abnormalities by Finding

20248897

Exam Type: External		0 ug/dose Group 1	100 ug/dose Group 2
	Number of Fetuses Examined:	278	308
	Number of Fetuses Evaluated:	278	308
	Number of Litters Examined:	21	22
	Number of Litters Evaluated:	21	22
Mouth			
Tongue, Protruding - Malformation	Fetuses N(%)	1(0.28)	0(0.00)
	Litters N(%)	1(4.8)	0(0.0)
Trunk			
Anus, Absent - Malformation	Fetuses N(%)	1(0.28)	0(0.00)
	Litters N(%)	1(4.8)	0(0.0)
Genital tubercle, Misshapen - Malformation	Fetuses N(%)	1(0.28)	0(0.00)
	Litters N(%)	1(4.8)	0(0.0)

[Fetuses %] - Kruskal-Wallis & Dunn
FetusesN(%) N=Group Fetal Incidence;(%)=Mean Litter % of Fetuses with the Abnormality

Table 18

Summary of Fetal Abnormalities by Finding

20248897

Exam Type: Fixed Head		0 ug/dose Group 1	100 ug/dose Group 2
Number of Fetuses Examined:		134	150
Number of Fetuses Evaluated:		278	308
Number of Litters Examined:		21	22
Number of Litters Evaluated:		21	22
Brain			
Lateral ventricle, Both, Dilatation, Moderate - Variation	Fetuses N(%)	1(0.60)	1(0.76)
	Litters N(%)	1(4.8)	1(4.5)

[Fetuses %] - Kruskal-Wallis & Dunn
FetusesN(%) N=Group Fetal Incidence;(%)=Mean Litter % of Fetuses with the Abnormality

Table 18

Summary of Fetal Abnormalities by Finding

20248897

Exam Type: FreshVisBody		0 ug/dose Group 1	100 ug/dose Group 2
Number of Fetuses Examined:		134	150
Number of Fetuses Evaluated:		278	308
Number of Litters Examined:		21	22
Number of Litters Evaluated:		21	22
Innominate artery			
Innominate artery, Absent - Variation	Fetuses N(%)	1(0.95)	0(0.00)
	Litters N(%)	1(4.8)	0(0.0)
Lung			
Lobe, Caudate process, Absent - Malformation	Fetuses N(%)	1(0.60)	0(0.00)
	Litters N(%)	1(4.8)	0(0.0)
Ureter			
Ureter, Both, Dilatation, Severe - Variation	Fetuses N(%)	1(0.60)	0(0.00)
	Litters N(%)	1(4.8)	0(0.0)
Ureter, Left, Dilatation, Moderate - Variation	Fetuses N(%)	0(0.00)	1(0.65)
	Litters N(%)	0(0.0)	1(4.5)

[Fetuses %] - Kruskal-Wallis & Dunn
FetusesN(%) N=Group Fetal Incidence;(%)=Mean Litter % of Fetuses with the Abnormality

Table 18

Summary of Fetal Abnormalities by Finding

20248897

Exam Type: Skeletal		0 ug/dose Group 1	100 ug/dose Group 2
	Number of Fetuses Examined:	144	158
	Number of Fetuses Evaluated:	278	308
	Number of Litters Examined:	21	22
	Number of Litters Evaluated:	21	22
Pelvic girdle			
Pubis, Both, Incomplete ossification - Variation	Fetuses N(%)	1(0.95)	0(0.00)
	Litters N(%)	1(4.8)	0(0.0)
Rib			
Rib, 1 or more, Incomplete ossification - Variation	Fetuses N(%)	0(0.00)	4(2.81)
	Litters N(%)	0(0.0)	3(13.6)
Rib, 1 or more, Nodule - Variation	Fetuses N(%)	0(0.00)	5(3.27)*
	Litters N(%)	0(0.0)	4(18.2)
Rib, 1 or more, Short - Variation	Fetuses N(%)	1(0.53)	0(0.00)
	Litters N(%)	1(4.8)	0(0.0)
Rib, 1 or more, Wavy rib - Variation	Fetuses N(%)	0(0.00)	6(4.03)*
	Litters N(%)	0(0.0)	4(18.2)
Skull			
Frontal, Both, Incomplete ossification - Variation	Fetuses N(%)	6(4.70)	5(3.22)
	Litters N(%)	5(23.8)	3(13.6)
Nasal, Both, Incomplete ossification - Variation	Fetuses N(%)	0(0.00)	1(0.57)
	Litters N(%)	0(0.0)	1(4.5)
Parietal, Both, Incomplete ossification - Variation	Fetuses N(%)	10(6.91)	7(4.71)
	Litters N(%)	7(33.3)	4(18.2)
Parietal, Left, Incomplete ossification - Variation	Fetuses N(%)	0(0.00)	1(0.76)
	Litters N(%)	0(0.0)	1(4.5)
Parietal, Right, Incomplete ossification - Variation	Fetuses N(%)	0(0.00)	1(0.57)
	Litters N(%)	0(0.0)	1(4.5)
Squamosal, Both, Incomplete ossification - Variation	Fetuses N(%)	6(4.55)	12(7.57)
	Litters N(%)	4(19.0)	6(27.3)
Squamosal, Left, Incomplete ossification - Variation	Fetuses N(%)	1(0.68)	0(0.00)
	Litters N(%)	1(4.8)	0(0.0)
Squamosal, Right, Incomplete ossification - Variation	Fetuses N(%)	0(0.00)	1(0.65)
	Litters N(%)	0(0.0)	1(4.5)
Supraoccipital, Incomplete ossification - Variation	Fetuses N(%)	1(0.95)	0(0.00)
	Litters N(%)	1(4.8)	0(0.0)
Zygomatic arch, Both, Incomplete ossification - Variation	Fetuses N(%)	9(6.82)	15(9.65)
	Litters N(%)	5(23.8)	8(36.4)
Zygomatic arch, Left, Incomplete ossification - Variation	Fetuses N(%)	0(0.00)	1(0.65)
	Litters N(%)	0(0.0)	1(4.5)
Zygomatic arch, Right, Incomplete ossification - Variation	Fetuses N(%)	1(1.59)	1(0.76)
	Litters N(%)	1(4.8)	1(4.5)

[Fetuses %] - Kruskal-Wallis & Dunn: * = $p \leq 0.05$
FetusesN(%) N=Group Fetal Incidence;(%)=Mean Litter % of Fetuses with the Abnormality

Table 18

Summary of Fetal Abnormalities by Finding

20248897

Exam Type: Skeletal		0 ug/dose Group 1	100 ug/dose Group 2
Number of Fetuses Examined:		144	158
Number of Fetuses Evaluated:		278	308
Number of Litters Examined:		21	22
Number of Litters Evaluated:		21	22
Sternebra			
Sternebra, 1 or more, Misshapen - Variation	Fetuses N(%)	0(0.00)	1(0.65)
	Litters N(%)	0(0.0)	1(4.5)
Sternebra, 1 or more, Incomplete ossification - Variation	Fetuses N(%)	1(0.60)	1(0.65)
	Litters N(%)	1(4.8)	1(4.5)
Supernumerary rib			
Cervical, 1 or more, Short - Variation	Fetuses N(%)	1(0.68)	1(0.76)
	Litters N(%)	1(4.8)	1(4.5)
Vertebra			
Cervical arch, 1 or more, Misshapen - Variation	Fetuses N(%)	1(0.53)	2(1.41)
	Litters N(%)	1(4.8)	2(9.1)
Cervical arch, 1 or more, Incomplete ossification - Variation	Fetuses N(%)	4(3.33)	3(1.89)
	Litters N(%)	2(9 5)	2(9 1)
Thoracic centrum, 1 or more, Incomplete ossification - Variation	Fetuses N(%)	3(2.07)	1(0.65)
	Litters N(%)	3(14.3)	1(4.5)

[Fetuses %] - Kruskal-Wallis & Dunn
FetusesN(%) N=Group Fetal Incidence;(%)=Mean Litter % of Fetuses with the Abnormality

Table 19

Summary of Mean Fetal Skeletal Ossification Sites

20248897

Sex: Female Day(s) Relative to Mating (Litter: A)		0 ug/dose Group 1	100 ug/dose Group 2
Hyoid [k]	Mean	1.00	1.00
	SD	0.00	0.00
	N	21	22
	%Diff	-	0.00
Cervical Vertebrae [k]	Mean	7.00	7.00
	SD	0.00	0.00
	N	21	22
	%Diff	-	0.00
Thoracic Vertebrae [k]	Mean	13.06	13.02
	SD	0.22	0.05
	N	21	22
	%Diff	-	-0.29
Lumbar Vertebrae [k]	Mean	5.94	5.98
	SD	0.22	0.05
	N	21	22
	%Diff	-	0.64
Sacral Vertebrae [k]	Mean	4.00	4.00
	SD	0.00	0.00
	N	21	22
	%Diff	-	0.00
Caudal Vertebrae [k]	Mean	6.23	6.05
	SD	0.51	0.64
	N	21	22
	%Diff	-	-2.91
Ribs,Paired [k]	Mean	13.04	13.01
	SD	0.15	0.03
	N	21	22
	%Diff	-	-0.22
Manubrium [k]	Mean	1.00	1.00
	SD	0.00	0.00
	N	21	22
	%Diff	-	0.00

[k] - Kruskal-Wallis & Dunn

Table 19

Summary of Mean Fetal Skeletal Ossification Sites

20248897

Sex: Female Day(s) Relative to Mating (Litter: A)		0 ug/dose Group 1	100 ug/dose Group 2
Sternal Centra [k]	Mean	4.00	4.00
	SD	0.00	0.00
	N	21	22
	%Diff	-	0.00
Xiphoid [k]	Mean	1.00	1.00
	SD	0.00	0.00
	N	21	22
	%Diff	-	0.00
Carpals [k]	Mean	0.00	0.00
	SD	0.00	0.00
	N	21	22
	%Diff	-	-
Metacarpals [k]	Mean	4.00	4.00
	SD	0.00	0.00
	N	21	22
	%Diff	-	0.00
Forelimb Digits [k]	Mean	5.00	5.00
	SD	0.00	0.00
	N	21	22
	%Diff	-	0.00
Forelimb Phalanges [k]	Mean	7.87	7.91
	SD	0.73	0.87
	N	21	22
	%Diff	-	0.47
Tarsals [k]	Mean	0.01	0.00
	SD	0.03	0.00
	N	21	22
	%Diff	-	-100.00
Metatarsals [k]	Mean	4.80	4.81
	SD	0.20	0.22
	N	21	22
	%Diff	-	0.25

[k] - Kruskal-Wallis & Dunn

Table 19

Summary of Mean Fetal Skeletal Ossification Sites

20248897

Sex: Female Day(s) Relative to Mating (Litter: A)		0 ug/dose Group 1	100 ug/dose Group 2
Hindlimb Digits [k]	Mean	5.00	5.00
	SD	0.00	0.00
	N	21	22
	%Diff	-	0.00
Hindlimb Phalanges [k]	Mean	6.01	6.01
	SD	1.04	0.85
	N	21	22
	%Diff	-	-0.07

[k] - Kruskal-Wallis & Dunn

Table 20

Summary of Macroscopic Pathology: Gestation

20248897

Removal Reason(s): TERMINAL EUTHANASIA Summary: Incidence	Female 0 ug/dose Group 1	100 ug/dose Group 2
Number of Animals:	22	24
ANIMAL IDENTIFICATION		
Submitted	1	0
No Visible Lesions	1	.
ARTERY, AORTA		
Submitted	1	0
No Visible Lesions	1	.
BODY CAVITY, NASAL		
Submitted	1	0
No Visible Lesions	1	.
BONE, FEMUR		
Submitted	1	0
No Visible Lesions	1	.
BONE, STERNUM		
Submitted	1	0
No Visible Lesions	1	.
BRAIN		
Submitted	1	0
No Visible Lesions	1	.
ESOPHAGUS		
Submitted	1	0
No Visible Lesions	1	.
EYE		
Submitted	1	0
No Visible Lesions	1	.
GALT		
Submitted	1	0
No Visible Lesions	1	.
GANGLION, DORSAL ROOT, LUMBAR		
Submitted	1	0
No Visible Lesions	1	.
GLAND, ADRENAL		
Submitted	1	0
No Visible Lesions	1	.

Table 20

Summary of Macroscopic Pathology: Gestation

20248897

Removal Reason(s): TERMINAL EUTHANASIA Summary: Incidence	Female 0 ug/dose Group 1	100 ug/dose Group 2
Number of Animals:	22	24
GLAND, CLITORAL		
Submitted	1	0
No Visible Lesions	1	.
GLAND, HARDERIAN		
Submitted	1	0
No Visible Lesions	1	.
GLAND, LACRIMAL		
Submitted	1	0
No Visible Lesions	1	.
GLAND, MAMMARY		
Submitted	1	0
No Visible Lesions	1	.
GLAND, PARATHYROID		
Submitted	1	0
No Visible Lesions	1	.
GLAND, PITUITARY		
Submitted	1	0
No Visible Lesions	1	.
GLAND, SALIVARY, MANDIBULAR		
Submitted	1	0
No Visible Lesions	1	.
GLAND, SALIVARY, PAROTID		
Submitted	1	0
No Visible Lesions	1	.
GLAND, SALIVARY, SUBLINGUAL		
Submitted	1	0
No Visible Lesions	1	.
GLAND, THYROID		
Submitted	1	0
No Visible Lesions	1	.
GLAND, ZYMBALS		
Submitted	1	0
No Visible Lesions	1	.

Table 20

Summary of Macroscopic Pathology: Gestation

20248897

Removal Reason(s): TERMINAL EUTHANASIA Summary: Incidence	Female 0 ug/dose Group 1	100 ug/dose Group 2
Number of Animals:	22	24
HEART		
Submitted	1	0
No Visible Lesions	1	.
JOINT, FEMOROTIBIAL		
Submitted	1	0
No Visible Lesions	1	.
KIDNEY		
Submitted	2	0
No Visible Lesions	1	.
Dilatation; pelvis	1	.
LARGE INTESTINE, CECUM		
Submitted	1	0
No Visible Lesions	1	.
LARGE INTESTINE, COLON		
Submitted	1	0
No Visible Lesions	1	.
LARGE INTESTINE, RECTUM		
Submitted	1	0
No Visible Lesions	1	.
LARYNX		
Submitted	1	0
No Visible Lesions	1	.
LIVER		
Submitted	1	0
No Visible Lesions	1	.
LUNG		
Submitted	1	0
No Visible Lesions	1	.
LYMPH NODE		
Submitted	1	0
No Visible Lesions	1	.
LYMPH NODE, MANDIBULAR		
Submitted	1	0
No Visible Lesions	1	.

Table 20

Summary of Macroscopic Pathology: Gestation

20248897

Removal Reason(s): TERMINAL EUTHANASIA Summary: Incidence	Female 0 ug/dose Group 1	100 ug/dose Group 2
Number of Animals:	22	24
LYMPH NODE, MESENTERIC		
Submitted	1	0
No Visible Lesions	1	.
MUSCLE, SKELETAL		
Submitted	1	0
No Visible Lesions	1	.
NERVE, OPTIC		
Submitted	1	0
No Visible Lesions	1	.
NERVE, SCIATIC		
Submitted	1	0
No Visible Lesions	1	.
NERVE, TIBIAL		
Submitted	1	0
No Visible Lesions	1	.
OVARY		
Submitted	2	2
No Visible Lesions	2	2
OVIDUCT		
Submitted	1	0
No Visible Lesions	1	.
PANCREAS		
Submitted	1	0
No Visible Lesions	1	.
PLACENTA		
Submitted	0	1
Adhesion	.	1
SITE, ADMINISTRATION		
Submitted	22	24
No Visible Lesions	22	24
SKIN		
Submitted	1	0
No Visible Lesions	1	.

Table 20

Summary of Macroscopic Pathology: Gestation

20248897

Removal Reason(s): TERMINAL EUTHANASIA Summary: Incidence	Female 0 ug/dose Group 1	100 ug/dose Group 2
Number of Animals:	22	24
SMALL INTESTINE, DUODENUM		
Submitted	1	0
No Visible Lesions	1	.
SMALL INTESTINE, ILEUM		
Submitted	1	0
No Visible Lesions	1	.
SMALL INTESTINE, JEJUNUM		
Submitted	1	0
No Visible Lesions	1	.
SPINAL CORD		
Submitted	1	0
No Visible Lesions	1	.
SPLEEN		
Submitted	1	0
No Visible Lesions	1	.
STOMACH		
Submitted	1	0
No Visible Lesions	1	.
THYMUS		
Submitted	1	0
No Visible Lesions	1	.
TONGUE		
Submitted	1	0
No Visible Lesions	1	.
TRACHEA		
Submitted	1	0
No Visible Lesions	1	.
URETER		
Submitted	1	0
No Visible Lesions	1	.
URINARY BLADDER		
Submitted	1	0
No Visible Lesions	1	.

Table 20

Summary of Macroscopic Pathology: Gestation

20248897

Removal Reason(s): TERMINAL EUTHANASIA Summary: Incidence	Female 0 ug/dose Group 1	100 ug/dose Group 2
Number of Animals:	22	24
UTERUS		
Submitted	1	2
No Visible Lesions	1	2
VAGINA		
Submitted	1	0
No Visible Lesions	1	.
UTERUS/CERVIX		
Submitted	1	0
No Visible Lesions	1	.

Table 21

Summary of Macroscopic Pathology: No Confirmed Date of Mating

20248897

Removal Reason(s): TERMINAL EUTHANASIA Summary: Incidence	Female 0 ug/dose Group 1	100 ug/dose Group 2
Number of Animals:	2	5
OVARY		
Submitted	2	5
No Visible Lesions	1	5
Cyst, clear	1	0
SITE, ADMINISTRATION		
Submitted	2	5
No Visible Lesions	2	5
UTERUS		
Submitted	2	5
No Visible Lesions	2	5

Table 22

Summary of Macroscopic Pathology: Lactation

20248897

Removal Reason(s): TERMINAL EUTHANASIA Summary: Incidence	Female 0 ug/dose Group 1	100 ug/dose Group 2
Number of Animals:	19	15
ANIMAL IDENTIFICATION		
Submitted	0	0
ARTERY, AORTA		
Submitted	0	0
BODY CAVITY, NASAL		
Submitted	0	0
BONE, FEMUR		
Submitted	0	0
BONE, STERNUM		
Submitted	0	0
BRAIN		
Submitted	0	0
ESOPHAGUS		
Submitted	0	0
EYE		
Submitted	0	0
GANGLION, DORSAL ROOT, LUMBAR		
Submitted	0	0
GLAND, ADRENAL		
Submitted	0	0
GLAND, CLITORAL		
Submitted	0	0
GLAND, HARDERIAN		
Submitted	0	0
GLAND, LACRIMAL		
Submitted	0	0
GLAND, MAMMARY		
Submitted	0	0
GLAND, PARATHYROID		
Submitted	0	0

Table 22

Summary of Macroscopic Pathology: Lactation

20248897

Removal Reason(s): TERMINAL EUTHANASIA Summary: Incidence	Female 0 ug/dose Group 1	100 ug/dose Group 2
Number of Animals:	19	15
GLAND, PITUITARY		
Submitted	0	0
GLAND, SALIVARY, PAROTID		
Submitted	0	0
GLAND, SALIVARY, SUBLINGUAL		
Submitted	0	0
GLAND, THYROID		
Submitted	0	0
GLAND, ZYMBALS		
Submitted	0	0
HEART		
Submitted	0	0
JOINT, FEMOROTIBIAL		
Submitted	0	0
KIDNEY		
Submitted	0	0
LARGE INTESTINE, CECUM		
Submitted	0	0
LARGE INTESTINE, COLON		
Submitted	0	0
LARGE INTESTINE, RECTUM		
Submitted	0	0
LARYNX		
Submitted	0	0
LIVER		
Submitted	0	0
LUNG		
Submitted	0	0
LYMPH NODE, ILIAC		
Submitted	0	0

Table 22

Summary of Macroscopic Pathology: Lactation

20248897

Removal Reason(s): TERMINAL EUTHANASIA Summary: Incidence	Female 0 ug/dose Group 1	100 ug/dose Group 2
Number of Animals:	19	15
LYMPH NODE, INGUINAL		
Submitted	0	0
LYMPH NODE, MANDIBULAR		
Submitted	0	0
LYMPH NODE, MESENTERIC		
Submitted	0	0
MUSCLE, SKELETAL		
Submitted	0	0
NERVE, OPTIC		
Submitted	0	0
NERVE, SCIATIC		
Submitted	0	0
OVARY		
Submitted	0	0
OVIDUCT		
Submitted	0	0
PANCREAS		
Submitted	0	0
SITE, ADMINISTRATION		
Submitted	19	15
No Visible Lesions	19	15
SKIN		
Submitted	0	0
SMALL INTESTINE, DUODENUM		
Submitted	0	0
SMALL INTESTINE, ILEUM		
Submitted	0	0
SMALL INTESTINE, JEJUNUM		
Submitted	0	0
SPINAL CORD		
Submitted	0	0

Table 22

Summary of Macroscopic Pathology: Lactation

20248897

Removal Reason(s): TERMINAL EUTHANASIA Summary: Incidence	Female 0 ug/dose Group 1	100 ug/dose Group 2
Number of Animals:	19	15
SPLEEN		
Submitted	0	0
STOMACH		
Submitted	0	0
THYMUS		
Submitted	0	0
TONGUE		
Submitted	0	0
TRACHEA		
Submitted	0	0
URETER		
Submitted	0	0
URINARY BLADDER		
Submitted	0	0
UTERUS		
Submitted	0	0
VAGINA		
Submitted	0	0

Table 22

Summary of Macroscopic Pathology: Lactation

20248897

Removal Reason(s): Euthanized No Surviving Pups Summary: Incidence	Female 0 ug/dose Group 1
Number of Animals:	1
ANIMAL IDENTIFICATION	
Submitted	1
No Visible Lesions	1
ARTERY, AORTA	
Submitted	1
No Visible Lesions	1
BODY CAVITY, NASAL	
Submitted	1
No Visible Lesions	1
BONE, FEMUR	
Submitted	1
No Visible Lesions	1
BONE, STERNUM	
Submitted	1
No Visible Lesions	1
BRAIN	
Submitted	1
No Visible Lesions	1
ESOPHAGUS	
Submitted	1
No Visible Lesions	1
EYE	
Submitted	1
No Visible Lesions	1
GANGLION, DORSAL ROOT, LUMBAR	
Submitted	1
No Visible Lesions	1
GLAND, ADRENAL	
Submitted	1
No Visible Lesions	1
GLAND, CLITORAL	
Submitted	1
No Visible Lesions	1

Table 22

Summary of Macroscopic Pathology: Lactation

20248897

Removal Reason(s): Euthanized No Surviving Pups Summary: Incidence	Female 0 ug/dose Group 1
Number of Animals:	1
GLAND, HARDERIAN	
Submitted	1
No Visible Lesions	1
GLAND, LACRIMAL	
Submitted	1
No Visible Lesions	1
GLAND, MAMMARY	
Submitted	1
No Visible Lesions	1
GLAND, PARATHYROID	
Submitted	1
No Visible Lesions	1
GLAND, PITUITARY	
Submitted	1
No Visible Lesions	1
GLAND, SALIVARY, PAROTID	
Submitted	1
No Visible Lesions	1
GLAND, SALIVARY, SUBLINGUAL	
Submitted	1
No Visible Lesions	1
GLAND, THYROID	
Submitted	1
No Visible Lesions	1
GLAND, ZYMBALS	
Submitted	1
No Visible Lesions	1
HEART	
Submitted	1
No Visible Lesions	1
JOINT, FEMOROTIBIAL	
Submitted	1
No Visible Lesions	1

Table 22

Summary of Macroscopic Pathology: Lactation

20248897

Removal Reason(s): Euthanized No Surviving Pups Summary: Incidence	Female 0 ug/dose Group 1
Number of Animals:	1
KIDNEY	
Submitted	1
No Visible Lesions	1
LARGE INTESTINE, CECUM	
Submitted	1
No Visible Lesions	1
LARGE INTESTINE, COLON	
Submitted	1
No Visible Lesions	1
LARGE INTESTINE, RECTUM	
Submitted	1
No Visible Lesions	1
LARYNX	
Submitted	1
No Visible Lesions	1
LIVER	
Submitted	1
No Visible Lesions	1
LUNG	
Submitted	1
No Visible Lesions	1
LYMPH NODE, ILIAC	
Submitted	1
No Visible Lesions	1
LYMPH NODE, INGUINAL	
Submitted	1
No Visible Lesions	1
LYMPH NODE, MANDIBULAR	
Submitted	1
No Visible Lesions	1
LYMPH NODE, MESENTERIC	
Submitted	1
No Visible Lesions	1

Table 22

Summary of Macroscopic Pathology: Lactation

20248897

Removal Reason(s): Euthanized No Surviving Pups Summary: Incidence	Female 0 ug/dose Group 1
Number of Animals:	1
MUSCLE, SKELETAL	
Submitted	1
No Visible Lesions	1
NERVE, OPTIC	
Submitted	1
No Visible Lesions	1
NERVE, SCIATIC	
Submitted	1
No Visible Lesions	1
OVARY	
Submitted	1
No Visible Lesions	1
OVIDUCT	
Submitted	1
No Visible Lesions	1
PANCREAS	
Submitted	1
No Visible Lesions	1
SITE, ADMINISTRATION	
Submitted	1
No Visible Lesions	1
SKIN	
Submitted	1
No Visible Lesions	1
SMALL INTESTINE, DUODENUM	
Submitted	1
No Visible Lesions	1
SMALL INTESTINE, ILEUM	
Submitted	1
No Visible Lesions	1
SMALL INTESTINE, JEJUNUM	
Submitted	1
No Visible Lesions	1

Table 22

Summary of Macroscopic Pathology: Lactation

20248897

Removal Reason(s): Euthanized No Surviving Pups Summary: Incidence	Female 0 ug/dose Group 1
Number of Animals:	1
SPINAL CORD	
Submitted	1
No Visible Lesions	1
SPLEEN	
Submitted	1
No Visible Lesions	1
STOMACH	
Submitted	1
No Visible Lesions	1
THYMUS	
Submitted	1
No Visible Lesions	1
TONGUE	
Submitted	1
No Visible Lesions	1
TRACHEA	
Submitted	1
No Visible Lesions	1
URETER	
Submitted	1
No Visible Lesions	1
URINARY BLADDER	
Submitted	1
No Visible Lesions	1
UTERUS	
Submitted	1
No Visible Lesions	1
VAGINA	
Submitted	1
No Visible Lesions	1

Table 23

Summary of Maternal Observations: Lactation

20248897

Observation Type: All Types Sex: Female From Day 0 (Littering (A)) to 21 (Littering)	0 ug/dose Group 1	100 ug/dose Group 2
Grooming of pups - normal		
Number of Animals Affected	20	15
Number of Times Recorded	20	15
% of Affected Animals	100	100
First to Last seen	0 - 1	0 - 1
AmntcSacPlcntaUmbilicaRem-norm		
Number of Animals Affected	20	15
Number of Times Recorded	20	15
% of Affected Animals	100	100
First to Last seen	0 - 1	0 - 1
Not nursing pups		
Number of Animals Affected	1	0
Number of Times Recorded	2	0
% of Affected Animals	5	0
First to Last seen	1 - 2	-
Nursing activity – normal		
Number of Animals Affected	19	15
Number of Times Recorded	410	326
% of Affected Animals	95	100
First to Last seen	0 - 21	0 - 21
Nesting activity – normal		
Number of Animals Affected	20	15
Number of Times Recorded	412	326
% of Affected Animals	100	100
First to Last seen	0 - 21	0 - 21

Table 24

Summary of Natural Delivery Observations

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)		0 ug/dose Group 1	100 ug/dose Group 2
Group Size - Females		22	22
Number of Females Pregnant [f]	N+ve	20	15
	%	90.9	68.2
Gestation Length (Days) [k]	Mean	21.6	21.7
	SD	0.7	0.5
	N	20	15
	%Diff	-	0.3
Gestation Index [f]	%	100.0	100.0
	ProA	20/20	15/15
Females Completing Delivery [f]	N+ve	20	15
Females with Liveborn [f]	N+ve	20	15
Female with no Liveborn Pups [f]	N+ve	0	0
Fem w/ Stillborn Pups [f]	N+ve	2	2
Stillborn Pups/Litter [k]	Mean	0.68	1.03
	SD	2.11	2.73
	N	20	15
	%Diff	-	52.01
Number Pups Stillborn	Sum	2	2
Number Live Newborn Pups [k]	Mean	13.6	13.5
	SD	2.3	2.5
	N	20	15
	%Diff	-	-0.5
	Sum	272	203
Live Birth Index (%) [k]	Mean	99.32	98.97
	SD	2.11	2.73
	N	20	15
	%Diff	-	-0.36
Live Male Pups/Litter (%) Birth [G]	Mean	52.01	43.90
	SD	12.88	17.57
	N	20	15
	%Diff	-	-15.59

[f] - Fisher's Exact
[k] - Kruskal-Wallis & Dunn
[G] - Anova & Dunnett

Table 24

Summary of Natural Delivery Observations

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)		0 ug/dose Group 1	100 ug/dose Group 2
Implantation Sites - Total [k]	Mean	15.1	14.6
	SD	1.5	2.3
	N	20	15
	%Diff	-	-3.3
Post-implant Loss/Litter (%) [k]	Mean	8.97	5.84
	SD	14.10	11.42
	N	20	15
	%Diff	-	-34.85

[k] - Kruskal-Wallis & Dunn

Table 25

Summary of Pup Clinical Observations: F1 Generation

Group 1 - Control Article

Group 2 - mRNA-1273 100 µg/dose

		GROUP 1	GROUP 2
LITTERS EXAMINED	N	20	15
Skin, Scab			
Number of Times Recorded	N	3	6
Number of Litters Affected	N	1	1
Dehydrated Suspected			
Number of Times Recorded	N	1	0
Number of Litters Affected	N	1	0
Cold to Touch			
Number of Times Recorded	N	24	1
Number of Litters Affected	N	2	1
Discharge, Red			
Number of Times Recorded	N	1	0
Number of Litters Affected	N	1	0
Fur, Ungroomed			
Number of Times Recorded	N	0	8
Number of Litters Affected	N	0	1
No Milk Band Present			
Number of Times Recorded	N	0	1
Number of Litters Affected	N	0	1
Skin Discolored, Pale, Purple or Black			
Number of Times Recorded	N	8	1
Number of Litters Affected	N	3	1

20248897

Table 26

Summary of Litter Observations

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)		0 ug/dose Group 1	100 ug/dose Group 2
Group Size - Females		20	15
Females with Liveborn	N+ve	20	15
Viability Index % [k]	Mean	91.01	96.84
	SD	24.63	7.03
	N	20	15
	%Diff	-	6.42
Lactation Index [k]	Mean	99.34	100.00
	SD	2.87	0.00
	N	19	15
	%Diff	-	0.66
Live Male Pups/Litter (%) 21 [G]	Mean	50.69	46.67
	SD	7.79	12.91
	N	19	15
	%Diff	-	-7.94

[k] - Kruskal-Wallis & Dunn
[G] - Anova & Dunnett

Table 27
Summary of Litter Mean Pup Body Weights: F1 Generation

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)			0 ug/dose Group 1	100 ug/dose Group 2
Litter Mean Pup BW	1 [G]	Mean	7.24	7.36
		SD	0.79	0.66
		N	20	15
		%Diff	-	1.65
	4 [G]	Mean	10.39	10.67
		SD	1.26	0.98
		N	19	15
		%Diff	-	2.63
	7 [G]	Mean	17.00	17.75
		SD	2.21	1.39
		N	19	15
		%Diff	-	4.42
	10 [G]	Mean	24.67	26.29*
		SD	2.61	1.55
		N	19	15
		%Diff	-	6.57
	14 [G]	Mean	35.26	37.23*
		SD	2.99	2.48
		N	19	15
		%Diff	-	5.61

[G] - Anova & Dunnett: * = $p \leq 0.05$

Table 27
Summary of Litter Mean Pup Body Weights: F1 Generation

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)			0 ug/dose Group 1	100 ug/dose Group 2
Litter Mean Pup BW	18 [G]	Mean	45.61	47.52
		SD	3.13	3.18
		N	19	15
		%Diff	-	4.19
	21 [G]	Mean	58.99	61.36
		SD	4.32	3.71
		N	19	15
		%Diff	-	4.01
Litter Mean Pup BW M	1 [G]	Mean	7.38	7.59
		SD	0.83	0.76
		N	20	15
		%Diff	-	2.83
	4 [G]	Mean	10.61	10.92
		SD	1.22	1.12
		N	19	15
		%Diff	-	2.94
	7 [G]	Mean	17.37	18.05
		SD	2.28	1.29
		N	19	15
		%Diff	-	3.96

[G] - Anova & Dunnett

Table 27
Summary of Litter Mean Pup Body Weights: F1 Generation

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)			0 ug/dose Group 1	100 ug/dose Group 2
Litter Mean Pup BW M	10 [G]	Mean	25.14	26.66
		SD	2.74	1.73
		N	19	15
		%Diff	-	6.05
	14 [G]	Mean	35.78	37.63
		SD	3.12	2.66
		N	19	15
		%Diff	-	5.15
	18 [G]	Mean	46.29	48.11
		SD	3.21	3.42
		N	19	15
		%Diff	-	3.92
	21 [G]	Mean	60.18	62.38
		SD	4.55	4.19
		N	19	15
		%Diff	-	3.65
Litter Mean Pup BW F	1 [G]	Mean	7.08	7.14
		SD	0.79	0.67
		N	20	15
		%Diff	-	0.73

[G] - Anova & Dunnett

Table 27
Summary of Litter Mean Pup Body Weights: F1 Generation

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)			0 ug/dose Group 1	100 ug/dose Group 2
Litter Mean Pup BW F	4 [G]	Mean	10.14	10.39
		SD	1.34	1.03
		N	19	15
		%Diff	-	2.45
	7 [G]	Mean	16.62	17.43
		SD	2.23	1.56
		N	19	15
		%Diff	-	4.88
	10 [G]	Mean	24.18	25.92*
		SD	2.62	1.69
		N	19	15
		%Diff	-	7.18
	14 [G]	Mean	34.71	36.81*
		SD	3.07	2.51
		N	19	15
		%Diff	-	6.04
	18 [G]	Mean	44.90	46.92
		SD	3.32	3.06
		N	19	15
		%Diff	-	4.50

[G] - Anova & Dunnett: * = $p \leq 0.05$

Table 27
Summary of Litter Mean Pup Body Weights: F1 Generation

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)			0 ug/dose Group 1	100 ug/dose Group 2
Litter Mean Pup BW F	21 [G]	Mean	57.78	60.24
		SD	4.44	3.44
		N	19	15
		%Diff	-	4.26
LM Post-cull Pup BW	4 [G]	Mean	10.36	10.64
		SD	1.24	1.05
		N	19	15
		%Diff	-	2.65
LM Postcull Pup BW M	4 [G]	Mean	10.61	10.86
		SD	1.22	1.10
		N	19	15
		%Diff	-	2.33
LM Postcull Pup BW F	4 [G]	Mean	10.10	10.39
		SD	1.32	1.11
		N	19	15
		%Diff	-	2.84

[G] - Anova & Dunnett

Table 28

Summary of Pup Gross Pathology F1 Generation

20248897
Litter: A

Exam Type: Pup Necropsy - Unscheduled		0 ug/dose Group 1	100 ug/dose Group 2
Number of Pups Examined:		18	5
Number of Litters Examined:		6	4
Brain			
Brain, Dilatation, Moderate	Pups N(%)	1(5.6)	0(0.0)
	Litters N(%)	1(16.7)	0(0.0)

Pups N(%) N=Group Pup Incidence;(%)=Group % of Pups with the Abnormality
Litters N(%) N=Group Litter Incidence,(%)=Group % Litters with the Abnormality

Table 28

Summary of Pup Gross Pathology F1 Generation

20248897
Litter: A

Exam Type: Pup Necropsy 2		0 ug/dose Group 1	100 ug/dose Group 2
Number of Pups Examined:		148	118
Number of Litters Examined:		19	15
Kidney			
Renal papilla, Both, Small, Moderate - Variation	Pups N(%)	0(0.0)	1(0.8)
	Litters N(%)	0(0.0)	1(6.7)
Renal papilla, Left, Small, Moderate - Variation	Pups N(%)	0(0.0)	1(0.8)
	Litters N(%)	0(0.0)	1(6.7)

Pups N(%) N=Group Pup Incidence;(%)=Group % of Pups with the Abnormality
Litters N(%) N=Group Litter Incidence,(%)=Group % Litters with the Abnormality

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DEVIATIONS

All deviations that occurred during Testing Facility Study No. 20248897 have been authorized/acknowledged by the Study Director, assessed for impact, and documented in the study records. All GLP and protocol deviations are listed below. Minor SOP deviations have been retained in the raw data.

None of the deviations were considered to have impacted the overall integrity of the study or the interpretation of the study results and conclusions.

GLP = Good Laboratory Practice; LD= Lactation Day; GD = Gestation Day; SD = Study Day.

GLP

- On 21 Aug 2020, For female rat PO 506, euthanasia was performed on 08 Jul 2020, and necropsy and euthanasia via anesthesia and exsanguination were documented as occurring on 21 Aug 2020, with no explanation. A necropsy was not required by protocol, as the rat was considered extra. All PO file spaces were removed on the same date and the disposition has 5 females on it for the same date and specifically documents the PO #s. This deviation did not have an adverse impact on the study because the PO rats were not required for study assignment and all PO and study rats have been accounted for.

In-life Observations, Measurements, and Evaluations

- On SD 26 (25 Jul 2020), viability checks were only performed once in the AM. All rats were alive with access to food and water at the viability check on DS 27 in the AM. This deviation did not have an adverse impact on the study because all rats were alive with access to food and water at the following viability check.
- On GD 10 (13 Aug 2020), body weights were not recorded for rats 5539 and 5543 (Group 1) and 5551, 5553, 5558, 5562 and 5576 (Group 2). This deviation did not have an adverse impact on the study because there are sufficient body weights available for the interpretation of the study.
- On 31 Aug 2020, the following cohort 2 females did not have feed remaining or initial values recorded: LD 7: 5544 (Group 1), LD 10: 5526,5529,5536 (Group 1), and 5579, 5580, 5581, 5582, 5586, 5587, and 5588 (Group 2). This deviation did not have an adverse impact on the study because the omitted values do not adversely impact the interpretation of the study.

Laboratory Evaluations

- On 30 Jun 2020, the DS 1 antibody sample for rats 5525-5528 (Group 1) were not allowed to clot for at least 20 minutes prior to centrifugation. The serum sample from rat 5525 was placed in the centrifuge 1 minute early and rats 5526-5528 were placed in the centrifuge 3 minutes early. This deviation does not have an adverse impact on the study because this did not have any impact on sample analysis and these samples did not demonstrate aberrant results.

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- On DS 15 (14 Jul 2020), a second aliquot of serum was unable to be obtained for rats 5521 and 5543 (Group 1). This deviation did not have an adverse impact on the study because the first aliquot was successfully analyzed. This deviation did not have an adverse impact on the study because the first aliquot was successfully analyzed.
- On GD 21 (18 to 21 Aug 2020), the required 1.0 mL pooled was not collected from the following litters: 5503 (0.6 mL), 5505 (0.5 mL), 5509 (0.55 mL), 5510 (0.4 mL), 5511 (0.4 mL), 5512 (0.6 mL), 5513 (0.6 mL), 5516 (0.4 mL), 5523 (0.5 mL), 5502 (0.6 mL), 5504 (0.6 mL), 5507 (0.55 mL), 5522 (0.8 mL), 5508 (0.55 mL), 5515 (0.55 mL), 5518 (0.7 mL), 5521 (0.6 mL), 5501 (0.8 mL), 5506 (0.8 mL), 5519 (0.7 mL) (Group 1), and 5545 (0.5 mL), 5548 (0.55 mL), 5549 (0.7 mL), 5552 (0.3 mL), 5554 (0.5 mL), 5559 (0.55 mL), 5564 (0.3 mL), 5566 (0.3 mL), 5568 (0.4 mL), 5570 (0.5 mL), 5550 (0.5 mL), 5561 (0.6 mL), 5565 (0.6 mL), 5546 (0.7 mL), 5547 (0.7 mL), 5555 (0.7 mL), 5557 (0.7 mL), 5563 (0.7 mL), 5567 (0.7 mL), and 5569 (0.7 mL). This deviation did not have an adverse impact on the study because there was a suffient volume available for analysis. This deviation did not have an adverse impact on the study because there was a suffient volume available for analysis.
- On LD 21 (12 Sep 2020), F0 generation Cohort 2 female 5571 (Group 2) had the antibody blood sample processed 18 minutes after blood collection, instead of being processed at least 20 minutes after blood collection as required by the protocol. This deviation does not have an adverse impact on the study because this did not have any impact on sample analysis and this sample did not demonstrate aberrant results.

Postmortem and Pathology

- On 18 Aug 2020, an incomplete Aliquot 1 (240 uL) and no Aliquot 2 (remainder) was obtained for the following Fetal Pooled serum samples due to low sample volume at blood collection: Group 1: 5505, 5510, 5511, 5516, 5523 and Group 2: 5552, 5564, 5566, 5568, 5570. This deviation did not have an adverse impact on the study because the first aliquot as successfully analyzed.
- On 18 Aug 2020, no gravid uterus weight was recorded for F0 generation female rat 5568 in Group 2 (cohort 1). This deviation did not have an adverse impact on the study because there were sufficient weights available for data interpretation. This deviation did not have an adverse impact on the study because there were sufficient weights available for data interpretation.
- On 18 and 21 Aug 2020, a gross examination at necropsy was required for cohort 1 animals. 5528 (21 Aug 2020) and 5570 (18 Aug 2020) do not indicate that a gross necropsy examination was performed. This deviation does not have an adverse impact on the study because there is sufficient gross necropsy data for the interpretation of study results.
- On GD 21 (18 Aug 2020), the following rat fetuses assigned to decapitation blood collection did not have the method of euthanasia documented: 5516-2, 5516-4, 5516-6, 5516-8, 5516-10, 5516-12, 5501-2, 5501-4, 5501-6, 5501-8, 5501-10, 5506-2, 5506-4, 5506-6, 5506-8, 5506-10, 5506-12, 5506-14, 5519-2, 5519-4, 5519-6, 5519-9, 5519-11, 5528-2, 5528-4,

Appendix 1

5528-6, 5528-8, 5528-10 and 5528-12 (Group 1), and 5556-2, 5556-4, 5556-6, 5556-8, 5556-10, 5556-13, 5560-2, 5560-4, 5560-7, 5560-9, 5560-11 and 5560-13 (Group 2). However, the route of blood collection was documented as decapitation. This deviation did not have an adverse impact on the study because it is presumed to be a documentation error based on decapitation itself being the standard method of euthanasia utilized when decapitation for blood collection is required.

- On 19 and 20 Aug 2020, per protocol section 15.2.1, found dead on day 0 or 1 were to be evaluated for vital status at birth. Per facility SOPs, this is done by a trained litter technician. Found dead pups 5575-6 (male, Group 2) and 5584-9 (male, Group 2) were both evaluated for vital status and then retained in 10% NBF per protocol. Per SOP, all unscheduled and found dead animals are to be necropsied to the extent required by protocol as soon as possible but not more than 20 hours after discovery and should be held refrigerated prior to necropsy. Pup 5575-6 was retained in 10% NBF for 6 days prior to discovery necropsy was incomplete and pup 5584-9 was retained in 10% NBF for 7 days prior to discovery necropsy was incomplete. This deviation did not have an adverse impact on the study because there is sufficient necropsy data from other pups available for interpretation.
- On 21 Aug 2020, for the following Cohort 1 rat litters, there is no documentation that fetuses not selected for blood collection were euthanized via intraperitoneal injection of Fatal Plus: 5501, 5506, 5519 and 5528 (Group 1), and 5556 and 5560 (Group 2). However, evisceration was documented for all the above litters, therefore, euthanasia must have occurred for the fetuses not selected for blood collection, as evisceration occurred for said fetuses. Therefore, only the method of euthanasia is unknown. This deviation did not have an adverse impact on the study because the method of euthanasia for these fetuses does not adversely impact any study endpoint.
- On 22 Aug 2020, per protocol, all found dead, unscheduled, and still born pups were to receive a complete necropsy. For the following F1 pups only a gross necropsy was documented: 5526-17 (Group 1, female), 5536-16,17 (Group 1, female), 5580- 18 (Group 2, female), and 5585-15 (Group 2, female). This deviation did not have an adverse impact on the study because histopathological evaluation of the tissues was not required for the interpretation of the study.
- On 23 Aug 2020 and 08 Sep 2020, for F1 rat pups: 5577-2 (PND 21, Group 2, male, Cohort 2), 5577-10 (PND 21, Group 2, female, Cohort 2) and 5585-10 (PND 4, Group 2, male, Cohort 2), no necropsy observations were collected. However, for 5577-2 and 5577-10, it was documented that a gross examination was performed. This deviation did not have an adverse impact on the study because the omitted observations do not adversely impact the interpretation of the study.
- On 10 Sep 2020, for Cohort 2 F1 male rat 5524-6 (Group 1), the pituitary gland was lost during processing; this male had been randomly selected for complete tissue retention. This deviation did not have an adverse impact on the study because the pituitary gland was not required for evaluation.

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Other

- The residual aliquot 1 samples were archived at the Test Site and the aliquot 2 antibody analysis samples maintained at the Testing Facility as backup samples were archived at the Testing Facility rather than returned to the Sponsor. This deviation did not have an adverse impact on the study because the samples are archived.
- Uteri and ovaries of apparently nonpregnant rats retained in 10% neutral buffered formalin were archived at the Testing Facility rather than discarded. This deviation did not have an adverse impact on the study because the tissues are archived.
- The plates were to be coated with SARS-CoV2 S Protein (sino Biological) and read at OD 450nm and then antibody units were to be calculated using a SoftMax software, however, the the plates were coated with SARS-CoV2 S2P protein (GenScript), read at OD 650nm and the results were then calculated using VersaMax. This deviation did not have an adverse impact on the study because this was a discrepancy in the protocol and the analysis was conducted appropriately.

Appendix 1

charles river

PROTOCOL AMENDMENT NO. 4

Testing Facility Study No. 20248897

A GLP Intramuscular Combined Developmental and Perinatal/Postnatal Reproductive Toxicity Study of mRNA-1273 in Rats

SPONSOR:
Moderna TX, Inc.
200 Technology Square
Cambridge, MA 02139
United States

TESTING FACILITY:
Charles River Laboratories, Inc.
905 Sheehy Drive
Horsham, PA 19044
United States

Appendix 1

SUMMARY OF CHANGES AND JUSTIFICATIONS

Protocol effective date: 16 Jun 2020

Note: When applicable, additions are indicated in bold underlined text and deletions are indicated in bold strikethrough text in the affected sections of the document.

Item or Section(s)	Justification
Amendment 1	**Date: 29 Jun 2020**
2. PROPOSED STUDY SCHEDULE	This change removes the audited draft report date for the antibody analysis report as this phase of the study is being performed non-GLP.
5.2. Test Material Identification	This change removes an erroneous footnote.
6.1. Preparation of Formulations	These changes clarify the storage conditions for the test and control articles.
6.3. Sample Collection and Analysis	This change adds a footnote to the first preparation to clarify the homogeneity results.
6.3.1.1. Concentration and Homogeneity Analysis	This change corrects the header for the concentration and homogeneity analysis.
7.3.1. F0 Generation	This change clarifies when animals will be assigned to cohorts.
10. IN-LIFE PROCEDURES, OBSREVATIONS, AND MEASUREMENTS – F0 GENERATION	This change clarifies that food consumption will not be recorded during the cohabitation period. These changes also clarify the directive for the females that do not mate after the 7-day cohabitation period and clarify that females will be assigned to Cohorts 1 or 2 following cohabitation.
12.1.1. Maternal Samples (Cohorts 1 and 2)	This change removes the footnote for collection prior to dose administration on LD 21 as the animals will not be dosed on this day.
12.3. Antibody Sample Analysis	This change corrects the disposition of the antibody samples 6 months following issuance of the Draft Report.
13. TERMINAL PROCEDURES – F0 Generation	These changes correct the references to the attachments for the tissue collections.
ATTACHMENT B, ATTACHMENT C	These changes remove erroneous footnotes, clarifies that the number in the collection column refers to the number to be collected, and removes animal identification from the tissues to be collected for the F1 generation as they will not be individually identified.
ATTACHMENT D	This change adjusts the shipment date for first preparation dose formulation samples.
Amendment 2	**Date: 23 Jul 2020**
Summary of Changes and Justifications – Amendment 1	This change corrects a typographical error.
5.3. Control Article Identification, 6.2.1. Preparation of Control Article	These changes correct the control article identification.
12.3. Antibody Sample Analysis	This change removes the draft report type.
15.2.1. Days 0 to 21 Postpartum	This change clarifies that the whole pup will be retained for any pups PNDs 0-10. Individual tissues will be collected for any pups PNDs 11-21.
ATTACHMENT B	This change clarifies the lymph nodes to be collected.

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Item or Section(s)	Justification
Amendment 3	**Date: 17 Aug 2020**
12.1.2. Fetal Samples (Cohort 1)	These changes clarify which animals are to be used for antibody evaluation fetal sample collections and changes the route of collection to decapitation for animals assigned to the visceral examinations with the option to use the carotid artery from fetuses assigned to the skeletal evaluations in cases where there are not enough viable fetuses assigned to visceral exams.
14. FETAL EXAMINATIONS – COHORT 1	These changes correct/clarify the fetal examinations for Cohort 1.
Amendment 4	**Date: 18 Nov 2020**
16. STATISTICAL ANALYSIS, 16.2. Constructed Variables, and 16.3. Inferential Statistical Methods	These changes remove statistical analysis for preweaning pup necropsy observations, add the statistical analysis performed on the corrected body weights and gravid uterine weights, and adjust the footnotes and in the statistical matrix table.

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1. OBJECTIVE

The objective of this study is to assess the potential effects of mRNA-1273, a vaccine development candidate against SARS-CoV-2 infection, on fertility and pre and postnatal development in the pregnant and lactating female on Sprague Dawley CD (Crl:CD[SD]) rat.

2. PROPOSED STUDY SCHEDULE

Proposed study dates are listed below. Actual dates will be included in the Final Report.

Animal Arrival:	23 Jun 2020
Initiation of Dosing:	30 Jun 2020
Initiation of Estrous Cycle Evaluations:	14 Jul 2020
Initiation of F0 Generation Cohabitation:	27 Jul 2020
First Possible Gestation Day 0:	28 Jul 2020
First Possible Delivery:	18 Aug 2020 (GD 21)
Last Possible Delivery:	28 Aug 2020 (GD 25)
Completion of In-Life:	18 Sep 2020 (Last possible date of necropsy)
Unaudited Draft Report:	16 Nov 2020
Audited Draft Report:	16 Dec 2020

The contributions from Principal Investigators to Study Director are proposed at the dates indicated below to allow inclusion in Unaudited/Audited Draft Reports.

Unaudited Antibody Analysis Draft Report:	09 Nov 2020
Unaudited Dose Formulation Draft Report:	09 Nov 2020
Audited Dose Formulation Draft Report:	09 Dec 2020

FDA-CBER-2022-4207-0123

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3. SPONSOR

Role/Phase	Name	Contact Information
Sponsor Representative/Study Monitor	(b) (6)	Address as cited for the Sponsor Tel: (b) (6) E-mail: (b) (6)
Toxicology Director of Toxicology		Address as cited for the Sponsor Tel: (b) (6) E-mail: (b) (6)
Infectious Disease Biomarkers		Address as cited for the Sponsor Tel: (b) (6) E-mail: (b) (6)
Analytical Development		Address as cited for the Sponsor Tel: (b) (6) E-mail: (b) (6)

4. RESPONSIBLE PERSONNEL

Role/Phase	Quality Assurance Unit (QAU)	Name	Contact Information
Study Director	Charles River	(b) (6)	Address as cited for Testing Facility Tel: (b) (6) Fax: (b) (6) E-(b) (6)
Testing Facility Management	Charles River		Address as cited for Testing Facility Tel: (b) (6) Fax: (b) (6) E-(b) (6)
Scientific Reviewer	Charles River		Address as cited for Testing Facility Tel: (b) (6) Fax: (b) (6) E-mail (b) (6)
Testing Facility QAU	Charles River		Address as cited for Testing Facility Tel: (b) (6) E-mail (b) (6)
Principal Investigator (PI)			
Analytical Chemistry[a]	Charles River	(b) (6)	Charles River Laboratories Montreal ULC Senneville Site (CR-SEN) 22022 Transcanadienne Senneville, QC H9X 3R3 Canada Tel: (b) (6) E-mail: (b) (6)

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Role/Phase	Quality Assurance Unit (QAU)	Name	Contact Information
Antibody Analysis[b]	N/A (Non-GLP)	(b) (6)	Integrated Biotherapeutics, Inc. 4 Research Court, Suite 300, Rockville, MD 20850 USA Tel (b) (6) E-mail (b) (6)

[a] Testing Facility designated Test Site
[b] Sponsor designated Test Site.

Each PI is required to report all deviations or other circumstances that could affect the quality or integrity of the study to the Study Director in a timely manner for authorization/acknowledgement. Each PI, will provide a report addressing their assigned phase of the study, which will be included as an appendix to the Final Report.

The PI phase report will include the following:

- A Statement of Compliance (if the applicable phase is GLP)
- A QA Statement (if the applicable phase is GLP)
- The archive site for all records, samples, specimens and reports generated from the phase or segment (alternatively, details regarding the retention of the materials may be provided to the Study Director for inclusion in the Final Report)
- A listing of critical computerized systems used in the conduct and/or interpretation of the assigned study phase

5. TEST MATERIALS

5.1. Test and Control Article Characterization

The Sponsor will provide to the Testing Facility documentation of the identity, strength, purity, composition, and stability for the test and control article(s). A Certificate of Analysis or equivalent documentation will be provided for inclusion in the Final Report.

The Sponsor has appropriate documentation on file concerning the method of synthesis, fabrication or derivation of the test and control article(s), and this information is available to the appropriate regulatory agencies should it be requested.

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5.2. Test Material Identification

Test Article Identification

	Test Article
Identification:	mRNA-1273 LNP Solution
Batch/Lot No.:	DH-03026
Expiration:	18 Nov 2020
Physical Description:	White to off-white dispersion; essentially free of visible particles.
Supplied Stock Concentration:	0.76 mg/mL
Correction Factor:	None
Storage Conditions (temperature set to maintain):	Ultrafrozen -60°C to -90°C
Provided by:	Sponsor
Test Article Contact:	(b) (6) E-Mail:

5.3. Control Article Identification

Control Article Identification

	Control Article (Dilution Buffer)
Identification:	20 mM Tris, 8.7% Sucrose, pH 7.5
Batch/Lot No.:	DH-03026.2
Expiration Date:	18 Nov 2020
Physical Description:	Clear colorless solution free from visible particulates
Storage Conditions (temperature set to maintain):	Ultrafrozen -60°C to -90°C
Provided by:	Sponsor

5.4. Reserve Samples

For each batch (lot) of Test Article and Control Article, a reserve sample will be collected and maintained under the appropriate storage conditions by the Testing Facility.

5.5. Test and Control Article Inventory and Disposition

Records of the receipt, distribution, storage, and disposition of test materials will be maintained. All unused Sponsor-supplied bulk test materials, with the exception of reserve samples, will be returned to the Sponsor following issuance of the Draft Report, discarded, or retained for use on future studies.

5.6. Safety

The Safety Precautions for the study follow the standards for a Charles River Occupational Exposure Band (No. 3) categorized material.

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6. DOSE FORMULATION AND ANALYSIS

6.1. Preparation of Formulations

Dose formulations will be prepared fresh daily on each day of dosing and may be divided into aliquots, when required.

Test and Control Article dosing formulations will be used for dose administration within 4 hours of preparation.

Preparation Details

Dose Formulation	Administration Dose Form	Frequency of Preparation	Storage Conditions (temperature set to maintain)[a]
Control Article	Solution	Daily	Ambient/room temperature conditions for <4 hours or <8 hours refrigerated (2-8°C) if not used within 3 hours of preparation
Test Article	Solution	Daily	Ambient/room temperature conditions for <4 hours or <8 hours refrigerated (2-8°C) if not used within 3 hours of preparation

[a] Unopened vials may be refrozen after thawing.

6.2. Preparation Details

6.2.1. Preparation of Control Article

Dose formulations will be performed under a biological safety cabinet using aseptic procedures.

The Control Article, 20 mM Tris, 8.7% Sucrose, pH 7.5, will be administered as received. The bulk control article will be removed from the freezer and allowed to thaw at room temperature for no more than 1 hour before dose formulation preparation. The storage of control article dose formulations at room temperature should not exceed 4 hours from the time of preparation to the time of dose administration. The control article dosing formulations may be stored refrigerated (2-8°C) for up to 8 hours if not used for dose administration within 3 hours of preparation. If refrigerated storage is necessary, the control article dosing formulation aliquots will be removed from the refrigerator and allowed to equilibrate at ambient/room temperature for at least 30 minutes before dosing. The formulation will NOT be vortexed or sonicated but may be gently swirled to ensure even mixing during formulation. Thawed Control Article vials will be used only on the day of dose formulation preparation once thawed and will not be used on subsequent dosing days.
Detailed preparation procedures (i.e., Formulation Batch Records [FBR]) will be maintained in the raw data.

Any residual volumes will be retained and discarded prior to study finalization upon Sponsor and Study Director authorization.

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6.2.2. Preparation of Test Article

Dose formulation preparations will be performed under a biological safety cabinet using aseptic procedures.

The bulk Test Article stock will be removed from the freezer and allowed to thaw at room temperature for at least 30 minutes (no more than 1 hour) before dose formulation preparation. The test article dosing formulations will be prepared by diluting the bulk Test Article with the Control Article as necessary to the target concentration for administration and should not be filtered. The storage of test article dosing formulations at room temperature should not exceed 4 hours from the time of preparation to the time of dose administration. The test article dosing formulations may be stored refrigerated (2-8°C) for up to 8 hours if not used for dose administration within 3 hours of preparation. If refrigerated storage is necessary, the test article dosing formulation aliquots will be removed from the refrigerator and allowed to equilibrate at ambient/room temperature for at least 30 minutes before dosing. The formulation will NOT be vortexed or sonicated but may be gently inverted 20 times to ensure even mixing during formulation. Stock vials will be used only on the day of dose formulation preparation once thawed and will not be used on subsequent dosing days.
Detailed preparation procedures (i.e., FBR) will be maintained in the raw data.

Any residual volumes will be retained and discarded prior to study finalization upon Sponsor and Study Director authorization.

6.3. Sample Collection and Analysis

Dose formulation samples will be collected for analysis as indicated in the following table. Additional samples may be collected and analyzed at the discretion of the Study Director.

Dose Formulation Sample Collection Schedule

Interval	Concentration	Sampling From
First Preparation: Day 1	Group 1: 3 x 0.5 mL (middle)	Preparation vessel
	Group 2: 5 x 0.5 mL (top, middle, bottom)[a]	
Approximate Middle Preparation: GD 1	Groups 1 and 2: 5 x 0.5 mL (middle)	Preparation vessel
Last Preparation: GD 13	Groups 1 and 2: 5 x 0.5 mL (middle)	Preparation vessel

[a] The homogeneity results obtained from the top, middle, and bottom preparations will be averaged and utilized as the concentration results.

All samples to be analyzed will be shipped (on dry ice) to Charles River Laboratories Montreal, see ATTACHMENT D. Samples will be shipped on the date prepared, when possible.

The analytical laboratory and Sponsor Representative will be notified before shipment of the samples. Upon receipt at the analytical laboratory, the samples will be stored under ultrafrozen conditions at -60°C to -90°C.

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A temperature monitoring device will be coordinated with the shipping service and added to the shipment by the shipping service. Any temperature monitoring of the shipment will be the responsibility of the Sponsor and/or shipping service and will be outside the scope of the Protocol.

6.3.1. Analytical Method

Analyses described below will be performed under Test Site Study Number 2100930 by Ion-Exchange High Performance Liquid Chromotography (IEX-HPLC) using a validated analytical procedure (CR-SEN validation study 2100933).

6.3.1.1. Concentration and Homogeneity Analysis

Sample Allocation:	Duplicate for analysis, one for backup for Group 1. Duplicate for analysis, triplicate for backup for Group 2. Backup samples may be analyzed at the discretion of the Study Director.
Storage Conditions:	Temperature set to maintain -60°C to -90°C. Samples will be placed into autoclaved amber glass vials.
Acceptance Criteria:	For concentration, the criteria for acceptability will be mean sample concentration results within or equal to ± 15% of theoretical concentration. Each individual sample concentration result within or equal to ± 20%. For homogeneity, the criteria for acceptability will be a relative standard deviation (RSD) of concentrations of ≤ 5% for each group.

7. TEST SYSTEM

Species:	Rat
Strain:	Crl:CD(SD) Sprague Dawley rat
Condition:	Females, virgin
Source:	Charles River Laboratories, Inc.
Number of Females Ordered:	93
Number of Females to be Assigned:	88
Target Age at Arrival:	60 to 70 days
Target Weight at Arrival	200 g to 225 g

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The actual age and weight of the animals at the initiation of dosing will be listed in the Final Report.

Male rats of the same source and strain that are maintained by the Testing Facility will be used only as breeders and are not considered part of the Test System.

7.1. Animal Identification

Method: A subcutaneously implanted electronic identification chip or other approved identification method such indelible ink where required.

7.2. Environmental Acclimation

Method: After receipt at the Testing Facility, the rats will be acclimated for at least 7 days prior to initiation of dosing.

7.3. Selection, Assignment, Replacement, and Disposition of Animals

Replacement: Before the initiation of dosing, any assigned animals considered unsuitable for use in the study will be replaced by alternate animals obtained from the same shipment and maintained under the same environmental conditions, at the discretion of the Study Director. After initiation of dosing, study animals may be replaced during the replacement period with alternate animals in the event of accidental injury, non-test article-related health issues, or similar circumstances, at the discretion of the Study Director.

Disposition: The disposition of all animals will be documented in the study records.

7.3.1. F0 Generation

Selection and Assignment: Female rats will be selected for study on the basis of physical condition and body weights recorded during acclimation. Female rats will be assigned to groups using a computer-based randomization procedure based on body weights recorded during the acclimation period.

Animals in poor health or at extremes of body weight range will not be assigned to groups.

Eighty eight (88) female rats will be assigned to 2 dose groups, 44 rats per group. Additionally, each dose group will consist of two cohorts, 22 rats in each of Cohorts 1 and 2 as described in the following table. Animals will be assigned to cohorts following cohabitation.

Group No.	Cohort 1 (Caesarean – Sectioning Phase)	Cohort 2 (Natural Delivery Phase)
1	22	22
2	22	22

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7.3.2. F1 Generation

Selection and Assignment:	Day 0 of lactation (postpartum) is defined as the day the delivery of the litter appears to be completed. If the litter is observed to be completed at the morning viability check, Day 0 of lactation (postpartum) is defined as the previous day. Day 1 of lactation (postpartum) is defined as the first day on which all pups in a litter are individually weighed and clinical observations are recorded. On Day 0/1 of lactation (postpartum) all pups in a litter will be sexed. On Lactation Day 4 (LD 4) a randomization program will be used to select F1 generation pups to be culled, and litters will be reduced to eight pups each (when possible). Whenever possible, the same number of male and female pups per litter will be continued on study.

8. HUSBANDRY

8.1. Housing

Housing:	Control group animals will be housed on a separate rack from the Test Article-treated animals. F0 generation rats will be co-housed (where possible) in solid-bottomed cages by dose group (no more than 2 per cage) until cohabitation, unless deemed inappropriate by the Study Director and/or Clinical Veterinarian. During the cohabitation period, one breeder male rat and one female rat will be pair housed in the breeder male rat's solid-bottomed cage. After cohabitation, female rats will be individually housed until the day of scheduled euthanasia (Cohort 1) or until parturition (Cohort 2), at which time, each dam and delivered litter will be housed in a common nesting box during the postpartum period. The male breeder rats will be returned to co-housing with their previous same box mates, whenever possible. Any rats not assigned to study may be trio-housed to avoid having a single-housed animal, whenever possible.
Caging:	Polycarbonate cages containing appropriate bedding.

Housing set-up is as described in the *Guide for the Care and Use of Laboratory Animals*.[1] Animals will be separated during designated procedures/activities or will be separated as required for monitoring and/or health purposes, as deemed appropriate by Study Director and/or Clinical Veterinarian. Cages will be arranged on the racks in group order.

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8.2. Animal Enrichment

Type/Frequency:	For psychological/environmental enrichment, animals will be socially housed and will be provided with Crink-l'Nest™, stainless steel resting lofts, and a chewing item such as *ad libitum* pelleted rodent feed, except when interrupted by study procedures/activities.
Analysis:	There are no known contaminants in the animal enrichment that would interfere with the objectives of the study.

8.3. Bedding

Type:	Bed-o'Cobs®
Frequency:	Changed as often as necessary to keep the animals dry and clean.
Analysis:	Results of analysis for environmental contaminants are on file at the Testing Facility. It is considered that there are no known contaminants in the bedding that would interfere with the objectives of the study.

8.4. Environmental Conditions

The targeted conditions for animal room environment will be as follows:

Temperature:	68°F to 79°F (20°C to 26°C)
Humidity:	30% to 70%
Light Cycle:	12 hours light and 12 hours dark (except during designated procedures)
Ventilation:	At least 10 changes per hour of fresh air that has been passed through 99.97% HEPA filters

8.5. Food

Diet:	Certified Rodent Diet® #5002 (PMI® Nutrition International)
Type:	Pellets (alternate diet may be provided on individual animal basis as warranted as approved by the Study Director)
Frequency:	Ad libitum, except during designated procedures
Analysis:	Results of analysis for nutritional components and environmental contaminants are on file at the Testing Facility. It is considered that there are no known contaminants in the feed that would interfere with the objectives of the study.

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8.6. Water

Type:	All water will be from a local source and passed through a reverse osmosis membrane before use. Chlorine will be added to the processed water as a bacteriostat; processed water is expected to contain no more than 1.2 ppm chlorine at the time of analysis.
Frequency/Ration:	Available *ad libitum* from an automatic watering access system and/or individual water bottles attached to the nesting boxes (except during designated procedures).
Analysis:	Periodic analysis of the water is performed, and results of these analyses are on file at the Testing Facility. It is considered that there are no known contaminants in the water that could interfere with the outcome of the study.

8.7. Veterinary Care

Veterinary care will be available throughout the course of the study and animals will be examined by the veterinary staff as warranted by clinical signs or other changes. In the event that animals show signs of illness or distress, the responsible Veterinarian may make initial recommendations about treatment of the animal(s) and/or alteration of study procedures, which must be approved by the Study Director or Scientific designate. Treatment of the animal(s) for minor injuries or ailments may be approved without prior consultation with the Sponsor Representative when such treatment does not impact fulfillment of the study objectives. If the condition of the animal(s) warrants significant therapeutic intervention or alterations in study procedures, the Sponsor Representative will be contacted, when possible, to discuss appropriate action. If the condition of the animal(s) is such that emergency measures must be taken, the Study Director (or Scientific designate) and/or attending Veterinarian will attempt to consult with the Sponsor representative prior to responding to the medical crisis, but the Study Director (or Scientific designate) and/or Veterinarian has authority to act immediately at his/her discretion to alleviate suffering. The Sponsor Representative will be fully informed of any such events.

9. EXPERIMENTAL DESIGN

Experimental Design – F0 Generation

Group No.	Test Material	Dose Level (µg/dose)	Dose Concentration (mg/mL)	Dose Volume (µL/dose)	No. of Females	
					Cohort 1 (Cesaearan-Sectioning Phase)	Cohort 2 (Natural Delivery Phase)
1	Control Article	0	0	200	22	22
2	mRNA-1273	100	0.5	200	22	22

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9.1. Administration of Test and Control Articles

9.1.1. F0 Generation

Dose Route:	Intramuscular injection into the quadriceps on the hindlimbs; alternating on each dosing occasion.
Frequency:	Once on each day of dose administration
Duration:	Premating Period: Study Day (SD) 1 (28 days prior to mating) and SD 15 (14 days prior to mating). Study Day 1 is defined as the first day of dose administration. Gestation Period: Gestation Days (GDs) 1 and 13.
Special Procedures:	The initiation of dose administration will occur at approximately the same time each day, when possible. • Under no circumstances, the dosing formulations will be subject to vortexing and vigorously shaking to avoid disruption of the Test Article. Before withdrawing a dose formulation into syringes, the dose formulation container will be gently swirled to achieve homogeneity and this step will be documented. • The Control Article will be maintained on a separate cart from the Test Article during dose procedures and will be transported in a separate carrier, when possible. Only the Control Article will be in the study room during dose administration of Group 1, when possible. • Dose procedures for the Control Article group will be completed before dosing for Group 2 is initiated. • Dose administration will be conducted in a Group number sequence order from Group 1 to 2, in order to minimize any potential risk of Test Article cross-contamination. • Personal Protective Equipment (PPE) used for dosing will be changed between groups. • The Control Article will be removed from the study room before dosing for Group 2 is initiated.

9.1.2. F1 Generation

F1 generation pups will not be directly given the Test Article and/or the Control Article formulations, but may be possibly exposed to the Test Article and/or the Control Article formulations article during maternal gestation (*in utero* exposure) or via maternal milk during the lactation period.

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10. IN-LIFE PROCEDURES, OBSERVATIONS, AND MEASUREMENTS – F0 GENERATION

The in-life procedures, observations, and measurements listed below will be performed as per table below.

General In-life Assessments – F0 Generation Females

Parameter	Frequency (minimum required)	Comments
Viability	• At least twice daily	-
Clinical Observations: General	• At least once weekly during the acclimation period • Daily before each dose is administered and daily on non-dosing days • Daily during the postdose period (including the day of scheduled euthanasia).	-
Clinical Observations: Postdose Observations	• 6 hours following dose administration.	Time intervals for postdose observations may be adjusted if deemed appropriate by the Study Director during the course of the study. Such adjustments will be documented in the raw data.
Maternal Observations:	• Daily during the postpartum period (Cohort 2).	Maternal behavior will be recorded.
Individual Body Weights	• On the day of or day after arrival and at least once weekly during acclimation. • On SDs, 1,8, 15, 22, and 28 and on GDs 0, 1, 6, 10, 13, 15, 18, 21, and 25 (if necessary). • Lactation Day (LD) 1, 4, 7, 10, 14, 18 and 21 (Cohort 2)	-
Food Consumption	• Once weekly during the dose period until cohabitation. • On GDs 0, 1, 6, 10, 13, 15, 18, 21, and 25 (if necessary). • On LDs 1, 4, 7, 10 and 14 (Cohort 2)	Food consumption values will be recorded. During cohabitation, when two rats occupy the same nesting box with one food jar, replenishment of the food jars will be documented. Individual values will not be recorded or tabulated. Food consumption will not be tabulated after Day 14 postpartum, when it is expected that pups will begin to consume maternal food. Food consumption values may be recorded more frequently if it is necessary to replenish the food. These intervals will not be tabulated.

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Parameter	Frequency (minimum required)	Comments
Estrous Cycle Evaluations	Samples will be collected from females for 14 consecutive days before initiation of the cohabitation period and then until spermatozoa are observed in a smear of the vaginal contents and/or a copulatory plug is observed in situ during the cohabitation period.	Estrous cycles will be evaluated by examining the vaginal cytology of samples obtained by vaginal lavage.
Reproductive Capacity	Within each dose group, rats will be assigned to cohabitation (i.e., pairing), one breeder male per one female. The cohabitation period will consist of a maximum of 7 days. Females observed with spermatozoa in a smear of the vaginal contents and/or a copulatory plug observed in situ will be considered to be at GD 0 and assigned to individual housing. Females not mated after completion of the 7-day cohabitation period will be considered to be at GD 0 on the last day of cohabitation, assigned to individual housing (i.e., solid bottom or wire-bottom cages) and will be euthanized 25 days after the end of the cohabitation period (for rats that do not deliver a litter) or continued on study to be assigned to Cohort 2 as needed (for rats that do deliver a litter) at the discretion of the Study Director. Animals will be assigned to either Cohort 1 or 2 following cohabitation.	-
Natural Delivery Observations	Female rats will be evaluated for: • Adverse clinical signs observed • Duration of Gestation (GD 0 to the time the first pup is observed) • Litter Size (defined as all pups delivered) • Pup Viability at Birth	-

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11. IN-LIFE PROCEDURES, OBSERVATIONS, AND MEASUREMENTS – F1 GENERATION (COHORT 2)

11.1. Preweaning

The in-life procedures, observations, and measurements listed below will be performed for all F1 litters, with the litter as the unit of measure.

General In-life Assessments – F1 Generation (Preweaning)

Parameter	Frequency (minimum required)	Comments
Viability	Litters will be observed for dead pups at least twice daily and the pups in each litter will be counted at least once daily during the preweaning period.	-
Clinical Observations: General Appearance	At least once daily.	Clinical observations may be recorded more frequently than cited.
Individual Body Weights	Day 1, 4, 7, 10, 14, 18, and 21 postpartum.	-

12. ANTIBODY EVALUATION

12.1. Antibody Sample Collection

12.1.1. Maternal Samples (Cohorts 1 and 2)

Antibody Sample Collection

Group Nos.	Cohort	Time Points					
		SD 1[a]	SD 15[a]	GD 1[a]	GD 13[a]	GD 21[b]	LD 21[b]
1-2	1	X	X	X	X	X	-
1-2	2	X	X	X	X	-	X
Unscheduled euthanasia (when possible)		X					

Method/Comments:	Jugular vein (SD 1, 15, GD 1, 13 in-life blood collections) or via the vena cava while under isoflurane/oxygen anesthesia (GD 21 and LD 21 terminal blood collections). If necessary, in-life blood samples may be collected from an alternate site (lateral tail vein); if so, the alternate site will be documented in the raw data. Additional blood samples may be obtained (e.g. due to sample quality) if permissible sampling frequency and blood volume are not exceeded. Blood will be collected from unscheduled euthanized animals, when possible.
Target Volume (mL):	1.0 mL
Anticoagulant:	None, in SST
Special Requirements:	None
Processing:	Serum

X = Sample to be collected; - = Not applicable, SST = serum separator tube
[a] Sample collected prior to dose administration.
[b] Terminal blood sample collection.

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12.1.2. Fetal Samples (Cohort 1)

On GD 21, pooled fetal blood will be collected via decapitation from at least the first 5 fetuses assigned to visceral examination, to achieve target volume (more can be used if deemed necessary and documented in the raw data). In cases where there are not enough viable fetuses assigned to visceral examinations, the carotid blood collection route will be utilized from fetuses assigned to skeletal examination.

Target Volume: 1.0 mL pooled per litter

Anticoagulant: None/Serum separator tube

12.1.3. Pup Samples (Cohort 2)

On the day of scheduled euthanasia (LD 21), blood will be collected from 2 pups per litter (1 male and 1 female , when possible) via the inferior vena cava while under isofluorane/oxygen anesthesia.

Target Volume: 1.0 mL pooled per litter

Anticoagulant: None/Serum separator tube

12.2. Antibody Analysis Sample Processing

Antibody Sample Processing

Centrifugation	Aliquot 1 Volume	Aliquot 2 Volume	Storage Conditions
1800 g for 10 minutes Approximately 4°C	At least 240 µL (serum)	Remaining (serum)	-70°C

Theoretical number of samples: up to 220 samples x 2 aliquots (dams), 44 samples x 2 aliquots (fetuses) and 44 samples x 2 aliquots (pups).

The blood samples will be mixed gently and will be centrifuged as soon as practical following an at least 20 minute clot time (not to exceed 1 hour). Blood samples will be centrifuged for 10 minutes at 1800 g in refrigerated centrifuge (4°C). The resultant serum will be separated into two aliquots as described in the table above, transferred to uniquely labeled clear polypropylene tubes, and frozen immediately over dry ice until stored in a freezer set to maintain -70°C.

The first set of samples (aliquot 1/occasion) will be shipped on dry ice with a temperature monitor to the Test Site for antibody analysis, see ATTACHMENT D, after the end of the treatment period. The second set of samples (aliquot 2/occasion) will be maintained at the Testing Facility as back up samples. The Test Site for antibody analysis and the Sponsor Representative will be notified before shipment of the samples. Samples will be stored at the Test Site in a freezer set to maintain -80°C until analysis.

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12.3. Antibody Sample Analysis

The samples will be analyzed for antibodies produced as a result of mRNA-1273 administration using a qualified analytical procedure (insert analytical procedure number).

Antibody responses to SARS-CoV2 S protein will be evaluated using optimized indirect ELISA assay.

In brief, 96-well microtiter plates will be coated with SARS-CoV2 S protein (Sino Biological) and incubated overnight. 5-Step serial dilutions of rat or pup sera will be added, and the bound antibody detected with HRP-conjugated goat anti-rat IgG (KPL), followed by incubation with TMB substrate (KPL). The absorbance measured at OD450nm.

Antibody titers will be calculated as "Antibody Units/mL" based on the four-parameter logistic curve fit (4PL) of a hyperimmune rat standard curve using a using Softmax software (Molecular devices Inc.).

Any residual/retained samples will be maintained for a minimum of 6 months following issuance of the Draft Report after which the samples will be returned to the Sponsor. An earlier determination of the disposition of these residual/retained samples may also be requested and authorized by the Study Director in consultation with the Sponsor following confirmation by the Sponsor Representative. An Antibody Report will be included as an appendix to the Final Report.

13. TERMINAL PROCEDURES – F0 GENERATION

Terminal procedures are summarized in the following tables:

F0 Generation Females – Cohort 1

Group No.	Scheduled Euthanasia Day	Necropsy Procedures				Histology Processing and Microscopic Evaluation
		Ovarian/ Uterine Examination	Necropsy	Tissue Collection[a]	Organ Weights	
1	GD 21	X	X	X	X[b]	-
2						
Unscheduled Deaths		X	X	X	X	-

X = Procedure to be conducted; - = Not applicable; GD = Gestation Day

[a] See Tissue Collection and Evaluation table – F0 Generation Scheduled Euthanasia, ATTACHMENT A and Tissue Collection and Evaluation table – F0 and F1 Generation – Unscheduled Euthanasia, ATTACHMENT B for list of tissues applicable to each procedure.

[b] The gravid uterus and the placentae will be weighed for all rats that survive to scheduled euthanasia.

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F0 Generation Females – Cohort 2

Group No.	Scheduled Euthanasia Day	Necropsy Procedures				Histology Processing and Microscopic Evaluation
		Ovarian/ Uterine Examination	Necropsy	Tissue Collection[a]	Organ Weights	
1	LD 21	X	X	X	-	-
2						
Unscheduled Deaths		X	X	X	-	-
Dams that did Not Deliver	GD 25	X	X	X	-	-
Dams with No Surviving Pups	b	X	X	X	-	-

X = Procedure to be conducted; - = Not applicable; GD = Gestation Day; LD = Lactation Day
[a] See Tissue Collection and Evaluation table– F0 Generation Scheduled Euthanasia, ATTACHMENT A and Tissue Collection and Evaluation table – F0 and F1 Generation – Unscheduled Euthanasia, ATTACHMENT B for list of tissues applicable to each procedure.
[b] On the day the observation is made.

13.1. Method of Euthanasia

F0 generation rats euthanized before scheduled termination will be euthanized by carbon dioxide asphyxiation.

All surviving rats will be euthanized via exsanguination following blood sample collection from the inferior vena cava while under isoflurane/oxygen anesthesia.

All live fetuses selected for Cohort 1 blood collections will be euthanized by decapitatioan.. All other fetuses will be euthanized by an intraperitoneal injection of sodium pentobarbital (390 mg/mL)

13.2. Unscheduled Euthanasia

Images may be generated for illustration of or consultation on gross observations. Generation of such images will be documented. Images and associated documentation will be retained and archived at the Testing Facility.

13.2.1. Cohorts 1 and 2

Rats assigned to Cohorts 1 and 2 that die or are euthanized before scheduled termination will be examined for the cause of death or condition as soon as possible after the observation is made. A complete necropsy will be performed (including examination of the injection site). See Section 13.5. (Tissue Collection and Preservation) for tissues that will be retained for possible future evaluation.

	Complete Necropsy (Section 13.4.)	Ovarian and Uterine Examination (Section 13.3.3.)	Tissue Retention (Section 13.5.)
Females - Before Cohabitation	X	-	X
Females - After Cohabitation	X	X[a]	X

X = Procedure to be conducted; - = Not Applicable
[a] The number of implantation sites and corpora lutea will be recorded.

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Pregnancy status and uterine contents will be recorded, and the aborted fetuses, conceptuses *in utero*, and/or delivered pups will be examined to the extent possible, using the same methods described for term fetuses.

Uteri of apparently nonpregnant animals will be examined while being pressed between glass plates to confirm the absence of implantation sites. Uteri and ovaries of apparently nonpregnant animals will be retained in 10% neutral buffered formalin and will be discarded when authorized by the Study Director in consultation with the Sponsor.

13.3. Scheduled Euthanasia

13.3.1. Cohort 1

On GD 21, all surviving female rats assigned to Cohort 1 will be euthanized, blood samples will be collected as described in Section 12. (Antibody Evaluation), and animals will be examined for ovarian and uterine contents (Section 13.3.3., Ovarian and Uterine Examinations) and gross lesions (Section 13.4, Necropsy) (including examination of the injection site). See Section 13.5. (Tissue Collection and Preservation) for tissues to be retained for possible future evaluation.

13.3.2. Cohort 2

After completion of the 21-Day postpartum period, F0 generation female rats will be euthanized, blood samples will be collected as described in Section 12. (Antibody Evaluation), and animals will be examined for gross lesions (including examination of the injection site). Dams with no surviving pups will be euthanized after the last pup is found dead or missing, presumed cannibalized.

The rats will be examined as described in Sections 13.3.3. (Ovarian and Uterine Examinations) and Section 13.4. (Necropsy). See Section 13.5. (Tissue Collection and Preservation) for tissues to be retained for possible future evaluation.

Females that did not mate after the completion of the 7-day cohabitation period will be euthanized 25 days after the end of the cohabitation period (females that do not deliver a litter) or will continue on study (females that deliver) at the discretion of the Study Director. If euthanized, animals will be examined for gross lesions (including examination of the injection site). The rats will be examined as described in Sections 13.3.3. (Ovarian and Uterine Examinations) and Section 13.4. (Necropsy). See Section 13.5. (Tissue Collection and Preservation) for tissues to be retained for possible future evaluation.

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13.3.3. Ovarian and Uterine Examinations

13.3.3.1. Cohort 1

The reproductive tract will be dissected from the abdominal cavity. The gravid uterus will be weighed. The uterus will be opened and the contents will be examined. The fetuses will be removed from the uterus and placed in individual containers. Each placenta will be weighed.

- Corpora lutea
- Implantation sites
- Placentae (size, color or shape) – any abnormalities will be recorded
- Live and dead fetuses
- Early and late resorptions

Uteri of apparently nonpregnant animals will be examined while being pressed between glass plates to confirm the absence of implantation sites. Uteri and ovaries of apparently nonpregnant animals that are found dead or euthanized before scheduled termination will be retained in 10% neutral buffered formalin and may be discarded when authorized by the Study Director in consultation with the Sponsor.

13.3.3.2. Cohort 2

The reproductive tract will be dissected from the abdominal cavity. The number and distribution of implantation sites will be recorded.

Uteri of apparently nonpregnant animals will be examined while being pressed between glass plates to confirm the absence of implantation sites. Uteri and ovaries of apparently nonpregnant animals will be retained in 10% neutral buffered formalin and will be discarded when authorized by the Study Director in consultation with the Sponsor.

13.4. Necropsy

Animals unscheduled euthanized and found dead will be subjected to a complete necropsy examination, which will include evaluation of the carcass and musculoskeletal system; all external surfaces and orifices; cranial cavity and external surfaces of the brain; and thoracic, abdominal, and pelvic cavities with their associated organs and tissues.
A gross necropsy of the thoracic, abdominal and pelvic viscera will be performed for each scheduled euthanized animal.

Images may be generated for illustration of or consultation on gross observations. These images will not be used for data generation or interpretation and will not be archived or included in the Final Report.

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13.5. Tissue Collection and Preservation

Representative samples of tissues will be collected and preserved in 10% neutral buffered formalin, except for tissues requiring alternate fixatives as defined by standard operating procedures, as detailed in ATTACHMENT A (Tissue Collection and Evaluation – F0 Generation Scheduled Euthanasia) and ATTACHMENT B (Tissue Collection and Evaluation – F0 Generation Unscheduled Euthanasia). Additional tissue samples may be collected to elucidate abnormal findings and will be discarded before finalization of the study.

14. FETAL EXAMINATIONS – COHORT 1

Representative photographs of external, visceral and skeletal abnormalities will be taken at the discretion of the Study Director or designee for illustration of, or consultation on, observations. Photographs will not be included in the Report, but will be retained as electronic images and archived with the raw data. Abnormalities will be classified as malformations, variations, and incidental.

Examination	Procedure
Aborted/Conceptuses *in utero*/Delivered Pups	Examined for external, visceral, and/or skeletal abnormalities to the extent possible.
Late Resorptions	Examined for external abnormalities to the extent possible, and discarded without further examination
Dead Fetuses	Examined to the extent possible.
Body Weights	Recorded for each live fetus.
External	All fetuses will be examined for sex and for external abnormalities.
Visceral	Approximately one-half of the fetuses in each litter will be examined for visceral abnormalities by using a modification of the microdissection technique of Staples.[2] Each fetus will be fixed in Bouin's solution and the heads will subsequently be examined by free-hand sectioning;[3] head sections with abnormal findings will be stored in alcohol. All other head sections will be discarded. The decapitated carcasses will not be retained.
Skeletal	The remaining fetuses (approximately one-half of the fetuses in each litter) will be examined for skeletal abnormalities after staining with alizarin red S.[4] Following examination, skeletal preparations will be retained in glycerin with thymol added as a preservative.

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15. TERMINAL PROCEDURES – F1 GENERATION (COHORT 2)

15.1. Method of Euthanasia

F1 generation pups assigned to Cohorts 2 blood collections will be euthanized via exsanguination following blood sample collections.

All other F1 generation pups will be euthanized by an intraperitoneal injection of sodium pentobarbital (390 mg/mL) (pups ≤ 14 days of age) or by carbon dioxide asphyxiation (pups ≥15 days of age).

15.2. Unscheduled Deaths

15.2.1. Days 0 to 21 Postpartum

Pups that are found dead during delivery or at the completion of littering (Days 0 or 1 postpartum) will be evaluated for vital status at birth. The lungs will be removed and immersed in water. Pups with lungs that sink will be identified as stillborn; pups with lungs that float will be identified as liveborn and to have died shortly after birth. Pups (whole animal) will be preserved in 10% neutral buffered formalin for possible future evaluation.

Pups that die (Days 1 to 21 postpartum) or are euthanized (Days 0 to 21 postpartum) before scheduled termination will be examined for gross lesions and the cause of death or condition as soon as possible after the observation is made. Pups euthanized on Days 0 to 4 postpartum or found on Days 1 to 4 postpartum will be preserved in 10 % neutral buffered formalin (whole animal) for possible future evaluation. Tissues will be collected from pups euthanized or found on Days 5 to 21 postpartum as described in Section 15.5 (Tissue Collection and Preservation). For any premature pups (Days 5 to 21 postpartum), the whole animal will be fixed in 10 % neutral buffered formalin if tissue collection is not feasible due to the small size of the animal (i.e., PNDs 0-10 collect whole animal including eyes/optic nerves/harderian glands and testes for retention in the appropriate fixative; PNDs 11-21 collect individual tissues).

