TRADE SECRET

FINAL REPORT
Volume 1 of 2 (Text, Tables, and Appendices A-D)

STUDY TITLE

AN ORAL (GAVAGE) PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS

STUDY NUMBER

WIL-189223

DATA REQUIREMENT

OPPTS Guideline 870.3700
OECD Guideline 414

STUDY DIRECTOR

Tammye L. Edwards, B.S., L.A.T.

STUDY INITIATION DATE

12 October 2009

STUDY COMPLETION DATE

2 July 2010

PERFORMING LABORATORY

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18405-841

SPONSOR

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Wilmington, Delaware 19898
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GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

This study was conducted in compliance with U.S. EPA FIFRA (40 CFR part 160) and TSCA (40 CFR Part 792) Good Laboratory Practice Standards, which are compatible with current OECD Good Laboratory Practices, the standard operating procedures of WIL Research Laboratories, LLC, the protocol, and protocol amendments as approved by the Sponsor.

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QUALITY ASSURANCE UNIT STATEMENT

Phases Inspected

Date(s) of Inspection(s)	Phase Inspected	Date(s) Findings Reported to Study Director	Date(s) Findings Reported to WIL Management	Auditor(s)
02-Nov-2009	Oral Gavage Test Article Administration	02-Nov-2009	21-Dec-2009	R.Rohr
10-Nov-2009	Gestational Body and Food Weights	10-Nov-2009	21-Dec-2009	R.Rohr
18-Nov-2009	Laparohysterectomy and Fetal Examination	18-Nov-2009	21-Dec-2009	R.Rohr
02-Dec-2009, 09-Dec-2009, 10-Dec-2009, 11-Dec-2009	Study Records (I-1)	11-Dec-2009	25-Jan-2010	J.Adams
11-Dec-2009, 18-Dec-2009, 21-Dec-2009	Study Records (Rx-1)	21-Dec-2009	25-Jan-2010	K.Mentzer / J.Adams
31-Dec-2009, 06-Jan-2010, 07-Jan-2010	Study Records (N-1)	07-Jan-2010	22-Feb-2010	J.Adams
30-Dec-2009, 31-Dec-2009, 07-Jan-2010	Study Records (N-2)	07-Jan-2010	22-Feb-2010	J.Adams
15-Jan-2010, 18-Jan-2010	Study Records (A-1)	18-Jan-2010	22-Feb-2010	C.Heifner
19-Jan-2010	Draft Report (Analytical Chemistry)	19-Jan-2010	22-Feb-2010	C.Heifner
07-Jan-2010, 08-Jan-2010, 11-Jan-2010, 12-Jan-2010, 21-Jan-2010, 22-Jan-2010	Draft Report (Excluding Analytical Appendix)	22-Jan-2010	22-Feb-2010	J.Adams / K.Mentzer
24-Jun-2010	Study Records (H-1)	24-Jun-2010	02-Jul-2010	J.Adams

This study was inspected in accordance with the U.S. EPA Good Laboratory Practice Regulations (40 CFR Parts 160 and 792), the OECD Principles of Good Laboratory Practice, the standard operating procedures of WIL Research Laboratories, LLC, and the Sponsor's protocol and protocol amendments with the following exception. The data located in Appendix B (Certificate of Analysis) were the responsibility of the Sponsor. Data located in Appendix E (Pathology Report) were the responsibility of the Sponsor. Quality Assurance findings, derived from the inspections during the conduct of the study and from the inspections of the raw data and draft report, are documented and have been reported to the Study Director. Review of the protocol and protocol amendments as well as a yearly internal facility inspection are conducted by the WIL Quality Assurance Unit. A status report is submitted to management monthly.

This report accurately reflects the data generated during the study. The methods and procedures used in the study were those specified in the protocol, its amendments, and the standard operating procedures of WIL Research Laboratories, LLC.

The specimens, raw data, the retention sample, and the final report will be stored in the Archives at WIL Research Laboratories, LLC, or another location specified by the sponsor.

APPROVAL

This study was inspected according to the criteria discussed in the Quality Assurance Unit Statement.