15.3. Scheduled Euthanasia

Pups culled on Day 4 postpartum will be examined for gross lesions as described in Section 15.4 (Necropsy). Necropsy will include a single cross-section of the head at the level of the frontal-parietal suture and examination of the cross-sectioned brain for apparent hydrocephaly.

On Day 21 postpartum, F1 generation rats will be euthanized and examined for gross lesions (Section 15.4., Necropsy). Necropsy will include a single cross-section of the head at the level of the frontal-parietal suture and examination of the cross-sectioned brain for apparent hydrocephaly. See Section 15.5. (Tissue Collection and Preservation) for tissues to be retained for possible future evaluation.

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15.4. Necropsy

A gross necropsy of the thoracic, abdominal and pelvic viscera will be performed for each animal.

Images may be generated for illustration of or consultation on gross observations. Generation of such images will be documented. Images and associated documentation will be retained and archived.

15.5. Tissue Collection and Preservation

Representative samples of tissues will be collected and preserved in 10% neutral buffered formalin, except for tissues requiring alternate fixatives as defined by standard operating procedures, as detailed in ATTACHMENT B (Tissue Collection and Evaluation – F1 Generation Unscheduled Euthanasia) and ATTACHMENT C (Tissue Collection and Evaluation – F1 Generation Scheduled Euthanasia). Additional tissue samples may be collected to elucidate abnormal findings and will discarded before finalization of the study.

16. STATISTICAL ANALYSIS

Any data collected during the predose period will not be tabulated or summarized, unless applicable to analyses in the proceeding sections. Litter values will be used, where appropriate. Additional procedures and/or analyses may be performed if deemed appropriate.

Clinical and necropsy observations data ~~**(with the exception of preweaning pup necropsy observations [inferential statistics will be performed on incidences])**~~ will be summarized but no inferential statistical analysis will be performed.

Numerical data collected on scheduled occasions will be summarized and statistically analyzed as indicated below according to sex and occasion or by litter.

Additional procedures and/or analyses may be performed, if appropriate; however may involve additional cost and a reporting time longer than that specified in the study contract.

16.1. Descriptive Statistical Analyses

Means, standard deviations (or % coefficient of variation or standard error, when deemed appropriate), ratio, percentages, numbers, and/or incidences will be reported as appropriate by dataset.

16.2. Constructed Variables

F0 Generation

Body weight changes	Calculated between each scheduled interval.
Food Consumption	Calculated between each scheduled interval.
Corrected Body Weight (CBW)	**Terminal Bodyweight – Gravid Uterus Weight**
Corrected Body Weight Gains	**CBW - Bodyweight on Day 0**

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Additional or alternative body weight or food consumption intervals may be evaluated to elucidate study results at the discretion of the Study Director.

The following parental indices and litter calculations will be included, where applicable:

Female Mating Index = $\frac{\text{Number of Females with Evidence of Mating (or no confirmed mating date and pregnant)}}{\text{Number of Females Paired}}$

Female Fertility Index = $\frac{\text{Number of Pregnant Females}}{\text{Number of Females with Evidence of Mating (or no confirmed mating date and pregnant)}}$

Female Pregnancy Index = $\frac{\text{Number of Pregnant Females}}{\text{Number of Females Paired}}$

Pre-Implantation Loss = $\frac{\text{Number of Corpora Lutea – Number of Implants}}{\text{Number of Corpora Lutea}} \times 100$

Post-Implantation Loss = $\frac{\text{Number of Implants – Number of Live Fetuses}}{\text{Number of Implants}} \times 100$

Sex Ratio (% males) = $\frac{\text{Number Male Fetuses}}{\text{Total Number of Fetuses}} \times 100$

Litter % of Fetuses with Abnormalities = $\frac{\text{Number of Fetuses in Litter with a given Finding}}{\text{Number of Fetuses in Litter Examined}} \times 100$

The following natural delivery/reproductive parameters will be included, as appropriate:

- Gestation Length: The gestation length is calculated from GD 0 to the day the first pup is observed.
- Female Pregnancy Index: $\frac{\text{Number of Pregnant Females}}{\text{Number of Females Paired}}$
- Gestation Index: Percentage of pregnancies that result in birth of live litters

  $\frac{\text{Number of Animals with Live Offspring}}{\text{Number of Animals Pregnant}} \times 100$
- Live Birth Index: Percentage of pups born alive.

  $\frac{\text{Number of Live Newborn Pups}}{\text{Number of Newborn Pups}} \times 100$
- Viability Index: Percentage of pups born that survive 4 days postpartum

  $\frac{\text{Number of Live Pups on Day 4 Postpartum}}{\text{Number of Live Newborn Pups}} \times 100$

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- Lactation Index: Percentage of pups that survive 21 days postpartum

  $$\frac{\text{Number of Live Pups on Day 21 Postpartum}}{\text{Number of Live Pups on Day 4 (postculling) Postpartum}} \times 100$$

- Post-Implantation Loss/Litter

  $$\frac{\text{Number of Implants} - \text{Total Newborn Pups}}{\text{Number of Implants}} \times 100$$

- Sex Ratio (% males) Percentage of male pups per litter

  $$\frac{\text{Number of Live Male Pups}}{\text{Total Number of Live Pups}} \times 100$$

16.3. Inferential Statistical Methods

All statistical tests will be conducted at the 5% significance level. All pairwise comparisons will be conducted using two sided tests and will be reported at the 1% and 5% levels, unless otherwise noted.

Analyses will be conducted and pairwise comparisons of interest will be carried out as listed below:

F0 Generation/Litters (Preweaning)		
Group 2	vs.	Group 1

Analyses will be performed according to the matrix below when possible, but will exclude any group with less than 3 observations.

Statistical Matrix

Variables for Inferential Analysis	**Statistical Method**		
	Parametric/ Non-Parametric	**Non-Parametric**	**Incidence**
General Data			
Body Weight[a]	X	-	-
Body Weight Gains[a]	X	-	-
Food Consumption[a]	X	-	-
Parental Indices and Mortality	-	-	X
Gravid Uterine Weight and Corrected Maternal Body Weights[a]	**X**	**-**	**-**
Natural Delivery and Litter Data			
Natural Delivery and Litter Observations (Proportional) (e.g. Pregnant, Females with Liveborn, Gestation Index, Female with Liveborn)	-	-	X
Natural Delivery and Litter Observations (Count) (e.g. Gestation Length, Live Pups, Implantation Sites)	-	X	-
Litter Observations (Continuous) (e.g. Sex Ratio - Males, Mean Litter Bodyweights)	X	-	-

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Variables for Inferential Analysis	Statistical Method		
	Parametric/ Non-Parametric	Non-Parametric	Incidence
Live Birth Index	-	X	-
~~Litter Incidence of Adverse Necropsy Findings per Group~~	-	-	~~X[b]~~
~~Pup Incidence of Adverse Necropsy Findings per Group~~	-	-	~~X[b]~~
Estrous Cycling, Mating and Fertility			
Number of Estrous Cycles and Mean Cycle Length	-	X	-
Pregnancy, Mating and Fertility Indices	-	-	X
Precoital Interval[b e]	-	X	-
Caesarean-section Late Gestation[d]			
Ovarian and Uterine Examinations[b e]	-	X	-
Litter Observations (Litter Means)[b e, d e]	X		-
Litter % of Fetuses with Gross/External/Visceral/Skeletal Abnormalities[e f]	-	X	-
Mean Fetal Ossification Sites[e f]	-	X	-

[a] Excludes animals not pregnant from the gestation phase summarization and statistical analysis.
~~[b] Inferential statistical analysis will be restricted to pups euthanized on Postnatal Day 21.~~
[b e] Excludes animals with no confirmed mating date from summarization and statistical analysis.
[c ~~d~~] Excludes animals euthanized preterminally from summarization and statistical analysis.
[d e] Presented for males, females and sexes combined; live fetuses only.
[e f] Presented for sexes combined; live fetuses only.

16.4. Parametric/Non-parametric

Levene's test will be used to assess the homogeneity of group variances. The groups will be compared using a Dunnett's test if Levene's test is not significant or Dunn's test if it is significant.

16.5. Non-Parametric

Datasets will be compared using a Dunn's test.

16.6. Incidence

A Fisher's exact test will be used to conduct pairwise group comparisons of interest.

17. COMPUTERIZED SYSTEMS

The following critical computerized systems may be used in the study. The actual critical computerized systems used will be specified in the Final Report.

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Critical Computerized Systems

System Name	Description of Data Collected and/or Analyzed
(b) (4)	Test material receipt, accountability, formulation activities, in-life (e.g., clinical observations, body weights, food consumption), and/or postmortem (e.g., pathology, ovarian and uterine contents, and fetal parameters)
	Temperature, humidity and light cycle times
	Deviations
	In-life; postmortem
	Reporting
	Collection of Part 11 compliant signature
	Data acquisition for dose formulation analysis, including regression analysis and measurement of concentration and recovery of dose formulations using HPLC

Data for parameters not required by the Protocol, which are automatically generated by analytical devices used, will be retained on file but not reported. Statistical analysis results that are generated by the program but are not required by the Protocol and/or are not scientifically relevant will be retained on file but will not be included in the tabulations.

18. REGULATORY COMPLIANCE

The study will be performed in accordance with the U.S. Department of Health and Human Services, Food and Drug Administration, United States Code of Federal Regulations, Title 21, Part 58: Good Laboratory Practice for Nonclinical Laboratory Studies and as accepted by Regulatory Authorities throughout the European Union (OECD Principles of Good Laboratory Practice), Japan (MHLW), and other countries that are signatories to the OECD Mutual Acceptance of Data Agreement.

Any portion of this study conducted in Canada will be performed in accordance with the OECD Principles of Good Laboratory Practice and as accepted by Regulatory Authorities throughout the European Union, United States of America (FDA), Japan (MHLW), and other countries that are signatories to the OECD Mutual Acceptance of Data Agreement.

Exceptions to GLPs include the following study elements:

- Characterization of the Test and Control articles will be performed by the Sponsor or Sponsor subcontractor at a laboratory that follows FDA Good Manufacturing Practice (GMP) regulations.
- Stability testing of the supplied Test and Control articles was performed by the Sponsor or Sponsor subcontractor at a laboratory that follows FDA GMP regulations.
- Stability of the Test Article formulations will not be determined in this study.
- The antibody analysis will not comply with Good Laboratory Practice (GLP) regulations. This analysis will be performed using established SOPs, controls, approved test methodologies, and good scientific practices.

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19. QUALITY ASSURANCE

19.1. Testing Facility

The Testing Facility Quality Assurance Unit (QAU) will monitor the study to assure the facilities, equipment, personnel, methods, practices, records, and controls are in conformance with Good Laboratory Practice regulations. The QAU will review the Protocol, conduct inspections at intervals adequate to assure the integrity of the study, and audit the Final Report to assure that it accurately describes the methods and standard operating procedures and that the reported results accurately reflect the raw data of the study.

19.2. Test Site(s)/Subcontractor(s)

For all study phase(s) inspected by test site/subcontractor QAU(s), copies of each periodic inspection report will be made available to the Study Director, Testing Facility Management, and the Testing Facility QAU.

20. AMENDMENTS AND DEVIATIONS

Changes to the approved Protocol shall be made in the form of an Amendment, which will be signed and dated by the Study Director. Every reasonable effort will be made to discuss any necessary protocol changes in advance with the Sponsor. The Study Director will notify the Sponsor of deviations that may result in a significant impact on the study as soon as possible.

21. RETENTION AND DISPOSITION OF RECORDS, SAMPLES, AND SPECIMENS

All study-specific raw data, electronic data, documentation, Protocol (and amendments, if any), retained samples and specimens, and final reports will be archived by no later than the date of final report issue. All materials generated by Charles River from this study will be transferred to a Charles River archive. At least 1 year after issue of the Draft Report, the Sponsor will be contacted.

Disposition of residual/retained analytical samples will be as described in the table below.

Disposition of Residual/Retained Samples

Sample Type	Disposition	Schedule
Analytical Chemistry (Dose Formulation Samples)	Discard or Archive	Samples will be maintained for a minimum of 6 months following issuance of the Draft Report or at an alternate time point prior to finalization as requested and authorized by the Study Director in consultation with the Sponsor.
Antibody Serum Samples	Returned to Sponsor	

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Records to be maintained will include, but will not be limited to, documentation and data for the following:

- Protocol, Protocol amendments, and deviations
- Study schedule
- Study-related correspondence
- Test system receipt, health, and husbandry
- Test and control article receipt, identification, preparation, and analysis
- Mating history
- In-life measurements and observations
- Antibody serum sample collection and evaluation
- Gross observations and related data
- Ovarian/Uterine and fetal observations
- Photographs, if any
- Statistical analysis results
- Natural Delivery Observations
- Litter Observations

22. REPORTING

A comprehensive Draft Report will be prepared following completion of the study and will be finalized following consultation with the Sponsor. The report will include all information necessary to provide a complete and accurate description of the experimental methods and results and any circumstances that may have affected the quality or integrity of the study.

The Sponsor will receive an electronic version of the Draft and Final Reports provided in Adobe Acrobat PDF format (hyperlinked and searchable) along with a Microsoft Word version of the text. The PDF document will be created from native electronic files to the extent possible, including text and tables generated by the Testing Facility. Report components not available in native electronic files and/or original signature pages will be scanned and converted to PDF image files for incorporation.

Reports should be finalized within 6 months of issue of the Draft Report. If the Sponsor has not provided comments to the report within 6 months of draft issue, the report will be finalized by the Testing Facility unless other arrangements are made by the Sponsor.

23. JUSTIFICATIONS AND GUIDELINES

23.1. Justification of Test System and Number of Animals

The test system was selected because: 1) this strain of rat has been demonstrated to be sensitive to reproductive and developmental toxins and has been widely used throughout industry for reproductive and developmental toxicity evaluations; 2) historical data and experience exist at the Testing Facility; and 3) the Test Article is pharmacologically active in the species and strain.

The number of animals chosen for this study is the smallest number considered necessary to provide the minimum number of pregnancies recommended by the applicable guidelines.

23.2. Justification of Route and Dose Levels

The intramuscular route of exposure was selected because this is the intended route of human exposure.

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The dose level for this study (100µg/dose) was chosen to approximate the human clinical dose.

23.3. Guidelines for Study

The design of this study was based on the study objective(s), the overall product development strategy for the Test Article, and the following study design guidelines:

- ICH Harmonised Tripartite Guideline S5 (R3). *Guideline on Reproductive Toxicology : Detection of Toxicity to Reproduction for Human Pharmaceuticals.*
- ICH Harmonised Tripartite Guideline M3 (R2). *Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals.*
- Food and Drug Administration (FDA). Guidance for Industry: Considerations for developmental toxicity studies for preventative and therapeutic vaccines for infectious disease indications, CBER Division of Vaccines and related products (February 2006).

24. ANIMAL WELFARE

This study will comply with all applicable sections of the Final Rules of the Animal Welfare Act regulations (Code of Federal Regulations, Title 9), the *Public Health Service Policy on Humane Care and Use of Laboratory Animals* from the Office of Laboratory Animal Welfare, and the *Guide for the Care and Use of Laboratory Animals* from the National Research Council.[1,5] The Protocol and any amendments or procedures involving the care or use of animals in this study will be reviewed and approved by the Testing Facility Institutional Animal Care and Use Committee before the initiation of such procedures.

If an animal is determined to be in overt pain/distress, or appears moribund and is beyond the point where recovery appears reasonable, the animal will be euthanized for humane reasons in accordance with the *American Veterinary Medical Association (AVMA) Guidelines for the Euthanasia of Animals* and with the procedures outlined in the Protocol.[6]

By approving this Protocol, the Sponsor affirms that there are no acceptable non-animal alternatives for this study, that this study is required by a relevant government regulatory agency(ies) and that it does not unnecessarily duplicate any previous experiments.

Appendix 1

25. REFERENCES

1. National Research Council. *Guide for the Care and Use of Laboratory Animals*. 8th edition. Washington, DC: National Academy Press. 2011.
2. Staples RE. Detection of visceral alterations in mammalian fetuses. *Teratology* 1974;9(3):A37-A38.
3. Wilson JG. Methods for administering agents and detecting malformations in experimental animals. In: Wilson JG, Warkany J, editors. *Teratology: principles and techniques*. Chicago (IL): University of Chicago Press; 1965. p. 262-77.
4. Staples RE, Schnell VL. Refinements in rapid clearing technic in the KOH-alizarin red S method for fetal bone. *Stain Technol* 1964;39:61-3.
5. Office of Laboratory Animal Welfare. *Public Health Services Policy on Humane Care and Use of Laboratory Animals*. Bethesda, MD: National Institutes of Health. 2015.
6. American Veterinary Medical Association. *AVMA Guidelines for the Euthanasia of Animals*. 2020 edition.

Appendix 1

AMENDMENT APPROVAL

DocuSigned by:
(b) (6)
Signer Name: (b) (6)
Signing Reason: I approve this document
Signing Time: 18-Nov-2020 | 12:05:01 EST
21C2CFF6B9FE4A5EBB9C44F8F9E9C519

(b) (6)

Appendix 1

SPONSOR APPROVAL

The Protocol Amendment was approved by the Sponsor by e-mail on the date designated below. The correspondence giving approval will be archived, as appropriate with other Sponsor communications.

17 Nov 2020
Date of Sponsor Approval

Appendix 1

ATTACHMENT A

Tissue, Collection, and Evaluation Table – F0 Generation Scheduled Euthanasia

A table of random units will be used to select one control group rat from which all tissues examined at necropsy will be retained, in order to provide control tissues for any possible future evaluations of gross lesions.

Tissue Collection and Preservation – F0 Generation Scheduled Euthanasia

Tissue	Weigh	Collect	Comment
Administration site	-	X	All scheduled euthanized animals
Gravid Uterus	X	-	All pregnant animals at scheduled euthanasia
Gross lesions/masses	-	X	All scheduled euthanized animals
Placentae	X	-	All pregnant animals at scheduled euthanasia

X = Procedure to be conducted

Appendix 1

ATTACHMENT B

Tissue Collection and Evaluation Table – F0 and F1 Generation – Unscheduled Euthanasia

Tissue Collection and Preservation – F0 and F1 Generation Unscheduled Euthanized and Found Dead Animals

Tissue	Collect (number of tissues to be collected)	Microscopic Evaluation	Comment
Animal Identification	X	-	F0 generation
Artery, aorta	X	-	-
Body cavity, nasal	X	-	-
Bone marrow, sternum	X	-	Unscheduled euthanized animals only. Bone marrow smears are allowed to air dry and are not fixed in formalin.
Bone, femur	X (1)	-	-
Bone, sternum	X	-	-
Brain	X	-	Seven brain levels .[7] to be examined to include olfactory bulb (Examine in Body cavity, nasal section level 4[8])
Epididymis	X (2)	-	Paired examination.
Esophagus	X	-	-
Eye	X (2)	-	Paired examination; Preserve in Davidson's fixative.
Ganglion, dorsal root, lumbar	X	-	Collect with spinal column.
Gland, adrenal	X (2)	-	Paired examination.
Gland, clitoral	X (2)	-	-
Gland, Harderian	X (2)	-	-
Gland, lacrimal	X (2) (extra-orbital)	-	-
Gland, mammary	X	-	For males, examine only if present in routine section of skin. Collect with inguinal skin.
Gland, parathyroid	X (2)	-	Examine only if present in the routine section of thyroid.
Gland, pituitary	X	-	-
Gland, preputial	X (2)	-	-
Gland, prostate	X	-	-
Gland, salivary, submandibular	X (2)	-	-
Gland, salivary, sublingual	X (2)	-	-
Gland salivary, parotid	X (2)	-	-
Gland, seminal vesicle	X (2)	-	Paired examination.
Gland, thyroid	X (2)	-	Paired examination
Gland, Zymbal's	X (2)	-	-
Gut-associated lymphoid tissue[b]	X	-	Examine only if present in routine section of intestine.

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Tissue	Collect (number of tissues to be collected)	Microscopic Evaluation	Comment
Heart	X	-	-
Joint, femorotibial	X (1)	-	-
Kidney	X (2)	-	Paired examination.
Large intestine, cecum	X	-	-
Large intestine, colon	X	-	-
Large intestine, rectum	X	-	-
Larynx	X	-	Examine level 2[9]
Liver	X	-	-
Lung	X	-	-
Lymph node(s) draining administration site	X (2)	-	Collect lymph nodes that would be expected to receive primary exposure to the test article (i.e. lymph node draining the administration site [iliac and inguinal]).
Lymph node, mandibular	X (2)	-	-
Lymph node, mesenteric	X	-	-
Muscle, skeletal	X (2)	-	-
Nerve, optic	X (2)	-	Examine only if present in the routine section of the eye. Preserve in Davidson's fixative.
Nerve, sciatic	X (2)	-	-
Nerve, tibial	X (2)	-	-
Ovary	X (2)	-	Paired examination.
Oviduct	X (2)	-	-
Pancreas	X	-	-
Site(s), administration	X	-	Right and left quadriceps.
Skin	X	-	-
Small intestine, duodenum	X	-	-
Small intestine, ileum	X	-	-
Small intestine, jejunum	X	-	-
Spinal cord	X	-	Examine one transverse and one longitudinal section from each of the following areas cranial cervical, mid-thoracic, lumbar (intumescence)
Spleen	X	-	-
Stomach	X	-	-
Testis	X (2)	-	Paired examination; Preserve in Modified Davidson's fixative.
Thymus	X	-	-
Tongue	X	-	-
Trachea	X	-	-
Ureter	X (2)	-	-
Urinary bladder	X	-	-
Uterus/Cervix	X	-	-

Appendix 1

Tissue	Collect (number of tissues to be collected)	Microscopic Evaluation	Comment
Vagina	X	-	-

[7] Bolon, B., Garman, R. H., Pardo, I. D, Jensen, K., Sills, R., Roulois, A., Radovsky, A. E., Bradley, A., Andrews-Jones, L., Butt, M., Guimprecht, L. STP Position Paper: Recommended practices for sampling and processing the nervous system (brain, spinal cord, nerve and eye) during nonclinical general toxicity studies. *Toxicol Pathol*. 41, 2013. 1028-1048.

[8] Young, J. Histopathologic Examination of the Rat Nasal Cavity, Fundamental and Applied Toxicology, 1:309-312 (July/August 1981).

[9] Roger A. Renne, Katherine M. Gideon, Rodney A. Miller, Paul W. Mellick, and Sandra L. Grumbein. Histologic Methods and Interspecies variations in the Laryngeal Histology of F344/N Rats and B6G3F1 Mice, Toxicologic Pathology, Vol 20, Number 1, 1992 pp 44-51.

Appendix 1

ATTACHMENT C

Tissue Weighing, Collection, and Evaluation Table – F1 Generation Scheduled Euthanasia

A table of random units will be used to select one F1 generation control group rat of each sex from which all tissues examined at necropsy will be retained, in order to provide control tissues for any possible histopathological evaluations of gross lesions.

Tissue Collection and Preservation – F1 Generation Scheduled Euthanasia

Tissue	Weigh	Collect	Comment
Gross lesions/masses	-	X	All scheduled euthanized animals.

X = Procedure to be conducted; - = Not applicable.

Appendix 1

ATTACHMENT D

Shipment of Samples and Study Records

Matrix	Purpose	Day/ Week/ Aliquot	Proposed Shipment Date	Conditions for Shipment	Recipient/Address
Dose formulation samples	Analytical chemistry	First Preparation	01 Jul 2020	Dry Ice with a temperature monitor	Charles River Laboratories Montreal ULC Senneville Site (CR-SEN) 22022 Transcanadienne Senneville, QC H9X 3R3 Canada Tel: (b) (6) E-mail: (b) (6)
		Middle Preparation	29 Jul 2020		
		Last Preparation	17 Aug 2020		
Serum	Antibody Analysis	Aliquot 1: SDs 1 and 15 GDs 1, 13, and 21 LD 21	22 Sep 2020	Dry Ice with a temperature monitor	Integrated Biotherapeutics, Inc 4 Research Court, Suite 300, Rockville, MD 20850 Tel: (b) (6) E-mail: (b) (6)

Appendix 1

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FINAL PROTOCOL

Testing Facility Study No. 20248897

A GLP Intramuscular Combined Developmental and Perinatal/Postnatal Reproductive Toxicity Study of mRNA-1273 in Rats

SPONSOR:
Moderna TX, Inc.
200 Technology Square
Cambridge, MA 02139
United States

TESTING FACILITY:
Charles River Laboratories, Inc.
905 Sheehy Drive
Horsham, PA 19044
United States

Appendix 1

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Appendix 1

1. OBJECTIVE

The objective of this study is to assess the potential effects of mRNA-1273, a vaccine development candidate against SARS-CoV-2 infection, on fertility and pre and postnatal development in the pregnant and lactating female on Sprague Dawley CD (Crl:CD[SD]) rat.

2. PROPOSED STUDY SCHEDULE

Proposed study dates are listed below. Actual dates will be included in the Final Report.

Animal Arrival:	23 Jun 2020
Initiation of Dosing:	30 Jun 2020
Initiation of Estrous Cycle Evaluations:	14 Jul 2020
Initiation of F0 Generation Cohabitation:	27 Jul 2020
First Possible Gestation Day 0:	28 Jul 2020
First Possible Delivery:	18 Aug 2020 (GD 21)
Last Possible Delivery:	28 Aug 2020 (GD 25)
Completion of In-Life:	18 Sep 2020 (Last possible date of necropsy)
Unaudited Draft Report:	16 Nov 2020
Audited Draft Report:	16 Dec 2020

The contributions from Principal Investigators to Study Director are proposed at the dates indicated below to allow inclusion in Unaudited/Audited Draft Reports.

Unaudited Antibody Analysis Draft Report:	09 Nov 2020
Audited Antibody Analysis Draft Report	09 Dec 2020
Unaudited Dose Formulation Draft Report:	09 Nov 2020
Audited Dose Formulation Draft Report:	09 Dec 2020

Appendix 1

3. SPONSOR

Role/Phase	Name	Contact Information
Sponsor Representative/Study Monitor	(b) (6)	Address as cited for the Sponsor Tel: (b) (6) E-mail (b) (6)
Toxicology Director of Toxicology		Address as cited for the Sponsor Tel: (b) (6) E-mail: (b) (6)
Infectious Disease Biomarkers		Address as cited for the Sponsor Tel: (b) (6) E-mail: (b) (6)
Analytical Development		Address as cited for the Sponsor Tel: (b) (6) E-mail: (b) (6)

4. RESPONSIBLE PERSONNEL

Role/Phase	Quality Assurance Unit (QAU)	Name	Contact Information
Study Director	Charles River	(b) (6)	Address as cited for Testing Facility Tel: (b) (6) Fax: (b) (6) E-mail: (b) (6)
Testing Facility Management	Charles River		Address as cited for Testing Facility Tel: (b) (6) Fax: (b) (6) E-mail: (b) (6)
Scientific Reviewer	Charles River		Address as cited for Testing Facility Tel: (b) (6) Fax: (b) (6) E-mail: (b) (6)
Testing Facility QAU	Charles River		Address as cited for Testing Facility Tel: (b) (6) E-mail: (b) (6)
Principal Investigator (PI)			
Analytical Chemistry[a]	Charles River	(b) (6)	Charles River Laboratories Montreal ULC Senneville Site (CR-SEN) 22022 Transcanadienne Senneville, QC H9X 3R3 Canada Tel: (b) (6) E-mail: (b) (6)

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Role/Phase	Quality Assurance Unit (QAU)	Name	Contact Information
Antibody Analysis[b]	N/A (Non-GLP)	(b) (6)	Integrated Biotherapeutics, Inc. 4 Research Court, Suite 300, Rockville, MD 20850 USA Tel (b) (6) E-mail (b) (6)

[a] Testing Facility designated Test Site
[b] Sponsor designated Test Site.

Each PI is required to report all deviations or other circumstances that could affect the quality or integrity of the study to the Study Director in a timely manner for authorization/acknowledgement. Each PI, will provide a report addressing their assigned phase of the study, which will be included as an appendix to the Final Report.

The PI phase report will include the following:

- A Statement of Compliance (if the applicable phase is GLP)
- A QA Statement (if the applicable phase is GLP)
- The archive site for all records, samples, specimens and reports generated from the phase or segment (alternatively, details regarding the retention of the materials may be provided to the Study Director for inclusion in the Final Report)
- A listing of critical computerized systems used in the conduct and/or interpretation of the assigned study phase

5. TEST MATERIALS

5.1. Test and Control Article Characterization

The Sponsor will provide to the Testing Facility documentation of the identity, strength, purity, composition, and stability for the test and control article(s). A Certificate of Analysis or equivalent documentation will be provided for inclusion in the Final Report.

The Sponsor has appropriate documentation on file concerning the method of synthesis, fabrication or derivation of the test and control article(s), and this information is available to the appropriate regulatory agencies should it be requested.

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5.2. Test Material Identification

Test Article Identification

	Test Article
Identification:	mRNA-1273 LNP Solution
Batch/Lot No.:	DH-03026
Expiration[a]:	18 Nov 2020
Physical Description:	White to off-white dispersion; essentially free of visible particles.
Supplied Stock Concentration:	0.76 mg/mL
Correction Factor:	None
Storage Conditions (temperature set to maintain):	Ultrafrozen -60°C to -90°C
Provided by:	Sponsor
Test Article Contact:	(b) (6) [redacted]

5.3. Control Article Identification

Control Article Identification

	Control Article (Dilution Buffer)
Identification:	20 mM Tris, 17.5 mM Sodium Acetate, 87 g/L Sucrose, pH 7.5
Batch/Lot No.:	DH-03026.2
Expiration Date:	18 Nov 2020
Physical Description:	Clear colorless solution free from visible particulates
Storage Conditions (temperature set to maintain):	Ultrafrozen -60°C to -90°C
Provided by:	Sponsor

5.4. Reserve Samples

For each batch (lot) of Test Article and Control Article, a reserve sample will be collected and maintained under the appropriate storage conditions by the Testing Facility.

5.5. Test and Control Article Inventory and Disposition

Records of the receipt, distribution, storage, and disposition of test materials will be maintained. All unused Sponsor-supplied bulk test materials, with the exception of reserve samples, will be returned to the Sponsor following issuance of the Draft Report, discarded, or retained for use on future studies.

5.6. Safety

The Safety Precautions for the study follow the standards for a Charles River Occupational Exposure Band (No. 3) categorized material.

Appendix 1

6. DOSE FORMULATION AND ANALYSIS

6.1. Preparation of Formulations

Dose formulations will be prepared fresh daily on each day of dosing and may be divided into aliquots, when required.

Test and Control Article dosing formulations will be kept at ambient/room temperature conditions and will be used for dose administration within 4 hours of preparation.

Preparation Details

Dose Formulation	Administration Dose Form	Frequency of Preparation	Storage Conditions (temperature set to maintain)[a]
Control Article	Solution	Daily	Ambient/room temperature conditions for <8 hours
Test Article	Solution	Daily	Ambient/room temperature conditions for <4 hours or <8 hours refrigerated

[a] The dosing formulations may be stored refrigerated (2-8°C) for up to 24 hours after preparation or at room temperature for a maximum of 8 hours. Unopened vials may be refrozen after thawing.

6.2. Preparation Details

6.2.1. Preparation of Control Article

Dose formulations will be performed under a biological safety cabinet using aseptic procedures.

The Control Article, 20 mM Tris,17.5 mM Sodium Acetate, 87 g/L Sucrose, pH 7.5, will be administered as received. The bulk control article will be removed from the freezer and allowed to thaw at room temperature for no more than 1 hour before dose formulation preparation. The storage of control article dose formulations at room temperature should not exceed 4 hours from the time of preparation to the time of dose administration. The control article dosing formulations may be stored refrigerated (2-8 °C) for up to 8 hours if not used for dose administration within 3 hours of preparation. If refrigerated storage is necessary, the control article dosing formulation aliquots will be removed from the refrigerator and allowed to equilibrate at ambient/room temperature for at least 30 minutes before dosing. The formulation will NOT be vortexed or sonicated but may be gently swirled to ensure even mixing during formulation. Thawed Control Article vials will be used only on the day of dose formulation preparation once thawed and will not be used on subsequent dosing days.
Detailed preparation procedures (i.e., Formulation Batch Records [FBR]) will be maintained in the raw data.

Any residual volumes will be retained and discarded prior to study finalization upon Sponsor and Study Director authorization.

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6.2.2. Preparation of Test Article

Dose formulation preparations will be performed under a biological safety cabinet using aseptic procedures.

The bulk Test Article stock will be removed from the freezer and allowed to thaw at room temperature for at least 30 minutes (no more than 1 hour) before dose formulation preparation. The test article dosing formulations will be prepared by diluting the bulk Test Article with the Control Article as necessary to the target concentration for administration and should not be filtered. The storage of test article dosing formulations at room temperature should not exceed 4 hours from the time of preparation to the time of dose administration. The test article dosing formulations may be stored refrigerated (2-8 °C) for up to 8 hours if not used for dose administration within 3 hours of preparation. If refrigerated storage is necessary, the test article dosing formulation aliquots will be removed from the refrigerator and allowed to equilibrate at ambient/room temperature for at least 30 minutes before dosing. The formulation will NOT be vortexed or sonicated but may be gently inverted 20 times to ensure even mixing during formulation. Stock vials will be used only on the day of dose formulation preparation once thawed and will not be used on subsequent dosing days.
Detailed preparation procedures (i.e., FBR) will be maintained in the raw data.

Any residual volumes will be retained and discarded prior to study finalization upon Sponsor and Study Director authorization.

6.3. Sample Collection and Analysis

Dose formulation samples will be collected for analysis as indicated in the following table. Additional samples may be collected and analyzed at the discretion of the Study Director.

Dose Formulation Sample Collection Schedule

Interval	Concentration	Sampling From
First Preparation: Day 1	Group 1: 3 x 0.5 mL (middle)	Preparation vessel
	Group 2: 5 x 0.5 mL (top, middle, bottom)	
Approximate Middle Preparation: GD 1	Groups 1 and 2: 5 x 0.5 mL (middle)	Preparation vessel
Last Preparation: GD 13	Groups 1 and 2: 5 x 0.5 mL (middle)	Preparation vessel

All samples to be analyzed will be shipped (on dry ice) to Charles River Laboratories Montreal, see ATTACHMENT D. Samples will be shipped on the date prepared, when possible.

The analytical laboratory and Sponsor Representative will be notified before shipment of the samples. Upon receipt at the analytical laboratory, the samples will be stored under ultrafrozen conditions at -60°C to -90°C.

A temperature monitoring device will be coordinated with the shipping service and added to the shipment by the shipping service. Any temperature monitoring of the shipment will be the responsibility of the Sponsor and/or shipping service and will be outside the scope of the Protocol.

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6.3.1. Analytical Method

Analyses described below will be performed under Test Site Study Number 2100930 by Ion-Exchange High Performance Liquid Chromotography (IEX-HPLC) using a validated analytical procedure (CR-SEN validation study 2100933).

6.3.1.1. Concentration Analysis

Sample Allocation:	Duplicate for analysis, one for backup for Group 1. Duplicate for analysis, triplicate for backup for Group 2. Backup samples may be analyzed at the discretion of the Study Director.
Storage Conditions:	Temperature set to maintain -60°C to -90°C. Samples will be placed into autoclaved amber glass vials.
Acceptance Criteria:	For concentration, the criteria for acceptability will be mean sample concentration results within or equal to ± 15% of theoretical concentration. Each individual sample concentration result within or equal to ± 20%. For homogeneity, the criteria for acceptability will be a relative standard deviation (RSD) of concentrations of ≤ 5% for each group.

7. TEST SYSTEM

Species:	Rat
Strain:	Crl:CD(SD) Sprague Dawley rat
Condition:	Females, virgin
Source:	Charles River Laboratories, Inc.
Number of Females Ordered:	93
Number of Females to be Assigned:	88
Target Age at Arrival:	60 to 70 days
Target Weight at Arrival	200 g to 225 g

The actual age and weight of the animals at the initiation of dosing will be listed in the Final Report.

Male rats of the same source and strain that are maintained by the Testing Facility will be used only as breeders and are not considered part of the Test System.

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7.1. Animal Identification

Method: A subcutaneously implanted electronic identification chip or other approved identification method such indelible ink where required.

7.2. Environmental Acclimation

Method: After receipt at the Testing Facility, the rats will be acclimated for at least 7 days prior to initiation of dosing.

7.3. Selection, Assignment, Replacement, and Disposition of Animals

Replacement: Before the initiation of dosing, any assigned animals considered unsuitable for use in the study will be replaced by alternate animals obtained from the same shipment and maintained under the same environmental conditions, at the discretion of the Study Director. After initiation of dosing, study animals may be replaced during the replacement period with alternate animals in the event of accidental injury, non-test article-related health issues, or similar circumstances, at the discretion of the Study Director.

Disposition: The disposition of all animals will be documented in the study records.

7.3.1. F0 Generation

Selection and Assignment: Female rats will be selected for study on the basis of physical condition and body weights recorded during acclimation. Female rats will be assigned to groups using a computer-based randomization procedure based on body weights recorded during the acclimation period.

Animals in poor health or at extremes of body weight range will not be assigned to groups.

Eighty eight (88) female rats will be assigned to 2 dose groups, 44 rats per group. Additionally, each dose group will consist of two cohorts, 22 rats in each of Cohorts 1 and 2 as described in the following table.

Group No.	Cohort 1 (Caesarean – Sectioning Phase)	Cohort 2 (Natural Delivery Phase)
1	22	22
2	22	22

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7.3.2. F1 Generation

Selection and Assignment:	Day 0 of lactation (postpartum) is defined as the day the delivery of the litter appears to be completed. If the litter is observed to be completed at the morning viability check, Day 0 of lactation (postpartum) is defined as the previous day. Day 1 of lactation (postpartum) is defined as the first day on which all pups in a litter are individually weighed and clinical observations are recorded. On Day 0/1 of lactation (postpartum) all pups in a litter will be sexed. On Lactation Day 4 (LD 4) a randomization program will be used to select F1 generation pups to be culled, and litters will be reduced to eight pups each (when possible). Whenever possible, the same number of male and female pups per litter will be continued on study.

8. HUSBANDRY

8.1. Housing

Housing:	Control group animals will be housed on a separate rack from the Test Article-treated animals. F0 generation rats will be co-housed (where possible) in solid-bottomed cages by dose group (no more than 2 per cage) until cohabitation, unless deemed inappropriate by the Study Director and/or Clinical Veterinarian. During the cohabitation period, one breeder male rat and one female rat will be pair housed in the breeder male rat's solid-bottomed cage. After cohabitation, female rats will be individually housed until the day of scheduled euthanasia (Cohort 1) or until parturition (Cohort 2), at which time, each dam and delivered litter will be housed in a common nesting box during the postpartum period. The male breeder rats will be returned to co-housing with their previous same box mates, whenever possible. Any rats not assigned to study may be trio-housed to avoid having a single-housed animal, whenever possible.
Caging:	Polycarbonate cages containing appropriate bedding.

Housing set-up is as described in the *Guide for the Care and Use of Laboratory Animals*.[1] Animals will be separated during designated procedures/activities or will be separated as required for monitoring and/or health purposes, as deemed appropriate by Study Director and/or Clinical Veterinarian. Cages will be arranged on the racks in group order.

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8.2. Animal Enrichment

Type/Frequency:	For psychological/environmental enrichment, animals will be socially housed and will be provided with Crink-l'Nest™, stainless steel resting lofts, and a chewing item such as *ad libitum* pelleted rodent feed, except when interrupted by study procedures/activities.
Analysis:	There are no known contaminants in the animal enrichment that would interfere with the objectives of the study.

8.3. Bedding

Type:	Bed-o'Cobs®
Frequency:	Changed as often as necessary to keep the animals dry and clean.
Analysis:	Results of analysis for environmental contaminants are on file at the Testing Facility. It is considered that there are no known contaminants in the bedding that would interfere with the objectives of the study.

8.4. Environmental Conditions

The targeted conditions for animal room environment will be as follows:

Temperature:	68°F to 79°F (20°C to 26°C)
Humidity:	30% to 70%
Light Cycle:	12 hours light and 12 hours dark (except during designated procedures)
Ventilation:	At least 10 changes per hour of fresh air that has been passed through 99.97% HEPA filters

8.5. Food

Diet:	Certified Rodent Diet® #5002 (PMI® Nutrition International)
Type:	Pellets (alternate diet may be provided on individual animal basis as warranted as approved by the Study Director)
Frequency:	Ad libitum, except during designated procedures
Analysis:	Results of analysis for nutritional components and environmental contaminants are on file at the Testing Facility. It is considered that there are no known contaminants in the feed that would interfere with the objectives of the study.

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8.6. Water

Type:	All water will be from a local source and passed through a reverse osmosis membrane before use. Chlorine will be added to the processed water as a bacteriostat; processed water is expected to contain no more than 1.2 ppm chlorine at the time of analysis.
Frequency/Ration:	Available *ad libitum* from an automatic watering access system and/or individual water bottles attached to the nesting boxes (except during designated procedures).
Analysis:	Periodic analysis of the water is performed, and results of these analyses are on file at the Testing Facility. It is considered that there are no known contaminants in the water that could interfere with the outcome of the study.

8.7. Veterinary Care

Veterinary care will be available throughout the course of the study and animals will be examined by the veterinary staff as warranted by clinical signs or other changes. In the event that animals show signs of illness or distress, the responsible Veterinarian may make initial recommendations about treatment of the animal(s) and/or alteration of study procedures, which must be approved by the Study Director or Scientific designate. Treatment of the animal(s) for minor injuries or ailments may be approved without prior consultation with the Sponsor Representative when such treatment does not impact fulfillment of the study objectives. If the condition of the animal(s) warrants significant therapeutic intervention or alterations in study procedures, the Sponsor Representative will be contacted, when possible, to discuss appropriate action. If the condition of the animal(s) is such that emergency measures must be taken, the Study Director (or Scientific designate) and/or attending Veterinarian will attempt to consult with the Sponsor representative prior to responding to the medical crisis, but the Study Director (or Scientific designate) and/or Veterinarian has authority to act immediately at his/her discretion to alleviate suffering. The Sponsor Representative will be fully informed of any such events.

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9. EXPERIMENTAL DESIGN

Experimental Design – F0 Generation

Group No.	Test Material	Dose Level (µg/dose)	Dose Concentration (mg/mL)	Dose Volume (µL/dose)	No. of Females	
					Cohort 1 (Cesaearan-Sectioning Phase)	Cohort 2 (Natural Delivery Phase)
1	Control Article	0	0	200	22	22
2	mRNA-1273	100	0.5	200	22	22

9.1. Administration of Test and Control Articles

9.1.1. F0 Generation

Dose Route: Intramuscular injection into the quadriceps on the hindlimbs; alternating on each dosing occasion.

Frequency: Once on each day of dose administration

Duration: Premating Period: Study Day (SD) 1 (28 days prior to mating) and SD 15 (14 days prior to mating). Study Day 1 is defined as the first day of dose administration.

Gestation Period: Gestation Days (GDs) 1 and 13.

Special Procedures: The initiation of dose administration will occur at approximately the same time each day, when possible.

- Under no circumstances, the dosing formulations will be subject to vortexing and vigorously shaking to avoid disruption of the Test Article. Before withdrawing a dose formulation into syringes, the dose formulation container will be gently swirled to achieve homogeneity and this step will be documented.
- The Control Article will be maintained on a separate cart from the Test Article during dose procedures and will be transported in a separate carrier, when possible. Only the Control Article will be in the study room during dose administration of Group 1, when possible.
- Dose procedures for the Control Article group will be completed before dosing for Group 2 is initiated.
- Dose administration will be conducted in a Group number sequence order from Group 1 to 2, in order to minimize any potential risk of Test Article cross-contamination.
- Personal Protective Equipment (PPE) used for dosing will be changed between groups.

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- The Control Article will be removed from the study room before dosing for Group 2 is initiated.

9.1.2. F1 Generation

F1 generation pups will not be directly given the Test Article and/or the Control Article formulations, but may be possibly exposed to the Test Article and/or the Control Article formulations article during maternal gestation (*in utero* exposure) or via maternal milk during the lactation period.

10. IN-LIFE PROCEDURES, OBSERVATIONS, AND MEASUREMENTS – F0 GENERATION

The in-life procedures, observations, and measurements listed below will be performed as per table below.

General In-life Assessments – F0 Generation Females

Parameter	Frequency (minimum required)	Comments
Viability	• At least twice daily	-
Clinical Observations: General	• At least once weekly during the acclimation period • Daily before each dose is administered and daily on non-dosing days • Daily during the postdose period (including the day of scheduled euthanasia).	-
Clinical Observations: Postdose Observations	• 6 hours following dose administration.	Time intervals for postdose observations may be adjusted if deemed appropriate by the Study Director during the course of the study. Such adjustments will be documented in the raw data.
Maternal Observations:	• Daily during the postpartum period (Cohort 2).	Maternal behavior will be recorded.
Individual Body Weights	• On the day of or day after arrival and at least once weekly during acclimation. • On SDs, 1,8, 15, 22, and 28 and on GDs 0, 1, 6, 10, 13, 15, 18, 21, and 25 (if necessary). • Lactation Day (LD) 1, 4, 7, 10, 14, 18 and 21 (Cohort 2)	-

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Parameter	Frequency (minimum required)	Comments
Food Consumption	• Once weekly during the dose period • On GDs 0, 1, 6, 10, 13, 15, 18, 21, and 25 (if necessary). • On LDs 1, 4, 7, 10 and 14 (Cohort 2)	Food consumption values will be recorded. Food consumption will not be tabulated after Day 14 postpartum, when it is expected that pups will begin to consume maternal food. Food consumption values may be recorded more frequently if it is necessary to replenish the food. These intervals will not be tabulated.
Estrous Cycle Evaluations	Samples will be collected from females for 14 consecutive days before initiation of the cohabitation period and then until spermatozoa are observed in a smear of the vaginal contents and/or a copulatory plug is observed in situ during the cohabitation period.	Estrous cycles will be evaluated by examining the vaginal cytology of samples obtained by vaginal lavage.
Reproductive Capacity	Within each dose group, rats will be assigned to cohabitation (i.e., pairing), one breeder male per one female. The cohabitation period will consist of a maximum of 7 days. Females observed with spermatozoa in a smear of the vaginal contents and/or a copulatory plug observed in situ will be considered to be at GD 0 and assigned to individual housing. Females not mated after completion of the 7-day cohabitation period will be considered to be at GD 0 on the last day of cohabitation, assigned to individual housing (i.e., solid bottom or wire-bottom cages) and will be euthanized 25 days after the end of the cohabitation period (for rats that do not deliver a litter) or continued on study (for rats that do deliver a litter) at the discretion of the Study Director.	-
Natural Delivery Observations	Female rats will be evaluated for: • Adverse clinical signs observed • Duration of Gestation (GD 0 to the time the first pup is observed) • Litter Size (defined as all pups delivered) • Pup Viability at Birth	-

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11. IN-LIFE PROCEDURES, OBSERVATIONS, AND MEASUREMENTS – F1 GENERATION (COHORT 2)

11.1. Preweaning

The in-life procedures, observations, and measurements listed below will be performed for all F1 litters, with the litter as the unit of measure.

General In-life Assessments – F1 Generation (Preweaning)

Parameter	Frequency (minimum required)	Comments
Viability	Litters will be observed for dead pups at least twice daily and the pups in each litter will be counted at least once daily during the preweaning period.	-
Clinical Observations: General Appearance	At least once daily.	Clinical observations may be recorded more frequently than cited.
Individual Body Weights	Day 1, 4, 7, 10, 14, 18, and 21 postpartum.	-

12. ANTIBODY EVALUATION

12.1. Antibody Sample Collection

12.1.1. Maternal Samples (Cohorts 1 and 2)

Antibody Sample Collection

Group Nos.	Cohort	Time Points					
		SD 1[a]	SD 15[a]	GD 1[a]	GD 13[a]	GD 21[b]	LD 21[a,b]
1-2	1	X	X	X	X	X	-
1-2	2	X	X	X	X	-	X
Unscheduled euthanasia (when possible)		X					

Method/Comments:	Jugular vein (SD 1, 15, GD 1, 13 in-life blood collections) or via the vena cava while under isoflurane/oxygen anesthesia (GD 21 and LD 21 terminal blood collections). If necessary, in-life blood samples may be collected from an alternate site (lateral tail vein); if so, the alternate site will be documented in the raw data. Additional blood samples may be obtained (e.g. due to sample quality) if permissible sampling frequency and blood volume are not exceeded. Blood will be collected from unscheduled euthanized animals, when possible.
Target Volume (mL):	1.0 mL
Anticoagulant:	None, in SST
Special Requirements:	None
Processing:	Serum

X = Sample to be collected; - = Not applicable, SST = serum separator tube
[a] Sample collected prior to dose administration.
[b] Terminal blood sample collection.

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12.1.2. Fetal Samples (Cohort 1)

On GD 21, blood will be collected via the carotid artery from all viable fetuses in Cohort 1 (pooled per litter).

Target Volume: 1.0 mL pooled per litter

Anticoagulant: None/Serum separator tube

12.1.3. Pup Samples (Cohort 2)

On the day of scheduled euthanasia (LD 21), blood will be collected from 2 pups per litter (1 male and 1 female , when possible) via the inferior vena cava while under isofluorane/oxygen anesthesia.

Target Volume: 1.0 mL pooled per litter

Anticoagulant: None/Serum separator tube

12.2. Antibody Analysis Sample Processing

Antibody Sample Processing

Centrifugation	Aliquot 1 Volume	Aliquot 2 Volume	Storage Conditions
1800 g for 10 minutes Approximately 4°C	At least 240 µL (serum)	Remaining (serum)	-70°C

Theoretical number of samples: up to 220 samples x 2 aliquots (dams), 44 samples x 2 aliquots (fetuses) and 44 samples x 2 aliquots (pups).

The blood samples will be mixed gently and will be centrifuged as soon as practical following an at least 20 minute clot time (not to exceed 1 hour). Blood samples will be centrifuged for 10 minutes at 1800 g in refrigerated centrifuge (4°C). The resultant serum will be separated into two aliquots as described in the table above, transferred to uniquely labeled clear polypropylene tubes, and frozen immediately over dry ice until stored in a freezer set to maintain -70°C.

The first set of samples (aliquot 1/occasion) will be shipped on dry ice with a temperature monitor to the Test Site for antibody analysis, see ATTACHMENT D, after the end of the treatment period. The second set of samples (aliquot 2/occasion) will be maintained at the Testing Facility as back up samples. The Test Site for antibody analysis and the Sponsor Representative will be notified before shipment of the samples. Samples will be stored at the Test Site in a freezer set to maintain -80°C until analysis.

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12.3. Antibody Sample Analysis

The samples will be analyzed for antibodies produced as a result of mRNA-1273 administration using a qualified analytical procedure (insert analytical procedure number).

Antibody responses to SARS-CoV2 S protein will be evaluated using optimized indirect ELISA assay.

In brief, 96-well microtiter plates will be coated with SARS-CoV2 S protein (Sino Biological) and incubated overnight. 5-Step serial dilutions of rat or pup sera will be added, and the bound antibody detected with HRP-conjugated goat anti-rat IgG (KPL), followed by incubation with TMB substrate (KPL). The absorbance measured at OD450nm.

Antibody titers will be calculated as "Antibody Units/mL" based on the four-parameter logistic curve fit (4PL) of a hyperimmune rat standard curve using a using Softmax software (Molecular devices Inc.).

Any residual/retained samples will be maintained for a minimum of 6 months following issuance of the Audited Draft Report after which the disposition of the samples will be determined in consultation with Sponsor. An earlier determination of the disposition of these residual/retained samples may also be requested and authorized by the Study Director in consultation with the Sponsor following confirmation by the Sponsor Representative. An Antibody Report will be included as an appendix to the Final Report.

13. TERMINAL PROCEDURES – F0 GENERATION

Terminal procedures are summarized in the following tables:

F0 Generation Females – Cohort 1

Group No.	Scheduled Euthanasia Day	Necropsy Procedures				Histology Processing and Microscopic Evaluation
		Ovarian/ Uterine Examination	Necropsy	Tissue Collection[a]	Organ Weights	
1	GD 21	X	X	X	X[b]	-
2						
Unscheduled Deaths		X	X	X	X	-

X = Procedure to be conducted; - = Not applicable; GD = Gestation Day

[a] See Tissue Weighing, Collection, Processing and Evaluation table, ATTACHMENT B for list of tissues applicable to each procedure.

[b] The gravid uterus and the placentae will be weighed for all rats that survive to scheduled euthanasia.

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F0 Generation Females – Cohort 2

Group No.	Scheduled Euthanasia Day	Necropsy Procedures				Histology Processing and Microscopic Evaluation
		Ovarian/ Uterine Examination	Necropsy	Tissue Collection[a]	Organ Weights	
1	LD 21	X	X	X	-	-
2						
Unscheduled Deaths		X	X	X	-	-
Dams that did Not Deliver	GD 25	X	X	X	-	-
Dams with No Surviving Pups	b	X	X	X	-	-

X = Procedure to be conducted; - = Not applicable; GD = Gestation Day; LD = Lactation Day
[a] See Tissue Weighing, Collection, Processing and Evaluation table, ATTACHMENT B for list of tissues applicable to each procedure.
[b] On the day the observation is made.

13.1. Method of Euthanasia

F0 generation rats euthanized before scheduled termination will be euthanized by carbon dioxide asphyxiation.

All surviving rats will be euthanized via exsanguination following blood sample collection from the inferior vena cava while under isoflurane/oxygen anesthesia.

All live fetuses (including those selected for Cohort 1 blood collections) will be euthanized by an intraperitoneal injection of sodium pentobarbital (390 mg/mL).

13.2. Unscheduled Euthanasia

Images may be generated for illustration of or consultation on gross observations. Generation of such images will be documented. Images and associated documentation will be retained and archived at the Testing Facility.

13.2.1. Cohorts 1 and 2

Rats assigned to Cohorts 1 and 2 that die or are euthanized before scheduled termination will be examined for the cause of death or condition as soon as possible after the observation is made. A complete necropsy will be performed (including examination of the injection site). See Section 13.5. (Tissue Collection and Preservation) for tissues that will be retained for possible future evaluation.

	Complete Necropsy (Section 13.4.)	Ovarian and Uterine Examination (Section 13.3.3.)	Tissue Retention (Section 13.5.)
Females - Before Cohabitation	X	-	X
Females - After Cohabitation	X	X[a]	X

X = Procedure to be conducted; - = Not Applicable
[a] The number of implantation sites and corpora lutea will be recorded.

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Pregnancy status and uterine contents will be recorded, and the aborted fetuses, conceptuses *in utero*, and/or delivered pups will be examined to the extent possible, using the same methods described for term fetuses.

Uteri of apparently nonpregnant animals will be examined while being pressed between glass plates to confirm the absence of implantation sites. Uteri and ovaries of apparently nonpregnant animals will be retained in 10% neutral buffered formalin and will be discarded when authorized by the Study Director in consultation with the Sponsor.

13.3. Scheduled Euthanasia

13.3.1. Cohort 1

On GD 21, all surviving female rats assigned to Cohort 1 will be euthanized, blood samples will be collected as described in Section 12. (Antibody Evaluation), and animals will be examined for ovarian and uterine contents (Section 13.3.3., Ovarian and Uterine Examinations) and gross lesions (Section 13.4, Necropsy) (including examination of the injection site). See Section 13.5. (Tissue Collection and Preservation) for tissues to be retained for possible future evaluation.

13.3.2. Cohort 2

After completion of the 21-Day postpartum period, F0 generation female rats will be euthanized, blood samples will be collected as described in Section 12. (Antibody Evaluation), and animals will be examined for gross lesions (including examination of the injection site). Dams with no surviving pups will be euthanized after the last pup is found dead or missing, presumed cannibalized.

The rats will be examined as described in Sections 13.3.3. (Ovarian and Uterine Examinations) and Section 13.4. (Necropsy). See Section 13.5. (Tissue Collection and Preservation) for tissues to be retained for possible future evaluation.

Females that did not mate after the completion of the 7-day cohabitation period will be euthanized 25 days after the end of the cohabitation period (females that do not deliver a litter) or will continue on study (females that deliver) at the discretion of the Study Director. If euthanized, animals will be examined for gross lesions (including examination of the injection site). The rats will be examined as described in Sections 13.3.3. (Ovarian and Uterine Examinations) and Section 13.4. (Necropsy). See Section 13.5. (Tissue Collection and Preservation) for tissues to be retained for possible future evaluation.

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13.3.3. Ovarian and Uterine Examinations

13.3.3.1. Cohort 1

The reproductive tract will be dissected from the abdominal cavity. The gravid uterus will be weighed. The uterus will be opened and the contents will be examined. The fetuses will be removed from the uterus and placed in individual containers. Each placenta will be weighed.

- Corpora lutea
- Implantation sites
- Placentae (size, color or shape) – any abnormalities will be recorded
- Live and dead fetuses
- Early and late resorptions

Uteri of apparently nonpregnant animals will be examined while being pressed between glass plates to confirm the absence of implantation sites. Uteri and ovaries of apparently nonpregnant animals that are found dead or euthanized before scheduled termination will be retained in 10% neutral buffered formalin and may be discarded when authorized by the Study Director in consultation with the Sponsor.

13.3.3.2. Cohort 2

The reproductive tract will be dissected from the abdominal cavity. The number and distribution of implantation sites will be recorded.

Uteri of apparently nonpregnant animals will be examined while being pressed between glass plates to confirm the absence of implantation sites. Uteri and ovaries of apparently nonpregnant animals will be retained in 10% neutral buffered formalin and will be discarded when authorized by the Study Director in consultation with the Sponsor.

13.4. Necropsy

Animals unscheduled euthanized and found dead will be subjected to a complete necropsy examination, which will include evaluation of the carcass and musculoskeletal system; all external surfaces and orifices; cranial cavity and external surfaces of the brain; and thoracic, abdominal, and pelvic cavities with their associated organs and tissues.
A gross necropsy of the thoracic, abdominal and pelvic viscera will be performed for each scheduled euthanized animal.

Images may be generated for illustration of or consultation on gross observations. These images will not be used for data generation or interpretation and will not be archived or included in the Final Report.

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13.5. Tissue Collection and Preservation

Representative samples of tissues will be collected and preserved in 10% neutral buffered formalin, except for tissues requiring alternate fixatives as defined by standard operating procedures, as detailed in ATTACHMENT A (Tissue Collection and Evaluation – F0 Generation Scheduled Euthanasia) and ATTACHMENT B (Tissue Collection and Evaluation – F0 Generation Unscheduled Euthanasia). Additional tissue samples may be collected to elucidate abnormal findings and will be discarded before finalization of the study.

14. FETAL EXAMINATIONS – COHORT 1

Representative photographs of external, visceral and skeletal abnormalities will be taken at the discretion of the Study Director or designee for illustration of, or consultation on, observations. Photographs will not be included in the Report, but will be retained as electronic images and archived with the raw data. Abnormalities will be classified as malformations and variations.

Examination	Procedure
Aborted/Delivered Pups	Examined for external and visceral abnormalities to the extent possible and discarded without further examination.
Dead Fetuses	Examined to the extent possible and discarded without further evaluation..
Body Weights	Recorded for each live fetus.
External	All fetuses will be examined for sex and for external abnormalities.
Visceral	Approximately one-half of the fetuses in each litter will be examined for visceral abnormalities by using a modification of the microdissection technique of Staples.[2] Each fetus will be fixed in Bouin's solution and the heads will subsequently be examined by free-hand sectioning;[3] head sections with abnormal findings will be stored in alcohol. All other head sections will be discarded. The decapitated carcasses will not be retained.
Skeletal	The remaining fetuses (approximately one-half of the fetuses in each litter) will be examined for skeletal abnormalities after staining with alizarin red S.[4] Following examination, skeletal preparations will be retained in glycerin with thymol added as a preservative.

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15. TERMINAL PROCEDURES – F1 GENERATION (COHORT 2)

15.1. Method of Euthanasia

F1 generation pups assigned to Cohorts 2 blood collections will be euthanized via exsanguination following blood sample collections.

All other F1 generation pups will be euthanized by an intraperitoneal injection of sodium pentobarbital (390 mg/mL) (pups ≤ 14 days of age) or by carbon dioxide asphyxiation (pups ≥15 days of age).

15.2. Unscheduled Deaths

15.2.1. Days 0 to 21 Postpartum

Pups that are found dead during delivery or at the completion of littering (Days 0 or 1 postpartum) will be evaluated for vital status at birth. The lungs will be removed and immersed in water. Pups with lungs that sink will be identified as stillborn; pups with lungs that float will be identified as liveborn and to have died shortly after birth. Pups (whole animal) will be preserved in 10% neutral buffered formalin for possible future evaluation.

Pups that die (Days 1 to 21 postpartum) or are euthanized (Days 0 to 21 postpartum) before scheduled termination will be examined for gross lesions and the cause of death or condition as soon as possible after the observation is made. Pups euthanized on Days 0 to 4 postpartum or found on Days 1 to 4 postpartum will be preserved in 10 % neutral buffered formalin (whole animal) for possible future evaluation. Tissues will be collected from pups euthanized or found on Days 5 to 21 postpartum as described in Section 15.5. (Tissue Collection and Preservation). For any premature pups (Days 5 to 21 postpartum), the whole animal will be fixed in 10 % neutral buffered formalin if tissue collection is not feasible due to the small size of the animal.

15.3. Scheduled Euthanasia

Pups culled on Day 4 postpartum will be examined for gross lesions as described in Section 15.4 (Necropsy). Necropsy will include a single cross-section of the head at the level of the frontal-parietal suture and examination of the cross-sectioned brain for apparent hydrocephaly.

On Day 21 postpartum, F1 generation rats will be euthanized and examined for gross lesions (Section 15.4., Necropsy). Necropsy will include a single cross-section of the head at the level of the frontal-parietal suture and examination of the cross-sectioned brain for apparent hydrocephaly. See Section 15.5. (Tissue Collection and Preservation) for tissues to be retained for possible future evaluation.

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15.4. Necropsy

A gross necropsy of the thoracic, abdominal and pelvic viscera will be performed for each animal.

Images may be generated for illustration of or consultation on gross observations. Generation of such images will be documented. Images and associated documentation will be retained and archived.

15.5. Tissue Collection and Preservation

Representative samples of tissues will be collected and preserved in 10% neutral buffered formalin, except for tissues requiring alternate fixatives as defined by standard operating procedures, as detailed in ATTACHMENT B (Tissue Collection and Evaluation – F1 Generation Unscheduled Euthanasia) and ATTACHMENT C (Tissue Collection and Evaluation – F1 Generation Scheduled Euthanasia). Additional tissue samples may be collected to elucidate abnormal findings and will discarded before finalization of the study.

16. STATISTICAL ANALYSIS

Any data collected during the predose period will not be tabulated or summarized, unless applicable to analyses in the proceeding sections. Litter values will be used, where appropriate. Additional procedures and/or analyses may be performed if deemed appropriate.

Clinical and necropsy observations data (with the exception of preweaning pup necropsy observations [inferential statistics will be performed on incidences]) will be summarized but no inferential statistical analysis will be performed.

Numerical data collected on scheduled occasions will be summarized and statistically analyzed as indicated below according to sex and occasion or by litter.

Additional procedures and/or analyses may be performed, if appropriate; however may involve additional cost and a reporting time longer than that specified in the study contract.

16.1. Descriptive Statistical Analyses

Means, standard deviations (or % coefficient of variation or standard error, when deemed appropriate), ratio, percentages, numbers, and/or incidences will be reported as appropriate by dataset.

Appendix 1

16.2. Constructed Variables

F0 Generation

Body weight changes	Calculated between each scheduled interval.
Food Consumption	Calculated between each scheduled interval.

Additional or alternative body weight or food consumption intervals may be evaluated to elucidate study results at the discretion of the Study Director.

The following parental indices and litter calculations will be included, where applicable:

Female Mating Index = $\frac{\text{Number of Females with Evidence of Mating (or no confirmed mating date and pregnant)}}{\text{Number of Females Paired}}$

Female Fertility Index = $\frac{\text{Number of Pregnant Females}}{\text{Number of Females with Evidence of Mating (or no confirmed mating date and pregnant)}}$

Female Pregnancy Index = $\frac{\text{Number of Pregnant Females}}{\text{Number of Females Paired}}$

Pre-Implantation Loss = $\frac{\text{Number of Corpora Lutea – Number of Implants}}{\text{Number of Corpora Lutea}} \times 100$

Post-Implantation Loss = $\frac{\text{Number of Implants – Number of Live Fetuses}}{\text{Number of Implants}} \times 100$

Sex Ratio (% males) = $\frac{\text{Number Male Fetuses}}{\text{Total Number of Fetuses}} \times 100$

Litter % of Fetuses with Abnormalities = $\frac{\text{Number of Fetuses in Litter with a given Finding}}{\text{Number of Fetuses in Litter Examined}} \times 100$

The following natural delivery/reproductive parameters will be included, as appropriate:

- Gestation Length: The gestation length is calculated from GD 0 to the day the first pup is observed.
- Female Pregnancy Index: $\frac{\text{Number of Pregnant Females}}{\text{Number of Females Paired}}$
- Gestation Index: Percentage of pregnancies that result in birth of live litters

  $\frac{\text{Number of Animals with Live Offspring}}{\text{Number of Animals Pregnant}} \times 100$

Appendix 1

- Live Birth Index: Percentage of pups born alive.

  $$\frac{\text{Number of Live Newborn Pups}}{\text{Number of Newborn Pups}} \times 100$$

- Viability Index: Percentage of pups born that survive 4 days postpartum

  $$\frac{\text{Number of Live Pups on Day 4 Postpartum}}{\text{Number of Live Newborn Pups}} \times 100$$

- Lactation Index: Percentage of pups that survive 21 days postpartum

  $$\frac{\text{Number of Live Pups on Day 21 Postpartum}}{\text{Number of Live Pups on Day 4 (postculling) Postpartum}} \times 100$$

- Post-Implantation Loss/Litter

  $$\frac{\text{Number of Implants} - \text{Total Newborn Pups}}{\text{Number of Implants}} \times 100$$

- Sex Ratio (% males) Percentage of male pups per litter

  $$\frac{\text{Number of Live Male Pups}}{\text{Total Number of Live Pups}} \times 100$$

16.3. Inferential Statistical Methods

All statistical tests will be conducted at the 5% significance level. All pairwise comparisons will be conducted using two sided tests and will be reported at the 1% and 5% levels, unless otherwise noted.

Analyses will be conducted and pairwise comparisons of interest will be carried out as listed below:

F0 Generation/Litters (Preweaning)		
Group 2	vs.	Group 1

Analyses will be performed according to the matrix below when possible, but will exclude any group with less than 3 observations.

Appendix 1

Statistical Matrix

Variables for Inferential Analysis	Statistical Method		
	Parametric/ Non-Parametric	**Non-Parametric**	**Incidence**
General Data			
Body Weight[a]	X	-	-
Body Weight Gains[a]	X	-	-
Food Consumption[a]	X	-	-
Parental Indices and Mortality	-	-	X
Natural Delivery and Litter Data			
Natural Delivery and Litter Observations (Proportional) (e.g. Pregnant, Females with Liveborn, Gestation Index, Female with Liveborn)	-	-	X
Natural Delivery and Litter Observations (Count) (e.g. Gestation Length, Live Pups, Implantation Sites)	-	X	-
Litter Observations (Continuous) (e.g. Sex Ratio - Males, Mean Litter Bodyweights)	X	-	-
Live Birth Index	-	X	-
Litter Incidence of Adverse Necropsy Findings per Group	-	-	X[b]
Pup Incidence of Adverse Necropsy Findings per Group	-	-	X[b]
Estrous Cycling, Mating and Fertility			
Number of Estrous Cycles and Mean Cycle Length	-	X	-
Pregnancy, Mating and Fertility Indices	-	-	X
Precoital Interval[c]	-	X	-
Caesarean-section Late Gestation[d]			
Ovarian and Uterine Examinations[c]	-	X	-
Litter Observations (Litter Means)[c,e]	X		-
Litter % of Fetuses with Gross/External/Visceral/Skeletal Abnormalities[f]	-	X	-
Mean Fetal Ossification Sites[f]	-	X	-

[a] Excludes animals not pregnant from the gestation phase summarization and statistical analysis.
[b] Inferential statistical analysis will be restricted to pups euthanized on Postnatal Day 21.
[c] Excludes animals with no confirmed mating date from summarization and statistical analysis.
[d] Excludes animals euthanized preterminally from summarization and statistical analysis.
[e] Presented for males, females and sexes combined; live fetuses only.
[f] Presented for sexes combined; live fetuses only.

Appendix 1

16.4. Parametric/Non-parametric

Levene's test will be used to assess the homogeneity of group variances. The groups will be compared using a Dunnett's test if Levene's test is not significant or Dunn's test if it is significant.

16.5. Non-Parametric

Datasets will be compared using a Dunn's test.

16.6. Incidence

A Fisher's exact test will be used to conduct pairwise group comparisons of interest.

17. COMPUTERIZED SYSTEMS

The following critical computerized systems may be used in the study. The actual critical computerized systems used will be specified in the Final Report.

Critical Computerized Systems

System Name	Description of Data Collected and/or Analyzed
(b) (4)	Test material receipt, accountability, formulation activities, in-life (e.g., clinical observations, body weights, food consumption), and/or postmortem (e.g., pathology, ovarian and uterine contents, and fetal parameters)
	Temperature, humidity and light cycle times
	Deviations
	In-life; postmortem
	Reporting
	Collection of Part 11 compliant signature
	Data acquisition for dose formulation analysis, including regression analysis and measurement of concentration and recovery of dose formulations using HPLC

Data for parameters not required by the Protocol, which are automatically generated by analytical devices used, will be retained on file but not reported. Statistical analysis results that are generated by the program but are not required by the Protocol and/or are not scientifically relevant will be retained on file but will not be included in the tabulations.

Appendix 1

18. REGULATORY COMPLIANCE

The study will be performed in accordance with the U.S. Department of Health and Human Services, Food and Drug Administration, United States Code of Federal Regulations, Title 21, Part 58: Good Laboratory Practice for Nonclinical Laboratory Studies and as accepted by Regulatory Authorities throughout the European Union (OECD Principles of Good Laboratory Practice), Japan (MHLW), and other countries that are signatories to the OECD Mutual Acceptance of Data Agreement.

Any portion of this study conducted in Canada will be performed in accordance with the OECD Principles of Good Laboratory Practice and as accepted by Regulatory Authorities throughout the European Union, United States of America (FDA), Japan (MHLW), and other countries that are signatories to the OECD Mutual Acceptance of Data Agreement.

Exceptions to GLPs include the following study elements:

- Characterization of the Test and Control articles will be performed by the Sponsor or Sponsor subcontractor at a laboratory that follows FDA Good Manufacturing Practice (GMP) regulations.
- Stability testing of the supplied Test and Control articles was performed by the Sponsor or Sponsor subcontractor at a laboratory that follows FDA GMP regulations.
- Stability of the Test Article formulations will not be determined in this study.
- The antibody analysis will not comply with Good Laboratory Practice (GLP) regulations. This analysis will be performed using established SOPs, controls, approved test methodologies, and good scientific practices.

19. QUALITY ASSURANCE

19.1. Testing Facility

The Testing Facility Quality Assurance Unit (QAU) will monitor the study to assure the facilities, equipment, personnel, methods, practices, records, and controls are in conformance with Good Laboratory Practice regulations. The QAU will review the Protocol, conduct inspections at intervals adequate to assure the integrity of the study, and audit the Final Report to assure that it accurately describes the methods and standard operating procedures and that the reported results accurately reflect the raw data of the study.

19.2. Test Site(s)/Subcontractor(s)

For all study phase(s) inspected by test site/subcontractor QAU(s), copies of each periodic inspection report will be made available to the Study Director, Testing Facility Management, and the Testing Facility QAU.

Appendix 1

20. AMENDMENTS AND DEVIATIONS

Changes to the approved Protocol shall be made in the form of an Amendment, which will be signed and dated by the Study Director. Every reasonable effort will be made to discuss any necessary protocol changes in advance with the Sponsor. The Study Director will notify the Sponsor of deviations that may result in a significant impact on the study as soon as possible.

21. RETENTION AND DISPOSITION OF RECORDS, SAMPLES, AND SPECIMENS

All study-specific raw data, electronic data, documentation, Protocol (and amendments, if any), retained samples and specimens, and final reports will be archived by no later than the date of final report issue. All materials generated by Charles River from this study will be transferred to a Charles River archive. At least 1 year after issue of the Draft Report, the Sponsor will be contacted.

Disposition of residual/retained analytical samples will be as described in the table below.

Disposition of Residual/Retained Samples

Sample Type	Disposition	Schedule
Analytical Chemistry (Dose Formulation Samples)	Discard or Archive	Samples will be maintained for a minimum of 6 months following issuance of the Draft Report or at an alternate time point prior to finalization as requested and authorized by the Study Director in consultation with the Sponsor.
Antibody Serum Samples	Returned to Sponsor	

Records to be maintained will include, but will not be limited to, documentation and data for the following:

- Protocol, Protocol amendments, and deviations
- Study schedule
- Study-related correspondence
- Test system receipt, health, and husbandry
- Test and control article receipt, identification, preparation, and analysis
- Mating history
- In-life measurements and observations
- Antibody serum sample collection and evaluation
- Gross observations and related data
- Ovarian/Uterine and fetal observations
- Photographs, if any
- Statistical analysis results
- Natural Delivery Observations
- Litter Observations

Appendix 1

22. REPORTING

A comprehensive Draft Report will be prepared following completion of the study and will be finalized following consultation with the Sponsor. The report will include all information necessary to provide a complete and accurate description of the experimental methods and results and any circumstances that may have affected the quality or integrity of the study.

The Sponsor will receive an electronic version of the Draft and Final Reports provided in Adobe Acrobat PDF format (hyperlinked and searchable) along with a Microsoft Word version of the text. The PDF document will be created from native electronic files to the extent possible, including text and tables generated by the Testing Facility. Report components not available in native electronic files and/or original signature pages will be scanned and converted to PDF image files for incorporation.

Reports should be finalized within 6 months of issue of the Draft Report. If the Sponsor has not provided comments to the report within 6 months of draft issue, the report will be finalized by the Testing Facility unless other arrangements are made by the Sponsor.

23. JUSTIFICATIONS AND GUIDELINES

23.1. Justification of Test System and Number of Animals

The test system was selected because: 1) this strain of rat has been demonstrated to be sensitive to reproductive and developmental toxins and has been widely used throughout industry for reproductive and developmental toxicity evaluations; 2) historical data and experience exist at the Testing Facility; and 3) the Test Article is pharmacologically active in the species and strain.

The number of animals chosen for this study is the smallest number considered necessary to provide the minimum number of pregnancies recommended by the applicable guidelines.

23.2. Justification of Route and Dose Levels

The intramuscular route of exposure was selected because this is the intended route of human exposure.

The dose level for this study (100µg/dose) was chosen to approximate the human clinical dose.

Appendix 1

23.3. Guidelines for Study

The design of this study was based on the study objective(s), the overall product development strategy for the Test Article, and the following study design guidelines:

- ICH Harmonised Tripartite Guideline S5 (R3). *Guideline on Reproductive Toxicology : Detection of Toxicity to Reproduction for Human Pharmaceuticals.*
- ICH Harmonised Tripartite Guideline M3 (R2). *Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals.*
- Food and Drug Administration (FDA). Guidance for Industry: Considerations for developmental toxicity studies for preventative and therapeutic vaccines for infectious disease indications, CBER Division of Vaccines and related products (February 2006).

24. ANIMAL WELFARE

This study will comply with all applicable sections of the Final Rules of the Animal Welfare Act regulations (Code of Federal Regulations, Title 9), the *Public Health Service Policy on Humane Care and Use of Laboratory Animals* from the Office of Laboratory Animal Welfare, and the *Guide for the Care and Use of Laboratory Animals* from the National Research Council.[1,5] The Protocol and any amendments or procedures involving the care or use of animals in this study will be reviewed and approved by the Testing Facility Institutional Animal Care and Use Committee before the initiation of such procedures.

If an animal is determined to be in overt pain/distress, or appears moribund and is beyond the point where recovery appears reasonable, the animal will be euthanized for humane reasons in accordance with the *American Veterinary Medical Association (AVMA) Guidelines for the Euthanasia of Animals* and with the procedures outlined in the Protocol.[6]

By approving this Protocol, the Sponsor affirms that there are no acceptable non-animal alternatives for this study, that this study is required by a relevant government regulatory agency(ies) and that it does not unnecessarily duplicate any previous experiments.

Appendix 1

25. REFERENCES

1. National Research Council. *Guide for the Care and Use of Laboratory Animals*. 8th edition. Washington, DC: National Academy Press. 2011.
2. Staples RE. Detection of visceral alterations in mammalian fetuses. *Teratology* 1974;9(3):A37-A38.
3. Wilson JG. Methods for administering agents and detecting malformations in experimental animals. In: Wilson JG, Warkany J, editors. *Teratology: principles and techniques*. Chicago (IL): University of Chicago Press; 1965. p. 262-77.
4. Staples RE, Schnell VL. Refinements in rapid clearing technic in the KOH-alizarin red S method for fetal bone. *Stain Technol* 1964;39:61-3.
5. Office of Laboratory Animal Welfare. *Public Health Services Policy on Humane Care and Use of Laboratory Animals*. Bethesda, MD: National Institutes of Health. 2015.
6. American Veterinary Medical Association. *AVMA Guidelines for the Euthanasia of Animals*. 2020 edition.

Appendix 1

TESTING FACILITY APPROVAL

The signature below indicates that Testing Facility Management approves the Study Director identified in this Protocol and management's responsibility to the study as defined by the relevant GLP regulations.

DocuSigned by:
(b) (6)
Signer Name: (b) (6)
Signing Reason: I have reviewed this document
Signing Time: 16-Jun-2020 | 12:25:22 EDT
78BAB4040E994EC394A576D8ACD5E23C

(b) (6)

The signature below indicates that the Study Director approves the Protocol.

DocuSigned by:
(b) (6)
Signer Name (b) (6)
Signing Reason: I approve this document
Signing Time: 16-Jun-2020 | 12:30:31 EDT
21C2CFF6B9FE4A5EBB9C44F8F9E9C519

(b) (6)

Appendix 1

SPONSOR APPROVAL

The Protocol was approved by the Sponsor by e-mail on the date designated below. The correspondence giving approval will be archived, as appropriate with other Sponsor communications.

15 Jun 2020
Date of Sponsor Approval

Appendix 1

ATTACHMENT A

Tissue, Collection, and Evaluation Table – F0 Generation Scheduled Euthanasia

A table of random units will be used to select one control group rat from which all tissues examined at necropsy will be retained, in order to provide control tissues for any possible future evaluations of gross lesions.

Tissue Collection and Preservation – F0 Generation Scheduled Euthanasia

Tissue	Weigh	Collect	Comment
Administration site	-	X	All scheduled euthanized animals
Gravid Uterus	X	-	All pregnant animals at scheduled euthanasia
Gross lesions/masses	-	X	All scheduled euthanized animals
Placentae	X	-	All pregnant animals at scheduled euthanasia

X = Procedure to be conducted

Appendix 1

ATTACHMENT B

Tissue Collection and Evaluation Table – F0 and F1 Generation – Unscheduled Euthanasia

Tissue Collection and Preservation – F0 and F1 Generation Unscheduled Euthanized and Found Dead Animals

Tissue	Collect	Microscopic Evaluation	Comment
Animal Identification	X	-	-
Artery, aorta	X	-	-
Body cavity, nasal	X	-	-
Bone marrow, sternum	X	-	Unscheduled euthanized animals only. Bone marrow smears are allowed to air dry and are not fixed in formalin.
Bone, femur	X (1)	-	-
Bone, sternum	X	-	-
Brain	X	-	Seven brain levels .[7] to be examined to include olfactory bulb (Examine in Body cavity, nasal section level 4[8])
Epididymis	X (2)	-	Paired examination.
Esophagus	X	-	-
Eye	X (2)[a]	-	Paired examination; Preserve in Davidson's fixative.
Ganglion, dorsal root, lumbar	X	-	Collect with spinal column.
Gland, adrenal	X (2)	-	Paired examination.
Gland, clitoral	X (2)	-	-
Gland, Harderian	X (2)	-	-
Gland, lacrimal	X (2) (extra-orbital)	-	-
Gland, mammary	X	-	For males, examine only if present in routine section of skin. Collect with inguinal skin.
Gland, parathyroid	X (2)	-	Examine only if present in the routine section of thyroid.
Gland, pituitary	X	-	-
Gland, preputial	X (2)	-	-
Gland, prostate	X	-	-
Gland, salivary, submandibular	X (2)	-	-
Gland, salivary, sublingual	X (2)	-	-
Gland salivary, parotid	X (2)	-	-
Gland, seminal vesicle	X (2)	-	Paired examination.
Gland, thyroid	X (2)	-	Paired examination
Gland, Zymbal's	X (2)	-	-
Gut-associated lymphoid tissue[b]	X	-	Examine only if present in routine section of intestine.
Heart	X	-	-

Appendix 1

Tissue	Collect	Microscopic Evaluation	Comment
Joint, femorotibial	X (1)	-	-
Kidney	X (2)	-	Paired examination.
Large intestine, cecum	X	-	-
Large intestine, colon	X	-	-
Large intestine, rectum	X	-	-
Larynx	X	-	Examine level 2[9]
Liver	X	-	-
Lung	X	-	-
Lymph node(s) draining administration site	X (2)	-	Collect lymph nodes that would be expected to receive primary exposure to the test article (i.e. lymph node draining the administration site
Lymph node, mandibular	X (2)	-	-
Lymph node, mesenteric	X	-	-
Muscle, skeletal	X (2)	-	-
Nerve, optic	X (2)[a]	-	Examine only if present in the routine section of the eye. Preserve in Davidson's fixative.
Nerve, sciatic	X (2)	-	-
Nerve, tibial	X (2)	-	-
Ovary	X (2)	-	Paired examination.
Oviduct	X (2)	-	-
Pancreas	X	-	-
Site(s), administration	X	-	Right and left quadriceps.
Skin	X	-	-
Small intestine, duodenum	X	-	-
Small intestine, ileum	X	-	-
Small intestine, jejunum	X	-	-
Spinal cord	X	-	Examine one transverse and one longitudinal section from each of the following areas cranial cervical, mid-thoracic, lumbar (intumescence)
Spleen	X	-	-
Stomach	X	-	-
Testis	X (2)[a]	-	Paired examination; Preserve in Modified Davidson's fixative.
Thymus	X	-	-
Tongue	X	-	-
Trachea	X	-	-
Ureter	X (2)	-	-
Urinary bladder	X	-	-
Uterus/Cervix	X	-	-
Vagina	X	-	-

Appendix 1

[7] Bolon, B., Garman, R. H., Pardo, I. D, Jensen, K., Sills, R., Roulois, A., Radovsky, A. E., Bradley, A., Andrews-Jones, L., Butt, M., Guimprecht, L. STP Position Paper: Recommended practices for sampling and processing the nervous system (brain, spinal cord, nerve and eye) during nonclinical general toxicity studies. *Toxicol Pathol*. **41**, 2013. 1028-1048.

[8] Young, J. Histopathologic Examination of the Rat Nasal Cavity, Fundamental and Applied Toxicology, 1:309-312 (July/August 1981).

[9] Roger A. Renne, Katherine M. Gideon, Rodney A. Miller, Paul W. Mellick, and Sandra L. Grumbein. Histologic Methods and Interspecies variations in the Laryngeal Histology of F344/N Rats and B6G3F1 Mice, Toxicologic Pathology, Vol 20, Number 1, 1992 pp 44-51.

Appendix 1

ATTACHMENT C

Tissue Weighing, Collection, and Evaluation Table – F1 Generation Scheduled Euthanasia

A table of random units will be used to select one F1 generation control group rat of each sex from which all tissues examined at necropsy will be retained, in order to provide control tissues for any possible histopathological evaluations of gross lesions.

Tissue Collection and Preservation – F1 Generation Scheduled Euthanasia

Tissue	Weigh	Collect	Comment
Animal Identification	-	X	All scheduled euthanized animals, only collect if gross lesions are present.
Gross lesions/masses	-	X	All scheduled euthanized animals.

X = Procedure to be conducted; - = Not applicable.

Appendix 1

ATTACHMENT D

Shipment of Samples and Study Records

Matrix	Purpose	Day/ Week/ Aliquot	Proposed Shipment Date	Conditions for Shipment	Recipient/Address
Dose formulation samples	Analytical chemistry	First Preparation	30 Jun 2020	Dry Ice with a temperature monitor	Charles River Laboratories Montreal ULC Senneville Site (CR-SEN) 22022 Transcanadienne Senneville, QC H9X 3R3 Canada Tel: (b) (6) E-mail:
		Middle Preparation	29 Jul 2020		
		Last Preparation	17 Aug 2020		
Serum	Antibody Analysis	Aliquot 1: SDs 1 and 15 GDs 1, 13, and 21 LD 21	22 Sep 2020	Dry Ice with a temperature monitor	Integrated Biotherapeutics, Inc 4 Research Court, Suite 300, Rockville, MD 20850 Tel: (b) (6) E-mail:

Appendix 2

moderna
200 Tech Square • Cambridge MA 02139
phone 617-714-6500 • fax 617-583-1998

SUMMARY OF ANALYSIS

(b) (4)

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Appendix 2

Number: DPAD-00735 Version: 1.0 Approved Date: 05 Jun 2020
Summary of Analysis: Lot DH-03026 Release

moderna

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REVISION HISTORY

Revision #	Change Details	Author	Effective Date
1.0	Introduction of a New Document	(b) (6)	Date of Approval

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Appendix 2

Number: DPAD-00735 Version: 1.0 Approved Date: 05 Jun 2020
Summary of Analysis: Lot DH-03026 Release

Document Approvals

Approved Date: 05 Jun 2020

Approve Verdict: Approved	(b) (6) Development 05-Jun-2020 18:35:33 GMT+0000

Approve Verdict: Approved	(b) (6) Development 05-Jun-2020 18:36:04 GMT+0000

Appendix 2

Number: DPAD-00745 Version: 1.0 Approved Date: 08 Jun 2020
Summary of Analysis: Lot DH-03026.2 Formulation Buffer

moderna

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SUMMARY OF ANALYSIS

(b) (4)

REVISION HISTORY

Revision #	Change Details	Author	Effective Date
1.0	Introduction of a New Document	(b) (6)	Date of Approval

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Appendix 2

Number: DPAD-00745 Version: 1.0 Approved Date: 08 Jun 2020
Summary of Analysis: Lot DH-03026.2 Formulation Buffer

Document Approvals

Approved Date: 08 Jun 2020

Approve Verdict: Approved	(b) (6) Development 08-Jun-2020 20:01:11 GMT+0000
Approve Verdict: Approved	(b) (6) 08-Jun-2020 21:03:28 GMT+0000

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Appendix 3

charles river

FINAL REPORT

Study Phase: Analytical Chemistry

Test Site Reference No. 2100930

Test Facility Study No. 20248897

A GLP Intramuscular Combined Development and Perinatal/Postnatal Reproductive Toxicity Study of mRNA-1273 in Rats

TEST FACILITY:
Charles River Laboratories, Inc.
905 Sheehy Drive
Horsham, PA 19044
United States

TEST SITE:
Charles River Laboratories Montreal ULC
Senneville Site (CR-SEN)
22022 Transcanadienne
Senneville, QC H9X 3R3
Canada

Appendix 3

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QUALITY ASSURANCE STATEMENT

Study Number: 20248897

This phase has been audited by Quality Assurance in accordance with the applicable Good Laboratory Practice regulations. Reports were submitted in accordance with standard operating procedures as follows:

QA INSPECTION DATES

Date(s) of Audit	Phase(s) Audited	Dates Findings Submitted to: Principal Investigator	Principal Investigator Management	Study Director	Study Director Management
06-Jul-2020	Sample Analysis	07-Jul-2020	07-Jul-2020	07-Jul-2020	07-Jul-2020
23-Sep-2020 - 24-Sep-2020	Data Review - Analytical Chemistry	25-Sep-2020	25-Sep-2020	25-Sep-2020	25-Sep-2020
23-Sep-2020 - 24-Sep-2020	Phase Report - Analytical Chemistry	25-Sep-2020	25-Sep-2020	25-Sep-2020	25-Sep-2020
04-Nov-2020 - 05-Nov-2020	Final Phase Report - Analytical Chemistry	05-Nov-2020	05-Nov-2020	05-Nov-2020	05-Nov-2020

Process-based inspections relevant to this study were conducted according to a predetermined schedule. The outcome of each inspection was reported to Management and, where relevant for processes seen as part of a study, the Study Director.