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STUDY INFORMATION

Substance Tested:	HFPO Dimer Acid Ammonium Salt 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propionic acid, ammonium salt 62037-80-3 (CAS Number) H-28548
Haskell Number:	28548
Composition:	Proprietary
Purity:	84%
Physical Characteristics:	Clear and colorless liquid
Stability:	The test substance appeared to be stable under the conditions of the study; no evidence of instability was observed.
Study Initiated/Completed:	12 October 2009 / 2 July 2010
Experimental Starting:	13 October 2009
Experimental Start/ Termination, Completion:	2 November 2009 / 16 February 2010
In-Life Initiated/Completed:	27 October 2009 / 22 November 2009

SUMMARY

A. Objective

The objective of this study was to determine the potential of H-28548 to induce developmental toxicity after maternal exposure during the critical period of organogenesis, to characterize maternal toxicity at the exposure levels tested, and to determine a no-observed-adverse-effect level (NOAEL) for maternal and developmental toxicity.

B. Test Guidelines

The protocol was designed to be in compliance with the U.S. EPA Health Effects Test Guidelines OPPTS 870.3700, Prenatal Developmental Toxicity Study, August 1998, and the Organisation of Economic Cooperation and Development (OECD) Guidelines for Testing of Chemicals Guideline 414, Prenatal Developmental Toxicity Study, January 2001.

C. Study Design

The test substance, H-28548, in the vehicle, deionized water, was administered orally by gavage to 3 groups of 22 bred female Crl:CD(SD) rats once daily from gestation day 6 through 20. Dosage levels were 10, 100, and 1000 mg/kg/day administered at a dosage volume of 10 mL/kg. A concurrent control group of 22 bred females received the vehicle (deionized water) on a comparable regimen.

All animals were observed twice daily for mortality and moribundity. Clinical observations, body weights, and food consumption were recorded at appropriate intervals. On gestation day 21, a laparohysterectomy was performed on each surviving female. The uteri, placentae, and ovaries were examined, and the numbers of fetuses, early and late resorptions, total implantations, and corpora lutea were recorded. Gravid uterine weights were recorded, and the net body weights and net body weight changes were calculated. Kidney and liver weights were recorded and preserved in 10% neutral-buffered formalin; microscopic examination of these tissues was conducted. The fetuses were weighed, sexed, and examined for external, visceral, and skeletal malformations and developmental variations.

D. Results

One female in the 1000 mg/kg/day was found dead on gestation day 20. This female had lower mean body weight gains and/or food consumption compared to the control group during gestation days 12-18. The test substance-related liver and kidney changes (moderate coagulative necrosis in the liver and fibrin thrombi in the glomerular capillaries) noted microscopically were considered the cause of death in this animal. Four and 9 females in the 100 and 1000 mg/kg/day groups, respectively, delivered early on gestation day 21. The mortality in the 1000 mg/kg/day group and early deliveries in the 100 and 1000 mg/kg/day groups were considered test substance-related. All other females survived to the scheduled laparohysterectomy.

Test substance-related clinical findings were noted in the 1000 mg/kg/day group and consisted of yellow material on various body surfaces and salivation or evidence thereof (clear material around the mouth). No test substance-related clinical findings were observed in the 10 and 100 mg/kg/day groups.

A transient mean body weight loss was observed in the 1000 mg/kg/day following administration of the first dose (gestation days 6-7), resulting in a lower mean body weight gain during gestation days 6-9. Correspondingly lower mean food consumption was also observed in the 1000 mg/kg/day group. The lower mean body weight gain early in gestation was considered test substance-related. Mean body weight gain was also lower in this group during gestation days 18-21 and when the entire treatment period (gestation days 6-21) was evaluated. The lower mean body weight gain late in gestation in this group as well as a lower mean gravid uterine weight and lower mean body weight on gestation day 21 (8.4% lower than the control group) was attributed to the test substance-related lower mean fetal body weights observed at 1000 mg/kg/day, supported by the lack of effect on mean net body weight and net body weight gain. Mean body weights, body weight gains, net body weights, net body weight gains, gravid uterine weights, and food consumption in the 10 and 100 mg/kg/day groups were similar to the control group, with the following exception. A lower mean gravid uterine weight was noted in the 100 mg/kg/day group and was attributed to the lower mean fetal weights observed in this group.