Facilities relevant to this study are included in Charles River's annual facility inspection programme. The outcome of each inspection is reported to Management.

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Appendix 3

COMPLIANCE STATEMENT AND REPORT APPROVAL

The dose formulation analysis phase of this study conducted in Canada at CR-SEN was performed in accordance with the OECD Principles of Good Laboratory Practice as accepted by Regulatory Authorities throughout the European Union, United States of America (FDA), Japan (MHLW), and other countries that are signatories to the OECD Mutual Acceptance of Data Agreement.

This phase of the study was conducted in accordance with the procedures described herein. The report represents an accurate and complete record of the results obtained for this study phase.

There were no deviations from the above regulations that affected the overall integrity of this study phase or the interpretation of the phase results and conclusions.

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Appendix 3

1. SUMMARY

Dose formulation samples have been analyzed by Ion Exchange High Performance Liquid Chromatography (IEX-HPLC) for the determination of mRNA-1273.

The dose formulations were within specification. Homogeneity testing showed that the formulation technique used produced homogeneous preparations.

2. INTRODUCTION

This report describes the analytical evaluation of mRNA-1273 in dose formulations (mRNA-1273 Diluent Buffer; 20 mM Tris, 8.7% sucrose, pH 7.5) from Study 20248897.

For the work detailed in this report, the analytical phase experimental start date was 06 Jul 2020, and the analytical phase experimental completion date was 20 Aug 2020.

3. EXPERIMENTAL DESIGN

3.1. Dose Formulation Analysis

Analysis of dose formulations was carried out with regard to concentration and homogeneity.

Duplicate samples were collected from the top, middle and bottom strata of Group 2 from the first preparation for concentration and homogeneity verification while duplicate samples were collected from the middle strata of Group 2 from the approximately middle (GD1) and last (GD13) preparation for concentration verification.

Duplicate samples were also collected from the middle stata of Group 1 (control group) from the first, approximately middle and last preparation.

The samples were shipped on dry ice and stored in the freezer set to maintain -80°C until analysis within established stability (21 days).

4. MATERIALS AND METHODS

4.1. Materials

4.1.1. Reference Standard

Identification:	mRNA-1273, MTDS20002, CX-024414
Physical Description:	Clear, colorless solution, essentially free of visible particles
Moderna Lot No.:	DH-02689.1
Concentration:	4.76 mg/mL
Retest Date:	31 Mar 2022
Storage Conditions:	Kept in a freezer set to maintain -20°C
Supplier:	Moderna, TX, Inc.

Appendix 3

4.1.2. Reference Material (Bulk Test Item)

Identification:	mRNA-1273 LNP
Physical Description:	White to off-white dispersion; essentially free of visible particulates
Moderna Lot No.:	DH-03026
Concentration:	0.76 mg/mL
Expiry Date:	18 Nov 2020
Storage Conditions:	Kept in a freezer set to maintain -80°C
Supplier:	Moderna, TX, Inc.

4.1.3. Vehicle

Identification:	mRNA-1273 Diluent Buffer (20 mM Tris, 8.7% sucrose, pH 7.5)
Moderna Lot No.:	DH-03026.2
Expiry Date:	18 Nov 2020
Storage Conditions:	Kept in a freezer set to maintain -80°C
Supplier:	Moderna, TX, Inc.

4.1.4. Characterization of Reference Standard, Reference Material and Vehicle

The Sponsor provided the documentation for the identity, strength, purity, composition, and stability for the reference standard, reference material and vehicle. Copies of the supplied Summary of Analysis (SoA) or equivalent documentation are presented in Appendix 2.

4.1.5. Inventory and Disposition of Reference Standard, Reference Material and Vehicle

Records of the receipt, distribution, and storage of the reference standard, reference material and vehicle were maintained. All unused Sponsor-supplied reference standard, reference material and vehicle were retained for use on subsequent studies for the Sponsor.

4.2. Methods

4.2.1. Analytical Procedures

The method for concentration analysis is documented in Analytical Procedure AP.2100930.SP.02 (Appendix 1) and was previously validated under Study No. 2100933. Concentration stability data were generated by the department of Analytical Chemistry, Charles River, CR-SEN for 1 day, 7 days, and 21 days, for formulation samples stored at ambient temperature, in a refrigerator set to maintain 4°C and in a freezer set to maintain -80°C, respectively, over the concentration range of 0.0100 – 0.760 mg/mL, under Study No. 2100933.

Appendix 3

4.3. Computerized Systems

Critical computerized systems used in this study phase are listed below (see Text Table 1).

Text Table 1
Computerized Systems

System Name	Version No.	Description of Data Collected and/or Analyzed
(b) (4)		Data acquisition for dose formulation analysis, including regression analysis and measurement of concentration and recovery of dose formulations using HPLC
		Continuous Monitoring System. Monitoring of standalone fridges, freezers, incubators, and selected laboratories to measure temperature, relative humidity, and CO_2, as appropriate
		Building Automation System. Control of HVAC and other building systems, as well as temperature/humidity control and trending in selected laboratories and animal rooms
		Deviations
		Reporting
		Collection of Part 11 compliant signature

4.4. Disposition of Study Materials

All study-specific raw data, documentation and the Final Report generated from this study phase will be sent to Charles River Montreal archive for a period of at least one year.

Electronic data generated by the Test Site were archived as noted above, except reporting files stored on SDMS and the study deviations, which were archived electronically at the Charles River Laboratories facility location in Wilmington, MA.

Appendix 3

5. RESULTS AND DISCUSSIONS

All results presented in the tables of the report are calculated using non-rounded values as per the raw data rounding procedure and may not be exactly reproduced from the individual data presented.

5.1. Dose Formulation Analysis

All study samples analyzed had mean concentrations within or equal to the acceptance criteria of ± 15% (individual values within or equal to ± 20%) of their theoretical concentrations. Results are presented in Table 1.

For homogeneity, the RSD of concentrations for all samples in each group tested was within the acceptance criteria of ≤ 5%. Results are presented in Table 1.

6. CONCLUSION

The dose formulations were within specification. Homogeneity testing showed that the formulation technique used produced homogeneous preparations.

Appendix 3

Table 1 Study Samples - Concentration and Homogeneity

Occasion (Sampling Date)	Group Id	Theoretical Concentration (mg/mL)	Sampling Location	Measured Concentration (mg/mL)	Percent of Theoretical	RSD (%)
First preparation (30 Jun 2020)	1	0	Middle	ND	-	-
				ND	-	
			Mean	ND	-	
	2	0.5	Top	0.485	97.0	4.6
				0.509	102	
			Middle	0.489	97.8	
				0.548	110	
			Bottom	0.499	99.7	
				0.493	98.7	
			Mean	0.504	101	
Middle preparation: GD1 (29 Jul 2020)	1	0	Middle	ND	-	-
				ND	-	
			Mean	ND	-	
	2	0.5	Middle	0.462	92.4	
				0.481	96.2	
			Mean	0.472	94.3	
Last preparation: GD13 (16 Aug 2020)	1	0	Middle	ND	-	-
				ND	-	
			Mean	ND	-	
	2	0.5	Middle	0.485	97.1	
				0.515	103	
			Mean	0.500	100	

ND = None detected.

Appendix 3

Appendix 1
Analytical Procedure

Appendix 3

Analytical Procedure (AP.2100930.SP.02)

Determination of mRNA-1273 in Dose Formulations by Ion Exchange High Performance Chromatography Using Ultraviolet/Visible Detection

Reference Standard, Reference Material and Vehicle

Reference Standard	mRNA-1273, MTDS20002, CX-024414
Lot number	DH-02689.1
Concentration (actual)	4.76 mg/mL
Reference Material	mRNA-1273 LNP
Description	White to off-white dispersion; essentially free of visible particulates
Lot number	DH-03026
Concentration (nominal)	0.76 mg/mL (to be used for calculations)
Vehicle	mRNA-1273 Diluent Buffer (20 mM Tris, 8.7% sucrose, pH 7.5)
Lot number	DH-03026.2

For storage conditions for reference standard, reference material and vehicle supplied by the Sponsor, refer to the corresponding log sheets.

NOTES:

- ❑ Modifications may be made to the chromatographic conditions in order to optimize the chromatography.
- ❑ Solution volumes throughout this AP (including reagent solutions, blanks, standard stocks, standards and spiked samples) may be scaled up or down as long as the final concentration remains the same as specified in the procedure.
- ❑ Any changes made are to be documented in the raw data of the run.
- ❑ Unless otherwise indicated, information relating to the time of mixing/stirring, temperature or mixing method used in the preparation of solutions, diluents, mobile phases and vehicle will be considered non-critical. If a step is deemed critical, it will be noted within the procedure, and a positive entry will be made in the raw data
- ❑ **The compound is a mRNA, benchwork and handling should be performed under clean conditions to limit RNase contamination. When possible use RNase free tubes, pipette and repeater tips for reference standard/test item dilutions. DO NOT VORTEX, mix manually by inversion.**
- ❑ The analytical method was previously validated under study No. 2100933.

Appendix 3

Analytical Procedure (AP.2100930.SP.02)

HPLC Conditions

System: Agilent Technologies 1260 series
Column: Thermofisher Proswift WAX-1S Monolithic (50 x 4.6 mm)
Column temperature: set at 60°C
Mobile phase: A: 20 mM NaOH/Glycine, 25 mM sodium perchlorate in 20% Ethanol
B: 20 mM NaOH/Glycine, 500 mM sodium perchlorate in 20% Ethanol

Time (min)	A%	B%
0	100	0
2.0	0	100
4.0	0	100
4.5	100	0
7.0	100	0

Flow rate: 1.0 mL/min
Detection wavelength: 260 nm
Injection volume: 10 µL (20 µL for cleaning blanks)
Sample tray: set at 4°C
Retention time: ~1.6 min
Run time: 7 min

Rinse settings (if applicable)

S1	water *
S2	Mobile Phase A

Auto-sampler Multi Wash:
Step 1: S1, needle wash/seat back flush, 3 sec
Step 2: S2, needle wash/seat back flush, 3 sec
Step 3: Off
Start Cond.: S2

* Water as rinsing solution can be used for 7 days when stored at room temperature.

Reagents
Unless specified, reagents with appropriate grade (A.C.S., USP et al) or numerical purity will be used.

- Water (ultra pure water, UPW; in-house); RNase free water (molecular biology grade); Ethanol (200 proof, HPLC grade also acceptable); glycine (HPLC grade (>99%), 75.07 g/mol); sodium perchlorate monohydrate (ACS grade, supplier Millipore, 140.46 g/mol); TRIS-EDTA (TE buffer, Fisher Scientific # BP1338) 100X solution; Triton X-100 reduced (Sigma-Aldrich # 282103 or equivalent), sodium chloride (biological grade, 58.44 g/mol) 10/1N hydrochloric acid (HCl) and 10/1N sodium hydroxide (NaOH); Phosphate-buffered Saline (PBS 1X, pH 7.2, without magnesium and calcium).

Appendix 3

Analytical Procedure (AP.2100930.SP.02)

Preparation of Solutions

Stock Mobile Phase Buffer 1 (25 mM NaOH/Glycine, pH 10.9 (pH 10 at column temp of 60°C))
- Weigh 7.66±0.05 g of glycine and transfer in a solution bottle.
- Add 10.0 mL of 10 N NaOH.
- Add 4000 mL of water (UPW) and mix to dissolve.
- Measure and adjust pH to 10.9±0.1 using 10N NaOH or 10N HCl solution.
- Store solution at ambient room temperature (expiry: two weeks).

Stock Mobile Phase Buffer 2 (20 mM NaOH/Glycine, pH 10.9 (pH 10 at column temp of 60°C) in 20% Ethanol)
- Transfer 3200 mL of Stock Mobile Phase buffer 1 in a solution bottle.
- Add 800 mL of Ethanol and mix well.
- Store solution at ambient room temperature (expiry: two weeks).

Mobile Phase A (20 mM NaOH/Glycine, 25 mM sodium perchlorate in 20% Ethanol)
- Transfer 2000 mL of Stock Mobile Phase Buffer 2 into a solution bottle.
- Add 7.0±0.05 g of sodium perchlorate monohydrate.
- Mix to dissolve.
- Store solution at ambient room temperature (expiry: two weeks).

Mobile Phase B (20 mM NaOH/Glycine, 500 mM sodium perchlorate in 20% Ethanol)
- Transfer 1600 mL of Stock Mobile Phase Buffer 2 into a solution bottle.
- Add 112.5±0.2 g of sodium perchlorate monohydrate.
- Mix to dissolve.
- Store solution at ambient room temperature (expiry: two weeks).

Diluent (2% Triton in 1X-TE Buffer and 150 mM sodium chloride)
- Add 100 mL of RNase free water into a clean container.
- Remove 1 mL of water from the tube.
- Add 1 mL of 100X TE buffer and mix.
- Add 2 g of **Triton X-100 reduced** and 0.876±0.01 g of sodium chloride.
- Mix well.
- Store solution at ambient room temperature (expiry: two weeks).

Appendix 3

Analytical Procedure (AP.2100930.SP.02)

Preparation of Standards (STDs)

Standard stocks (STD STK; nominal concentration 4.76 mg/mL)
- Thaw the reference standard (4.76 mg/mL) as supplied at room temperature.
- Mix well prior to use.
- Store the remaining bulk test item under the original storage conditions.

Standard Working Solution (STD WS; nominal concentration 0.0300 mg/mL)
- Using a pipette, add 7.950 mL of diluent into an appropriate size tube and add 50.4 µL of STD STK (final volume = 8 mL).
- Mix.
- Store remaining in a refrigerator set to maintain 4°C (expiry: 3 days).

System calibration solution (CAL; 6.00 µg/mL)
- Use STD D as CAL solution.

Standards
- Add the required volume of the diluent into appropriate size polypropylene tubes as per Table 1.
- Add the aliquots of the STD WS (0.0300 mg/mL) into the tube.
- Cap and mix.
- Transfer into an injection vial for analysis.
- Store the standard solutions in a refrigerator set to maintain 4°C (expiry: 3 days).

Table 1: Preparation of standards

STD identification	Volume of diluent (µL)	Aliquot of STD WS (µL)	Final volume (µL)	Nominal Concentration (µg/mL)
STD A	1000	--	1000	0
STD B	900	100	1000	3.00
STD C	850	150	1000	4.50
STD D	4000	1000	5000	6.00
STD E	600	400	1000	12.0
STD F	250	750	1000	22.5
STD G	--	1000	1000	30.0

Preparation of Blanks

Diluent blanks (Diluent BLK: n=2)
- Transfer approximately 1.00 mL of the **diluent** into injection vials.
- Store the blanks under the same storage conditions as standards.

Vehicle blank (V-BLK: n=2)
- Transfer 500 µL of diluent into a polypropylene tube.
- Add 500 µL of vehicle directly in the tube.
- Mix.
- Aliquot into injection vials for analysis.
- Store the vehicle blanks under the same storage conditions as for spike solutions.

Appendix 3

Analytical Procedure (AP.2100930.SP.02)

Preparation of Spikes

High spikes (SPK B; 0.760 mg/mL; n = 1)
- Thaw the reference material (0.76 mg/mL) as supplied at room temperature.
- Mix well prior to use.
- Store the remaining bulk material under the original storage conditions.

Low spikes (SPK A; 0.0100 mg/mL; n = 1)
- Accurately add 20.0 mL of **vehicle** into an appropriate size tube.
- Remove 263 µL of vehicle from the tube.
- Aliquot 263 µL of reference material (0.76 mg/mL) into the tube.
- Cap and mix.
- Store unprocessed spikes in a refrigerator set to maintain 4°C (expiry: 7 days).

Dilution of spikes
- Aliquot the required amount of diluent directly into an appropriate size tube.
- Add the aliquots of spikes to each tube.
- Cap and mix.
- Sonicate for 15 minutes.
- Transfer into an injection vial for analysis.
- Store solutions in a refrigerator set to maintain 4°C (expiry: 3 days).

Table 2. Dilution of spiked samples

SPK ID	Volume of diluent (µL)	Aliquot of SPK (µL)	Final Volume (mL)	Injected concentration (µg/mL)	Dilution Factor
SPK A (n=2)	1000	1000	2.00	5.00	2
SPK B (n=2)	2925	75.0	3.00	19.0	40

Appendix 3

Analytical Procedure (AP.2100930.SP.02)

Analysis of Suspension Formulation Samples

Sampling

- Request samples (0.5 mL) are taken from the dose formulations and transferred into appropriate containers by the formulation laboratory.
- Store samples in a freezer set to maintain -80°C (expiry: 21 days).

Sampling preparation

- Aliquot the required amount of diluent directly into an appropriate size tube as per Table 3.
- Add the aliquots of sample to each tube.
- Cap and mix.
- Sonicate for 15 minutes.
- Transfer into an injection vial for analysis.
- Store processed samples in a refrigerator set to maintain a temperature of 4°C (expiry: 3 days).

Table 3. Dilution of dose formulation samples

Sample identification	Dilution			Injected concentration (µg/mL)	Dilution factor
	Volume of diluent (µL)	Aliquot of sample (µL)	Final volume in diluent (mL)		
Group 1 (0 mg/mL)	2925	75.0	3	0	40
Group 2 (0.5 mg/mL)	2925	75.0	3	12.5	40

Injection Sequence (suggested sequence)

Note: To minimize and control carry-over, inject standards, blanks and spiked samples in group from low to high concentration. After injection of each group and prior to injection of each set of CAL, inject diluent in triplicate (injection volume: 20 µL) to clean up carry-over.

- Inject a CAL in triplicate to verify system suitability (ensure that %RSD is ≤3% before proceeding with further injection).
- Inject diluent in triplicate (not reported, to clean up carry-over).
- In sequence, inject standards, Diluent BLKs, Vehicle BLKs, spikes and study samples, inserting a CAL after a certain number (preferably ~10) of injections (changes may be made to this sequence).
- Inject a CAL solution in triplicate at the end (the % RSD should be ≤ 3% and the percentage difference with the beginning should be ±10%).

Appendix 3

Analytical Procedure (AP.2100930.SP.02)

Calculations

System suitability

- Calculate the relative standard deviation (%RSD) in response of CAL (n = 3) using the following equation:
  % RSD= (SD ÷ A) × 100
  SD – standard deviation in response
  A – average response
- Calculate system stability using the following equation:
  $(A_2 - A_1) \div A_1 \times 100$
  A_1 – average response (n = 3) of CAL at the beginning of the run.
  A_2 – average response (n = 3) of CAL at the end of the run.

Standard curve

- Perform the least squares fit regression of peak area versus concentration (type of curve fit: linear; weighting factor: none).

Calculation of concentrations

- Using (b) (4) Custom Field, calculate concentrations and accuracies of spikes and study samples.

Integration

- Integration algorithm: Traditional

Acceptance criteria

Unless specified in the following or in the Study Plan, refer to SOP CAD-002 and SOP CAD-003 for acceptance criteria.

Formulation Samples:	For concentration, the criteria for acceptability will be mean sample concentration results within or equal to ± 15% of theoretical concentration. Each individual sample concentration result within or equal to ± 20%. For homogeneity, the criteria for acceptability will be a relative standard deviation (RSD) of concentrations of ≤ 5% for each group.

AP Version Control

First update (supersedes AP.2100930.SP.01):
• Included missing expiry period for samples.

Verified by (b) (6)

Approved by

Authorized b

Scientific Director

(b) (6)

FDA-CBER-2022-4207-0228

Appendix 3

Appendix 2
Certificates of Analysis

Appendix 3

Number: DSAD-SOA-0254 Version: 2.0 Approved Date: 24 Apr 2020
MTDS20002, CX-024414 SofA

moderna

200 Technology Square • Cambridge, MA 02139
Phone 617.714.6500 • Fax 617.583.1998

SUMMARY OF ANALYSIS

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Number: DSAD-SOA-0254 Version: 2.0 Approved Date: 24 Apr 2020
MTDS20002, CX-024414 SofA

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SUMMARY OF ANALYSIS

Test	Method	Target Attribute	Result

Version History:

1. SOA of Release
2. Updated target attributes in accordance with SPC-0995.

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SUMMARY OF ANALYSIS

(b) (4)

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REVISION HISTORY

Revision #	Change Details	Author	Effective Date
1.0	Introduction of a New Document	(b) (6)	Date of Approval

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Appendix 3

Number: DPAD-00735 Version: 1.0 Approved Date: 05 Jun 2020
Summary of Analysis: Lot DH-03026 Release

Document Approvals
Approved Date: 05 Jun 2020

Approve Verdict: Approved	(b) (6) Development 05-Jun-2020 18:35:33 GMT+0000

Approve Verdict: Approved	(b) (6) Development 05-Jun-2020 18:36:04 GMT+0000

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Appendix 3

Number: DPAD-00745 Version: 1.0 Approved Date: 08 Jun 2020
Summary of Analysis: Lot DH-03026.2 Formulation Buffer

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REVISION HISTORY

Revision #	Change Details	Author	Effective Date
1.0	Introduction of a New Document	(b) (6)	Date of Approval

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Appendix 3

Number: DPAD-00745 Version: 1.0 Approved Date: 08 Jun 2020
Summary of Analysis: Lot DH-03026.2 Formulation Buffer

Document Approvals
Approved Date: 08 Jun 2020

Approve Verdict: Approved	(b) (6)	Development 08-Jun-2020 20:01:11 GMT+0000
Approve Verdict: Approved	(b) (6)	08-Jun-2020 21:03:28 GMT+0000

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Individual Appendices Explanation Page

All Day(s) referenced throughout the outputs generated are Study Day, Gestation Day, or Lactation Day (F0 Generation) or Day Postpartum (F1 Generation

Abbreviations consistent throughout the Individual Appendices

Note: All of the abbreviations listed on these pages may not be applicable to this report.

Abbreviation	Description
(g)	Grams
(Litter A)	First Litter
OA, NC	Omitted Activity, Not Calculable
!	Result Marker
NBF	Neutral Buffered Formalin
M, F, B,U	Male, Female, Both, Unsexed

Dosing Information

Dosing information is abbreviated on various data outputs; the following represents the dosing information for this study:

Group No.	Test Material	Dose Level (µg/dose)	Dose Concentration (mg/mL)	Dose Volume (µL/dose)
1	Control Article	0	0	200
2	mRNA-1273	100	0.5	200

Individual Mortality Data

Abbreviation	Description	Abbreviation	Description
FD	Found dead	NR	Not recorded
TE or TERM	Terminal euthanasia	UE, UNSC or Unsc	Unscheduled euthanasia
DELI	Delivered	AM SIR	Observed during AM Mortality/Moribundity check
ABOR	Aborted	DE	Detailed Examination
ENSP	Euthanized, no surviving pups		

Individual Clinical and Maternal Observations

Abbreviation	Description	Abbreviation	Description
AM SIRT	Anything observed during the AM Mortality/Moribundity checks	PM SIRT	Anything observed during the PM Mortality/Moribundity checks
DE	Anything observed during scheduled detailed examinations	Unsc #	Anything observed that is not in a scheduled activity
Unsc Pre-Rx #	Anything observed prior to dosing but not in a scheduled activity	Unsc during Rx #	Anything observed that is not in a scheduled activity during dosing
Unsc Post-Rx #	Anything observed after dosing, but not in a scheduled activity	Vet Aid	Anything observed by Vet Aid
Pre Rx	Anything scheduled to be completed prior to dosing when the same activity must also occur following dosing	Post Rx #	Anything scheduled to occur following dosing when the same activity occurs more than one occasion in a day
CSO	Anything observed during scheduled cage side observations	CSO Post and CSO PostRx	Anything observed during cage side observations after dosing
During Rx	Anything observed during dosing	X	Present
. (period)	Period indicates no observation; all other entries indicate observation present	PT	Permanent
TERM	Terminal	6H	6 hours postdose
Unsc	Unscheduled	AmntcSacPlcntaUmbilicaRem-norm	Removal of pup amniotic sac, pup placenta and umbilical cord from delivered pups - normal

Note: Only animals with findings and only days when any animal in the study had a finding are presented in the clinical observations appendix.

Individual Body Weights and Body Weight Gains

Abbreviation	Description
-	Not scheduled to be performed or animal was an early death

Note: A body weight of 342 g was recorded for female 5520 (Group 1) prior to the completion of delivery. A second body weight was collected for this female after the completion of delivery and is reported on the appendix.

Individual Gravid Uterine Weights and Corrected Body Weight

Abbreviation	Description	Abbreviation	Description
Corrected BW	Terminal body weight - gravid uterine	Corrected BWG (0-TBW)	(Terminal body weight - Day 0 body weight)

	weight	- gravid uterine weigh
- or .	Animal not pregnant or was an early death	

Individual Food Consumption

Abbreviation	Description	Abbreviation	Description
Cons	Consumption	. or -	Not scheduled to be performed, not calculable, or animal was an early death
SPIL	Food Spill		

Note: Included on the premating food consumption appendix are the cage assignments before the cohabitation period. After mating, females were assigned to individual housing, and assigned a cage number based on the animal number.

Individual Estrous Cycling

Values are tabulated based on the first day of pairing (Days -13 to 0 are the precohabitation estrous evaluations).

The Number of Estrus Cycles are tabulated based on the Number of Days Estrus (E) was observed.

The Number of Cycles are tabulated based on the following:

Start of cycle is E:

- If consecutive E's exist, start of the cycle is defined as the first E
- If the first value in the reporting period is E, it is ignored as a cycle start
- Last E or assumed E (as indicated below) is ignored as a cycle start (it is however used to calculate cycle length of the last full cycle)

Start of a cycle for Assumed E:

- If P is followed by M (i.e. E is missing), start of cycle is taken as the P immediately before the M
- If P is followed by D (i.e. E & M are missing), start of cycle is taken as the P immediately before the D

Mean cycle length = the sum of the number of days in each complete cycle/the number of complete cycles

Abbreviation	Description	Abbreviation	Description
-	Not calculable or not scheduled to be performed	+	Sperm Positive

Individual Reproductive Performance

Pre-coital Interval (Days): The number of pairing days until a confirmed mating was observed. Animals without a confirmed mating are presented as a dash (-).

Individual Maternal Performance

Abbreviation	Description	Abbreviation	Description
Fem	Female	-	No data recorded or not calculable
TERM	Terminal euthanasia	DELI	Delivered
FD	Found dead	ABOR	Aborted
UNSC	Unscheduled euthanasia, unscheduled		

Individual Macroscopic Pathology

Animals appeared normal at necropsy, unless otherwise noted.

Individual Ovarian and Uterine Examinations and Litter Observations

Abbreviation	Description	Abbreviation	Description
-	Animal not pregnant or was an early death	CorporaLutea	Corpora Lutea
Implant	Implantations	(M)/(F)/(B)	Male/Female/Both Sexes
Pre-implant Loss (%)	Percentage of Preimplantation Loss [(Number of Corpora Lutea – Number of Implantations)/ Number of Corpora Lutea] x 100	Post-implant Loss (%)	Percentage of Postimplantation Loss [(Number of Implantations – Number of Live Fetuses)/ Number of Implantations] x 100
Live Male Fetus/Litter (%)	Percentage of Male fetuses (Number of Male Fetuses/Number of Fetuses) x 100		

Cohort 1 female 5517 (Group 1) was not pregnant and not included on this appendix.

Note: Total Fetuses = Number of Live and Dead Fetuses

Note: Dead Fetuses = Number of Dead Fetuses (Dead Fetuses and Empty implantation sites are included in this calculation)

Note: Mean Fetal Weight by sex is reported for litters that consisted of at least one fetus of the sex.

Individual Fetal Data

Abbreviation	Description	Abbreviation	Description
Implant Type Abbr	Implant Type Abbreviation	M,F,U	Male, Female, Unsexed
R-#, L#	First column is fetal position, second column is fetus number as examined		

Cohort 1 female 5517 (Group 1) was not pregnant and not included on this appendix.

Individual Natural Delivery Observations

Abbreviation	Description	Abbreviation	Description
Post-implantation Loss/Litter (%)	Percentage of Postimplantation Loss [(Number of Implantations – Number of Live pups)/Number of Implantations] x 100	Live Birth Index (%)	Percentage of pups born alive (Number of Live Newborn Pups/Number of Newborn Pups) x 100
-, .	Not calculable	Stillborn Pups/Litter	Percentage of stillborn pups (Number of Stillborn Pups/Number of Newborn Pups) x 100

Individual Litter Observations

Abbreviation	Description	Abbreviation	Description
-	Not calculable	Live Male Pups/Litter (%) Birth	Percentage of Live Male pups (Number of Male Pups/Number of Pups) x 100 at Birth
Viability Index	Percentage of pups born that survive 4 days postpartum (Number of Live Pups on Day 4 Postpartum/Number of Liveborn Pups on Day 1 Postpartum) x 100	Lactation Index	Percentage of pups that survive 21 days postpartum (Number of Live Pups on Day 21 Postpartum/ Number of Live Pups on Day 4 Postpartum) x 100

Note: Cohort 2 females 5539, 5543 (Group 1), 5551, 5553, 5558, 5562, 5572, 5576, 5578 (Group 2) were not pregnant, and are not included on this appendix.

Individual Pup Sex and Status

Abbreviation	Description	Abbreviation	Description
M	Male	F	Female
U	Unsexed		

Individual Pup Clinical Observations

Abbreviation	Description	Abbreviation	Description
N/N	Number of pups affected/Total number of pups in litter	DE	Anything observed during scheduled detailed examinations

Note: Only animals with findings and only days when any animal in the study had a finding are presented in this appendix.

Individual Pup Body Weights and Litter Mean Pup Body Weights

Abbreviation	Description	Abbreviation	Description
Meas.	Measurement	-	Not calculable

Note: Cohort 2 females 5539, 5543 (Group 1), 5551, 5553, 5558, 5562, 5572, 5576, 5578 (Group 2) were not pregnant, and are not included on this appendix.

Individual Pup Gross Pathology

Note: When abnormalities were detected, only the abnormalities were included on the appendix.
Note: The appendix reports all early deaths as unscheduled.

Appendix 4

Individual Mortality: Gestation

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

0 ug/dose Group 1	Day of Death	Removal Date	Path Removal Reason
5501	21	21-Aug-2020	TERM
5502	21	19-Aug-2020	TERM
5503	21	18-Aug-2020	TERM
5504	21	19-Aug-2020	TERM
5505	21	18-Aug-2020	TERM
5506	21	21-Aug-2020	TERM
5507	21	19-Aug-2020	TERM
5508	21	20-Aug-2020	TERM
5509	21	18-Aug-2020	TERM
5510	21	18-Aug-2020	TERM
5511	21	18-Aug-2020	TERM
5512	21	18-Aug-2020	TERM
5513	21	18-Aug-2020	TERM
5515	21	20-Aug-2020	TERM
5516	21	18-Aug-2020	TERM
5517	21	19-Aug-2020	TERM

TE/TERM = Terminal Euthanasia FD = Found Dead UE/UNSC = Unscheduled Euthanasia
DELI = Delivered ABOR = Aborted

Appendix 4

Individual Mortality: Gestation

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

0 ug/dose Group 1	Day of Death	Removal Date	Path Removal Reason
5518	21	20-Aug-2020	TERM
5519	21	21-Aug-2020	TERM
5521	21	20-Aug-2020	TERM
5522	21	19-Aug-2020	TERM
5523	21	18-Aug-2020	TERM
5528	21	21-Aug-2020	TERM

TE/TERM = Terminal Euthanasia FD = Found Dead UE/UNSC = Unscheduled Euthanasia
DELI = Delivered ABOR = Aborted

Appendix 4

Individual Mortality: Gestation

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

100 ug/dose Group 2	Day of Death	Removal Date	Path Removal Reason
5545	21	18-Aug-2020	TERM
5546	21	20-Aug-2020	TERM
5547	21	20-Aug-2020	TERM
5548	21	18-Aug-2020	TERM
5549	21	18-Aug-2020	TERM
5550	21	19-Aug-2020	TERM
5552	21	18-Aug-2020	TERM
5554	21	18-Aug-2020	TERM
5555	21	20-Aug-2020	TERM
5556	21	21-Aug-2020	TERM
5557	21	20-Aug-2020	TERM
5559	21	18-Aug-2020	TERM
5560	21	21-Aug-2020	TERM
5561	21	19-Aug-2020	TERM
5563	21	20-Aug-2020	TERM
5564	21	18-Aug-2020	TERM

TE/TERM = Terminal Euthanasia FD = Found Dead UE/UNSC = Unscheduled Euthanasia
DELI = Delivered ABOR = Aborted

Appendix 4

Individual Mortality: Gestation

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

100 ug/dose Group 2	Day of Death	Removal Date	Path Removal Reason
5565	21	19-Aug-2020	TERM
5566	21	18-Aug-2020	TERM
5567	21	20-Aug-2020	TERM
5568	21	18-Aug-2020	TERM
5569	21	20-Aug-2020	TERM
5570	21	18-Aug-2020	TERM
5572	25	22-Aug-2020	TERM
5578	25	22-Aug-2020	TERM

TE/TERM = Terminal Euthanasia FD = Found Dead UE/UNSC = Unscheduled Euthanasia
DELI = Delivered ABOR = Aborted

Appendix 4

Individual Mortality: Gestation

20248897

Key Page

General Footnotes

TE/TERM = Terminal Euthanasia FD = Found Dead UE/UNSC = Unscheduled Euthanasia
DELI = Delivered ABOR = Aborted

Measurement Descriptions

Headings Used	Description
Day of Death	Day of Death
Removal Date	Removal Date
Path Removal Reason	Path Removal Reason

Time-Points/Ranges

Measurement	From	To	Report As
Day of Death	-9,999	9,999	-
Removal Date	-9,999	9,999	-
Path Removal Reason	-9,999	9,999	-

Group Information

Short Name	Long Name	Type	Report Headings 1-4		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Appendix 5

Individual Mortality: No Confirmed Date of Mating

20248897

Sex: Female Day(s): - Relative to Start Date

0 ug/dose Group 1	Day of Death	Removal Date	Path Removal Reason
5539	60	28-Aug-2020	TERM
5543	60	28-Aug-2020	TERM

TE/TERM = Terminal Euthanasia FD = Found Dead UE/UNSC = Unscheduled Euthanasia
DELI = Delivered ABOR = Aborted

Appendix 5

Individual Mortality: No Confirmed Date of Mating

20248897

Sex: Female Day(s): - Relative to Start Date

100 ug/dose Group 2	Day of Death	Removal Date	Path Removal Reason
5551	60	28-Aug-2020	TERM
5553	60	28-Aug-2020	TERM
5558	60	28-Aug-2020	TERM
5562	60	28-Aug-2020	TERM
5576	60	28-Aug-2020	TERM

TE/TERM = Terminal Euthanasia FD = Found Dead UE/UNSC = Unscheduled Euthanasia
DELI = Delivered ABOR = Aborted

Appendix 5

Individual Mortality: No Confirmed Date of Mating

20248897

Key Page

General Footnotes

TE/TERM = Terminal Euthanasia FD = Found Dead UE/UNSC = Unscheduled Euthanasia
DELI = Delivered ABOR = Aborted

Measurement Descriptions

Headings Used	Description
Day of Death	Day of Death
Removal Date	Removal Date
Path Removal Reason	Path Removal Reason

Time-Points/Ranges

Measurement	From	To	Report As
Day of Death	-9,999	9,999	-
Removal Date	-9,999	9,999	-
Path Removal Reason	-9,999	9,999	-

Group Information

Short Name	Long Name	Type	Report Headings 1-4		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Appendix 6

Individual Mortality: Lactation

20248897

Sex: Female Day(s): - Relative to Littering (Litter: A)

0 ug/dose Group 1	Day of Death	Removal Date	Path Removal Reason
5514	21	12-Sep-2020	TERM
5520	3	21-Aug-2020	ENSP
5524	21	10-Sep-2020	TERM
5525	21	10-Sep-2020	TERM
5526	21	11-Sep-2020	TERM
5527	21	08-Sep-2020	TERM
5529	21	11-Sep-2020	TERM
5530	21	10-Sep-2020	TERM
5531	21	09-Sep-2020	TERM
5532	21	09-Sep-2020	TERM
5533	21	08-Sep-2020	TERM
5534	21	09-Sep-2020	TERM
5535	21	09-Sep-2020	TERM
5536	21	11-Sep-2020	TERM
5537	21	09-Sep-2020	TERM
5538	21	09-Sep-2020	TERM

TE/TERM = Terminal Euthanasia FD = Found Dead UE/UNSC = Unscheduled Euthanasia
ENSP = Euthanized due to No Surviving Pups

Appendix 6

Individual Mortality: Lactation

20248897

Sex: Female Day(s): - Relative to Littering (Litter: A)

0 ug/dose Group 1	Day of Death	Removal Date	Path Removal Reason
5540	21	13-Sep-2020	TERM
5541	21	10-Sep-2020	TERM
5542	21	09-Sep-2020	TERM
5544	21	14-Sep-2020	TERM

TE/TERM = Terminal Euthanasia FD = Found Dead UE/UNSC = Unscheduled Euthanasia
ENSP = Euthanized due to No Surviving Pups

Appendix 6

Individual Mortality: Lactation

20248897

Sex: Female Day(s): - Relative to Littering (Litter: A)

100 ug/dose Group 2	Day of Death	Removal Date	Path Removal Reason
5571	21	12-Sep-2020	TERM
5573	21	10-Sep-2020	TERM
5574	21	09-Sep-2020	TERM
5575	21	09-Sep-2020	TERM
5577	21	08-Sep-2020	TERM
5579	21	11-Sep-2020	TERM
5580	21	11-Sep-2020	TERM
5581	21	11-Sep-2020	TERM
5582	21	11-Sep-2020	TERM
5583	21	08-Sep-2020	TERM
5584	21	09-Sep-2020	TERM
5585	21	09-Sep-2020	TERM
5586	21	11-Sep-2020	TERM
5587	21	11-Sep-2020	TERM
5588	21	11-Sep-2020	TERM

TE/TERM = Terminal Euthanasia FD = Found Dead UE/UNSC = Unscheduled Euthanasia
ENSP = Euthanized due to No Surviving Pups

Appendix 6

Individual Mortality: Lactation

20248897

Key Page

General Footnotes

TE/TERM = Terminal Euthanasia FD = Found Dead UE/UNSC = Unscheduled Euthanasia
ENSP = Euthanized due to No Surviving Pups

Measurement Descriptions

Headings Used	Description
Day of Death	Day of Death
Removal Date	Removal Date
Path Removal Reason	Path Removal Reason

Time-Points/Ranges

Measurement	From	To	Report As
Day of Death	-9,999	9,999	-
Removal Date	-9,999	9,999	-
Path Removal Reason	-9,999	9,999	-

Group Information

Short Name	Long Name	Type	Report Headings 1-4		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Appendix 7

Individual Clinical Observations Premating

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date (A)						
		15 6H	16 DE	17 DE	19 DE	20 DE	21 DE	22 DE
5519	Skin, Scab, Cranium	.	.	.	.	.	.	.
5531	Fur, Thin Cover, Ventral Aspect Generalized	.	.	.	.	.	.	.

Appendix 7

Individual Clinical Observations Premating

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date (A)						
		23 DE	24 DE	25 DE	26 DE	27 DE	28 DE	29 DE
5519	Skin, Scab, Cranium	.	.	.	.	.	X	X
5531	Fur, Thin Cover, Ventral Aspect Generalized	.	X	X	X	X	X	X

X=Present

Appendix 7

Individual Clinical Observations Premating

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date (A)						
		30 DE	31 DE	32 DE	33 DE	34 DE	46 DE	47 DE
5519	Skin, Scab, Cranium	X	X	.	.	.	.	.
5531	Fur, Thin Cover, Ventral Aspect Generalized	.	.	.	.	.	.	.

X=Present

Appendix 7

Individual Clinical Observations Premating

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date (A)						
		48 DE	48 6H	49 DE	50 DE	51 DE	52 DE	53 DE
5519	Skin, Scab, Cranium	.	.	.	.	.	.	.
5531	Fur, Thin Cover, Ventral Aspect Generalized	.	.	.	.	.	.	.

Appendix 7

Individual Clinical Observations Premating

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date (A)						
		54 DE	55 DE	56 DE	57 DE	58 DE	59 DE	60 TERM
5519	Skin, Scab, Cranium	.	.	.	.	.	.	.
5531	Fur, Thin Cover, Ventral Aspect Generalized	.	.	.	.	.	.	.

Appendix 7

Individual Clinical Observations: Premating

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date (A)						
		15 6H	16 DE	17 DE	19 DE	20 DE	21 DE	22 DE
5551	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Skin, Scab, Hindlimb, Right	.	.	.	X	X	X	X
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5553	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5558	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5562	Fur, Thin Cover, Forelimb, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Forelimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
	Discharge, Color, Eye, Right, Red	X	X	X	.	.	.	.
5574	Fur, Thin Cover, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
5575	Fur, Thin Cover, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Forepaw, Right	.	.	.	.	.	.	.
5576	Fur, Thin Cover, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5579	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
5581	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
5586	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.

X=Present

Appendix 7

Individual Clinical Observations: Premating

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date (A)						
		23 DE	24 DE	25 DE	26 DE	27 DE	28 DE	29 DE
5551	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Skin, Scab, Hindlimb, Right	X	X	X	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5553	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5558	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5562	Fur, Thin Cover, Forelimb, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Forelimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
	Discharge, Color, Eye, Right, Red	.	.	.	.	.	.	.
5574	Fur, Thin Cover, Forepaw, Left	.	X	X	X	X	.	.
	Fur, Thin Cover, Forepaw, Right	.	X	X	X	X	.	.
	Fur, Thin Cover, Hindlimb, Right	.	X	X	X	X	X	.
5575	Fur, Thin Cover, Forepaw, Left	.	X	X	X	X	X	.
	Fur, Thin Cover, Forepaw, Right	.	X	X	X	X	X	.
5576	Fur, Thin Cover, Forepaw, Left	.	.	.	.	.	X	X
	Fur, Thin Cover, Forepaw, Right	.	.	.	.	.	X	X
	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5579	Fur, Thin Cover, Hindlimb, Right	.	X	X	X	X	X	X
5581	Fur, Thin Cover, Hindlimb, Right	.	X	X	X	X	X	X
5586	Fur, Thin Cover, Hindlimb, Right	.	X	X	X	X	X	X

X=Present

Appendix 7

Individual Clinical Observations: Premating

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date (A)						
		30 DE	31 DE	32 DE	33 DE	34 DE	46 DE	47 DE
5551	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	X	X
	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	X	X
	Skin, Scab, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5553	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5558	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5562	Fur, Thin Cover, Forelimb, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Forelimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
	Discharge, Color, Eye, Right, Red	.	.	.	.	.	.	.
5574	Fur, Thin Cover, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
5575	Fur, Thin Cover, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Forepaw, Right	.	.	.	.	.	.	.
5576	Fur, Thin Cover, Forepaw, Left	X	X	X	X	X	.	.
	Fur, Thin Cover, Forepaw, Right	X	X	X	X	X	.	.
	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5579	Fur, Thin Cover, Hindlimb, Right	X	.	.	.	.	.	.
5581	Fur, Thin Cover, Hindlimb, Right	X	.	.	.	.	.	.
5586	Fur, Thin Cover, Hindlimb, Right	X	.	.	.	.	.	.

X=Present

Appendix 7

Individual Clinical Observations: Premating

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date (A)						
		48 DE	48 6H	49 DE	50 DE	51 DE	52 DE	53 DE
5551	Fur, Thin Cover, Hindlimb, Left	X	X	X	X	X	X	X
	Fur, Thin Cover, Hindlimb, Right	X	X	X	X	X	X	X
	Skin, Scab, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	X	X	X	X
5553	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	X	.	.	.	.	.
5558	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	X	X	X	.
5562	Fur, Thin Cover, Forelimb, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Forelimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	X	X	X	.
	Discharge, Color, Eye, Right, Red	.	.	.	.	.	.	.
5574	Fur, Thin Cover, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
5575	Fur, Thin Cover, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Forepaw, Right	.	.	.	.	.	.	.
5576	Fur, Thin Cover, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Left	.	.	.	X	X	X	X
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	X	X	X	X
5579	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
5581	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
5586	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.

X=Present

Appendix 7

Individual Clinical Observations: Premating

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Start Date (A)						
		54 DE	55 DE	56 DE	57 DE	58 DE	59 DE	60 TERM
5551	Fur, Thin Cover, Hindlimb, Left	X	X	X	X	.	.	.
	Fur, Thin Cover, Hindlimb, Right	X	X	X	X	X	X	X
	Skin, Scab, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	X	.	.	.	.	.	.
5553	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5558	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	X	X	X
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5562	Fur, Thin Cover, Forelimb, Left	.	.	X	X	X	X	X
	Fur, Thin Cover, Forelimb, Right	.	.	X	X	X	X	X
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
	Discharge, Color, Eye, Right, Red	.	.	.	.	.	.	.
5574	Fur, Thin Cover, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
5575	Fur, Thin Cover, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Forepaw, Right	.	.	.	.	.	.	.
5576	Fur, Thin Cover, Forepaw, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Forepaw, Right	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Left	X	X	X	X	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	X	X	.	.	.	.	.
5579	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
5581	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
5586	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.

X=Present

Appendix 7

Individual Clinical Observations: Premating

20248897

Key Page

Group Information

Short Name	Long Name	Type	Report Headings		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Timeslot Definition

Abbreviation	Description
DE	DE
6H	6 Hours Post Dose
TERM	Terminal

Appendix 8

Individual Clinical Observations Gestation

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: All Types	Day(s) Relative to Mating (A)						
		0 DE	1 DE	1 6H	2 DE	3 DE	4 DE	5 DE
5517	Fur, Loss, Severity Not Recorded	.	.	.	.	.	.	.
	Skin, Scab, Scapular, Left	.	.	.	.	.	.	.
5519	Skin, Scab, Cranium	X	X	X	X	X	X	.
5542	Hunched Posture	.	.	.	.	.	.	.
	Thin	.	.	.	.	.	.	.

X=Present

Appendix 8

Individual Clinical Observations Gestation

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: All Types	Day(s) Relative to Mating (A)						
		6 DE	7 DE	8 DE	9 DE	10 DE	11 DE	12 DE
5517	Fur, Loss, Severity Not Recorded	.	.	.	.	.	.	.
	Skin, Scab, Scapular, Left	.	.	.	.	.	.	.
5519	Skin, Scab, Cranium	.	.	.	.	.	.	.
5542	Hunched Posture	X	X	X	X	X	X	.
	Thin	.	X	X	X	X	X	X

X=Present

Appendix 8

Individual Clinical Observations Gestation

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: All Types	Day(s) Relative to Mating (A)						
		13 DE	13 6H	14 DE	14 Unsc	15 DE	16 DE	17 DE
5517	Fur, Loss, Severity Not Recorded	.	.	.	.	X	X	X
	Skin, Scab, Scapular, Left	.	.	.	.	X	.	.
5519	Skin, Scab, Cranium	.	.	.	.	.	.	.
5542	Hunched Posture	.	.	.	.	.	.	.
	Thin	X	X	X	.	.	.	.

X=Present

Appendix 8

Individual Clinical Observations Gestation

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: All Types	Day(s) Relative to Mating (A)						
		18 DE	19 DE	20 DE	21 DE	21 TERM	22 DE	23 DE
5517	Fur, Loss, Severity Not Recorded	X	X	X	.	.	.	.
	Skin, Scab, Scapular, Left	.	.	.	.	.	.	.
5519	Skin, Scab, Cranium	.	.	.	.	.	.	.
5542	Hunched Posture	.	.	.	.	.	.	.
	Thin	.	.	.	.	.	.	.

X=Present

Appendix 8

Individual Clinical Observations Gestation

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: All Types	Day(s) Relative to Mating (A)						
		24 DE	25 TERM					
5517	Fur, Loss, Severity Not Recorded	.	.					
	Skin, Scab, Scapular, Left	.	.					
5519	Skin, Scab, Cranium	.	.					
5542	Hunched Posture	.	.					
	Thin	.	.					

Appendix 8

Individual Clinical Observations: Gestation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Mating (A)						
		0 DE	1 DE	1 6H	2 DE	3 DE	4 DE	5 DE
5545	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5546	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5547	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5548	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5549	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5550	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5552	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5554	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5555	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5556	Fur, Thin Cover, Forelimb, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Forelimb, Right	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5557	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5559	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5560	Fur, Thin Cover, Forelimb, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Forelimb, Right	.	.	.	.	.	.	.

Appendix 8

Individual Clinical Observations: Gestation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Mating (A)						
		0 DE	1 DE	1 6H	2 DE	3 DE	4 DE	5 DE
5560	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5561	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5563	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5564	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5565	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5566	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5567	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5568	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5569	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5570	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5571	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5572	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.

Appendix 8

Individual Clinical Observations: Gestation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Mating (A)						
		0 DE	1 DE	1 6H	2 DE	3 DE	4 DE	5 DE
5572	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5573	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Fur, Thin Cover, Treatment Site No.01	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5574	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Right	X	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5575	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5577	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5578	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5579	Fur, Thin Cover, Hindlimb, Right	X	X	X	X	X	X	X
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5580	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5581	Fur, Thin Cover, Hindlimb, Right	X	X	X	X	X	X	X
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5582	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5583	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5584	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.

X=Present

Appendix 8

Individual Clinical Observations: Gestation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Mating (A)						
		0 DE	1 DE	1 6H	2 DE	3 DE	4 DE	5 DE
5584	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5585	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5586	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Right	X	X	X	X	X	X	X
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5587	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5588	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
	Discharge, Color, Vagina, Red	X	.	.	.	.	.	.
	Discharge, Consistency, Vagina, Mucoid	X	.	.	.	.	.	.

X=Present

Appendix 8

Individual Clinical Observations: Gestation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Mating (A)						
		6 DE	7 DE	8 DE	9 DE	10 DE	11 DE	12 DE
5545	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5546	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5547	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5548	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5549	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5550	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5552	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5554	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5555	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5556	Fur, Thin Cover, Forelimb, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Forelimb, Right	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5557	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5559	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5560	Fur, Thin Cover, Forelimb, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Forelimb, Right	.	.	.	.	.	.	.

Appendix 8

Individual Clinical Observations: Gestation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Mating (A)						
		6 DE	7 DE	8 DE	9 DE	10 DE	11 DE	12 DE
5560	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5561	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5563	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5564	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5565	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5566	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5567	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5568	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5569	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5570	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5571	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5572	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.

Appendix 8

Individual Clinical Observations: Gestation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Mating (A)						
		6 DE	7 DE	8 DE	9 DE	10 DE	11 DE	12 DE
5572	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5573	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Fur, Thin Cover, Treatment Site No.01	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5574	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5575	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5577	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5578	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5579	Fur, Thin Cover, Hindlimb, Right	X	X	X	X	X	X	X
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5580	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5581	Fur, Thin Cover, Hindlimb, Right	X	X	X	X	X	X	X
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5582	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5583	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5584	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.

X=Present

Appendix 8

Individual Clinical Observations: Gestation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Mating (A)						
		6 DE	7 DE	8 DE	9 DE	10 DE	11 DE	12 DE
5584	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5585	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5586	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5587	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5588	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
	Discharge, Color, Vagina, Red	.	.	.	.	.	.	.
	Discharge, Consistency, Vagina, Mucoid	.	.	.	.	.	.	.

Appendix 8

Individual Clinical Observations: Gestation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Mating (A)						
		13 DE	13 6H	14 DE	14 Unsc	15 DE	16 DE	17 DE
5545	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	X	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	X	.	X	X	.
5546	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	X	X	.	X	.	.
5547	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	X	X	.	X	X	X
5548	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	X	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	X	.	X	X	X
5549	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	X	.	X	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	X	.	X	.	.
5550	Limited Usage, Hindlimb, Right, Severity Not Recorded	X	.	X	X	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	X	.	X	X	X	X	.
5552	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	X	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	X	.	X	X	.
5554	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	X	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	X	.	X	X	X
5555	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	X	X	.	X	X	X
5556	Fur, Thin Cover, Forelimb, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Forelimb, Right	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	X	.	X	X	.
5557	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	X	X	.	X	.	.
5559	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	.	X
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	X	.	X	X	.
5560	Fur, Thin Cover, Forelimb, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Forelimb, Right	.	.	.	.	.	.	.

X=Present

Appendix 8

Individual Clinical Observations: Gestation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Mating (A)						
		13 DE	13 6H	14 DE	14 Unsc	15 DE	16 DE	17 DE
5560	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	X	.	X	X	X
5561	Limited Usage, Hindlimb, Right, Severity Not Recorded	X	.	.	X	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	X	.	X	X	X	.	.
5563	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	X	X	.	X	.	.
5564	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	X	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	X	.	X	X	.
5565	Limited Usage, Hindlimb, Right, Severity Not Recorded	X	.	.	X	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	X	.	X	X	X	.	.
5566	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	X	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	X	.	X	X	.
5567	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	X	X	.	X	.	.
5568	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	X	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	X	.	X	X	.
5569	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	X	X	X
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	X	X	.	X	.	.
5570	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	X	.	X	.	.
	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	.	X
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	X	.	X	X	.
5571	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	X	X	.	X	X	.
5572	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	X	.	.	.	.
	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	.	X
	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.

X=Present

Appendix 8

Individual Clinical Observations: Gestation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Mating (A)						
		13 DE	13 6H	14 DE	14 Unsc	15 DE	16 DE	17 DE
5572	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	X	.	X	X	.
5573	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	X	X
	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	X	X
	Fur, Thin Cover, Treatment Site No.01	.	.	.	.	X	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	X	X	.	X	.	.
5574	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	X	.	.	.	.
	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	X	.	X	X	.
5575	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	X	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	X	.	X	X	.
5577	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	X	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	X	.	X	X	X
5578	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	X	.	X	.	.
	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	X	.	X	X	.
5579	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	X	.	.
5580	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	X	X	.	X	.	.
5581	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	X	X	.	X	.	.
5582	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	X	.	X	X	.
5583	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	X	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	X	.	X	.	.
5584	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	X	.	.	.	.

X=Present

Appendix 8

Individual Clinical Observations: Gestation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Mating (A)						
		13 DE	13 6H	14 DE	14 Unsc	15 DE	16 DE	17 DE
5584	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	X	.	X	X	.
5585	Limited Usage, Hindlimb, Right, Severity Not Recorded	X	.	.	X	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	X	.	X	X	X	.	.
5586	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	X	X	X
	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	X	X	.	X	X	X
5587	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	X	X	.	X	X	X
5588	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	X	X	.	X	X	X
	Discharge, Color, Vagina, Red	.	.	.	.	.	.	.
	Discharge, Consistency, Vagina, Mucoid	.	.	.	.	.	.	.

X=Present

Appendix 8

Individual Clinical Observations: Gestation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Mating (A)						
		18 DE	19 DE	20 DE	21 DE	21 TERM	22 DE	23 DE
5545	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5546	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5547	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5548	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5549	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5550	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5552	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5554	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5555	Fur, Thin Cover, Hindlimb, Right	.	X	X	.	X	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5556	Fur, Thin Cover, Forelimb, Left	.	.	.	.	X	.	.
	Fur, Thin Cover, Forelimb, Right	.	.	.	.	X	.	.
	Fur, Thin Cover, Hindlimb, Right	X	X	X	.	X	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5557	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5559	Fur, Thin Cover, Hindlimb, Left	X	X	X	.	X	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5560	Fur, Thin Cover, Forelimb, Left	.	.	.	.	X	.	.
	Fur, Thin Cover, Forelimb, Right	.	.	.	.	X	.	.

X=Present

Appendix 8

Individual Clinical Observations: Gestation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Mating (A)						
		18 DE	19 DE	20 DE	21 DE	21 TERM	22 DE	23 DE
5560	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	X	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	X	X	X	.	.	.	.
5561	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5563	Fur, Thin Cover, Hindlimb, Right	.	X	X	.	X	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5564	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5565	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5566	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5567	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5568	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5569	Fur, Thin Cover, Hindlimb, Left	X	X	X	.	X	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5570	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Left	X	X	X	.	X	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5571	Fur, Thin Cover, Hindlimb, Right	X	X	X	X	.	X	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5572	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Left	X	X	X	.	.	.	.
	Fur, Thin Cover, Hindlimb, Right	X	X	X	X	.	X	X

X=Present

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Individual Clinical Observations: Gestation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Mating (A)						
		18 DE	19 DE	20 DE	21 DE	21 TERM	22 DE	23 DE
5572	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5573	Fur, Thin Cover, Hindlimb, Left	X	X	X	X	.	.	.
	Fur, Thin Cover, Hindlimb, Right	X	X	X	X	.	.	.
	Fur, Thin Cover, Treatment Site No.01	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5574	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5575	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5577	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5578	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Right	.	.	.	X	.	X	X
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5579	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5580	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5581	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5582	Fur, Thin Cover, Hindlimb, Right	X	X	X	X	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5583	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5584	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.

X=Present

Appendix 8

Individual Clinical Observations: Gestation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Mating (A)						
		18 DE	19 DE	20 DE	21 DE	21 TERM	22 DE	23 DE
5584	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5585	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.	.	.	.	.	.
5586	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Right	.	.	.	.	.	.	.
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5587	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
5588	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.	.	.	.	.	.
	Discharge, Color, Vagina, Red	.	.	.	.	.	.	.
	Discharge, Consistency, Vagina, Mucoid	.	.	.	.	.	.	.

Appendix 8

Individual Clinical Observations: Gestation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Mating (A)						
		24 DE	25 TERM					
5545	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.					
5546	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.					
5547	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.					
5548	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.					
5549	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.					
5550	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.					
5552	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.					
5554	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.					
5555	Fur, Thin Cover, Hindlimb, Right	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.					
5556	Fur, Thin Cover, Forelimb, Left	.	.					
	Fur, Thin Cover, Forelimb, Right	.	.					
	Fur, Thin Cover, Hindlimb, Right	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.					
5557	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.					
5559	Fur, Thin Cover, Hindlimb, Left	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.					
5560	Fur, Thin Cover, Forelimb, Left	.	.					
	Fur, Thin Cover, Forelimb, Right	.	.					

Appendix 8

Individual Clinical Observations: Gestation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Mating (A)						
		24 DE	25 TERM					
5560	Fur, Thin Cover, Hindlimb, Right	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.					
5561	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.					
5563	Fur, Thin Cover, Hindlimb, Right	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.					
5564	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.					
5565	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.					
5566	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.					
5567	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.					
5568	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.					
5569	Fur, Thin Cover, Hindlimb, Left	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.					
5570	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.					
	Fur, Thin Cover, Hindlimb, Left	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.					
5571	Fur, Thin Cover, Hindlimb, Right	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.					
5572	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.					
	Fur, Thin Cover, Hindlimb, Left	.	.					
	Fur, Thin Cover, Hindlimb, Right	X	X					

X=Present

Appendix 8

Individual Clinical Observations: Gestation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Mating (A)						
		24 DE	25 TERM					
5572	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.					
5573	Fur, Thin Cover, Hindlimb, Left	.	.					
	Fur, Thin Cover, Hindlimb, Right	.	.					
	Fur, Thin Cover, Treatment Site No.01	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.					
5574	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.					
	Fur, Thin Cover, Hindlimb, Right	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.					
5575	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.					
5577	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.					
5578	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.					
	Fur, Thin Cover, Hindlimb, Right	X	X					
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.					
5579	Fur, Thin Cover, Hindlimb, Right	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.					
5580	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.					
5581	Fur, Thin Cover, Hindlimb, Right	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.					
5582	Fur, Thin Cover, Hindlimb, Right	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.					
5583	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.					
5584	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.					

X=Present

Appendix 8

Individual Clinical Observations: Gestation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: All Types	Day(s) Relative to Mating (A)						
		24 DE	25 TERM					
5584	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.					
5585	Limited Usage, Hindlimb, Right, Severity Not Recorded	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Soft	.	.					
5586	Fur, Thin Cover, Hindlimb, Left	.	.					
	Fur, Thin Cover, Hindlimb, Right	.	.					
	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.					
5587	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.					
5588	Swollen, Hindlimb, Right, Severity Not Recorded, Firm	.	.					
	Discharge, Color, Vagina, Red	.	.					
	Discharge, Consistency, Vagina, Mucoid	.	.					

Appendix 8

Individual Clinical Observations: Gestation

20248897

Key Page

Group Information

Short Name	Long Name	Type	Report Headings		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Timeslot Definition

Abbreviation	Description
DE	DE
6H	6 Hours Post Dose
TERM	Terminal
Unsc	unscheduled

Appendix 9

Individual Clinical Observations Lactation

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: Toxicology Observations	Day(s) Relative to Littering (A)						
		1 DE	2 DE	3 DE	4 DE	5 DE	6 DE	7 DE
5529	Fur, Thin Cover, Ventral Aspect Generalized	.	.	.	.	.	.	X

X=Present

Appendix 9

Individual Clinical Observations Lactation

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: Toxicology Observations	Day(s) Relative to Littering (A)						
		8 DE	9 DE	10 DE	11 DE	12 DE	13 DE	14 DE
5529	Fur, Thin Cover, Ventral Aspect Generalized	X	X	X	X	X	X	X

X=Present

Appendix 9

Individual Clinical Observations Lactation

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: Toxicology Observations	Day(s) Relative to Littering (A)						
		15 DE	16 DE	17 DE	18 DE			
5529	Fur, Thin Cover, Ventral Aspect Generalized	X	.	.	.			

X=Present

Appendix 9

Individual Clinical Observations Lactation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: Toxicology Observations	Day(s) Relative to Littering (A)						
		1 DE	2 DE	3 DE	4 DE	5 DE	6 DE	7 DE
5571	Fur, Thin Cover, Hindlimb, Right	X	X	X	X	X	X	X
5573	Fur, Thin Cover, Hindlimb, Left	X	X	X	X	X	.	.
	Fur, Thin Cover, Hindlimb, Right	X	X	X	X	X	X	X
5579	Fur, Thin Cover, Hindlimb, Right	.	.	.	X	X	X	X
5582	Fur, Thin Cover, Hindlimb, Right	X	X	X	X	X	X	X

X=Present

Appendix 9

Individual Clinical Observations Lactation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: Toxicology Observations	Day(s) Relative to Littering (A)						
		8 DE	9 DE	10 DE	11 DE	12 DE	13 DE	14 DE
5571	Fur, Thin Cover, Hindlimb, Right	X	X	X	X	X	X	X
5573	Fur, Thin Cover, Hindlimb, Left	.	.	.	.	.	.	.
	Fur, Thin Cover, Hindlimb, Right	X	X	X	X	X	X	X
5579	Fur, Thin Cover, Hindlimb, Right	X	X	X	X	X	X	X
5582	Fur, Thin Cover, Hindlimb, Right	X	X	X	.	.	.	.

X=Present

Appendix 9

Individual Clinical Observations Lactation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: Toxicology Observations	Day(s) Relative to Littering (A)						
		15 DE	16 DE	17 DE	18 DE			
5571	Fur, Thin Cover, Hindlimb, Right	X	X	.	.			
5573	Fur, Thin Cover, Hindlimb, Left	.	.	.	.			
	Fur, Thin Cover, Hindlimb, Right	X	X	X	X			
5579	Fur, Thin Cover, Hindlimb, Right	X	X	X	.			
5582	Fur, Thin Cover, Hindlimb, Right	.	.	.	.			

X=Present

Appendix 9

Individual Clinical Observations: Lactation

20248897

Key Page

Group Information

Short Name	Long Name	Type	Report Headings		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Timeslot Definition

Abbreviation	Description
DE	DE

Appendix 10
Individual Body Weights: Premating

20248897
Sex: Female Bodyweight (g)

0 ug/dose Group 1	Day(s) Relative to Start Date						
	1	8	15	22	28	35	36
5501	244	261	261	281	279	-	-
5502	260	275	286	292	295	-	-
5503	236	253	258	269	266	-	-
5504	254	267	282	281	297	-	-
5505	241	250	264	272	278	-	-
5506	254	264	274	285	284	-	-
5507	247	264	279	284	295	-	-
5508	230	251	260	267	282	-	-
5509	250	261	275	284	282	-	-
5510	243	256	277	285	287	-	-
5511	251	261	282	283	287	-	-
5512	241	255	278	284	292	-	-
5513	250	272	289	298	300	-	-
5514	233	257	269	277	292	-	-
5515	247	263	271	290	289	-	-
5516	254	272	286	300	310	-	-

Appendix 10
Individual Body Weights: Premating

20248897
Sex: Female Bodyweight (g)

0 ug/dose Group 1	Day(s) Relative to Start Date					
	41	48	50	53	56	60
5501	-	-	-	-	-	-
5502	-	-	-	-	-	-
5503	-	-	-	-	-	-
5504	-	-	-	-	-	-
5505	-	-	-	-	-	-
5506	-	-	-	-	-	-
5507	-	-	-	-	-	-
5508	-	-	-	-	-	-
5509	-	-	-	-	-	-
5510	-	-	-	-	-	-
5511	-	-	-	-	-	-
5512	-	-	-	-	-	-
5513	-	-	-	-	-	-
5514	-	-	-	-	-	-
5515	-	-	-	-	-	-
5516	-	-	-	-	-	-

Appendix 10
Individual Body Weights: Premating

20248897
Sex: Female Bodyweight (g)

0 ug/dose Group 1	Day(s) Relative to Start Date						
	1	8	15	22	28	35	36
5517	217	229	236	232	251	-	-
5518	239	254	265	273	287	-	-
5519	242	246	258	270	263	-	-
5520	249	263	275	270	295	-	-
5521	255	270	276	289	298	-	-
5522	238	258	273	277	285	-	-
5523	239	252	269	271	267	-	-
5524	247	258	271	281	290	-	-
5525	244	248	263	272	277	-	-
5526	250	264	277	286	287	-	-
5527	242	258	275	282	288	-	-
5528	269	283	300	309	309	-	-
5529	234	243	256	265	256	-	-
5530	246	265	279	280	295	-	-
5531	251	268	285	293	305	-	-
5532	239	249	264	262	275	-	-

Appendix 10
Individual Body Weights: Premating

20248897
Sex: Female Bodyweight (g)

0 ug/dose Group 1	Day(s) Relative to Start Date					
	41	48	50	53	56	60
5517	-	-	-	-	-	-
5518	-	-	-	-	-	-
5519	-	-	-	-	-	-
5520	-	-	-	-	-	-
5521	-	-	-	-	-	-
5522	-	-	-	-	-	-
5523	-	-	-	-	-	-
5524	-	-	-	-	-	-
5525	-	-	-	-	-	-
5526	-	-	-	-	-	-
5527	-	-	-	-	-	-
5528	-	-	-	-	-	-
5529	-	-	-	-	-	-
5530	-	-	-	-	-	-
5531	-	-	-	-	-	-
5532	-	-	-	-	-	-

Appendix 10
Individual Body Weights: Premating

20248897
Sex: Female Bodyweight (g)

0 ug/dose Group 1	Day(s) Relative to Start Date						
	1	8	15	22	28	35	36
5533	239	254	274	284	283	-	-
5534	252	270	290	297	287	-	-
5535	233	249	273	292	300	-	-
5536	266	279	290	303	309	-	-
5537	263	283	302	309	319	-	-
5538	253	265	283	289	300	-	-
5539	243	262	289	298	318	332	317
5540	244	262	274	275	274	-	-
5541	244	265	283	287	293	-	-
5542	248	264	282	287	287	-	-
5543	258	275	285	294	303	324	330
5544	241	257	278	293	308	-	-
Mean	245.9	260.8	275.4	283.0	289.2	328.0	323.5
SD	9.8	10.7	12.2	13.8	15.0	5.7	9.2
N	44	44	44	44	44	2	2

Appendix 10
Individual Body Weights: Premating

20248897
Sex: Female Bodyweight (g)

0 ug/dose Group 1	Day(s) Relative to Start Date					
	41	48	50	53	56	60
5533	-	-	-	-	-	-
5534	-	-	-	-	-	-
5535	-	-	-	-	-	-
5536	-	-	-	-	-	-
5537	-	-	-	-	-	-
5538	-	-	-	-	-	-
5539	311	334	340	342	345	346
5540	-	-	-	-	-	-
5541	-	-	-	-	-	-
5542	-	-	-	-	-	-
5543	323	330	328	329	335	332
5544	-	-	-	-	-	-
Mean	317.0	332.0	334.0	335.5	340.0	339.0
SD	8.5	2.8	8.5	9.2	7.1	9.9
N	2	2	2	2	2	2

Appendix 10
Individual Body Weights: Premating

20248897
Sex: Female Bodyweight (g)

100 ug/dose Group 2	Day(s) Relative to Start Date						
	1	8	15	22	28	35	36
5545	253	255	280	282	304	-	-
5546	248	261	280	292	306	-	-
5547	244	258	275	278	285	-	-
5548	246	254	269	275	283	-	-
5549	236	243	267	275	283	-	-
5550	245	257	283	295	323	-	-
5551	242	250	264	274	274	306	304
5552	234	240	248	255	269	-	-
5553	240	265	262	274	276	303	298
5554	253	264	284	290	297	-	-
5555	263	273	288	302	319	-	-
5556	242	271	268	283	272	-	-
5557	244	260	269	277	282	-	-
5558	244	252	268	276	267	309	309
5559	231	244	253	261	275	-	-
5560	265	275	287	295	297	-	-

Appendix 10
Individual Body Weights: Premating

20248897
Sex: Female Bodyweight (g)

100 ug/dose Group 2	Day(s) Relative to Start Date					
	41	48	50	53	56	60
5545	-	-	-	-	-	-
5546	-	-	-	-	-	-
5547	-	-	-	-	-	-
5548	-	-	-	-	-	-
5549	-	-	-	-	-	-
5550	-	-	-	-	-	-
5551	303	305	310	294	317	326
5552	-	-	-	-	-	-
5553	309	301	308	290	310	322
5554	-	-	-	-	-	-
5555	-	-	-	-	-	-
5556	-	-	-	-	-	-
5557	-	-	-	-	-	-
5558	318	314	316	296	304	309
5559	-	-	-	-	-	-
5560	-	-	-	-	-	-

Appendix 10
Individual Body Weights: Premating

20248897
Sex: Female Bodyweight (g)

100 ug/dose Group 2	Day(s) Relative to Start Date						
	1	8	15	22	28	35	36
5561	260	274	296	296	300	-	-
5562	239	271	298	286	268	314	322
5563	236	255	262	272	271	-	-
5564	243	254	273	281	280	-	-
5565	246	264	275	288	296	-	-
5566	241	249	270	280	275	-	-
5567	245	256	267	273	279	-	-
5568	256	267	282	290	298	-	-
5569	224	240	251	255	266	-	-
5570	219	225	239	244	240	-	-
5571	255	266	281	292	286	-	-
5572	255	267	277	295	286	-	-
5573	244	262	276	276	288	-	-
5574	258	268	287	294	284	-	-
5575	242	247	263	270	270	-	-
5576	266	279	280	294	291	333	346

Appendix 10
Individual Body Weights: Premating

20248897
Sex: Female Bodyweight (g)

100 ug/dose Group 2	Day(s) Relative to Start Date					
	41	48	50	53	56	60
5561	-	-	-	-	-	-
5562	316	306	296	289	312	328
5563	-	-	-	-	-	-
5564	-	-	-	-	-	-
5565	-	-	-	-	-	-
5566	-	-	-	-	-	-
5567	-	-	-	-	-	-
5568	-	-	-	-	-	-
5569	-	-	-	-	-	-
5570	-	-	-	-	-	-
5571	-	-	-	-	-	-
5572	-	-	-	-	-	-
5573	-	-	-	-	-	-
5574	-	-	-	-	-	-
5575	-	-	-	-	-	-
5576	328	327	323	319	325	329

Appendix 10
Individual Body Weights: Premating

20248897
Sex: Female Bodyweight (g)

100 ug/dose Group 2	Day(s) Relative to Start Date						
	1	8	15	22	28	35	36
5577	255	266	280	281	288	-	-
5578	263	265	277	284	290	-	-
5579	226	242	253	265	274	-	-
5580	269	295	313	318	335	-	-
5581	242	249	272	275	287	-	-
5582	244	254	268	274	277	-	-
5583	247	259	282	292	292	-	-
5584	240	245	262	265	270	-	-
5585	251	270	274	275	287	-	-
5586	249	261	283	290	304	-	-
5587	235	253	268	275	282	-	-
5588	240	256	263	269	272	-	-
Mean	245.9	258.7	273.1	280.3	285.2	313.0	315.8
SD	11.1	12.5	13.7	13.7	16.8	11.9	19.1
N	44	44	44	44	44	5	5
%Diff	0.0	-0.8	-0.8	-1.0	-1.4	-4.6	-2.4

Appendix 10
Individual Body Weights: Premating

20248897
Sex: Female Bodyweight (g)

100 ug/dose Group 2	Day(s) Relative to Start Date					
	41	48	50	53	56	60
5577	-	-	-	-	-	-
5578	-	-	-	-	-	-
5579	-	-	-	-	-	-
5580	-	-	-	-	-	-
5581	-	-	-	-	-	-
5582	-	-	-	-	-	-
5583	-	-	-	-	-	-
5584	-	-	-	-	-	-
5585	-	-	-	-	-	-
5586	-	-	-	-	-	-
5587	-	-	-	-	-	-
5588	-	-	-	-	-	-
Mean	314.8	310.6	310.6	297.6	313.6	322.8
SD	9.5	10.3	10.0	12.3	7.9	8.2
N	5	5	5	5	5	5
%Diff	-0.7	-6.4	-7.0	-11.3	-7.8	-4.8

Appendix 10

Individual Body Weights: Premating

20248897

Key Page

Measurement Descriptions

Headings Used	Description
Bodyweight	Bodyweight

Measurement/Statistics

Measurement	Descriptive
Bodyweight	Mean
	Standard Deviation
	Count
	% Difference from Control

Group Information

Short Name	Long Name	Type	Report Headings 1-4		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Appendix 11

Individual Body Weight Gains (g): Premating

20248897

Sex: Female Bodyweight Gain (Interval)

0 ug/dose Group 1	Day(s) Relative to Start Date						
	1 → 8	8 → 15	15 → 22	22 → 28	28 → 35	35 → 36	36 → 41
5501	17	0	20	-2	-	-	-
5502	15	11	6	3	-	-	-
5503	17	5	11	-3	-	-	-
5504	13	15	-1	16	-	-	-
5505	9	14	8	6	-	-	-
5506	10	10	11	-1	-	-	-
5507	17	15	5	11	-	-	-
5508	21	9	7	15	-	-	-
5509	11	14	9	-2	-	-	-
5510	13	21	8	2	-	-	-
5511	10	21	1	4	-	-	-
5512	14	23	6	8	-	-	-
5513	22	17	9	2	-	-	-
5514	24	12	8	15	-	-	-
5515	16	8	19	-1	-	-	-
5516	18	14	14	10	-	-	-

Appendix 11

Individual Body Weight Gains (g): Premating

20248897

Sex: Female Bodyweight Gain (Interval)

0 ug/dose Group 1	Day(s) Relative to Start Date				
	41 → 48	48 → 50	50 → 53	53 → 56	56 → 60
5501	-	-	-	-	-
5502	-	-	-	-	-
5503	-	-	-	-	-
5504	-	-	-	-	-
5505	-	-	-	-	-
5506	-	-	-	-	-
5507	-	-	-	-	-
5508	-	-	-	-	-
5509	-	-	-	-	-
5510	-	-	-	-	-
5511	-	-	-	-	-
5512	-	-	-	-	-
5513	-	-	-	-	-
5514	-	-	-	-	-
5515	-	-	-	-	-
5516	-	-	-	-	-

Appendix 11

Individual Body Weight Gains (g): Premating

20248897

Sex: Female Bodyweight Gain (Interval)

0 ug/dose Group 1	Day(s) Relative to Start Date						
	1 → 8	8 → 15	15 → 22	22 → 28	28 → 35	35 → 36	36 → 41
5517	12	7	-4	19	-	-	-
5518	15	11	8	14	-	-	-
5519	4	12	12	-7	-	-	-
5520	14	12	-5	25	-	-	-
5521	15	6	13	9	-	-	-
5522	20	15	4	8	-	-	-
5523	13	17	2	-4	-	-	-
5524	11	13	10	9	-	-	-
5525	4	15	9	5	-	-	-
5526	14	13	9	1	-	-	-
5527	16	17	7	6	-	-	-
5528	14	17	9	0	-	-	-
5529	9	13	9	-9	-	-	-
5530	19	14	1	15	-	-	-
5531	17	17	8	12	-	-	-
5532	10	15	-2	13	-	-	-

Appendix 11

Individual Body Weight Gains (g): Premating

20248897

Sex: Female Bodyweight Gain (Interval)

0 ug/dose	Day(s) Relative to Start Date				
Group 1	41 → 48	48 → 50	50 → 53	53 → 56	56 → 60
5517	-	-	-	-	-
5518	-	-	-	-	-
5519	-	-	-	-	-
5520	-	-	-	-	-
5521	-	-	-	-	-
5522	-	-	-	-	-
5523	-	-	-	-	-
5524	-	-	-	-	-
5525	-	-	-	-	-
5526	-	-	-	-	-
5527	-	-	-	-	-
5528	-	-	-	-	-
5529	-	-	-	-	-
5530	-	-	-	-	-
5531	-	-	-	-	-
5532	-	-	-	-	-

Appendix 11
Individual Body Weight Gains (g): Premating

20248897
Sex: Female Bodyweight Gain (Interval)

0 ug/dose	Day(s) Relative to Start Date						
Group 1	1 → 8	8 → 15	15 → 22	22 → 28	28 → 35	35 → 36	36 → 41
5533	15	20	10	-1	-	-	-
5534	18	20	7	-10	-	-	-
5535	16	24	19	8	-	-	-
5536	13	11	13	6	-	-	-
5537	20	19	7	10	-	-	-
5538	12	18	6	11	-	-	-
5539	19	27	9	20	14	-15	-6
5540	18	12	1	-1	-	-	-
5541	21	18	4	6	-	-	-
5542	16	18	5	0	-	-	-
5543	17	10	9	9	21	6	-7
5544	16	21	15	15	-	-	-
Mean	14.9	14.6	7.6	6.2	17.5	-4.5	-6.5
SD	4.3	5.3	5.5	7.9	4.9	14.8	0.7
N	44	44	44	44	2	2	2

Appendix 11
Individual Body Weight Gains (g): Premating

20248897
Sex: Female Bodyweight Gain (Interval)

0 ug/dose	Day(s) Relative to Start Date				
Group 1	41 → 48	48 → 50	50 → 53	53 → 56	56 → 60
5533	-	-	-	-	-
5534	-	-	-	-	-
5535	-	-	-	-	-
5536	-	-	-	-	-
5537	-	-	-	-	-
5538	-	-	-	-	-
5539	23	6	2	3	1
5540	-	-	-	-	-
5541	-	-	-	-	-
5542	-	-	-	-	-
5543	7	-2	1	6	-3
5544	-	-	-	-	-
Mean	15.0	2.0	1.5	4.5	-1.0
SD	11.3	5.7	0.7	2.1	2.8
N	2	2	2	2	2

Appendix 11

Individual Body Weight Gains (g): Premating

20248897

Sex: Female Bodyweight Gain (Interval)

100 ug/dose Group 2	Day(s) Relative to Start Date						
	1 → 8	8 → 15	15 → 22	22 → 28	28 → 35	35 → 36	36 → 41
5545	2	25	2	22	-	-	-
5546	13	19	12	14	-	-	-
5547	14	17	3	7	-	-	-
5548	8	15	6	8	-	-	-
5549	7	24	8	8	-	-	-
5550	12	26	12	28	-	-	-
5551	8	14	10	0	32	-2	-1
5552	6	8	7	14	-	-	-
5553	25	-3	12	2	27	-5	11
5554	11	20	6	7	-	-	-
5555	10	15	14	17	-	-	-
5556	29	-3	15	-11	-	-	-
5557	16	9	8	5	-	-	-
5558	8	16	8	-9	42	0	9
5559	13	9	8	14	-	-	-
5560	10	12	8	2	-	-	-

Appendix 11

Individual Body Weight Gains (g): Premating

20248897

Sex: Female Bodyweight Gain (Interval)

100 ug/dose Group 2	Day(s) Relative to Start Date				
	41 → 48	48 → 50	50 → 53	53 → 56	56 → 60
5545	-	-	-	-	-
5546	-	-	-	-	-
5547	-	-	-	-	-
5548	-	-	-	-	-
5549	-	-	-	-	-
5550	-	-	-	-	-
5551	2	5	-16	23	9
5552	-	-	-	-	-
5553	-8	7	-18	20	12
5554	-	-	-	-	-
5555	-	-	-	-	-
5556	-	-	-	-	-
5557	-	-	-	-	-
5558	-4	2	-20	8	5
5559	-	-	-	-	-
5560	-	-	-	-	-

Appendix 11

Individual Body Weight Gains (g): Premating

20248897

Sex: Female Bodyweight Gain (Interval)

100 ug/dose Group 2	Day(s) Relative to Start Date						
	1 → 8	8 → 15	15 → 22	22 → 28	28 → 35	35 → 36	36 → 41
5561	14	22	0	4	-	-	-
5562	32	27	-12	-18	46	8	-6
5563	19	7	10	-1	-	-	-
5564	11	19	8	-1	-	-	-
5565	18	11	13	8	-	-	-
5566	8	21	10	-5	-	-	-
5567	11	11	6	6	-	-	-
5568	11	15	8	8	-	-	-
5569	16	11	4	11	-	-	-
5570	6	14	5	-4	-	-	-
5571	11	15	11	-6	-	-	-
5572	12	10	18	-9	-	-	-
5573	18	14	0	12	-	-	-
5574	10	19	7	-10	-	-	-
5575	5	16	7	0	-	-	-
5576	13	1	14	-3	42	13	-18

Appendix 11

Individual Body Weight Gains (g): Premating

20248897

Sex: Female Bodyweight Gain (Interval)

100 ug/dose Group 2	Day(s) Relative to Start Date				
	41 → 48	48 → 50	50 → 53	53 → 56	56 → 60
5561	-	-	-	-	-
5562	-10	-10	-7	23	16
5563	-	-	-	-	-
5564	-	-	-	-	-
5565	-	-	-	-	-
5566	-	-	-	-	-
5567	-	-	-	-	-
5568	-	-	-	-	-
5569	-	-	-	-	-
5570	-	-	-	-	-
5571	-	-	-	-	-
5572	-	-	-	-	-
5573	-	-	-	-	-
5574	-	-	-	-	-
5575	-	-	-	-	-
5576	-1	-4	-4	6	4

Appendix 11
Individual Body Weight Gains (g): Premating

20248897
Sex: Female Bodyweight Gain (Interval)

100 ug/dose Group 2	Day(s) Relative to Start Date						
	1 → 8	8 → 15	15 → 22	22 → 28	28 → 35	35 → 36	36 → 41
5577	11	14	1	7	-	-	-
5578	2	12	7	6	-	-	-
5579	16	11	12	9	-	-	-
5580	26	18	5	17	-	-	-
5581	7	23	3	12	-	-	-
5582	10	14	6	3	-	-	-
5583	12	23	10	0	-	-	-
5584	5	17	3	5	-	-	-
5585	19	4	1	12	-	-	-
5586	12	22	7	14	-	-	-
5587	18	15	7	7	-	-	-
5588	16	7	6	3	-	-	-
Mean	12.8	14.5	7.2	4.9	37.8	2.8	-1.0
SD	6.5	7.0	5.1	9.2	7.9	7.5	11.8
N	44	44	44	44	5	5	5

Appendix 11

Individual Body Weight Gains (g): Premating

20248897

Sex: Female Bodyweight Gain (Interval)

100 ug/dose Group 2	Day(s) Relative to Start Date				
	41 → 48	48 → 50	50 → 53	53 → 56	56 → 60
5577	-	-	-	-	-
5578	-	-	-	-	-
5579	-	-	-	-	-
5580	-	-	-	-	-
5581	-	-	-	-	-
5582	-	-	-	-	-
5583	-	-	-	-	-
5584	-	-	-	-	-
5585	-	-	-	-	-
5586	-	-	-	-	-
5587	-	-	-	-	-
5588	-	-	-	-	-
Mean	-4.2	0.0	-13.0	16.0	9.2
SD	4.9	7.0	7.1	8.3	5.0
N	5	5	5	5	5

Appendix 11

Individual Body Weight Gains (g): Premating

20248897

Key Page

Measurement Descriptions

Headings Used	Description
Bodyweight Gain (Interval)	Bodyweight Gain (Interval)

Measurement/Statistics

Measurement	Descriptive
Bodyweight Gain (Interval)	Mean
	Standard Deviation
	Count

Group Information

Short Name	Long Name	Type	Report Headings 1-4		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Appendix 12
Individual Body Weights: Gestation

20248897
Sex: Female Bodyweight (g)

0 ug/dose Group 1	Day(s) Relative to Mating (Litter: A)				
	0	1	6	10	13
5501	285	292	316	320	341
5502	291	301	338	356	373
5503	262	269	292	312	318
5504	288	296	316	340	360
5505	279	293	317	329	337
5506	289	292	316	328	354
5507	293	299	311	318	333
5508	287	286	304	328	333
5509	281	295	316	333	334
5510	289	304	314	342	344
5511	284	296	327	343	358
5512	285	298	321	337	339
5513	293	298	331	352	359
5514	292	305	326	340	349
5515	297	306	330	339	356

Appendix 12
Individual Body Weights: Gestation

20248897
Sex: Female Bodyweight (g)

0 ug/dose Group 1	Day(s) Relative to Mating (Litter: A)		
	15	18	21
5501	354	387	443
5502	388	424	495
5503	328	366	414
5504	376	418	477
5505	348	393	449
5506	365	408	470
5507	341	366	413
5508	353	408	458
5509	339	365	404
5510	348	383	448
5511	356	386	438
5512	353	386	446
5513	371	399	461
5514	359	400	449
5515	368	431	492