An edematous pancreas was noted in 2 females that delivered early in the 1000 mg/kg/day group at necropsy; the relationship of this finding to the test substance is uncertain. Other macroscopic findings occurred in single females and/or are not uncommon in females that deliver. Higher mean liver weights were noted in the 100 and 1000 mg/kg/day group females, and higher mean kidney weight was observed in the 1000 mg/kg/day group**.** There were no microscopic correlates to the higher mean kidney weight. Focal necrosis of the liver was noted in some females in the 100 and 1000 mg/kg/day groups in a dose-related manner. In addition, test substance-related hepatocellular hypertrophy was noted at 1000 mg/kg/day; hypertrophy was morphologically consistent with a PPARα agonist.

Mean fetal weights were 8.8% and 28.1% lower in the 100 and 1000 mg/kg/day groups, respectively. No test substance-related effects on mean fetal weight were noted in the 10 mg/kg/day group. Intrauterine survival was not affected by test substance administration at any dosage level.

There were no test substance-related fetal malformations. A higher mean litter proportion of 14^{th} rudimentary ribs was observed in the 1000 mg/kg/day group, resulting in a higher mean litter proportion of total skeletal variations and total developmental variations. Although considered test substance-related, the increase in the number of fetuses with this finding was not considered adverse because it has been suggested that 14^{th} rudimentary ribs are resorbed during postnatal development (Holson et al, 2006; Wickramaratne, 1988). No test substance-related developmental variations were observed in the 10 and 100 mg/kg/day groups.

E. Conclusions

The no-observed-adverse-effect level (NOAEL) for maternal and developmental toxicity was considered to be 10 mg/kg/day based on mortality and lower mean body weight gains and food consumption at 1000 mg/kg/day and early deliveries, microscopic findings in the liver (focal necrosis), and lower mean fetal weights at 100 and 1000 mg/kg/day. At 1000 mg/kg/day, there were additional test substance-related effects that were not considered adverse and consisted of higher kidney and liver weights and hepatocellular hypertrophy.

INTRODUCTION

A. General Study Information

This report presents the data from "An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats." Due to software spacing constraints, the study title appears as "An Oral Prenatal Developmental Toxicity Study of H-28548 in Rats" on the report tables.

The following computer protocol was used for data collection during the study:

Computer Protocol(s)	Type of Data Collected
WIL-189223	Main study data

B. Key Study Dates

Date(s)	Event(s)
13 October 2009	Experimental starting date (animal receipt)
27 October 2009	First gestation day 0
2 November 2009	Experimental start date (first day of test substance administration)
2-21 November 2009	Test substance administration
22 November 2009	Last laparohysterectomy
16 February 2010	Experimental termination (completion) date (last microscopic examination)

STUDY DESIGN

EXPERIMENTAL PROCEDURES - MATERIALS AND METHODS

A. Test Substance and Vehicle

1. Test Substance Identification

The test substance, H-28548, was received from E. I. DuPont de Nemours Company, Newark, DE, on 13 October 2009, as follows:

Identification	Physical Description
H-28548 Lot no. E109540-44A Exp. date: 13 June 2011 [WIL ID no. 090123]	Clear, colorless liquid

Documentation regarding the purity and stability of the test substance is on file with the sponsor and WIL Research Laboratories, LLC. A Certificate of Analysis for the test substance was provided by the sponsor and is presented in Appendix B. The purity of the test substance was 84%. The test substance was stored at controlled room temperature and humidity, and was considered stable under these conditions. A reserve sample of the test substance was collected and stored in the Archives of WIL Research Laboratories, LLC.

2. Vehicle Identification

The vehicle used in preparation of the test substance formulations and for administration to the control group was deionized water (prepared on-site).

3. Preparation

The vehicle, deionized water, was placed in a labeled storage container. The vehicle was prepared approximately weekly and stirred continuously during sampling and dispensation. Aliquots of the vehicle were prepared for daily dispensation and stored refrigerated. The vehicle was stirred continuously throughout dosing.

Dosing formulations were prepared at the concentrations indicated in the following table:

Group Number	Test Substance	Dosage Level (mg/kg/day)	Test Substance Concentration (mg/mL)[a]
2	H-28548	10	1
3	H-28548	100	10
4	H-28548	1000	100

[a] = Test substance formulations were adjusted to account for a purity of 84%.

A 150 mg/mL stock solution of the test substance was prepared weekly for use in preparing the test substance dosing formulations. The stock solution was stirred during preparation and overnight in the refrigerator.

The test substance formulations were prepared approximately weekly as dilutions of the stock solution as single formulations for each dosage level, divided into aliquots for daily dispensation, and stored refrigerated, stirring overnight in the refrigerator. The test substance formulations were stirred continuously throughout the preparation, sampling, and dose administration procedures. The pH was measured for the formulations prepared for the first day of dose administration; the pH measurements for the 0, 1, 10, and 100 mg/mL formulations were 5.93, 8.55, 8.77, and 8.96, respectively. The first dosing formulations were visually inspected by the study director's designee and were found to be visibly homogeneous and acceptable for administration.

4. Sampling and Analyses

Stability and resuspension homogeneity were established in a previous study (Haas, 2009, WIL-189216). Test substance formulations were stable following 12 days of refrigerated (2-8°C) storage at concentrations of 0.01 and 100 mg/mL and were homogeneous after resuspension following 12 days of refrigerated storage (2-8°C). Therefore, stability and resuspension homogeneity analyses were not conducted in this study.

Prior to the initiation of dose administration, samples for homogeneity determination were collected from the top, middle, and bottom strata of the 1 and 100 mg/mL dosing formulations; the middle stratum of these formulations were used for concentration determination. Samples were also collected from the middle stratum of the 10 mg/mL formulation and the vehicle control for concentration analyses prior to the initiation of dose administration. Samples for concentration analyses were collected from the middle stratum of each dosing formulation (including the vehicle formulation administered to the control group) from the formulations prepared for the last week of dose administration. All analyses were conducted by the Analytical Chemistry Department, WIL Research Laboratories, LLC. The methodology and results of these analyses are presented in Appendix C and the results are summarized in Section A of the Results and Discussion.

B. Test System

Sexually mature, virgin female Crl:CD(SD) rats from Charles River Laboratories, Inc., Raleigh, NC, were used as the test system on this study.

This species and strain of animal is recognized as appropriate for developmental toxicity studies. WIL Research Laboratories, LLC has historical control data on the background incidence of fetal malformations and developmental variations in the Crl:CD(SD) rat. This animal model has been proven to be susceptible to the effects of developmental toxicants.

C. Organization of Test Groups, Dosage Levels, and Treatment Regimen

The vehicle and test substance formulations were administered orally by gavage, via an appropriately sized flexible, Teflon®-shafted, stainless steel ball-tipped dosing cannula (Natume, Japan), once daily during gestation days 6-20. The dosage volume for all groups was 10 mL/kg. Individual dosages were based on the most recently recorded body weights to provide the correct mg/kg/day dose. All animals were dosed at approximately the same time each day.

The following table presents the study group assignment:

Group Number	Treatment	Dosage Level (mg/kg/day)	Dosage Volume (mL/kg)	Number of Females
1	Vehicle	0	10	22
2	H-28548	10	10	22
3	H-28548	100	10	22
4	H-28548	1000	10	22

Dosage levels were selected based on the results of previous studies and were provided by the Sponsor after consultation with the Study Director.

The selected route of administration for this study was oral (gavage) because this is a potential route of exposure for humans. The number of animals selected for this study was based on the U.S. EPA Health Effects Test Guidelines OPPTS 870.3700 and the OECD Guidelines for Testing Chemicals Guideline 414.

D. Animal Receipt and Acclimation

One hundred ten sexually mature, virgin female Crl:CD(SD) rats were received in good health from Charles River Laboratories, Inc., Raleigh, NC, on 13 October 2009. The animals were approximately 70 days old upon receipt. Each female was examined by a qualified biologist. The day following receipt, all animals were weighed and clinical observations were recorded. Each rat was uniquely identified by a Monel® metal ear tag displaying the animal number and housed for 14 days for acclimation purposes. During the acclimation period, the rats were observed twice daily for mortality and changes in general appearance and behavior. Body weights were recorded prior to the initiation of breeding.