Appendix 12
Individual Body Weights: Gestation

20248897
Sex: Female Bodyweight (g)

0 ug/dose Group 1	Day(s) Relative to Mating (Litter: A)				
	0	1	6	10	13
5516	300	315	334	353	360
5517 NP	253 E	260 E	283 E	290 E	289 E
5518	282	294	315	340	364
5519	271	274	295	310	333
5520	287	292	311	330	339
5521	293	303	329	339	360
5522	291	296	308	325	338
5523	272	279	310	319	331
5524	280	287	316	327	337
5525	275	281	301	307	323
5526	290	301	324	337	354
5527	283	295	319	343	348
5528	315	318	341	345	368
5529	272	273	303	314	336
5530	296	302	317	331	351

E = Exclude

Appendix 12
Individual Body Weights: Gestation

20248897
Sex: Female Bodyweight (g)

0 ug/dose Group 1	Day(s) Relative to Mating (Litter: A)		
	15	18	21
5516	368	406	469
5517 NP	283 E	289 E	279 E
5518	370	420	482
5519	343	376	440
5520	349	379	-
5521	372	411	479
5522	356	386	450
5523	336	375	429
5524	346	391	449
5525	325	371	426
5526	361	409	461
5527	360	395	476
5528	384	430	502
5529	344	386	445
5530	358	395	455

E = Exclude

Appendix 12
Individual Body Weights: Gestation

20248897
Sex: Female Bodyweight (g)

0 ug/dose Group 1	Day(s) Relative to Mating (Litter: A)				
	0	1	6	10	13
5531	291	301	320	344	360
5532	273	279	291	305	320
5533	284	291	309	324	325
5534	286	297	318	338	348
5535	290	296	320	350	355
5536	310	320	343	345	356
5537	311	315	336	367	376
5538	297	303	321	344	345
5540	286	291	338	333	348
5541	295	305	325	344	361
5542	280	264	220	271	292
5544	314	326	351	370	362
Mean	288.3	295.8	316.8	333.5	345.8
SD	11.4	13.3	20.6	17.9	16.7
N	41	41	41	41	41

Appendix 12
Individual Body Weights: Gestation

20248897
Sex: Female Bodyweight (g)

0 ug/dose Group 1	Day(s) Relative to Mating (Litter: A)		
	15	18	21
5531	371	407	470
5532	329	370	438
5533	341	384	449
5534	360	397	453
5535	365	411	471
5536	366	408	469
5537	385	426	479
5538	356	393	442
5540	354	389	426
5541	373	416	490
5542	313	346	403
5544	370	412	482
Mean	356.1	395.3	454.8
SD	16.7	19.8	24.7
N	41	41	40

Appendix 12

Individual Body Weights: Gestation

20248897

Sex: Female Bodyweight (g)

100 ug/dose Group 2	Day(s) Relative to Mating (Litter: A)				
	0	1	6	10	13
5545	293	299	312	343	348
5546	305	312	334	355	372
5547	290	298	308	326	351
5548	281	292	311	338	340
5549	276	291	308	345	348
5550	313	310	333	352	371
5552	264	274	287	309	314
5554	292	301	322	346	354
5555	310	311	328	335	365
5556	298	307	330	355	372
5557	285	294	307	313	333
5559	271	279	298	323	334
5560	318	312	325	346	365
5561	309	311	316	351	363
5563	266	286	308	330	348

Appendix 12
Individual Body Weights: Gestation

20248897
Sex: Female Bodyweight (g)

100 ug/dose Group 2	Day(s) Relative to Mating (Litter: A)			
	15	18	21	25
5545	355	377	436	-
5546	383	437	502	-
5547	368	408	465	-
5548	345	370	428	-
5549	359	387	437	-
5550	382	426	478	-
5552	327	357	411	-
5554	371	411	474	-
5555	373	416	475	-
5556	372	418	489	-
5557	336	364	416	-
5559	343	381	448	-
5560	380	420	500	-
5561	364	399	463	-
5563	361	409	475	-

Appendix 12
Individual Body Weights: Gestation

20248897
Sex: Female Bodyweight (g)

100 ug/dose Group 2	Day(s) Relative to Mating (Litter: A)				
	0	1	6	10	13
5564	283	291	313	341	356
5565	299	304	330	348	358
5566	278	293	311	334	337
5567	278	283	305	313	333
5568	297	303	322	346	354
5569	274	288	307	322	341
5570	240	248	268	286	299
5571	306	312	334	354	377
5572 NP	278 E	285 E	319 E	349 E	323 E
5573	288	291	297	322	335
5574	289	296	316	335	349
5575	270	278	301	320	338
5577	289	306	334	357	372
5578 NP	285 E	299 E	321 E	351 E	355 E
5579	284	289	315	341	361

E = Exclude

Appendix 12
Individual Body Weights: Gestation

20248897
Sex: Female Bodyweight (g)

100 ug/dose Group 2	Day(s) Relative to Mating (Litter: A)			
	15	18	21	25
5564	363	401	472	-
5565	379	416	480	-
5566	344	387	448	-
5567	341	383	453	-
5568	362	395	455	-
5569	345	380	422	-
5570	304	333	394	-
5571	378	401	435	-
5572 NP	327 E	331 E	337 E	336 E
5573	341	390	-	-
5574	359	388	441	-
5575	346	384	446	-
5577	378	394	472	-
5578 NP	340 E	341 E	340 E	334 E
5579	369	403	445	-

E = Exclude

Appendix 12
Individual Body Weights: Gestation

20248897
Sex: Female Bodyweight (g)

100 ug/dose Group 2	Day(s) Relative to Mating (Litter: A)				
	0	1	6	10	13
5580	332	341	373	390	425
5581	280	291	307	316	340
5582	283	290	304	326	347
5583	291	310	317	339	342
5584	270	287	297	320	328
5585	278	288	303	306	331
5586	294	306	329	346	373
5587	292	298	323	344	367
5588	279	284	307	334	348
Mean	287.7	296.1	314.6	335.3	351.1
SD	17.2	15.2	17.3	18.7	21.3
N	37	37	37	37	37

Appendix 12
Individual Body Weights: Gestation

20248897
Sex: Female Bodyweight (g)

100 ug/dose Group 2	Day(s) Relative to Mating (Litter: A)			
	15	18	21	25
5580	429	471	535	-
5581	350	389	438	-
5582	353	380	-	-
5583	347	374	434	-
5584	338	369	433	-
5585	345	388	452	-
5586	384	421	469	-
5587	380	430	472	-
5588	364	407	467	-
Mean	359.9	396.3	456.0	-
SD	21.4	25.2	28.3	-
N	37	37	35	0

Appendix 12
Individual Body Weights: Gestation

20248897

Comments and Markers

Page	Measurement	Group	Sex	Subject	Day	Type	Marker
	Bodyweight	1	Female	5517	0	Quality Flag	E (Exclude)
	Bodyweight	1	Female	5517	1	Quality Flag	E (Exclude)
	Bodyweight	1	Female	5517	6	Quality Flag	E (Exclude)
	Bodyweight	1	Female	5517	10	Quality Flag	E (Exclude)
	Bodyweight	1	Female	5517	13	Quality Flag	E (Exclude)
	Bodyweight	1	Female	5517	15	Quality Flag	E (Exclude)
	Bodyweight	1	Female	5517	18	Quality Flag	E (Exclude)
	Bodyweight	1	Female	5517	21	Quality Flag	E (Exclude)
	Bodyweight	2	Female	5572	0	Quality Flag	E (Exclude)
	Bodyweight	2	Female	5572	1	Quality Flag	E (Exclude)
	Bodyweight	2	Female	5572	6	Quality Flag	E (Exclude)
	Bodyweight	2	Female	5572	10	Quality Flag	E (Exclude)
	Bodyweight	2	Female	5572	13	Quality Flag	E (Exclude)
	Bodyweight	2	Female	5578	0	Quality Flag	E (Exclude)
	Bodyweight	2	Female	5578	1	Quality Flag	E (Exclude)
	Bodyweight	2	Female	5578	6	Quality Flag	E (Exclude)
	Bodyweight	2	Female	5578	10	Quality Flag	E (Exclude)
	Bodyweight	2	Female	5578	13	Quality Flag	E (Exclude)
	Bodyweight	2	Female	5572	15	Quality Flag	E (Exclude)
	Bodyweight	2	Female	5572	18	Quality Flag	E (Exclude)
	Bodyweight	2	Female	5572	21	Quality Flag	E (Exclude)
	Bodyweight	2	Female	5572	25	Quality Flag	E (Exclude)
	Bodyweight	2	Female	5578	15	Quality Flag	E (Exclude)
	Bodyweight	2	Female	5578	18	Quality Flag	E (Exclude)
	Bodyweight	2	Female	5578	21	Quality Flag	E (Exclude)
	Bodyweight	2	Female	5578	25	Quality Flag	E (Exclude)

Appendix 12

Individual Body Weights: Gestation

20248897

Subject Comments/Exclusions

Subject	Marker	Comment/Exclusion
5517	NP	Not Pregnant
5572	NP	Not Pregnant
5578	NP	Not Pregnant

Appendix 12

Individual Body Weights: Gestation

20248897

Key Page

Quality Flags

Symbol	IES Status	Description
E	Excluded	Exclude

Measurement Descriptions

Headings Used	Description
Bodyweight	Bodyweight

Measurement/Statistics

Measurement	Descriptive
Bodyweight	Mean
	Standard Deviation
	Count

Group Information

Short Name	Long Name	Type	Report Headings 1-4		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Appendix 13

Individual Body Weight Gains (g): Gestation

20248897

Sex: Female Bodyweight Gain (Interval)

0 ug/dose Group 1	Day(s) Relative to Mating (Litter: A)						
	0 → 1	1 → 6	6 → 10	10 → 13	13 → 15	15 → 18	18 → 21
5501	7	24	4	21	13	33	56
5502	10	37	18	17	15	36	71
5503	7	23	20	6	10	38	48
5504	8	20	24	20	16	42	59
5505	14	24	12	8	11	45	56
5506	3	24	12	26	11	43	62
5507	6	12	7	15	8	25	47
5508	-1	18	24	5	20	55	50
5509	14	21	17	1	5	26	39
5510	15	10	28	2	4	35	65
5511	12	31	16	15	-2	30	52
5512	13	23	16	2	14	33	60
5513	5	33	21	7	12	28	62
5514	13	21	14	9	10	41	-
5515	9	24	9	17	12	63	61

Appendix 13

Individual Body Weight Gains (g): Gestation

20248897

Sex: Female Bodyweight Gain (Interval)

0 ug/dose Group 1	Day(s) Relative to Mating (Litter: A)						
	0 → 1	1 → 6	6 → 10	10 → 13	13 → 15	15 → 18	18 → 21
5516	15	19	19	7	8	38	63
5517 NP	7 E	23 E	7 E	-1 E	-6 E	6 E	-10 E
5518	12	21	25	24	6	50	62
5519	3	21	15	23	10	33	64
5520	5	19	19	9	10	30	-
5521	10	26	10	21	12	39	68
5522	5	12	17	13	18	30	64
5523	7	31	9	12	5	39	54
5524	7	29	11	10	9	45	58
5525	6	20	6	16	2	46	-
5526	11	23	13	17	7	48	52
5527	12	24	24	5	12	35	-
5528	3	23	4	23	16	46	72
5529	1	30	11	22	8	42	-
5530	6	15	14	20	7	37	60

E = Exclude

Appendix 13

Individual Body Weight Gains (g): Gestation

20248897

Sex: Female Bodyweight Gain (Interval)

0 ug/dose Group 1	Day(s) Relative to Mating (Litter: A)						
	0 → 1	1 → 6	6 → 10	10 → 13	13 → 15	15 → 18	18 → 21
5531	10	19	24	16	11	36	-
5532	6	12	14	15	9	41	-
5533	7	18	15	1	16	43	-
5534	11	21	20	10	12	37	56
5535	6	24	30	5	10	46	60
5536	10	23	2	11	10	42	61
5537	4	21	31	9	9	41	53
5538	6	18	23	1	11	37	49
5540	5	47	-5	15	6	35	37
5541	10	20	19	17	12	43	74
5542	-16	-44	51	21	21	33	57
5544	12	25	19	-8	8	42	70
Mean	7.5	21.0	16.6	12.3	10.3	39.2	58.2
SD	5.4	12.5	9.5	7.9	4.6	7.6	8.6
N	41	41	41	41	41	41	33

Appendix 13

Individual Body Weight Gains (g): Gestation

20248897

Sex: Female Bodyweight Gain (Interval)

100 ug/dose Group 2	Day(s) Relative to Mating (Litter: A)						
	0 → 1	1 → 6	6 → 10	10 → 13	13 → 15	15 → 18	18 → 21
5545	6	13	31	5	7	22	59
5546	7	22	21	17	11	54	65
5547	8	10	18	25	17	40	57
5548	11	19	27	2	5	25	58
5549	15	17	37	3	11	28	50
5550	-3	23	19	19	11	44	52
5552	10	13	22	5	13	30	54
5554	9	21	24	8	17	40	63
5555	1	17	7	30	8	43	59
5556	9	23	25	17	0	46	71
5557	9	13	6	20	3	28	52
5559	8	19	25	11	9	38	67
5560	-6	13	21	19	15	40	80
5561	2	5	35	12	1	35	64
5563	20	22	22	18	13	48	66

Appendix 13

Individual Body Weight Gains (g): Gestation

20248897

Sex: Female Bodyweight Gain (Interval)

100 ug/dose Group 2	Day(s) Relative to Mating (Litter: A) 21 → 25
5545	-
5546	-
5547	-
5548	-
5549	-
5550	-
5552	-
5554	-
5555	-
5556	-
5557	-
5559	-
5560	-
5561	-
5563	-

Appendix 13

Individual Body Weight Gains (g): Gestation

20248897

Sex: Female Bodyweight Gain (Interval)

100 ug/dose Group 2	Day(s) Relative to Mating (Litter: A)						
	0 → 1	1 → 6	6 → 10	10 → 13	13 → 15	15 → 18	18 → 21
5564	8	22	28	15	7	38	71
5565	5	26	18	10	21	37	64
5566	15	18	23	3	7	43	61
5567	5	22	8	20	8	42	70
5568	6	19	24	8	8	33	60
5569	14	19	15	19	4	35	42
5570	8	20	18	13	5	29	61
5571	6	22	20	23	1	23	34
5572 NP	7 E	34 E	30 E	-26 E	4 E	4 E	6 E
5573	3	6	25	13	6	49	-
5574	7	20	19	14	10	29	53
5575	8	23	19	18	8	38	62
5577	17	28	23	15	6	16	-
5578 NP	14 E	22 E	30 E	4 E	-15 E	1 E	-1 E
5579	5	26	26	20	8	34	42

E = Exclude

Appendix 13

Individual Body Weight Gains (g): Gestation

20248897

Sex: Female Bodyweight Gain (Interval)

100 ug/dose Group 2	Day(s) Relative to Mating (Litter: A) 21 → 25
5564	-
5565	-
5566	-
5567	-
5568	-
5569	-
5570	-
5571	-
5572 NP	-1 E
5573	-
5574	-
5575	-
5577	-
5578 NP	-6 E
5579	-

E = Exclude

Appendix 13

Individual Body Weight Gains (g): Gestation

20248897

Sex: Female Bodyweight Gain (Interval)

100 ug/dose Group 2	Day(s) Relative to Mating (Litter: A)						
	0 → 1	1 → 6	6 → 10	10 → 13	13 → 15	15 → 18	18 → 21
5580	9	32	17	35	4	42	64
5581	11	16	9	24	10	39	49
5582	7	14	22	21	6	27	-
5583	19	7	22	3	5	27	-
5584	17	10	23	8	10	31	64
5585	10	15	3	25	14	43	-
5586	12	23	17	27	11	37	48
5587	6	25	21	23	13	50	42
5588	5	23	27	14	16	43	60
Mean	8.4	18.5	20.7	15.7	8.9	36.4	58.3
SD	5.5	6.2	7.3	8.1	4.8	8.6	10.0
N	37	37	37	37	37	37	32

Appendix 13

Individual Body Weight Gains (g): Gestation

20248897

Sex: Female Bodyweight Gain (Interval)

100 ug/dose Group 2	Day(s) Relative to Mating (Litter: A) 21 → 25
5580	-
5581	-
5582	-
5583	-
5584	-
5585	-
5586	-
5587	-
5588	-
Mean	-
SD	-
N	0

Appendix 13
Individual Body Weight Gains (g): Gestation

20248897

Comments and Markers

Page	Measurement	Group	Sex	Subject	Day	Type	Marker
	Bodyweight Gain (Interval)	1	Female	5517	0 - 1	Quality Flag	E (Exclude)
	Bodyweight Gain (Interval)	1	Female	5517	1 - 6	Quality Flag	E (Exclude)
	Bodyweight Gain (Interval)	1	Female	5517	6 - 10	Quality Flag	E (Exclude)
	Bodyweight Gain (Interval)	1	Female	5517	10 - 13	Quality Flag	E (Exclude)
	Bodyweight Gain (Interval)	1	Female	5517	13 - 15	Quality Flag	E (Exclude)
	Bodyweight Gain (Interval)	1	Female	5517	15 - 18	Quality Flag	E (Exclude)
	Bodyweight Gain (Interval)	1	Female	5517	18 - 21	Quality Flag	E (Exclude)
	Bodyweight Gain (Interval)	2	Female	5572	0 - 1	Quality Flag	E (Exclude)
	Bodyweight Gain (Interval)	2	Female	5572	1 - 6	Quality Flag	E (Exclude)
	Bodyweight Gain (Interval)	2	Female	5572	6 - 10	Quality Flag	E (Exclude)
	Bodyweight Gain (Interval)	2	Female	5572	10 - 13	Quality Flag	E (Exclude)
	Bodyweight Gain (Interval)	2	Female	5572	13 - 15	Quality Flag	E (Exclude)
	Bodyweight Gain (Interval)	2	Female	5572	15 - 18	Quality Flag	E (Exclude)
	Bodyweight Gain (Interval)	2	Female	5572	18 - 21	Quality Flag	E (Exclude)
	Bodyweight Gain (Interval)	2	Female	5578	0 - 1	Quality Flag	E (Exclude)
	Bodyweight Gain (Interval)	2	Female	5578	1 - 6	Quality Flag	E (Exclude)
	Bodyweight Gain (Interval)	2	Female	5578	6 - 10	Quality Flag	E (Exclude)
	Bodyweight Gain (Interval)	2	Female	5578	10 - 13	Quality Flag	E (Exclude)
	Bodyweight Gain (Interval)	2	Female	5578	13 - 15	Quality Flag	E (Exclude)
	Bodyweight Gain (Interval)	2	Female	5578	15 - 18	Quality Flag	E (Exclude)
	Bodyweight Gain (Interval)	2	Female	5578	18 - 21	Quality Flag	E (Exclude)
	Bodyweight Gain (Interval)	2	Female	5572	21 - 25	Quality Flag	E (Exclude)
	Bodyweight Gain (Interval)	2	Female	5578	21 - 25	Quality Flag	E (Exclude)

Subject Comments/Exclusions

Subject	Marker	Comment/Exclusion
5517	NP	Not Pregnant
5572	NP	Not Pregnant
5578	NP	Not Pregnant

Appendix 13

Individual Body Weight Gains (g): Gestation

20248897

Key Page

Quality Flags

Symbol	IES Status	Description
E	Excluded	Exclude

Measurement Descriptions

Headings Used	Description
Bodyweight Gain (Interval)	Bodyweight Gain (Interval)

Measurement/Statistics

Measurement	Descriptive
Bodyweight Gain (Interval)	Mean
	Standard Deviation
	Count

Group Information

Short Name	Long Name	Type	Report Headings 1-4		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Appendix 14
Individual Body Weights: Lactation

20248897
Sex: Female Bodyweight (g)

0 ug/dose Group 1	Day(s) Relative to Littering (Litter: A)			
	1	3	4	7
5514	324	-	348	356
5520	336	333 E[a]	-	-
5524	301	-	308	320
5525	304	-	313	325
5526	314	-	330	337
5527	342	-	367	356
5529	311	-	324	339
5530	325	-	333	340
5531	353	-	362	378
5532	288	-	329	345
5533	321	-	342	345
5534	341	-	352	363
5535	332	-	367	373
5536	319	-	334	352
5537	362	-	386	378

E = Exclude
[a] [FC:Female was euthanized due to no surviving pups, excluded as per SD.]

Appendix 14

Individual Body Weights: Lactation

20248897

Sex: Female Bodyweight (g)

0 ug/dose Group 1	Day(s) Relative to Littering (Litter: A)			
	10	14	18	21
5514	370	359	366	366
5520	-	-	-	-
5524	357	326	341	329
5525	353	330	347	346
5526	353	361	352	340
5527	389	394	368	358
5529	366	367	353	341
5530	356	366	368	347
5531	381	374	396	385
5532	339	345	348	349
5533	358	356	354	345
5534	378	372	380	359
5535	388	384	377	360
5536	383	377	378	358
5537	372	376	391	394

Appendix 14
Individual Body Weights: Lactation

20248897
Sex: Female Bodyweight (g)

0 ug/dose Group 1	Day(s) Relative to Littering (Litter: A)			
	1	3	4	7
5538	328	-	355	360
5540	336	-	346	355
5541	368	-	359	357
5542	305	-	316	323
5544	354	-	380	372
Mean	328.2	-	344.8	351.3
SD	21.3	-	22.3	17.7
N	20	0	19	19

Appendix 14
Individual Body Weights: Lactation

20248897
Sex: Female Bodyweight (g)

0 ug/dose Group 1	Day(s) Relative to Littering (Litter: A)			
	10	14	18	21
5538	357	366	370	350
5540	367	365	375	367
5541	375	367	371	354
5542	328	355	359	348
5544	369	382	357	357
Mean	365.2	364.3	365.8	355.4
SD	16.1	17.1	15.0	15.3
N	19	19	19	19

Appendix 14
Individual Body Weights: Lactation

20248897
Sex: Female Bodyweight (g)

100 ug/dose Group 2	Day(s) Relative to Littering (Litter: A)			
	1	4	7	10
5571	374	380	382	394
5573	319	337	353	365
5574	320	332	345	347
5575	315	340	364	353
5577	373	387	405	424
5579	339	342	384	393
5580	391	401	416	419
5581	306	334	341	341
5582	312	320	341	358
5583	328	342	347	370
5584	316	323	328	338
5585	318	339	351	356
5586	361	380	395	412
5587	358	378	406	411

Appendix 14
Individual Body Weights: Lactation

20248897
Sex: Female Bodyweight (g)

100 ug/dose Group 2	Day(s) Relative to Littering (Litter: A)		
	14	18	21
5571	369	393	383
5573	349	365	348
5574	341	351	343
5575	381	364	371
5577	434	429	407
5579	405	396	371
5580	432	422	414
5581	348	335	351
5582	354	355	342
5583	364	382	378
5584	337	335	337
5585	352	350	358
5586	395	396	381
5587	426	432	400

Appendix 14
Individual Body Weights: Lactation

20248897
Sex: Female Bodyweight (g)

100 ug/dose Group 2	Day(s) Relative to Littering (Litter: A)			
	1	4	7	10
5588	305	330	343	351
Mean	335.7	351.0	366.7	375.5
SD	28.2	26.3	28.6	30.3
N	15	15	15	15

Appendix 14

Individual Body Weights: Lactation

20248897

Sex: Female Bodyweight (g)

100 ug/dose Group 2	Day(s) Relative to Littering (Litter: A)		
	14	18	21
5588	347	353	341
Mean	375.6	377.2	368.3
SD	34.4	32.8	25.3
N	15	15	15

Appendix 14
Individual Body Weights: Lactation

20248897

Comments and Markers

Page	Measurement	Group	Sex	Subject	Day	Type	Marker
	Bodyweight	1	Female	5520	3	Quality Flag	E (Exclude)

Comment: Female was euthanized due to no surviving pups, excluded as per SD.

Appendix 14

Individual Body Weights: Lactation

20248897

Key Page

Quality Flags

Symbol	IES Status	Description
E	Excluded	Exclude

Measurement Descriptions

Headings Used	Description
Bodyweight	Bodyweight

Measurement/Statistics

Measurement	Descriptive
Bodyweight	Mean
	Standard Deviation
	Count

Group Information

Short Name	Long Name	Type	Report Headings 1-4		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Comment Abbreviations

FC = Flag Comment

Appendix 15
Individual Body Weight Gains (g): Lactation

20248897
Sex: Female Bodyweight Gain (Interval)

0 ug/dose Group 1	Day(s) Relative to Littering (Litter: A)					
	1 → 4	4 → 7	7 → 10	10 → 14	14 → 18	18 → 21
5514	24	8	14	-11	7	0
5524	7	12	37	-31	15	-12
5525	9	12	28	-23	17	-1
5526	16	7	16	8	-9	-12
5527	25	-11	33	5	-26	-10
5529	13	15	27	1	-14	-12
5530	8	7	16	10	2	-21
5531	9	16	3	-7	22	-11
5532	41	16	-6	6	3	1
5533	21	3	13	-2	-2	-9
5534	11	11	15	-6	8	-21
5535	35	6	15	-4	-7	-17
5536	15	18	31	-6	1	-20
5537	24	-8	-6	4	15	3
5538	27	5	-3	9	4	-20
5540	10	9	12	-2	10	-8
5541	-9	-2	18	-8	4	-17
5542	11	7	5	27	4	-11

Appendix 15

Individual Body Weight Gains (g): Lactation

20248897

Sex: Female Bodyweight Gain (Interval)

0 ug/dose	Day(s) Relative to Littering (Litter: A)					
Group 1	1 → 4	4 → 7	7 → 10	10 → 14	14 → 18	18 → 21
5544	26	-8	-3	13	-25	0
Mean	17.0	6.5	13.9	-0.9	1.5	-10.4
SD	11.5	8.5	13.2	13.0	13.1	7.9
N	19	19	19	19	19	19

Appendix 15
Individual Body Weight Gains (g): Lactation

20248897
Sex: Female Bodyweight Gain (Interval)

100 ug/dose Group 2	Day(s) Relative to Littering (Litter: A)					
	1 → 4	4 → 7	7 → 10	10 → 14	14 → 18	18 → 21
5571	6	2	12	-25	24	-10
5573	18	16	12	-16	16	-17
5574	12	13	2	-6	10	-8
5575	25	24	-11	28	-17	7
5577	14	18	19	10	-5	-22
5579	3	42	9	12	-9	-25
5580	10	15	3	13	-10	-8
5581	28	7	0	7	-13	16
5582	8	21	17	-4	1	-13
5583	14	5	23	-6	18	-4
5584	7	5	10	-1	-2	2
5585	21	12	5	-4	-2	8
5586	19	15	17	-17	1	-15
5587	20	28	5	15	6	-32
5588	25	13	8	-4	6	-12
Mean	15.3	15.7	8.7	0.1	1.6	-8.9
SD	7.7	10.2	8.6	14.0	11.8	13.1
N	15	15	15	15	15	15

Appendix 15

Individual Body Weight Gains (g): Lactation

20248897

Key Page

Measurement Descriptions

Headings Used	Description
Bodyweight Gain (Interval)	Bodyweight Gain (Interval)

Measurement/Statistics

Measurement	Descriptive
Bodyweight Gain (Interval)	Mean
	Standard Deviation
	Count

Group Information

Short Name	Long Name	Type	Report Headings 1-4		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Appendix 16
Individual Food Consumption: Premating

20248897
Sex: Female Daily Food Cons Per Animal (g)

0 ug/dose Group 1	No. in Cage	Day(s) Relative to Animal Start Date			
		1 → 8	8 → 15	15 → 22	22 → 28
1	2	20	18	19	17
2	2	19	19	17	15
3	2	18	18	17	17
4	2	19	18	18	17
5	2	20	19	18	18
6	2	21	22	19	18
7	2	19	19	18	18
8	2	19	19	19	18
9	2	18	18	17	18
10	2	19	18	17	16
11	2	20	19	18	18
12	2	19	19	17	16
13	2	17	17	16	15
14	2	21	20	20	19
15	2	20	20	19	19
16	2	20	21	19	20

Appendix 16

Individual Food Consumption: Premating

20248897

Sex: Female Daily Food Cons Per Animal (g)

0 ug/dose Group 1	No. in Cage	Day(s) Relative to Animal Start Date			
		1 → 8	8 → 15	15 → 22	22 → 28
17	2	21	19	19	17
18	2	19	19	19	18
19	2	20	19	19	19
20	2	20	21	19	18
21	2	18	17	17	16
22	2	21	21	20	22
	Mean	19.4	19.1	18.1	17.6
	SD	1.1	1.2	1.1	1.5
	N	22	22	22	22

Appendix 16

Individual Food Consumption: Premating

20248897

Sex: Female Daily Food Cons Per Animal (g)

100 ug/dose Group 2	No. in Cage	Day(s) Relative to Animal Start Date			
		1 → 8	8 → 15	15 → 22	22 → 28
23	2	18	19	17	19
24	2	25	29	23	20
25	2	18	20	17	21
26	2	17	18	16	17
27	2	20	20	18	20
28	2	19	19	18	18
29	2	18	19	18	17
30	2	18	19	14	18
31	2	18	20	16	18
32	2	19	19	18	17
33	2	18	18	17	17
34	2	18	18	16	16
35	2	19	17	18	17
36	2	19	19	19	17
37	2	19	21	17	19
38	2	20	20	19	19

Appendix 16

Individual Food Consumption: Premating

20248897

Sex: Female Daily Food Cons Per Animal (g)

100 ug/dose Group 2	No. in Cage	Day(s) Relative to Animal Start Date			
		1 → 8	8 → 15	15 → 22	22 → 28
39	2	20	19	17	18
40	2	20	19	19	21
41	2	17	19	17	17
42	2	18	19	17	19
43	2	19	18	18	19
44	2	19	19	17	18
	Mean	18.9	19.5	17.4	18.3
	SD	1.7	2.2	1.7	1.3
	N	22	22	22	22
	%Diff	-2.8	2.3	-3.6	4.1

Appendix 16

Individual Food Consumption: Premating

20248897

Key Page

Cage Contents

Cage Number	Animal Numbers	Cage Number	Animal Numbers
1	5501, 5502	2	5503, 5504
3	5505, 5506	4	5507, 5508
5	5509, 5510	6	5511, 5512
7	5513, 5514	8	5515, 5516
9	5517, 5518	10	5519, 5520
11	5521, 5522	12	5523, 5524
13	5525, 5526	14	5527, 5528
15	5529, 5530	16	5531, 5532
17	5533, 5534	18	5535, 5536
19	5537, 5538	20	5539, 5540
21	5541, 5542	22	5543, 5544
23	5545, 5546	24	5547, 5548
25	5549, 5550	26	5551, 5552
27	5553, 5554	28	5555, 5556
29	5557, 5558	30	5559, 5560
31	5561, 5562	32	5563, 5564
33	5565, 5566	34	5567, 5568
35	5569, 5570	36	5571, 5572
37	5573, 5574	38	5575, 5576
39	5577, 5578	40	5579, 5580
41	5581, 5582	42	5583, 5584
43	5585, 5586	44	5587, 5588

Measurement Descriptions

Headings Used	Description
Daily Food Cons Per Animal	Mean Daily Food Cons. Per Animal

Appendix 16

Individual Food Consumption: Premating

20248897

Key Page

Measurement/Statistics

Measurement	Descriptive
Daily Food Cons Per Animal	Mean
	Standard Deviation
	Count
	% Difference from Control

Group Information

Short Name	Long Name	Type	Report Headings 1-4		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Appendix 17

Individual Food Consumption: Gestation

20248897

Sex: Female Food Mean Daily Consumption (g/animal/day)

0 ug/dose Group 1	Day(s) Relative to Mating (Litter: A)						
	0 → 1	1 → 6	6 → 10	10 → 13	13 → 15	15 → 18	18 → 21
5501	23	23	26	25	25	25	28
5502	21	25	27	26	28	29	27
5503	18	17	20	22	23	23	21
5504	17	21	26	27	28	30	27
5505	29	20	23	23	25	27	26
5506	17	18	21	22	22	25	26
5507	20	20	21	22	22	26	23
5508	17	17	23	22	24	27	25
5509	31	21	22	23	24	26	28
5510	25	20	23	23	25	22	33
5511	25	19	22	24	23	22	24
5512	30	20	23	24	24	23	26
5513	23	19	23	24	26	23	27
5514	21	23	27	28	27	31	7 E[a]
5515	28	21	22	26	25	28	28

E = Exclude

[a] [FC:Suspected aberrant value. Excluded per Study Director.]

Appendix 17

Individual Food Consumption: Gestation

20248897

Sex: Female Food Mean Daily Consumption (g/animal/day)

0 ug/dose Group 1	Day(s) Relative to Mating (Litter: A)						
	0 → 1	1 → 6	6 → 10	10 → 13	13 → 15	15 → 18	18 → 21
5516	25	20	25	22	26	21	23
5517 NP	22 E	21 E	23 E	23 E	17 E	18 E	18 E
5518	20	23	30	31	21	26	28
5519	16	21	23	25	25	24	27
5520	19	20	23	21	23	26	.
5521	26	20	24	25	27	26	29
5522	23	21	22	25	25	28	25
5523	24	20	21	22	24	24	26
5524	21	22	22	21	21	25	25
5525	21	19	20	23	21	23	26
5526	16	21	24	23	20	26	25
5527	24	20	24	23	25	26	29
5528	24	23	23	27	26	29	30
5529	19	22	21	24	21	27	29
5530	24	25	25	23	26	27	28

E = Exclude

Appendix 17

Individual Food Consumption: Gestation

20248897

Sex: Female Food Mean Daily Consumption (g/animal/day)

0 ug/dose Group 1	Day(s) Relative to Mating (Litter: A)						
	0 → 1	1 → 6	6 → 10	10 → 13	13 → 15	15 → 18	18 → 21
5531	21	22	25	24	27	28	9 E[a]
5532	26	20	20	25	22	26	26
5533	26	19	22	26	27	25	28
5534	25	19	23	25	25	23	27
5535	23	19	25	26	28	26	30
5536	22	22	24	24	22	23	28
5537	27	17	25	25	26	25	27
5538	27	20	23	25	24	26	27
5540	18	25	24	27	33	29	35
5541	35	20	21	26	28	24	30
5542	17	3 E[a]	21	16	28	22	24
5544	22	29	29	29	24	29	32
Mean	22.83	20.81	23.23	24.21	24.54	25.57	27.18
SD	4.36	2.42	2.25	2.55	2.55	2.45	2.69
N	41	40	41	41	41	41	38

E = Exclude

[a] [FC:Suspected aberrant value. Excluded per Study Director.]

Appendix 17

Individual Food Consumption: Gestation

20248897

Sex: Female Food Mean Daily Consumption (g/animal/day)

100 ug/dose Group 2	Day(s) Relative to Mating (Litter: A)						
	0 → 1	1 → 6	6 → 10	10 → 13	13 → 15	15 → 18	18 → 21
5545	28	17	24	24	20	24	24
5546	26	21	26	27	20	29	29
5547	24	19	24	26	20	27	27
5548	28	19	26	26	22	24	25
5549	25	19	25	25	20	26	25
5550	18	22	25	25	22	26	25
5552	33	17	22	23	22	23	24
5554	31	20	25	29	24	29	31
5555	1 E[a]	18	20	25	20	28	26
5556	21	21	25	24	19	25	28
5557	23	18	20	22	19	21	28
5559	28	19	23	30	23	29	29
5560	13	19	24	24	23	29	29
5561	19	19	26	27	17	31	32
5563	20	20	25	27	19	27	29

E = Exclude

[a] [FC:Suspected aberrant value. Excluded per Study Director.]

Appendix 17

Individual Food Consumption: Gestation

20248897

Sex: Female Food Mean Daily Consumption (g/animal/day)

100 ug/dose Group 2	Day(s) Relative to Mating (Litter: A) 21 → 25
5545	.
5546	.
5547	.
5548	.
5549	.
5550	.
5552	.
5554	.
5555	.
5556	.
5557	.
5559	.
5560	.
5561	.
5563	.

Appendix 17

Individual Food Consumption: Gestation

20248897

Sex: Female Food Mean Daily Consumption (g/animal/day)

100 ug/dose Group 2	Day(s) Relative to Mating (Litter: A)						
	0 → 1	1 → 6	6 → 10	10 → 13	13 → 15	15 → 18	18 → 21
5564	26	21	26	29	23	25	28
5565	22	24	27	28	24	31	26
5566	21	17	22	24	19	26	27
5567	24	19	23	22	20	24	28
5568	26	19	23	25	22	26	30
5569	29	21	26	25	20	25	26
5570	26	17	21	24	19	22	25
5571	20	21	25	26	21	26	31
5572 NP	17 E	19 E	26 E	21 E	20 E	21 E	22 E
5573	27	18	26	28	18	29	.
5574	28	18	23	27	23	24	30
5575	27	20	24	29	24	28	30
5577	35	21	25	29	25	28	36
5578 NP	27 E	19 E	26 E	29 E	19 E	18 E	21 E
5579	26	23	30	30	23	27	30

E = Exclude

Appendix 17

Individual Food Consumption: Gestation

20248897

Sex: Female Food Mean Daily Consumption (g/animal/day)

100 ug/dose Group 2	Day(s) Relative to Mating (Litter: A) 21 → 25
5564	.
5565	.
5566	.
5567	.
5568	.
5569	.
5570	.
5571	.
5572 NP	14 E
5573	.
5574	.
5575	.
5577	.
5578 NP	15 E
5579	.

E = Exclude

Appendix 17

Individual Food Consumption: Gestation

20248897

Sex: Female Food Mean Daily Consumption (g/animal/day)

100 ug/dose Group 2	Day(s) Relative to Mating (Litter: A)						
	0 → 1	1 → 6	6 → 10	10 → 13	13 → 15	15 → 18	18 → 21
5580	23	25	32	32	26	27	33
5581	20	18	23	25	17	22	26
5582	22	21	26	30	24	22	.
5583	31	16	22	23	19	22	28
5584	32	17	23	27	20	26	29
5585	21	20	19	22	21	27	28
5586	25	22	26	29	25	27	37
5587	23	22	25	29	25	35	36
5588	21	21	26	27	20	26	33
Mean	24.78	19.63	24.21	26.27	21.00	26.25	28.82
SD	4.62	2.01	2.57	2.53	2.35	2.94	3.31
N	36	37	37	37	37	37	35

Appendix 17

Individual Food Consumption: Gestation

20248897

Sex: Female Food Mean Daily Consumption (g/animal/day)

100 ug/dose Group 2	Day(s) Relative to Mating (Litter: A) 21 → 25
5580	.
5581	.
5582	.
5583	.
5584	.
5585	.
5586	.
5587	.
5588	.
Mean	.
SD	.
N	0

Appendix 17

Individual Food Consumption: Gestation

20248897

Comments and Markers

Page	Measurement	Group	Sex	Subject	Day	Type	Marker
	Food Mean Daily Consumption	1	Female	5514	18 - 21	Quality Flag	E (Exclude)
	Comment: Suspected aberrant value. Excluded per Study Director.						
	Food Mean Daily Consumption	1	Female	5517	0 - 1	Quality Flag	E (Exclude)
	Food Mean Daily Consumption	1	Female	5517	1 - 6	Quality Flag	E (Exclude)
	Food Mean Daily Consumption	1	Female	5517	6 - 10	Quality Flag	E (Exclude)
	Food Mean Daily Consumption	1	Female	5517	10 - 13	Quality Flag	E (Exclude)
	Food Mean Daily Consumption	1	Female	5517	13 - 15	Quality Flag	E (Exclude)
	Food Mean Daily Consumption	1	Female	5517	15 - 18	Quality Flag	E (Exclude)
	Food Mean Daily Consumption	1	Female	5517	18 - 21	Quality Flag	E (Exclude)
	Food Mean Daily Consumption	1	Female	5531	18 - 21	Quality Flag	E (Exclude)
	Comment: Suspected aberrant value. Excluded per Study Director.						
	Food Mean Daily Consumption	1	Female	5542	1 - 6	Quality Flag	E (Exclude)
	Comment: Suspected aberrant value. Excluded per Study Director.						
	Food Mean Daily Consumption	2	Female	5555	0 - 1	Quality Flag	E (Exclude)
	Comment: Suspected aberrant value. Excluded per Study Director.						
	Food Mean Daily Consumption	2	Female	5572	0 - 1	Quality Flag	E (Exclude)
	Food Mean Daily Consumption	2	Female	5572	1 - 6	Quality Flag	E (Exclude)
	Food Mean Daily Consumption	2	Female	5572	6 - 10	Quality Flag	E (Exclude)
	Food Mean Daily Consumption	2	Female	5572	10 - 13	Quality Flag	E (Exclude)
	Food Mean Daily Consumption	2	Female	5572	13 - 15	Quality Flag	E (Exclude)
	Food Mean Daily Consumption	2	Female	5572	15 - 18	Quality Flag	E (Exclude)
	Food Mean Daily Consumption	2	Female	5572	18 - 21	Quality Flag	E (Exclude)
	Food Mean Daily Consumption	2	Female	5578	0 - 1	Quality Flag	E (Exclude)
	Food Mean Daily Consumption	2	Female	5578	1 - 6	Quality Flag	E (Exclude)
	Food Mean Daily Consumption	2	Female	5578	6 - 10	Quality Flag	E (Exclude)
	Food Mean Daily Consumption	2	Female	5578	10 - 13	Quality Flag	E (Exclude)
	Food Mean Daily Consumption	2	Female	5578	13 - 15	Quality Flag	E (Exclude)
	Food Mean Daily Consumption	2	Female	5578	15 - 18	Quality Flag	E (Exclude)
	Food Mean Daily Consumption	2	Female	5578	18 - 21	Quality Flag	E (Exclude)

Appendix 17

Individual Food Consumption: Gestation

20248897

Comments and Markers

Page	Measurement	Group	Sex	Subject	Day	Type	Marker
	Food Mean Daily Consumption	2	Female	5572	21 - 25	Quality Flag	E (Exclude)
	Food Mean Daily Consumption	2	Female	5578	21 - 25	Quality Flag	E (Exclude)

Subject Comments/Exclusions

Subject	Marker	Comment/Exclusion
5517	NP	Not Pregnant
5572	NP	Not Pregnant
5578	NP	Not Pregnant

Appendix 17

Individual Food Consumption: Gestation

20248897

Key Page

Quality Flags

Symbol	IES Status	Description
E	Excluded	Exclude

Measurement Descriptions

Headings Used	Description
Food Mean Daily Consumption	Food Mean Consumption per Animal

Measurement/Statistics

Measurement	Descriptive
Food Mean Daily Consumption	Mean
	Standard Deviation
	Count

Group Information

Short Name	Long Name	Type	Report Headings 1-4		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Comment Abbreviations

FC = Flag Comment

Appendix 18

Individual Food Consumption: Lactation

20248897

Sex: Female Food Mean Daily Consumption (g/animal/day)

0 ug/dose Group 1	Day(s) Relative to Littering (Litter: A)				
	1 → 3	1 → 4	4 → 7	7 → 10	10 → 14
5514	.	25	31	41	50
5520	17 E[a]	.	.	.	.
5524	.	30	37	59	64
5525	.	32	37	55	63
5526	.	34	38	OA	.
5527	.	39	44	59	65
5529	.	32	41	OA	.
5530	.	40	45	60	72
5531	.	36	50	58	65
5532	.	38	48	58	60
5533	.	37	48	58	66
5534	.	34	50	65	65
5535	.	43	44	55	63
5536	.	37	46	OA	.
5537	.	34	43	48	58
5538	.	36	46	48	58
5540	.	32	47	56	70
5541	.	28	32	44	51
5542	.	30	39	47	58

E = Exclude

[a] [FC:No Surviving Pups, Unscheduled Sacrificed]

Appendix 18

Individual Food Consumption: Lactation

20248897

Sex: Female Food Mean Daily Consumption (g/animal/day)

0 ug/dose	Day(s) Relative to Littering (Litter: A)				
Group 1	1 → 3	1 → 4	4 → 7	7 → 10	10 → 14
5544	.	44	OA	.	64
Mean	.	34.98	42.65	54.09	61.89
SD	.	4.92	5.90	6.85	6.07
N	0	19	18	15	16

Appendix 18
Individual Food Consumption: Lactation

20248897
Sex: Female Food Mean Daily Consumption (g/animal/day)

100 ug/dose Group 2	Day(s) Relative to Littering (Litter: A)			
	1 → 4	4 → 7	7 → 10	10 → 14
5571	30	43	54	60
5573	35	43	63	70
5574	27	44	51	60
5575	35	52	53	69
5577	45	63	65	83
5579	43	55	OA	.
5580	41	46	OA	.
5581	37	45	OA	.
5582	35	44	OA	.
5583	32	47	57	70
5584	35	44	57	60
5585	33	46	58	67
5586	46	52	OA	.
5587	45	42	OA	.
5588	39	41	OA	.
Mean	37.13	47.20	57.33	67.25
SD	5.74	5.95	4.68	7.86
N	15	15	8	8

Appendix 18

Individual Food Consumption: Lactation

20248897

Comments and Markers

Page	Measurement	Group	Sex	Subject	Day	Type	Marker
	Food Mean Daily Consumption	1	Female	5520	1 - 3	Quality Flag	E (Exclude)

Comment: No Surviving Pups, Unscheduled Sacrificed

Appendix 18

Individual Food Consumption: Lactation

20248897

Key Page

Quality Flags

Symbol	IES Status	Description
E	Excluded	Exclude

Measurement Descriptions

Headings Used	Description
Food Mean Daily Consumption	Food Mean Consumption per Animal

Measurement/Statistics

Measurement	Descriptive
Food Mean Daily Consumption	Mean
	Standard Deviation
	Count

Group Information

Short Name	Long Name	Type	Report Headings 1-4		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Comment Abbreviations

FC = Flag Comment

Appendix 19

Individual Estrous Cycles: Precohabitation

20248897

Sex: Female Day(s) Relative to Pairing (Litter: A)

0 ug/dose Group 1	Number of Cycles	Mean Length (Days)	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start
	-13 → 0	-13 → 0	-13	-12	-11	-10	-9	-8
5501	1	11.0	D	P	/E	D	D	D
5502	2	4.0	D	D	P	/E	D	D
5503	2	4.5	E	D	D	P	/E	D
5504	2	4.0	D	D	P	/E	D	D
5505	2	4.0	D	P	/E	D	D	P
5506	3	4.0	P	/E	D	D	P	/E
5507	3	3.7	D	D	P	/E	D	D
5508	2	4.0	E	D	D	P	/E	D
5509	2	4.0	D	P	/E	D	D	P
5510	2	4.5	P	/E	E	D	D	P
5511	2	4.0	D	P	/E	D	D	P
5512	2	4.0	D	D	/E	D	D	P
5513	2	4.0	D	P	/E	D	D	P
5514	2	4.0	E	E	M	D	D	D
5515	2	4.0	E	D	D	P	/E	D
5516	2	4.0	D	P	/E	D	D	D

E - Estrus; M - Metestrus; D - Diestrus; P - Proestrus
/ - Denotes the Start of Estrous Cycle

Appendix 19

Individual Estrous Cycles: Precohabitation

20248897

Sex: Female Day(s) Relative to Pairing (Litter: A)

0 ug/dose Group 1	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start
	-7	-6	-5	-4	-3	-2	-1	0
5501	D	D	D	D	D	D	D	P
5502	D	/E	D	D	P	E	D	D
5503	D	D	/E	E	D	D	D	E
5504	P	/E	D	D	P	E	D	D
5505	/E	D	D	P	E	D	D	P
5506	D	D	D	/E	D	D	P	E
5507	P	/E	D	D	P	/E	E	D
5508	D	D	/E	E	D	D	E	D
5509	/E	D	D	P	E	D	D	P
5510	/E	D	D	P	E	D	D	P
5511	/E	D	D	P	E	D	D	P
5512	/E	D	D	P	E	D	D	P
5513	/E	D	D	P	E	D	D	P
5514	/E	E	D	P	/E	D	D	P
5515	D	P	/E	D	D	P	E	D
5516	/E	D	D	P	E	D	D	P

E - Estrus; M - Metestrus; D - Diestrus; P - Proestrus
/ - Denotes the Start of Estrous Cycle

Appendix 19

Individual Estrous Cycles: Precohabitation

20248897

Sex: Female Day(s) Relative to Pairing (Litter: A)

0 ug/dose Group 1	Number of Cycles	Mean Length (Days)	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start
	-13 → 0	-13 → 0	-13	-12	-11	-10	-9	-8
5517	2	4.0	D	D	P	/E	D	D
5518	2	4.0	E	D	D	P	/E	D
5519	3	4.0	P	/E	D	D	P	/E
5520	3	3.7	D	D	P	/E	D	D
5521	2	4.0	E	D	D	P	/E	D
5522	2	4.0	D	D	P	/E	D	D
5523	2	4.0	D	P	/E	D	D	P
5524	2	4.0	E	E	D	D	D	D
5525	2	4.0	E	D	D	P	/E	D
5526	2	4.0	D	D	D	P	/E	D
5527	2	4.0	D	P	/E	D	D	D
5528	3	4.0	P	/E	D	D	P	/E
5529	3	4.0	P	/E	D	D	P	/E
5530	2	4.0	D	D	P	/E	D	D
5531	3	3.7	D	D	P	/E	D	D
5532	1	9.0	D	P	/E	E	D	D

E - Estrus; M - Metestrus; D - Diestrus; P - Proestrus
/ - Denotes the Start of Estrous Cycle

Appendix 19

Individual Estrous Cycles: Precohabitation

20248897

Sex: Female Day(s) Relative to Pairing (Litter: A)

0 ug/dose Group 1	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start
	-7	-6	-5	-4	-3	-2	-1	0
5517	D	/E	D	D	P	E	D	D
5518	D	P	/E	D	D	P	E	D
5519	D	D	P	/E	D	D	P	E
5520	P	/E	D	D	P	/E	D	D
5521	D	D	/E	D	D	D	E	D
5522	/P	D	D	D	P	E	D	D
5523	/E	D	D	P	E	D	D	P
5524	/E	D	D	P	P	/E	D	D
5525	D	D	/E	D	D	P	E	D
5526	D	D	/E	D	D	D	E	D
5527	/E	D	D	P	E	D	D	P
5528	D	D	P	/E	D	D	P	E
5529	D	D	D	/E	D	D	P	E
5530	P	/E	D	D	P	E	D	D
5531	/E	D	D	D	P	/E	D	D
5532	D	D	D	D	P	E	M	D

E - Estrus; M - Metestrus; D - Diestrus; P - Proestrus
/ - Denotes the Start of Estrous Cycle

Appendix 19

Individual Estrous Cycles: Precohabitation

20248897

Sex: Female Day(s) Relative to Pairing (Litter: A)

0 ug/dose Group 1	Number of Cycles	Mean Length (Days)	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start
	-13 → 0	-13 → 0	-13	-12	-11	-10	-9	-8
5533	2	4.0	D	P	/E	D	D	P
5534	2	4.0	D	P	/E	D	D	P
5535	2	4.0	D	P	/E	D	D	P
5536	2	4.0	M	D	D	P	/E	D
5537	2	4.0	D	P	/E	D	D	D
5538	2	4.0	D	P	/E	D	D	P
5539	1	3.0	P	D	D	D	D	/E
5540	2	4.5	D	P	/E	E	D	D
5541	2	4.0	D	P	/E	D	D	D
5542	2	4.0	D	P	/E	D	D	D
5543	3	4.0	P	/E	D	D	P	/E
5544	2	5.0	D	D	P	/E	D	D
Mean	2.1	4.28	-	-	-	-	-	-
SD	0.5	1.31	-	-	-	-	-	-
N	44	44	-	-	-	-	-	-

E - Estrus; M - Metestrus; D - Diestrus; P - Proestrus
/ - Denotes the Start of Estrous Cycle

Appendix 19

Individual Estrous Cycles: Precohabitation

20248897

Sex: Female Day(s) Relative to Pairing (Litter: A)

0 ug/dose Group 1	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start
	-7	-6	-5	-4	-3	-2	-1	0
5533	/E	D	D	P	E	D	D	P
5534	/E	D	D	P	E	D	D	P
5535	/E	D	D	P	E	D	D	P
5536	D	P	/E	E	D	P	E	M
5537	/E	D	D	P	E	D	D	P
5538	/E	D	D	P	E	D	D	P
5539	D	D	E	D	D	D	D	P
5540	D	D	/E	D	D	E	E	M
5541	/E	D	D	P	E	D	D	P
5542	/E	D	D	P	E	D	D	P
5543	D	D	D	/E	D	D	P	E
5544	D	D	P	/E	D	D	P	E
Mean	-	-	-	-	-	-	-	-
SD	-	-	-	-	-	-	-	-
N	-	-	-	-	-	-	-	-

E - Estrus; M - Metestrus; D - Diestrus; P - Proestrus
/ - Denotes the Start of Estrous Cycle

Appendix 19

Individual Estrous Cycles: Precohabitation

20248897

Sex: Female Day(s) Relative to Pairing (Litter: A)

100 ug/dose Group 2	Number of Cycles	Mean Length (Days)	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start
	-13 → 0	-13 → 0	-13	-12	-11	-10	-9	-8
5545	3	3.7	D	P	/E	E	D	D
5546	2	4.0	D	D	D	P	/E	D
5547	2	5.0	D	P	/E	E	D	D
5548	2	4.0	D	P	/E	D	D	P
5549	2	4.0	D	P	/E	D	D	P
5550	-	-	D	D	P	E	D	D
5551	3	4.0	P	/E	D	D	P	/E
5552	1	5.0	E	D	D	P	/E	E
5553	2	4.0	E	E	D	D	P	/E
5554	2	3.5	D	P	/E	D	D	P
5555	2	4.0	E	D	D	P	/E	D
5556	2	5.0	E	D	D	/E	E	D
5557	2	4.5	D	D	P	/E	E	D
5558	3	4.0	D	/E	D	D	P	/E
5559	1	6.0	E	D	P	/E	D	D
5560	3	4.0	P	/E	D	D	P	/E

E - Estrus; M - Metestrus; D - Diestrus; P - Proestrus
/ - Denotes the Start of Estrous Cycle

Appendix 19

Individual Estrous Cycles: Precohabitation

20248897

Sex: Female Day(s) Relative to Pairing (Litter: A)

100 ug/dose Group 2	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start
	-7	-6	-5	-4	-3	-2	-1	0
5545	/E	E	D	/E	E	D	D	E
5546	D	D	/E	D	D	P	E	D
5547	D	P	/E	D	D	P	E	D
5548	/E	D	D	P	E	D	D	P
5549	/E	D	D	P	E	D	D	P
5550	D	D	D	D	D	D	D	D
5551	D	D	D	/E	D	D	P	E
5552	D	D	P	E	M	D	D	P
5553	D	D	D	/E	D	D	D	E
5554	/E	D	D	P	D	D	D	P
5555	D	/P	D	D	D	P	E	D
5556	D	D	D	P	/E	D	P	E
5557	D	P	/E	D	D	P	E	D
5558	D	D	P	/E	D	D	P	E
5559	D	D	D	E	E	D	D	P
5560	D	D	P	/E	D	D	P	E

E - Estrus; M - Metestrus; D - Diestrus; P - Proestrus
/ - Denotes the Start of Estrous Cycle

Appendix 19

Individual Estrous Cycles: Precohabitation

20248897

Sex: Female Day(s) Relative to Pairing (Litter: A)

100 ug/dose Group 2	Number of Cycles	Mean Length (Days)	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start
	-13 → 0	-13 → 0	-13	-12	-11	-10	-9	-8
5561	2	4.5	D	P	/E	E	D	D
5562	2	5.5	D	P	/E	D	P	/E
5563	1	8.0	D	D	D	P	/E	D
5564	1	7.0	D	D	/E	E	M	D
5565	2	5.5	D	D	P	/E	D	D
5566	2	4.0	D	P	/E	D	D	P
5567	2	4.5	D	D	P	/E	E	D
5568	2	4.0	D	P	/E	D	D	D
5569	3	3.0	D	D	P	/E	E	D
5570	2	4.5	D	/E	E	D	D	D
5571	3	4.0	P	/E	D	D	P	/E
5572	2	4.5	E	D	D	P	/E	E
5573	2	4.5	D	D	P	/E	E	D
5574	1	8.0	D	P	/E	E	D	D
5575	2	4.0	D	P	/E	D	D	/P
5576	2	4.0	E	E	D	D	P	/E

E - Estrus; M - Metestrus; D - Diestrus; P - Proestrus
/ - Denotes the Start of Estrous Cycle

Appendix 19

Individual Estrous Cycles: Precohabitation

20248897

Sex: Female Day(s) Relative to Pairing (Litter: A)

100 ug/dose Group 2	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start
	-7	-6	-5	-4	-3	-2	-1	0
5561	D	/E	D	D	P	E	D	D
5562	D	D	D	D	D	D	P	E
5563	D	D	D	D	D	P	E	D
5564	D	D	D	E	D	D	D	P
5565	D	D	D	P	P	/E	E	D
5566	/E	D	D	P	E	D	D	P
5567	D	D	D	/P	D	P	E	M
5568	/E	D	D	D	E	D	D	P
5569	D	/P	D	/E	D	D	E	D
5570	/E	D	D	P	E	M	D	P
5571	D	D	P	/E	D	D	P	E
5572	D	D	D	/P	D	D	P	E
5573	D	/E	E	D	D	P	E	D
5574	D	D	D	P	E	D	D	P
5575	D	D	D	P	E	D	D	P
5576	D	D	D	/E	D	D	P	E

E - Estrus; M - Metestrus; D - Diestrus; P - Proestrus
/ - Denotes the Start of Estrous Cycle

Appendix 19

Individual Estrous Cycles: Precohabitation

20248897

Sex: Female Day(s) Relative to Pairing (Litter: A)

100 ug/dose Group 2	Number of Cycles	Mean Length (Days)	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start
	-13 → 0	-13 → 0	-13	-12	-11	-10	-9	-8
5577	2	4.0	P	/E	D	D	D	/E
5578	2	4.0	D	P	/E	D	D	D
5579	1	4.0	D	D	D	P	/E	D
5580	2	4.0	D	D	D	P	/E	D
5581	2	5.0	D	P	/E	E	D	D
5582	2	4.5	E	D	D	P	/E	E
5583	2	4.0	D	P	/E	D	D	D
5584	2	4.0	D	P	/E	D	D	P
5585	2	4.0	D	D	P	/E	D	D
5586	2	4.5	D	D	P	/E	D	D
5587	2	4.5	D	P	/E	E	D	D
5588	2	4.0	D	D	D	P	/E	D
Mean	2.0	4.53	-	-	-	-	-	-
SD	0.5	1.04	-	-	-	-	-	-
N	43	43	-	-	-	-	-	-

E - Estrus; M - Metestrus; D - Diestrus; P - Proestrus
/ - Denotes the Start of Estrous Cycle

Appendix 19

Individual Estrous Cycles: Precohabitation

20248897

Sex: Female Day(s) Relative to Pairing (Litter: A)

100 ug/dose Group 2	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start	Estrus Stage Cycle Start
	-7	-6	-5	-4	-3	-2	-1	0
5577	E	D	D	E	E	M	D	D
5578	/E	D	D	P	E	M	D	D
5579	D	D	E	D	D	D	D	D
5580	D	D	D	/E	D	P	E	D
5581	D	P	/E	D	D	D	E	D
5582	D	D	D	/E	D	D	D	E
5583	/E	D	D	P	E	D	D	P
5584	/E	D	D	P	E	M	D	P
5585	P	/E	E	D	P	E	M	D
5586	D	/P	D	D	D	P	E	D
5587	D	/E	D	D	P	E	E	D
5588	D	P	/E	D	D	P	E	D
Mean	-	-	-	-	-	-	-	-
SD	-	-	-	-	-	-	-	-
N	-	-	-	-	-	-	-	-

E - Estrus; M - Metestrus; D - Diestrus; P - Proestrus
/ - Denotes the Start of Estrous Cycle

Appendix 19

Individual Estrous Cycles: Precohabitation

20248897

Key Page

General Footnotes

E - Estrus; M - Metestrus; D - Diestrus; P - Proestrus
/ - Denotes the Start of Estrous Cycle

Measurement Descriptions

Headings Used	Description
Number of Cycles	Number of Cycles
Mean Length	Mean of Cycle Lengths
Estrus Stage Cycle Start	Estrus Stage with Cycle Start

Unit Descriptions

Headings Used	Description
Days	DAYS

Measurement/Statistics

Measurement	Descriptive
Number of Cycles	Mean
	Standard Deviation
	Count
Mean Length	Mean
	Standard Deviation
	Count

Appendix 19

Individual Estrous Cycles: Precohabitation

20248897

Key Page

Group Information

Short Name	Long Name	Type	Report Headings 1-4		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Appendix 20

Individual Estrous Cycles: Pairing

20248897

Sex: Female Estrous Cycles plus Outcome.

0 ug/dose Group 1	Day(s) Relative to Pairing (Litter: A)						
	1	2	3	4	5	6	7
5501	D	D	P	1	-	-	-
5502	P	+	-	-	-	-	-
5503	+	-	-	-	-	-	-
5504	D	1	-	-	-	-	-
5505	1	-	-	-	-	-	-
5506	D	D	P	1	-	-	-
5507	E	+	-	-	-	-	-
5508	D	D	1	-	-	-	-
5509	+	-	-	-	-	-	-
5510	1	-	-	-	-	-	-
5511	+	-	-	-	-	-	-
5512	1	-	-	-	-	-	-
5513	1	-	-	-	-	-	-
5514	E	D	D	P	1	-	-
5515	D	P	1	-	-	-	-
5516	1	-	-	-	-	-	-
5517	P	1	-	-	-	-	-
5518	D	P	1	-	-	-	-

E - Estrus; M - Metestrus; D - Diestrus; P - Proestrus
/ - Denotes the Start of Estrous Cycle
+ Sperm +ve; 1 - Plug in animal; 2 - Plug in cage; 3 - Plug in animal and cage

Appendix 20

Individual Estrous Cycles: Pairing

20248897

Sex: Female Estrous Cycles plus Outcome.

0 ug/dose Group 1	Day(s) Relative to Pairing (Litter: A)						
	1	2	3	4	5	6	7
5519	D	D	P	1	-	-	-
5520	E	+	-	-	-	-	-
5521	D	P	1	-	-	-	-
5522	P	+	-	-	-	-	-
5523	+	-	-	-	-	-	-
5524	E	+	-	-	-	-	-
5525	D	P	1	-	-	-	-
5526	D	D	+	-	-	-	-
5527	1	-	-	-	-	-	-
5528	D	D	P	1	-	-	-
5529	D	D	P	1	-	-	-
5530	P	1	-	-	-	-	-
5531	E	1	-	-	-	-	-
5532	D	+	-	-	-	-	-
5533	1	-	-	-	-	-	-
5534	1	-	-	-	-	-	-
5535	1	-	-	-	-	-	-
5536	D	P	1	-	-	-	-

E - Estrus; M - Metestrus; D - Diestrus; P - Proestrus
/ - Denotes the Start of Estrous Cycle
+ Sperm +ve; 1 - Plug in animal; 2 - Plug in cage; 3 - Plug in animal and cage

Appendix 20

Individual Estrous Cycles: Pairing

20248897

Sex: Female Estrous Cycles plus Outcome.

0 ug/dose	Day(s) Relative to Pairing (Litter: A)						
Group 1	1	2	3	4	5	6	7
5537	1	-	-	-	-	-	-
5538	1	-	-	-	-	-	-
5539 NM	D	D	D	D	D	D	D
5540	D	D	D	P	1	-	-
5541	1	-	-	-	-	-	-
5542	1	-	-	-	-	-	-
5543 NM	D	D	D	D	D	D	D
5544	D	D	D	D	P	1	-

E - Estrus; M - Metestrus; D - Diestrus; P - Proestrus
/ - Denotes the Start of Estrous Cycle
+ Sperm +ve; 1 - Plug in animal; 2 - Plug in cage; 3 - Plug in animal and cage

Appendix 20

Individual Estrous Cycles: Pairing

20248897

Sex: Female Estrous Cycles plus Outcome.

100 ug/dose Group 2	Day(s) Relative to Pairing (Litter: A)						
	1	2	3	4	5	6	7
5545	1	-	-	-	-	-	-
5546	D	P	1	-	-	-	-
5547	D	P	1	-	-	-	-
5548	1	-	-	-	-	-	-
5549	+	-	-	-	-	-	-
5550	D	1	-	-	-	-	-
5551 NM	D	D	D	D	D	D	D
5552	1	-	-	-	-	-	-
5553 NM	D	D	D	D	D	D	D
5554	1	-	-	-	-	-	-
5555	D	P	1	-	-	-	-
5556	D	D	P	1	-	-	-
5557	D	P	+	-	-	-	-
5558 NM	D	D	D	D	D	D	D
5559	+	-	-	-	-	-	-
5560	D	D	P	1	-	-	-
5561	D	+	-	-	-	-	-
5562 NM	D	D	D	D	D	D	D

E - Estrus; M - Metestrus; D - Diestrus; P - Proestrus
/ - Denotes the Start of Estrous Cycle
+ Sperm +ve; 1 - Plug in animal; 2 - Plug in cage; 3 - Plug in animal and cage

Appendix 20

Individual Estrous Cycles: Pairing

20248897

Sex: Female Estrous Cycles plus Outcome.

100 ug/dose Group 2	Day(s) Relative to Pairing (Litter: A)						
	1	2	3	4	5	6	7
5563	D	P	1	-	-	-	-
5564	1	-	-	-	-	-	-
5565	E	+	-	-	-	-	-
5566	+	-	-	-	-	-	-
5567	D	P	1	-	-	-	-
5568	1	-	-	-	-	-	-
5569	D	P	1	-	-	-	-
5570	1	-	-	-	-	-	-
5571	D	D	P	1	-	-	-
5572	1	-	-	-	-	-	-
5573	D	P	1	-	-	-	-
5574	1	-	-	-	-	-	-
5575	1	-	-	-	-	-	-
5576 NM	D	D	D	D	D	D	D
5577	1	-	-	-	-	-	-
5578	1	-	-	-	-	-	-
5579	D	P	1	-	-	-	-
5580	D	P	1	-	-	-	-

E - Estrus; M - Metestrus; D - Diestrus; P - Proestrus
/ - Denotes the Start of Estrous Cycle
+ Sperm +ve; 1 - Plug in animal; 2 - Plug in cage; 3 - Plug in animal and cage

Appendix 20

Individual Estrous Cycles: Pairing

20248897

Sex: Female Estrous Cycles plus Outcome.

100 ug/dose Group 2	Day(s) Relative to Pairing (Litter: A)						
	1	2	3	4	5	6	7
5581	D	D	1	-	-	-	-
5582	D	D	D	1	-	-	-
5583	1	-	-	-	-	-	-
5584	+	-	-	-	-	-	-
5585	P	1	-	-	-	-	-
5586	D	P	1	-	-	-	-
5587	D	P	1	-	-	-	-
5588	D	P	1	-	-	-	-

E - Estrus; M - Metestrus; D - Diestrus; P - Proestrus
/ - Denotes the Start of Estrous Cycle
+ Sperm +ve; 1 - Plug in animal; 2 - Plug in cage; 3 - Plug in animal and cage

Appendix 20

Individual Estrous Cycles: Pairing

20248897

Subject Comments/Exclusions

Subject	Marker	Comment/Exclusion
5539	NM	No Mating Date
5543	NM	No Mating Date
5551	NM	No Mating Date
5553	NM	No Mating Date
5558	NM	No Mating Date
5562	NM	No Mating Date
5576	NM	No Mating Date

Appendix 20

Individual Estrous Cycles: Pairing

20248897

Key Page

General Footnotes

E - Estrus; M - Metestrus; D - Diestrus; P - Proestrus
/ - Denotes the Start of Estrous Cycle
+ Sperm +ve; 1 - Plug in animal; 2 - Plug in cage; 3 - Plug in animal and cage

Measurement Descriptions

Headings Used	Description
Estrous Cycles plus Outcome.	Stage of Estrous with Start plus Outcome & Estrous

Group Information

Short Name	Long Name	Type	Report Headings 1-4		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Appendix 21

Individual Reproductive Performance

20248897

Sex: Female Day(s) Relative to Pairing (Litter: A)

0 ug/dose Group 1	1st Pairing Date	Confirmed Mating Date	Pre-coital Interval (Days)	Pregnancy Type
	-	-	-	-
5501	27-Jul-2020	31-Jul-2020	4	Pregnant
5502	27-Jul-2020	29-Jul-2020	2	Pregnant
5503	27-Jul-2020	28-Jul-2020	1	Pregnant
5504	27-Jul-2020	29-Jul-2020	2	Pregnant
5505	27-Jul-2020	28-Jul-2020	1	Pregnant
5506	27-Jul-2020	31-Jul-2020	4	Pregnant
5507	27-Jul-2020	29-Jul-2020	2	Pregnant
5508	27-Jul-2020	30-Jul-2020	3	Pregnant
5509	27-Jul-2020	28-Jul-2020	1	Pregnant
5510	27-Jul-2020	28-Jul-2020	1	Pregnant
5511	27-Jul-2020	28-Jul-2020	1	Pregnant
5512	27-Jul-2020	28-Jul-2020	1	Pregnant
5513	27-Jul-2020	28-Jul-2020	1	Pregnant
5514	27-Jul-2020	01-Aug-2020	5	-
5515	27-Jul-2020	30-Jul-2020	3	Pregnant
5516	27-Jul-2020	28-Jul-2020	1	Pregnant

Appendix 21

Individual Reproductive Performance

20248897

Sex: Female Day(s) Relative to Pairing (Litter: A)

0 ug/dose Group 1	1st Pairing Date	Confirmed Mating Date	Pre-coital Interval (Days)	Pregnancy Type
	-	-	-	-
5517	27-Jul-2020	29-Jul-2020	2	Not Pregnant [a]
5518	27-Jul-2020	30-Jul-2020	3	Pregnant
5519	27-Jul-2020	31-Jul-2020	4	Pregnant
5520	27-Jul-2020	29-Jul-2020	2	-
5521	27-Jul-2020	30-Jul-2020	3	Pregnant
5522	27-Jul-2020	29-Jul-2020	2	Pregnant
5523	27-Jul-2020	28-Jul-2020	1	Pregnant
5524	27-Jul-2020	29-Jul-2020	2	-
5525	27-Jul-2020	30-Jul-2020	3	-
5526	27-Jul-2020	30-Jul-2020	3	-
5527	27-Jul-2020	28-Jul-2020	1	-
5528	27-Jul-2020	31-Jul-2020	4	Pregnant
5529	27-Jul-2020	31-Jul-2020	4	-
5530	27-Jul-2020	29-Jul-2020	2	-
5531	27-Jul-2020	29-Jul-2020	2	-
5532	27-Jul-2020	29-Jul-2020	2	-

[a] [RC:Uterus pressed between glass plates. No implantation sites present.]

Appendix 21

Individual Reproductive Performance

20248897

Sex: Female Day(s) Relative to Pairing (Litter: A)

0 ug/dose Group 1	1st Pairing Date	Confirmed Mating Date	Pre-coital Interval (Days)	Pregnancy Type
	-	-	-	-
5533	27-Jul-2020	28-Jul-2020	1	-
5534	27-Jul-2020	28-Jul-2020	1	-
5535	27-Jul-2020	28-Jul-2020	1	-
5536	27-Jul-2020	30-Jul-2020	3	-
5537	27-Jul-2020	28-Jul-2020	1	-
5538	27-Jul-2020	28-Jul-2020	1	-
5539 NM	27-Jul-2020	-	-	Not Pregnant [a]
5540	27-Jul-2020	01-Aug-2020	5	-
5541	27-Jul-2020	28-Jul-2020	1	-
5542	27-Jul-2020	28-Jul-2020	1	-
5543 NM	27-Jul-2020	-	-	Not Pregnant [a]
5544	27-Jul-2020	02-Aug-2020	6	-

[a] [RC:Uterus pressed between glass plates. No implantation sites present.]

Appendix 21
Individual Reproductive Performance

20248897

Sex: Female Day(s) Relative to Pairing (Litter: A)

100 ug/dose Group 2	1st Pairing Date	Confirmed Mating Date	Pre-coital Interval (Days)	Pregnancy Type
	-	-	-	-
5545	27-Jul-2020	28-Jul-2020	1	Pregnant
5546	27-Jul-2020	30-Jul-2020	3	Pregnant
5547	27-Jul-2020	30-Jul-2020	3	Pregnant
5548	27-Jul-2020	28-Jul-2020	1	Pregnant
5549	27-Jul-2020	28-Jul-2020	1	Pregnant
5550	27-Jul-2020	29-Jul-2020	2	Pregnant
5551 NM	27-Jul-2020	-	-	Not Pregnant [a]
5552	27-Jul-2020	28-Jul-2020	1	Pregnant
5553 NM	27-Jul-2020	-	-	Not Pregnant [a]
5554	27-Jul-2020	28-Jul-2020	1	Pregnant
5555	27-Jul-2020	30-Jul-2020	3	Pregnant
5556	27-Jul-2020	31-Jul-2020	4	Pregnant
5557	27-Jul-2020	30-Jul-2020	3	Pregnant
5558 NM	27-Jul-2020	-	-	Not Pregnant [a]
5559	27-Jul-2020	28-Jul-2020	1	Pregnant
5560	27-Jul-2020	31-Jul-2020	4	Pregnant

[a] [RC:Uterus pressed between glass plates. No implantation sites present.]

Appendix 21
Individual Reproductive Performance

20248897

Sex: Female Day(s) Relative to Pairing (Litter: A)

100 ug/dose Group 2	1st Pairing Date	Confirmed Mating Date	Pre-coital Interval (Days)	Pregnancy Type
	-	-	-	-
5561	27-Jul-2020	29-Jul-2020	2	Pregnant
5562 NM	27-Jul-2020	-	-	Not Pregnant [a]
5563	27-Jul-2020	30-Jul-2020	3	Pregnant
5564	27-Jul-2020	28-Jul-2020	1	Pregnant
5565	27-Jul-2020	29-Jul-2020	2	Pregnant
5566	27-Jul-2020	28-Jul-2020	1	Pregnant
5567	27-Jul-2020	30-Jul-2020	3	Pregnant
5568	27-Jul-2020	28-Jul-2020	1	Pregnant
5569	27-Jul-2020	30-Jul-2020	3	Pregnant
5570	27-Jul-2020	28-Jul-2020	1	Pregnant
5571	27-Jul-2020	31-Jul-2020	4	-
5572	27-Jul-2020	28-Jul-2020	1	Not Pregnant [a]
5573	27-Jul-2020	30-Jul-2020	3	-
5574	27-Jul-2020	28-Jul-2020	1	-
5575	27-Jul-2020	28-Jul-2020	1	-
5576 NM	27-Jul-2020	-	-	Not Pregnant [a]

[a] [RC:Uterus pressed between glass plates. No implantation sites present.]

Appendix 21

Individual Reproductive Performance

20248897

Sex: Female Day(s) Relative to Pairing (Litter: A)

100 ug/dose Group 2	1st Pairing Date	Confirmed Mating Date	Pre-coital Interval (Days)	Pregnancy Type
	-	-	-	-
5577	27-Jul-2020	28-Jul-2020	1	-
5578	27-Jul-2020	28-Jul-2020	1	Not Pregnant [a]
5579	27-Jul-2020	30-Jul-2020	3	-
5580	27-Jul-2020	30-Jul-2020	3	-
5581	27-Jul-2020	30-Jul-2020	3	-
5582	27-Jul-2020	31-Jul-2020	4	-
5583	27-Jul-2020	28-Jul-2020	1	-
5584	27-Jul-2020	28-Jul-2020	1	-
5585	27-Jul-2020	29-Jul-2020	2	-
5586	27-Jul-2020	30-Jul-2020	3	-
5587	27-Jul-2020	30-Jul-2020	3	-
5588	27-Jul-2020	30-Jul-2020	3	-

[a] [RC:Uterus pressed between glass plates. No implantation sites present.]

Appendix 21
Individual Reproductive Performance

20248897

Comments and Markers

Page	Day	Group	Sex	Subject	Measurement	Type	Marker
	-	1	Female	5517	Pregnancy Type	Result	
			Comment: Uterus pressed between glass plates. No implantation sites present.				
	-	1	Female	5539	Pregnancy Type	Result	
			Comment: Uterus pressed between glass plates. No implantation sites present.				
	-	1	Female	5543	Pregnancy Type	Result	
			Comment: Uterus pressed between glass plates. No implantation sites present.				
	-	2	Female	5551	Pregnancy Type	Result	
			Comment: Uterus pressed between glass plates. No implantation sites present.				
	-	2	Female	5553	Pregnancy Type	Result	
			Comment: Uterus pressed between glass plates. No implantation sites present.				
	-	2	Female	5558	Pregnancy Type	Result	
			Comment: Uterus pressed between glass plates. No implantation sites present.				
	-	2	Female	5562	Pregnancy Type	Result	
			Comment: Uterus pressed between glass plates. No implantation sites present.				
	-	2	Female	5572	Pregnancy Type	Result	
			Comment: Uterus pressed between glass plates. No implantation sites present.				
	-	2	Female	5576	Pregnancy Type	Result	
			Comment: Uterus pressed between glass plates. No implantation sites present.				
	-	2	Female	5578	Pregnancy Type	Result	
			Comment: Uterus pressed between glass plates. No implantation sites present.				

Appendix 21

Individual Reproductive Performance

20248897

Subject Comments/Exclusions

Subject	Marker	Comment/Exclusion
5539	NM	No Mating Date
5543	NM	No Mating Date
5551	NM	No Mating Date
5553	NM	No Mating Date
5558	NM	No Mating Date
5562	NM	No Mating Date
5576	NM	No Mating Date

Appendix 21
Individual Reproductive Performance

20248897

Key Page

Measurement Descriptions

Headings Used	Description
1st Pairing Date	1st Pairing Date
Confirmed Mating Date	Confirmed Mating Date
Pre-coital Interval	Pre-coital Interval (All Pairings)
Pregnancy Type	Pregnancy Type

Unit Descriptions

Headings Used	Description
Days	DAYS

Time-Points/Ranges

Measurement	From	To	Report As
1st Pairing Date	-9,999	9,999	-
Confirmed Mating Date	-9,999	9,999	-
Pre-coital Interval	-9,999	9,999	-
Pregnancy Type	-9,999	9,999	-

Group Information

Short Name	Long Name	Type	Report Headings 1-4		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Comment Abbreviations

RC = Result Comment

Appendix 22
Individual Maternal Performance

20248897

Sex: Female Day(s) Relative to Mating (Litter: A)

0 ug/dose Group 1	Pregnancy Type	Female with Live Fetuses	Female with Resorptions	Fem w/all Nonviable	Path Removal Reason
	-	-	-	-	-
5501	Pregnant	Yes	No	No	TERM
5502	Pregnant	Yes	Yes	No	TERM
5503	Pregnant	Yes	No	No	TERM
5504	Pregnant	Yes	No	No	TERM
5505	Pregnant	Yes	No	No	TERM
5506	Pregnant	Yes	No	No	TERM
5507	Pregnant	Yes	Yes	No	TERM
5508	Pregnant	Yes	No	No	TERM
5509	Pregnant	Yes	Yes	No	TERM
5510	Pregnant	Yes	Yes	No	TERM
5511	Pregnant	Yes	Yes	No	TERM
5512	Pregnant	Yes	No	No	TERM
5513	Pregnant	Yes	No	No	TERM
5515	Pregnant	Yes	No	No	TERM
5516	Pregnant	Yes	No	No	TERM
5517	Not Pregnant [a]	-	-	-	TERM

[a] [RC:Uterus pressed between glass plates. No implantation sites present.]

Appendix 22

Individual Maternal Performance

20248897

Sex: Female Day(s) Relative to Mating (Litter: A)

0 ug/dose Group 1	Pregnancy Type	Female with Live Fetuses	Female with Resorptions	Fem w/all Nonviable	Path Removal Reason
	-	-	-	-	-
5518	Pregnant	Yes	No	No	TERM
5519	Pregnant	Yes	Yes	No	TERM
5521	Pregnant	Yes	No	No	TERM
5522	Pregnant	Yes	No	No	TERM
5523	Pregnant	Yes	No	No	TERM
5528	Pregnant	Yes	No	No	TERM

Appendix 22

Individual Maternal Performance

20248897

Sex: Female Day(s) Relative to Mating (Litter: A)

100 ug/dose Group 2	Pregnancy Type	Female with Live Fetuses	Female with Resorptions	Fem w/all Nonviable	Path Removal Reason
	-	-	-	-	-
5545	Pregnant	Yes	Yes	No	TERM
5546	Pregnant	Yes	Yes	No	TERM
5547	Pregnant	Yes	No	No	TERM
5548	Pregnant	Yes	No	No	TERM
5549	Pregnant	Yes	No	No	TERM
5550	Pregnant	Yes	Yes	No	TERM
5552	Pregnant	Yes	No	No	TERM
5554	Pregnant	Yes	Yes	No	TERM
5555	Pregnant	Yes	No	No	TERM
5556	Pregnant	Yes	Yes	No	TERM
5557	Pregnant	Yes	Yes	No	TERM
5559	Pregnant	Yes	Yes	No	TERM
5560	Pregnant	Yes	Yes	No	TERM
5561	Pregnant	Yes	No	No	TERM
5563	Pregnant	Yes	No	No	TERM
5564	Pregnant	Yes	No	No	TERM

Appendix 22

Individual Maternal Performance

20248897

Sex: Female Day(s) Relative to Mating (Litter: A)

100 ug/dose Group 2	Pregnancy Type	Female with Live Fetuses	Female with Resorptions	Fem w/all Nonviable	Path Removal Reason
	-	-	-	-	-
5565	Pregnant	Yes	No	No	TERM
5566	Pregnant	Yes	No	No	TERM
5567	Pregnant	Yes	No	No	TERM
5568	Pregnant	Yes	No	No	TERM
5569	Pregnant	Yes	No	No	TERM
5570	Pregnant	Yes	Yes	No	TERM

Appendix 22
Individual Maternal Performance

20248897

Comments and Markers

Page	Day	Group	Sex	Subject	Measurement	Type	Marker
	-	1	Female	5517	Pregnancy Type	Result	

Comment: Uterus pressed between glass plates. No implantation sites present.