E. Animal Housing

Upon arrival and until pairing, all rats were individually housed (except during mating) in solid bottom cages (plastic maternity cages) containing ground corncob nesting material (Bed-O'Cobs; The Andersons, Cob Products Division, Maumee, OH). The rats were paired for mating in the home cage of the male (stainless steel wire-mesh cages suspended above cage-board). Following positive evidence of mating, the females were returned to individual plastic maternity cages. Animals were maintained in accordance with the *Guide for the Care and Use of Laboratory Animals* (National Research Council, 1996). The animal facilities at WIL Research Laboratories, LLC are fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC International). All animals were offered Nestlets™ that were replaced as needed.

F. Diet, Drinking Water and Maintenance

The basal diet used in this study, PMI Nutrition International, LLC Certified Rodent LabDiet® 5002, is a certified feed with appropriate analyses performed by the manufacturer and provided to WIL Research Laboratories, LLC. Feed lots used during the study are documented in the study records. The feeders were changed and sanitized once per week. Municipal water supplying the facility is regularly sampled for contaminants according to standard operating procedures. The results of the diet and water analyses are maintained at WIL Research Laboratories, LLC. No contaminants were present in animal feed or water at concentrations sufficient to interfere with the objectives of this study. Reverse osmosis-purified (on-site) drinking water, delivered by an automatic watering system, and the basal diet were provided ad libitum throughout the acclimation period and during the study.

G. Environmental Conditions

All rats were housed throughout the acclimation period and during the study in an environmentally controlled room. The room temperature and humidity controls were set to maintain environmental conditions of 71°F ± 5°F (22°C ± 3°C) and 50% ± 20% relative humidity. Room temperature and relative humidity were controlled and monitored using the Metasys® DDC Electronic Environmental control system. These data were recorded approximately hourly and are summarized in Appendix D. Actual mean daily temperature ranged from 70.4°F to 71.6°F (21.3°C to 22.0°C) and mean daily relative humidity ranged from 43.5% to 51.1% during the study. Light timers were calibrated to provide a 12-hour light (0600 hours to 1800 hours)/12-hour dark photoperiod. Air handling units were set to provide a minimum of 10 fresh air changes per hour.

H. Assignment of Animals to Treatment Groups

At the conclusion of the acclimation period, all available females were weighed and examined in detail for physical abnormalities. At the discretion of the Study Director, each animal judged to be in good health and meeting acceptable body weight requirements (a minimum of 220 g) was placed in a suspended wire-mesh cage with a resident male from the same strain and source for breeding. Resident males were untreated, sexually mature rats utilized exclusively for breeding. These rats were maintained under similar laboratory conditions as the females. A breeding

record containing the male and female identification numbers and the dates of cohabitation was prepared. The selected females were approximately 12 weeks old when paired for breeding.

Positive evidence of mating was confirmed by the presence of a vaginal copulatory plug or the presence of sperm in a vaginal lavage and verified by a second biologist. Each mating pair was examined daily. The day on which evidence of mating was identified was termed gestation day 0 and the animals were separated.

The experimental design for WIL-189223 consisted of 3 test substance-treated groups and 1 control group, composed of 22 rats per group. The bred females were assigned to groups using a WIL Toxicology Data Management System (WTDMS™) computer program which randomized the animals based on stratification of the gestation day 0 body weights in a block design. Body weight values ranged from 228 g to 285 g on gestation day 0.

PARAMETERS EVALUATED

A. Clinical Observations and Mortality

All rats were observed twice daily, once in the morning and once in the afternoon, for moribundity and mortality. Individual clinical observations were recorded from gestation days 0 through 21 (prior to dose administration during the treatment period). Animals were also observed for signs of toxicity approximately 1-2 hours following dose administration. The absence or presence of findings was recorded for individual animals. In addition, the presence of findings at the time of dose administration was recorded for individual animals.

B. Body Weights and Gravid Uterine Weights

Individual maternal body weights were recorded on gestation days 0 and 6-21 (daily). Group mean body weights were calculated for each of these days. Mean body weight changes were calculated for each corresponding interval and also for gestation days 6-9, 9-12, 12-18, 18-21, and 6-21. When body weights could not be determined for an animal during a given interval (due to an unscheduled death, weighing error, etc.), group mean values were calculated for that interval using the available data. The time periods when body weight values were unavailable for a given animal were designated as "NA" (Not Applicable) on the individual report tables. Body weights were not recorded on gestation day 21 for females that initiated delivery prior to body weight collection (4 and 7 females in the 100 and 1000 mg/kg/day groups, respectively).

With the exception of females that delivered, gravid uterine weight was collected and net body weight (the gestation day 21 body weight exclusive of the weight of the uterus and contents) and net body weight change (the gestation day 0-21 body weight change exclusive of the weight of the uterus and contents) were calculated and presented for each gravid female at the scheduled laparohysterectomy.

C. Food Consumption

Individual food consumption was recorded on gestation days 0 and 6-21 (daily). Food intake was reported as g/animal/day and g/kg/day for the corresponding body weight change intervals. When food consumption could not be determined for an animal during a given interval (due to an unscheduled death, weighing error, food spillage, obvious erroneous value, etc.), group mean values were calculated for that interval using the available data. The time periods when food consumption values were unavailable for a given animal were designated as "NA" (Not Applicable) on the individual report tables.

D. Anatomic Pathology and Laparohysterectomy

A gross necropsy was performed on the female that died during the course of the study. The kidneys and liver were retained in 10% neutral-buffered formalin for histopathologic examination. The number and location of implantation sites, corpora lutea, and viable fetuses were recorded. Recognizable fetuses were examined externally and preserved in 10% neutral-buffered formalin. The carcass of the female was discarded.

Laparohysterectomies and macroscopic examinations were performed blind to treatment group. All surviving females (including females that delivered) were euthanized by carbon dioxide inhalation on gestation day 21. The thoracic, abdominal, and pelvic cavities were opened by a ventral mid-line incision, and the contents were examined. In all instances, the postmortem findings were correlated with the antemortem comments, and any abnormalities were recorded. The uterus and ovaries were then exposed and excised. The number of corpora lutea on each ovary was recorded. The trimmed uterus was weighed (except for females that delivered) and opened, and the number and location of all fetuses, early and late resorptions, and the total number of implantation sites were recorded. The placentae were also examined. The individual uterine distribution of implantation sites was documented using the following procedure. All implantation sites, including resorptions, were numbered in consecutive order beginning with the left distal to the left proximal uterine horn, noting the position of the cervix, and continuing from the right proximal to the right distal uterine horn.

Uteri with no macroscopic evidence of implantation were opened and subsequently placed in 10% ammonium sulfide solution for detection of early implantation loss (Salewski, 1964).

The kidneys (weighed paired) and liver were weighed from each female at the scheduled laparohysterectomy. The kidneys, liver, and other maternal tissues (only as indicated by the gross findings) were preserved in 10% neutral-buffered formalin for histopathologic examination. Representative sections of corresponding organs from a sufficient number of control animals were retained for comparison. The carcass of each female was then discarded.

Microscopic examination was performed on the kidneys and livers from all females. After fixation, protocol specified tissues were trimmed according to WIL SOPs and the protocol. Trimmed tissues were processed into paraffin blocks, sectioned at 4 to 8 microns, mounted on glass microscope slides, and stained with hematoxylin and eosin. Slides were shipped to the Sponsor to forward to the Principal Investigator, Steven R. Frame, D.V.M., Ph.D., D.A.C.V.P., Stine-Haskell Research Center, for microscopic examination. The pathology report is presented in Appendix E. The date of necropsy noted on the individual pathology report tables refers to the date of microscopic examination.

Intrauterine data were summarized using 2 methods of calculation. An example of each method of calculation follows:

1. Group Mean Litter Basis:

$$\text{Postimplantation Loss/Litter} = \frac{\text{No. Dead Fetuses, Resorptions (Early/Late)/Group}}{\text{No. Gravid Females/Group}}$$

2. Proportional Litter Basis:

$$\text{Summation Per Group (\%)} = \frac{\text{Sum of Postimplantation Loss/Litter (\%)}}{\text{No. Litters/Group}}$$

Where:

$$\text{Postimplantation Loss/Litter (\%)} = \frac{\text{No. Dead Fetuses, Resorptions (Early/Late)/Litter}}{\text{No. Implantation Sites/Litter}} \times 100$$

E. Fetal Morphological Evaluation

Fetal examinations were performed blind to treatment group. Each viable fetus was examined externally, individually sexed, weighed, euthanized by hypothermia followed by an intrathoracic injection of sodium pentobarbital (if necessary), and tagged for identification. Findings for delivered pups are included on the fetal tables. Fetal tags contained the WIL study number, the female number, and the fetus number. The detailed external examination of each fetus included, but was not limited to, an examination of the eyes, palate, and external orifices, and each finding was recorded. Crown-rump measurements and degrees of autolysis were recorded for late resorptions, a gross external examination was performed (if possible), and the tissues were discarded.