Appendix 22
Individual Maternal Performance

20248897

Key Page

Measurement Descriptions

Headings Used	Description
Pregnancy Type	Pregnancy Type
Female with Live Fetuses	Female with Live Fetuses
Female with Resorptions	Female with Resorptions
Fem w/all Nonviable	Fem. w/all Nonviable
Path Removal Reason	Path Removal Reason

Time-Points/Ranges

Measurement	From	To	Report As
Pregnancy Type	-9,999	9,999	-
Female with Live Fetuses	-9,999	9,999	-
Female with Resorptions	-9,999	9,999	-
Fem w/all Nonviable	-9,999	9,999	-
Path Removal Reason	-9,999	9,999	-

Group Information

Short Name	Long Name	Type	Report Headings 1-4		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Comment Abbreviations

RC = Result Comment

Appendix 23

Individual Ovarian and Uterine Examinations and Litter Observations

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

0 ug/dose Group 1	Number of CorporaLutea	CorporaLutea -Left	CorporaLutea -Right	Number of Implants	Implant -Left-	Implant -Right-	Pre-implant Loss (%)
5501	14	9	5	12	9	3	14.3
5502	21	11	10	17	10	7	19.0
5503	19	9	10	12	7	5	36.8
5504	14	7	7	13	6	7	7.1
5505	14	8	6	14	8	6	0.0
5506	19	10	9	17	10	7	10.5
5507	12	8	4	12	8	4	0.0
5508	19	9	10	17	7	10	10.5
5509	14	7	7	7	5	2	50.0
5510	16	8	8	12	7	5	25.0
5511	13	6	7	11	5	6	15.4
5512	16	8	8	14	8	6	12.5
5513	14	9	5	12	9	3	14.3
5515	18	10	8	17	10	7	5.6

Appendix 23

Individual Ovarian and Uterine Examinations and Litter Observations

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

0 ug/dose Group 1	Total Number Resorptions	No. of Early Resorptions	No. of Late Resorptions	Total Number of Fetuses	Live Fetuses	Live Male Fetuses	Live Female Fetuses
5501	0	0	0	12	12	7	5
5502	2	2	0	15	15	8	7
5503	0	0	0	12	12	10	2
5504	0	0	0	13	13	7	6
5505	0	0	0	14	14	6	8
5506	0	0	0	17	17	8	9
5507	3	3	0	9	9	4	5
5508	0	0	0	17	17	12	5
5509	1	1	0	6	6	2	4
5510	1	1	0	11	11	5	6
5511	1	1	0	10	10	5	5
5512	0	0	0	14	14	6	8
5513	0	0	0	12	12	6	6
5515	0	0	0	17	17	9	8

Appendix 23

Individual Ovarian and Uterine Examinations and Litter Observations

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

0 ug/dose Group 1	Dead Fetuses	Post-implant Loss (%)	Live Male Fetus/Litter (%)	Mean Fetal Weight all (g)	Mean Fetal Weight (m) (g)	Mean Fetal Weight (f) (g)	Placental Wt Live Mean (g)
5501	0	0.0	58.3	5.82	6.05	5.51	0.58
5502	0	11.8	53.3	5.70	5.75	5.65	0.55
5503	0	0.0	83.3	5.57	5.66	5.16	0.59
5504	0	0.0	53.8	6.04	6.38	5.63	0.58
5505	0	0.0	42.9	6.18	6.41	6.00	0.61
5506	0	0.0	47.1	5.38	5.58	5.20	0.51
5507	0	25.0	44.4	6.10	6.23	6.00	0.57
5508	0	0.0	70.6	5.47	5.50	5.41	0.52
5509	0	14.3	33.3	5.97	6.27	5.82	0.65
5510	0	8.3	45.5	5.89	6.09	5.73	0.56
5511	0	9.1	50.0	6.40	6.66	6.15	0.62
5512	0	0.0	42.9	5.74	5.79	5.70	0.60
5513	0	0.0	50.0	6.06	6.20	5.92	0.61
5515	0	0.0	52.9	5.57	5.77	5.34	0.50

Appendix 23

Individual Ovarian and Uterine Examinations and Litter Observations

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

0 ug/dose Group 1	Number of CorporaLutea	CorporaLutea -Left	CorporaLutea -Right	Number of Implants	Implant -Left-	Implant -Right-	Pre-implant Loss (%)
5516	17	11	6	14	8	6	17.6
5518	15	8	7	15	8	7	0.0
5519	14	7	7	14	7	7	0.0
5521	14	6	8	14	6	8	0.0
5522	16	7	9	15	6	9	6.3
5523	16	8	8	14	7	7	12.5
5528	17	8	9	15	6	9	11.8
Mean	15.8	8.3	7.5	13.7	7.5	6.2	12.82
SD	2.4	1.4	1.7	2.4	1.5	2.0	12.53
N	21	21	21	21	21	21	21

Appendix 23

Individual Ovarian and Uterine Examinations and Litter Observations

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

0 ug/dose Group 1	Total Number Resorptions	No. of Early Resorptions	No. of Late Resorptions	Total Number of Fetuses	Live Fetuses	Live Male Fetuses	Live Female Fetuses
5516	0	0	0	14	14	5	9
5518	0	0	0	15	15	7	8
5519	2	1	1	12	12	3	9
5521	0	0	0	14	14	8	6
5522	0	0	0	15	15	6	9
5523	0	0	0	14	14	6	8
5528	0	0	0	15	15	6	9
Mean	0.5	0.4	0.0	13.2	13.2	6.5	6.8
SD	0.9	0.8	0.2	2.7	2.7	2.3	2.0
N	21	21	21	21	21	21	21

Appendix 23

Individual Ovarian and Uterine Examinations and Litter Observations

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

0 ug/dose Group 1	Dead Fetuses	Post-implant Loss (%)	Live Male Fetus/Litter (%)	Mean Fetal Weight all (g)	Mean Fetal Weight (m) (g)	Mean Fetal Weight (f) (g)	Placental Wt Live Mean (g)
5516	0	0.0	35.7	5.82	5.99	5.73	0.58
5518	0	0.0	46.7	5.49	5.66	5.35	0.54
5519	0	14.3	25.0	5.61	5.90	5.51	0.54
5521	0	0.0	57.1	5.95	5.94	5.96	0.51
5522	0	0.0	40.0	5.72	5.83	5.65	0.58
5523	0	0.0	42.9	5.27	5.41	5.17	0.50
5528	0	0.0	40.0	5.88	5.87	5.88	0.62
Mean	0.0	3.94	48.37	5.793	5.949	5.642	0.567
SD	0.0	7.06	12.58	0.283	0.324	0.293	0.044
N	21	21	21	21	21	21	21

Appendix 23

Individual Ovarian and Uterine Examinations and Litter Observations

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

100 ug/dose Group 2	Number of CorporaLutea	CorporaLutea -Left	CorporaLutea -Right	Number of Implants	Implant -Left-	Implant -Right-	Pre-implant Loss (%)
5545	13	7	6	12	7	5	7.7
5546	19	7	12	17	5	12	10.5
5547	16	7	9	16	7	9	0.0
5548	19	10	9	12	5	7	36.8
5549	15	6	9	14	5	9	6.7
5550	20	10	10	18	9	9	10.0
5552	17	5	12	14	4	10	17.6
5554	16	7	9	16	7	9	0.0
5555	18	6	12	16	6	10	11.1
5556	15	7	8	15	7	8	0.0
5557	15	7	8	9	7	2	40.0
5559	17	7	10	16	6	10	5.9
5560	15	6	9	15	6	9	0.0
5561	13	7	6	13	7	6	0.0

Appendix 23

Individual Ovarian and Uterine Examinations and Litter Observations

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

100 ug/dose Group 2	Total Number Resorptions	No. of Early Resorptions	No. of Late Resorptions	Total Number of Fetuses	Live Fetuses	Live Male Fetuses	Live Female Fetuses
5545	1	1	0	11	11	7	4
5546	1	1	0	16	16	9	7
5547	0	0	0	16	16	7	9
5548	0	0	0	12	12	4	8
5549	0	0	0	14	14	8	6
5550	2	2	0	16	16	8	8
5552	0	0	0	14	14	6	8
5554	1	1	0	15	15	8	7
5555	0	0	0	16	16	10	6
5556	1	1	0	14	14	7	7
5557	1	1	0	8	8	3	5
5559	2	2	0	14	14	6	8
5560	1	1	0	14	14	8	6
5561	0	0	0	13	13	5	8

Appendix 23

Individual Ovarian and Uterine Examinations and Litter Observations

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

100 ug/dose Group 2	Dead Fetuses	Post-implant Loss (%)	Live Male Fetus/Litter (%)	Mean Fetal Weight all (g)	Mean Fetal Weight (m) (g)	Mean Fetal Weight (f) (g)	Placental Wt Live Mean (g)
5545	0	8.3	63.6	5.78	5.83	5.69	0.61
5546	0	5.9	56.3	5.88	6.01	5.70	0.59
5547	0	0.0	43.8	5.40	5.54	5.29	0.51
5548	0	0.0	33.3	5.86	5.90	5.84	0.61
5549	0	0.0	57.1	5.80	5.97	5.58	0.63
5550	0	11.1	50.0	5.78	5.97	5.58	0.47
5552	0	0.0	42.9	5.32	5.64	5.08	0.66
5554	0	6.3	53.3	6.07	6.21	5.92	0.54
5555	0	0.0	62.5	5.71	5.97	5.30	0.53
5556	0	6.7	50.0	5.53	5.57	5.49	0.59
5557	0	11.1	37.5	6.18	6.51	5.98	0.71
5559	0	12.5	42.9	6.12	6.29	6.00	0.71
5560	0	6.7	57.1	6.46	6.56	6.31	0.57
5561	0	0.0	38.5	5.45	5.63	5.34	0.55

Appendix 23

Individual Ovarian and Uterine Examinations and Litter Observations

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

100 ug/dose Group 2	Number of CorporaLutea	CorporaLutea -Left	CorporaLutea -Right	Number of Implants	Implant -Left-	Implant -Right-	Pre-implant Loss (%)
5563	19	9	10	18	8	10	5.3
5564	17	7	10	15	6	9	11.8
5565	17	10	7	15	9	6	11.8
5566	15	7	8	14	6	8	6.7
5567	15	9	6	15	9	6	0.0
5568	16	9	7	13	6	7	18.8
5569	14	8	6	14	8	6	0.0
5570	14	4	10	13	3	10	7.1
Mean	16.1	7.4	8.8	14.5	6.5	8.0	9.44
SD	2.0	1.6	1.9	2.1	1.6	2.2	10.98
N	22	22	22	22	22	22	22

Appendix 23

Individual Ovarian and Uterine Examinations and Litter Observations

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

100 ug/dose Group 2	Total Number Resorptions	No. of Early Resorptions	No. of Late Resorptions	Total Number of Fetuses	Live Fetuses	Live Male Fetuses	Live Female Fetuses
5563	0	0	0	18	18	14	4
5564	0	0	0	15	15	7	8
5565	0	0	0	15	15	3	12
5566	0	0	0	14	14	6	8
5567	0	0	0	15	15	8	7
5568	0	0	0	13	13	3	10
5569	0	0	0	14	14	8	6
5570	2	2	0	11	11	7	4
Mean	0.5	0.5	0.0	14.0	14.0	6.9	7.1
SD	0.7	0.7	0.0	2.1	2.1	2.5	1.9
N	22	22	22	22	22	22	22

Appendix 23

Individual Ovarian and Uterine Examinations and Litter Observations

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

100 ug/dose Group 2	Dead Fetuses	Post-implant Loss (%)	Live Male Fetus/Litter (%)	Mean Fetal Weight all (g)	Mean Fetal Weight (m) (g)	Mean Fetal Weight (f) (g)	Placental Wt Live Mean (g)
5563	0	0.0	77.8	5.62	5.70	5.35	0.51
5564	0	0.0	46.7	5.29	5.38	5.20	0.58
5565	0	0.0	20.0	5.78	5.85	5.76	0.59
5566	0	0.0	42.9	5.86	5.85	5.87	0.65
5567	0	0.0	53.3	5.61	5.75	5.46	0.65
5568	0	0.0	23.1	5.80	6.02	5.73	0.54
5569	0	0.0	57.1	5.48	5.66	5.23	0.56
5570	0	15.4	63.6	6.39	6.53	6.15	0.70
Mean	0.0	3.81	48.78	5.779	5.924	5.629	0.594
SD	0.0	5.13	13.59	0.319	0.328	0.332	0.067
N	22	22	22	22	22	22	22

Appendix 23

Individual Ovarian and Uterine Examinations and Litter Observations

20248897

Key Page

Measurement Descriptions

Headings Used	Description
Number of CorporaLutea	Number of Corpora Lutea
CorporaLutea -Left	Corpora Lutea - Left
CorporaLutea -Right	Corpora Lutea - Right
Number of Implants	Number of Implantations
Implant -Left-	Implantations - Left
Implant -Right-	Implantations - Right
Pre-implant Loss	Percentage Pre-implantation Loss
Total Number Resorptions	Total Number of Resorptions
No. of Early Resorptions	Number of Early Resorptions
No. of Late Resorptions	Number of Late Resorptions
Total Number of Fetuses	Total Number of Fetuses
Live Fetuses	Number of Live Fetuses
Live Male Fetuses	Number of Live Male Fetuses
Live Female Fetuses	Number of Live Female Fetuses
Dead Fetuses	Number of Dead Fetuses
Post-implant Loss	Percentage Post-implantation Loss
Live Male Fetus/Litter	Percentage Live Male Fetuses Per Litter
Mean Fetal Weight all	Mean Fetal Weight all (2 dec)
Mean Fetal Weight (m)	Mean Fetal Weight males (2 dec)
Mean Fetal Weight (f)	Mean Fetal Weight females (2 dec)
Placental Wt Live Mean	Live Mean Placental Weight

Unit Descriptions

Headings Used	Description
%	%
g	g

Appendix 23

Individual Ovarian and Uterine Examinations and Litter Observations

20248897

Key Page

Time-Points/Ranges

Measurement	From	To	Report As
Number of CorporaLutea	-9,999	9,999	-
CorporaLutea -Left	-9,999	9,999	-
CorporaLutea -Right	-9,999	9,999	-
Number of Implants	-9,999	9,999	-
Implant -Left-	-9,999	9,999	-
Implant -Right-	-9,999	9,999	-
Pre-implant Loss	-9,999	9,999	-
Total Number Resorptions	-9,999	9,999	-
No. of Early Resorptions	-9,999	9,999	-
No. of Late Resorptions	-9,999	9,999	-
Total Number of Fetuses	-9,999	9,999	-
Live Fetuses	-9,999	9,999	-
Live Male Fetuses	-9,999	9,999	-
Live Female Fetuses	-9,999	9,999	-
Dead Fetuses	-9,999	9,999	-
Post-implant Loss	-9,999	9,999	-
Live Male Fetus/Litter	-9,999	9,999	-
Mean Fetal Weight all	-9,999	9,999	-
Mean Fetal Weight (m)	-9,999	9,999	-
Mean Fetal Weight (f)	-9,999	9,999	-
Placental Wt Live Mean	-9,999	9,999	-

Measurement/Statistics

Measurement	Descriptive

Appendix 23
Individual Ovarian and Uterine Examinations and Litter Observations

20248897

Key Page

Measurement/Statistics (Continued)

Measurement	Descriptive
Number of CorporaLutea	Mean
	Standard Deviation
	Count
CorporaLutea -Left	Mean
	Standard Deviation
	Count
CorporaLutea -Right	Mean
	Standard Deviation
	Count
Number of Implants	Mean
	Standard Deviation
	Count
Implant -Left-	Mean
	Standard Deviation
	Count
Implant -Right-	Mean
	Standard Deviation
	Count
Pre-implant Loss	Mean
	Standard Deviation
	Count
Total Number Resorptions	Mean
	Standard Deviation
	Count
No. of Early Resorptions	Mean
	Standard Deviation
	Count

Appendix 23
Individual Ovarian and Uterine Examinations and Litter Observations

20248897

Key Page

Measurement/Statistics (Continued)

Measurement	Descriptive
No. of Late Resorptions	Mean
	Standard Deviation
	Count
Total Number of Fetuses	Mean
	Standard Deviation
	Count
Live Fetuses	Mean
	Standard Deviation
	Count
Live Male Fetuses	Mean
	Standard Deviation
	Count
Live Female Fetuses	Mean
	Standard Deviation
	Count
Dead Fetuses	Mean
	Standard Deviation
	Count
Post-implant Loss	Mean
	Standard Deviation
	Count
Live Male Fetus/Litter	Mean
	Standard Deviation
	Count
Mean Fetal Weight all	Mean
	Standard Deviation
	Count

Appendix 23
Individual Ovarian and Uterine Examinations and Litter Observations

20248897

Key Page

Measurement/Statistics (Continued)

Measurement	Descriptive
Mean Fetal Weight (m)	Mean
	Standard Deviation
	Count
Mean Fetal Weight (f)	Mean
	Standard Deviation
	Count
Placental Wt Live Mean	Mean
	Standard Deviation
	Count

Group Information

Short Name	Long Name	Type	Report Headings 1-4		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Appendix 24
Individual Ovarian and Uterine Examinations

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

0 ug/dose Group 1	Pregnancy Type
5539 NP	Not Pregnant E[a]
5543 NP	Not Pregnant E[a]

E = Exclude
[a] [RC:Uterus pressed between glass plates. No implantation sites present.]

Appendix 24
Individual Ovarian and Uterine Examinations

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

100 ug/dose Group 2	Pregnancy Type
5551 NP	Not Pregnant E[a]
5553 NP	Not Pregnant E[a]
5558 NP	Not Pregnant E[b]
5562 NP	Not Pregnant E[a]
5572 NP	Not Pregnant E[b]
5576 NP	Not Pregnant E[b]
5578 NP	Not Pregnant E[a]

E = Exclude
[a] [RC:Uterus pressed between glass plates. No implantation sites present.]
[b] [RC:Uterus pressed between glass plates, no implantation sites present.]

Appendix 24
Individual Ovarian and Uterine Examinations

20248897

Comments and Markers

Page	Day	Group	Sex	Subject	Measurement	Type	Marker
	-	1	Female	5539	Pregnancy Type	Quality Flag	E (Exclude)
	-	1	Female	5539	Pregnancy Type	Result	
			Comment:	Uterus pressed between glass plates. No implantation sites present.			
	-	1	Female	5543	Pregnancy Type	Quality Flag	E (Exclude)
	-	1	Female	5543	Pregnancy Type	Result	
			Comment:	Uterus pressed between glass plates. No implantation sites present.			
	-	2	Female	5551	Pregnancy Type	Quality Flag	E (Exclude)
	-	2	Female	5551	Pregnancy Type	Result	
			Comment:	Uterus pressed between glass plates. No implantation sites present.			
	-	2	Female	5553	Pregnancy Type	Quality Flag	E (Exclude)
	-	2	Female	5553	Pregnancy Type	Result	
			Comment:	Uterus pressed between glass plates. No implantation sites present.			
	-	2	Female	5558	Pregnancy Type	Quality Flag	E (Exclude)
	-	2	Female	5558	Pregnancy Type	Result	
			Comment:	Uterus pressed between glass plates, no implantation sites present.			
	-	2	Female	5562	Pregnancy Type	Quality Flag	E (Exclude)
	-	2	Female	5562	Pregnancy Type	Result	
			Comment:	Uterus pressed between glass plates. No implantation sites present.			
	-	2	Female	5572	Pregnancy Type	Quality Flag	E (Exclude)
	-	2	Female	5572	Pregnancy Type	Result	
			Comment:	Uterus pressed between glass plates, no implantation sites present.			
	-	2	Female	5576	Pregnancy Type	Quality Flag	E (Exclude)
	-	2	Female	5576	Pregnancy Type	Result	
			Comment:	Uterus pressed between glass plates, no implantation sites present.			
	-	2	Female	5578	Pregnancy Type	Quality Flag	E (Exclude)
	-	2	Female	5578	Pregnancy Type	Result	
			Comment:	Uterus pressed between glass plates. No implantation sites present.			

Appendix 24

Individual Ovarian and Uterine Examinations

20248897

Subject Comments/Exclusions

Subject	Marker	Comment/Exclusion
5539	NP	Not Pregnant
5543	NP	Not Pregnant
5551	NP	Not Pregnant
5553	NP	Not Pregnant
5558	NP	Not Pregnant
5562	NP	Not Pregnant
5572	NP	Not Pregnant
5576	NP	Not Pregnant
5578	NP	Not Pregnant

Appendix 24
Individual Ovarian and Uterine Examinations

20248897

Key Page

Quality Flags

Symbol	IES Status	Description
E	Excluded	Exclude

Measurement Descriptions

Headings Used	Description
Pregnancy Type	Pregnancy Type

Time-Points/Ranges

Measurement	From	To	Report As
Pregnancy Type	-9,999	9,999	-

Group Information

Short Name	Long Name	Type	Report Headings 1-4		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Comment Abbreviations
RC = Result Comment

Appendix 25

Individual Gravid Uterine Weights and Corrected Body Weights: Gestation

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

0 ug/dose Group 1	Bodyweight on Day 0 (g)	Terminal Body Wt (g)	Gravid Uterus (g)	Corrected BW (g)	Corrected BWG (0-TBW) (g)
5501	285	443	92.3	351	66
5502	291	495	110.7	384	93
5503	262	414	87.3	327	65
5504	288	477	100.0	377	89
5505	279	449	115.5	334	55
5506	289	470	111.5	359	70
5507	293	413	72.4	341	48
5508	287	458	121.4	337	50
5509	281	404	49.6	354	73
5510	289	448	86.3	362	73
5511	284	438	82.4	356	72
5512	285	446	107.3	339	54
5513	293	461	98.0	363	70
5515	297	492	125.5	367	70

Appendix 25

Individual Gravid Uterine Weights and Corrected Body Weights: Gestation

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

0 ug/dose Group 1	Bodyweight on Day 0 (g)	Terminal Body Wt (g)	Gravid Uterus (g)	Corrected BW (g)	Corrected BWG (0-TBW) (g)
5516	300	469	111.3	358	58
5518	282	482	113.0	369	87
5519	271	440	91.1	349	78
5521	293	479	108.3	371	78
5522	291	450	114.5	336	45
5523	272	429	96.3	333	61
5528	315	502	105.6	396	81
Mean	287.0	455.2	100.01	355.2	68.2
SD	11.1	27.4	17.85	18.4	13.7
N	21	21	21	21	21

Appendix 25

Individual Gravid Uterine Weights and Corrected Body Weights: Gestation

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

100 ug/dose Group 2	Bodyweight on Day 0 (g)	Terminal Body Wt (g)	Gravid Uterus (g)	Corrected BW (g)	Corrected BWG (0-TBW) (g)
5545	293	436	84.3	352	59
5546	305	502	123.7	378	73
5547	290	465	113.6	351	61
5548	281	428	94.0	334	53
5549	276	437	110.2	327	51
5550	313	478	119.0	359	46
5552	264	411	97.7	313	49
5554	292	474	116.2	358	66
5555	310	475	117.3	358	48
5556	298	489	105.0	384	86
5557	285	416	66.3	350	65
5559	271	448	113.8	334	63
5560	318	500	122.3	378	60
5561	309	463	93.9	369	60

Appendix 25

Individual Gravid Uterine Weights and Corrected Body Weights: Gestation

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

100 ug/dose Group 2	Bodyweight on Day 0 (g)	Terminal Body Wt (g)	Gravid Uterus (g)	Corrected BW (g)	Corrected BWG (0-TBW) (g)
5563	266	475	134.5	341	75
5564	283	472	109.3	363	80
5565	299	480	110.4	370	71
5566	278	448	109.1	339	61
5567	278	453	108.1	345	67
5568	297	455	OA	-	-
5569	274	422	101.4	321	47
5570	240	394	90.6	303	63
Mean	287.3	455.5	106.70	348.8	62.0
SD	18.7	29.2	15.21	21.8	10.9
N	22	22	21	21	21

Appendix 25

Individual Gravid Uterine Weights and Corrected Body Weights: Gestation

20248897

Comments and Markers

Page	Day	Group	Sex	Subject	Measurement	Type	Marker
	-	2	Female	5568	Gravid Uterus	Replacement	OA

Appendix 25

Individual Gravid Uterine Weights and Corrected Body Weights: Gestation

20248897

Key Page

Replacement Values

Value	Description
OA	Omitted activity

Measurement Descriptions

Headings Used	Description
Bodyweight on Day 0	Bodyweight on Day 0
Terminal Body Wt	Terminal BW
Gravid Uterus	Gravid Uterus Weight
Corrected BW	Corrected Bodyweight
Corrected BWG (0-TBW)	Corrected Bodyweight Gain (from Day 0)

Unit Descriptions

Headings Used	Description
g	g

Time-Points/Ranges

Measurement	From	To	Report As
Bodyweight on Day 0	-9,999	9,999	-
Terminal Body Wt	-9,999	9,999	-
Gravid Uterus	-9,999	9,999	-
Corrected BW	-9,999	9,999	-
Corrected BWG (0-TBW)	-9,999	9,999	-

Appendix 25

Individual Gravid Uterine Weights and Corrected Body Weights: Gestation

20248897

Key Page

Measurement/Statistics

Measurement	Descriptive
Bodyweight on Day 0	Mean
	Standard Deviation
	Count
Terminal Body Wt	Mean
	Standard Deviation
	Count
Gravid Uterus	Mean
	Standard Deviation
	Count
Corrected BW	Mean
	Standard Deviation
	Count
Corrected BWG (0-TBW)	Mean
	Standard Deviation
	Count

Group Information

Short Name	Long Name	Type	Report Headings 1-4		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Appendix 26

Individual Fetal Data and Placental Weights

20248897

0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5501 Implant ID	Pregnancy Type: Pregnant			Path Removal Reason: TERM	
R1	LF	M	5.78	0.67	.....External, No abnormalities detected .....Skeletal, Skull Zygomatic arch, Both, Incomplete ossification - Variation .....Skeletal, Vertebra Cervical arch, 1 or more, Incomplete ossification - Variation, [5th and 6th right]
R2	LF	M	6.56	0.64	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	M	5.64	0.69	.....External, No abnormalities detected .....Skeletal, Skull Zygomatic arch, Both, Incomplete ossification - Variation
L4	LF	F	5.05	0.41	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L5	LF	M	5.88	0.57	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L6	LF	F	5.40	0.48	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L7	LF	M	6.08	0.66	.....External, No abnormalities detected .....Skeletal, Skull Frontal, Both, Incomplete ossification - Variation Squamosal, Both, Incomplete ossification - Variation Zygomatic arch, Both, Incomplete ossification - Variation .....Skeletal, Vertebra Cervical arch, 1 or more, Incomplete

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

Appendix 26

Individual Fetal Data and Placental Weights

20248897

0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5501 Implant ID	(Continued...)				
					ossification - Variation, [4th right]
L8	LF	M	6.20	0.57	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L9	LF	F	5.76	0.52	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L10	LF	F	5.46	0.52	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L11	LF	M	6.19	0.54	.....External, No abnormalities detected .....Skeletal, Vertebra Cervical arch, 1 or more, Incomplete ossification - Variation, [4th and 5th right]
L12	LF	F	5.89	0.65	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
Dam: 5502 Implant ID	Pregnancy Type: Pregnant		Path Removal Reason: TERM		
R1	LF	F	5.37	0.56	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	F	5.88	0.56	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	F	5.92	0.67	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	ER				
R5	LF	F	5.51	0.58	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R6	LF	M	5.13	0.58	.....External, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

Appendix 26

Individual Fetal Data and Placental Weights

20248897

0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5502 Implant ID	(Continued...)				
R7	LF	F	6.06	0.62	.....Skeletal, No abnormalities detected .....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L8	LF	F	5.24	0.45	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L9	ER				
L10	LF	M	6.01	0.58	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L11	LF	M	5.68	0.55	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L12	LF	M	5.63	0.55	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L13	LF	F	5.54	0.55	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L14	LF	M	5.91	0.56	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L15	LF	M	5.94	0.41	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L16	LF	M	5.76	0.58	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L17	LF	M	5.95	0.44	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
Dam: 5503 Implant ID	Pregnancy Type: Pregnant		Path Removal Reason: TERM		
R1	LF	M	5.36	0.54 [a]	.....External, No abnormalities detected

[a] [RC:recorded to 0.5405g]
LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

Appendix 26

Individual Fetal Data and Placental Weights

20248897

0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5503 Implant ID	(Continued...)				
R2	LF	M	5.87	0.56 [a]	.....Skeletal, No abnormalities detected .....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	M	6.08	0.68 [b]	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	M	5.63	0.64	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	M	5.68	0.51	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L6	LF	F	5.17	0.65	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L7	LF	M	5.55	0.62	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L8	LF	M	5.51	0.54	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L9	LF	M	5.68	0.53	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L10	LF	M	5.36	0.56	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L11	LF	F	5.14	0.60	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L12	LF	M	5.84	0.65	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected

[a] [RC:recorded to 0.5588g]
[b] [RC:recorded to 0.6781g]
LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

Appendix 26

Individual Fetal Data and Placental Weights

20248897

0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5504 Implant ID	Pregnancy Type: Pregnant			Path Removal Reason: TERM	
R1	LF	M	6.10	0.53	.....External, No abnormalities detected .....Skeletal, Skull Parietal, Both, Incomplete ossification - Variation
R2	LF	F	5.97	0.63	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	M	6.61	0.63	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	M	6.39	0.62	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	M	6.40	0.77	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R6	LF	M	6.06	0.64	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R7	LF	F	5.51	0.42	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L8	LF	F	5.36	0.48	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L9	LF	M	6.34	0.60	.....External, No abnormalities detected .....Skeletal, Skull Parietal, Both, Incomplete ossification - Variation
L10	LF	M	6.79	0.65	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L11	LF	F	5.66	0.57	.....External, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

Appendix 26

Individual Fetal Data and Placental Weights

20248897

0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5504 Implant ID	(Continued...)				
L12	LF	F	5.82	0.55	.....Skeletal, No abnormalities detected .....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L13	LF	F	5.48	0.46	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
Dam: 5505 Implant ID	Pregnancy Type: Pregnant		Path Removal Reason: TERM		
R1	LF	F	5.72	0.60	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	F	6.19	0.58	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	M	6.86	0.65	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	F	6.30	0.66	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	M	6.52	0.74	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R6	LF	M	6.09	0.57	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L7	LF	M	6.44	0.63	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L8	LF	F	6.12	0.68	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L9	LF	M	6.63	0.67	.....External, No abnormalities detected .....Skeletal, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

20248897

0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5505 Implant ID	(Continued...)				
L10	LF	F	5.65	0.60	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L11	LF	M	5.90	0.54	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L12	LF	F	6.01	0.53	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L13	LF	F	6.10	0.52	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L14	LF	F	5.93	0.51	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
Dam: 5506 Implant ID	Pregnancy Type: Pregnant		Path Removal Reason: TERM		
R1	LF	M	5.55	0.59	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	F	5.34	0.35	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	F	5.28	0.52	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	F	5.66	0.49	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	F	5.35	0.58	.....External, No abnormalities detected .....Skeletal, Rib, [Selected for photography] Rib, 1 or more, Short - Variation, [13th left]

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

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0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5506 Implant ID	(Continued...)				
R6	LF	F	5.15	0.64	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R7	LF	M	5.87	0.57	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L8	LF	M	5.52	0.63	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L9	LF	F	5.25	0.72	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L10	LF	F	4.89	0.39	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L11	LF	M	5.65	0.47	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L12	LF	M	5.85	0.40	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L13	LF	F	5.01	0.47	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L14	LF	M	5.50	0.48	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L15	LF	M	4.91	0.52	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L16	LF	F	4.84	0.50	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L17	LF	M	5.78	0.41	.....External, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

20248897

0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5506 Implant ID	(Continued...)				
					.....Skeletal, No abnormalities detected
Dam: 5507 Implant ID	Pregnancy Type: Pregnant		Path Removal Reason: TERM		
R1	LF	F	5.93	0.58	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	ER				
R3	LF	F	5.91	0.66	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R4	LF	F	6.03	0.54	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L5	LF	M	6.29	0.59	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L6	LF	F	6.00	0.61	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L7	ER				
L8	LF	F	6.13	0.51	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L9	ER				
L10	LF	M	6.45	0.66	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L11	LF	M	6.26	0.60	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L12	LF	M	5.92	0.41	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
Dam: 5508 Implant ID	Pregnancy Type: Pregnant		Path Removal Reason: TERM		

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

20248897

0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5508 Implant ID	(Continued...)				
R1	LF	M	5.45	0.44	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	M	5.65	0.52	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	F	5.40	0.49	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	F	5.32	0.56	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	M	5.57	0.54	.....External, No abnormalities detected .....Skeletal, Skull Parietal, Both, Incomplete ossification - Variation Squamosal, Both, Incomplete ossification - Variation Zygomatic arch, Both, Incomplete ossification - Variation
R6	LF	M	5.75	0.62	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R7	LF	M	5.92	0.52	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R8	LF	F	5.06	0.48	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R9 !	LF	M	4.91	0.51	.....External, Mouth, [photograph taken] Tongue, Protruding - Malformation .....External, Trunk, [Photograph taken] Anus, Absent - Malformation, [No opening present]

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

20248897

0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5508 Implant ID	(Continued...)				
					Genital tubercle, Misshapen - Malformation, [Opening in skin inferior to the genital tubercle.] .....Fixed Head, Brain, [Saved in 70% ETOH] Lateral ventricle, Both, Dilatation, Moderate - Variation .....FreshVisBody, Lung, [Photograph taken. Saved in NBF] Lobe, Caudate process, Absent - Malformation .....FreshVisBody, Ureter, [Photograph taken, Tissue saved in NBF] Ureter, Both, Dilatation, Severe - Variation
R10	LF	M	5.20	0.57	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L11	LF	M	5.68	0.49	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L12	LF	F	5.57	0.53	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L13	LF	M	5.80	0.59	.....External, No abnormalities detected .....Skeletal, Skull Frontal, Both, Incomplete ossification - Variation Parietal, Both, Incomplete ossification - Variation Squamosal, Both, Incomplete ossification - Variation Zygomatic arch, Both, Incomplete ossification - Variation .....Skeletal, Vertebra, [Selected for photography]

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

Appendix 26

Individual Fetal Data and Placental Weights

20248897

0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5508 Implant ID	(Continued...)				
					Cervical arch, 1 or more, Misshapen - Variation, [7th right, accelerated development of the transverse process]
L14	LF	M	5.41	0.53	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L15	LF	M	5.04	0.34	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L16	LF	M	5.65	0.50	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L17	LF	M	5.66	0.57	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
Dam: 5509 Implant ID	Pregnancy Type: Pregnant		Path Removal Reason: TERM		
R1	LF	F	5.74	0.60	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	ER				
L3	LF	F	6.31	0.52	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L4	LF	M	6.18	0.73	.....External, No abnormalities detected .....Skeletal, Skull Zygomatic arch, Right, Incomplete ossification - Variation
L5	LF	F	5.57	0.73	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L6	LF	M	6.36	0.74	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L7	LF	F	5.66	0.56	.....External, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

20248897

0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5509 Implant ID	(Continued...)				
					.....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
Dam: 5510 Implant ID	Pregnancy Type: Pregnant		Path Removal Reason: TERM		
R1	LF	M	5.90	0.57	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	ER				
R3	LF	M	5.97	0.56	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R4	LF	F	5.78	0.61	.....External, No abnormalities detected .....Skeletal, Skull Frontal, Both, Incomplete ossification - Variation Parietal, Both, Incomplete ossification - Variation Squamosal, Both, Incomplete ossification - Variation Zygomatic arch, Both, Incomplete ossification - Variation
R5	LF	F	5.68	0.51	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L6	LF	M	5.95	0.69	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L7	LF	F	5.59	0.57	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L8	LF	F	5.58	0.61	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L9	LF	M	6.23	0.58	.....External, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

20248897

0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5510 Implant ID	(Continued...)				
L10	LF	M	6.40	0.51	.....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected .....External, No abnormalities detected .....Skeletal, No abnormalities detected
L11	LF	F	5.74	0.55	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L12	LF	F	6.02	0.44	.....External, No abnormalities detected .....Skeletal, Vertebra Thoracic centrum, 1 or more, Incomplete ossification - Variation, [13th bipartite]
Dam: 5511 Implant ID	Pregnancy Type: Pregnant		Path Removal Reason: TERM		
R1	LF	F	6.36	0.58	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	F	6.07	0.64	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	ER				
R4	LF	F	5.91	0.55	.....External, No abnormalities detected .....Skeletal, Pelvic girdle, [Selected for photography] Pubis, Both, Incomplete ossification - Variation .....Skeletal, Skull, [Selected for photography] Frontal, Both, Incomplete ossification - Variation Parietal, Both, Incomplete ossification - Variation Squamosal, Both, Incomplete ossification - Variation

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

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0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5511 Implant ID	(Continued...)				
					Supraoccipital, Incomplete ossification - Variation Zygomatic arch, Both, Incomplete ossification - Variation .....Skeletal, Vertebra Cervical arch, 1 or more, Incomplete ossification - Variation, [3rd through 6th right; 2nd through 6th left]
R5	LF	F	6.38	0.57	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R6	LF	F	6.02	0.55	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L7	LF	M	6.82	0.62	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L8	LF	M	6.95	0.76	.....External, No abnormalities detected .....Skeletal, Skull Frontal, Both, Incomplete ossification - Variation Squamosal, Both, Incomplete ossification - Variation Zygomatic arch, Both, Incomplete ossification - Variation
L9	LF	M	6.14	0.53	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, Innominate artery, [Photograph taken, surrounding tissue saved in NBF] Innominate artery, Absent - Variation
L10	LF	M	6.44	0.57	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L11	LF	M	6.95	0.79	.....External, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

20248897

0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5511 Implant ID	(Continued...)				
					.....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
Dam: 5512 Implant ID	Pregnancy Type: Pregnant		Path Removal Reason: TERM		
R1	LF	M	5.65	0.66	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	F	5.88	0.56	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	M	5.87	0.67	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	F	5.52	0.64	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	F	5.70	0.51	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R6	LF	F	5.97	0.55	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L7	LF	F	5.65	0.53	.....External, No abnormalities detected .....Skeletal, Vertebra Thoracic centrum, 1 or more, Incomplete ossification - Variation, [11th bipartite]
L8	LF	F	5.40	0.61	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L9	LF	F	5.56	0.59	.....External, No abnormalities detected .....Skeletal, Supernumerary rib Cervical, 1 or more, Short - Variation, [right 7th]

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

20248897

0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5512 Implant ID	(Continued...)				
L10	LF	M	5.54	0.58	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L11	LF	M	5.65	0.57	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L12	LF	M	6.19	0.65	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L13	LF	F	5.91	0.52	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L14	LF	M	5.83	0.71	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
Dam: 5513 Implant ID	Pregnancy Type: Pregnant		Path Removal Reason: TERM		
R1	LF	M	6.24	0.56	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	F	5.71	0.65	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	F	6.09	0.64	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L4	LF	F	5.95	0.66	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L5	LF	F	5.97	0.75	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L6	LF	M	6.21	0.63	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

20248897

0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5513 (Continued...) Implant ID					
					detected
L7	LF	M	6.26	0.57	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L8	LF	F	5.99	0.59	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L9	LF	M	5.97	0.64	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L10	LF	M	6.42	0.61	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L11	LF	M	6.09	0.55	.....External, No abnormalities detected .....Skeletal, Skull Parietal, Both, Incomplete ossification - Variation
L12	LF	F	5.79	0.49	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
Dam: 5515 Pregnancy Type: Pregnant Path Removal Reason: TERM Implant ID					
R1	LF	F	4.65	0.51	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	M	5.95	0.43	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	F	5.45	0.53	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	M	5.47	0.62	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

20248897

0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5515 Implant ID	(Continued...)				
R5	LF	F	5.34	0.39	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R6	LF	M	5.52	0.54	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R7	LF	M	5.67	0.63	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L8	LF	M	5.86	0.44	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L9	LF	F	5.37	0.49	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L10	LF	F	5.65	0.51	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L11	LF	F	5.56	0.49	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L12	LF	F	5.17	0.58	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L13	LF	M	5.85	0.48	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L14	LF	M	6.07	0.65	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L15	LF	M	5.82	0.33	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L16	LF	M	5.76	0.47	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

20248897

0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5515 Implant ID	(Continued...)				
L17	LF	F	5.56	0.41	detected .....External, No abnormalities detected .....Skeletal, No abnormalities detected
Dam: 5516 Implant ID	Pregnancy Type: Pregnant		Path Removal Reason: TERM		
R1	LF	F	5.60	0.51	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	F	5.53	0.59	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	M	5.73	0.61	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	M	6.16	0.66	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	M	6.04	0.55	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R6	LF	F	5.64	0.38	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L7	LF	M	6.11	0.63	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L8	LF	M	5.92	0.62	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L9	LF	F	5.74	0.60	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L10	LF	F	5.82	0.55	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

20248897

0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5516 (Continued...) Implant ID					
L11	LF	F	5.95	0.61	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L12	LF	F	5.64	0.53	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L13	LF	F	5.68	0.66	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L14	LF	F	5.97	0.61	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
Dam: 5518 Pregnancy Type: Pregnant Path Removal Reason: TERM Implant ID					
R1	LF	F	5.14	0.51	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	F	5.34	0.67	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	M	5.98	0.47	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	F	5.56	0.64	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	F	5.25	0.63	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R6	LF	M	5.80	0.43	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R7	LF	F	5.10	0.72	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L8	LF	M	5.61	0.53	.....External, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

20248897

0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5518 (Continued...) Implant ID					
L9	LF	F	5.30	0.58	.....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected .....External, No abnormalities detected .....Skeletal, Sternebra, [selected for photography] Sternebra, 1 or more, Incomplete ossification - Variation, [2nd]
L10	LF	M	5.19	0.46	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L11	LF	F	5.53	0.44	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L12	LF	M	5.46	0.52	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L13	LF	F	5.58	0.52	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L14	LF	M	5.84	0.56	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L15	LF	M	5.72	0.41	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
Dam: 5519 Pregnancy Type: Pregnant Path Removal Reason: TERM Implant ID					
R1	LF	F	4.06	0.45	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	F	5.54	0.56	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	F	5.45	0.31	.....External, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

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0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5519 Implant ID	(Continued...)				
R4	LF	M	5.92	0.52	.....Skeletal, No abnormalities detected .....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	M	5.36	0.33	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R6	LF	F	5.99	0.69	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R7	LF	F	5.84	0.69	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L8	ER				
L9	LF	F	5.62	0.50	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L10	LF	F	5.60	0.52	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L11	LF	F	5.82	0.45	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L12 !	LR				
L13	LF	M	6.42	0.73	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L14	LF	F	5.69	0.69	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
Dam: 5521 Implant ID	Pregnancy Type: Pregnant		Path Removal Reason: TERM		
R1	LF	M	5.88	0.46	.....External, No abnormalities detected .....Skeletal, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

20248897

0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5521 Implant ID	(Continued...)				
R2	LF	F	6.05	0.56	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	F	5.75	0.49	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	M	6.55	0.59	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	F	5.67	0.58	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R6	LF	M	5.93	0.49	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R7	LF	M	5.87	0.54	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R8	LF	M	6.05	0.48	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L9	LF	M	5.99	0.41	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L10	LF	M	5.67	0.52	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L11	LF	F	6.07	0.45	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L12	LF	M	5.86	0.62	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L13	LF	F	6.23	0.43	.....External, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

20248897

0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5521 Implant ID	(Continued...)				
L14	LF	M	5.72	0.45	.....Skeletal, No abnormalities detected .....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
Dam: 5522 Implant ID	Pregnancy Type: Pregnant		Path Removal Reason: TERM		
R1	LF	M	5.91	0.76	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	F	5.33	0.46	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	F	5.44	0.55	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	M	5.70	0.48	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	M	5.57	0.67	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R6	LF	F	5.81	0.62	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R7	LF	F	5.51	0.49	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R8	LF	F	5.82	0.61	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R9	LF	F	6.22	0.55	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L10	LF	M	5.74	0.60	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

20248897

0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5522 Implant ID	(Continued...)				
					.....FreshVisBody, No abnormalities detected
L11	LF	M	5.80	0.57	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L12	LF	F	5.12	0.53	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L13	LF	F	5.61	0.68	.....External, No abnormalities detected .....Skeletal, Vertebra, [Selected for photography] Thoracic centrum, 1 or more, Incomplete ossification - Variation, [12th bipartite]
L14	LF	F	6.00	0.57	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L15	LF	M	6.27	0.58	.....External, No abnormalities detected .....Skeletal, Skull Parietal, Both, Incomplete ossification - Variation
Dam: 5523 Implant ID	Pregnancy Type: Pregnant		Path Removal Reason: TERM		
R1	LF	F	5.39	0.57	.....External, No abnormalities detected .....Skeletal, Skull Parietal, Both, Incomplete ossification - Variation Squamosal, Left, Incomplete ossification - Variation
R2	LF	M	5.58	0.55	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	F	4.96	0.45	.....External, No abnormalities detected .....Skeletal, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

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0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5523 Implant ID	(Continued...)				
R4	LF	M	5.56	0.50	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	M	5.54	0.43	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R6	LF	F	5.50	0.46	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R7	LF	F	5.26	0.50	.....External, No abnormalities detected .....Skeletal, Skull Frontal, Both, Incomplete ossification - Variation Parietal, Both, Incomplete ossification - Variation Zygomatic arch, Both, Incomplete ossification - Variation
L8	LF	F	5.53	0.55	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L9	LF	M	4.75	0.39	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L10	LF	F	5.47	0.60	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L11	LF	F	4.18	0.40	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L12	LF	M	5.61	0.52	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L13	LF	F	5.09	0.50	.....External, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

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0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5523 Implant ID	(Continued...)				
L14	LF	M	5.39	0.52	.....Skeletal, No abnormalities detected .....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
Dam: 5528 Implant ID	Pregnancy Type: Pregnant		Path Removal Reason: TERM		
R1	LF	M	5.70	0.63	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	F	5.39	0.34	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	F	5.86	0.48	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	M	5.66	0.68	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	M	6.05	0.60	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R6	LF	F	6.32	0.59	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R7	LF	F	5.84	0.78	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R8	LF	F	5.53	0.82	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R9	LF	F	5.94	0.78	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L10	LF	M	5.72	0.50	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

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0 ug/dose Group 1	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5528 Implant ID	(Continued...)				
					.....FreshVisBody, No abnormalities detected
L11	LF	M	6.00	0.47	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L12	LF	F	5.58	0.69	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L13	LF	F	6.33	0.49	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L14	LF	M	6.09	0.75	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L15	LF	F	6.16	0.71	.....External, No abnormalities detected .....Skeletal, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

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100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5545 Pregnancy Type: Pregnant Path Removal Reason: TERM Implant ID					
R1	LF	F	5.07	0.67	.....External, No abnormalities detected .....Skeletal, Rib Rib, 1 or more, Incomplete ossification - Variation, [10th-11th left] Rib, 1 or more, Nodule - Variation, [4th-7th right, medial; 4th-8th left, medial] Rib, 1 or more, Wavy rib - Variation, [8th-12th right; 10th-12th left] .....Skeletal, Skull Frontal, Both, Incomplete ossification - Variation Parietal, Both, Incomplete ossification - Variation Squamosal, Both, Incomplete ossification - Variation Zygomatic arch, Both, Incomplete ossification - Variation
R2	LF	M	5.84	0.69	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	M	5.86	0.55	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	F	6.40	0.70	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	F	5.90	0.68	.....External, No abnormalities detected .....Skeletal, Rib Rib, 1 or more, Incomplete ossification - Variation, [10th-12th right ; 9th-12th left] Rib, 1 or more, Wavy rib - Variation, [10th right; 9th-10th left] .....Skeletal, Skull Parietal, Both, Incomplete ossification -

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

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100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5545 Implant ID	(Continued...)				
					Variation Squamosal, Both, Incomplete ossification - Variation Zygomatic arch, Both, Incomplete ossification - Variation
L6	LF	F	5.39	0.70	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L7	LF	M	5.74	0.50	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L8	ER				
L9	LF	M	6.18	0.60	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L10	LF	M	5.37	0.49	.....External, No abnormalities detected .....Skeletal, Skull Parietal, Left, Incomplete ossification - Variation
L11	LF	M	5.89	0.54	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L12	LF	M	5.91	0.62	.....External, No abnormalities detected .....Skeletal, Skull Parietal, Both, Incomplete ossification - Variation Squamosal, Both, Incomplete ossification - Variation Zygomatic arch, Both, Incomplete ossification - Variation
Dam: 5546 Implant ID	Pregnancy Type: Pregnant		Path Removal Reason: TERM		
R1	LF	M	5.85	0.61	.....External, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

Appendix 26

Individual Fetal Data and Placental Weights

20248897

100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5546 Implant ID	(Continued...)				
R2	LF	F	5.96	0.58	.....Skeletal, No abnormalities detected .....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	M	5.89	0.64	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	F	5.80	0.59	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	M	5.85	0.60	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R6	LF	M	5.89	0.44	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R7	LF	M	6.49	0.65	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R8	ER				
R9	LF	F	5.42	0.41	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R10	LF	M	5.87	0.66	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R11	LF	F	5.78	0.55	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R12	LF	F	5.70	0.55	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L13	LF	M	5.94	0.63	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

Appendix 26

Individual Fetal Data and Placental Weights

20248897

100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5546 (Continued...) Implant ID					
					detected
L14	LF	F	5.59	0.72	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L15	LF	M	5.73	0.59	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L16	LF	M	6.58	0.70	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L17	LF	F	5.68	0.53	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
Dam: 5547 Pregnancy Type: Pregnant Path Removal Reason: TERM Implant ID					
R1	LF	F	5.14	0.48	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	F	5.21	0.68	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	F	5.62	0.42	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	F	5.19	0.45	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	F	5.44	0.46	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R6	LF	F	5.51	0.57	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R7	LF	M	5.07	0.43	.....External, No abnormalities detected .....Skeletal, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

Appendix 26

Individual Fetal Data and Placental Weights

20248897

100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5547 (Continued...) Implant ID					
R8	LF	M	5.47	0.56	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R9	LF	M	6.04	0.46	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L10	LF	F	4.73	0.45	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L11	LF	F	4.99	0.48	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L12	LF	M	5.59	0.65	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L13	LF	M	5.65	0.47	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L14	LF	M	5.62	0.53	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L15	LF	M	5.37	0.51	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L16	LF	F	5.80	0.50	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
Dam: 5548 Pregnancy Type: Pregnant Path Removal Reason: TERM Implant ID					
R1	LF	M	5.92	0.57	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	F	5.83	0.46	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

Appendix 26

Individual Fetal Data and Placental Weights

20248897

100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5548 Implant ID	(Continued...)				
					detected
R3	LF	F	5.95	0.57	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	F	6.18	0.96 [a]	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	F	5.64	0.58	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R6	LF	M	5.56	0.57	.....External, No abnormalities detected .....Fixed Head, Brain, [Photograph taken, head sections saved in 70%ETOH] Lateral ventricle, Both, Dilatation, Moderate - Variation .....FreshVisBody, No abnormalities detected
R7	LF	F	6.24	0.60	.....External, No abnormalities detected .....Skeletal, Vertebra Cervical arch, 1 or more, Misshapen - Variation, [6th left, reduced ventral process]
L8	LF	M	5.73	0.69	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L9	LF	M	6.39	0.58	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L10	LF	F	6.12	0.66	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L11	LF	F	4.97	0.57	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L12	LF	F	5.80	0.45	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected

[a] [RC:recorded value]
LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

20248897

100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5548 (Continued...) Implant ID					
					.....FreshVisBody, No abnormalities detected
Dam: 5549 Pregnancy Type: Pregnant Path Removal Reason: TERM Implant ID					
R1	LF	M	5.65	0.53	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	M	5.97	0.59	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	M	6.48	0.56	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	F	6.02	0.87	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	M	5.96	0.58	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R6	LF	F	5.65	0.63	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R7	LF	M	6.18	0.60	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R8	LF	F	4.65	1.05 [a]	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R9	LF	M	5.46		.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L10	LF	M	5.93	0.67	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L11	LF	F	5.70	0.57	.....External, No abnormalities detected

[a] [RC:Placenta fused at implant site 8 and 9.]
LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

20248897

100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5549 (Continued...) Implant ID					
L12	LF	M	6.11	0.49	.....Skeletal, No abnormalities detected .....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L13	LF	M	5.71	0.59	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L14	LF	F	5.74	0.51	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
Dam: 5550 Pregnancy Type: Pregnant Path Removal Reason: TERM Implant ID					
R1	LF	F	5.23	0.40	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	F	5.82	0.56	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	F	5.42	0.37	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	M	5.83	0.43	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	ER				
R6	LF	F	5.61	0.45	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R7	LF	M	5.82	0.42	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R8	ER				
R9	LF	M	6.25	0.63	.....External, No abnormalities detected .....Skeletal, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

20248897

100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5550 (Continued...) Implant ID					
L10	LF	F	5.49	0.42	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L11	LF	F	5.39	0.44	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L12	LF	M	5.99	0.50	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L13	LF	F	5.83	0.64	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L14	LF	M	6.21	0.39	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L15	LF	F	5.85	0.51	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L16	LF	M	5.83	0.45	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L17	LF	M	5.97	0.40	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L18	LF	M	5.86	0.51	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
Dam: 5552 Pregnancy Type: Pregnant Path Removal Reason: TERM Implant ID					
R1	LF	M	5.40	0.77	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	F	5.01	0.59	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

20248897

100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5552 Implant ID	(Continued...)				
					detected
R3	LF	M	5.83	0.53	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	F	5.45	0.63	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	F	5.79	0.83	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R6	LF	F	3.19	0.48	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R7	LF	F	5.55	0.80	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R8	LF	M	5.89	0.67	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R9	LF	F	5.19	0.55	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R10	LF	M	5.57	0.81	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L11	LF	F	5.61	0.62	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L12	LF	M	5.52	0.74	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L13	LF	F	5.24	0.65	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L14	LF	F	5.20	0.51	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

20248897

100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5552 Implant ID	(Continued...)				
					.....FreshVisBody, No abnormalities detected
Dam: 5554 Implant ID	Pregnancy Type: Pregnant		Path Removal Reason: TERM		
R1	LF	M	6.17	0.67	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	F	6.40	0.47	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	M	6.30	0.65	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	F	5.97	0.58	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	M	6.18	0.52	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R6	LF	F	5.78	0.54	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R7	LF	M	6.49	0.47	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R8	LF	M	5.87	0.52	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R9	ER				
L10	LF	F	5.81	0.56	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L11	LF	M	6.22	0.50	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

20248897

100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5554 (Continued...) Implant ID					
L12	LF	M	6.36	0.59	.....External, No abnormalities detected .....Skeletal, Rib Rib, 1 or more, Nodule - Variation, [7th, 8th ,9th right, medial] Rib, 1 or more, Wavy rib - Variation, [10th-11th right]
L13	LF	M	6.08	0.56	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L14	LF	F	5.89	0.44	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L15	LF	F	5.58	0.50	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L16	LF	F	5.98	0.47	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
Dam: 5555 Pregnancy Type: Pregnant Path Removal Reason: TERM Implant ID					
R1	LF	F	4.70	0.62	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	F	5.38	0.54	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	M	6.00	0.59	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	F	5.32	0.45	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	M	5.92	0.63	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R6	LF	M	5.54	0.51	.....External, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

20248897

100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5555 Implant ID	(Continued...)				
					.....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R7	LF	M	6.18	0.47	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R8	LF	M	5.72	0.56	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R9	LF	F	5.33	0.44	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R10	LF	M	5.13	0.49	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L11	LF	M	6.17	0.49	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L12	LF	M	6.51	0.52	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L13	LF	F	5.39	0.50	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L14	LF	M	6.29	0.61	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L15	LF	M	6.20	0.56	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L16	LF	F	5.65	0.53	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

20248897

100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5556 Pregnancy Type: Pregnant Path Removal Reason: TERM Implant ID					
R1	LF	M	5.59	0.53	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	F	5.42	0.73	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	M	5.34	0.51	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	M	5.76	0.57	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	F	5.54	0.59	.....External, No abnormalities detected .....Skeletal, Skull Squamosal, Right, Incomplete ossification - Variation Zygomatic arch, Left, Incomplete ossification - Variation
R6	LF	M	5.62	0.78	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R7	LF	M	5.60	0.61	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R8	LF	M	5.44	0.48	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L9	LF	F	5.10	0.63	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L10	LF	M	5.65	0.49	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L11	LF	F	5.23	0.47	.....External, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

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100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5556 Implant ID	(Continued...)				
					.....Skeletal, No abnormalities detected
L12	ER				
L13	LF	F	5.65	0.61	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L14	LF	F	5.77	0.60	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L15	LF	F	5.69	0.62	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
Dam: 5557 Implant ID	Pregnancy Type: Pregnant		Path Removal Reason: TERM		
R1	LF	M	6.54	0.76	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	F	6.19	0.78	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L3	LF	F	5.95	0.57	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L4	LF	F	5.25	0.63	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L5	LF	F	6.41	0.81	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L6	ER				
L7	LF	M	6.34	0.73	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L8	LF	F	6.11	0.68	.....External, No abnormalities detected .....Skeletal, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

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100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5557 (Continued...) Implant ID					
L9	LF	M	6.66	0.75	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
Dam: 5559 Pregnancy Type: Pregnant Path Removal Reason: TERM Implant ID					
R1	LF	M	6.04	0.75	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	F	5.26	0.50	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	F	6.01	0.73	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	F	6.19	0.68	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	M	6.40	0.61	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R6	LF	M	6.25	0.71	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R7	LF	M	6.22	0.79	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R8	ER				
R9	LF	M	6.35	0.84	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R10	LF	M	6.46	0.64	.....External, No abnormalities detected .....Skeletal, Skull Parietal, Both, Incomplete ossification - Variation

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

20248897

100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5559 (Continued...) Implant ID					
L11	ER				
L12	LF	F	6.14	0.77	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L13	LF	F	6.08	0.73	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L14	LF	F	6.01	0.82	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L15	LF	F	6.26	0.70	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L16	LF	F	6.02	0.67	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
Dam: 5560 Pregnancy Type: Pregnant Path Removal Reason: TERM Implant ID					
R1	LF	M	6.58	0.71	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	F	6.17	0.74	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, Ureter, [Tissue saved in NBF] Ureter, Left, Dilatation, Moderate - Variation
R3	LF	F	6.97	0.58	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	M	6.74	0.60	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	M	6.73	0.48	.....External, No abnormalities detected .....Skeletal, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

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100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5560 (Continued...) Implant ID					
R6	ER				
R7	LF	M	6.99	0.47	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R8	LF	F	6.27	0.57	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R9	LF	M	6.38	0.56	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L10	LF	M	6.18	0.55	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L11	LF	F	5.98	0.64	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L12	LF	M	6.45	0.47	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L13	LF	F	6.47	0.55	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L14	LF	M	6.46	0.45	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L15	LF	F	6.01	0.67	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
Dam: 5561 Pregnancy Type: Pregnant Path Removal Reason: TERM Implant ID					
R1	LF	F	5.40	0.52	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	M	5.44	0.49	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

Appendix 26

Individual Fetal Data and Placental Weights

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100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5561 Implant ID	(Continued...)				
					.....FreshVisBody, No abnormalities detected
R3	LF	F	5.33	0.50	.....External, No abnormalities detected .....Skeletal, Vertebra, [Selected for photography] Cervical arch, 1 or more, Misshapen - Variation, [6th left, reduced ventral process]
R4	LF	F	5.41	0.58	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	M	5.76	0.56	.....External, No abnormalities detected .....Skeletal, Rib, [Selected for photography] Rib, 1 or more, Nodule - Variation, [8th and 9th right, medial] Rib, 1 or more, Wavy rib - Variation, [10th-12th bilateral]
R6	LF	F	5.17	0.39	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L7	LF	M	5.55	0.48	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L8	LF	F	5.37	0.58	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L9	LF	F	5.30	0.62	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L10	LF	F	5.48	0.56	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

20248897

100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5561 (Continued...) Implant ID					
L11	LF	M	6.02	0.64	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L12	LF	F	5.22	0.70	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L13	LF	M	5.37	0.56	.....External, No abnormalities detected .....Skeletal, Rib, [Selected for photography] Rib, 1 or more, Incomplete ossification - Variation, [10th right] Rib, 1 or more, Nodule - Variation, [6th-9th, right; 6th-11th left , medial] Rib, 1 or more, Wavy rib - Variation, [10th-12th right] .....Skeletal, Skull Squamosal, Both, Incomplete ossification - Variation Zygomatic arch, Both, Incomplete ossification - Variation
Dam: 5563 Pregnancy Type: Pregnant Path Removal Reason: TERM Implant ID					
R1	LF	M	5.66	0.57	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	M	5.26	0.36	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	M	5.23	0.40	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	M	5.51	0.44	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	M	6.09	0.61	.....External, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

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100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5563 Implant ID	(Continued...)				
R6	LF	M	5.77	0.66	.....Skeletal, No abnormalities detected .....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R7	LF	F	5.53	0.48	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R8	LF	F	5.40	0.46	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R9	LF	F	5.06	0.43	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R10	LF	M	5.68	0.53	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L11	LF	M	5.78	0.50	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L12	LF	M	5.62	0.59	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L13	LF	M	5.64	0.45	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L14	LF	M	6.07	0.54	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L15	LF	M	6.03	0.60	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L16	LF	F	5.39	0.51	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

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100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5563 (Continued...) Implant ID					
L17	LF	M	5.79	0.60	.....External, No abnormalities detected .....Skeletal, Skull Squamosal, Both, Incomplete ossification - Variation Zygomatic arch, Both, Incomplete ossification - Variation
L18	LF	M	5.64	0.44	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
Dam: 5564 Pregnancy Type: Pregnant Path Removal Reason: TERM Implant ID					
R1	LF	M	5.58	0.43	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	M	5.38	0.68	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	F	4.98	0.49	.....External, No abnormalities detected .....Skeletal, Skull Frontal, Both, Incomplete ossification - Variation Parietal, Right, Incomplete ossification - Variation Squamosal, Both, Incomplete ossification - Variation Zygomatic arch, Both, Incomplete ossification - Variation
R4	LF	F	5.51	0.56	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	F	5.32	0.52	.....External, No abnormalities detected .....Skeletal, Skull, [Selected for photography]

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

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100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5564 (Continued...) Implant ID					
R6	LF	F	5.22	0.47	Frontal, Both, Incomplete ossification - Variation Nasal, Both, Incomplete ossification - Variation Parietal, Both, Incomplete ossification - Variation Squamosal, Both, Incomplete ossification - Variation Zygomatic arch, Both, Incomplete ossification - Variation .....Skeletal, Vertebra, [Selected for photography] Cervical arch, 1 or more, Incomplete ossification - Variation, [5th left] .....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R7	LF	M	5.27	0.72	.....External, No abnormalities detected .....Skeletal, Skull Frontal, Both, Incomplete ossification - Variation Parietal, Both, Incomplete ossification - Variation Squamosal, Both, Incomplete ossification - Variation Zygomatic arch, Both, Incomplete ossification - Variation .....Skeletal, Vertebra Cervical arch, 1 or more, Incomplete ossification - Variation, [4th and 5th right]
R8	LF	M	4.65	0.73	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

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100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5564 (Continued...) Implant ID					
R9	LF	F	4.72	0.54	.....External, No abnormalities detected .....Skeletal, Skull Squamosal, Both, Incomplete ossification - Variation Zygomatic arch, Both, Incomplete ossification - Variation
L10	LF	M	5.08	0.54	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L11	LF	F	5.36	0.63	.....External, No abnormalities detected .....Skeletal, Skull Squamosal, Both, Incomplete ossification - Variation Zygomatic arch, Both, Incomplete ossification - Variation
L12	LF	F	5.48	0.66	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L13	LF	M	5.76	0.60	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L14	LF	F	5.03	0.67	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L15	LF	M	5.94	0.52	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
Dam: 5565 Pregnancy Type: Pregnant Path Removal Reason: TERM Implant ID					
R1	LF	F	5.39	0.46	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	M	5.59	0.57	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

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100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5565 Implant ID	(Continued...)				
					detected
R3	LF	F	6.00	0.56	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	F	6.19	0.56	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	F	5.65	0.50	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R6	LF	F	5.73	0.60	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L7	LF	F	5.84	0.60	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L8	LF	M	6.19	0.74	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L9	LF	F	5.90	0.62	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L10	LF	M	5.77	0.61	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L11	LF	F	5.60	0.61	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L12	LF	F	5.48	0.54	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L13	LF	F	5.88	0.55	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L14	LF	F	5.42	0.64	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

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100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5565 (Continued...) Implant ID					
L15	LF	M	6.05	0.62	.....FreshVisBody, No abnormalities detected .....External, No abnormalities detected .....Skeletal, Skull Zygomatic arch, Both, Incomplete ossification - Variation
Dam: 5566 Pregnancy Type: Pregnant Path Removal Reason: TERM Implant ID					
R1	LF	M	6.09	0.50	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	M	6.16	0.58	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	F	5.95	0.76	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	F	6.09	0.68	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	F	5.87	0.63	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R6	LF	F	5.21	0.53	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R7	LF	F	6.25	0.64	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R8	LF	F	6.21	0.72	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L9	LF	M	5.59	0.62	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L10	LF	F	5.76	0.67	.....External, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

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100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5566 (Continued...) Implant ID					
					.....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L11	LF	M	5.66	0.66	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L12	LF	M	5.95	0.78	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L13	LF	M	5.62	0.73	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L14	LF	F	5.60	0.61	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
Dam: 5567 Pregnancy Type: Pregnant Path Removal Reason: TERM Implant ID					
R1	LF	F	5.08	0.59	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	M	5.38	0.57	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	F	5.51	0.69	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	F	5.54	0.74	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	F	5.51	0.74	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R6	LF	F	5.37	0.55	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

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100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5567 (Continued...) Implant ID					
L7	LF	M	5.58	0.56	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L8	LF	M	6.21	0.62	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L9	LF	M	5.67	0.55	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L10	LF	M	5.80	0.58	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L11	LF	F	5.88	0.77	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L12	LF	F	5.31	0.69	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L13	LF	M	5.24	0.62	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L14	LF	M	5.18	0.61	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L15	LF	M	6.90	0.80	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
Dam: 5568 Pregnancy Type: Pregnant Path Removal Reason: TERM Implant ID					
R1	LF	F	6.03	0.51	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	F	6.19	0.55	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	M	6.03	0.61	.....External, No abnormalities detected

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

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100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5568 Implant ID	(Continued...)				
					.....Skeletal, Rib Rib, 1 or more, Incomplete ossification - Variation, [9th-11th right] Rib, 1 or more, Nodule - Variation, [7th, 9th right, medial ; 8th right distal;] Rib, 1 or more, Wavy rib - Variation, [10th right] .....Skeletal, Skull Squamosal, Both, Incomplete ossification - Variation Zygomatic arch, Both, Incomplete ossification - Variation
R4	LF	F	6.13	0.49	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	F	5.96	0.58	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R6	LF	F	5.79	0.36	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R7	LF	F	5.99	0.58	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L8	LF	M	5.80	0.50	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L9	LF	F	5.53	0.55	.....External, No abnormalities detected .....Skeletal, Sternebra Sternebra, 1 or more, Incomplete ossification - Variation, [2nd]
L10	LF	F	4.09	0.28	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

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100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5568 (Continued...) Implant ID					
					detected
L11	LF	M	6.23	0.80	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L12	LF	F	5.95	0.58	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L13	LF	F	5.62	0.68	.....External, No abnormalities detected .....Skeletal, Vertebra Thoracic centrum, 1 or more, Incomplete ossification - Variation, [13th bipartite]
Dam: 5569 Pregnancy Type: Pregnant Path Removal Reason: TERM Implant ID					
R1	LF	F	5.01	0.47	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	LF	M	5.16	0.61	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R3	LF	M	5.39	0.57	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R4	LF	M	5.84	0.58	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R5	LF	M	5.61	0.51	.....External, No abnormalities detected .....Skeletal, Skull Parietal, Both, Incomplete ossification - Variation Squamosal, Both, Incomplete ossification - Variation Zygomatic arch, Both, Incomplete ossification - Variation .....Skeletal, Sternebra, [Selected for photography]

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

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100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5569 (Continued...) Implant ID					
					Sternebra, 1 or more, Misshapen - Variation, [6th]
R6	LF	F	4.60	0.52	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L7	LF	F	5.00	0.49	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L8	LF	M	5.36	0.48	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L9	LF	F	5.19	0.72	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L10	LF	M	6.06	0.48	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L11	LF	M	6.18	0.63	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L12	LF	F	5.77	0.65	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L13	LF	F	5.83	0.64	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
L14	LF	M	5.70	0.54	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
Dam: 5570 Pregnancy Type: Pregnant Path Removal Reason: TERM Implant ID					
R1	LF	F	5.81	0.59	.....External, No abnormalities detected .....Skeletal, No abnormalities detected
R2	ER				

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

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100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5570 Implant ID	(Continued...)				
R3	LF	M	6.51	0.66	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R4	LF	F	5.91	0.68	.....External, No abnormalities detected .....Skeletal, Skull Zygomatic arch, Both, Incomplete ossification - Variation
R5	LF	M	6.57	0.69	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R6	LF	M	6.41	0.76	.....External, No abnormalities detected .....Skeletal, Skull Zygomatic arch, Both, Incomplete ossification - Variation .....Skeletal, Vertebra Cervical arch, 1 or more, Incomplete ossification - Variation, [6th bilateral]
R7	LF	M	6.70	0.73	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R8	LF	M	6.31	0.70	.....External, No abnormalities detected .....Skeletal, Supernumerary rib, [Selected for photography] Cervical, 1 or more, Short - Variation, [7th right]
R9	LF	F	6.40	0.68	.....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
R10	LF	M	6.64	0.78	.....External, No abnormalities detected .....Skeletal, Skull Zygomatic arch, Right, Incomplete

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Individual Fetal Data and Placental Weights

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100 ug/dose Group 2	Implant Type Abbr	Fetal Sex	Fetal Weight (g)	Placental Weight (g)	Findings
Dam: 5570 (Continued...) Implant ID					
L11	LF	M	6.54	0.77	ossification - Variation .....External, No abnormalities detected .....Fixed Head, No abnormalities detected .....FreshVisBody, No abnormalities detected
L12	ER				
L13	LF	F	6.49	0.66	.....External, No abnormalities detected .....Skeletal, Skull Frontal, Both, Incomplete ossification - Variation

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

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Fetal Result Comments and Markers

Group	Dam	Implant	Sex	Measurement	Type	Marker
1	5503	R1	Male	Placental Weight	Result	
	Comment: recorded to 0.5405g					
1	5503	R2	Male	Placental Weight	Result	
	Comment: recorded to 0.5588g					
1	5503	R3	Male	Placental Weight	Result	
	Comment: recorded to 0.6781g					
2	5548	R4	Female	Placental Weight	Result	
	Comment: recorded value					
2	5549	R8	Female	Placental Weight	Result	
	Comment: Placenta fused at implant site 8 and 9.					

Fetus Comments

Dam	Implant	Comment
5508	R9 !	Colon empties into blind pouch (due to external observation of anal opening absent)
5519	L12 !	Autolysis precludes further evaluation, tissues discarded

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Individual Fetal Data and Placental Weights

20248897

Key Page

Dam Measurement Descriptions

Headings Used	Description
Pregnancy Type	Pregnancy Type
Path Removal Reason	Path Removal Reason

Fetal Measurement Descriptions

Headings Used	Description
Implant Type Abbr	Implant Type Abbreviation
Fetal Sex	Fetal Sex
Fetal Weight	Fetal Weight
Placental Weight	Placental Weight

Fetal Measurement Unit Descriptions

Headings Used	Description
g	g

General Footnotes

LF=Live Fetus DF=Dead Fetus ER=Early Resorption LR=Late Resorption
U=Unsexed DFE=Dead Fetus Examined EI=Empty Implantation LRE=Late Resorption Examined

Group Information

Short Name	Long Name	Type	Report Headings		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Appendix 27

Individual Mean Fetal Skeletal Ossification Sites

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

0 ug/dose Group 1	Hyoid	Cervical Vertebrae	Thoracic Vertebrae	Lumbar Vertebrae	Sacral Vertebrae	Caudal Vertebrae	Ribs, Paired
5501	1.0	7.0	13.2	5.8	4.0	6.3	13.1
5502	1.0	7.0	13.0	6.0	4.0	5.4	13.0
5503	1.0	7.0	13.0	6.0	4.0	6.2	13.0
5504	1.0	7.0	13.0	6.0	4.0	6.0	13.0
5505	1.0	7.0	13.1	5.9	4.0	6.9	13.1
5506	1.0	7.0	13.0	6.0	4.0	5.9	13.0
5507	1.0	7.0	13.0	6.0	4.0	7.2	13.0
5508	1.0	7.0	13.0	6.0	4.0	5.7	13.0
5509	1.0	7.0	13.0	6.0	4.0	5.7	13.0
5510	1.0	7.0	13.0	6.0	4.0	7.0	13.0
5511	1.0	7.0	14.0	5.0	4.0	6.2	13.7
5512	1.0	7.0	13.0	6.0	4.0	6.3	13.0
5513	1.0	7.0	13.0	6.0	4.0	6.3	13.0
5515	1.0	7.0	13.0	6.0	4.0	6.6	13.0
5516	1.0	7.0	13.0	6.0	4.0	5.9	13.0
5518	1.0	7.0	13.0	6.0	4.0	6.1	13.0
5519	1.0	7.0	13.0	6.0	4.0	6.2	13.0
5521	1.0	7.0	13.0	6.0	4.0	7.1	13.0
5522	1.0	7.0	13.0	6.0	4.0	6.6	13.0
5523	1.0	7.0	13.0	6.0	4.0	5.9	13.0

Appendix 27

Individual Mean Fetal Skeletal Ossification Sites

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

0 ug/dose Group 1	Manubrium	Sternal Centra	Xiphoid	Carpals	Metacarpals	Forelimb Digits	Forelimb Phalanges
5501	1.0	4.0	1.0	0.0	4.0	5.0	6.8
5502	1.0	4.0	1.0	0.0	4.0	5.0	6.9
5503	1.0	4.0	1.0	0.0	4.0	5.0	8.7
5504	1.0	4.0	1.0	0.0	4.0	5.0	8.9
5505	1.0	4.0	1.0	0.0	4.0	5.0	8.9
5506	1.0	4.0	1.0	0.0	4.0	5.0	7.6
5507	1.0	4.0	1.0	0.0	4.0	5.0	8.6
5508	1.0	4.0	1.0	0.0	4.0	5.0	8.4
5509	1.0	4.0	1.0	0.0	4.0	5.0	6.7
5510	1.0	4.0	1.0	0.0	4.0	5.0	8.2
5511	1.0	4.0	1.0	0.0	4.0	5.0	7.2
5512	1.0	4.0	1.0	0.0	4.0	5.0	8.9
5513	1.0	4.0	1.0	0.0	4.0	5.0	8.2
5515	1.0	4.0	1.0	0.0	4.0	5.0	7.3
5516	1.0	4.0	1.0	0.0	4.0	5.0	7.6
5518	1.0	4.0	1.0	0.0	4.0	5.0	7.2
5519	1.0	4.0	1.0	0.0	4.0	5.0	7.2
5521	1.0	4.0	1.0	0.0	4.0	5.0	8.3
5522	1.0	4.0	1.0	0.0	4.0	5.0	8.0
5523	1.0	4.0	1.0	0.0	4.0	5.0	7.6

Appendix 27

Individual Mean Fetal Skeletal Ossification Sites

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

0 ug/dose Group 1	Tarsals	Metatarsals	Hindlimb Digits	Hindlimb Phalanges
5501	0.0	4.3	5.0	5.0
5502	0.0	4.4	5.0	5.0
5503	0.0	4.8	5.0	7.2
5504	0.0	5.0	5.0	6.7
5505	0.1	5.0	5.0	8.3
5506	0.0	4.8	5.0	5.2
5507	0.0	5.0	5.0	7.6
5508	0.0	5.0	5.0	6.9
5509	0.0	5.0	5.0	5.0
5510	0.0	4.8	5.0	6.8
5511	0.0	4.7	5.0	5.0
5512	0.0	5.0	5.0	7.4
5513	0.0	4.8	5.0	5.0
5515	0.0	4.7	5.0	5.0
5516	0.0	4.9	5.0	6.1
5518	0.0	4.8	5.0	5.1
5519	0.0	4.7	5.0	6.3
5521	0.0	5.0	5.0	6.1
5522	0.0	4.8	5.0	5.6
5523	0.0	4.7	5.0	5.9

Appendix 27

Individual Mean Fetal Skeletal Ossification Sites

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

0 ug/dose Group 1	Hyoid	Cervical Vertebrae	Thoracic Vertebrae	Lumbar Vertebrae	Sacral Vertebrae	Caudal Vertebrae	Ribs, Paired
5528	1.0	7.0	13.0	6.0	4.0	5.6	13.0
Mean	1.00	7.00	13.06	5.94	4.00	6.23	13.04
SD	0.00	0.00	0.22	0.22	0.00	0.51	0.15
N	21	21	21	21	21	21	21

Appendix 27

Individual Mean Fetal Skeletal Ossification Sites

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

0 ug/dose Group 1	Manubrium	Sternal Centra	Xiphoid	Carpals	Metacarpals	Forelimb Digits	Forelimb Phalanges
5528	1.0	4.0	1.0	0.0	4.0	5.0	8.5
Mean	1.00	4.00	1.00	0.00	4.00	5.00	7.87
SD	0.00	0.00	0.00	0.00	0.00	0.00	0.73
N	21	21	21	21	21	21	21

Appendix 27

Individual Mean Fetal Skeletal Ossification Sites

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

0 ug/dose Group 1	Tarsals	Metatarsals	Hindlimb Digits	Hindlimb Phalanges
5528	0.0	4.7	5.0	5.0
Mean	0.01	4.80	5.00	6.01
SD	0.03	0.20	0.00	1.04
N	21	21	21	21

Appendix 27

Individual Mean Fetal Skeletal Ossification Sites

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

100 ug/dose Group 2	Hyoid	Cervical Vertebrae	Thoracic Vertebrae	Lumbar Vertebrae	Sacral Vertebrae	Caudal Vertebrae	Ribs, Paired
5545	1.0	7.0	13.0	6.0	4.0	5.7	13.0
5546	1.0	7.0	13.0	6.0	4.0	6.9	13.0
5547	1.0	7.0	13.1	5.9	4.0	5.8	13.1
5548	1.0	7.0	13.2	5.8	4.0	5.7	13.1
5549	1.0	7.0	13.0	6.0	4.0	5.7	13.0
5550	1.0	7.0	13.0	6.0	4.0	7.3	13.0
5552	1.0	7.0	13.0	6.0	4.0	5.7	13.0
5554	1.0	7.0	13.0	6.0	4.0	5.4	13.0
5555	1.0	7.0	13.1	5.9	4.0	5.1	13.1
5556	1.0	7.0	13.0	6.0	4.0	5.1	13.0
5557	1.0	7.0	13.0	6.0	4.0	6.5	13.0
5559	1.0	7.0	13.0	6.0	4.0	6.7	13.0
5560	1.0	7.0	13.0	6.0	4.0	6.6	13.0
5561	1.0	7.0	13.0	6.0	4.0	5.1	13.0
5563	1.0	7.0	13.0	6.0	4.0	6.3	13.0
5564	1.0	7.0	13.1	5.9	4.0	6.5	13.1
5565	1.0	7.0	13.0	6.0	4.0	6.8	13.0
5566	1.0	7.0	13.0	6.0	4.0	6.1	13.0
5567	1.0	7.0	13.0	6.0	4.0	6.0	13.0
5568	1.0	7.0	13.0	6.0	4.0	6.4	13.0

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Individual Mean Fetal Skeletal Ossification Sites

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

100 ug/dose Group 2	Manubrium	Sternal Centra	Xiphoid	Carpals	Metacarpals	Forelimb Digits	Forelimb Phalanges
5545	1.0	4.0	1.0	0.0	4.0	5.0	6.3
5546	1.0	4.0	1.0	0.0	4.0	5.0	9.0
5547	1.0	4.0	1.0	0.0	4.0	5.0	8.1
5548	1.0	4.0	1.0	0.0	4.0	5.0	7.0
5549	1.0	4.0	1.0	0.0	4.0	5.0	8.1
5550	1.0	4.0	1.0	0.0	4.0	5.0	8.4
5552	1.0	4.0	1.0	0.0	4.0	5.0	7.4
5554	1.0	4.0	1.0	0.0	4.0	5.0	7.5
5555	1.0	4.0	1.0	0.0	4.0	5.0	7.3
5556	1.0	4.0	1.0	0.0	4.0	5.0	9.0
5557	1.0	4.0	1.0	0.0	4.0	5.0	8.3
5559	1.0	4.0	1.0	0.0	4.0	5.0	8.4
5560	1.0	4.0	1.0	0.0	4.0	5.0	8.0
5561	1.0	4.0	1.0	0.0	4.0	5.0	6.9
5563	1.0	4.0	1.0	0.0	4.0	5.0	8.6
5564	1.0	4.0	1.0	0.0	4.0	5.0	5.9
5565	1.0	4.0	1.0	0.0	4.0	5.0	8.6
5566	1.0	4.0	1.0	0.0	4.0	5.0	9.0
5567	1.0	4.0	1.0	0.0	4.0	5.0	8.1
5568	1.0	4.0	1.0	0.0	4.0	5.0	8.9

Appendix 27

Individual Mean Fetal Skeletal Ossification Sites

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

100 ug/dose Group 2	Tarsals	Metatarsals	Hindlimb Digits	Hindlimb Phalanges
5545	0.0	5.0	5.0	5.5
5546	0.0	5.0	5.0	8.1
5547	0.0	4.9	5.0	5.4
5548	0.0	4.5	5.0	5.3
5549	0.0	4.7	5.0	6.4
5550	0.0	5.0	5.0	6.5
5552	0.0	4.8	5.0	5.1
5554	0.0	4.8	5.0	5.9
5555	0.0	4.3	5.0	5.0
5556	0.0	4.4	5.0	5.0
5557	0.0	5.0	5.0	5.5
5559	0.0	5.0	5.0	6.6
5560	0.0	5.0	5.0	6.0
5561	0.0	4.7	5.0	5.6
5563	0.0	4.9	5.0	6.2
5564	0.0	4.6	5.0	5.8
5565	0.0	5.0	5.0	6.3
5566	0.0	5.0	5.0	7.9
5567	0.0	4.8	5.0	6.1
5568	0.0	5.0	5.0	7.1

Appendix 27

Individual Mean Fetal Skeletal Ossification Sites

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

100 ug/dose Group 2	Hyoid	Cervical Vertebrae	Thoracic Vertebrae	Lumbar Vertebrae	Sacral Vertebrae	Caudal Vertebrae	Ribs, Paired
5569	1.0	7.0	13.0	6.0	4.0	5.1	13.0
5570	1.0	7.0	13.0	6.0	4.0	6.7	13.0
Mean	1.00	7.00	13.02	5.98	4.00	6.05	13.01
SD	0.00	0.00	0.05	0.05	0.00	0.64	0.03
N	22	22	22	22	22	22	22

Appendix 27

Individual Mean Fetal Skeletal Ossification Sites

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

100 ug/dose Group 2	Manubrium	Sternal Centra	Xiphoid	Carpals	Metacarpals	Forelimb Digits	Forelimb Phalanges
5569	1.0	4.0	1.0	0.0	4.0	5.0	7.4
5570	1.0	4.0	1.0	0.0	4.0	5.0	7.8
Mean	1.00	4.00	1.00	0.00	4.00	5.00	7.91
SD	0.00	0.00	0.00	0.00	0.00	0.00	0.87
N	22	22	22	22	22	22	22

Appendix 27

Individual Mean Fetal Skeletal Ossification Sites

20248897

Sex: Female Day(s): - Relative to Mating (Litter: A)

100 ug/dose Group 2	Tarsals	Metatarsals	Hindlimb Digits	Hindlimb Phalanges
5569	0.0	4.6	5.0	5.0
5570	0.0	4.8	5.0	6.0
Mean	0.00	4.81	5.00	6.01
SD	0.00	0.22	0.00	0.85
N	22	22	22	22

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Individual Mean Fetal Skeletal Ossification Sites

20248897

Key Page

Measurement Descriptions

Headings Used	Description
Hyoid	Litter Mean Hyoid
Cervical Vertebrae	Litter Mean Cervical Vertebrae
Thoracic Vertebrae	Litter Mean Thoracic Vertebrae
Lumbar Vertebrae	Litter Mean Lumbar Vertebrae
Sacral Vertebrae	Litter Mean Sacral Vertebrae
Caudal Vertebrae	Litter Mean Caudal Vertebrae
Ribs, Paired	Litter Mean Ribs,Paired
Manubrium	Litter Mean Manubrium
Sternal Centra	Litter Mean Sternal Centra
Xiphoid	Litter Mean Xiphoid
Carpals	Litter Mean Carpals
Metacarpals	Litter Mean Metacarpals
Forelimb Digits	Litter Mean Forelimb Digits
Forelimb Phalanges	Litter Mean Forelimb Phalanges
Tarsals	Litter Mean Tarsals
Metatarsals	Litter Mean Metatarsals
Hindlimb Digits	Litter Mean Hindlimb Digits
Hindlimb Phalanges	Litter Mean Hindlimb Phalanges

Time-Points/Ranges

Measurement	From	To	Report As
Hyoid	-9,999	9,999	-
Cervical Vertebrae	-9,999	9,999	-
Thoracic Vertebrae	-9,999	9,999	-
Lumbar Vertebrae	-9,999	9,999	-
Sacral Vertebrae	-9,999	9,999	-

Appendix 27
Individual Mean Fetal Skeletal Ossification Sites

20248897

Key Page

Time-Points/Ranges (Continued)

Measurement	From	To	Report As
Caudal Vertebrae	-9,999	9,999	-
Ribs, Paired	-9,999	9,999	-
Manubrium	-9,999	9,999	-
Sternal Centra	-9,999	9,999	-
Xiphoid	-9,999	9,999	-
Carpals	-9,999	9,999	-
Metacarpals	-9,999	9,999	-
Forelimb Digits	-9,999	9,999	-
Forelimb Phalanges	-9,999	9,999	-
Tarsals	-9,999	9,999	-
Metatarsals	-9,999	9,999	-
Hindlimb Digits	-9,999	9,999	-
Hindlimb Phalanges	-9,999	9,999	-

Measurement/Statistics

Measurement	Descriptive
Hyoid	Mean
	Standard Deviation
	Count
Cervical Vertebrae	Mean
	Standard Deviation
	Count
Thoracic Vertebrae	Mean
	Standard Deviation
	Count

Appendix 27
Individual Mean Fetal Skeletal Ossification Sites

20248897

Key Page

Measurement/Statistics (Continued)

Measurement	Descriptive
Lumbar Vertebrae	Mean
	Standard Deviation
	Count
Sacral Vertebrae	Mean
	Standard Deviation
	Count
Caudal Vertebrae	Mean
	Standard Deviation
	Count
Ribs, Paired	Mean
	Standard Deviation
	Count
Manubrium	Mean
	Standard Deviation
	Count
Sternal Centra	Mean
	Standard Deviation
	Count
Xiphoid	Mean
	Standard Deviation
	Count
Carpals	Mean
	Standard Deviation
	Count
Metacarpals	Mean
	Standard Deviation
	Count

Appendix 27

Individual Mean Fetal Skeletal Ossification Sites

20248897

Key Page

Measurement/Statistics (Continued)

Measurement	Descriptive
Forelimb Digits	Mean
	Standard Deviation
	Count
Forelimb Phalanges	Mean
	Standard Deviation
	Count
Tarsals	Mean
	Standard Deviation
	Count
Metatarsals	Mean
	Standard Deviation
	Count
Hindlimb Digits	Mean
	Standard Deviation
	Count
Hindlimb Phalanges	Mean
	Standard Deviation
	Count

Group Information

Short Name	Long Name	Type	Report Headings 1-4		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5501	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5502	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5503	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5504	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5505	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5506	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5507	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5508	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5509	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5510	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5511	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5512	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5513	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Complete gross examination was performed. Tissues submitted into 10% neutral buffered formalin except eyes, optic nerves, and Harderian glands submitted in Davidson`s Fixative.

Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

LYMPH NODE : (Comment) iliac and inguinal

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5515	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5516	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5517	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Not-Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5518	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5519	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

GENERAL OBSERVATIONS : (Comment) Photograph(s) Taken.
KIDNEY : Dilatation; right, pelvis : (Comment) mild (TGL)

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5521	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5522	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5523	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5528	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Gestation

20248897

Animal: 5545	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Gestation

20248897

Animal: 5546	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5547	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Gestation

20248897

Animal: 5548	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Gestation

20248897

Animal: 5549	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

GENERAL OBSERVATIONS : (Comment) Photograph taken
PLACENTA : Adhesion : (Comment) placentae fused at sites 8 and 9 (TGL)

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5550	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5552	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5554	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Gestation

20248897

Animal: 5555	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5556	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5557	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 28

Individual Macroscopic Pathology: Gestation

20248897

Animal: 5559	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Gestation

20248897

Animal: 5560	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Gestation

20248897

Animal: 5561	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Gestation

20248897

Animal: 5563	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Gestation

20248897

Animal: 5564	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Gestation

20248897

Animal: 5565	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Gestation

20248897

Animal: 5566	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Gestation

20248897

Animal: 5567	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Gestation

20248897

Animal: 5568	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Gestation

20248897

Animal: 5569	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Gestation

20248897

Animal: 5570	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Tissues submitted in 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Gestation

20248897

Animal: 5572	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Not-Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA CARBON DIOXIDE

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Gestation

20248897

Animal: 5578	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Not-Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA CARBON DIOXIDE

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Gestation

20248897

Key Page

Codes

(TGL) = Trackable Gross Lesion, (MPF) = Major Pathological Finding, (?) = Questionable, (E) = Excluded,
(C) = Clinical Observation, (M) = Mass, (G) = Gross Pathology, (H) = Histopathology

Report Request Items

Animals Included:	5501, 5502, 5503, 5504, 5505, 5506, 5507, 5508, 5509, 5510, 5511, 5512, 5513, 5515, 5516, 5517, 5518, 5519, 5521, 5522, 5523, 5528, 5545, 5546, 5547, 5548, 5549, 5550, 5552, 5554, 5555, 5556, 5557, 5559, 5560, 5561, 5563, 5564, 5565, 5566, 5567, 5568, 5569, 5570, 5572, 5578
Groups:	1, 2
Observation Type:	Gross
Tissues:	All
Removal Reasons:	All

Group Information

Short Name	Long Name	Type
1	1	Control
2	2	Dose

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Individual Macroscopic Pathology: No Confirmed Date of Mating

20248897

Animal: 5539	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Not-Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA CARBON DIOXIDE

Gross Pathology Observations [Correlation]:

OVARY : Cyst, clear; right : (Comment) Measuring 0.7 cm x 0.3 cm x 0.3 cm in size. (TGL)

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 29

Individual Macroscopic Pathology: No Confirmed Date of Mating

20248897

Animal: 5543	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Not-Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA CARBON DIOXIDE

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 29

Individual Macroscopic Pathology: No Confirmed Date of Mating

20248897

Animal: 5551	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Not-Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA CARBON DIOXIDE

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 29

Individual Macroscopic Pathology: No Confirmed Date of Mating

20248897

Animal: 5553	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Not-Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA CARBON DIOXIDE

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 29

Individual Macroscopic Pathology: No Confirmed Date of Mating

20248897

Animal: 5558	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Not-Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA CARBON DIOXIDE

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 29

Individual Macroscopic Pathology: No Confirmed Date of Mating

20248897

Animal: 5562	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Not-Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA CARBON DIOXIDE

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 29

Individual Macroscopic Pathology: No Confirmed Date of Mating

20248897

Animal: 5576	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Pregnancy Status: Not-Pregnant
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA CARBON DIOXIDE

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 29

Individual Macroscopic Pathology: No Confirmed Date of Mating

20248897

Key Page

Codes

(TGL) = Trackable Gross Lesion, (MPF) = Major Pathological Finding, (?) = Questionable, (E) = Excluded, (C) = Clinical Observation, (M) = Mass, (G) = Gross Pathology, (H) = Histopathology

Report Request Items

Animals Included:	5539, 5543, 5551, 5553, 5558, 5562, 5576
Groups:	1, 2
Observation Type:	Gross
Tissues:	All
Removal Reasons:	All

Group Information

Short Name	Long Name	Type
1	1	Control
2	2	Dose

Appendix 30

Individual Macroscopic Pathology: Lactation

20248897

Animal: 5514	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted in 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 30

Individual Macroscopic Pathology: Lactation

20248897

Animal:	5520	Group:	1	Sex:	Female
Species:	Rat	Strain:	Sprague Dawley		
		Dose:	0 ug/dose Group 1		
		Removal Reason:	Euthanized No Surviving Pups		
				Gross Status:	Complete

Gross Pathology Animal Details:

Animal Comment: Complete gross examination was performed. Tissues submitted into 10% neutral buffered formalin except eyes, optic nerves, and Harderian glands submitted in Davidson`s Fixative.