Each viable fetus was subjected to a visceral examination using a modification of the Stuckhardt and Poppe fresh dissection technique to include the heart and major blood vessels (Stuckhardt and Poppe, 1984). The sex of each fetus was confirmed by internal examination. Fetal kidneys were examined and graded for renal papillae development (Woo and Hoar, 1972). Heads from approximately one-half of the fetuses in each litter were placed in Bouin's fixative for subsequent soft tissue examination by the Wilson sectioning technique (Wilson, 1965). The heads from the remaining one-half of the fetuses were examined by a mid-coronal slice. All carcasses were eviscerated and fixed in 100% ethyl alcohol.

Following fixation in alcohol, each fetus was macerated in potassium hydroxide and stained with Alizarin Red S (Dawson, 1926). External, visceral, and skeletal findings were recorded as developmental variations (alterations in anatomic structure that are considered to have no

significant biological effect on animal health or body conformity and/or occur at high incidence, representing slight deviations from normal) or malformations (those structural anomalies that alter general body conformity, disrupt or interfere with normal body function, or may be incompatible with life).

The fetal developmental findings were summarized by: 1) presenting the incidence of a given finding both as the number of fetuses and the number of litters available for examination in the group; and 2) considering the litter as the basic unit for comparison and calculating the number of affected fetuses in a litter on a proportional basis as follows:

$$\text{Summation per Group (\%)} = \frac{\text{Sum of Viable Fetuses Affected/Litter (\%)}}{\text{No. Litters/Group}}$$

Where:

$$\text{Viable Fetuses Affected/Litter (\%)} = \frac{\text{No. Viable Fetuses Affected/Litter}}{\text{No. Viable Fetuses/Litter}} \times 100$$

F. Statistical Methods

All statistical tests were performed using appropriate computing devices or programs. Analyses were conducted using two-tailed tests (except as noted otherwise) for minimum significance levels of 1% and 5%, comparing each test substance-treated group to the control group. Each mean was presented with the standard deviation (S.D.), standard error (S.E.), and the number of animals (N) used to calculate the mean. Data obtained from nongravid animals were excluded from statistical analyses. Due to the different rounding conventions inherent in the types of software used, the means, standard deviations, and standard errors on the summary and individual tables may differ by ±1 in the last significant figure. Where applicable, the litter was used as the experimental unit.

Mean maternal body weights (absolute and net), body weight changes (absolute and net), food consumption, gravid uterine weights, organ weights, numbers of corpora lutea, implantation sites, and viable fetuses, and fetal body weights (separately by sex and combined) were subjected to a parametric one-way analysis of variance (ANOVA) (Snedecor and Cochran, 1980) to determine intergroup differences between the control and test substance-treated groups. If the ANOVA revealed significant ($p<0.05$) intergroup variance, Dunnett's test (Dunnett, 1964) was used to compare the test substance-treated groups to the control group. Mean litter proportions (percent per litter) of prenatal data (viable and nonviable fetuses, early and late resorptions, total resorptions, pre- and postimplantation loss, and fetal sex distribution), total fetal malformations and developmental variations (external, visceral, skeletal, and combined) and each particular external, visceral, and skeletal malformation or variation were subjected to the Kruskal-Wallis nonparametric ANOVA test (Kruskal and Wallis, 1952) to determine intergroup differences between the control and test substance-treated groups. If the ANOVA revealed significant ($p<0.05$) intergroup variance, Dunn’s test (Dunn, 1964) was used to compare the test substance-treated groups to the control group.

G. Data Retention

The Sponsor has title to all documentation records, raw data, specimens, or other work product generated during the performance of the study. Any remaining formulations samples will be discarded upon issuance of the final report. All work product generated by WIL Research Laboratories, LLC, including raw paper data, skeletal specimens, and blocks, are retained in the Archives at WIL Research Laboratories, LLC as specified in the study protocol. The Sponsor is responsible for archiving the raw data, slides, and tissues associated with the conduct of the pathology examination.