Animal Notes: EUTHANASIA VIA CARBON DIOXIDE

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Lactation

20248897

Animal: 5524	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Lactation

20248897

Animal: 5525	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 30

Individual Macroscopic Pathology: Lactation

20248897

Animal: 5526	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 30

Individual Macroscopic Pathology: Lactation

20248897

Animal: 5527	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Lactation

20248897

Animal: 5529	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Lactation

20248897

Animal: 5530	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Lactation

20248897

Animal: 5531	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Lactation

20248897

Animal: 5532	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 30

Individual Macroscopic Pathology: Lactation

20248897

Animal: 5533	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Lactation

20248897

Animal: 5534	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 30

Individual Macroscopic Pathology: Lactation

20248897

Animal: 5535	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Lactation

20248897

Animal: 5536	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 30

Individual Macroscopic Pathology: Lactation

20248897

Animal: 5537	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 30

Individual Macroscopic Pathology: Lactation

20248897

Animal: 5538	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Lactation

20248897

Animal: 5540	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Lactation

20248897

Animal: 5541	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Lactation

20248897

Animal: 5542	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Lactation

20248897

Animal: 5544	Group: 1	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 0 ug/dose Group 1	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 30

Individual Macroscopic Pathology: Lactation

20248897

Animal: 5571	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted in 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 30

Individual Macroscopic Pathology: Lactation

20248897

Animal: 5573	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 30

Individual Macroscopic Pathology: Lactation

20248897

Animal: 5574	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Lactation

20248897

Animal: 5575	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Lactation

20248897

Animal: 5577	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Lactation

20248897

Animal: 5579	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Lactation

20248897

Animal: 5580	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Lactation

20248897

Animal: 5581	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Lactation

20248897

Animal: 5582	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Lactation

20248897

Animal: 5583	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Lactation

20248897

Animal: 5584	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Lactation

20248897

Animal: 5585	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Lactation

20248897

Animal:	5586	Group:	2	Sex:	Female
Species:	Rat	Strain:	Sprague Dawley		
		Dose:	100 ug/dose Group 2		
		Removal Reason:	Terminal Euthanasia		
				Gross Status:	Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Lactation

20248897

Animal: 5587	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

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Individual Macroscopic Pathology: Lactation

20248897

Animal: 5588	Group: 2	Sex: Female
Species: Rat	Strain: Sprague Dawley	
	Dose: 100 ug/dose Group 2	
	Removal Reason: Terminal Euthanasia	
		Gross Status: Complete

Gross Pathology Animal Details:

Animal Comment: Gross examination was performed. Tissues submitted into 10% neutral buffered formalin.
Animal Notes: EUTHANASIA VIA ANESTHESIA AND EXSANGUINATION

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Gross Pathology - The following Tissues were Not Examined:

None

Appendix 30

Individual Macroscopic Pathology: Lactation

20248897

Key Page

Codes

(TGL) = Trackable Gross Lesion, (MPF) = Major Pathological Finding, (?) = Questionable, (E) = Excluded,
(C) = Clinical Observation, (M) = Mass, (G) = Gross Pathology, (H) = Histopathology

Report Request Items

Animals Included:	5514, 5520, 5524, 5525, 5526, 5527, 5529, 5530, 5531, 5532, 5533, 5534, 5535, 5536, 5537, 5538, 5540, 5541, 5542, 5544, 5571, 5573, 5574, 5575, 5577, 5579, 5580, 5581, 5582, 5583, 5584, 5585, 5586, 5587, 5588
Groups:	1, 2
Observation Type:	Gross
Tissues:	All
Removal Reasons:	All

Group Information

Short Name	Long Name	Type
1	1	Control
2	2	Dose

Appendix 31

Individual Maternal Observations: Lactation

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		0	1	2	3	4	5	6
5514	Grooming of pups - normal	.	X	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	X	.	.	.	.	.
	Nursing activity – normal	.	X	X	X	X	X	X
	Nesting activity – normal	.	X	X	X	X	X	X
5520	Grooming of pups - normal	.	X	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	X	.	.	.	.	.
	Not nursing pups	.	X	X	.	.	.	.
	Nesting activity – normal	.	X	X	.	.	.	.
5524	Grooming of pups - normal	X	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	X	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5525	Grooming of pups - normal	.	X	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	X	.	.	.	.	.
	Nursing activity – normal	.	X	X	X	X	X	X
	Nesting activity – normal	.	X	X	X	X	X	X
5526	Grooming of pups - normal	.	X	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	X	.	.	.	.	.
	Nursing activity – normal	.	X	X	X	X	X	X
	Nesting activity – normal	.	X	X	X	X	X	X
5527	Grooming of pups - normal	.	X	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	X	.	.	.	.	.
	Nursing activity – normal	.	X	X	X	X	X	X
	Nesting activity – normal	.	X	X	X	X	X	X
5529	Grooming of pups - normal	.	X	.	.	.	.	.

X=Present

Appendix 31

Individual Maternal Observations: Lactation

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		0	1	2	3	4	5	6
5529	AmntcSacPlcntaUmbilicaRem-norm	.	X	.	.	.	.	.
	Nursing activity – normal	.	X	X	X	X	X	X
	Nesting activity – normal	.	X	X	X	X	X	X
5530	Grooming of pups - normal	X	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	X	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5531	Grooming of pups - normal	.	X	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	X	.	.	.	.	.
	Nursing activity – normal	.	X	X	X	X	X	X
	Nesting activity – normal	.	X	X	X	X	X	X
5532	Grooming of pups - normal	.	X	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	X	.	.	.	.	.
	Nursing activity – normal	.	X	X	X	X	X	X
	Nesting activity – normal	.	X	X	X	X	X	X
5533	Grooming of pups - normal	.	X	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	X	.	.	.	.	.
	Nursing activity – normal	.	X	X	X	X	X	X
	Nesting activity – normal	.	X	X	X	X	X	X
5534	Grooming of pups - normal	X	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	X	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5535	Grooming of pups - normal	X	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	X	.	.	.	.	.	.

X=Present

Appendix 31

Individual Maternal Observations: Lactation

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		0	1	2	3	4	5	6
5535	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5536	Grooming of pups - normal	X	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	X	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5537	Grooming of pups - normal	X	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	X	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5538	Grooming of pups - normal	X	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	X	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5540	Grooming of pups - normal	X	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	X	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5541	Grooming of pups - normal	X	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	X	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5542	Grooming of pups - normal	X	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	X	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X

X=Present

Appendix 31

Individual Maternal Observations Lactation

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		0	1	2	3	4	5	6
5542	Nesting activity – normal	X	X	X	X	X	X	X
5544	Grooming of pups - normal	X	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	X	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X

X=Present

Appendix 31

Individual Maternal Observations: Lactation

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		7	8	9	10	11	12	13
5514	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5520	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Not nursing pups	.	.	.	.	.	.	.
	Nesting activity – normal	.	.	.	.	.	.	.
5524	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5525	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5526	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5527	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5529	Grooming of pups - normal	.	.	.	.	.	.	.

X=Present

Appendix 31

Individual Maternal Observations: Lactation

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		7	8	9	10	11	12	13
5529	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5530	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5531	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5532	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5533	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5534	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5535	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.

X=Present

Appendix 31

Individual Maternal Observations: Lactation

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		7	8	9	10	11	12	13
5535	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5536	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5537	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5538	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5540	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5541	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5542	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X

X=Present

Appendix 31

Individual Maternal Observations Lactation

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		7	8	9	10	11	12	13
5542	Nesting activity – normal	X	X	X	X	X	X	X
5544	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X

X=Present

Appendix 31

Individual Maternal Observations: Lactation

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		14	15	16	17	18	19	20
5514	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5520	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Not nursing pups	.	.	.	.	.	.	.
	Nesting activity – normal	.	.	.	.	.	.	.
5524	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5525	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5526	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5527	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5529	Grooming of pups - normal	.	.	.	.	.	.	.

X=Present

Appendix 31

Individual Maternal Observations: Lactation

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		14	15	16	17	18	19	20
5529	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5530	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5531	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5532	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5533	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5534	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5535	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.

X=Present

Appendix 31

Individual Maternal Observations: Lactation

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		14	15	16	17	18	19	20
5535	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5536	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5537	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5538	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5540	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5541	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5542	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X

X=Present

Appendix 31

Individual Maternal Observations Lactation

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		14	15	16	17	18	19	20
5542	Nesting activity – normal	X	X	X	X	X	X	X
5544	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X

X=Present

Appendix 31

Individual Maternal Observations: Lactation

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		21						
5514	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5520	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Not nursing pups	.						
	Nesting activity – normal	.						
5524	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5525	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5526	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5527	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5529	Grooming of pups - normal	.						

X=Present

Appendix 31

Individual Maternal Observations: Lactation

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		21						
5529	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5530	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5531	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5532	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5533	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5534	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5535	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						

X=Present

Appendix 31

Individual Maternal Observations: Lactation

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		21						
5535	Nursing activity – normal	X						
	Nesting activity – normal	X						
5536	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5537	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5538	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5540	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5541	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5542	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						

X=Present

Appendix 31

Individual Maternal Observations Lactation

20248897

0 ug/dose Group 1 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		21						
5542 5544	Nesting activity – normal	X						
	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						

X=Present

Appendix 31

Individual Maternal Observations: Lactation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		0	1	2	3	4	5	6
5571	Grooming of pups - normal	.	X	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	X	.	.	.	.	.
	Nursing activity – normal	.	X	X	X	X	X	X
	Nesting activity – normal	.	X	X	X	X	X	X
5573	Grooming of pups - normal	X	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	X	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5574	Grooming of pups - normal	X	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	X	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5575	Grooming of pups - normal	X	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	X	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5577	Grooming of pups - normal	.	X	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	X	.	.	.	.	.
	Nursing activity – normal	.	X	X	X	X	X	X
	Nesting activity – normal	.	X	X	X	X	X	X
5579	Grooming of pups - normal	X	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	X	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5580	Grooming of pups - normal	X	.	.	.	.	.	.

X=Present

Appendix 31

Individual Maternal Observations: Lactation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		0	1	2	3	4	5	6
5580	AmntcSacPlcntaUmbilicaRem-norm	X	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5581	Grooming of pups - normal	X	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	X	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5582	Grooming of pups - normal	X	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	X	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5583	Grooming of pups - normal	.	X	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	X	.	.	.	.	.
	Nursing activity – normal	.	X	X	X	X	X	X
	Nesting activity – normal	.	X	X	X	X	X	X
5584	Grooming of pups - normal	X	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	X	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5585	Grooming of pups - normal	X	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	X	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5586	Grooming of pups - normal	X	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	X	.	.	.	.	.	.

X=Present

Appendix 31

Individual Maternal Observations: Lactation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		0	1	2	3	4	5	6
5586	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5587	Grooming of pups - normal	X	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	X	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5588	Grooming of pups - normal	X	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	X	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X

X=Present

Appendix 31

Individual Maternal Observations: Lactation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		7	8	9	10	11	12	13
5571	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5573	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5574	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5575	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5577	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5579	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5580	Grooming of pups - normal	.	.	.	.	.	.	.

X=Present

Appendix 31

Individual Maternal Observations: Lactation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		7	8	9	10	11	12	13
5580	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5581	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5582	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5583	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5584	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5585	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5586	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.

X=Present

Appendix 31

Individual Maternal Observations: Lactation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		7	8	9	10	11	12	13
5586	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5587	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5588	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X

X=Present

Appendix 31

Individual Maternal Observations: Lactation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		14	15	16	17	18	19	20
5571	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5573	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5574	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5575	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5577	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5579	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	.
	Nesting activity – normal	X	X	X	X	X	X	.
5580	Grooming of pups - normal	.	.	.	.	.	.	.

X=Present

Appendix 31

Individual Maternal Observations: Lactation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		14	15	16	17	18	19	20
5580	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5581	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5582	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5583	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5584	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5585	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5586	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.

X=Present

Appendix 31

Individual Maternal Observations: Lactation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		14	15	16	17	18	19	20
5586	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5587	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X
5588	Grooming of pups - normal	.	.	.	.	.	.	.
	AmntcSacPlcntaUmbilicaRem-norm	.	.	.	.	.	.	.
	Nursing activity – normal	X	X	X	X	X	X	X
	Nesting activity – normal	X	X	X	X	X	X	X

X=Present

Appendix 31

Individual Maternal Observations: Lactation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		21						
5571	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5573	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5574	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5575	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5577	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5579	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5580	Grooming of pups - normal	.						

X=Present

Appendix 31

Individual Maternal Observations: Lactation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		21						
5580	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5581	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5582	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5583	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5584	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5585	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5586	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						

X=Present

Appendix 31

Individual Maternal Observations: Lactation

20248897

100 ug/dose Group 2 Sex: Female	Observation Type: Maternal Observations	Day(s) Relative to Littering (A)						
		21						
5586	Nursing activity – normal	X						
	Nesting activity – normal	X						
5587	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						
5588	Grooming of pups - normal	.						
	AmntcSacPlcntaUmbilicaRem-norm	.						
	Nursing activity – normal	X						
	Nesting activity – normal	X						

X=Present

Appendix 31

Individual Maternal Observations: Lactation

20248897

Key Page

Group Information

Short Name	Long Name	Type	Report Headings		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Appendix 32

Individual Natural Delivery Observations

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

0 ug/dose Group 1	Gestation Length (Days)	Total Number Newborn Pups	Number Live Newborn Pups	Live Birth Index (%)	Number Pups Stillborn	Stillborn Pups/Litter	Live Male Pups/Litter (%)
	-	Birth	Birth	Birth	Birth	Birth	Birth
5514	21	13	13	100.0	0	0.0	58.3
5520	20	13	13	100.0	0	0.0	46.2
5524	22	15	15	100.0	0	0.0	53.3
5525	21	13	13	100.0	0	0.0	38.5
5526	22	17	16	94.1	1	5.9	31.3
5527	21	14	14	100.0	0	0.0	50.0
5529	21	14	14	100.0	0	0.0	64.3
5530	22	16	16	100.0	0	0.0	50.0
5531	21	12	12	100.0	0	0.0	75.0
5532	21	16	16	100.0	0	0.0	56.3
5533	21	13	13	100.0	0	0.0	61.5
5534	22	13	12	92.3	1	7.7	50.0
5535	22	16	16	100.0	0	0.0	62.5
5536	22	17	17	100.0	0	0.0	46.7
5537	22	14	14	100.0	0	0.0	50.0

Appendix 32

Individual Natural Delivery Observations

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

0 ug/dose Group 1	Implants -Total	Implants -Right	Implants -Left	Post Implant Loss/Litter (%)
	-	-	-	-
5514	14	8	6	7.1
5520	15	7	8	13.3
5524	15	10	5	0.0
5525	14	5	9	7.1
5526	18	6	12	5.6
5527	14	6	8	0.0
5529	14	7	7	0.0
5530	17	9	8	5.9
5531	13	4	9	7.7
5532	16	10	6	0.0
5533	13	7	6	0.0
5534	16	7	9	18.8
5535	16	6	10	0.0
5536	17	11	6	0.0
5537	15	6	9	6.7

Appendix 32

Individual Natural Delivery Observations

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

0 ug/dose Group 1	Gestation Length (Days)	Total Number Newborn Pups	Number Live Newborn Pups	Live Birth Index (%)	Number Pups Stillborn	Stillborn Pups/Litter	Live Male Pups/Litter (%)
	-	Birth	Birth	Birth	Birth	Birth	Birth
5538	22	13	13	100.0	0	0.0	69.2
5539 NP	-	-	-	-	.	-	-
5540	22	10	10	100.0	0	0.0	70.0
5541	23	7	7	100.0	0	0.0	28.6
5542	22	14	14	100.0	0	0.0	42.9
5543 NP	-	-	-	-	.	-	-
5544	22	14	14	100.0	0	0.0	35.7
Mean	21.6	13.7	13.6	99.32	0.1	0.68	52.01
SD	0.7	2.3	2.3	2.11	0.3	2.11	12.88
N	20	20	20	20	20	20	20

Appendix 32

Individual Natural Delivery Observations

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

0 ug/dose Group 1	Implants -Total	Implants -Right	Implants -Left	Post Implant Loss/Litter (%)
	-	-	-	-
5538	13	5	8	0.0
5539 NP	-	-	-	-
5540	15	7	8	33.3
5541	16	11	5	56.3
5542	14	8	6	0.0
5543 NP	-	-	-	-
5544	17	10	7	17.6
Mean	15.1	7.5	7.6	8.97
SD	1.5	2.1	1.8	14.10
N	20	20	20	20

Appendix 32

Individual Natural Delivery Observations

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

100 ug/dose Group 2	Gestation Length (Days)	Total Number Newborn Pups	Number Live Newborn Pups	Live Birth Index (%)	Number Pups Stillborn	Stillborn Pups/Litter	Live Male Pups/Litter (%)
	-	Birth	Birth	Birth	Birth	Birth	Birth
5551 NP	-	-	-	-	.	-	-
5553 NP	-	-	-	-	.	-	-
5558 NP	-	-	-	-	.	-	-
5562 NP	-	-	-	-	.	-	-
5571	22	9	9	100.0	0	0.0	33.3
5573	21	13	13	100.0	0	0.0	30.8
5574	22	12	12	100.0	0	0.0	41.7
5575	22	14	13	92.9	1	7.1	46.2
5577	21	12	12	100.0	0	0.0	41.7
5579	22	14	14	100.0	0	0.0	42.9
5580	22	19	19	100.0	0	0.0	42.1
5581	22	14	14	100.0	0	0.0	50.0
5582	21	15	15	100.0	0	0.0	13.3
5583	21	11	11	100.0	0	0.0	36.4
5584	22	12	11	91.7	1	8.3	72.7

Appendix 32

Individual Natural Delivery Observations

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

100 ug/dose Group 2	Implants -Total	Implants -Right	Implants -Left	Post Implant Loss/Litter (%)
	-	-	-	-
5551 NP	-	-	-	-
5553 NP	-	-	-	-
5558 NP	-	-	-	-
5562 NP	-	-	-	-
5571	16	8	8	43.8
5573	13	6	7	0.0
5574	12	6	6	0.0
5575	14	7	7	0.0
5577	12	5	7	0.0
5579	16	8	8	12.5
5580	19	9	10	0.0
5581	14	7	7	0.0
5582	16	7	9	6.3
5583	11	4	7	0.0
5584	12	7	5	0.0

Appendix 32

Individual Natural Delivery Observations

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

100 ug/dose Group 2	Gestation Length (Days)	Total Number Newborn Pups	Number Live Newborn Pups	Live Birth Index (%)	Number Pups Stillborn	Stillborn Pups/Litter	Live Male Pups/Litter (%)
	-	Birth	Birth	Birth	Birth	Birth	Birth
5585	21	15	15	100.0	0	0.0	73.3
5586	22	13	13	100.0	0	0.0	15.4
5587	22	15	15	100.0	0	0.0	60.0
5588	22	17	17	100.0	0	0.0	58.8
Mean	21.7	13.7	13.5	98.97	0.1	1.03	43.90
SD	0.5	2.4	2.5	2.73	0.4	2.73	17.57
N	15	15	15	15	15	15	15

Appendix 32

Individual Natural Delivery Observations

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

100 ug/dose Group 2	Implants -Total	Implants -Right	Implants -Left	Post Implant Loss/Litter (%)
	-	-	-	-
5585	16	7	9	6.3
5586	14	4	10	7.1
5587	17	8	9	11.8
5588	17	7	10	0.0
Mean	14.6	6.7	7.9	5.84
SD	2.3	1.4	1.5	11.42
N	15	15	15	15

Appendix 32

Individual Natural Delivery Observations

20248897

Subject Comments/Exclusions

Subject	Marker	Comment/Exclusion
5539	NP	Not Pregnant
5543	NP	Not Pregnant
5551	NP	Not Pregnant
5553	NP	Not Pregnant
5558	NP	Not Pregnant
5562	NP	Not Pregnant

Appendix 32

Individual Natural Delivery Observations

20248897

Key Page

Measurement Descriptions

Headings Used	Description
Gestation Length	Gestation Length
Total Number Newborn Pups	Total Number Newborn Pups
Number Live Newborn Pups	Number Live Newborn Pups
Live Birth Index	Live Birth Index - (Mean % / litter)
Number Pups Stillborn	Cmb - Stillborn
Stillborn Pups/Litter	Cmb - Stillborn Pups/Litter %
Live Male Pups/Litter	Cmb - Sex Ratio Range
Implants -Total	Implantation Sites - Total (Lactation)
Implants -Right	Implantation Sites - Right (Lactation)
Implants -Left	Implantation Sites - Left (Lactation)
Post Implant Loss/Litter	Post Implantation Loss % /Litter (Pups)

Unit Descriptions

Headings Used	Description
%	%
Days	DAYS

Time-Points/Ranges

Measurement	From	To	Report As
Gestation Length	-9,999	9,999	-
Total Number Newborn Pups	-9,999	9,999	Birth
Number Live Newborn Pups	-9,999	9,999	Birth
Live Birth Index	-9,999	9,999	Birth

Appendix 32

Individual Natural Delivery Observations

20248897

Key Page

Time-Points/Ranges (Continued)

Measurement	From	To	Report As
Number Pups Stillborn	-9,999	9,999	Birth
Stillborn Pups/Litter	-9,999	9,999	Birth
Live Male Pups/Litter	0	1	Birth
Implants -Total	-9,999	9,999	-
Implants -Right	-9,999	9,999	-
Implants -Left	-9,999	9,999	-
Post Implant Loss/Litter	-9,999	9,999	-

Measurement/Statistics

Measurement	Descriptive
Gestation Length	Mean
	Standard Deviation
	Count
Total Number Newborn Pups	Mean
	Standard Deviation
	Count
Number Live Newborn Pups	Mean
	Standard Deviation
	Count
Live Birth Index	Mean
	Standard Deviation
	Count
Number Pups Stillborn	Mean
	Standard Deviation
	Count

Appendix 32

Individual Natural Delivery Observations

20248897

Key Page

Measurement/Statistics (Continued)

Measurement	Descriptive
Stillborn Pups/Litter	Mean
	Standard Deviation
	Count
Live Male Pups/Litter	Mean
	Standard Deviation
	Count
Implants -Total	Mean
	Standard Deviation
	Count
Implants -Right	Mean
	Standard Deviation
	Count
Implants -Left	Mean
	Standard Deviation
	Count
Post Implant Loss/Litter	Mean
	Standard Deviation
	Count

Group Information

Short Name	Long Name	Type	Report Headings 1-4		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Appendix 33

Individual Pup Clinical Observations: F1 Generation

20248897

0 ug/dose Group 1	Day(s) Relative to Littering (A)	Number of Pups	Observation Type All Types
5514	2	10/10	Cold to Touch
	4	1/6	Skin, Discolored, Cranium, Purple
	21	1/6	Discharge, Color, Eye, Left, Red
5520	1	13/13	Cold to Touch
	2	1/1	Dehydrated Suspected, Moderate
		1/1	Cold to Touch
5526	14	1/8	Skin, Scab, Anus
	15	1/8	Skin, Scab, Anus
	16	1/8	Skin, Scab, Anus
5532	7	1/8	Skin, Discolored, Tip of Tail, Black
	8	1/8	Skin, Discolored, Tip of Tail, Black
	9	1/8	Skin, Discolored, Tip of Tail, Black
	10	1/8	Skin, Discolored, Tip of Tail, Black
	11	1/8	Skin, Discolored, Tip of Tail, Black
5534	0	1/12	Skin, Discolored, Nose, Purple
	1	1/12	Skin, Discolored, Nose, Purple

Appendix 33

Individual Pup Clinical Observations: F1 Generation

20248897

100 ug/dose Group 2	Day(s) Relative to Littering (A)	Number of Pups	Observation Type All Types
5575	0	1/13	Skin, Discolored, Generalized, Pale
		1/13	Cold to Touch
		1/13	No Milk Band Present
	14	8/8	Fur, Ungroomed
5586	4	1/13	Skin, Scab, Forelimb, Right
		1/13	Skin, Scab, Inguinal, Right
	5	1/8	Skin, Scab, Forelimb, Right
		1/8	Skin, Scab, Inguinal, Right
	6	1/8	Skin, Scab, Forelimb, Right
		1/8	Skin, Scab, Inguinal, Right

Appendix 33

Individual Pup Clinical Observations: F1 Generation

20248897

Key Page

Group Information

Short Name	Long Name	Type	Report Headings		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Appendix 34
Individual Litter Observations

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

0 ug/dose Group 1	Live Pups on Day 1	Live Males on Day 1	Live Females on Day 1	Live Pups on Day 4	Live Males on Day 4	Live Females on Day 4	Live Pups Postcull
	-	-	-	-	-	-	-
5514	12	7	5	6	4	2	6
5520	13	6	7	-	-	-	0
5524	15	8	7	15	8	7	8
5525	13	5	8	13	5	8	8
5526	16	5	11	16	5	11	8
5527	14	7	7	14	7	7	8
5529	14	9	5	14	9	5	8
5530	16	8	8	16	8	8	8
5531	12	9	3	12	9	3	8
5532	16	9	7	16	9	7	8
5533	13	8	5	13	8	5	8
5534	12	6	6	12	6	6	8
5535	16	10	6	16	10	6	8

Appendix 34

Individual Litter Observations

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

0 ug/dose Group 1	Postcull Live Males	Postcull Live Females	Live Pups on Day 7	Live Males on Day 7	Live Females on Day 7	Live Pups on Day 10	Live Males on Day 10
	4	4	-	-	-	-	-
5514	4	2	6	4	2	6	4
5520	-	-	-	-	-	-	-
5524	4	4	8	4	4	8	4
5525	4	4	8	4	4	8	4
5526	4	4	8	4	4	8	4
5527	4	4	8	4	4	8	4
5529	4	4	8	4	4	8	4
5530	4	4	8	4	4	8	4
5531	5	3	8	5	3	8	5
5532	4	4	8	4	4	8	4
5533	4	4	8	4	4	8	4
5534	4	4	8	4	4	8	4
5535	4	4	8	4	4	8	4

Appendix 34
Individual Litter Observations

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

0 ug/dose Group 1	Live Females on Day 10	Live Pups on Day 14	Live Males on Day 14	Live Females on Day 14	Live Pups on Day 21	Live Males on Day 21	Live Females on Day 21
	-	-	-	-	-	-	-
5514	2	6	4	2	6	4	2
5520	-	-	-	-	-	-	-
5524	4	8	4	4	8	4	4
5525	4	8	4	4	8	4	4
5526	4	8	4	4	8	4	4
5527	4	8	4	4	8	4	4
5529	4	8	4	4	8	4	4
5530	4	8	4	4	8	4	4
5531	3	8	5	3	8	5	3
5532	4	8	4	4	8	4	4
5533	4	8	4	4	8	4	4
5534	4	8	4	4	8	4	4
5535	4	8	4	4	8	4	4

Appendix 34
Individual Litter Observations

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

0 ug/dose Group 1	Viability Index	Lactation Index	Live Male Pups/Litter (%)
	1-4	4Postcull-21	21
5514	46.2	100.0	66.7
5520	0.0	NC	-
5524	100.0	100.0	50.0
5525	100.0	100.0	50.0
5526	100.0	100.0	50.0
5527	100.0	100.0	50.0
5529	100.0	100.0	50.0
5530	100.0	100.0	50.0
5531	100.0	100.0	62.5
5532	100.0	100.0	50.0
5533	100.0	100.0	50.0
5534	100.0	100.0	50.0
5535	100.0	100.0	50.0

Appendix 34
Individual Litter Observations

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

0 ug/dose Group 1	Live Pups on Day 1	Live Males on Day 1	Live Females on Day 1	Live Pups on Day 4	Live Males on Day 4	Live Females on Day 4	Live Pups Postcull
	-	-	-	-	-	-	-
5536	15	7	8	15	7	8	8
5537	14	7	7	14	7	7	8
5538	13	9	4	13	9	4	8
5540	10	7	3	10	7	3	8
5541	7	2	5	7	2	5	7
5542	13	6	7	13	6	7	8
5544	14	5	9	13	5	8	8
Mean	13.4	7.0	6.4	13.1	6.9	6.2	7.5
SD	2.2	1.9	2.0	2.8	2.1	2.2	1.8
N	20	20	20	19	19	19	20

Appendix 34
Individual Litter Observations

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

0 ug/dose Group 1	Postcull Live Males	Postcull Live Females	Live Pups on Day 7	Live Males on Day 7	Live Females on Day 7	Live Pups on Day 10	Live Males on Day 10
	4	4	-	-	-	-	-
5536	4	4	8	4	4	8	4
5537	4	4	8	4	4	8	4
5538	4	4	8	4	4	8	4
5540	5	3	8	5	3	8	5
5541	2	5	7	2	5	7	2
5542	4	4	8	4	4	8	4
5544	4	4	7	3	4	7	3
Mean	4.0	3.8	7.8	3.9	3.8	7.8	3.9
SD	0.6	0.6	0.5	0.6	0.6	0.5	0.6
N	19	19	19	19	19	19	19

Appendix 34
Individual Litter Observations

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

0 ug/dose Group 1	Live Females on Day 10	Live Pups on Day 14	Live Males on Day 14	Live Females on Day 14	Live Pups on Day 21	Live Males on Day 21	Live Females on Day 21
	-	-	-	-	-	-	-
5536	4	8	4	4	8	4	4
5537	4	8	4	4	8	4	4
5538	4	8	4	4	8	4	4
5540	3	8	5	3	8	5	3
5541	5	7	2	5	7	2	5
5542	4	8	4	4	8	4	4
5544	4	7	3	4	7	3	4
Mean	3.8	7.8	3.9	3.8	7.8	3.9	3.8
SD	0.6	0.5	0.6	0.6	0.5	0.6	0.6
N	19	19	19	19	19	19	19

Appendix 34
Individual Litter Observations

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

0 ug/dose Group 1	Viability Index	Lactation Index	Live Male Pups/Litter (%)
	1-4	4Postcull-21	21
5536	88.2	100.0	50.0
5537	100.0	100.0	50.0
5538	100.0	100.0	50.0
5540	100.0	100.0	62.5
5541	100.0	100.0	28.6
5542	92.9	100.0	50.0
5544	92.9	87.5	42.9
Mean	91.01	99.34	50.69
SD	24.63	2.87	7.79
N	20	19	19

Appendix 34
Individual Litter Observations

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

100 ug/dose Group 2	Live Pups on Day 1	Live Males on Day 1	Live Females on Day 1	Live Pups on Day 4	Live Males on Day 4	Live Females on Day 4	Live Pups Postcull
	-	-	-	-	-	-	-
5571	9	3	6	9	3	6	8
5573	13	4	9	13	4	9	8
5574	12	5	7	12	5	7	8
5575	12	5	7	12	5	7	8
5577	12	5	7	12	5	7	8
5579	14	6	8	14	6	8	8
5580	15	6	9	14	5	9	8
5581	14	7	7	14	7	7	8
5582	14	1	13	14	1	13	8
5583	11	4	7	11	4	7	8
5584	11	8	3	11	8	3	8
5585	15	11	4	14	11	3	8
5586	13	2	11	13	2	11	8

Appendix 34
Individual Litter Observations

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

100 ug/dose Group 2	Postcull Live Males	Postcull Live Females	Live Pups on Day 7	Live Males on Day 7	Live Females on Day 7	Live Pups on Day 10	Live Males on Day 10
	4	4	-	-	-	-	-
5571	3	5	8	3	5	8	3
5573	4	4	8	4	4	8	4
5574	4	4	8	4	4	8	4
5575	4	4	8	4	4	8	4
5577	4	4	8	4	4	8	4
5579	4	4	8	4	4	8	4
5580	4	4	8	4	4	8	4
5581	4	4	8	4	4	8	4
5582	1	7	8	1	7	8	1
5583	4	4	8	4	4	8	4
5584	5	3	8	5	3	8	5
5585	5	3	8	5	3	8	5
5586	2	6	8	2	6	8	2

Appendix 34
Individual Litter Observations

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

100 ug/dose Group 2	Live Females on Day 10	Live Pups on Day 14	Live Males on Day 14	Live Females on Day 14	Live Pups on Day 21	Live Males on Day 21	Live Females on Day 21
	-	-	-	-	-	-	-
5571	5	8	3	5	8	3	5
5573	4	8	4	4	8	4	4
5574	4	8	4	4	8	4	4
5575	4	8	4	4	8	4	4
5577	4	8	4	4	8	4	4
5579	4	8	4	4	8	4	4
5580	4	8	4	4	8	4	4
5581	4	8	4	4	8	4	4
5582	7	8	1	7	8	1	7
5583	4	8	4	4	8	4	4
5584	3	8	5	3	8	5	3
5585	3	8	5	3	8	5	3
5586	6	8	2	6	8	2	6

Appendix 34
Individual Litter Observations

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

100 ug/dose Group 2	Viability Index	Lactation Index	Live Male Pups/Litter (%)
	1-4	4Postcull-21	21
5571	100.0	100.0	37.5
5573	100.0	100.0	50.0
5574	100.0	100.0	50.0
5575	92.3	100.0	50.0
5577	100.0	100.0	50.0
5579	100.0	100.0	50.0
5580	73.7	100.0	50.0
5581	100.0	100.0	50.0
5582	93.3	100.0	12.5
5583	100.0	100.0	50.0
5584	100.0	100.0	62.5
5585	93.3	100.0	62.5
5586	100.0	100.0	25.0

Appendix 34

Individual Litter Observations

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

100 ug/dose Group 2	Live Pups on Day 1	Live Males on Day 1	Live Females on Day 1	Live Pups on Day 4	Live Males on Day 4	Live Females on Day 4	Live Pups Postcull
	-	-	-	-	-	-	-
5587	15	9	6	15	9	6	8
5588	17	10	7	17	10	7	8
Mean	13.1	5.7	7.4	13.0	5.7	7.3	8.0
SD	2.0	2.9	2.5	1.9	2.9	2.6	0.0
N	15	15	15	15	15	15	15

Appendix 34

Individual Litter Observations

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

100 ug/dose Group 2	Postcull Live Males	Postcull Live Females	Live Pups on Day 7	Live Males on Day 7	Live Females on Day 7	Live Pups on Day 10	Live Males on Day 10
	4	4	-	-	-	-	-
5587	4	4	8	4	4	8	4
5588	4	4	8	4	4	8	4
Mean	3.7	4.3	8.0	3.7	4.3	8.0	3.7
SD	1.0	1.0	0.0	1.0	1.0	0.0	1.0
N	15	15	15	15	15	15	15

Appendix 34

Individual Litter Observations

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

100 ug/dose Group 2	Live Females on Day 10	Live Pups on Day 14	Live Males on Day 14	Live Females on Day 14	Live Pups on Day 21	Live Males on Day 21	Live Females on Day 21
	-	-	-	-	-	-	-
5587	4	8	4	4	8	4	4
5588	4	8	4	4	8	4	4
Mean	4.3	8.0	3.7	4.3	8.0	3.7	4.3
SD	1.0	0.0	1.0	1.0	0.0	1.0	1.0
N	15	15	15	15	15	15	15

Appendix 34
Individual Litter Observations

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

100 ug/dose Group 2	Viability Index	Lactation Index	Live Male Pups/Litter (%)
	1-4	4Postcull-21	21
5587	100.0	100.0	50.0
5588	100.0	100.0	50.0
Mean	96.84	100.00	46.67
SD	7.03	0.00	12.91
N	15	15	15

Appendix 34
Individual Litter Observations

20248897

Comments and Markers

Page	Day	Group	Sex	Subject	Measurement	Type	Marker
	4Postcull-21	1	Female	5520	Lactation Index	Replacement	NC

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Individual Litter Observations

20248897

Key Page

Replacement Values

Value	Description
NC	Not Calculable

Measurement Descriptions

Headings Used	Description
Live Pups on Day 1	ILD - Live Pups on Day 1
Live Males on Day 1	ILD - Live Males on Day 1
Live Females on Day 1	ILD - Live Females on Day 1
Live Pups on Day 4	ILD - Live Pups on Day 4
Live Males on Day 4	ILD - Live Males on Day 4
Live Females on Day 4	ILD - Live Females on Day 4
Live Pups Postcull	Live Pups Post Cull in litter
Postcull Live Males	Live Males - Post Cull
Postcull Live Females	Live Females - Post Cull
Live Pups on Day 7	ILD - Live Pups on Day 7
Live Males on Day 7	ILD - Live Males on Day 7
Live Females on Day 7	ILD - Live Females on Day 7
Live Pups on Day 10	ILD - Live Pups on Day 10
Live Males on Day 10	ILD - Live Males on Day 10
Live Females on Day 10	ILD - Live Females on Day 10
Live Pups on Day 14	ILD - Live Pups on Day 14
Live Males on Day 14	ILD - Live Males on Day 14
Live Females on Day 14	ILD - Live Females on Day 14
Live Pups on Day 21	ILD - Live Pups on Day 21
Live Males on Day 21	ILD - Live Males on Day 21
Live Females on Day 21	ILD - Live Females on Day 21
Viability Index	Viability Index

Appendix 34
Individual Litter Observations

20248897

Key Page

Measurement Descriptions (Continued)

Headings Used	Description
Lactation Index	Lactation Index
Live Male Pups/Litter	Cmb - Sex Ratio Range

Unit Descriptions

Headings Used	Description
%	%

Time-Points/Ranges

Measurement	From	To	Report As
Live Pups on Day 1	-9,999	9,999	-
Live Males on Day 1	-9,999	9,999	-
Live Females on Day 1	-9,999	9,999	-
Live Pups on Day 4	-9,999	9,999	-
Live Males on Day 4	-9,999	9,999	-
Live Females on Day 4	-9,999	9,999	-
Live Pups Postcull	-9,999	9,999	-
Live Pups on Day 7	-9,999	9,999	-
Live Males on Day 7	-9,999	9,999	-
Live Females on Day 7	-9,999	9,999	-
Live Pups on Day 10	-9,999	9,999	-
Live Males on Day 10	-9,999	9,999	-
Live Females on Day 10	-9,999	9,999	-
Live Pups on Day 14	-9,999	9,999	-
Live Males on Day 14	-9,999	9,999	-
Live Females on Day 14	-9,999	9,999	-

Appendix 34
Individual Litter Observations

20248897

Key Page

Time-Points/Ranges (Continued)

Measurement	From	To	Report As
Live Pups on Day 21	-9,999	9,999	-
Live Males on Day 21	-9,999	9,999	-
Live Females on Day 21	-9,999	9,999	-
Viability Index	-9,999	9,999	1-4
Lactation Index	-9,999	9,999	4Postcull-21
Live Male Pups/Litter	21	21	21

Measurement/Statistics

Measurement	Descriptive
Live Pups on Day 1	Mean
	Standard Deviation
	Count
Live Males on Day 1	Mean
	Standard Deviation
	Count
Live Females on Day 1	Mean
	Standard Deviation
	Count
Live Pups on Day 4	Mean
	Standard Deviation
	Count
Live Males on Day 4	Mean
	Standard Deviation
	Count

Appendix 34
Individual Litter Observations

20248897

Key Page

Measurement/Statistics (Continued)

Measurement	Descriptive
Live Females on Day 4	Mean
	Standard Deviation
	Count
Live Pups Postcull	Mean
	Standard Deviation
	Count
Postcull Live Males	Mean
	Standard Deviation
	Count
Postcull Live Females	Mean
	Standard Deviation
	Count
Live Pups on Day 7	Mean
	Standard Deviation
	Count
Live Males on Day 7	Mean
	Standard Deviation
	Count
Live Females on Day 7	Mean
	Standard Deviation
	Count
Live Pups on Day 10	Mean
	Standard Deviation
	Count
Live Males on Day 10	Mean
	Standard Deviation
	Count

Appendix 34
Individual Litter Observations

20248897

Key Page

Measurement/Statistics (Continued)

Measurement	Descriptive
Live Females on Day 10	Mean
	Standard Deviation
	Count
Live Pups on Day 14	Mean
	Standard Deviation
	Count
Live Males on Day 14	Mean
	Standard Deviation
	Count
Live Females on Day 14	Mean
	Standard Deviation
	Count
Live Pups on Day 21	Mean
	Standard Deviation
	Count
Live Males on Day 21	Mean
	Standard Deviation
	Count
Live Females on Day 21	Mean
	Standard Deviation
	Count
Viability Index	Mean
	Standard Deviation
	Count
Lactation Index	Mean
	Standard Deviation
	Count

Appendix 34
Individual Litter Observations

20248897

Key Page

Measurement/Statistics (Continued)

Measurement	Descriptive
Live Male Pups/Litter	Mean
	Standard Deviation
	Count

Group Information

Short Name	Long Name	Type	Report Headings 1-4		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Appendix 35
Individual Pup Body Weights: F1 Generation

20248897
Day: 1 Relative to Littering (Litter: A)

0 ug/dose Group 1 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5514	Male	PBWT	6.1	6.3	6.8	5.9	6.5	6.3	4.6	6.0	-	-	-	-	-	-
	Female	PBWT	5.5	5.5	5.2	5.7	5.9	5.4	-	-	-	-	-	-	-	-
5520	Male	PBWT	5.0	5.1	4.6	4.7	5.0	5.2	5.1	-	-	-	-	-	-	-
	Female	PBWT	4.9	5.2	4.9	5.0	4.5	4.8	4.8	5.1	-	-	-	-	-	-
5524	Male	PBWT	7.7	8.0	7.3	7.4	8.0	8.0	7.2	7.8	8.0	-	-	-	-	-
	Female	PBWT	7.6	7.8	8.4	7.3	7.4	7.4	6.6	8.2	-	-	-	-	-	-
5525	Male	PBWT	7.2	7.4	7.4	6.6	7.2	7.4	-	-	-	-	-	-	-	-
	Female	PBWT	6.9	6.8	7.3	6.7	6.9	6.7	6.8	6.8	7.0	-	-	-	-	-
5526	Male	PBWT	6.5	6.1	7.0	6.2	6.9	6.5	-	-	-	-	-	-	-	-
	Female	PBWT	6.7	7.4	6.4	6.9	6.3	7.1	5.8	7.1	7.3	6.8	6.3	6.5	-	-
5527	Male	PBWT	7.1	6.7	7.6	7.3	6.6	7.6	6.9	6.9	-	-	-	-	-	-
	Female	PBWT	7.0	6.8	6.8	7.0	7.7	6.9	7.0	6.6	-	-	-	-	-	-
5529	Male	PBWT	7.7	8.0	7.2	7.6	7.6	8.0	7.4	8.1	7.8	7.9	-	-	-	-
	Female	PBWT	6.9	7.0	7.1	7.4	6.9	6.2	-	-	-	-	-	-	-	-
5530	Male	PBWT	8.0	7.3	8.5	8.1	7.9	8.2	7.7	8.0	8.0	-	-	-	-	-
	Female	PBWT	7.3	7.6	6.9	6.7	7.1	7.7	7.3	7.1	8.1	-	-	-	-	-
5531	Male	PBWT	7.3	6.6	7.1	7.7	7.4	6.7	7.4	7.8	7.6	7.2	-	-	-	-
	Female	PBWT	7.1	7.0	7.2	7.0	-	-	-	-	-	-	-	-	-	-

Appendix 35
Individual Pup Body Weights: F1 Generation

20248897
Day: 1 Relative to Littering (Litter: A)

0 ug/dose Group 1 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5532	Male	PBWT	6.8	6.8	6.8	6.6	6.9	7.1	6.3	7.3	6.3	7.0	-	-	-	-
	Female	PBWT	6.5	6.8	6.8	5.3	6.7	6.6	6.6	6.5	-	-	-	-	-	-
5533	Male	PBWT	7.3	7.4	7.2	7.4	6.8	8.1	7.2	7.3	7.0	-	-	-	-	-
	Female	PBWT	7.0	6.6	6.8	7.0	7.2	7.3	-	-	-	-	-	-	-	-
5534	Male	PBWT	8.0	8.2	8.0	7.6	8.5	7.5	8.2	-	-	-	-	-	-	-
	Female	PBWT	7.9	7.3	8.0	8.0	8.3	8.2	7.8	-	-	-	-	-	-	-
5535	Male	PBWT	7.5	6.7	7.7	7.7	8.2	7.9	7.1	8.1	7.7	7.6	6.6	-	-	-
	Female	PBWT	7.2	7.3	7.1	6.4	7.2	7.3	7.7	-	-	-	-	-	-	-
5536	Male	PBWT	8.1	8.7	7.5	8.9	7.3	8.5	8.2	7.4	-	-	-	-	-	-
	Female	PBWT	7.6	8.0	7.1	8.6	7.5	7.8	7.7	7.3	6.5	-	-	-	-	-
5537	Male	PBWT	8.0	7.7	8.2	7.9	8.2	7.8	8.1	8.3	-	-	-	-	-	-
	Female	PBWT	7.7	7.3	7.4	7.8	7.8	8.2	7.6	7.5	-	-	-	-	-	-
5538	Male	PBWT	8.3	8.7	7.9	7.8	7.7	8.1	8.4	8.6	8.7	8.5	-	-	-	-
	Female	PBWT	7.9	7.3	8.0	8.1	8.0	-	-	-	-	-	-	-	-	-
5540	Male	PBWT	7.9	7.4	8.6	7.7	8.3	6.8	8.5	8.1	-	-	-	-	-	-
	Female	PBWT	8.2	8.2	8.2	8.2	-	-	-	-	-	-	-	-	-	-
5541	Male	PBWT	7.0	7.8	6.2	-	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	7.1	6.1	7.6	7.8	7.4	6.5	-	-	-	-	-	-	-	-

Appendix 35
Individual Pup Body Weights: F1 Generation

20248897
Day: 1 Relative to Littering (Litter: A)

0 ug/dose Group 1 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5542	Male	PBWT	7.7	7.1	7.8	7.8	8.2	7.6	7.6	-	-	-	-	-	-	-
	Female	PBWT	7.0	7.2	7.6	6.9	7.1	6.9	6.9	6.7	-	-	-	-	-	-
5544	Male	PBWT	8.5	9.0	8.6	8.2	8.5	8.1	-	-	-	-	-	-	-	-
	Female	PBWT	7.8	8.2	6.5	8.1	7.5	7.2	7.4	8.7	8.8	8.1	-	-	-	-

Appendix 35

Individual Pup Body Weights: F1 Generation

20248897

Day: 1 Relative to Littering (Litter: A)

100 ug/dose Group 2 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5571	Male	PBWT	7.4	6.4	8.5	7.3	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	7.6	7.9	8.5	6.1	8.4	7.9	6.7	-	-	-	-	-	-	-
5573	Male	PBWT	6.8	7.1	7.0	6.6	6.6	-	-	-	-	-	-	-	-	-
	Female	PBWT	6.4	5.9	6.7	6.5	6.0	6.5	6.9	6.8	5.3	7.0	-	-	-	-
5574	Male	PBWT	7.8	7.3	8.0	8.1	7.7	8.1	-	-	-	-	-	-	-	-
	Female	PBWT	7.5	7.2	7.3	7.8	7.0	7.7	7.9	7.4	-	-	-	-	-	-
5575	Male	PBWT	8.0	6.5	8.4	8.3	8.3	8.3	-	-	-	-	-	-	-	-
	Female	PBWT	8.0	7.5	8.9	8.0	8.0	7.7	7.7	8.0	-	-	-	-	-	-
5577	Male	PBWT	6.8	6.2	7.3	7.1	6.7	6.6	-	-	-	-	-	-	-	-
	Female	PBWT	6.7	5.6	7.1	7.1	6.9	6.6	6.8	6.9	-	-	-	-	-	-
5579	Male	PBWT	8.4	8.5	7.5	8.2	8.8	8.8	8.3	-	-	-	-	-	-	-
	Female	PBWT	7.7	7.7	8.1	7.4	7.7	8.1	7.5	7.2	8.1	-	-	-	-	-
5580	Male	PBWT	7.8	6.8	7.1	8.4	8.3	7.8	8.3	-	-	-	-	-	-	-
	Female	PBWT	7.1	7.7	7.0	7.0	7.2	7.6	6.9	6.2	7.2	7.2	-	-	-	-
5581	Male	PBWT	7.7	7.4	7.8	7.3	7.5	7.9	8.1	8.0	-	-	-	-	-	-
	Female	PBWT	6.8	7.9	7.2	7.2	6.7	6.8	5.5	6.5	-	-	-	-	-	-
5582	Male	PBWT	6.1	6.1	-	-	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	6.1	6.5	5.6	5.9	6.2	6.1	6.8	5.8	5.7	6.5	6.4	5.7	6.4	5.8

Appendix 35

Individual Pup Body Weights: F1 Generation

20248897

Day: 1 Relative to Littering (Litter: A)

100 ug/dose Group 2 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5583	Male	PBWT	8.6	9.0	7.3	9.0	9.2	-	-	-	-	-	-	-	-	-
	Female	PBWT	7.4	7.0	7.4	7.7	7.8	6.3	8.1	7.4	-	-	-	-	-	-
5584	Male	PBWT	8.6	8.6	9.0	9.4	8.3	8.8	9.0	7.6	8.3	-	-	-	-	-
	Female	PBWT	7.5	7.7	8.2	6.7	-	-	-	-	-	-	-	-	-	-
5585	Male	PBWT	6.5	6.4	5.4	7.2	6.8	6.1	6.5	5.9	6.5	7.2	6.5	6.6	-	-
	Female	PBWT	5.6	5.8	6.2	5.2	5.3	-	-	-	-	-	-	-	-	-
5586	Male	PBWT	8.1	8.0	8.1	-	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	7.7	8.2	7.3	8.1	8.3	7.5	7.3	7.3	6.9	7.8	8.2	7.7	-	-
5587	Male	PBWT	7.8	8.2	7.9	7.3	8.0	7.7	8.1	7.4	7.5	7.9	-	-	-	-
	Female	PBWT	7.5	7.5	7.0	7.6	6.9	7.9	7.8	-	-	-	-	-	-	-
5588	Male	PBWT	7.5	8.0	7.2	6.9	7.7	8.2	8.0	7.7	7.6	6.8	7.2	-	-	-
	Female	PBWT	7.4	7.7	7.2	7.3	6.7	6.8	8.2	8.1	-	-	-	-	-	-

Appendix 35
Individual Pup Body Weights: F1 Generation

20248897
Day: 4 Relative to Littering (Litter: A)

0 ug/dose Group 1 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5514	Male	PBWT	7.4	7.5	7.1	7.5	7.3	-	-	-	-	-	-	-	-	-
	Female	PBWT	6.6	7.0	6.2	-	-	-	-	-	-	-	-	-	-	-
5524	Male	PBWT	10.6	10.7	10.3	11.2	10.3	11.2	10.6	10.4	10.1	-	-	-	-	-
	Female	PBWT	9.9	9.1	10.3	9.3	10.7	10.9	8.5	10.8	-	-	-	-	-	-
5525	Male	PBWT	9.7	8.5	10.3	10.4	9.6	9.9	-	-	-	-	-	-	-	-
	Female	PBWT	9.2	9.0	9.1	9.4	9.2	9.5	9.3	9.3	9.1	-	-	-	-	-
5526	Male	PBWT	9.2	8.9	9.2	8.6	10.1	9.1	-	-	-	-	-	-	-	-
	Female	PBWT	8.8	10.0	9.1	9.6	8.5	8.3	9.4	7.6	7.8	8.8	9.2	8.9	-	-
5527	Male	PBWT	10.0	10.2	10.3	10.1	9.2	9.2	10.4	10.5	-	-	-	-	-	-
	Female	PBWT	9.9	10.0	10.0	9.4	9.7	9.4	10.4	10.1	-	-	-	-	-	-
5529	Male	PBWT	10.6	11.1	10.2	10.8	10.9	10.2	10.0	10.5	10.7	10.6	-	-	-	-
	Female	PBWT	9.4	9.7	9.4	8.4	10.0	9.6	-	-	-	-	-	-	-	-
5530	Male	PBWT	11.0	11.5	11.3	10.9	10.1	10.6	11.5	10.9	11.1	-	-	-	-	-
	Female	PBWT	9.8	10.4	9.6	10.1	8.6	8.7	9.4	10.2	11.1	-	-	-	-	-
5531	Male	PBWT	10.6	11.0	10.5	11.5	9.9	9.7	11.1	10.6	11.0	10.4	-	-	-	-
	Female	PBWT	10.3	10.4	10.4	10.2	-	-	-	-	-	-	-	-	-	-
5532	Male	PBWT	8.8	8.4	9.6	8.6	8.8	9.0	8.4	8.7	8.8	8.8	-	-	-	-
	Female	PBWT	8.6	8.7	8.9	9.1	8.6	9.1	8.7	7.1	-	-	-	-	-	-

Appendix 35
Individual Pup Body Weights: F1 Generation

20248897
Day: 4 Relative to Littering (Litter: A)

0 ug/dose Group 1 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5533	Male	PBWT	10.9	11.0	11.1	10.8	10.6	11.2	10.9	10.6	11.2	-	-	-	-	-
	Female	PBWT	10.2	9.9	10.2	10.8	10.2	10.0	-	-	-	-	-	-	-	-
5534	Male	PBWT	12.2	12.5	12.2	11.6	12.8	12.0	12.2	-	-	-	-	-	-	-
	Female	PBWT	11.9	10.9	12.4	12.1	12.1	12.4	11.6	-	-	-	-	-	-	-
5535	Male	PBWT	10.5	10.8	11.0	9.0	10.1	11.2	10.5	11.2	8.9	11.7	10.7	-	-	-
	Female	PBWT	10.1	9.0	9.7	10.8	10.1	10.1	10.8	-	-	-	-	-	-	-
5536	Male	PBWT	10.7	10.1	10.0	11.9	10.2	10.9	10.0	11.5	-	-	-	-	-	-
	Female	PBWT	10.2	10.3	9.7	9.6	9.8	10.1	11.4	9.6	10.8	-	-	-	-	-
5537	Male	PBWT	11.4	11.5	10.8	11.3	11.7	11.2	11.7	11.4	-	-	-	-	-	-
	Female	PBWT	10.8	10.4	10.8	10.9	10.7	11.3	11.3	10.3	-	-	-	-	-	-
5538	Male	PBWT	12.1	12.0	12.1	12.6	11.5	11.5	11.9	11.8	12.7	12.8	-	-	-	-
	Female	PBWT	11.6	11.2	11.7	11.7	11.6	-	-	-	-	-	-	-	-	-
5540	Male	PBWT	11.7	12.1	12.9	9.3	11.3	12.5	12.2	11.6	-	-	-	-	-	-
	Female	PBWT	12.1	11.7	12.4	12.2	-	-	-	-	-	-	-	-	-	-
5541	Male	PBWT	11.8	10.5	13.0	-	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	12.1	12.6	11.6	12.5	12.8	10.8	-	-	-	-	-	-	-	-
5542	Male	PBWT	10.7	11.5	10.9	11.0	9.9	10.3	10.8	-	-	-	-	-	-	-
	Female	PBWT	10.0	10.8	9.9	9.9	9.5	9.5	10.3	9.8	-	-	-	-	-	-

Appendix 35

Individual Pup Body Weights: F1 Generation

20248897

Day: 4 Relative to Littering (Litter: A)

0 ug/dose Group 1 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5544	Male	PBWT	11.8	11.4	12.3	12.0	11.5	11.7	-	-	-	-	-	-	-	-
	Female	PBWT	11.2	11.5	10.1	10.8	10.8	12.0	12.1	12.0	10.3	-	-	-	-	-

Appendix 35

Individual Pup Body Weights: F1 Generation

20248897

Day: 4 Relative to Littering (Litter: A)

100 ug/dose Group 2 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5571	Male	PBWT	10.6	11.0	12.8	8.0	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	11.3	9.4	12.3	12.0	12.6	12.3	8.9	-	-	-	-	-	-	-
5573	Male	PBWT	9.8	10.0	10.2	9.5	9.6	-	-	-	-	-	-	-	-	-
	Female	PBWT	9.2	9.8	7.8	8.5	9.6	9.8	9.6	9.6	9.0	9.3	-	-	-	-
5574	Male	PBWT	11.7	12.2	12.2	11.3	11.6	11.3	-	-	-	-	-	-	-	-
	Female	PBWT	11.3	11.6	11.4	11.0	10.9	11.6	11.7	10.8	-	-	-	-	-	-
5575	Male	PBWT	12.3	13.2	12.9	13.1	12.9	9.5	-	-	-	-	-	-	-	-
	Female	PBWT	11.9	12.0	12.2	12.3	13.5	10.1	11.7	11.8	-	-	-	-	-	-
5577	Male	PBWT	10.5	11.0	10.9	9.4	10.5	10.9	-	-	-	-	-	-	-	-
	Female	PBWT	10.6	10.5	11.2	11.3	10.5	8.7	10.8	11.1	-	-	-	-	-	-
5579	Male	PBWT	11.4	11.2	11.2	11.4	11.8	11.7	11.3	-	-	-	-	-	-	-
	Female	PBWT	10.7	11.1	10.6	11.0	10.7	10.7	10.3	10.6	10.7	-	-	-	-	-
5580	Male	PBWT	10.8	10.0	11.5	9.5	11.8	11.4	-	-	-	-	-	-	-	-
	Female	PBWT	10.7	10.8	11.0	11.5	10.9	10.7	10.4	10.3	9.4	11.0	-	-	-	-
5581	Male	PBWT	10.4	10.7	9.6	10.9	10.4	10.2	10.9	10.3	-	-	-	-	-	-
	Female	PBWT	9.6	9.9	9.8	10.4	8.3	10.0	9.9	9.2	-	-	-	-	-	-
5582	Male	PBWT	9.2	9.2	-	-	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	9.3	9.7	10.1	9.0	9.0	8.4	10.0	10.1	8.6	9.2	10.0	9.0	9.2	9.0

Appendix 35
Individual Pup Body Weights: F1 Generation

20248897
Day: 4 Relative to Littering (Litter: A)

100 ug/dose Group 2 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5583	Male	PBWT	12.3	12.7	13.1	12.6	10.7	-	-	-	-	-	-	-	-	-
	Female	PBWT	10.9	11.8	11.7	11.2	10.6	11.0	11.0	9.2	-	-	-	-	-	-
5584	Male	PBWT	12.5	13.4	12.1	12.8	12.1	13.3	12.7	12.7	11.1	-	-	-	-	-
	Female	PBWT	11.1	10.5	11.7	11.2	-	-	-	-	-	-	-	-	-	-
5585	Male	PBWT	9.3	9.9	8.5	10.7	8.5	10.1	9.0	9.8	8.6	7.1	10.3	9.9	-	-
	Female	PBWT	8.1	7.2	9.3	7.8	-	-	-	-	-	-	-	-	-	-
5586	Male	PBWT	12.2	12.4	11.9	-	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	11.3	11.6	11.5	10.6	11.5	11.6	10.7	12.1	11.5	11.8	11.1	10.5	-	-
5587	Male	PBWT	10.9	10.6	11.4	10.9	11.1	10.3	11.5	11.1	10.4	11.2	-	-	-	-
	Female	PBWT	9.9	9.9	9.7	9.5	10.5	9.6	9.9	-	-	-	-	-	-	-
5588	Male	PBWT	9.7	9.5	9.9	8.6	10.2	9.7	10.2	9.3	10.5	9.8	9.3	-	-	-
	Female	PBWT	9.9	11.0	10.4	9.5	10.5	8.7	10.4	8.5	-	-	-	-	-	-

Appendix 35
Individual Pup Body Weights: F1 Generation

20248897
Day: 7 Relative to Littering (Litter: A)

0 ug/dose Group 1 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5514	Male	PBWT	10.8	10.9	11.2	9.8	11.3	-	-	-	-	-	-	-	-	-
	Female	PBWT	10.2	9.2	11.1	-	-	-	-	-	-	-	-	-	-	-
5524	Male	PBWT	17.5	17.2	17.9	17.3	17.7	-	-	-	-	-	-	-	-	-
	Female	PBWT	16.6	18.1	15.8	15.1	17.4	-	-	-	-	-	-	-	-	-
5525	Male	PBWT	15.6	14.0	15.6	16.4	16.4	-	-	-	-	-	-	-	-	-
	Female	PBWT	15.1	15.3	15.6	15.0	14.5	-	-	-	-	-	-	-	-	-
5526	Male	PBWT	15.1	15.2	14.2	13.7	17.2	-	-	-	-	-	-	-	-	-
	Female	PBWT	15.6	15.0	15.4	15.7	16.1	-	-	-	-	-	-	-	-	-
5527	Male	PBWT	16.6	16.8	16.4	16.6	16.5	-	-	-	-	-	-	-	-	-
	Female	PBWT	15.7	15.6	16.1	16.2	14.9	-	-	-	-	-	-	-	-	-
5529	Male	PBWT	17.6	17.2	17.9	17.6	17.6	-	-	-	-	-	-	-	-	-
	Female	PBWT	15.7	15.8	16.2	16.4	14.2	-	-	-	-	-	-	-	-	-
5530	Male	PBWT	17.9	18.0	18.9	16.8	17.9	-	-	-	-	-	-	-	-	-
	Female	PBWT	16.5	16.7	15.5	17.0	16.9	-	-	-	-	-	-	-	-	-
5531	Male	PBWT	17.5	17.1	18.1	19.1	16.8	16.2	-	-	-	-	-	-	-	-
	Female	PBWT	17.3	17.4	17.2	17.4	-	-	-	-	-	-	-	-	-	-
5532	Male	PBWT	14.9	14.7	14.2	15.3	15.2	-	-	-	-	-	-	-	-	-
	Female	PBWT	14.1	15.6	14.9	14.8	11.1	-	-	-	-	-	-	-	-	-

Appendix 35
Individual Pup Body Weights: F1 Generation

20248897
Day: 7 Relative to Littering (Litter: A)

0 ug/dose Group 1 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5533	Male	PBWT	18.3	18.4	18.0	18.8	17.8	-	-	-	-	-	-	-	-	-
	Female	PBWT	17.4	16.6	18.4	17.2	17.5	-	-	-	-	-	-	-	-	-
5534	Male	PBWT	20.0	20.0	20.5	19.8	19.6	-	-	-	-	-	-	-	-	-
	Female	PBWT	19.5	18.5	19.8	20.0	19.5	-	-	-	-	-	-	-	-	-
5535	Male	PBWT	16.6	17.4	17.2	17.2	14.5	-	-	-	-	-	-	-	-	-
	Female	PBWT	16.1	16.0	14.7	17.1	16.7	-	-	-	-	-	-	-	-	-
5536	Male	PBWT	18.6	19.9	17.2	17.6	19.8	-	-	-	-	-	-	-	-	-
	Female	PBWT	17.2	16.6	17.9	16.1	18.1	-	-	-	-	-	-	-	-	-
5537	Male	PBWT	18.3	18.1	18.5	18.9	17.8	-	-	-	-	-	-	-	-	-
	Female	PBWT	17.5	16.5	17.4	17.8	18.1	-	-	-	-	-	-	-	-	-
5538	Male	PBWT	20.1	21.0	20.1	20.4	19.0	-	-	-	-	-	-	-	-	-
	Female	PBWT	18.5	18.6	18.9	18.0	18.6	-	-	-	-	-	-	-	-	-
5540	Male	PBWT	19.4	16.2	20.5	20.1	21.4	19.0	-	-	-	-	-	-	-	-
	Female	PBWT	19.6	19.1	20.1	19.6	-	-	-	-	-	-	-	-	-	-
5541	Male	PBWT	17.9	19.3	16.4	-	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	18.0	16.6	18.6	18.5	17.6	18.8	-	-	-	-	-	-	-	-
5542	Male	PBWT	16.7	16.8	15.9	17.6	16.6	-	-	-	-	-	-	-	-	-
	Female	PBWT	15.6	17.3	14.8	15.1	15.0	-	-	-	-	-	-	-	-	-

Appendix 35

Individual Pup Body Weights: F1 Generation

20248897

Day: 7 Relative to Littering (Litter: A)

0 ug/dose Group 1 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5544	Male	PBWT	20.7	20.6	20.5	21.0	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	19.7	21.1	18.5	20.7	18.6	-	-	-	-	-	-	-	-	-

Appendix 35
Individual Pup Body Weights: F1 Generation

20248897
Day: 7 Relative to Littering (Litter: A)

100 ug/dose Group 2 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5571	Male	PBWT	17.2	20.7	18.5	12.3	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	18.1	19.7	20.8	19.3	14.3	16.5	-	-	-	-	-	-	-	-
5573	Male	PBWT	16.1	16.8	15.6	16.0	16.1	-	-	-	-	-	-	-	-	-
	Female	PBWT	14.6	15.8	16.1	12.6	14.0	-	-	-	-	-	-	-	-	-
5574	Male	PBWT	18.2	17.7	18.9	18.5	17.7	-	-	-	-	-	-	-	-	-
	Female	PBWT	17.8	17.1	17.9	18.7	17.6	-	-	-	-	-	-	-	-	-
5575	Male	PBWT	18.9	20.1	20.3	15.6	19.7	-	-	-	-	-	-	-	-	-
	Female	PBWT	19.4	19.7	20.0	19.0	18.8	-	-	-	-	-	-	-	-	-
5577	Male	PBWT	18.4	18.4	16.2	20.0	19.0	-	-	-	-	-	-	-	-	-
	Female	PBWT	18.4	19.1	16.0	19.4	19.1	-	-	-	-	-	-	-	-	-
5579	Male	PBWT	18.9	18.8	18.8	19.2	18.8	-	-	-	-	-	-	-	-	-
	Female	PBWT	17.7	17.7	18.0	17.4	17.5	-	-	-	-	-	-	-	-	-
5580	Male	PBWT	18.3	16.5	17.2	20.0	19.3	-	-	-	-	-	-	-	-	-
	Female	PBWT	18.4	19.0	18.2	18.2	18.3	-	-	-	-	-	-	-	-	-
5581	Male	PBWT	17.7	16.5	17.6	17.6	19.1	-	-	-	-	-	-	-	-	-
	Female	PBWT	16.3	17.3	14.4	16.7	16.9	-	-	-	-	-	-	-	-	-
5582	Male	PBWT	16.9	16.9	-	-	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	16.0	14.9	15.8	16.1	15.7	16.7	15.7	17.0	-	-	-	-	-	-

Appendix 35
Individual Pup Body Weights: F1 Generation

20248897
Day: 7 Relative to Littering (Litter: A)

100 ug/dose Group 2 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5583	Male	PBWT	20.2	21.0	20.7	21.0	18.2	-	-	-	-	-	-	-	-	-
	Female	PBWT	19.0	18.1	19.7	18.2	19.9	-	-	-	-	-	-	-	-	-
5584	Male	PBWT	19.0	20.3	18.7	18.6	17.4	20.0	-	-	-	-	-	-	-	-
	Female	PBWT	17.5	16.3	18.1	18.0	-	-	-	-	-	-	-	-	-	-
5585	Male	PBWT	16.0	16.5	18.9	16.7	12.4	15.3	-	-	-	-	-	-	-	-
	Female	PBWT	14.9	13.2	13.7	17.7	-	-	-	-	-	-	-	-	-	-
5586	Male	PBWT	20.1	20.8	19.3	-	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	20.0	20.5	19.3	19.1	19.4	20.9	20.7	-	-	-	-	-	-	-
5587	Male	PBWT	18.3	19.4	17.1	17.5	19.0	-	-	-	-	-	-	-	-	-
	Female	PBWT	17.0	16.6	17.9	17.1	16.5	-	-	-	-	-	-	-	-	-
5588	Male	PBWT	16.8	18.4	16.8	15.1	16.7	-	-	-	-	-	-	-	-	-
	Female	PBWT	16.4	15.1	15.7	17.3	17.5	-	-	-	-	-	-	-	-	-

Appendix 35
Individual Pup Body Weights: F1 Generation

20248897
Day: 10 Relative to Littering (Litter: A)

0 ug/dose Group 1 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5514	Male	PBWT	18.2	19.1	18.9	18.1	16.5	-	-	-	-	-	-	-	-	-
	Female	PBWT	17.0	16.1	17.9	-	-	-	-	-	-	-	-	-	-	-
5524	Male	PBWT	26.3	27.2	24.7	26.2	27.1	-	-	-	-	-	-	-	-	-
	Female	PBWT	24.9	26.7	24.1	26.2	22.7	-	-	-	-	-	-	-	-	-
5525	Male	PBWT	23.2	23.3	24.2	24.2	21.2	-	-	-	-	-	-	-	-	-
	Female	PBWT	22.8	23.2	22.7	22.0	23.2	-	-	-	-	-	-	-	-	-
5526	Male	PBWT	21.2	23.2	20.1	19.5	22.1	-	-	-	-	-	-	-	-	-
	Female	PBWT	22.7	22.9	22.5	22.2	23.0	-	-	-	-	-	-	-	-	-
5527	Male	PBWT	24.1	23.7	24.4	24.6	23.8	-	-	-	-	-	-	-	-	-
	Female	PBWT	22.8	23.0	23.6	21.0	23.4	-	-	-	-	-	-	-	-	-
5529	Male	PBWT	26.0	25.6	25.9	26.0	26.3	-	-	-	-	-	-	-	-	-
	Female	PBWT	23.8	23.3	22.3	24.8	24.8	-	-	-	-	-	-	-	-	-
5530	Male	PBWT	26.2	26.0	26.0	27.4	25.4	-	-	-	-	-	-	-	-	-
	Female	PBWT	24.4	24.1	25.2	25.5	22.7	-	-	-	-	-	-	-	-	-
5531	Male	PBWT	25.5	24.9	27.3	24.1	26.8	24.2	-	-	-	-	-	-	-	-
	Female	PBWT	25.2	25.2	25.5	24.9	-	-	-	-	-	-	-	-	-	-
5532	Male	PBWT	22.8	23.8	21.5	22.6	23.3	-	-	-	-	-	-	-	-	-
	Female	PBWT	21.8	23.1	23.3	23.2	17.7	-	-	-	-	-	-	-	-	-

Appendix 35
Individual Pup Body Weights: F1 Generation

20248897
Day: 10 Relative to Littering (Litter: A)

0 ug/dose Group 1 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5533	Male	PBWT	26.4	26.6	27.1	25.9	25.8	-	-	-	-	-	-	-	-	-
	Female	PBWT	24.7	24.5	25.8	24.2	24.4	-	-	-	-	-	-	-	-	-
5534	Male	PBWT	28.8	30.1	28.5	27.8	28.7	-	-	-	-	-	-	-	-	-
	Female	PBWT	28.1	28.9	26.8	28.2	28.4	-	-	-	-	-	-	-	-	-
5535	Male	PBWT	24.2	20.3	25.1	25.5	25.9	-	-	-	-	-	-	-	-	-
	Female	PBWT	23.4	22.6	23.9	21.8	25.2	-	-	-	-	-	-	-	-	-
5536	Male	PBWT	26.9	25.3	29.2	26.2	26.7	-	-	-	-	-	-	-	-	-
	Female	PBWT	25.3	25.6	26.6	24.9	24.1	-	-	-	-	-	-	-	-	-
5537	Male	PBWT	25.4	25.8	25.8	25.0	24.8	-	-	-	-	-	-	-	-	-
	Female	PBWT	24.5	23.2	25.3	25.1	24.3	-	-	-	-	-	-	-	-	-
5538	Male	PBWT	27.0	27.6	27.7	25.4	27.1	-	-	-	-	-	-	-	-	-
	Female	PBWT	25.1	25.0	25.2	24.4	25.8	-	-	-	-	-	-	-	-	-
5540	Male	PBWT	27.7	29.0	29.4	28.3	28.0	23.9	-	-	-	-	-	-	-	-
	Female	PBWT	27.8	27.2	28.1	28.0	-	-	-	-	-	-	-	-	-	-
5541	Male	PBWT	24.3	22.5	26.0	-	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	24.6	25.0	25.1	24.4	25.3	23.1	-	-	-	-	-	-	-	-
5542	Male	PBWT	23.6	23.7	23.1	24.3	23.1	-	-	-	-	-	-	-	-	-
	Female	PBWT	21.9	23.7	21.7	20.9	21.2	-	-	-	-	-	-	-	-	-

Appendix 35

Individual Pup Body Weights: F1 Generation

20248897

Day: 10 Relative to Littering (Litter: A)

0 ug/dose Group 1 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5544	Male	PBWT	30.2	30.0	30.2	30.5	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	28.9	30.3	27.1	30.6	27.5	-	-	-	-	-	-	-	-	-

Appendix 35
Individual Pup Body Weights: F1 Generation

20248897
Day: 10 Relative to Littering (Litter: A)

100 ug/dose Group 2 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5571	Male	PBWT	24.2	28.4	18.0	26.2	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	25.6	23.2	28.1	27.1	28.8	20.6	-	-	-	-	-	-	-	-
5573	Male	PBWT	24.9	26.0	24.9	24.1	24.4	-	-	-	-	-	-	-	-	-
	Female	PBWT	22.4	21.8	19.9	23.9	24.1	-	-	-	-	-	-	-	-	-
5574	Male	PBWT	26.4	26.9	25.6	27.4	25.8	-	-	-	-	-	-	-	-	-
	Female	PBWT	25.5	25.4	25.4	26.6	24.5	-	-	-	-	-	-	-	-	-
5575	Male	PBWT	26.1	27.4	27.9	27.1	21.9	-	-	-	-	-	-	-	-	-
	Female	PBWT	26.7	27.0	26.6	26.7	26.4	-	-	-	-	-	-	-	-	-
5577	Male	PBWT	27.2	25.5	27.5	27.0	28.8	-	-	-	-	-	-	-	-	-
	Female	PBWT	27.0	27.3	29.0	28.0	23.6	-	-	-	-	-	-	-	-	-
5579	Male	PBWT	28.1	28.1	27.6	28.7	28.1	-	-	-	-	-	-	-	-	-
	Female	PBWT	26.9	26.5	26.5	27.1	27.4	-	-	-	-	-	-	-	-	-
5580	Male	PBWT	27.2	29.9	25.1	27.0	26.6	-	-	-	-	-	-	-	-	-
	Female	PBWT	28.4	28.7	29.1	27.2	28.4	-	-	-	-	-	-	-	-	-
5581	Male	PBWT	27.2	27.6	25.4	28.5	27.2	-	-	-	-	-	-	-	-	-
	Female	PBWT	24.9	22.2	25.8	25.6	26.1	-	-	-	-	-	-	-	-	-
5582	Male	PBWT	25.7	25.7	-	-	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	25.2	24.8	25.3	25.3	25.5	24.1	24.6	26.9	-	-	-	-	-	-

Appendix 35
Individual Pup Body Weights: F1 Generation

20248897
Day: 10 Relative to Littering (Litter: A)

100 ug/dose Group 2 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5583	Male	PBWT	28.5	26.4	29.2	29.3	29.0	-	-	-	-	-	-	-	-	-
	Female	PBWT	26.9	25.6	25.7	28.1	28.0	-	-	-	-	-	-	-	-	-
5584	Male	PBWT	27.6	28.9	26.4	27.2	28.1	27.2	-	-	-	-	-	-	-	-
	Female	PBWT	25.5	24.6	25.5	26.3	-	-	-	-	-	-	-	-	-	-
5585	Male	PBWT	24.3	20.0	23.6	25.5	27.5	25.0	-	-	-	-	-	-	-	-
	Female	PBWT	23.4	22.0	26.6	21.6	-	-	-	-	-	-	-	-	-	-
5586	Male	PBWT	30.1	30.9	29.3	-	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	28.7	29.2	28.8	29.2	28.0	28.5	28.7	-	-	-	-	-	-	-
5587	Male	PBWT	28.1	28.8	27.5	27.3	28.8	-	-	-	-	-	-	-	-	-
	Female	PBWT	27.0	27.2	27.4	26.7	26.7	-	-	-	-	-	-	-	-	-
5588	Male	PBWT	24.5	22.7	27.4	22.5	25.3	-	-	-	-	-	-	-	-	-
	Female	PBWT	24.9	26.1	23.6	24.1	25.6	-	-	-	-	-	-	-	-	-

Appendix 35
Individual Pup Body Weights: F1 Generation

20248897
Day: 14 Relative to Littering (Litter: A)

0 ug/dose Group 1 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5514	Male	PBWT	29.2	29.0	30.2	30.2	27.5	-	-	-	-	-	-	-	-	-
	Female	PBWT	27.6	28.7	26.4	-	-	-	-	-	-	-	-	-	-	-
5524	Male	PBWT	37.1	37.7	38.5	34.3	37.8	-	-	-	-	-	-	-	-	-
	Female	PBWT	35.9	34.6	37.5	38.7	32.9	-	-	-	-	-	-	-	-	-
5525	Male	PBWT	34.5	36.2	34.9	34.4	32.5	-	-	-	-	-	-	-	-	-
	Female	PBWT	34.3	33.5	35.3	33.8	34.5	-	-	-	-	-	-	-	-	-
5526	Male	PBWT	31.4	28.2	33.5	30.9	32.8	-	-	-	-	-	-	-	-	-
	Female	PBWT	33.0	31.7	33.2	33.4	33.8	-	-	-	-	-	-	-	-	-
5527	Male	PBWT	34.1	34.9	31.6	35.8	34.2	-	-	-	-	-	-	-	-	-
	Female	PBWT	35.1	35.6	35.5	35.3	34.1	-	-	-	-	-	-	-	-	-
5529	Male	PBWT	36.2	36.4	35.8	37.0	35.4	-	-	-	-	-	-	-	-	-
	Female	PBWT	33.7	33.3	35.2	31.6	34.8	-	-	-	-	-	-	-	-	-
5530	Male	PBWT	37.2	39.2	36.4	36.8	36.5	-	-	-	-	-	-	-	-	-
	Female	PBWT	34.9	34.0	33.1	35.8	36.5	-	-	-	-	-	-	-	-	-
5531	Male	PBWT	36.5	38.4	35.5	35.4	34.7	38.7	-	-	-	-	-	-	-	-
	Female	PBWT	36.4	36.7	37.1	35.4	-	-	-	-	-	-	-	-	-	-
5532	Male	PBWT	33.2	32.8	33.6	34.3	31.9	-	-	-	-	-	-	-	-	-
	Female	PBWT	31.5	33.8	33.0	32.5	26.6	-	-	-	-	-	-	-	-	-

Appendix 35
Individual Pup Body Weights: F1 Generation

20248897
Day: 14 Relative to Littering (Litter: A)

0 ug/dose Group 1 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5533	Male	PBWT	37.6	37.9	39.2	35.5	37.9	-	-	-	-	-	-	-	-	-
	Female	PBWT	35.2	36.8	35.8	33.6	34.7	-	-	-	-	-	-	-	-	-
5534	Male	PBWT	40.4	39.4	39.8	41.1	41.2	-	-	-	-	-	-	-	-	-
	Female	PBWT	39.2	39.5	38.0	40.0	39.1	-	-	-	-	-	-	-	-	-
5535	Male	PBWT	36.5	38.6	31.4	37.5	38.3	-	-	-	-	-	-	-	-	-
	Female	PBWT	34.9	35.3	38.5	33.1	32.6	-	-	-	-	-	-	-	-	-
5536	Male	PBWT	38.6	40.3	40.3	37.1	36.7	-	-	-	-	-	-	-	-	-
	Female	PBWT	37.0	38.2	35.8	36.3	37.8	-	-	-	-	-	-	-	-	-
5537	Male	PBWT	34.4	34.0	33.2	33.9	36.5	-	-	-	-	-	-	-	-	-
	Female	PBWT	33.8	35.4	32.2	33.8	33.6	-	-	-	-	-	-	-	-	-
5538	Male	PBWT	36.0	34.9	34.7	37.6	36.6	-	-	-	-	-	-	-	-	-
	Female	PBWT	34.0	35.0	32.3	34.0	34.7	-	-	-	-	-	-	-	-	-
5540	Male	PBWT	39.1	40.8	34.8	41.4	38.5	40.0	-	-	-	-	-	-	-	-
	Female	PBWT	39.2	38.3	40.2	39.0	-	-	-	-	-	-	-	-	-	-
5541	Male	PBWT	32.8	30.9	34.6	-	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	32.9	32.5	33.2	32.7	32.5	33.6	-	-	-	-	-	-	-	-
5542	Male	PBWT	33.5	33.1	34.2	33.4	33.2	-	-	-	-	-	-	-	-	-
	Female	PBWT	30.6	29.5	29.7	32.7	30.4	-	-	-	-	-	-	-	-	-

Appendix 35
Individual Pup Body Weights: F1 Generation

20248897
Day: 14 Relative to Littering (Litter: A)

0 ug/dose Group 1 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5544	Male	PBWT	41.8	42.0	42.2	41.3	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	40.4	39.6	38.3	42.1	41.7	-	-	-	-	-	-	-	-	-

Appendix 35
Individual Pup Body Weights: F1 Generation

20248897
Day: 14 Relative to Littering (Litter: A)

100 ug/dose Group 2 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5571	Male	PBWT	34.7	37.5	38.8	27.8	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	35.5	39.5	29.3	36.8	34.0	38.1	-	-	-	-	-	-	-	-
5573	Male	PBWT	36.6	37.2	36.0	37.3	36.0	-	-	-	-	-	-	-	-	-
	Female	PBWT	33.6	35.8	35.1	30.5	32.9	-	-	-	-	-	-	-	-	-
5574	Male	PBWT	36.0	36.0	35.6	34.3	38.1	-	-	-	-	-	-	-	-	-
	Female	PBWT	35.2	35.8	35.8	33.7	35.3	-	-	-	-	-	-	-	-	-
5575	Male	PBWT	34.0	35.7	29.8	35.4	35.2	-	-	-	-	-	-	-	-	-
	Female	PBWT	33.8	33.9	34.6	33.3	33.5	-	-	-	-	-	-	-	-	-
5577	Male	PBWT	41.4	43.7	38.4	42.9	40.5	-	-	-	-	-	-	-	-	-
	Female	PBWT	40.8	36.0	43.5	40.0	43.6	-	-	-	-	-	-	-	-	-
5579	Male	PBWT	39.4	39.0	39.2	40.7	38.7	-	-	-	-	-	-	-	-	-
	Female	PBWT	38.5	37.4	38.5	38.2	39.9	-	-	-	-	-	-	-	-	-
5580	Male	PBWT	39.2	37.9	43.8	37.1	37.9	-	-	-	-	-	-	-	-	-
	Female	PBWT	40.4	38.7	40.1	41.4	41.2	-	-	-	-	-	-	-	-	-
5581	Male	PBWT	37.4	37.6	35.4	39.1	37.3	-	-	-	-	-	-	-	-	-
	Female	PBWT	34.8	36.6	34.7	35.4	32.4	-	-	-	-	-	-	-	-	-
5582	Male	PBWT	36.1	36.1	-	-	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	35.9	38.3	35.9	34.5	35.4	35.6	34.5	37.0	-	-	-	-	-	-

Appendix 35
Individual Pup Body Weights: F1 Generation

20248897
Day: 14 Relative to Littering (Litter: A)

100 ug/dose Group 2 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5583	Male	PBWT	40.4	41.9	40.3	41.0	38.4	-	-	-	-	-	-	-	-	-
	Female	PBWT	38.3	39.6	36.8	37.8	39.0	-	-	-	-	-	-	-	-	-
5584	Male	PBWT	38.8	38.0	38.1	40.6	37.9	39.5	-	-	-	-	-	-	-	-
	Female	PBWT	36.3	36.2	37.7	35.1	-	-	-	-	-	-	-	-	-	-
5585	Male	PBWT	35.4	36.5	37.0	31.1	34.4	37.8	-	-	-	-	-	-	-	-
	Female	PBWT	34.6	32.7	37.6	33.5	-	-	-	-	-	-	-	-	-	-
5586	Male	PBWT	40.7	41.6	39.8	-	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	40.1	40.2	39.1	40.8	40.1	40.5	39.7	-	-	-	-	-	-	-
5587	Male	PBWT	40.9	42.3	42.4	39.4	39.6	-	-	-	-	-	-	-	-	-
	Female	PBWT	39.5	41.2	38.7	38.7	39.2	-	-	-	-	-	-	-	-	-
5588	Male	PBWT	33.5	36.3	31.6	34.1	31.8	-	-	-	-	-	-	-	-	-
	Female	PBWT	35.0	34.2	36.1	36.3	33.2	-	-	-	-	-	-	-	-	-

Appendix 35
Individual Pup Body Weights: F1 Generation

20248897
Day: 18 Relative to Littering (Litter: A)

0 ug/dose Group 1 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5514	Male	PBWT	39.7	38.2	40.5	39.5	40.6	-	-	-	-	-	-	-	-	-
	Female	PBWT	37.9	36.4	39.4	-	-	-	-	-	-	-	-	-	-	-
5524	Male	PBWT	46.9	46.9	47.8	47.8	45.0	-	-	-	-	-	-	-	-	-
	Female	PBWT	45.0	48.7	46.2	40.2	44.7	-	-	-	-	-	-	-	-	-
5525	Male	PBWT	43.9	44.6	43.6	44.4	42.8	-	-	-	-	-	-	-	-	-
	Female	PBWT	43.0	42.4	42.4	43.9	43.1	-	-	-	-	-	-	-	-	-
5526	Male	PBWT	42.3	44.0	44.3	41.1	39.6	-	-	-	-	-	-	-	-	-
	Female	PBWT	43.9	44.4	43.1	44.9	43.3	-	-	-	-	-	-	-	-	-
5527	Male	PBWT	46.0	45.9	45.6	46.2	46.2	-	-	-	-	-	-	-	-	-
	Female	PBWT	45.3	41.9	46.5	47.4	45.5	-	-	-	-	-	-	-	-	-
5529	Male	PBWT	45.7	47.5	44.5	45.7	45.1	-	-	-	-	-	-	-	-	-
	Female	PBWT	43.2	45.0	43.9	43.0	40.7	-	-	-	-	-	-	-	-	-
5530	Male	PBWT	48.7	47.5	48.3	47.8	51.2	-	-	-	-	-	-	-	-	-
	Female	PBWT	45.3	47.1	45.2	42.4	46.4	-	-	-	-	-	-	-	-	-
5531	Male	PBWT	47.8	47.1	49.8	50.2	45.7	46.0	-	-	-	-	-	-	-	-
	Female	PBWT	47.3	45.2	49.1	47.5	-	-	-	-	-	-	-	-	-	-
5532	Male	PBWT	43.3	43.7	43.2	44.1	42.1	-	-	-	-	-	-	-	-	-
	Female	PBWT	40.8	43.2	43.7	42.0	34.4	-	-	-	-	-	-	-	-	-

Appendix 35
Individual Pup Body Weights: F1 Generation

20248897
Day: 18 Relative to Littering (Litter: A)

0 ug/dose Group 1 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5533	Male	PBWT	46.1	46.6	45.6	47.1	45.1	-	-	-	-	-	-	-	-	-
	Female	PBWT	44.0	42.3	44.9	45.3	43.4	-	-	-	-	-	-	-	-	-
5534	Male	PBWT	50.6	51.7	51.1	48.9	50.7	-	-	-	-	-	-	-	-	-
	Female	PBWT	49.1	50.0	48.8	50.5	47.1	-	-	-	-	-	-	-	-	-
5535	Male	PBWT	47.9	50.4	49.9	41.4	50.0	-	-	-	-	-	-	-	-	-
	Female	PBWT	46.6	45.5	49.7	44.5	46.6	-	-	-	-	-	-	-	-	-
5536	Male	PBWT	51.3	49.8	53.5	54.2	47.6	-	-	-	-	-	-	-	-	-
	Female	PBWT	49.2	47.4	48.9	51.0	49.4	-	-	-	-	-	-	-	-	-
5537	Male	PBWT	45.3	46.1	47.7	43.5	43.7	-	-	-	-	-	-	-	-	-
	Female	PBWT	44.2	47.0	41.3	44.0	44.6	-	-	-	-	-	-	-	-	-
5538	Male	PBWT	46.7	49.2	47.6	45.9	44.2	-	-	-	-	-	-	-	-	-
	Female	PBWT	44.2	43.2	42.3	46.2	45.0	-	-	-	-	-	-	-	-	-
5540	Male	PBWT	48.8	49.7	45.4	48.4	49.4	51.3	-	-	-	-	-	-	-	-
	Female	PBWT	50.0	51.0	50.4	48.7	-	-	-	-	-	-	-	-	-	-
5541	Male	PBWT	42.4	40.1	44.7	-	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	42.8	42.5	42.3	42.4	42.9	43.7	-	-	-	-	-	-	-	-
5542	Male	PBWT	44.7	44.5	46.4	45.7	42.0	-	-	-	-	-	-	-	-	-
	Female	PBWT	41.0	45.4	40.8	37.7	39.9	-	-	-	-	-	-	-	-	-

Appendix 35

Individual Pup Body Weights: F1 Generation

20248897

Day: 18 Relative to Littering (Litter: A)

0 ug/dose Group 1 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5544	Male	PBWT	51.7	53.0	52.1	50.1	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	50.5	47.9	52.8	49.8	51.6	-	-	-	-	-	-	-	-	-

Appendix 35
Individual Pup Body Weights: F1 Generation

20248897
Day: 18 Relative to Littering (Litter: A)

100 ug/dose Group 2 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5571	Male	PBWT	44.2	49.2	45.5	37.9	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	44.5	49.1	42.5	48.1	37.0	45.8	-	-	-	-	-	-	-	-
5573	Male	PBWT	47.6	48.2	48.2	47.0	47.0	-	-	-	-	-	-	-	-	-
	Female	PBWT	43.4	38.4	45.4	47.0	42.6	-	-	-	-	-	-	-	-	-
5574	Male	PBWT	46.4	46.2	44.5	49.2	45.6	-	-	-	-	-	-	-	-	-
	Female	PBWT	45.1	43.6	44.5	46.4	46.0	-	-	-	-	-	-	-	-	-
5575	Male	PBWT	44.2	47.2	45.9	45.1	38.5	-	-	-	-	-	-	-	-	-
	Female	PBWT	44.4	44.6	44.2	45.2	43.4	-	-	-	-	-	-	-	-	-
5577	Male	PBWT	54.1	53.8	57.0	55.5	50.0	-	-	-	-	-	-	-	-	-
	Female	PBWT	52.5	51.8	48.4	55.7	54.2	-	-	-	-	-	-	-	-	-
5579	Male	PBWT	49.4	51.5	48.3	48.2	49.5	-	-	-	-	-	-	-	-	-
	Female	PBWT	48.4	47.5	48.0	47.3	50.8	-	-	-	-	-	-	-	-	-
5580	Male	PBWT	48.5	46.8	46.2	53.9	47.2	-	-	-	-	-	-	-	-	-
	Female	PBWT	50.8	51.3	48.4	49.8	53.6	-	-	-	-	-	-	-	-	-
5581	Male	PBWT	47.4	44.7	48.2	48.8	48.0	-	-	-	-	-	-	-	-	-
	Female	PBWT	44.9	42.3	45.2	46.9	45.3	-	-	-	-	-	-	-	-	-
5582	Male	PBWT	44.7	44.7	-	-	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	43.4	43.1	43.0	42.0	43.8	43.4	42.7	45.7	-	-	-	-	-	-

Appendix 35
Individual Pup Body Weights: F1 Generation

20248897
Day: 18 Relative to Littering (Litter: A)

100 ug/dose Group 2 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5583	Male	PBWT	53.5	54.5	55.0	52.5	51.8	-	-	-	-	-	-	-	-	-
	Female	PBWT	50.7	49.1	52.7	50.7	50.3	-	-	-	-	-	-	-	-	-
5584	Male	PBWT	50.1	51.7	49.1	50.2	49.6	49.8	-	-	-	-	-	-	-	-
	Female	PBWT	47.3	46.5	47.1	48.4	-	-	-	-	-	-	-	-	-	-
5585	Male	PBWT	45.4	47.4	46.2	41.4	44.1	48.1	-	-	-	-	-	-	-	-
	Female	PBWT	44.9	47.4	44.2	43.0	-	-	-	-	-	-	-	-	-	-
5586	Male	PBWT	48.5	47.2	49.8	-	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	48.8	50.5	48.1	49.2	49.1	46.5	49.2	-	-	-	-	-	-	-
5587	Male	PBWT	53.3	50.6	51.4	55.5	55.8	-	-	-	-	-	-	-	-	-
	Female	PBWT	50.2	49.8	51.7	49.5	49.6	-	-	-	-	-	-	-	-	-
5588	Male	PBWT	44.4	41.7	42.7	47.5	45.7	-	-	-	-	-	-	-	-	-
	Female	PBWT	44.7	46.6	44.0	43.5	44.5	-	-	-	-	-	-	-	-	-

Appendix 35
Individual Pup Body Weights: F1 Generation

20248897
Day: 21 Relative to Littering (Litter: A)

0 ug/dose Group 1 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5514	Male	PBWT	50.1	50.0	52.3	50.6	47.4	-	-	-	-	-	-	-	-	-
	Female	PBWT	47.6	46.4	48.7	-	-	-	-	-	-	-	-	-	-	-
5524	Male	PBWT	63.3	65.1	60.5	63.0	64.4	-	-	-	-	-	-	-	-	-
	Female	PBWT	60.1	66.6	58.2	60.4	55.3	-	-	-	-	-	-	-	-	-
5525	Male	PBWT	54.9	55.5	55.2	51.2	57.8	-	-	-	-	-	-	-	-	-
	Female	PBWT	53.6	52.9	53.9	53.6	54.0	-	-	-	-	-	-	-	-	-
5526	Male	PBWT	54.8	57.4	50.9	53.0	57.7	-	-	-	-	-	-	-	-	-
	Female	PBWT	55.6	54.3	55.4	55.1	57.4	-	-	-	-	-	-	-	-	-
5527	Male	PBWT	56.9	58.4	57.3	55.3	56.4	-	-	-	-	-	-	-	-	-
	Female	PBWT	55.4	55.6	55.2	51.4	59.2	-	-	-	-	-	-	-	-	-
5529	Male	PBWT	61.1	59.9	60.0	62.4	62.1	-	-	-	-	-	-	-	-	-
	Female	PBWT	56.1	61.0	51.0	55.0	57.4	-	-	-	-	-	-	-	-	-
5530	Male	PBWT	64.9	63.7	65.0	67.9	62.9	-	-	-	-	-	-	-	-	-
	Female	PBWT	58.3	59.2	61.3	54.4	58.1	-	-	-	-	-	-	-	-	-
5531	Male	PBWT	62.1	64.0	58.1	66.6	60.0	61.7	-	-	-	-	-	-	-	-
	Female	PBWT	60.4	63.8	59.6	57.9	-	-	-	-	-	-	-	-	-	-
5532	Male	PBWT	56.3	54.1	58.1	55.4	57.5	-	-	-	-	-	-	-	-	-
	Female	PBWT	53.1	56.5	44.7	54.3	56.9	-	-	-	-	-	-	-	-	-

Appendix 35

Individual Pup Body Weights: F1 Generation

20248897

Day: 21 Relative to Littering (Litter: A)

0 ug/dose Group 1 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5533	Male	PBWT	56.3	56.8	56.3	56.1	55.8	-	-	-	-	-	-	-	-	-
	Female	PBWT	54.6	59.6	56.0	51.9	50.9	-	-	-	-	-	-	-	-	-
5534	Male	PBWT	64.6	60.9	65.0	65.5	66.9	-	-	-	-	-	-	-	-	-
	Female	PBWT	63.7	62.3	65.5	63.9	62.9	-	-	-	-	-	-	-	-	-
5535	Male	PBWT	62.2	63.1	66.0	63.8	55.7	-	-	-	-	-	-	-	-	-
	Female	PBWT	60.4	59.0	58.7	58.4	65.5	-	-	-	-	-	-	-	-	-
5536	Male	PBWT	68.2	72.6	72.0	64.2	63.9	-	-	-	-	-	-	-	-	-
	Female	PBWT	65.6	68.0	66.0	62.6	65.7	-	-	-	-	-	-	-	-	-
5537	Male	PBWT	61.2	57.7	59.8	63.5	63.6	-	-	-	-	-	-	-	-	-
	Female	PBWT	58.5	54.6	63.9	56.9	58.5	-	-	-	-	-	-	-	-	-
5538	Male	PBWT	61.7	64.3	59.3	57.3	66.0	-	-	-	-	-	-	-	-	-
	Female	PBWT	58.2	56.7	60.9	53.3	61.7	-	-	-	-	-	-	-	-	-
5540	Male	PBWT	63.0	61.6	61.5	64.2	68.5	59.2	-	-	-	-	-	-	-	-
	Female	PBWT	63.7	62.8	64.5	63.9	-	-	-	-	-	-	-	-	-	-
5541	Male	PBWT	57.6	52.4	62.7	-	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	57.4	59.0	56.4	57.5	59.3	54.9	-	-	-	-	-	-	-	-
5542	Male	PBWT	59.0	60.8	56.7	59.3	59.3	-	-	-	-	-	-	-	-	-
	Female	PBWT	53.6	53.5	51.7	59.8	49.4	-	-	-	-	-	-	-	-	-

Appendix 35
Individual Pup Body Weights: F1 Generation

20248897
Day: 21 Relative to Littering (Litter: A)

0 ug/dose Group 1 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5544	Male	PBWT	65.6	67.0	65.4	64.4	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	62.1	59.0	60.3	67.5	61.6	-	-	-	-	-	-	-	-	-

Appendix 35
Individual Pup Body Weights: F1 Generation

20248897
Day: 21 Relative to Littering (Litter: A)

100 ug/dose Group 2 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5571	Male	PBWT	54.6	62.3	57.5	44.0	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	57.5	64.0	58.5	63.7	45.8	55.5	-	-	-	-	-	-	-	-
5573	Male	PBWT	60.9	62.0	61.2	60.4	60.0	-	-	-	-	-	-	-	-	-
	Female	PBWT	55.5	51.4	52.4	61.0	57.3	-	-	-	-	-	-	-	-	-
5574	Male	PBWT	62.5	61.4	60.1	61.8	66.8	-	-	-	-	-	-	-	-	-
	Female	PBWT	59.0	55.0	59.7	61.6	59.7	-	-	-	-	-	-	-	-	-
5575	Male	PBWT	62.0	67.6	63.5	51.9	65.0	-	-	-	-	-	-	-	-	-
	Female	PBWT	59.9	61.6	59.5	58.4	59.9	-	-	-	-	-	-	-	-	-
5577	Male	PBWT	64.2	67.2	63.7	65.0	60.8	-	-	-	-	-	-	-	-	-
	Female	PBWT	63.0	67.2	55.4	63.5	65.8	-	-	-	-	-	-	-	-	-
5579	Male	PBWT	64.1	61.4	65.4	66.9	62.8	-	-	-	-	-	-	-	-	-
	Female	PBWT	62.0	60.1	65.1	60.3	62.6	-	-	-	-	-	-	-	-	-
5580	Male	PBWT	63.6	60.3	68.5	65.1	60.3	-	-	-	-	-	-	-	-	-
	Female	PBWT	64.3	62.8	64.4	61.5	68.4	-	-	-	-	-	-	-	-	-
5581	Male	PBWT	60.3	60.8	61.8	57.7	61.0	-	-	-	-	-	-	-	-	-
	Female	PBWT	56.1	52.8	55.8	57.2	58.4	-	-	-	-	-	-	-	-	-
5582	Male	PBWT	55.9	55.9	-	-	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	54.4	53.9	52.0	53.8	54.2	55.1	53.9	57.9	-	-	-	-	-	-

Appendix 35
Individual Pup Body Weights: F1 Generation

20248897
Day: 21 Relative to Littering (Litter: A)

100 ug/dose Group 2 Dam	Pup Sex	Meas.	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13
5583	Male	PBWT	67.3	70.1	65.9	69.5	63.8	-	-	-	-	-	-	-	-	-
	Female	PBWT	62.9	65.5	66.6	60.6	58.7	-	-	-	-	-	-	-	-	-
5584	Male	PBWT	68.3	67.1	68.7	66.0	69.8	70.0	-	-	-	-	-	-	-	-
	Female	PBWT	63.2	64.2	63.4	61.9	-	-	-	-	-	-	-	-	-	-
5585	Male	PBWT	59.3	58.5	53.6	58.8	62.3	63.2	-	-	-	-	-	-	-	-
	Female	PBWT	58.2	56.1	63.2	55.2	-	-	-	-	-	-	-	-	-	-
5586	Male	PBWT	64.4	67.3	61.5	-	-	-	-	-	-	-	-	-	-	-
	Female	PBWT	64.9	61.8	62.5	64.7	69.2	65.4	66.0	-	-	-	-	-	-	-
5587	Male	PBWT	69.1	71.2	71.9	67.4	65.8	-	-	-	-	-	-	-	-	-
	Female	PBWT	63.8	65.1	63.5	61.9	64.5	-	-	-	-	-	-	-	-	-
5588	Male	PBWT	59.2	64.2	56.3	60.7	55.4	-	-	-	-	-	-	-	-	-
	Female	PBWT	59.2	58.9	62.0	59.0	56.7	-	-	-	-	-	-	-	-	-

Appendix 35

Individual Pup Body Weights: F1 Generation

20248897

Key Page

Measurement Descriptions

Headings Used	Description
PBWT	Pup Bodyweight

Group Information

Short Name	Long Name	Type	Report Headings 1-4		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Appendix 36

Individual Litter Mean Pup Body Weights: F1 Generation

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

0 ug/dose Group 1	Litter Mean Pup BW	Litter Mean Pup BW	Litter Mean Pup BW	Litter Mean Pup BW	Litter Mean Pup BW	Litter Mean Pup BW	Litter Mean Pup BW
	1	4	7	10	14	18	21
5514	5.8	7.1	10.6	17.8	28.7	39.1	49.2
5520	4.9	-	-	-	-	-	-
5524	7.7	10.3	17.1	25.6	36.5	45.9	61.7
5525	7.0	9.4	15.4	23.0	34.4	43.4	54.3
5526	6.7	8.9	15.3	21.9	32.2	43.1	55.2
5527	7.0	9.9	16.1	23.4	34.6	45.7	56.1
5529	7.4	10.2	16.6	24.9	34.9	44.4	58.6
5530	7.6	10.4	17.2	25.3	36.0	47.0	61.6
5531	7.2	10.6	17.4	25.4	36.5	47.6	61.5
5532	6.7	8.7	14.5	22.3	32.3	42.1	54.7
5533	7.2	10.7	17.8	25.5	36.4	45.0	55.4
5534	8.0	12.1	19.7	28.4	39.8	49.9	64.1
5535	7.4	10.4	16.4	23.8	35.7	47.3	61.3
5536	7.8	10.4	17.9	26.1	37.8	50.2	66.9
5537	7.8	11.1	17.9	24.9	34.1	44.7	59.8

Appendix 36

Individual Litter Mean Pup Body Weights: F1 Generation

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

0 ug/dose Group 1	Litter Mean Pup BW M	Litter Mean Pup BW M	Litter Mean Pup BW M	Litter Mean Pup BW M	Litter Mean Pup BW M	Litter Mean Pup BW M	Litter Mean Pup BW M
	1	4	7	10	14	18	21
5514	6.1	7.4	10.8	18.2	29.2	39.7	50.1
5520	5.0	-	-	-	-	-	-
5524	7.7	10.6	17.5	26.3	37.1	46.9	63.3
5525	7.2	9.7	15.6	23.2	34.5	43.9	54.9
5526	6.5	9.2	15.1	21.2	31.4	42.3	54.8
5527	7.1	10.0	16.6	24.1	34.1	46.0	56.9
5529	7.7	10.6	17.6	26.0	36.2	45.7	61.1
5530	8.0	11.0	17.9	26.2	37.2	48.7	64.9
5531	7.3	10.6	17.5	25.5	36.5	47.8	62.1
5532	6.8	8.8	14.9	22.8	33.2	43.3	56.3
5533	7.3	10.9	18.3	26.4	37.6	46.1	56.3
5534	8.0	12.2	20.0	28.8	40.4	50.6	64.6
5535	7.5	10.5	16.6	24.2	36.5	47.9	62.2
5536	8.1	10.7	18.6	26.9	38.6	51.3	68.2
5537	8.0	11.4	18.3	25.4	34.4	45.3	61.2

Appendix 36

Individual Litter Mean Pup Body Weights: F1 Generation

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

0 ug/dose Group 1	Litter Mean Pup BW F	Litter Mean Pup BW F	Litter Mean Pup BW F	Litter Mean Pup BW F	Litter Mean Pup BW F	Litter Mean Pup BW F	Litter Mean Pup BW F
	1	4	7	10	14	18	21
5514	5.5	6.6	10.2	17.0	27.6	37.9	47.6
5520	4.9	-	-	-	-	-	-
5524	7.6	9.9	16.6	24.9	35.9	45.0	60.1
5525	6.9	9.2	15.1	22.8	34.3	43.0	53.6
5526	6.7	8.8	15.6	22.7	33.0	43.9	55.6
5527	7.0	9.9	15.7	22.8	35.1	45.3	55.4
5529	6.9	9.4	15.7	23.8	33.7	43.2	56.1
5530	7.3	9.8	16.5	24.4	34.9	45.3	58.3
5531	7.1	10.3	17.3	25.2	36.4	47.3	60.4
5532	6.5	8.6	14.1	21.8	31.5	40.8	53.1
5533	7.0	10.2	17.4	24.7	35.2	44.0	54.6
5534	7.9	11.9	19.5	28.1	39.2	49.1	63.7
5535	7.2	10.1	16.1	23.4	34.9	46.6	60.4
5536	7.6	10.2	17.2	25.3	37.0	49.2	65.6
5537	7.7	10.8	17.5	24.5	33.8	44.2	58.5

Appendix 36

Individual Litter Mean Pup Body Weights: F1 Generation

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

0 ug/dose Group 1	LM Post-cull Pup BW	LM Postcull Pup BW M	LM Postcull Pup BW F
	4	4	4
5514	7.1	7.4	6.6
5520	-	-	-
5524	10.3	10.7	10.0
5525	9.5	9.6	9.3
5526	9.3	9.3	9.3
5527	10.0	10.3	9.6
5529	9.9	10.6	9.3
5530	10.2	10.8	9.7
5531	10.5	10.6	10.3
5532	8.6	8.7	8.5
5533	10.6	11.0	10.3
5534	12.1	12.3	11.9
5535	10.1	10.3	9.9
5536	10.4	10.9	9.9
5537	10.9	11.3	10.6

Appendix 36

Individual Litter Mean Pup Body Weights: F1 Generation

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

0 ug/dose Group 1	Litter Mean Pup BW	Litter Mean Pup BW	Litter Mean Pup BW	Litter Mean Pup BW	Litter Mean Pup BW	Litter Mean Pup BW	Litter Mean Pup BW
	1	4	7	10	14	18	21
5538	8.1	11.9	19.3	26.0	35.0	45.5	59.9
5540	8.0	11.8	19.5	27.7	39.1	49.3	63.3
5541	7.1	12.0	18.0	24.5	32.9	42.7	57.5
5542	7.3	10.3	16.1	22.7	32.0	42.8	56.3
5544	8.1	11.4	20.1	29.5	41.0	51.0	63.6
Mean	7.24	10.39	17.00	24.67	35.26	45.61	58.99
SD	0.79	1.26	2.21	2.61	2.99	3.13	4.32
N	20	19	19	19	19	19	19

Appendix 36

Individual Litter Mean Pup Body Weights: F1 Generation

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

0 ug/dose Group 1	Litter Mean Pup BW M	Litter Mean Pup BW M	Litter Mean Pup BW M	Litter Mean Pup BW M	Litter Mean Pup BW M	Litter Mean Pup BW M	Litter Mean Pup BW M
	1	4	7	10	14	18	21
5538	8.3	12.1	20.1	27.0	36.0	46.7	61.7
5540	7.9	11.7	19.4	27.7	39.1	48.8	63.0
5541	7.0	11.8	17.9	24.3	32.8	42.4	57.6
5542	7.7	10.7	16.7	23.6	33.5	44.7	59.0
5544	8.5	11.8	20.7	30.2	41.8	51.7	65.6
Mean	7.38	10.61	17.37	25.14	35.78	46.29	60.18
SD	0.83	1.22	2.28	2.74	3.12	3.21	4.55
N	20	19	19	19	19	19	19

Appendix 36

Individual Litter Mean Pup Body Weights: F1 Generation

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

0 ug/dose Group 1	Litter Mean Pup BW F	Litter Mean Pup BW F	Litter Mean Pup BW F	Litter Mean Pup BW F	Litter Mean Pup BW F	Litter Mean Pup BW F	Litter Mean Pup BW F
	1	4	7	10	14	18	21
5538	7.9	11.6	18.5	25.1	34.0	44.2	58.2
5540	8.2	12.1	19.6	27.8	39.2	50.0	63.7
5541	7.1	12.1	18.0	24.6	32.9	42.8	57.4
5542	7.0	10.0	15.6	21.9	30.6	41.0	53.6
5544	7.8	11.2	19.7	28.9	40.4	50.5	62.1
Mean	7.08	10.14	16.62	24.18	34.71	44.90	57.78
SD	0.79	1.34	2.23	2.62	3.07	3.32	4.44
N	20	19	19	19	19	19	19

Appendix 36

Individual Litter Mean Pup Body Weights: F1 Generation

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

0 ug/dose Group 1	LM Post-cull Pup BW	LM Postcull Pup BW M	LM Postcull Pup BW F
	4	4	4
5538	11.9	12.2	11.6
5540	11.8	11.6	12.1
5541	12.0	11.8	12.1
5542	10.5	10.8	10.1
5544	11.3	11.7	11.0
Mean	10.36	10.61	10.10
SD	1.24	1.22	1.32
N	19	19	19

Appendix 36

Individual Litter Mean Pup Body Weights: F1 Generation

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

100 ug/dose Group 2	Litter Mean Pup BW	Litter Mean Pup BW	Litter Mean Pup BW	Litter Mean Pup BW	Litter Mean Pup BW	Litter Mean Pup BW	Litter Mean Pup BW
	1	4	7	10	14	18	21
5571	7.5	11.0	17.8	25.1	35.2	44.4	56.4
5573	6.5	9.4	15.4	23.6	35.1	45.5	58.2
5574	7.6	11.5	18.0	26.0	35.6	45.8	60.8
5575	8.0	12.1	19.2	26.4	33.9	44.3	60.9
5577	6.7	10.6	18.4	27.1	41.1	53.3	63.6
5579	8.0	11.0	18.3	27.5	39.0	48.9	63.1
5580	7.4	10.7	18.3	27.8	39.8	49.7	63.9
5581	7.3	10.0	17.0	26.1	36.1	46.2	58.2
5582	6.1	9.3	16.1	25.3	35.9	43.6	54.6
5583	7.8	11.4	19.6	27.7	39.4	52.1	65.1
5584	8.3	12.1	18.4	26.8	37.9	49.1	66.4
5585	6.2	9.1	15.6	24.0	35.1	45.2	58.9
5586	7.7	11.4	20.0	29.1	40.2	48.7	64.8
5587	7.6	10.5	17.6	27.6	40.2	51.7	66.4

Appendix 36

Individual Litter Mean Pup Body Weights: F1 Generation

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

100 ug/dose Group 2	Litter Mean Pup BW M	Litter Mean Pup BW M	Litter Mean Pup BW M	Litter Mean Pup BW M	Litter Mean Pup BW M	Litter Mean Pup BW M	Litter Mean Pup BW M
	1	4	7	10	14	18	21
5571	7.4	10.6	17.2	24.2	34.7	44.2	54.6
5573	6.8	9.8	16.1	24.9	36.6	47.6	60.9
5574	7.8	11.7	18.2	26.4	36.0	46.4	62.5
5575	8.0	12.3	18.9	26.1	34.0	44.2	62.0
5577	6.8	10.5	18.4	27.2	41.4	54.1	64.2
5579	8.4	11.4	18.9	28.1	39.4	49.4	64.1
5580	7.8	10.8	18.3	27.2	39.2	48.5	63.6
5581	7.7	10.4	17.7	27.2	37.4	47.4	60.3
5582	6.1	9.2	16.9	25.7	36.1	44.7	55.9
5583	8.6	12.3	20.2	28.5	40.4	53.5	67.3
5584	8.6	12.5	19.0	27.6	38.8	50.1	68.3
5585	6.5	9.3	16.0	24.3	35.4	45.4	59.3
5586	8.1	12.2	20.1	30.1	40.7	48.5	64.4
5587	7.8	10.9	18.3	28.1	40.9	53.3	69.1

Appendix 36

Individual Litter Mean Pup Body Weights: F1 Generation

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

100 ug/dose Group 2	Litter Mean Pup BW F	Litter Mean Pup BW F	Litter Mean Pup BW F	Litter Mean Pup BW F	Litter Mean Pup BW F	Litter Mean Pup BW F	Litter Mean Pup BW F
	1	4	7	10	14	18	21
5571	7.6	11.3	18.1	25.6	35.5	44.5	57.5
5573	6.4	9.2	14.6	22.4	33.6	43.4	55.5
5574	7.5	11.3	17.8	25.5	35.2	45.1	59.0
5575	8.0	11.9	19.4	26.7	33.8	44.4	59.9
5577	6.7	10.6	18.4	27.0	40.8	52.5	63.0
5579	7.7	10.7	17.7	26.9	38.5	48.4	62.0
5580	7.1	10.7	18.4	28.4	40.4	50.8	64.3
5581	6.8	9.6	16.3	24.9	34.8	44.9	56.1
5582	6.1	9.3	16.0	25.2	35.9	43.4	54.4
5583	7.4	10.9	19.0	26.9	38.3	50.7	62.9
5584	7.5	11.1	17.5	25.5	36.3	47.3	63.2
5585	5.6	8.1	14.9	23.4	34.6	44.9	58.2
5586	7.7	11.3	20.0	28.7	40.1	48.8	64.9
5587	7.5	9.9	17.0	27.0	39.5	50.2	63.8

Appendix 36

Individual Litter Mean Pup Body Weights: F1 Generation

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

100 ug/dose Group 2	LM Post-cull Pup BW	LM Postcull Pup BW M	LM Postcull Pup BW F
	4	4	4
5571	10.9	10.6	11.0
5573	9.4	9.8	8.9
5574	11.5	11.8	11.2
5575	12.1	12.2	12.1
5577	10.4	10.4	10.5
5579	11.0	11.4	10.7
5580	10.7	10.6	10.9
5581	9.9	10.3	9.5
5582	9.2	9.2	9.2
5583	11.8	12.3	11.3
5584	11.9	12.3	11.1
5585	8.8	9.2	8.1
5586	11.8	12.2	11.7
5587	10.4	10.8	9.9

Appendix 36

Individual Litter Mean Pup Body Weights: F1 Generation

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

100 ug/dose Group 2	Litter Mean Pup BW	Litter Mean Pup BW	Litter Mean Pup BW	Litter Mean Pup BW	Litter Mean Pup BW	Litter Mean Pup BW	Litter Mean Pup BW
	1	4	7	10	14	18	21
5588	7.5	9.8	16.6	24.7	34.2	44.5	59.2
Mean	7.36	10.67	17.75	26.29	37.23	47.52	61.36
SD	0.66	0.98	1.39	1.55	2.48	3.18	3.71
N	15	15	15	15	15	15	15

Appendix 36

Individual Litter Mean Pup Body Weights: F1 Generation

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

100 ug/dose Group 2	Litter Mean Pup BW M	Litter Mean Pup BW M	Litter Mean Pup BW M	Litter Mean Pup BW M	Litter Mean Pup BW M	Litter Mean Pup BW M	Litter Mean Pup BW M
	1	4	7	10	14	18	21
5588	7.5	9.7	16.8	24.5	33.5	44.4	59.2
Mean	7.59	10.92	18.05	26.66	37.63	48.11	62.38
SD	0.76	1.12	1.29	1.73	2.66	3.42	4.19
N	15	15	15	15	15	15	15

Appendix 36

Individual Litter Mean Pup Body Weights: F1 Generation

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

100 ug/dose Group 2	Litter Mean Pup BW F	Litter Mean Pup BW F	Litter Mean Pup BW F	Litter Mean Pup BW F	Litter Mean Pup BW F	Litter Mean Pup BW F	Litter Mean Pup BW F
	1	4	7	10	14	18	21
5588	7.4	9.9	16.4	24.9	35.0	44.7	59.2
Mean	7.14	10.39	17.43	25.92	36.81	46.92	60.24
SD	0.67	1.03	1.56	1.69	2.51	3.06	3.44
N	15	15	15	15	15	15	15

Appendix 36

Individual Litter Mean Pup Body Weights: F1 Generation

20248897

Sex: Female Day(s) Relative to Littering (Litter: A)

100 ug/dose Group 2	LM Post-cull Pup BW	LM Postcull Pup BW M	LM Postcull Pup BW F
	4	4	4
5588	9.8	9.8	9.8
Mean	10.64	10.86	10.39
SD	1.05	1.10	1.11
N	15	15	15

Appendix 36

Individual Litter Mean Pup Body Weights: F1 Generation

20248897

Key Page

Measurement Descriptions

Headings Used	Description
Litter Mean Pup BW	Litter Mean Pup Bodyweight
Litter Mean Pup BW M	Litter Mean Pup Bodyweight - Males
Litter Mean Pup BW F	Litter Mean Pup Bodyweight - Females
LM Post-cull Pup BW	Post-cull Litter Mean Pup Bodyweight
LM Postcull Pup BW M	Post-cull Male Litter Mean Pup Bodyweight
LM Postcull Pup BW F	Post-cull Female Litter Mean Pup Bodyweight

Time-Points/Ranges

Measurement	From	To	Report As
LM Post-cull Pup BW	-9,999	9,999	4
LM Postcull Pup BW M	-9,999	9,999	4
LM Postcull Pup BW F	-9,999	9,999	4

Measurement/Statistics

Measurement	Descriptive
Litter Mean Pup BW	Mean
	Standard Deviation
	Count
Litter Mean Pup BW M	Mean
	Standard Deviation
	Count
Litter Mean Pup BW F	Mean
	Standard Deviation
	Count

Appendix 36

Individual Litter Mean Pup Body Weights: F1 Generation

20248897

Key Page

Measurement/Statistics (Continued)

Measurement	Descriptive
LM Post-cull Pup BW	Mean
	Standard Deviation
	Count
LM Postcull Pup BW M	Mean
	Standard Deviation
	Count
LM Postcull Pup BW F	Mean
	Standard Deviation
	Count

Group Information

Short Name	Long Name	Type	Report Headings 1-4		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Appendix 37

Individual Pup Sex and Status: F1 Generation

20248897

Group: 1 Day(s): - Relative to Littering (Litter: A)

Dam	Measurement	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
5514	Pup Sex and Status	13	MT21	MT21	MT21	MT21	MD3	MD2	MD2	MD1	FT21	FT21	FK3	FD3	FD3	-	-	-	-	-	-
5520	Pup Sex and Status	13	MK3	MD2	MK2	MK2	MK2	MK2	FD2	FD2	FD2	FD2	FD2	FK2	FK2	-	-	-	-	-	-
5524	Pup Sex and Status	15	MT21	MT21	MC4	MC4	MT21	MT21	MC4	MC4	FT21	FC4	FT21	FT21	FC4	FC4	FT21	-	-	-	-
5525	Pup Sex and Status	13	MT21	MC4	MT21	MT21	MT21	FC4	FC4	FT21	FC4	FT21	FT21	FC4	FT21	-	-	-	-	-	-
5526	Pup Sex and Status	17	MC4	MT21	MT21	MT21	MT21	FT21	FT21	FC4	FC4	FC4	FC4	FC4	FC4	FC4	FT21	FT21	FS1	-	-
5527	Pup Sex and Status	14	MC4	MT21	MT21	MC4	MC4	MT21	MT21	FT21	FC4	FT21	FT21	FT21	FC4	FC4	-	-	-	-	-
5529	Pup Sex and Status	14	MC4	MC4	MT21	MC4	MT21	MC4	MT21	MT21	MC4	FT21	FT21	FT21	FC4	FT21	-	-	-	-	-
5530	Pup Sex and Status	16	MC4	MC4	MT21	MT21	MC4	MC4	MT21	MT21	FT21	FC4	FC4	FC4	FT21	FT21	FT21	FC4	-	-	-
5531	Pup Sex and Status	12	MT21	MT21	MT21	MC4	MT21	MC4	MC4	MC4	MT21	FT21	FT21	FT21	-	-	-	-	-	-	-
5532	Pup Sex and Status	16	MT21	MC4	MT21	MC4	MT21	MC4	MC4	MC4	MT21	FT21	FT21	FT21	FC4	FC4	FC4	FT21	-	-	-
5533	Pup Sex and Status	13	MT21	MT21	MC4	MT21	MT21	MC4	MC4	MC4	FT21	FT21	FT21	FT21	FC4	-	-	-	-	-	-
5534	Pup Sex and Status	13	MT21	MT21	MT21	MT21	MC4	MC4	MS0	FT21	FT21	FT21	FT21	FC4	FC4	-	-	-	-	-	-
5535	Pup Sex and Status	16	MT21	MC4	MT21	MC4	MC4	MT21	MC4	MC4	MC4	MT21	FT21	FT21	FT21	FT21	FC4	FC4	-	-	-
5536	Pup Sex and Status	17	MC4	MC4	MT21	MT21	MC4	MT21	MT21	FT21	FT21	FC4	FC4	FT21	FC4	FT21	FC4	FD0	FD0	-	-
5537	Pup Sex and Status	14	MT21	MT21	MT21	MC4	MC4	MC4	MT21	FT21	FT21	FT21	FC4	FC4	FC4	FT21	-	-	-	-	-

A=Alive T=Terminal C=Culled D=Found Dead S=Stillborn N=Unscheduled X=Transferred
Y= Euthanized Maternal Death K=Missing; Presumed Cannibalized G=Missing Z=Accidental

Appendix 37

Individual Pup Sex and Status: F1 Generation

20248897

Group: 1 Day(s): - Relative to Littering (Litter: A)

Dam	Measurement	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
5538	Pup Sex and Status	13	MT21	MC4	MT21	MC4	MT21	MC4	MC4	MC4	MT21	FT21	FT21	FT21	FT21	-	-	-	-	-	-
5540	Pup Sex and Status	10	MT21	MT21	MT21	MT21	MT21	MC4	MC4	FT21	FT21	FT21	-	-	-	-	-	-	-	-	-
5541	Pup Sex and Status	7	MT21	MT21	FT21	FT21	FT21	FT21	FT21	-	-	-	-	-	-	-	-	-	-	-	-
5542	Pup Sex and Status	14	MT21	MT21	MT21	MT21	MC4	MC4	FT21	FT21	FT21	FC4	FC4	FC4	FT21	FK1	-	-	-	-	-
5544	Pup Sex and Status	14	MT21	MC4	MT21	MT21	MD5	FT21	FT21	FC4	FC4	FT21	FC4	FC4	FT21	FD3	-	-	-	-	-

A=Alive T=Terminal C=Culled D=Found Dead S=Stillborn N=Unscheduled X=Transferred
Y= Euthanized Maternal Death K=Missing; Presumed Cannibalized G=Missing Z=Accidental

Appendix 37

Individual Pup Sex and Status: F1 Generation

20248897

Group: 2 Day(s): - Relative to Littering (Litter: A)

Dam	Measurement	Mean/ Count	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
5571	Pup Sex and Status	9	MT21	MT21	MT21	FT21	FC4	FT21	FT21	FT21	FT21	-	-	-	-	-	-	-	-	-	-
5573	Pup Sex and Status	13	MT21	MT21	MT21	MT21	FT21	FT21	FT21	FC4	FC4	FC4	FT21	FC4	FC4	-	-	-	-	-	-
5574	Pup Sex and Status	12	MT21	MT21	MT21	MC4	MT21	FT21	FT21	FT21	FC4	FC4	FC4	FT21	-	-	-	-	-	-	-
5575	Pup Sex and Status	14	MT21	MT21	MT21	MC4	MT21	MD1	MS0	FT21	FT21	FT21	FC4	FC4	FC4	FT21	-	-	-	-	-
5577	Pup Sex and Status	12	MC4	MT21	MT21	MT21	MT21	FC4	FT21	FC4	FC4	FT21	FT21	FT21	-	-	-	-	-	-	-
5579	Pup Sex and Status	14	MT21	MT21	MT21	MT21	MC4	MC4	FC4	FT21	FT21	FT21	FC4	FT21	FC4	FC4	-	-	-	-	-
5580	Pup Sex and Status	19	MT21	MT21	MT21	MC4	MT21	MK4	MK1	MK1	FT21	FT21	FC4	FT21	FT21	FC4	FC4	FC4	FC4	FD1	FK1
5581	Pup Sex and Status	14	MC4	MT21	MT21	MT21	MT21	MC4	MC4	FT21	FC4	FC4	FT21	FT21	FT21	FC4	-	-	-	-	-
5582	Pup Sex and Status	15	MT21	MK1	FC4	FT21	FT21	FC4	FT21	FT21	FC4	FC4	FT21	FC4	FT21	FC4	FT21	-	-	-	-
5583	Pup Sex and Status	11	MT21	MT21	MT21	MT21	FT21	FT21	FC4	FT21	FC4	FT21	FC4	-	-	-	-	-	-	-	-
5584	Pup Sex and Status	12	MT21	MT21	MT21	MT21	MC4	MC4	MC4	MT21	MS0	FT21	FT21	FT21	-	-	-	-	-	-	-
5585	Pup Sex and Status	15	MT21	MC4	MT21	MT21	MC4	MC4	MC4	MC4	MT21	MC4	MT21	FT21	FT21	FT21	FD3	-	-	-	-
5586	Pup Sex and Status	13	MT21	MT21	FT21	FT21	FC4	FT21	FT21	FC4	FT21	FC4	FT21	FC4	FC4	-	-	-	-	-	-
5587	Pup Sex and Status	15	MC4	MC4	MC4	MC4	MT21	MT21	MT21	MT21	MC4	FT21	FT21	FT21	FT21	FC4	FC4	-	-	-	-
5588	Pup Sex and Status	17	MC4	MC4	MC4	MC4	MT21	MC4	MC4	MT21	MT21	MT21	FC4	FC4	FT21	FT21	FT21	FT21	FC4	-	-

A=Alive T=Terminal C=Culled D=Found Dead S=Stillborn N=Unscheduled X=Transferred
Y= Euthanized Maternal Death K=Missing; Presumed Cannibalized G=Missing Z=Accidental

Appendix 37

Individual Pup Sex and Status: F1 Generation

20248897

Key Page

General Footnotes

A=Alive T=Terminal C=Culled D=Found Dead S=Stillborn N=Unscheduled X=Transferred
Y= Euthanized Maternal Death K=Missing; Presumed Cannibalized G=Missing Z=Accidental

Measurement Descriptions

Headings Used	Description
J042	Pup Sex and Status

Time-Points/Ranges

Measurement	From	To	Report As
J042	-9,999	9,999	-

Group Information

Short Name	Long Name	Type	Report Headings 1-4		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Appendix 38

Individual Pup Gross Pathology: F1 Generation

20248897

Litter: A

0 ug/dose Group 1	Findings
Dam: 5514	
5514-1	.....Pup Necropsy 2, No abnormalities detected
5514-2	.....Pup Necropsy 2, No abnormalities detected
5514-3	.....Pup Necropsy 2, No abnormalities detected
5514-4	.....Pup Necropsy 2, No abnormalities detected
5514-5 !	.....Pup Necropsy - Unscheduled, No abnormalities detected
5514-6 !	.....Pup Necropsy - Unscheduled, No abnormalities detected
5514-7 !	.....Pup Necropsy - Unscheduled, No abnormalities detected
5514-8 !	.....Pup Necropsy - Unscheduled, No abnormalities detected
5514-9	.....Pup Necropsy 2, No abnormalities detected
5514-10	.....Pup Necropsy 2, No abnormalities detected
5514-12 !	.....Pup Necropsy - Unscheduled, No abnormalities detected
5514-13 !	.....Pup Necropsy - Unscheduled, No abnormalities detected
Dam: 5520	
5520-2 !	.....Pup Necropsy - Unscheduled, No abnormalities detected
5520-7 !	.....Pup Necropsy - Unscheduled, No abnormalities detected
5520-8 !	.....Pup Necropsy - Unscheduled, No abnormalities detected
5520-9 !	.....Pup Necropsy - Unscheduled, No abnormalities detected
5520-10 !	.....Pup Necropsy - Unscheduled, No abnormalities detected
5520-11 !	.....Pup Necropsy - Unscheduled, No abnormalities detected
Dam: 5524	
5524-1	.....Pup Necropsy 2, No abnormalities detected
5524-2	.....Pup Necropsy 2, No abnormalities detected
5524-3	.....Pup Necropsy, No abnormalities detected
5524-4	.....Pup Necropsy, No abnormalities detected
5524-5	.....Pup Necropsy 2, No abnormalities detected
5524-6	.....Pup Necropsy 2, No abnormalities detected
5524-7	.....Pup Necropsy, No abnormalities detected
5524-8	.....Pup Necropsy, No abnormalities detected
5524-9	.....Pup Necropsy 2, No abnormalities detected
5524-10	.....Pup Necropsy, No abnormalities detected
5524-11	.....Pup Necropsy 2, No abnormalities detected
5524-12	.....Pup Necropsy 2, No abnormalities detected
5524-13	.....Pup Necropsy, No abnormalities detected
5524-14	.....Pup Necropsy, No abnormalities detected
5524-15	.....Pup Necropsy 2, No abnormalities detected
Dam: 5525	
5525-1	.....Pup Necropsy 2, No abnormalities detected
5525-2	.....Pup Necropsy, No abnormalities detected
5525-3	.....Pup Necropsy 2, No abnormalities detected
5525-4	.....Pup Necropsy 2, No abnormalities detected
5525-5	.....Pup Necropsy 2, No abnormalities detected

Appendix 38

Individual Pup Gross Pathology: F1 Generation

20248897

Litter: A

0 ug/dose Group 1	Findings
Dam: 5525	(Continued...)
5525-6	.....Pup Necropsy, No abnormalities detected
5525-7	.....Pup Necropsy, No abnormalities detected
5525-8	.....Pup Necropsy 2, No abnormalities detected
5525-9	.....Pup Necropsy, No abnormalities detected
5525-10	.....Pup Necropsy 2, No abnormalities detected
5525-11	.....Pup Necropsy 2, No abnormalities detected
5525-12	.....Pup Necropsy, No abnormalities detected
5525-13	.....Pup Necropsy 2, No abnormalities detected
Dam: 5526	
5526-1	.....Pup Necropsy, No abnormalities detected
5526-2	.....Pup Necropsy 2, No abnormalities detected
5526-3	.....Pup Necropsy 2, No abnormalities detected
5526-4	.....Pup Necropsy 2, No abnormalities detected
5526-5	.....Pup Necropsy 2, No abnormalities detected
5526-6	.....Pup Necropsy 2, No abnormalities detected
5526-7	.....Pup Necropsy 2, No abnormalities detected
5526-8	.....Pup Necropsy, No abnormalities detected
5526-9	.....Pup Necropsy, No abnormalities detected
5526-10	.....Pup Necropsy, No abnormalities detected
5526-11	.....Pup Necropsy, No abnormalities detected
5526-12	.....Pup Necropsy, No abnormalities detected
5526-13	.....Pup Necropsy, No abnormalities detected
5526-14	.....Pup Necropsy, No abnormalities detected
5526-15	.....Pup Necropsy 2, No abnormalities detected
5526-16	.....Pup Necropsy 2, No abnormalities detected
5526-17 !	.....Pup Necropsy - Unscheduled, Brain, [Photograph taken.] Brain, Dilatation, Moderate
Dam: 5527	
5527-1	.....Pup Necropsy, No abnormalities detected
5527-2	.....Pup Necropsy 2, No abnormalities detected
5527-3	.....Pup Necropsy 2, No abnormalities detected
5527-4	.....Pup Necropsy, No abnormalities detected
5527-5	.....Pup Necropsy, No abnormalities detected
5527-6	.....Pup Necropsy 2, No abnormalities detected
5527-7	.....Pup Necropsy 2, No abnormalities detected
5527-8	.....Pup Necropsy 2, No abnormalities detected
5527-9	.....Pup Necropsy, No abnormalities detected
5527-10	.....Pup Necropsy 2, No abnormalities detected
5527-11	.....Pup Necropsy 2, No abnormalities detected
5527-12	.....Pup Necropsy 2, No abnormalities detected
5527-13	.....Pup Necropsy, No abnormalities detected

Appendix 38

Individual Pup Gross Pathology: F1 Generation

20248897

Litter: A

0 ug/dose Group 1	Findings
Dam: 5527	(Continued...)
5527-14	.....Pup Necropsy, No abnormalities detected
Dam: 5529	
5529-1	.....Pup Necropsy, No abnormalities detected
5529-2	.....Pup Necropsy, No abnormalities detected
5529-3	.....Pup Necropsy 2, No abnormalities detected
5529-4	.....Pup Necropsy, No abnormalities detected
5529-5	.....Pup Necropsy 2, No abnormalities detected
5529-6	.....Pup Necropsy, No abnormalities detected
5529-7	.....Pup Necropsy 2, No abnormalities detected
5529-8	.....Pup Necropsy 2, No abnormalities detected
5529-9	.....Pup Necropsy, No abnormalities detected
5529-10	.....Pup Necropsy 2, No abnormalities detected
5529-11	.....Pup Necropsy 2, No abnormalities detected
5529-12	.....Pup Necropsy 2, No abnormalities detected
5529-13	.....Pup Necropsy, No abnormalities detected
5529-14	.....Pup Necropsy 2, No abnormalities detected
Dam: 5530	
5530-1	.....Pup Necropsy, No abnormalities detected
5530-2	.....Pup Necropsy, No abnormalities detected
5530-3	.....Pup Necropsy 2, No abnormalities detected
5530-4	.....Pup Necropsy 2, No abnormalities detected
5530-5	.....Pup Necropsy, No abnormalities detected
5530-6	.....Pup Necropsy, No abnormalities detected
5530-7	.....Pup Necropsy 2, No abnormalities detected
5530-8	.....Pup Necropsy 2, No abnormalities detected
5530-9	.....Pup Necropsy 2, No abnormalities detected
5530-10	.....Pup Necropsy, No abnormalities detected
5530-11	.....Pup Necropsy, No abnormalities detected
5530-12	.....Pup Necropsy, No abnormalities detected
5530-13	.....Pup Necropsy 2, No abnormalities detected
5530-14	.....Pup Necropsy 2, No abnormalities detected
5530-15	.....Pup Necropsy 2, No abnormalities detected
5530-16	.....Pup Necropsy, No abnormalities detected
Dam: 5531	
5531-1	.....Pup Necropsy 2, No abnormalities detected
5531-2	.....Pup Necropsy 2, No abnormalities detected
5531-3	.....Pup Necropsy 2, No abnormalities detected
5531-4	.....Pup Necropsy, No abnormalities detected
5531-5	.....Pup Necropsy 2, No abnormalities detected
5531-6	.....Pup Necropsy, No abnormalities detected
5531-7	.....Pup Necropsy, No abnormalities detected

Appendix 38

Individual Pup Gross Pathology: F1 Generation

20248897

Litter: A

0 ug/dose Group 1	Findings
Dam: 5531	(Continued...)
5531-8	.....Pup Necropsy, No abnormalities detected
5531-9	.....Pup Necropsy 2, No abnormalities detected
5531-10	.....Pup Necropsy 2, No abnormalities detected
5531-11	.....Pup Necropsy 2, No abnormalities detected
5531-12	.....Pup Necropsy 2, No abnormalities detected
Dam: 5532	
5532-1	.....Pup Necropsy 2, No abnormalities detected
5532-2	.....Pup Necropsy, No abnormalities detected
5532-3	.....Pup Necropsy 2, No abnormalities detected
5532-4	.....Pup Necropsy, No abnormalities detected
5532-5	.....Pup Necropsy 2, No abnormalities detected
5532-6	.....Pup Necropsy, No abnormalities detected
5532-7	.....Pup Necropsy, No abnormalities detected
5532-8	.....Pup Necropsy, No abnormalities detected
5532-9	.....Pup Necropsy 2, No abnormalities detected
5532-10	.....Pup Necropsy 2, No abnormalities detected
5532-11	.....Pup Necropsy 2, No abnormalities detected
5532-12	.....Pup Necropsy 2, No abnormalities detected
5532-13	.....Pup Necropsy, No abnormalities detected
5532-14	.....Pup Necropsy, No abnormalities detected
5532-15	.....Pup Necropsy, No abnormalities detected
5532-16	.....Pup Necropsy 2, No abnormalities detected
Dam: 5533	
5533-1	.....Pup Necropsy 2, No abnormalities detected
5533-2	.....Pup Necropsy 2, No abnormalities detected
5533-3	.....Pup Necropsy, No abnormalities detected
5533-4	.....Pup Necropsy 2, No abnormalities detected
5533-5	.....Pup Necropsy 2, No abnormalities detected
5533-6	.....Pup Necropsy, No abnormalities detected
5533-7	.....Pup Necropsy, No abnormalities detected
5533-8	.....Pup Necropsy, No abnormalities detected
5533-9	.....Pup Necropsy 2, No abnormalities detected
5533-10	.....Pup Necropsy 2, No abnormalities detected
5533-11	.....Pup Necropsy 2, No abnormalities detected
5533-12	.....Pup Necropsy 2, No abnormalities detected
5533-13	.....Pup Necropsy, No abnormalities detected
Dam: 5534	
5534-1	.....Pup Necropsy 2, No abnormalities detected
5534-2	.....Pup Necropsy 2, No abnormalities detected
5534-3	.....Pup Necropsy 2, No abnormalities detected
5534-4	.....Pup Necropsy 2, No abnormalities detected

Appendix 38

Individual Pup Gross Pathology: F1 Generation

20248897

Litter: A

0 ug/dose Group 1	Findings
Dam: 5534	(Continued...)
5534-5	.....Pup Necropsy, No abnormalities detected
5534-6	.....Pup Necropsy, No abnormalities detected
5534-7 !	.....Pup Necropsy - Unscheduled, No abnormalities detected
5534-8	.....Pup Necropsy 2, No abnormalities detected
5534-9	.....Pup Necropsy 2, No abnormalities detected
5534-10	.....Pup Necropsy 2, No abnormalities detected
5534-11	.....Pup Necropsy 2, No abnormalities detected
5534-12	.....Pup Necropsy, No abnormalities detected
5534-13	.....Pup Necropsy, No abnormalities detected
Dam: 5535	
5535-1	.....Pup Necropsy 2, No abnormalities detected
5535-2	.....Pup Necropsy, No abnormalities detected
5535-3	.....Pup Necropsy 2, No abnormalities detected
5535-4	.....Pup Necropsy, No abnormalities detected
5535-5	.....Pup Necropsy, No abnormalities detected
5535-6	.....Pup Necropsy 2, No abnormalities detected
5535-7	.....Pup Necropsy, No abnormalities detected
5535-8	.....Pup Necropsy, No abnormalities detected
5535-9	.....Pup Necropsy, No abnormalities detected
5535-10	.....Pup Necropsy 2, No abnormalities detected
5535-11	.....Pup Necropsy 2, No abnormalities detected
5535-12	.....Pup Necropsy 2, No abnormalities detected
5535-13	.....Pup Necropsy 2, No abnormalities detected
5535-14	.....Pup Necropsy 2, No abnormalities detected
5535-15	.....Pup Necropsy, No abnormalities detected
5535-16	.....Pup Necropsy, No abnormalities detected
Dam: 5536	
5536-1	.....Pup Necropsy, No abnormalities detected
5536-2	.....Pup Necropsy, No abnormalities detected
5536-3	.....Pup Necropsy 2, No abnormalities detected
5536-4	.....Pup Necropsy 2, No abnormalities detected
5536-5	.....Pup Necropsy, No abnormalities detected
5536-6	.....Pup Necropsy 2, No abnormalities detected
5536-7	.....Pup Necropsy 2, No abnormalities detected
5536-8	.....Pup Necropsy 2, No abnormalities detected
5536-9	.....Pup Necropsy 2, No abnormalities detected
5536-10	.....Pup Necropsy, No abnormalities detected
5536-11	.....Pup Necropsy, No abnormalities detected
5536-12	.....Pup Necropsy 2, No abnormalities detected
5536-13	.....Pup Necropsy, No abnormalities detected
5536-14	.....Pup Necropsy 2, No abnormalities detected

Appendix 38

Individual Pup Gross Pathology: F1 Generation

20248897

Litter: A

0 ug/dose Group 1	Findings
Dam: 5536	(Continued...)
5536-15	.....Pup Necropsy, No abnormalities detected
5536-16	.....Pup Necropsy - Unscheduled, No abnormalities detected
5536-17	.....Pup Necropsy - Unscheduled, No abnormalities detected
Dam: 5537	
5537-1	.....Pup Necropsy 2, No abnormalities detected
5537-2	.....Pup Necropsy 2, No abnormalities detected
5537-3	.....Pup Necropsy 2, No abnormalities detected
5537-4	.....Pup Necropsy, No abnormalities detected
5537-5	.....Pup Necropsy, No abnormalities detected
5537-6	.....Pup Necropsy, No abnormalities detected
5537-7	.....Pup Necropsy 2, No abnormalities detected
5537-8	.....Pup Necropsy 2, No abnormalities detected
5537-9	.....Pup Necropsy 2, No abnormalities detected
5537-10	.....Pup Necropsy 2, No abnormalities detected
5537-11	.....Pup Necropsy, No abnormalities detected
5537-12	.....Pup Necropsy, No abnormalities detected
5537-13	.....Pup Necropsy, No abnormalities detected
5537-14	.....Pup Necropsy 2, No abnormalities detected
Dam: 5538	
5538-1	.....Pup Necropsy 2, No abnormalities detected
5538-2	.....Pup Necropsy, No abnormalities detected
5538-3	.....Pup Necropsy 2, No abnormalities detected
5538-4	.....Pup Necropsy, No abnormalities detected
5538-5	.....Pup Necropsy 2, No abnormalities detected
5538-6	.....Pup Necropsy, No abnormalities detected
5538-7	.....Pup Necropsy, No abnormalities detected
5538-8	.....Pup Necropsy, No abnormalities detected
5538-9	.....Pup Necropsy 2, No abnormalities detected
5538-10	.....Pup Necropsy 2, No abnormalities detected
5538-11	.....Pup Necropsy 2, No abnormalities detected
5538-12	.....Pup Necropsy 2, No abnormalities detected
5538-13	.....Pup Necropsy 2, No abnormalities detected
Dam: 5540	
5540-1	.....Pup Necropsy 2, No abnormalities detected
5540-2	.....Pup Necropsy 2, No abnormalities detected
5540-3	.....Pup Necropsy 2, No abnormalities detected
5540-4	.....Pup Necropsy 2, No abnormalities detected
5540-5	.....Pup Necropsy 2, No abnormalities detected
5540-6	.....Pup Necropsy, No abnormalities detected
5540-7	.....Pup Necropsy, No abnormalities detected
5540-8	.....Pup Necropsy 2, No abnormalities detected

Appendix 38

Individual Pup Gross Pathology: F1 Generation

20248897

Litter: A

0 ug/dose Group 1	Findings
Dam: 5540	(Continued...)
5540-9	.....Pup Necropsy 2, No abnormalities detected
5540-10	.....Pup Necropsy 2, No abnormalities detected
Dam: 5541	
5541-1	.....Pup Necropsy 2, No abnormalities detected
5541-2	.....Pup Necropsy 2, No abnormalities detected
5541-3	.....Pup Necropsy 2, No abnormalities detected
5541-4	.....Pup Necropsy 2, No abnormalities detected
5541-5	.....Pup Necropsy 2, No abnormalities detected
5541-6	.....Pup Necropsy 2, No abnormalities detected
5541-7	.....Pup Necropsy 2, No abnormalities detected
Dam: 5542	
5542-1	.....Pup Necropsy 2, No abnormalities detected
5542-2	.....Pup Necropsy 2, No abnormalities detected
5542-3	.....Pup Necropsy 2, No abnormalities detected
5542-4	.....Pup Necropsy 2, No abnormalities detected
5542-5	.....Pup Necropsy, No abnormalities detected
5542-6	.....Pup Necropsy, No abnormalities detected
5542-7	.....Pup Necropsy 2, No abnormalities detected
5542-8	.....Pup Necropsy 2, No abnormalities detected
5542-9	.....Pup Necropsy 2, No abnormalities detected
5542-10	.....Pup Necropsy, No abnormalities detected
5542-11	.....Pup Necropsy, No abnormalities detected
5542-12	.....Pup Necropsy, No abnormalities detected
5542-13	.....Pup Necropsy 2, No abnormalities detected
Dam: 5544	
5544-1	.....Pup Necropsy 2, No abnormalities detected
5544-2	.....Pup Necropsy, No abnormalities detected
5544-3	.....Pup Necropsy 2, No abnormalities detected
5544-4	.....Pup Necropsy 2, No abnormalities detected
5544-5 !	.....Pup Necropsy - Unscheduled, No abnormalities detected
5544-6	.....Pup Necropsy 2, No abnormalities detected
5544-7	.....Pup Necropsy 2, No abnormalities detected
5544-8	.....Pup Necropsy, No abnormalities detected
5544-9	.....Pup Necropsy, No abnormalities detected
5544-10	.....Pup Necropsy 2, No abnormalities detected
5544-11	.....Pup Necropsy, No abnormalities detected
5544-12	.....Pup Necropsy, No abnormalities detected
5544-13	.....Pup Necropsy 2, No abnormalities detected
5544-14 !	.....Pup Necropsy - Unscheduled, No abnormalities detected

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Individual Pup Gross Pathology: F1 Generation

20248897

Litter: A

100 ug/dose Group 2	Findings
Dam: 5571	
5571-1	.....Pup Necropsy 2, No abnormalities detected
5571-2	.....Pup Necropsy 2, No abnormalities detected
5571-3	.....Pup Necropsy 2, No abnormalities detected
5571-4	.....Pup Necropsy 2, No abnormalities detected
5571-5	.....Pup Necropsy, No abnormalities detected
5571-6	.....Pup Necropsy 2, No abnormalities detected
5571-7	.....Pup Necropsy 2, No abnormalities detected
5571-8	.....Pup Necropsy 2, No abnormalities detected
5571-9	.....Pup Necropsy 2, No abnormalities detected
Dam: 5573	
5573-1	.....Pup Necropsy 2, No abnormalities detected
5573-2	.....Pup Necropsy 2, No abnormalities detected
5573-3	.....Pup Necropsy 2, No abnormalities detected
5573-4	.....Pup Necropsy 2, No abnormalities detected
5573-5	.....Pup Necropsy 2, No abnormalities detected
5573-6	.....Pup Necropsy 2, No abnormalities detected
5573-7	.....Pup Necropsy 2, No abnormalities detected
5573-8	.....Pup Necropsy, No abnormalities detected
5573-9	.....Pup Necropsy, No abnormalities detected
5573-10	.....Pup Necropsy, No abnormalities detected
5573-11	.....Pup Necropsy 2, No abnormalities detected
5573-12	.....Pup Necropsy, No abnormalities detected
5573-13	.....Pup Necropsy, No abnormalities detected
Dam: 5574	
5574-1	.....Pup Necropsy 2, No abnormalities detected
5574-2	.....Pup Necropsy 2, No abnormalities detected
5574-3	.....Pup Necropsy 2, No abnormalities detected
5574-4	.....Pup Necropsy, No abnormalities detected
5574-5	.....Pup Necropsy 2, No abnormalities detected
5574-6	.....Pup Necropsy 2, No abnormalities detected
5574-7	.....Pup Necropsy 2, No abnormalities detected
5574-8	.....Pup Necropsy 2, No abnormalities detected
5574-9	.....Pup Necropsy, No abnormalities detected
5574-10	.....Pup Necropsy, No abnormalities detected
5574-11	.....Pup Necropsy, No abnormalities detected
5574-12	.....Pup Necropsy 2, No abnormalities detected
Dam: 5575	
5575-1	.....Pup Necropsy 2, No abnormalities detected
5575-2	.....Pup Necropsy 2, No abnormalities detected
5575-3	.....Pup Necropsy 2, No abnormalities detected
5575-4	.....Pup Necropsy, No abnormalities detected

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Individual Pup Gross Pathology: F1 Generation

20248897

Litter: A

100 ug/dose Group 2	Findings
Dam: 5575	(Continued...)
5575-5	.....Pup Necropsy 2, No abnormalities detected
5575-6 !	.....Pup Necropsy - Unscheduled, No abnormalities detected
5575-7 !	.....Pup Necropsy - Unscheduled, No abnormalities detected
5575-8	.....Pup Necropsy 2, No abnormalities detected
5575-9	.....Pup Necropsy 2, No abnormalities detected
5575-10	.....Pup Necropsy 2, No abnormalities detected
5575-11	.....Pup Necropsy, No abnormalities detected
5575-12	.....Pup Necropsy, No abnormalities detected
5575-13	.....Pup Necropsy, No abnormalities detected
5575-14	.....Pup Necropsy 2, No abnormalities detected
Dam: 5577	
5577-1	.....Pup Necropsy, No abnormalities detected
5577-3	.....Pup Necropsy 2, No abnormalities detected
5577-4	.....Pup Necropsy 2, No abnormalities detected
5577-5	.....Pup Necropsy 2, No abnormalities detected
5577-6	.....Pup Necropsy, No abnormalities detected
5577-7	.....Pup Necropsy 2, No abnormalities detected
5577-8	.....Pup Necropsy, No abnormalities detected
5577-9	.....Pup Necropsy, No abnormalities detected
5577-11	.....Pup Necropsy 2, No abnormalities detected
5577-12	.....Pup Necropsy 2, No abnormalities detected
Dam: 5579	
5579-1	.....Pup Necropsy 2, No abnormalities detected
5579-2	.....Pup Necropsy 2, No abnormalities detected
5579-3	.....Pup Necropsy 2, No abnormalities detected
5579-4	.....Pup Necropsy 2, No abnormalities detected
5579-5	.....Pup Necropsy, No abnormalities detected
5579-6	.....Pup Necropsy, No abnormalities detected
5579-7	.....Pup Necropsy, No abnormalities detected
5579-8	.....Pup Necropsy 2, No abnormalities detected
5579-9	.....Pup Necropsy 2, No abnormalities detected
5579-10	.....Pup Necropsy 2, No abnormalities detected
5579-11	.....Pup Necropsy, No abnormalities detected
5579-12	.....Pup Necropsy 2, No abnormalities detected
5579-13	.....Pup Necropsy, No abnormalities detected
5579-14	.....Pup Necropsy, No abnormalities detected
Dam: 5580	
5580-1	.....Pup Necropsy 2, No abnormalities detected
5580-2	.....Pup Necropsy 2, No abnormalities detected
5580-3	.....Pup Necropsy 2, No abnormalities detected
5580-4	.....Pup Necropsy, No abnormalities detected

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Individual Pup Gross Pathology: F1 Generation

20248897

Litter: A

100 ug/dose Group 2	Findings
Dam: 5580	(Continued...)
5580-5	.....Pup Necropsy 2, Kidney, [Photograph(s) Taken. Tissues submitted in 10% neutral buffered formalin.]
	Renal papilla, Both, Small, Moderate - Variation
5580-9	.....Pup Necropsy 2, Kidney, [Photograph(s) Taken. Tissues submitted in 10% neutral buffered formalin.]
	Renal papilla, Left, Small, Moderate - Variation
5580-10	.....Pup Necropsy 2, No abnormalities detected
5580-11	.....Pup Necropsy, No abnormalities detected
5580-12	.....Pup Necropsy 2, No abnormalities detected
5580-13	.....Pup Necropsy 2, No abnormalities detected
5580-14	.....Pup Necropsy, No abnormalities detected
5580-15	.....Pup Necropsy, No abnormalities detected
5580-16	.....Pup Necropsy, No abnormalities detected
5580-17	.....Pup Necropsy, No abnormalities detected
5580-18 !	.....Pup Necropsy - Unscheduled, No abnormalities detected
Dam: 5581	
5581-1	.....Pup Necropsy, No abnormalities detected
5581-2	.....Pup Necropsy 2, No abnormalities detected
5581-3	.....Pup Necropsy 2, No abnormalities detected
5581-4	.....Pup Necropsy 2, No abnormalities detected
5581-5	.....Pup Necropsy 2, No abnormalities detected
5581-6	.....Pup Necropsy, No abnormalities detected
5581-7	.....Pup Necropsy, No abnormalities detected
5581-8	.....Pup Necropsy 2, No abnormalities detected
5581-9	.....Pup Necropsy, No abnormalities detected
5581-10	.....Pup Necropsy, No abnormalities detected
5581-11	.....Pup Necropsy 2, No abnormalities detected
5581-12	.....Pup Necropsy 2, No abnormalities detected
5581-13	.....Pup Necropsy 2, No abnormalities detected
5581-14	.....Pup Necropsy, No abnormalities detected
Dam: 5582	
5582-1	.....Pup Necropsy 2, No abnormalities detected
5582-3	.....Pup Necropsy, No abnormalities detected
5582-4	.....Pup Necropsy 2, No abnormalities detected
5582-5	.....Pup Necropsy 2, No abnormalities detected
5582-6	.....Pup Necropsy, No abnormalities detected
5582-7	.....Pup Necropsy 2, No abnormalities detected
5582-8	.....Pup Necropsy 2, No abnormalities detected
5582-9	.....Pup Necropsy, No abnormalities detected
5582-10	.....Pup Necropsy, No abnormalities detected
5582-11	.....Pup Necropsy 2, No abnormalities detected

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Individual Pup Gross Pathology: F1 Generation

20248897

Litter: A

100 ug/dose Group 2	Findings
Dam: 5582	(Continued...)
5582-12	.....Pup Necropsy, No abnormalities detected
5582-13	.....Pup Necropsy 2, No abnormalities detected
5582-14	.....Pup Necropsy, No abnormalities detected
5582-15	.....Pup Necropsy 2, No abnormalities detected
Dam: 5583	
5583-1	.....Pup Necropsy 2, No abnormalities detected
5583-2	.....Pup Necropsy 2, No abnormalities detected
5583-3	.....Pup Necropsy 2, No abnormalities detected
5583-4	.....Pup Necropsy 2, No abnormalities detected
5583-5	.....Pup Necropsy 2, No abnormalities detected
5583-6	.....Pup Necropsy 2, No abnormalities detected
5583-7	.....Pup Necropsy, No abnormalities detected
5583-8	.....Pup Necropsy 2, No abnormalities detected
5583-9	.....Pup Necropsy, No abnormalities detected
5583-10	.....Pup Necropsy 2, No abnormalities detected
5583-11	.....Pup Necropsy, No abnormalities detected
Dam: 5584	
5584-1	.....Pup Necropsy 2, No abnormalities detected
5584-2	.....Pup Necropsy 2, No abnormalities detected
5584-3	.....Pup Necropsy 2, No abnormalities detected
5584-4	.....Pup Necropsy 2, No abnormalities detected
5584-5	.....Pup Necropsy, No abnormalities detected
5584-6	.....Pup Necropsy, No abnormalities detected
5584-7	.....Pup Necropsy, No abnormalities detected
5584-8	.....Pup Necropsy 2, No abnormalities detected
5584-9 !	.....Pup Necropsy - Unscheduled, No abnormalities detected
5584-10	.....Pup Necropsy 2, No abnormalities detected
5584-11	.....Pup Necropsy 2, No abnormalities detected
5584-12	.....Pup Necropsy 2, No abnormalities detected
Dam: 5585	
5585-1	.....Pup Necropsy 2, No abnormalities detected
5585-2	.....Pup Necropsy, No abnormalities detected
5585-3	.....Pup Necropsy 2, No abnormalities detected
5585-4	.....Pup Necropsy 2, No abnormalities detected
5585-5	.....Pup Necropsy, No abnormalities detected
5585-6	.....Pup Necropsy, No abnormalities detected
5585-7	.....Pup Necropsy, No abnormalities detected
5585-8	.....Pup Necropsy, No abnormalities detected
5585-9	.....Pup Necropsy 2, No abnormalities detected
5585-11	.....Pup Necropsy 2, No abnormalities detected
5585-12	.....Pup Necropsy 2, No abnormalities detected

Appendix 38

Individual Pup Gross Pathology: F1 Generation

20248897

Litter: A

100 ug/dose Group 2	Findings
Dam: 5585	(Continued...)
5585-13	.....Pup Necropsy 2, No abnormalities detected
5585-14	.....Pup Necropsy 2, No abnormalities detected
5585-15 !	.....Pup Necropsy - Unscheduled, No abnormalities detected
Dam: 5586	
5586-1	.....Pup Necropsy 2, No abnormalities detected
5586-2	.....Pup Necropsy 2, No abnormalities detected
5586-3	.....Pup Necropsy 2, No abnormalities detected
5586-4	.....Pup Necropsy 2, No abnormalities detected
5586-5	.....Pup Necropsy, No abnormalities detected
5586-6	.....Pup Necropsy 2, No abnormalities detected
5586-7	.....Pup Necropsy 2, No abnormalities detected
5586-8	.....Pup Necropsy, No abnormalities detected
5586-9	.....Pup Necropsy 2, No abnormalities detected
5586-10	.....Pup Necropsy, No abnormalities detected
5586-11	.....Pup Necropsy 2, No abnormalities detected
5586-12	.....Pup Necropsy, No abnormalities detected
5586-13	.....Pup Necropsy, No abnormalities detected
Dam: 5587	
5587-1	.....Pup Necropsy, No abnormalities detected
5587-2	.....Pup Necropsy, No abnormalities detected
5587-3	.....Pup Necropsy, No abnormalities detected
5587-4	.....Pup Necropsy, No abnormalities detected
5587-5	.....Pup Necropsy 2, No abnormalities detected
5587-6	.....Pup Necropsy 2, No abnormalities detected
5587-7	.....Pup Necropsy 2, No abnormalities detected
5587-8	.....Pup Necropsy 2, No abnormalities detected
5587-9	.....Pup Necropsy, No abnormalities detected
5587-10	.....Pup Necropsy 2, No abnormalities detected
5587-11	.....Pup Necropsy 2, No abnormalities detected
5587-12	.....Pup Necropsy 2, No abnormalities detected
5587-13	.....Pup Necropsy 2, No abnormalities detected
5587-14	.....Pup Necropsy, No abnormalities detected
5587-15	.....Pup Necropsy, No abnormalities detected
Dam: 5588	
5588-1	.....Pup Necropsy, No abnormalities detected
5588-2	.....Pup Necropsy, No abnormalities detected
5588-3	.....Pup Necropsy, No abnormalities detected
5588-4	.....Pup Necropsy, No abnormalities detected
5588-5	.....Pup Necropsy 2, No abnormalities detected
5588-6	.....Pup Necropsy, No abnormalities detected
5588-7	.....Pup Necropsy, No abnormalities detected

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Individual Pup Gross Pathology: F1 Generation

20248897

Litter: A

100 ug/dose Group 2	Findings
Dam: 5588	(Continued...)
5588-8	.....Pup Necropsy 2, No abnormalities detected
5588-9	.....Pup Necropsy 2, No abnormalities detected
5588-10	.....Pup Necropsy 2, No abnormalities detected
5588-11	.....Pup Necropsy, No abnormalities detected
5588-12	.....Pup Necropsy, No abnormalities detected
5588-13	.....Pup Necropsy 2, No abnormalities detected
5588-14	.....Pup Necropsy 2, No abnormalities detected
5588-15	.....Pup Necropsy 2, No abnormalities detected
5588-16	.....Pup Necropsy 2, No abnormalities detected
5588-17	.....Pup Necropsy, No abnormalities detected

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Individual Pup Gross Pathology: F1 Generation

20248897

Pup Comments

Dam	Pup	Comment
5514	5514-5 !	Complete gross examination was performed. Carcass submitted in 10% neutral buffered formalin. Severe degree of autolysis.
5514	5514-6 !	Complete gross examination was performed. Carcass submitted into 10% neutral buffered formalin.
5514	5514-7 !	Complete gross examination was performed. Carcass submitted into 10% neutral buffered formalin.
5514	5514-8 !	Carcass submitted in 10% neutral buffered formalin.
5514	5514-12 !	Complete gross examination was performed. Carcass submitted into 10% neutral buffered formalin. Severe degree of autolysis.
5514	5514-13 !	Complete gross examination was performed. Carcass submitted into 10% neutral buffered formalin. Severe degree of autolysis.
5520	5520-2 !	Complete gross examination was performed. Carcass submitted in 10% neutral buffered formalin.
5520	5520-7 !	Complete gross examination was performed. Carcass submitted in 10% neutral buffered formalin.
5520	5520-8 !	Complete gross examination was performed. Carcass submitted in 10% neutral buffered formalin.
5520	5520-9 !	Complete gross examination was performed. Carcass submitted in 10% neutral buffered formalin.
5520	5520-10 !	Complete gross examination was performed. Carcass submitted in 10% neutral buffered formalin.
5520	5520-11 !	Complete gross examination was performed. Carcass submitted in 10% neutral buffered formalin.
5526	5526-17 !	Carcass submitted into 10% neutral buffered formalin.
5534	5534-7 !	Pup preserved in 10% NBF as per protocol
5544	5544-5 !	Complete gross examination was performed. Carcass submitted into 10% neutral buffered formalin except eyes, optic nerves, and Haderian glands submitted in Davidson`s Fixative and testes in modified Davidson`s Fixative.
5544	5544-14 !	Complete gross examination was performed. Carcass submitted into 10% NBF.
5575	5575-6 !	Complete gross examination was performed. Carcass submitted into 10% neutral buffered formalin.
5575	5575-7 !	Carcass preserved in 10% NBF as per protocol
5580	5580-18 !	Carcass submitted into 10% neutral buffered formalin. Moderate degree of autolysis.
5584	5584-9 !	Carcass preserved in 10% NBF as per protocol
5585	5585-15 !	Severe degree of autolysis. Carcass submitted into 10% neutral buffered formalin.

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Individual Pup Gross Pathology: F1 Generation

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Key Page

Group Information

Short Name	Long Name	Type	Report Headings		
1	1	Control	0	ug/dose	Group 1
2	2	Dose	100	ug/dose	Group 2

Appendix 39

Study Phase: Serology ELISA to detect antibodies against SARS-CoV-2 Spike Protein

A GLP Intramuscular Combined Developmental and Perinatal/Postnatal Reproductive Toxicity Study of mRNA-1273 in Rats

Test Site Reference No. BS-3858
Test Facility Study No. 20248897

TEST SITE:
Integrated BioTherapeutics, Inc.
4 Research Court, Suite 300
Rockville, MD 20850

TEST FACILITY:
Charles River Laboratories, Inc.
905 Sheehy Drive
Horsham, PA 19044
United States

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Appendix 39

1. RESPONSIBLE PERSONNEL

Principal Investigator (b) (6)
Integrated BioTherapeutics, Inc.

2. INTRODUCTION

This report describes the detection of antibodies against SARS-CoV-2 Spike Protein, pre-fusion stabilized spike protein (S2P), antigen in immunized Sprague-Dawley rat sera from Charles River Laboratories Study No. 20248897, entitled "A GLP Intramuscular Combined Developmental and Perinatal/Postnatal Reproductive Toxicity Study of mRNA-1273 in Rats." The objective of this study is to assess the potential effects of mRNA-1273, a vaccine candidate against SARS-CoV-2 infection, on fertility and pre and postnatal development in the pregnant and lactating female Sprague-Dawley CD (Crl:CD[SD]) rat.

The study was sponsored by Moderna TX, Inc., Cambridge, Massachusetts. (b) (6) serves as Sponsor Representative for Moderna TX, Inc.

A total of 507 rat serum samples (430 maternal samples, 43 fetal-pooled and 34 pup-pooled serum samples) were received at Integrated BioTherapeutics, Inc. (IBT) from Charles River Laboratories on September 23rd, 2020 (**Table 1**).

Serum antibody analyses were not conducted in compliance with the regulations governing the conduct of Good Laboratory Practices (GLP) nonclinical laboratory studies. However, this non-GLP study phase was conducted in accordance with antibody analysis specific Standard Operating Procedures (SOPs) developed as a part of study BS-3857 and general laboratory SOPs at IBT, Inc.

Appendix 39

3. EXPERIMENTAL DESIGN

Table 1: Study Design

Group No.	Test Material	Dose Level (µg/dose)	Dose Concentration (mg/mL)	Dose Volume (µL/dose)	Cohort 1 (Cesarean-Sectioning Phase)	Cohort 2 (Natural Delivery Phase)
1	Control	0	0	200	22	22
2	mRNA-1273	100	0.5	200	22	22

Table 2: Bioanalytical Sample Collection

Group Nos.		Time Points					
	Cohort	SD 1[a]	SD 15[a]	GD 1[a]	GD 13[a]	GD21[b]	LD 21[b]
1-2	1	X	X	X	X	X	-
1-2	2	X	X	X	X	-	X
Unscheduled euthanasia (when possible)		X					

X = Sample to be collected; - = Not applicable

[a] Sample collected prior to dose administration

[b] Terminal blood sample collection

4. MATERIALS AND METHODS

Table 3: Equipment

Equipment	Manufacturer	Model	IBT equipment#
(b) (4)			

Table 4: Materials

Material	Vendor	Cat#	Lot#	Expiry date
(b) (4)				

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Table 5: Reagents

Reagent	Vendor	Cat#	Lot#	Expiry date
(b) (4)				

4.1. SARS-CoV-2 Spike Protein (S2P)

Identification:	SARS-CoV-2 protein (S2P)
Supplier:	GenScript
Batch/Lot No.:	Lot U578BFC29004/DS01FF001
Concentration:	1.22 mg/mL
Used concentration:	1.5 µg/mL
Expiry:	Not available
Retest Date:	N/A
Storage conditions:	Kept in a freezer set to maintain -80°C

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4.2. Standard

Identification:	Pooled rat serum from seven Sprague Dawley rats immunized with SARS-CoV-2 Spike Protein (S1+S2, ECD, His-tag) (Sino Biological) 50 µg/rat in 1:1 ratio with TiterMax® Gold adjuvant (Sigma-Aldrich), 100 µL, IM on days 0 and 14, terminal bleeds = day 28
Supplier:	IBT Bioservices BS-3848 study
Batch/Lot No.:	N/A
Concentration:	Not applicable
Expected Titer:	Historical mean 18,626 Antibody Units/mL
Expiry:	Not available
Retest Date:	N/A
Storage conditions:	Kept in a freezer set to maintain -80°C

4.3. Unknown test samples

Identification:	Immunized rat sera (Charles River Study Number 20248897)
Supplier:	Charles River Laboratories
Storage conditions:	Kept in a freezer set to maintain -80°C
Duration:	Test samples will be discarded 30 days from completion of the project unless otherwise instructed

4.4. Detection Antibody

Identification:	Goat anti-rat IgG (H+L)-HRP, mouse serum-adsorbed
Supplier:	KPL
Batch/Lot No.:	Catalog # 5220-0459, lot 1025591
Storage conditions:	Kept in a refrigerator set to maintain +4°C
Expiry:	Not available
Retest Date:	N/A
Storage conditions:	Kept in a freezer set to maintain -80°C

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4.5. Computerized Systems

Table 6: Computerized Systems

System Name	Version No.	Description of Data Collected and/or Analyzed
(b) (4)		• Collection of Absorbance Values at 650 nm • Calculations of "Antibody Units/mL" (X) based on Absorbance Values (Y) by interpolating from a four-parameter standard curve
		Data summary
		Graphs

4.6. Brief procedure

(b) (4)

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RESULTS AND DISCUSSIONS

4.7. Sample Dilution Scheme

Rat serum samples from Group 1 (Control) SD1, SD15, GD1, GD13, GD21 and LD21 timepoints and Group 2 (mRNA-1273) SD1 timepoint (before the first immunization) were tested at 1:500 dilution, followed by two 4-fold serial dilutions.

The original dilution scheme for testing maternal rat serum samples from Group 2 (mRNA-1273) SD15, GD1, GD13, GD21 and LD21 timepoints, started at 1:5,000 dilution, followed by five 4-fold serial dilutions and ended at 1:5,120,000 dilution. During the initial testing of 144 maternal samples from Group 2 (mRNA-1273), it was observed that most samples did not reach background-level signals even at 1:5,120,000 dilution. In order to report End-point titer, samples would need to be re-tested with additional dilutions.

A new dilution scheme was proposed to include 2.5-fold serial dilutions. Maternal serum samples were tested starting at 1:5,000 dilution, followed by ten 2.5-fold serial dilutions and ending at 1:47,700,000 dilution. Pup-pooled and fetal-pooled serum samples were tested starting at 1:500 dilution, followed by ten 2.5-fold serial dilutions and ending at 1:4,770,000 dilution. The new dilution scheme enables more points within the linear portion of the standard curve to calculate antibody titers in “Antibody Units/mL” and also provides additional granularity to the End-point titer values (Appendix).

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Table 7: Original vs. New Rat Serum Sample Dilution Schemes

Original Dilution Scheme			New Dilution Scheme		
Maternal sample			Maternal sample		
Dilution 1	5.00E+03	4-fold serial dilutions	Dilution 1	5.00E+03	2.5-fold serial dilutions
Dilution 2	2.00E+04		Dilution 2	1.25E+04	
Dilution 3	8.00E+04		Dilution 3	3.13E+04	
Dilution 4	3.20E+05		Dilution 4	7.81E+04	
Dilution 5	1.28E+06		Dilution 5	1.95E+05	
Dilution 6	5.12E+06		Dilution 6	4.88E+05	
			Dilution 7	1.22E+06	
			Dilution 8	3.05E+06	
			Dilution 9	7.63E+06	
			Dilution 10	1.91E+07	
			Dilution 11	4.77E+07	

Original Dilution Scheme			New Dilution Scheme		
Fetal-pooled or Pup-pooled sample			Fetal-pooled or Pup-pooled sample		
Dilution 1	5.00E+02		Dilution 1	5.00E+02	2.5-fold serial dilutions
Dilution 2	2.00E+03		Dilution 2	1.25E+03	
Dilution 3	8.00E+03		Dilution 3	3.13E+03	
Dilution 4	3.20E+04		Dilution 4	7.81E+03	
Dilution 5	1.28E+05		Dilution 5	1.95E+04	
Dilution 6	5.12E+05		Dilution 6	4.88E+04	
			Dilution 7	1.22E+05	
			Dilution 8	3.05E+05	
			Dilution 9	7.63E+05	
			Dilution 10	1.91E+06	
			Dilution 11	4.77E+06	

4.8. Antibody Titers (Antibody Units/mL)

"Antibody units/mL" (AU/mL) values were calculated from a four-parameter equation derived from the normalized standard curve tested on each plate. Individual antibody titers for Group 1 (Control) and Group 2 (mRNA-1273) are shown in **Table 8** and **Table 9**, respectively. Graphical representation of antibody titers is displayed in **Figure 1**.

Four maternal samples (animal ID's: 5506, 5509, 5515 and 5543) from Group 1 (Control) exhibited signals above the limit of detection, across timepoints SD1, SD15, GD1 and GD13. The elevated signals appeared to be inherent to these four rats (**Table 13**), since the re-tested data were consistent with the original data (**Table 14 and Table 15**). The elevated signals from these four rats decline over time (SD1 to GD13) and appear to be unrelated to any experimental manipulation of the rats or physical manipulation of the samples. The observed high background for these four rats should have no impact since these are animals in Group 1 (Control).

In brief, the mean antibody titers observed in the maternal samples in Group 2 (mRNA-1273) at different time points were: 44,362 AU/mL @ SD15; 220,596 AU/mL @ GD1; 442,138 AU/mL @ GD13; 149,443 AU/mL @ GD21; 117,903 AU/mL @ LD21. The mean antibody titers in GD21 fetuses and LD21 pups were 15,315 AU/mL and 167,478 AU/mL, respectively.

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Table 8: "Antibody Units/mL" Titers of Group 1 (Control) Animals

Group 1 (Control)	Maternal samples						Fetal-pooled	Pup-pooled
Animal Number	Study Day SD1	Study Day SD15	Study Day GD1	Study Day GD13	Study Day GD21	Study Day LD21	Study Day GD21	Study Day LD21
5501	<30	<30	<30	<30	<30		<30	
5502	<30	<30	<30	<30	<30		<30	
5503	<30	<30	<30	<30	<30		<30	
5504	<30	<30	<30	<30	<30		<30	
5505	<30	<30	<30	<30	<30		<30	
5506	<30	<30	<30	<30	<30		<30	
5507	<30	<30	<30	<30	<30		<30	
5508	<30	<30	<30	<30	<30		<30	
5509	43	<30	<30	<30	<30		<30	
5510	<30	<30	<30	<30	<30		<30	
5511	<30	<30	<30	<30	<30		<30	
5512	<30	<30	<30	<30	<30		<30	
5513	<30	<30	<30	<30	<30		<30	
5514	<30	<30	<30	<30		<30		<30
5515	202	157	108	55	<30		<30	
5516	<30	<30	<30	<30	<30		<30	
5517	<30	<30	<30	<30	<30			
5518	<30	<30	<30	<30	<30		<30	
5519	<30	<30	<30	<30	<30		<30	
5520	<30	<30	<30	<30			<30	
5521	<30	<30	<30	<30	<30		<30	
5522	<30	<30	<30	<30	<30		<30	
5523	<30	<30	<30	<30	<30			
5524	<30	<30	<30	<30		<30		<30
5525	<30	<30	<30	<30		<30		<30
5526	<30	<30	<30	<30		<30		<30
5527	<30	<30	<30	<30		<30		<30
5528	<30	<30	<30	<30	<30		<30	
5529	<30	<30	<30	<30		<30		<30
5530	<30	<30	<30	<30		<30		<30
5531	<30	<30	<30	<30		<30		<30
5532	<30	<30	<30	<30		<30		<30
5533	<30	<30	<30	<30		<30		<30
5534	<30	<30	<30	<30		<30		<30
5535	<30	<30	<30	<30		<30		<30
5536	<30	<30	<30	<30		<30		<30
5537	<30	<30	<30	<30		<30		<30
5538	<30	<30	<30	<30		<30		<30
5539	<30	<30	<30	<30				
5540	<30	<30	<30	<30		<30		<30
5541	<30	<30	<30	<30		<30		<30
5542	<30	<30	<30	<30		<30		<30
5543	218	186	101	81				
5544	<30	<30	<30	<30		<30		<30

*Note: "Not detected" antibody titers are reported as "<0.059 Antibody Units/mL * 500" since 1:500 is the lowest dilution factor used for these samples or "<30 Antibody Units/mL"*

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Table 9: "Antibody Units/mL" Titers of Group 2 (mRNA-1273) Animals

Group 2 (mRNA-1273)	Maternal samples						Fetal-pooled	Pup-pooled
Animal Number	Study Day SD1	Study Day SD15	Study Day GD1	Study Day GD13	Study Day GD21	Study Day LD21	Study Day GD21	Study Day LD21
5545	<30	47442	286620	537528	152350		18418	
5546	<30	45283	226273	478970	159235		16102	
5547	<30	40558	207250	421534	107718		10631	
5548	<30	29659	178047	364046	100347		11794	
5549	<30	30473	199911	322605	90047		11966	
5550	<30	23838	126960	266797	97816		11034	
5551	<30	49146	208084	369542				
5552	<30	34917	200591	292328	108430		7131	
5553	<30	27157	200751	423072				
5554	<30	66488	285170	612097	188710		8388	
5555	<30	43305	159854	438486	248460		17488	
5556	<30	47866	216845	435030	168899		13895	
5557	<30	34256	252725	454987	203171		29738	
5558	<30	74943	269995	557708				
5559	<30	52070	373161	731002	175357		23982	
5560	<30	38923	204188	419030	118485		16091	
5561	<30	35229	149317	304963	87645		12155	
5562	<30	63412	244191	493124				
5563	<30	38304	159223	370480	120657		11317	
5564	<30	51783	213796	492502	108103		13714	
5565	<30	23623	157200	320758	129645		14669	
5566	<30	31366	178384	347980	108655		14630	
5567	<30	46880	248594	722243	170392		21660	
5568	<30	55277	163553	406257	188011		14103	
5569	<30	49237	264297	461283	211829		18215	
5570	<30	62633	371683	642307	243779		19807	
5571	<30	40474	226373	426661		145033		173541
5572	<30	34740	191203	486072				
5573	<30	22146	140656	298391		81615		132444
5574	<30	29359	191254	354813		67670		156654
5575	<30	55236	263634	543706		98880		177786
5576	<30	45638	181210	460607				
5577	<30	65545	279286	545139		146319		283979
5578	<30	53336	227368	427357				
5579	<30	22090	152413	303600		77020		139422
5580	<30	50132	170552	258336		86328		124656
5581	<30	26207	163310	251827		66020		149459
5582	<30	87549	388481	571262		248427		221737
5583	<30	55787	222526	657364		176550		201182
5584	<30	31662	291552	479812		82278		114012
5585	<30	35453	137011	281801		74186		85847
5586	<30	26888	98091	206131		64914		92087
5587	<30	65828	380768	658199		231917		234314
5588	<30	59785	253888	556341		121387		225044

*Note: "Not detected" antibody titers are reported as "<0.059 Antibody Units/mL * 500" since 1:500 is the lowest dilution factor used for these samples or "<30 Antibody Units/mL"*

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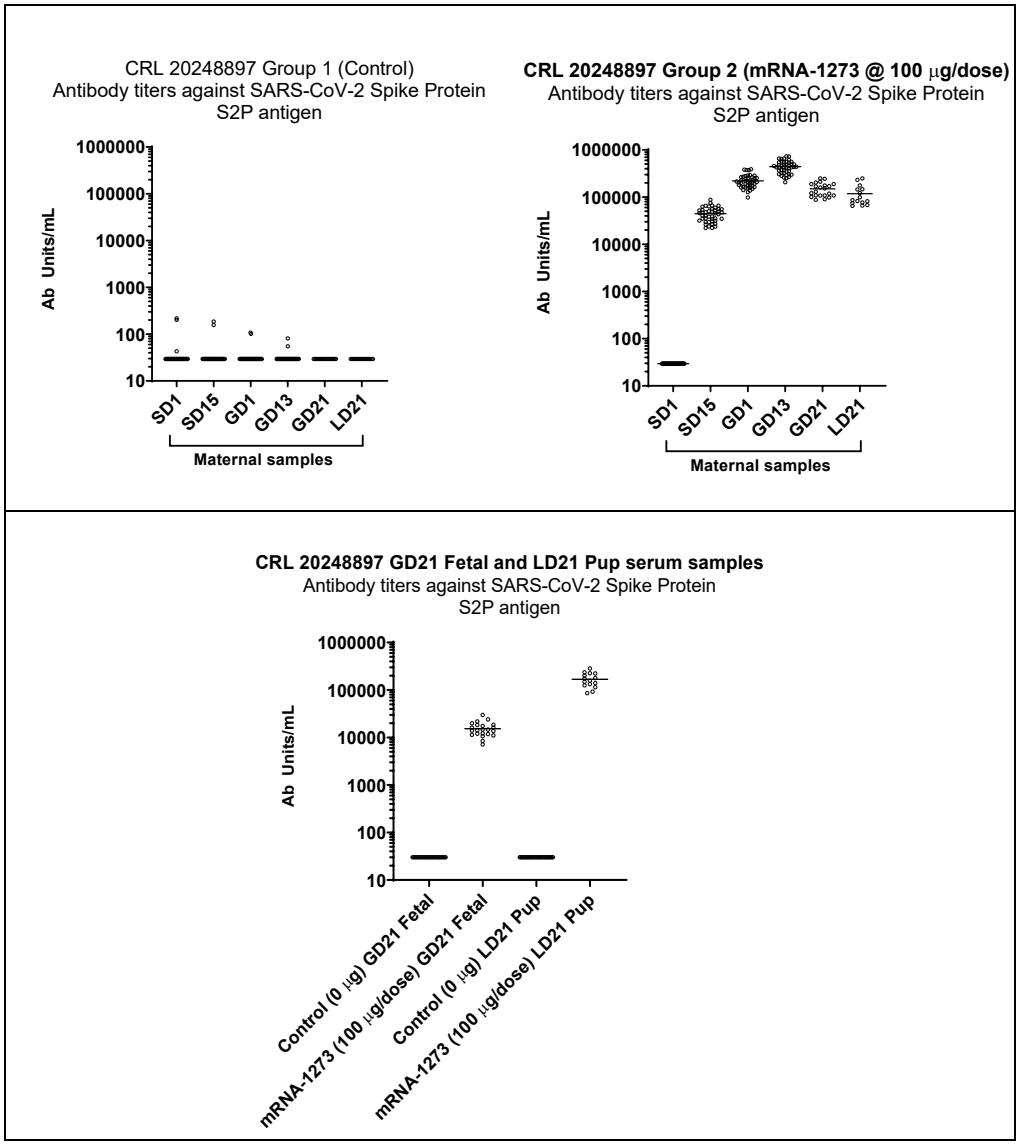
Figure 1: "Antibody Units/mL" Titers of Group 1 (Control) and Group 2 (mRNA-1273) Animals



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5. DEVIATION

EC_{50} values on plates 2, 3, 12, 14, 15, 21 and 94 did not meet plate acceptance criteria (**Section 9.1**). However, the EC_{50} values of these plates were within 10% of the maximum value of the expected EC_{50} range and are not expected to impact reporting of data. Samples on these plates, are from Group 1 (Control) and Group 2 at the SD1 timepoint (before immunization with mRNA-1273). These samples showed signals that were below the limit of detection except for four rats from Group 1 (Control) (**Appendix 9.3**). Samples on plates 2, 3, 12, 14, 15, 21 and 94 were re-tested and results were confirmed **(Table 10)**.

A deviation was observed in the ELISA run performed on September 29th, 2020. This was the second run in the series of sample analysis. It was observed that nine (9) of the twenty-four (24) standard curves and/or background controls failed to meet plate acceptance criteria. No operator error was reported, therefore, uneven washing by the plate washer was presumed to be the likely source of error. The plate washer was cleaned thoroughly per manufacturer's instructions before each run. This initiated a repeat of these plates in concordance with the approved protocol.

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Table 10: "Antibody Units/mL" values of re-tested serum samples on plates 2, 3, 12, 14, 15, 21 and 94

Group 1 (Control)	SD1 timepoint		AU/mL	
	Sample Number	Animal Number	Original Re-analyzed	Re-tested 06Nov2020
Plate 2	13	5513	<30	<30
	14	5514	<30	<30
	15	5515	202	238
	16	5516	<30	<30
	17	5517	<30	<30
	18	5518	<30	<30
	19	5519	<30	<30
	20	5520	<30	<30
	21	5521	<30	<30
	22	5522	<30	<30
	23	5523	<30	<30
	24	5524	<30	<30
Plate 3	25	5525	<30	<30
	26	5526	<30	<30
	27	5527	<30	<30
	28	5528	<30	<30
	29	5529	<30	<30
	30	5530	<30	<30
	31	5531	<30	<30
	32	5532	<30	<30
	33	5533	<30	<30
	34	5534	<30	<30
	35	5535	<30	<30
	36	5536	<30	<30

Group 1 (Control)	GD13 timepoint		AU/mL	
	Sample Number	Animal Number	Original Re-analyzed	Re-tested 06Nov2020
Plate 12	133	5503	<30	<30
	134	5505	<30	<30
	135	5509	<30	<30
	136	5510	<30	<30
	137	5511	<30	<30
	138	5512	<30	<30
	139	5513	<30	<30
	140	5516	<30	<30
	141	5523	<30	<30
	142	5527	<30	<30
	143	5533	<30	<30
	144	5534	<30	<30
Plate 14	157	5530	<30	<30
	158	5531	<30	<30
	159	5532	<30	<30
	160	5508	<30	<30
	161	5515	55	57
	162	5518	<30	<30
	163	5521	<30	<30
	164	5525	<30	<30
	165	5526	<30	<30
	166	5536	<30	<30
	167	5501	<30	<30
	168	5506	<30	<30
Plate 15	169	5519	<30	<30
	170	5528	<30	<30
	171	5529	<30	<30
	172	5514	<30	<30
	173	5540	<30	<30
	174	5544	<30	<30
	175	5539	<30	<30
	176	5543	81	79
	GD21 timepoint		AU/mL	
	Sample Number	Animal Number	Original Re-analyzed	Re-tested 06Nov2020
	177	5503	<30	<30
	178	5505	<30	<30
	179	5509	<30	<30
	180	5510	<30	<30

Group 1 (Control)		LD21 timepoint		AU/mL	
		Sample Number	Animal Number	Original Re-analyzed	Re-teste 06Nov202
Plate 94	Pup-pooled	4	5532	<30	<3
	Pup-pooled	5	5534	<30	<3
	Pup-pooled	6	5535	<30	<3
	Pup-pooled	7	5537	<30	<3
	Pup-pooled	8	5538	<30	<3
	Pup-pooled	9	5542	<30	<3
	Pup-pooled	10	5524	<30	<3
	Pup-pooled	11	5525	<30	<3
	Pup-pooled	12	5530	<30	<3
	Pup-pooled	13	5541	<30	<3
	Pup-pooled	14	5526	<30	<3
	Pup-pooled	15	5529	<30	<3

Group 2 (mRNA-1273)	SD1 timepoint		AU/mL	
	Sample Number	Animal Number	Original Re-analyzed	Re-tested 06Nov2020
Plate 21	241	5568	<30	<3
	242	5569	<30	<3
	243	5570	<30	<3
	244	5571	<30	<3
	245	5572	<30	<3
	246	5573	<30	<3
	247	5574	<30	<3
	248	5575	<30	<3
	249	5576	<30	<3
	250	5577	<30	<3
	251	5578	<30	<3
	252	5579	<30	<3

Appendix 39

6. CONCLUSION

The objective of this serological analysis phase was to assess IgG antibodies against SARS-CoV-2 Spike Protein antigen, in rat serum samples collected under Charles River Laboratories Study 20248897 using the ELISA against SARS-CoV-2 S2P antigen, according to SOPs developed as a part of IBT Study BS-3857.

A total of 507 rat serum samples were successfully tested to detect antibodies against SARS-CoV-2 S2P antigen. Titers in "Antibody Units/mL" are reported in **Section 4.8**. End-point titers are reported in the **Appendix 9.3**. Robust IgG titers were observed in the rats following four immunizations of mRNA-1273 vaccine. Peak titer was reached on GD13 and plateaued at parturition (GD21) and stayed constant through LD21. Strong maternal-to-fetal and maternal-to-pup transfer of antibodies was observed with mRNA-1273. Overall, the objectives of this serological analysis phase were met.

7. REPORT APPROVAL

(b) (6)

_____Date: November 20, 2020

Integrated BioTherapeutics, Inc.

Appendix 39

8. REFERENCES

1. Vu H, Holtsberg FW. BS-3857 Standard Operating Procedure: "Serology ELISA to detect antibodies against SARS-CoV-2 Spike Protein (S2P) in rat sera". Integrated Biotherapeutics Inc. 24Sep2020.

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9. APPENDIX:

9.1. Standard

The standard is a well-characterized anti-SARS-CoV-2 Spike protein pooled rat serum. Plate acceptance criteria were established during assay development (BS-3857 study): EC_{50} must be between 13,898 to 23,354 (Historical Mean EC_{50} ± 2 * Standard Deviation (Stdev)). According to the data presented in **Table 11**:

- 89/97 (92%) standard curves met the acceptance criterion.
- 8/97 (8%) standard curves did not meet the acceptance criterion:
    - 7/97 standard curves showed EC_{50} values that are within 10% above the 23,354 maximum value of the expected range. Results from plates 2, 3, 12, 14, 15, 21 and 94 are reported in the deviation section.
    - 1/97 standard curves on plate 67 showed EC_{50} value within 5% below the 13,898 minimum value of the expected range. Samples on plate 67 were repeated because Group 2 (mRNA-1273) maternal samples from animal numbers 5545, 5548, 5549 at GD1 timepoint were expected to show antibody responses.

The "Mean ± 2 * Stdev" ranges of EC_{50} values from assay development phase (BS-3857 study) and from sample analysis of 507 sera (BS-3858 study) mostly overlap each other **(Figure 2)**. The range for BS-3858 (n = 97) extended at the top, compared to the range for BS-3857 (n = 34).

All standard curves met other plate acceptance criteria **(Table 11)**:

- Hill slope between 0.9-1.2
- $R^2 \geq 0.99$

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Table 11: Combined standard curves during sample analysis

		A	B	C	D	R^2
Assay date: 27Sep2020	Plot#1	3.54	1.13	20200	0.071	1
	Plot#2	3.51	1.13	24500	0.063	0.999
	Plot#3	3.45	1.13	24500	0.059	1
	Plot#4	3.55	1.05	18700	0.053	1
	Plot#5	3.53	1.08	21400	0.054	1
	Plot#6	3.60	1.12	21000	0.056	1
	Plot#7	3.54	1.05	22300	0.044	1
	Plot#8	3.57	1.03	19000	0.054	1
	Plot#9	3.51	1.10	19200	0.071	1
	Plot#10	3.50	1.07	20800	0.561	1
	Plot#11	3.46	1.06	20600	0.057	1
	Plot#12	3.51	1.09	24000	0.062	1
	Plot#13	3.49	1.10	22500	0.060	1
	Plot#14	3.51	1.08	23600	0.057	1
	Plot#15	3.51	1.15	24500	0.072	1
	Plot#16	3.47	1.02	21800	0.045	1
	Plot#17	3.49	1.06	20700	0.052	1
	Plot#18	3.46	1.04	20100	0.048	1
	Plot#19	3.53	1.08	23000	0.075	1
	Plot#20	3.52	1.06	22500	0.051	1
	Plot#21	3.44	1.09	25700	0.059	1
	Plot#22	3.53	1.08	22900	0.059	1
Assay date: 09Oct2020	Plot#23	3.58	1.03	18500	0.067	1
	Plot#24	3.74	1.02	19100	0.053	1
	Plot#25	3.68	1.02	18200	0.047	1
	Plot#26	3.65	1.01	18800	0.052	1
	Plot#27	3.66	1.00	17000	0.051	1
	Plot#28	3.56	1.06	18400	0.061	1
	Plot#29	3.57	1.01	17800	0.047	1
	Plot#30	3.56	0.99	17500	0.046	1
	Plot#31	3.60	1.02	17900	0.050	1
	Plot#32	3.52	1.04	19300	0.052	1
Assay date: 11Oct2020	Plot#33	3.58	1.11	19000	0.071	1
	Plot#34	3.61	1.00	17900	0.046	1
	Plot#35	3.63	1.07	18100	0.065	1
	Plot#36	3.71	1.10	19500	0.062	1
	Plot#37	3.57	1.00	13900	0.047	1
	Plot#38	3.58	0.99	14900	0.055	1
	Plot#39	3.50	0.97	16000	0.032	1
	Plot#40	3.57	1.07	18000	0.059	1
	Plot#41	3.56	1.00	16800	0.057	1
	Plot#42	3.59	1.04	16600	0.054	1
	Plot#43	3.69	1.02	14500	0.064	1
	Plot#44	3.60	1.01	17300	0.045	1
	Plot#45	3.58	1.03	17300	0.050	1
	Plot#46	3.55	1.02	16600	0.050	1
	Plot#47	3.57	0.98	14800	0.044	1
	Plot#48	3.58	1.01	15800	0.043	1

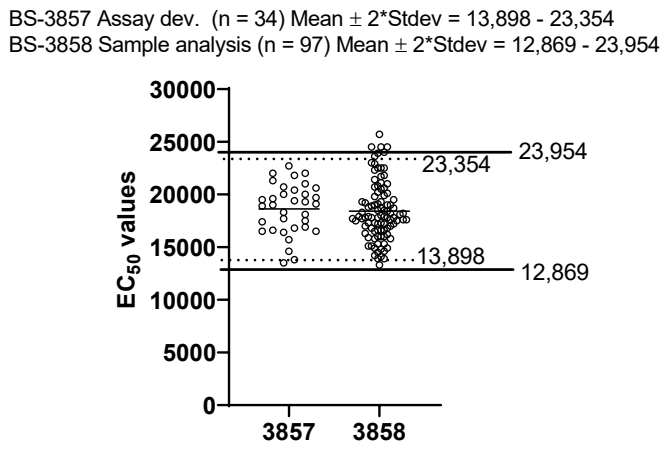
		A	B	C	D	R^2
Assay date 12Oct2020	Plot#49	3.68	1.03	17300	0.057	1
	Plot#50	3.57	1.07	18300	0.066	0.999
	Plot#51	3.60	1.04	19000	0.055	1
	Plot#52	3.61	1.03	17600	0.057	1
	Plot#53	3.60	1.00	17900	0.042	1
	Plot#54	3.67	1.00	15100	0.053	1
	Plot#55	3.48	1.03	17600	0.047	1
	Plot#56	3.65	0.98	17200	0.048	1
	Plot#57	3.53	1.04	15900	0.055	1
	Plot#58	3.57	1.03	16200	0.050	1
	Plot#59	3.51	0.96	15800	0.033	1
	Plot#60	3.53	1.01	16000	0.047	1
	Plot#61	3.64	1.03	14200	0.048	1
	Plot#62	3.63	1.03	15300	0.052	1
	Plot#63	3.56	1.03	15100	0.051	1
	Plot#64	3.55	1.05	16000	0.051	1
	Plot#65	3.59	1.06	16600	0.049	1
	Plot#66	3.62	1.04	16300	0.046	1
	Plot#67	3.65	1.04	13300	0.049	1
	Plot#68	3.54	1.00	13900	0.040	1
	Plot#69	3.51	1.01	15300	0.035	1
	Plot#70	3.62	1.02	14100	0.047	1
	Plot#71	3.52	0.99	14900	0.036	1
	Plot#72	3.56	1.01	14600	0.039	1
Assay date 16Oct2020	Plot#73	3.73	0.95	17000	0.039	1
	Plot#74	3.66	0.99	19800	0.033	0.999
	Plot#75	3.58	1.01	17800	0.048	1
	Plot#76	3.55	1.00	18200	0.041	1
	Plot#77	3.56	1.02	18700	0.046	1
	Plot#78	3.57	1.02	20500	0.042	1
	Plot#79	3.65	1.04	17500	0.060	1
	Plot#80	3.64	1.08	18500	0.079	1
	Plot#81	3.65	1.02	17700	0.051	1
	Plot#82	3.65	1.05	17700	0.066	1
	Plot#83	3.71	1.05	17600	0.054	1
	Plot#84	3.75	1.02	16800	0.050	1
	Plot#85	3.68	1.00	17800	0.043	1
	Plot#86	3.56	1.00	17800	0.055	1
	Plot#87	3.63	0.98	17200	0.045	1
	Plot#88	3.62	1.02	16500	0.055	1
	Plot#89	3.45	1.20	18900	0.081	0.999
	Plot#90	3.65	1.05	17800	0.052	1
	Plot#91	3.59	1.09	17200	0.061	1
Assay date 17Oct2020	Plot#92	3.54	1.09	21100	0.059	1
	Plot#93	3.51	1.05	22500	0.052	1
	Plot#94	3.48	1.07	23900	0.056	1
	Plot#95	3.50	1.05	21700	0.053	1
	Plot#96	3.65	1.00	19300	0.038	1
	Plot#67r	3.60	1.05	19900	0.051	1

Note: Highlighted cells indicate EC_{50} values that are outside of the expected range established during assay development.

Appendix 39

Figure 2: Comparison of EC_{50} values from BS-3857 and BS-3858 studies

	BS-3857 assay development	BS-3858 sample analysis of 507 sera
Number of plates	N = 34	N = 97
Mean EC_{50}	**18,626**	**18,411**
Stdev EC_{50}	2,364	2,771
Mean ± 2*Stdev	**13,898 – 23,354**	**12,869 – 23,954**
	2/34 fall out of the expected range	Based on 3858 data: 5/97 fall out of the expected range Based on 3857 data: 8/97 fall out of the expected range
Min to Max	13,500 – 22,700	13,300 – 25,700



Appendix 39

9.2. Background

Another plate acceptance criterion is for the average background value on each plate to be within 2 * Historical Mean of Background values. All mean background values on plates met the acceptance criterion of < 0.138 OD_{650} as shown in **Table 12**.

Table 12: Combined Mean Background

	Mean Background OD650	
Assay date: 27Sep2020	Plate#1	0.060
	Plate#2	0.051
	Plate#3	0.063
	Plate#4	0.055
	Plate#5	0.051
	Plate#6	0.048
	Plate#7	0.047
	Plate#8	0.058
	Plate#9	0.057
	Plate#10	0.048
	Plate#11	0.053
	Plate#12	0.058
	Plate#13	0.066
	Plate#14	0.053
	Plate#15	0.056
	Plate#16	0.053
	Plate#17	0.053
	Plate#18	0.052
	Plate#19	0.060
	Plate#20	0.058
	Plate#21	0.050
	Plate#22	0.055
Assay date: 09Oct2020	Plate#23	0.071
	Plate#24	0.067
	Plate#25	0.063
	Plate#26	0.070
	Plate#27	0.054
	Plate#28	0.062
	Plate#29	0.056
	Plate#30	0.058
	Plate#31	0.060
	Plate#32	0.063
Assay date: 11Oct2020	Plate#33	0.063
	Plate#34	0.058
	Plate#35	0.068
	Plate#36	0.061
	Plate#37	0.057
	Plate#38	0.060
	Plate#39	0.057
	Plate#40	0.079
	Plate#41	0.066
	Plate#42	0.059
	Plate#43	0.071
	Plate#44	0.062
	Plate#45	0.060
	Plate#46	0.069
	Plate#47	0.051
	Plate#48	0.059

	Mean Background OD650	
Assay date: 12Oct2020	Plate#49	0.066
	Plate#50	0.070
	Plate#51	0.065
	Plate#52	0.065
	Plate#53	0.057
	Plate#54	0.062
	Plate#55	0.060
	Plate#56	0.064
	Plate#57	0.066
	Plate#58	0.062
	Plate#59	0.070
	Plate#60	0.057
	Plate#61	0.066
	Plate#62	0.071
	Plate#63	0.055
	Plate#64	0.058
	Plate#65	0.054
	Plate#66	0.067
	Plate#67	0.060
	Plate#68	0.055
	Plate#69	0.052
	Plate#70	0.061
	Plate#71	0.053
	Plate#72	0.058
Assay date: 16Oct2020	Plate#73	0.058
	Plate#74	0.054
	Plate#75	0.061
	Plate#76	0.052
	Plate#77	0.056
	Plate#78	0.055
	Plate#79	0.076
	Plate#80	0.089
	Plate#81	0.059
	Plate#82	0.083
	Plate#83	0.062
	Plate#84	0.056
	Plate#85	0.056
	Plate#86	0.077
	Plate#87	0.056
	Plate#88	0.066
	Plate#89	0.068
	Plate#90	0.059
	Plate#91	0.060
Assay date: 17Oct2020	Plate#92	0.082
	Plate#93	0.054
	Plate#94	0.060
	Plate#95	0.055
	Plate#96	0.056
	Plate#67r	0.059

Appendix 39

9.3. End-point Titers

End-point titer is reported as the highest dilution at which absorbance value is higher than 2 * Historical Mean Background (>0.138 OD_{650}). Individual end-point titers for Groups 1 and 2 are shown in **Table 16** and **Table 17**, respectively. Graphical representation of end-point titers is displayed in **Figure 3**.

Four maternal samples from Group 1 (animal ID's: 5506, 5509, 5515 and 5543) exhibited signals above the limit of detection, across timepoints SD1, SD15, GD1 and GD13. The elevated signals appeared to be inherent to these four rats **(Table 13)** and not related to the standard curves with EC_{50} values exceeding the expected EC_{50} range, since the re-tested data were consistent with the original data **(Table 14** and **Table 15)**. In addition, animal ID 5587 in Group 2 did show an endpoint titer just above the background with an endpoint titer right at 500 for timepoint SD1 (**Table 17**). The elevated signals from these rats appear unrelated to any experimental manipulation of the rats or the samples.

Table 13: Four rat serum samples from Group 1 (Control) with signals above the limit of detection

	Plate 1	Plate 5	Plate 11	Plate 14*			Plate 1	Plate 5	Plate 8	Plate 12*	
CRL Sample number	6	50	124	168		CRL Sample number	9	53	91	135	
Animal number	**5506**	**5506**	**5506**	**5506**		**Animal number**	**5509**	**5509**	**5509**	**5509**	
Timepoint	**SD1**	**SD15**	**GD1**	**GD13**		**Timepoint**	**SD1**	**SD15**	**GD1**	**GD13**	
1:500	0.075	0.163	0.166	0.135		1 500	0.295	0.192	0.178	0.131	
1:2,000	0.064	0.081	0.077	0.074	Mean OD_{650}	1:2,000	0.122	0.091	0.090	0.070	Mean OD_6
1:8,000	0.070	0.056	0.058	0.061		1:8,000	0.070	0.068	0.070	0.058	
End-point Titer	**<500**	**5.00E+02**	**5.00E+02**	**<500**		**End-point Titer**	**5.00E+02**	**5.00E+02**	**5.00E+02**	**<500**	
AU/mL	**<30**	**<30**	**<30**	**<30**		**AU/mL**	**43**	**<30**	**<30**	**<30**	
	Plate 2*	**Plate 5**	**Plate 10**	**Plate 14***			**Plate 4**	**Plate 8**	**Plate 11**	**Plate 15***	
CRL Sample number	15	59	117	161		CRL Sample number	43	87	132	176	
Animal number	**5515**	**5515**	**5515**	**5515**		**Animal number**	**5543**	**5543**	**5543**	**5543**	
Timepoint	**SD1**	**SD15**	**GD1**	**GD13**		**Timepoint**	**SD1**	**SD15**	**GD1**	**GD13**	
1:500	1.372	1.067	0.678	0.422		1:500	1.460	1.135	0.725	0.574	
1:2,000	0.460	0.349	0.228	0.162	Mean OD_{650}	1:2,000	0.535	0.411	0.259	0.192	Mean OD_6
1 8,000	0.164	0.156	0.107	0.080		1:8,000	0.186	0.167	0.109	0.093	
End-point Titer	**8.00E+03**	**8.00E+03**	**2.00E+03**	**2.00E+03**		**End-point Titer**	**8.00E+03**	**8.00E+03**	**2.00E+03**	**2.00E+03**	
AU/mL	**202**	**157**	**108**	**55**		**AU/mL**	**218**	**186**	**101**	**81**	

- *Yellow-highlighted cells indicate the standard curves showed values that exceeded the maximum value of the expected EC_{50} range established during assay development.*
- *Pink-highlighted cells correspond to absorbance values that are greater than the limit of detection or > 2 * Historical background value or > 0.138, established during assay development.*

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Table 14: Comparison of re-testing data vs. original data for four rat samples from Group 1 (Control)

	Plate 2* original	P2 REPEAT	
CRL Sample number	15	15	
Animal number	**5515**	**5515**	
Timepoint	**SD1**	**SD1**	
1:500	1.372	1.256	Mean OD_{650}
1:2,000	0.460	0.453	
1:8,000	0.164	0.168	
End-point Titer	**8.00E+03**	**8.00E+03**	
AU/mL	**202**	**238**	

	Plate 14*	P14 REPEAT	
CRL Sample number	161	161	
Animal number	**5515**	**5515**	
Timepoint	**GD13**	**GD13**	
1:500	0.422	0.376	Mean OD_{650}
1:2,000	0.162	0.153	
1:8,000	0.080	0.087	
End-point Titer	**2.00E+03**	**2.00E+03**	
AU/mL	**55**	**57**	

	Plate 15* original	P15 REPEAT	
CRL Sample number	176	176	
Animal number	**5543**	**5543**	
Timepoint	**GD13**	**GD13**	
1:500	0.574	0.495	Mean OD_{650}
1:2,000	0.192	0.188	
1:8,000	0.093	0.098	
End-point Titer	**2.00E+03**	**2.00E+03**	
AU/mL	**81**	**79**	

	Plate 14* original	P14 REPEAT	
CRL Sample number	168	168	
Animal number	**5506**	**5506**	
Timepoint	**GD13**	**GD13**	
1:500	0.135	0.122	Mean OD_{650}
1:2,000	0.074	0.084	
1:8,000	0.061	0.077	
End-point Titer	**<500**	**<500**	
AU/mL	**<30**	**<30**	

	Plate 12* original	P12 REPEAT	
CRL Sample number	135	135	
Animal number	**5509**	**5509**	
Timepoint	**GD13**	**GD13**	
1:500	0.131	0.144	Mean OD_{650}
1:2,000	0.070	0.086	
1:8,000	0.058	0.072	
End-point Titer	**<500**	**5.00E+02**	
AU/mL	**<30**	**<30**	

Highlighted cells indicate absorbance values greater than the LOD or > 0.138

*Pink-highlighted cells correspond to absorbance values that are greater than the limit of detection or > 2 * Historical background value or > 0.138, established during assay development.*

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Table 15: End-point Titers of the re-tested samples on plates 2, 3, 12, 14, 15, 21 and 94

Group 1 (Control)	SD1 timepoint		End-point Titer	
	Sample Number	Animal Number	Original Re-analyzed	Re-tested 06Nov2020
Plate 2	13	5513	<500	<500
	14	5514	<500	<500
	15	5515	8.00E+03	8.00E+03
	16	5516	<500	<500
	17	5517	<500	<500
	18	5518	<500	<500
	19	5519	<500	<500
	20	5520	<500	<500
	21	5521	<500	<500
	22	5522	<500	<500
	23	5523	<500	<500
	24	5524	<500	<500
Plate 3	25	5525	<500	<500
	26	5526	<500	<500
	27	5527	<500	<500
	28	5528	<500	<500
	29	5529	<500	<500
	30	5530	<500	<500
	31	5531	<500	<500
	32	5532	<500	<500
	33	5533	<500	<500
	34	5534	<500	<500
	35	5535	<500	<500
	36	5536	<500	<500

Group 1 (Control)	GD13 timepoint		End-point Titer	
	Sample Number	Animal Number	Original Re-analyzed	Re-tested 06Nov2020
Plate 12	133	5503	<500	<500
	134	5505	<500	<500
	135	5509	<500	5.00E+02
	136	5510	<500	<500
	137	5511	<500	<500
	138	5512	<500	<500
	139	5513	<500	<500
	140	5516	<500	<500
	141	5523	<500	<500
	142	5527	<500	<500
	143	5533	<500	<500
	144	5534	<500	<500
Plate 14	157	5530	<500	<500
	158	5531	<500	<500
	159	5532	<500	<500
	160	5508	<500	<500
	161	5515	2.00E+03	2.00E+03
	162	5518	<500	<500
	163	5521	<500	<500
	164	5525	<500	<500
	165	5526	<500	<500
	166	5536	<500	<500
	167	5501	<500	<500
	168	5506	<500	<500
Plate 15	169	5519	<500	<500
	170	5528	<500	<500
	171	5529	<500	<500
	172	5514	<500	<500
	173	5540	<500	<500
	174	5544	<500	<500
	175	5539	<500	<500
	176	5543	2.00E+03	2.00E+03
	GD21 timepoint		**End-point Titer**	
	Sample Number	Animal Number	Original Re-analyzed	Re-tested 06Nov2020
	177	5503	<500	<500
	178	5505	<500	<500
	179	5509	<500	<500
	180	5510	<500	<500

Group 1 (Control)		LD21 timepoint		End-point Titer	
		Sample Number	Animal Number	Original Re-analyzed	Re-tested 06Nov2020
Plate 94	Pup-pooled	4	5532	<500	<500
	Pup-pooled	5	5534	<500	<500
	Pup-pooled	6	5535	<500	<500
	Pup-pooled	7	5537	<500	<500
	Pup-pooled	8	5538	<500	<500
	Pup-pooled	9	5542	<500	<500
	Pup-pooled	10	5524	<500	<500
	Pup-pooled	11	5525	<500	<500
	Pup-pooled	12	5530	<500	<500
	Pup-pooled	13	5541	<500	<500
	Pup-pooled	14	5526	<500	<500
	Pup-pooled	15	5529	<500	<500

Group 2 (mRNA-1273)	SD1 timepoint		End-point Titer	
	Sample Number	Animal Number	Original Re-analyzed	Re-tested 06Nov2020
Plate 21	241	5568	<500	<500
	242	5569	<500	<500
	243	5570	<500	<500
	244	5571	<500	<500
	245	5572	<500	<500
	246	5573	<500	<500
	247	5574	<500	<500
	248	5575	<500	<500
	249	5576	<500	<500
	250	5577	<500	<500
	251	5578	<500	<500
	252	5579	<500	<500

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Table 16: End-point Titers of Group 1 (Control) Animals

Group 1 (Control)	Maternal samples						Fetal-pooled	Pup-pooled
Animal Number	Study Day SD1	Study Day SD15	Study Day GD1	Study Day GD13	Study Day GD21	Study Day LD21	Study Day GD21	Study Day LD21
5501	<500	<500	<500	<500	<500		<500	
5502	<500	<500	<500	<500	<500		<500	
5503	<500	<500	<500	<500	<500		<500	
5504	<500	<500	<500	<500	<500		<500	
5505	<500	<500	<500	<500	<500		<500	
5506	<500	5.00E+02	5.00E+02	<500	<500		<500	
5507	<500	<500	<500	<500	<500		<500	
5508	<500	<500	<500	<500	<500		<500	
5509	5.00E+02	5.00E+02	5.00E+02	<500	<500		<500	
5510	<500	<500	<500	<500	<500		<500	
5511	<500	<500	<500	<500	<500		<500	
5512	<500	<500	<500	<500	<500		<500	
5513	<500	<500	<500	<500	<500		<500	
5514	<500	<500	<500	<500		<500		<500
5515	8.00E+03	8.00E+03	2.00E+03	2.00E+03	<500		<500	
5516	<500	<500	<500	<500	<500		<500	
5517	<500	<500	<500	<500	<500			
5518	<500	<500	<500	<500	<500		<500	
5519	<500	<500	<500	<500	<500		<500	
5520	<500	<500	<500	<500			<500	
5521	<500	<500	<500	<500	<500		<500	
5522	<500	<500	<500	<500	<500		5.00E+02	
5523	<500	<500	<500	<500	<500			
5524	<500	<500	<500	<500		<500		<500
5525	<500	<500	<500	<500		<500		<500
5526	<500	<500	<500	<500		<500		<500
5527	<500	<500	<500	<500		<500		<500
5528	<500	<500	<500	<500	<500		<500	
5529	<500	<500	<500	<500		<500		<500
5530	<500	<500	<500	<500		<500		<500
5531	<500	<500	<500	<500		<500		<500
5532	<500	<500	<500	<500		<500		<500
5533	<500	<500	<500	<500		<500		<500
5534	<500	<500	<500	<500		<500		<500
5535	<500	<500	<500	<500		<500		<500
5536	<500	<500	<500	<500		<500		<500
5537	<500	<500	<500	<500		5.00E+02		<500
5538	<500	<500	<500	<500		<500		<500
5539	<500	<500	<500	<500				
5540	<500	<500	<500	<500		<500		<500
5541	<500	<500	<500	<500		<500		<500
5542	<500	<500	<500	<500		<500		<500
5543	8.00E+03	8.00E+03	2.00E+03	2.00E+03				
5544	<500	<500	<500	<500		<500		<500

Note: "Not detected" antibody titers are reported as "<500" since 1:500 is the lowest dilution factor used for these samples.

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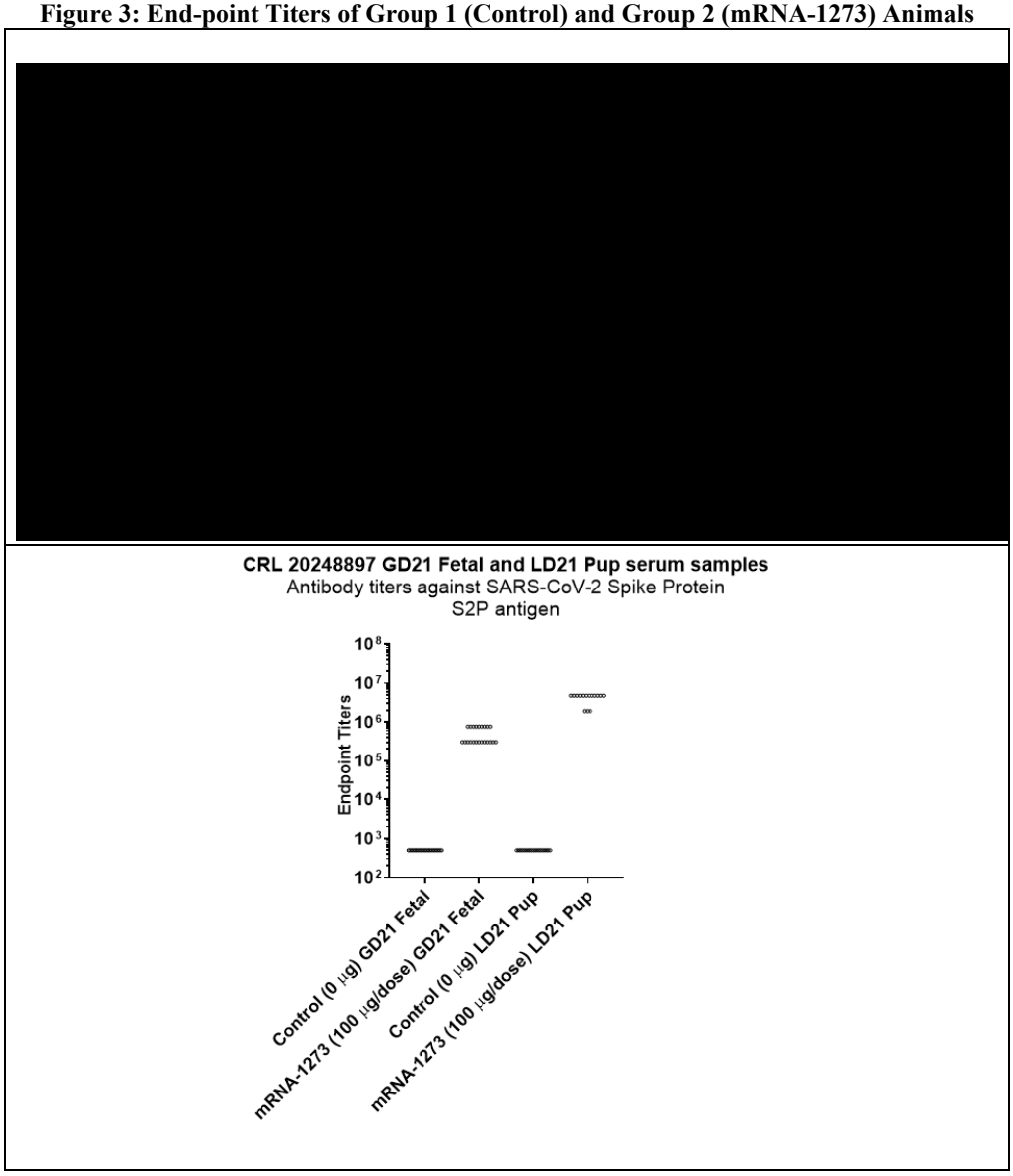
Table 17: End-point Titers of Group 2 (mRNA-1273) Animals

Group 2 (mRNA-1273)	Maternal samples						Fetal-pooled	Pup-pooled
Animal	Study Day	Study Day	Study Day	Study Day	Study Day	Study Day	Study Day	Study Day
Number	SD1	SD15	GD1	GD13	GD21	LD21	GD21	LD21
5545	<500	1.22E+06	7.63E+06	1.91E+07	3.05E+06		7.63E+05	
5546	<500	1.22E+06	7.63E+06	7.63E+06	3.05E+06		3.05E+05	
5547	<500	1.22E+06	3.05E+06	7.63E+06	3.05E+06		3.05E+05	
5548	<500	1.22E+06	3.05E+06	7.63E+06	3.05E+06		3.05E+05	
5549	<500	1.22E+06	3.05E+06	7.63E+06	3.05E+06		3.05E+05	
5550	<500	4.88E+05	3.05E+06	7.63E+06	3.05E+06		3.05E+05	
5551	<500	1.22E+06	7.63E+06	7.63E+06				
5552	<500	1.22E+06	7.63E+06	7.63E+06	3.05E+06		7.63E+05	
5553	<500	4.88E+05	7.63E+06	7.63E+06				
5554	<500	3.05E+06	7.63E+06	1.91E+07	3.05E+06		7.63E+05	
5555	<500	1.22E+06	7.63E+06	7.63E+06	7.63E+06		3.05E+05	
5556	<500	1.22E+06	7.63E+06	7.63E+06	3.05E+06		3.05E+05	
5557	<500	4.88E+05	7.63E+06	7.63E+06	3.05E+06		7.63E+05	
5558	<500	1.22E+06	7.63E+06	7.63E+06				
5559	<500	1.22E+06	7.63E+06	1.91E+07	3.05E+06		7.63E+05	
5560	<500	1.22E+06	7.63E+06	7.63E+06	3.05E+06		7.63E+05	
5561	<500	1.22E+06	3.05E+06	7.63E+06	1.22E+06		3.05E+05	
5562	<500	3.05E+06	7.63E+06	7.63E+06				
5563	<500	1.22E+06	3.05E+06	7.63E+06	3.05E+06		3.05E+05	
5564	<500	1.22E+06	7.63E+06	7.63E+06	3.05E+06		3.05E+05	
5565	<500	4.88E+05	3.05E+06	7.63E+06	3.05E+06		3.05E+05	
5566	<500	4.88E+05	3.05E+06	7.63E+06	3.05E+06		3.05E+05	
5567	<500	1.22E+06	7.63E+06	1.91E+07	3.05E+06		7.63E+05	
5568	<500	1.22E+06	3.05E+06	7.63E+06	3.05E+06		3.05E+05	
5569	<500	1.22E+06	7.63E+06	7.63E+06	7.63E+06		7.63E+05	
5570	<500	1.22E+06	7.63E+06	1.91E+07	3.05E+06		7.63E+05	
5571	<500	1.22E+06	7.63E+06	7.63E+06		3.05E+06		4.77E+06
5572	<500	1.22E+06	3.05E+06	7.63E+06				
5573	<500	4.88E+05	3.05E+06	7.63E+06		1.22E+06		4.77E+06
5574	<500	1.22E+06	3.05E+06	7.63E+06		1.22E+06		4.77E+06
5575	<500	1.22E+06	7.63E+06	1.91E+07		3.05E+06		4.77E+06
5576	<500	1.22E+06	3.05E+06	7.63E+06				
5577	<500	3.05E+06	7.63E+06	1.91E+07		3.05E+06		4.77E+06
5578	<500	1.22E+06	7.63E+06	7.63E+06				
5579	<500	4.88E+05	3.05E+06	7.63E+06		1.22E+06		4.77E+06
5580	<500	1.22E+06	3.05E+06	7.63E+06		3.05E+06		4.77E+06
5581	<500	4.88E+05	3.05E+06	7.63E+06		1.22E+06		4.77E+06
5582	<500	3.05E+06	1.91E+07	7.63E+06		7.63E+06		4.77E+06
5583	<500	1.22E+06	7.63E+06	1.91E+07		3.05E+06		4.77E+06
5584	<500	1.22E+06	7.63E+06	7.63E+06		3.05E+06		1.91E+06
5585	<500	1.22E+06	3.05E+06	7.63E+06		3.05E+06		1.91E+06
5586	<500	4.88E+05	7.63E+06	3.05E+06		1.22E+06		1.91E+06
5587	5.0E+02	1.22E+06	7.63E+06	1.91E+07		7.63E+06		4.77E+06
5588	<500	1.22E+06	7.63E+06	7.63E+06		3.05E+06		4.77E+06

Note: "Not detected" antibody titers are reported as "<500" since 1:500 is the lowest dilution factor used for these samples.

Appendix 39

Figure 3: End-point Titers of Group 1 (Control) and Group 2 (mRNA-1273) Animals



Appendix 40

REPRODUCTIVE INDICES
Crl:CD(SD) RATS
GESTATION DAY 21 CAESAREAN-SECTION

	FULL STUDIES	DOSE RANGE STUDIES
NO. OF STUDIES INCLUDED	82	50
NO. OF RATS TESTED	1883	348
NO. OF RATS PREGNANT	1822	339
NO. FOUND DEAD	4	0
NO. ABORTED	0	0
NO. DELIVERED	7	3
CAESAREAN-SECTIONED ON GD 21	1809	335
NO. OF RATS WITH SINGLE CONCEPTUS LITTER		
LIVE:	2	0
RESORBED:	0	0
ABORTED:	0	0

	MEAN	MIN	MAX	MEAN	MIN	MAX
PREGNANT (%)	96.9	75.0	100.0	97.6	80.0	100.0
CORPORA LUTEA	14.6	12.5	18.2	14.2	11.4	16.9
IMPLANTATIONS	13.7	11.5	16.0	13.2	10.0	16.3
PREIMPLANTATION LOSS (%)	5.3	0.0	16.4	6.8	0.0	25.5
LITTER SIZES						
LIVE FETUSES	13.1	10.7	15.1	12.5	8.6	15.6
DEAD FETUSES	0.0	0.0	0.0	0.0	0.0	0.2
TOTAL RESORPTIONS	0.6	0.2	1.1	0.6	0.0	2.0
EARLY RESORPTIONS	0.6	0.2	1.1	0.6	0.0	2.0
LATE RESORPTIONS	0.0	0.0	0.1	0.0	0.0	0.3
POSTIMPLANTATION LOSS (%)	4.3	1.4	8.8	5.0	0.0	21.5
DAMS WITH ANY RESORPTIONS (%)	40.8	15.0	70.0	38.8	0.0	75.0
DAMS WITH ALL CONCEPTUSES RESORBED (%)	0.0	0.0	0.0	0.0	0.0	0.0
DAMS WITH ONE OR MORE VIABLE FETUSES (%)	99.9	95.0	100.0	99.6	80.0	100.0

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Appendix 40

REPRODUCTIVE INDICES
Crl:CD(SD) RATS
GESTATION DAY 21 CAESAREAN-SECTION

	FULL STUDIES			DOSE RANGE STUDIES		
NO. OF STUDIES INCLUDED	82			50		
	MEAN	MIN	MAX	MEAN	MIN	MAX
SEX RATIO (% MALES/LITTER)	49.9	40.6	56.3	50.5	37.2	70.1
LIVE FETAL BODY WEIGHTS GRAMS/LITTER:	5.71	5.18	6.20	5.80	5.06	6.22
MALE FETUSES:	5.84	5.20	6.31	5.94	5.18	6.46
FEMALE FETUSES:	5 54	4.92	6.05	5.64	4.94	6.11
DAMS WITH NORMAL PLACENTAE (%)	99.7	95.0	100.0	99.0	80.0	100.0

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Appendix 40

FETAL EXTERNAL ABNORMALITIES
Crl:CD(SD) RATS
GESTATION DAY 21 CAESAREAN-SECTION
FULL STUDIES

NO OF STUDIES INCLUDED 21

NO LITTERS EXAMINED 468
NO LIVE FETUSES EXAMINED 5994

	ABNORMALITIES		N	RANGE/STUDY N	%
HEAD					
	: Exencephaly	L	3	0-1	(0-5 0)
		F	3	0-1	(0-0 4)
	: Fleshy protrusion	L	1	0-1	(0-4 3)
		F	1	0-1	(0-0 3)
	: Irregularly shaped	L	1	0-1	(0-4 3)
		F	1	0-1	(0-0 3)
	: Domed	L	2	0-1	(0-5 0)
		F	2	0-1	(0-0 3)
	: Meningocele	L	3	0-1	(0-4 5)
		F	3	0-1	(0-0 4)
EAR					
	: Pinna, absent	L	1	0-1	(0-5 0)
		F	1	0-1	(0-0 4)
EYE					
	: One or both eye bulges	L	8	0-1	(0-5 6)
	depressed	F	8	0-1	(0-0 4)
	: One or both eye lids	L	2	0-1	(0-5 6)
	open	F	2	0-1	(0-0 4)
	: Absent	L	1	0-1	(0-4 2)
		F	1	0-1	(0-0 8)
	: Protruding	L	1	0-1	(0-4 5)
		F	1	0-1	(0-0 4)
SNOUT					
	: Short	L	1	0-1	(0-5 6)
		F	1	0-1	(0-0 4)
	: Cleft	L	1	0-1	(0-4 3)
		F	1	0-1	(0-0 3)
	: Misshapen	L	2	0-1	(0-5 0)
		F	2	0-1	(0-0 4)
PALATE					
	: Cleft	L	1	0-1	(0-4 2)
		F	1	0-1	(0-0 3)
TONGUE					
	: Protruded	L	2	0-1	(0-5 6)
		F	2	0-1	(0-0 4)
	: Absent	L	1	0-1	(0-4 2)
		F	1	0-1	(0-0 3)
NOSE					
	: Nares, fused	L	2	0-1	(0-4 5)
		F	2	0-1	(0-0 4)

L: LITTER INCIDENCE
F: FETAL INCIDENCE
Note: All summary values are based on studies with fetal findings

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Appendix 40

FETAL EXTERNAL ABNORMALITIES
Crl:CD(SD) RATS
GESTATION DAY 21 CAESAREAN-SECTION
FULL STUDIES

	ABNORMALITIES		N	RANGE/STUDY N	%
MOUTH					
	: Small oral opening	L	2	0-1	(0-5 0)
		F	2	0-1	(0-0 4)
	: Absent	L	2	0-1	(0-4 5)
		F	2	0-1	(0-0 4)
JAW					
	: Micrognathia	L	2	0-1	(0-4 2)
		F	2	0-1	(0-0 3)
	: Agnathia	L	1	0-1	(0-4 2)
		F	1	0-1	(0-0 3)
	: Mandible, absent	L	2	0-1	(0-4 5)
		F	2	0-1	(0-0 4)
BODY					
	: Umbilical hernia	L	2	0-1	(0-4 5)
		F	2	0-1	(0-0 4)
	: Edema	L	2	0-1	(0-5 0)
		F	2	0-1	(0-0 4)
	: Trunk short	L	4	0-1	(0-5 6)
		F	4	0-1	(0-0 4)
	: Gastroschisis	L	1	0-1	(0-4 8)
		F	1	0-1	(0-0 4)
	: Craniorachischisis	L	2	0-1	(0-5 6)
		F	2	0-1	(0-0 4)
	: Spina bifida	L	1	0-1	(0-5 0)
		F	1	0-1	(0-0 3)
	: Trunk, thoracogastroschisis	L	1	0-1	(0-5 0)
		F	1	0-1	(0-0 4)
FORE AND/OR HINDLIMBS(S)					
	: Digit(s), extra	L	1	0-1	(0-4 0)
		F	1	0-1	(0-0 3)
	: Paw(s), flexed	L	3	0-1	(0-5 0)
		F	3	0-1	(0-0 4)
	: Limb(s), rotated	L	2	0-1	(0-4 5)
		F	2	0-1	(0-0 3)
	: Limb(s), flexed	L	1	0-1	(0-4 2)
		F	1	0-1	(0-0 3)
	: Malrotated	L	1	0-1	(0-5 0)
		F	1	0-1	(0-0 4)
ANUS					
	: No opening present	L	2	0-1	(0-5 0)
		F	2	0-1	(0-0 4)
TAIL					
	: Short	L	1	0-1	(0-4 2)
		F	1	0-1	(0-0 3)
	: Absent	L	1	0-1	(0-4 8)
		F	1	0-1	(0-0 3)
	: Misshapen	L	1	0-1	(0-5 0)
		F	1	0-1	(0-0 4)

L: LITTER INCIDENCE
F: FETAL INCIDENCE
Note: All summary values are based on studies with fetal findings

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Appendix 40

FETAL SOFT TISSUE ABNORMALITIES
Crl:CD(SD) RATS
GESTATION DAY 21 CAESAREAN-SECTION
FULL STUDIES

NO. OF STUDIES INCLUDED	31
NO. LITTERS EXAMINED	693
NO. FETUSES EXAMINED	4864
NO. HEADS ONLY EXAMINED	149
NO. BODIES ONLY EXAMINED	162

ABNORMALITIES			N	RANGE/STUDY N	%
BRAIN					
	: Lateral ventricles, dilation, slight	L	3	0-1	(0-5.3)
		F	3	0-1	(0-0.8)
	: Lateral ventricles, dilation, moderate	L	3	0-1	(0-4.5)
		F	3	0-1	(0-0.6)
EYE(S)					
	: Retina(s) folded	L	6	0-1	(0-5.3)
		F	6	0-1	(0-0.8)
	: Malpositioned	L	1	0-1	(0-4.2)
		F	1	0-1	(0-0.6)
	: Cup irregular	L	1	0-1	(0-4.2)
		F	1	0-1	(0-0.6)
	: Microphthalmia	L	8	0-3	(0-12.5)
		F	8	0-3	(0-1.9)
	: Absent	L	1	0-1	(0-4.8)
		F	1	0-1	(0-0.8)
TONGUE					
	: Small	L	1	0-1	(0-4.2)
		F	1	0-1	(0-0.6)
	: Absent	L	1	0-1	(0-4.2)
		F	1	0-1	(0-0.6)
PALATE					
	: Irregularly shaped	L	1	0-1	(0-4.2)
		F	1	0-1	(0-0.6)
NASOPHARYNX					
	: Misshapen	L	1	0-1	(0-4.2)
		F	1	0-1	(0-0.6)

L: LITTER INCIDENCE
F: FETAL INCIDENCE
Note: All summary values are based on studies with fetal findings

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FETAL SOFT TISSUE ABNORMALITIES
Crl:CD(SD) RATS
GESTATION DAY 21 CAESAREAN-SECTION
FULL STUDIES

	ABNORMALITIES		N	RANGE/STUDY N	%
HEART					
	: Interventricular septal defect	L	4	0-1	(0-4.8)
		F	4	0-1	(0-0.7)
	: Bicuspid valve, misshapen	L	1	0-1	(0-4.8)
		F	1	0-1	(0-0.7)
	: Lobe, misshapened	L	3	0-3	(0-14.3)
		F	3	0-3	(0-2.4)
VESSELS					
	: Innominate artery, absent	L	6	0-1	(0-5.0)
		F	6	0-1	(0-0.7)
	: Aorta passes dorsal to the trachea and esophagus	L	2	0-1	(0-5.0)
		F	2	0-1	(0-0.6)
	: Aortic arch, absent	L	1	0-1	(0-4.5)
		F	1	0-1	(0-0.8)
	: Aortic arch, interrupted	L	1	0-1	(0-4.8)
		F	1	0-1	(0-0.8)
	: Caroid artery, malpositioned	L	1	0-1	(0-4.5)
		F	1	0-1	(0-0.8)
	: Ductus arteriosus, patent	L	1	0-1	(0-5.0)
		F	3	0-3	(0-2.1)

L: LITTER INCIDENCE
F: FETAL INCIDENCE
Note: All summary values are based on studies with fetal findings

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FETAL SOFT TISSUE ABNORMALITIES
Crl:CD(SD) RATS
GESTATION DAY 21 CAESAREAN-SECTION
FULL STUDIES

	ABNORMALITIES		N	RANGE/STUDY N	%
VESSELS (CONT'D)					
	: Subclavian artery, malpositioned	L	1	0-1	(0-4.5)
		F	1	0-1	(0-0.8)
	: Vessels arise in incorrect order	L	1	0-1	(0-4.0)
		F	1	0-1	(0-0.6)
	: Right subclavian passes dorsal	L	1	0-1	(0-4.3)
	to trachea and esophagus	F	1	0-1	(0-0.6)
	: Right subclavian arises to the	L	1	0-1	(0-4.3)
	left of left subclavian	F	1	0-1	(0-0.6)
	: Pulmonary artery constricted	L	1	0-1	(0-4.3)
		F	1	0-1	(0-0.6)
	: Transposed	L	2	0-1	(0-4.0)
		F	2	0-1	(0-0.7)
	: Major vessels, malpositioned	L	1	0-1	(0-5.0)
		F	1	0-1	(0-0.6)
INTESTINES					
	: Portion protrudes through	L	1	0-1	(0-4.0)
	umbilicus	F	1	0-1	(0-0.6)
KIDNEYS					
	: Small	L	1	0-1	(0-4.5)
		F	1	0-1	(0-0.8)
URETER	: Dilated, slight	L	1	0-1	(0-5.0)
		F	1	0-1	(0-0.6)

L: LITTER INCIDENCE
F: FETAL INCIDENCE
Note: All summary values are based on studies with fetal findings

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FETAL SKELETAL ABNORMALITIES
Crl:CD(SD) RATS
GESTATION DAY 21 CAESAREAN-SECTION
FULL STUDIES

NO OF STUDIES INCLUDED 76

NO LITTERS EXAMINED 1680
NO FETUSES EXAMINED 11630

	ABNORMALITIES		N	RANGE/STUDY N	%
SKULL					
Frontals					
	: Contain an interfrontal	L	4	0-1	(0-5 0)
		F	4	0-1	(0-0 8)
	: Incompletely ossified	L	20	0-2	(0-10 5)
		F	24	0-5	(0-3 3)
	: Misshapen	L	1	0-1	(0-5 0)
		F	1	0-1	(0-0 7)
Nasal					
	: Short	L	1	0-1	(0-4 2)
		F	1	0-1	(0-0 6)
	: Misshapen	L	3	0-1	(0-5 0)
		F	3	0-1	(0-0 8)
Nasal-Frontal					
	: Suture, large	L	5	0-1	(0-5 9)
		F	5	0-1	(0-0 9)
Parietal					
	: Incompletely ossified	L	49	0-6	(0-30 0)
		F	63	0-8	(0-6 3)
	: Hole	L	2	0-1	(0-5 3)
		F	2	0-1	(0-0 7)
	: Misshapen	L	1	0-1	(0-5 0)
		F	1	0-1	(0-0 7)
Interparietals					
	: Unossified	L	2	0-1	(0-5 0)
		F	2	0-1	(0-0 7)
	: Incompletely ossified	L	14	0-6	(0-28 6)
		F	17	0-6	(0-4 5)
	: Absent	L	2	0-1	(0-5 0)
		F	2	0-1	(0-0 8)
Eye Socket					
	: Small	L	4	0-1	(0-4 8)
		F	4	0-1	(0-0 6)
Palate					
	: Incompletely ossified	L	2	0-1	(0-4 2)
		F	2	0-1	(0-0 6)
	: Irregularly shaped	L	2	0-1	(0-5 0)
		F	2	0-1	(0-0 7)
	: Absent	L	2	0-1	(0-4 5)
		F	2	0-1	(0-0 7)
Premaxilla					
	: Short	L	1	0-1	(0-4 2)
		F	1	0-1	(0-0 6)
	: Misshapen	L	2	0-1	(0-5 0)
		F	2	0-1	(0-0 7)

L LITTER INCIDENCE
F FETAL INCIDENCE
Note All summary values are based on studies with fetal findings.

Updated on 03 March 2019

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FETAL SKELETAL ABNORMALITIES
Crl:CD(SD) RATS
GESTATION DAY 21 CAESAREAN-SECTION
FULL STUDIES

				RANGE/STUDY	
		ABNORMALITIES	N	N	%
SKULL (CONT)					
	Maxilla				
		: Short	L 1	0-1	(0-4 2)
			F 1	0-1	(0-0 6)
		: Split	L 1	0-1	(0-4 2)
			F 1	0-1	(0-0 5)
		: Incompletely ossified	L 1	0-1	(0-4 8)
			F 2	0-2	(0-1 3)
		: Misshapen	L 3	0-1	(0-5 0)
			F 3	0-1	(0-0 8)
	Mandible				
		: Short	L 1	0-1	(0-4 2)
			F 1	0-1	(0-0 6)
		: Misshapen	L 1	0-1	(0-5 0)
			F 1	0-1	(0-0 7)
		: Absent	L 2	0-1	(0-4 5)
			F 2	0-1	(0-0 8)
	Squamosal				
		: Misshapen	L 4	0-1	(0-5 0)
			F 4	0-1	(0-0 8)
		: Incompletely ossified	L 91	0-7	(0-35 0)
			F 124	0-10	(0-8 3)
	Supraoccipital				
		: Incompletely ossified	L 4	0-1	(0-4 8)
			F 5	0-2	(0-1 3)
		: Hole	L 1	0-1	(0-5 3)
			F 1	0-1	(0-0 7)
		: Absent	L 1	0-1	(0-5 0)
			F 1	0-1	(0-0 7)
	Suture				
		: Large	L 2	0-1	(0-5 6)
			F 2	0-1	(0-0 8)
	Zygomatic Arch				
		: Incompletely ossified	L 131	0-11	(0-55 0)
			F 201	0-21	(0-19 0)
		: Fused	L 2	0-2	(0-9 5)
			F 2	0-2	(0-1 8)
		: Misshapen	L 4	0-1	(0-5 0)
			F 4	0-1	(0-0 8)
	Tympanic Rings				
		: Incompletely ossified	L 4	0-3	(0-13 6)
			F 5	0-4	(0-1 4)
		: Close set	L 1	0-1	(0-4 2)
			F 1	0-1	(0-0 5)
		: Absent	L 1	0-1	(0-5 0)
			F 1	0-1	(0-0 7)
		: Fused	L 2	0-1	(0-4 5)
			F 2	0-1	(0-0 8)
	Exoccipital				
		: Fused	L 1	0-1	(0-4 5)
			F 1	0-1	(0-0 7)
		: Absent	L 2	0-1	(0-5 0)
			F 2	0-1	(0-0 7)

L LITTER INCIDENCE
F FETAL INCIDENCE
Note All summary values are based on studies with fetal findings.

Updated on 03 March 2019

Appendix 40

FETAL SKELETAL ABNORMALITIES
Crl:CD(SD) RATS
GESTATION DAY 21 CAESAREAN-SECTION
FULL STUDIES

					RANGE/STUDY	
SKULL (CONT)		ABNORMALITIES		N	N	%
	Sphenoid					
		: Incompletely ossified	L	1	0-1	(0-4 2)
			F	1	0-1	(0-0 6)
	Basisphenoid					
		: Irregularly shaped	L	4	0-1	(0-5 0)
			F	4	0-1	(0-0 8)
	Basioccipital					
		: Irregularly shaped	L	2	0-1	(0-5 0)
			F	2	0-1	(0-0 7)
	Skull					
		: Unossified	L	1	0-1	(0-4 2)
			F	1	0-1	(0-0 5)
		: Short	L	1	0-1	(0-4 2)
			F	1	0-1	(0-0 5)
	Hyoid					
		: Unossified	L	4	0--2	(0-9 1)
			F	4	0-2	(0-1 6)
		: Body, incomplete ossification	L	6	0-4	(0-20 0)
			F	8	0-6	(0-3 9)
VERTEBRAE						
	Canal					
		: Absent	L	1	0-1	(0-5 0)
			F	1	0-1	(0-0 8)
	Cervical					
		: Arch, incompletely ossified	L	28	0-3	(0-14 3)
			F	33	0-4	(0-2 2)
		: Arch, reduced ventral process, 6th	L	29	0-3	(0-13 6)
			F	32	0-5	(0-3 0)
		: Arch, 7th cervical arch had the	L	6	0-2	(0-8 0)
		appearance of the 6th arch	F	6	0-2	(0-1 1)
		: Arch, fused	L	3	0-1	(0-4 2)
			F	3	0-1	(0-0 6)
		: Arch, open	L	1	0-1	(0-4 2)
			F	1	0-1	(0-0 5)
		: Arch, irregularly shaped	L	24	0-3	(0-13 6)
			F	24	0-3	(0-2 2)
		: Lateral ossification site	L	9	0-6	(0-27 3)
			F	9	0-6	(0-3 7)
		: Cervical rib present at 7th vertebra	L	64	0-4	(0-18 2)
			F	73	0-5	(0-4 0)
		: Hemivertebra	L	1	0-1	(0-4 0)
			F	1	0-1	(0-0 7)
		: Arch, small	L	1	0-1	(0-4 0)
			F	1	0-1	(0-0 7)
		: Supernumerary, short	L	17	0-3	(0-15 0)
			F	19	0-4	(0-3 2)
		: Supernumerary, full	L	1	0-1	(0-5 0)
			F	1	0-1	(0-0 8)

L LITTER INCIDENCE
F FETAL INCIDENCE
Note All summary values are based on studies with fetal findings.

Updated on 03 March 2019

Appendix 40

FETAL SKELETAL ABNORMALITIES
Crl:CD(SD) RATS
GESTATION DAY 21 CAESAREAN-SECTION
FULL STUDIES

				RANGE/STUDY	
		ABNORMALITIES		N	N	%
VERTEBRAE (CONT)						
	Thoracic					
		: Centrum, bifid	L	166	0-8	(0-34 8)
			F	186	0-10	(0-5 7)
		: Centrum, unilateral ossification	L	5	0-1	(0-5 0)
			F	5	0-1	(0-0 8)
		: Centrum, not ossified	L	2	0-1	(0-5 0)
			F	2	0-1	(0-0 6)
		: Arch, fused	L	4	0-1	(0-4 8)
			F	4	0-1	(0-0 8)
		: Arch, open	L	1	0-1	(0-4 2)
			F	1	0-1	(0-0 5)
		: Arch, misshapen	L	1	0-1	(0-4 8)
			F	1	0-1	(0-0 8)
		: Centrum, misshapen	L	1	0-1	(0-4 5)
			F	1	0-1	(0-0 7)
		: 7 present	L	1	0-1	(0-4 2)
			F	1	0-1	(0-0 6)
		: 11 present	L	1	0-1	(0-4 0)
			F	1	0-1	(0-0 6)
		: Arch, small	L	1	0-1	(0-4 0)
			F	1	0-1	(0-0 6)
	Lumbar					
		: Centrum, bifid	L	11	0-4	(0-18 2)
			F	11	0-4	(0-2 8)
		: Centrum, unilateral ossification	L	1	0-1	(0-4 2)
			F	1	0-1	(0-0 6)
		: Centrum, not ossified	L	1	0-1	(0-5 0)
			F	1	0-1	(0-0 8)
		: Centrum, irregularly shaped	L	1	0-1	(0-5 0)
			F	1	0-1	(0-0 8)
		: Centra, fused	L	1	0-1	(0-4 2)
			F	1	0-1	(0-0 6)
		: Arch, fused	L	1	0-1	(0-5 0)
			F	1	0-1	(0-0 8)
		: Arch, open	L	2	0-1	(0-5 0)
			F	2	0-1	(0-0 7)
		: Arch, irregularly shaped	L	1	0-1	(0-5 0)
			F	1	0-1	(0-0 8)
		: 10 present	L	1	0-1	(0-4 2)
			F	1	0-1	(0-0 6)
		: 5 present	L	1	0-1	(0-5 0)
			F	1	0-1	(0-0 8)
		: Supernumerary	L	1	0-1	(0-4 8)
			F	1	0-1	(0-0 7)
		: Arch, incompletely ossified	L	1	0-1	(0-5 0)
			F	1	0-1	(0-0 7)
	Sacral					
		: Arch, open	L	2	0-1	(0-5 0)
			F	2	0-1	(0-0 7)
		: Arch, incompletely ossified	L	4	0-2	(0-10 0)
			F	4	0-2	(0-1 6)
		: 0 present	L	1	0-1	(0-5 0)
			F	1	0-1	(0-0 8)

L LITTER INCIDENCE
F FETAL INCIDENCE
Note All summary values are based on studies with fetal findings.

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FETAL SKELETAL ABNORMALITIES
Crl:CD(SD) RATS
GESTATION DAY 21 CAESAREAN-SECTION
FULL STUDIES

	ABNORMALITIES		N	RANGE/STUDY N	%
VERTEBRAE (CONT)					
Caudal					
	: 4 present	L	1	0-1	(0-4 2)
		F	1	0-1	(0-0 6)
	: Arch, open	L	3	0-1	(0-5 0)
		F	3	0-1	(0-0 8)
	: Less than 26 pre-sacral vertebrae	L	1	0-1	(0-4 5)
		F	1	0-1	(0-0 8)
RIBS					
	: Wavy	L	37	0-3	(0-12 5)
		F	40	0-4	(0-2 4)
	: One or more incompletely ossified	L	44	0-3	(0-12 0)
	(hypoplastic) or not ossified	F	47	0-4	(0-2 4)
	: Fused	L	4	0-1	(0-4 5)
		F	4	0-1	(0-0 8)
	: Short	L	42	0-3	(0-12 5)
		F	45	0-3	(0-2 3)
	: Thickened	L	25	0-3	(0-12 5)
		F	29	0-4	(0-2 4)
	: 6 present	L	1	0-1	(0-4 2)
		F	1	0-1	(0-0 6)
	: 7 present	L	1	0-1	(0-4 2)
		F	1	0-1	(0-0 6)
	: Bent	L	1	0-1	(0-4 5)
		F	1	0-1	(0-0 6)
	: Broad	L	1	0-1	(0-4 5)
		F	1	0-1	(0-0 6)
	: Absent	L	2	0-1	(0-4 2)
		F	2	0-1	(0-0 5)
	: Nodulated	L	12	0-4	(0-20 0)
		F	14	0-5	(0-4 2)
	: Split	L	1	0-1	(0-4 0)
		F	1	0-1	(0-0 6)
	: 11 present	L	1	0-1	(0-4 0)
		F	1	0-1	(0-0 6)
	: T14, short	L	28	0-7	(0-31 8)
		F	49	0-15	(0-12 1)
	: T14, full	L	2	0-2	(0-9 5)
		F	2	0-2	(0-1 3)
	: Thoracolumbar, full	L	3	0-3	(0-14 3)
		F	3	0-3	(0-2 3)
	: Thoracolumbar, short	L	19	0-19	(0-90 5)
		F	66	0-66	(0-49 9)

L LITTER INCIDENCE
F FETAL INCIDENCE
Note All summary values are based on studies with fetal findings.

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FETAL SKELETAL ABNORMALITIES
Crl:CD(SD) RATS
GESTATION DAY 21 CAESAREAN-SECTION
FULL STUDIES

		ABNORMALITIES		N	RANGE/STUDY N	%
STERNUM						
	Sternebrae					
		: One or more incompletely ossified	L	24	0-2	(0-9 1)
		or not ossified	F	26	0-3	(0-2 4)
		: Asymmetric	L	13	0-2	(0-8 3)
			F	13	0-2	(0-1 1)
		: Irregularly shaped	L	9	0-2	(0-10 0)
			F	11	0-4	(0-3 7)
		: Fused	L	5	0-2	(0-10 2)
			F	5	0-2	(0-2 0)
		: Duplicated	L	9	0-1	(0-5 0)
			F	11	0-1	(0-0 7)
		: Bipartite ossification	L	5	0-1	(0-5 0)
			F	5	0-1	(0-0 8)
		: Split	L	1	0-1	(0-5 0)
			F	1	0-1	(0-0 7)
	Centra	: Not ossified	L	3	0-1	(0-5 3)
			F	3	0-1	(0-0 7)
		: Incompletely ossified	L	1	0-1	(0-5 3)
			F	1	0-1	(0-0 7)
		: Asymmetric	L	2	0-1	(0-5 3)
			F	3	0-2	(0-1 4)
		: 7 present	L	1	0-1	(0-4 8)
			F	1	0-1	(0-0 7)
		: Irregularly shaped	L	1	0-1	(0-4 8)
			F	1	0-1	(0-0 7)
		: Bifid	L	1	0-1	(0-5 0)
			F	1	0-1	(0-0 6)
	Manubrium					
		: Fused	L	2	0-1	(0-4 2)
			F	2	0-1	(0-0 6)
		: Irregularly shaped	L	4	0-1	(0-4 0)
			F	4	0-1	(0-0 5)
		: Duplicated	L	2	0-1	(0-5 3)
			F	2	0-1	(0-0 7)
		: Incompletely ossified	L	1	0-1	(0-4 8)
			F	1	0-1	(0-0 7)
	Xiphoid					
		: Irregularly shaped	L	1	0-1	(0-4 5)
			F	1	0-1	(0-0 7)
		: Incompletely ossified	L	2	0-1	(0-4 8)
			F	2	0-1	(0-0 7)
SCAPULAE						
	Body and Ala					
		: Bent	L	1	0-1	(0-4 2)
			F	1	0-1	(0-0 6)

L LITTER INCIDENCE
F FETAL INCIDENCE
Note All summary values are based on studies with fetal findings.

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FETAL SKELETAL ABNORMALITIES
Crl:CD(SD) RATS
GESTATION DAY 21 CAESAREAN-SECTION
FULL STUDIES

		ABNORMALITIES		N	RANGE/STUDY N	%
PELVIS						
	Pubis					
		: Incompletely ossified	L	17	0-2	(0-9 5)
			F	20	0-2	(0-2 6)
	Ishchium					
		: Incompletely ossified	L	12	0-2	(0-8 0)
			F	12	0-2	(0-1 1)
	Pelvis					
		: Close-set	L	1	0-1	(0-5 0)
			F	1	0-1	(0-0 8)
	Ilium					
		: Malpositioned	L	1	0-1	(0-5 0)
			F	1	0-1	(0-0 7)
FORELIMB (S)						
	Phalanx					
		: Absent	L	1	0-1	(0-4 5)
			F	1	0-1	(0-0 6)
		: Less than the expected number ossified	L	13	0-9	(0-42 8)
			F	24	0-20	(0-13 9)
		: Unossified	L	63	0-17	(0-81 0)
			F	204	0-71	(0-47 0)
	Digit					
		: Absent	L	1	0-1	(0-4 5)
			F	1	0-1	(0-0 6)
		: Short	L	1	0-1	(0-4 5)
			F	1	0-1	(0-0 6)
	Metacarpal					
		: Fused	L	1	0-1	(0-4 2)
			F	1	0-1	(0-0 6)
		: Less than the expected number ossified	L	2	0-2	(0-9 1)
			F	2	0-2	(0-1 2)
		: Misaligned	L	1	0-1	(0-4 5)
			F	1	0-1	(0-0 6)
HINDLIMB(S)						
	Digit					
		: Extra	L	2	0-1	(0-4 2)
			F	2	0-1	(0-0 6)
	Phalanx					
		: Extra	L	2	0-1	(0-4 2)
			F	2	0-1	(0-0 6)
		: Less than the expected number ossified	L	37	0-20	(0-95 2)
			F	167	0-101	(0-70 1)
	Metatarsal					
		: Unossified	L	12	0-5	(0-22 7)
			F	16	0-7	(0-5 5)

L LITTER INCIDENCE
F FETAL INCIDENCE
Note All summary values are based on studies with fetal findings.

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FETAL SKELETAL OSSIFICATION SITE AVERAGES
Crl:CD(SD) RATS
GESTATION DAY 21 CAESAREAN-SECTION
FULL STUDIES

NO. OF STUDIES INCLUDED	69
NO. LITTERS EXAMINED	1531
NO. FETUSES EXAMINED	10509

	MEAN	MINIMUM	MAXIMUM
HYOID	1.00	0.94	1.08
VERTEBRAE			
CERVICAL	7.00	6.98	7.00
THORACIC	13.07	13.01	13.30
LUMBAR	5.93	5.82	5.99
SACRAL	3.45	3.00	4.25
CAUDAL	7.14	5.98	8.14
RIBS (pairs)	13.04	13.01	13.12
STERNUM			
MANUBRIUM	1.00	1.00	1.02
STERNAL CENTERS	4.00	3.97	4.01
XIPHOID	1.00	0.99	1.04
FOREPAWS[a]			
CARPALS	0.00	0.00	0.00
METACARPALS	4.00	3.98	4.00
DIGITS	5.00	5.00	5.00
PHALANGES	8.22	7.54	8.80
HINDPAWS[a]			
TARSALS	0.03	0.00	0.13
METATARSALS	4.91	4.74	5.00
DIGITS	5.00	5.00	5.00
PHALANGES	6.65	5.73	7.93

a. Calculated as mean per limb

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NATURAL DELIVERY AND LITTER PARAMETERS
Crl:CD(SD) RATS
(STUDIES WITH CULLING)

		MEAN	MINIMUM	MAXIMUM	NO STUDIES INCLUDED
RATS ASSIGNED TO NATURAL DELIVERY	N	TOTAL =	215		
PREGNANT	N	TOTAL =	208		
	%	96 7	90 0	100 0	11
DELIVERED LITTERS	N	TOTAL =	121		
	%	99 6	95 4	100 0	11
DURATION OF GESTATION IN DAYS	MEAN	22 5	22 0	22 8	11
IMPLANTATION SITES PER DELIVERED LITTER	N	261 6	107	320	11
	MEAN	14 2	12 4	16 0	11
DAMS WITH STILLBORN PUPS	N	1 4	0	4	11
	%	6 8	0 0	16 7	11
DAMS WITH NO LIVEBORN PUPS	N	0 2	0	1	11
	%	0 8	0 0	4 8	11
GESTATION INDEX (NO RATS WITH LIVEBORN/NO PREGNANT RATS)	%	98 8	90 9	100 0	11
	N	18 5	8	24	11
	N	18 8	8	24	11
DAMS WITH ALL PUPS DYING DAYS 1-4 POSTPARTUM	N	0 1	0	1	11
	%	0 5	0 0	5 0	11
DAMS WITH ALL PUPS DYING DAYS 5-21 POSTPARTUM	N	0 1	0	1	11
	%	0 4	0 0	4 2	11
PUPS DELIVERED (TOTAL)	N	245 5	107	304	11
	MEAN	13 4	11 8	15 3	11
LIVEBORN	MEAN	13 3	11 7	15 2	11
	N	244 1	106	301	11
	%	99 4	98 3	100 0	11
STILLBORN	MEAN	0 0	0 0	0 2	11
	N	1 5	0	5	11
	%	0 6	0 0	1 7	11
UNKNOWN VITAL STATUS	N	0 0	0 0	0 0	10

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NATURAL DELIVERY AND LITTER PARAMETERS
Crl:CD(SD) RATS
(STUDIES WITH CULLING)

		MEAN	MINIMUM	MAXIMUM	NO STUDIES INCLUDED
PUPS FOUND DEAD OR PRESUMED CANNIBALIZED					
DAY 0	N	1 0	1	1	2
	N	168 5	133	204	2
	%	0 7	0 5	0 8	2
DAY 1	N	1 4	0	11	9
	N	260 9	106	301	9
	%	0 6	0 0	4 7	9
DAY 1-4	N	7 0	3	11	2
	N	167 5	132	203	2
	%	3 9	2 3	5 4	2
DAYS 2-4	N	3 0	0	13	9
	N	259 4	106	300	9
	%	1 0	0 0	4 6	9
DAYS 5-7	N	0 1	0	1	9
	N	149 7	64	184	9
	%	0 1	0 0	0 6	9
DAYS 5-9	N	1 0	1	1	1
	N	72 0	72	72	1
	%	1 4	1 4	1 4	1
DAYS 6-8	N	1 0	1	1	1
	N	176 0	176	176	1
	%	0 6	0 6	0 6	1
DAYS 8-14	N	0 0	0	0	6
	N	165 0	149	184	6
	%	0 0	0 0	0 0	6
DAYS 9-11	N	0 0	0	0	1
	N	175 0	175	175	1
	%	0 0	0 0	0 0	1
DAYS 8-14	N	0 0	0	0	2
	N	146 0	108	184	2
	%	0 0	0 0	0 0	2
DAYS 10-13	N	0 0	0	0	1
	N	71 0	71	71	1
	%	0 0	0 0	0 0	1
DAYS 11-14	N	0 1	0	1	7
	N	166 4	149	184	7
	%	0 1	0 0	0 6	7
DAYS 15-17	N	0 0	0	0	4
	N	148 0	108	175	4
	%	0 0	0 0	0 0	4
DAYS 15-18	N	0 0	0	0	4
	N	170 0	149	184	4
	%	0 0	0 0	0 0	4
DAYS 18-21	N	0 0	0	0	4
	N	148 0	108	175	4
	%	0 2	0 0	0 6	4
DAYS 19-21	N	0 0	0	0	4
	N	170 0	149	184	4
	%	0 0	0 0	0 0	4

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NATURAL DELIVERY AND LITTER PARAMETERS
Crl:CD(SD) RATS
(STUDIES WITH CULLING)

		MEAN	MINIMUM	MAXIMUM	NO STUDIES INCLUDED
PUPS FOUND DEAD OR PRESUMED CANNIBALIZED (CONT'D)					
DAYS 22-28	N	0 0	0	0	1
	N	159 0	159	159	1
	%	0 0	0 0	0 0	1
VIABILITY INDEX (No Live PPD4 / No Live PPD1)	%	97 8	94 1	100 0	11
	N	239 0	106	297	11
	N	244 1	106	301	11
LACTATION INDEX (No Live PPD21 / No Live PPD4)	%	99 6	98 6	100 0	10
	N	152 6	71	184	10
	N	153 1	72	184	10
SURVIVING PUPS/LITTER					
Day 0	MEAN	14 7	14 6	14 8	2
Day 1	MEAN	13 2	11 8	15 2	7
Day 2	MEAN	12 9	12 9	12 9	1
Day 4 (Preculling)	MEAN	13 3	11 2	15 0	9
Day 4 (Postculling)	MEAN	7 8	7 5	8 0	9
Day 5 (Preculling)	MEAN	12 9	12 9	12 9	1
Day 5 (Postculling)	MEAN	8 0	8 0	8 0	1
Day 7	MEAN	7 8	7 5	8 0	8
Day 8	MEAN	8 0	8 0	8 0	1
Day 9	MEAN	7 9	7 9	7 9	1
Day 10	MEAN	7 8	7 5	8 0	5
Day 11	MEAN	8 0	8 0	8 0	1
Day 13	MEAN	7 9	7 9	7 9	1
Day 14	MEAN	7 8	7 5	8 0	8
Day 17	MEAN	7 9	7 7	8 0	3
Day 18	MEAN	7 7	7 5	8 0	4
Day 20	MEAN	8 0	8 0	8 0	1
Day 21	MEAN	7 8	7 5	8 0	7
Day 28	MEAN	8 0	8 0	8 0	1

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NATURAL DELIVERY AND LITTER PARAMETERS
Crl:CD(SD) RATS
(STUDIES WITH CULLING)

		MEAN	MINIMUM	MAXIMUM	NO STUDIES INCLUDED
PERCENT MALE PUPS PER NUMBER OF PUPS SEXED					
Day 0	MEAN	47 5	42 5	52 5	2
Day 1	MEAN	50 8	47 9	53 9	7
Day 2	MEAN	46 6	46 6	46 6	1
Day 4 (Preculling)	MEAN	49 9	43 1	53 9	9
Day 4 (Postculling)	MEAN	50 0	48 4	52 2	9
Day 5 (Preculling)	MEAN	46 6	46 6	46 6	1
Day 5 (Postculling)	MEAN	48 3	48 3	48 3	1
Day 7	MEAN	50 3	49 1	52 2	8
Day 8	MEAN	48 0	48 0	48 0	1
Day 9	MEAN	49 2	49 2	49 2	1
Day 10	MEAN	50 6	49 4	52 2	5
Day 11	MEAN	48 0	48 0	48 0	1
Day 13	MEAN	49 2	49 2	49 2	1
Day 14	MEAN	50 0	48 0	52 2	8
Day 17	MEAN	49 0	48 0	50 0	3
Day 18	MEAN	50 5	49 1	52 2	4
Day 20	MEAN	48 0	48 0	48 0	1
Day 21	MEAN	50 3	49 1	52 2	7
Day 28	MEAN	50 0	50 0	50 0	1

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NATURAL DELIVERY AND LITTER PARAMETERS
Crl:CD(SD) RATS
(STUDIES WITH CULLING)

LIVE LITTER SIZE AT WEIGHING		MEAN	MINIMUM	MAXIMUM	NO STUDIES INCLUDED
Day 0	MEAN	14 7	14 5	14 8	2
Day 1	MEAN	13 2	11 8	15 2	7
Day 2	MEAN	12 9	12 9	12 9	1
Day 4 (Preculling)	MEAN	13 3	11 2	15 0	9
Day 4 (Postculling)	MEAN	7 8	7 5	8 0	8
Day 5 (Preculling)	MEAN	8 0	8 0	8 0	1
Day 5 (Postculling)	MEAN	8 0	8 0	8 0	1
Day 7	MEAN	7 9	7 6	8 0	8
Day 8	MEAN	8 0	8 0	8 0	1
Day 9	MEAN	7 9	7 9	7 9	1
Day 10	MEAN	7 8	7 6	8 0	5
Day 11	MEAN	8 0	8 0	8 0	1
Day 13	MEAN	7 9	7 9	7 9	1
Day 14	MEAN	7 9	7 6	8 0	8
Day 17	MEAN	7 9	7 7	8 0	3
Day 18	MEAN	7 8	7 6	8 0	4
Day 20	MEAN	8 0	8 0	8 0	1
Day 21	MEAN	7 8	7 6	8 0	7
Day 28	MEAN	8 0	8 0	8 0	1

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Appendix 40

NATURAL DELIVERY AND LITTER PARAMETERS
Crl:CD(SD) RATS
(STUDIES WITH CULLING)

PUP WEIGHT/LITTER (GRAMS)		MEAN	MINIMUM	MAXIMUM	NO STUDIES INCLUDED
Day 0	MEAN	6 7	6 6	6 7	2
Day 1	MEAN	6 9	6 4	7 3	7
Day 2	MEAN	7 3	7 3	7 3	1
Day 4 (Preculling)	MEAN	9 8	8 3	10 4	9
Day 4 (Postculling)	MEAN	9 9	8 4	10 7	9
Day 5 (Preculling)	MEAN	10 6	10 6	10 6	1
Day 5 (Postculling)	MEAN	10 8	10 8	10 8	1
Day 7	MEAN	16 1	12 8	18 0	8
Day 8	MEAN	17 4	17 4	17 4	1
Day 9	MEAN	22 6	22 6	22 6	1
Day 10	MEAN	23 9	23 1	24 8	5
Day 11	MEAN	25 5	25 5	25 5	1
Day 13	MEAN	32 4	32 4	32 4	1
Day 14	MEAN	34 2	31 6	37 4	8
Day 17	MEAN	42 1	40 1	44 6	3
Day 18	MEAN	43 0	39 8	46 2	4
Day 20	MEAN	49 3	49 3	49 3	1
Day 21	MEAN	54 7	50 6	58 1	7
Day 28	MEAN	91 0	91 0	91 0	1

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