Reserve samples of the test substance, pertinent electronic storage media, and the original final report are retained in the Archives at WIL Research Laboratories, LLC in compliance with regulatory requirements.

RESULTS AND DISCUSSION

A. Analytical Chemistry

Analytical Chemistry Report: Appendix C

The analyzed dosing formulations were within the WIL SOP range for suspensions (85% to 115%) and were homogeneous. Based on these results, the protocol-specified dosages of test article were administered to the animals. The test article was not detected in the vehicle formulation that was administered to the control group (Group 1).

Text Table 1. Results of Homogeneity Analyses

Homogeneity Assessment of the 29 October 2009 Dosing Formulations		
	Group 2 (1 mg/mL)	Group 4 (100 mg/mL)
Mean Concentration (mg/mL)	0.866	86.8
SD	0.025	0.81
RSD (%)	2.9	0.94
Mean % of Target	86.6	86.8

Text Table 2. Results of Concentration Analyses

	Mean Concentration, mg/mL (% of Target)		
Date of Preparation	Group 2 (1 mg/mL)	Group 3 (10 mg/mL)	Group 4 (100 mg/mL)
29 October 2009	0.883 (88.3)	8.64 (86.4)	86.2 (86.2)
12 November 2009	1.04 (104)	10.1 (101)	96.5 (96.5)

B. Clinical Observations and Mortality

Summary Data: Table 1, Table 2, Table 3
Individual Data: Table A1, Table A2, Table A3

Female no. 57328 in the 1000 mg/kg/day group was found dead on gestation day 20. Prior to death, this female had yellow material on various body surfaces at the daily examinations and 1-2 hours following dose administration beginning as early as gestation day 11. Salivation and/or evidence of salivation (clear material around the mouth) were also noted for this female 1-2 hours following dose administration beginning on gestation day 12. This female gained only 36 g during gestation days 12-18 compared to a mean of 62 g in the control group; lower

mean food consumption (11-17 g/animal/day) was observed for this female during gestation days 15-19. The test substance-related liver and kidney changes noted in Section G were considered the cause of death in this animal.

All other females survived to the scheduled necropsy on gestation day 21. However, 4 females in the 100 mg/kg/day group and 9 females in the 1000 mg/kg/day group delivered early in the morning on gestation day 21. Although rats often deliver on gestation day 21, the majority of these females had delivered in the morning (before 9:00 a.m.) before being sent to necropsy. No females (of 382 gravid) in the 17 datasets of the WIL developmental historical control data for gestation day 21 rats delivered prior to laparohysterectomy. Therefore, the early deliveries in the 100 and 1000 mg/kg/day groups were considered test substance-related. Test substance-related clinical findings noted for females (including those that delivered early) in the 1000 mg/kg/day group, consisted of yellow material on various body surfaces at the daily examinations and 1-2 hours following dose administration beginning as early as gestation day 8. Salivation and/or evidence thereof (clear material around the mouth) were also observed in the 1000 mg/kg/day group females prior to and/or 1-2 hours following dose administration beginning on gestation day 12.

Other clinical findings noted in the test substance-treated groups, including hair loss on the forelimbs and clear or red material around the nose, occurred infrequently, similarly in the control group, and/or were not observed in a dose-related manner. In addition, female no. 57316 that delivered early had a mass on the right forelimb, first observed on gestation day 14. No relationship to the test substance was evident.

C. Maternal Body Weights and Gravid Uterine Weights

Summary Data: Table 4, Table 5, Table 6
Individual Data: Table A4, Table A5, Table A6

A significant ($p<0.01$), mean maternal body weight loss (5 g) was observed in the 1000 mg/kg/day group females during gestation days 6-7, resulting in a significantly ($p<0.01$) lower mean body weight gain during gestation days 6-9 compared to the control group. This decrement in mean body weight gain was considered test substance-related. Mean body weight gain in this group was similar to that in the control group during gestation days 9-12 and 12-18. A significantly ($p<0.01$) lower mean body weight gain was noted in the 1000 mg/kg/day group females during gestation days 18-21. The lower mean body weight gain noted in these females late in gestation was attributed to the test substance-related lower mean fetal weights (see Section G). The decrements in mean body weight gain in the 1000 mg/kg/day group resulted in lower mean body weight gain when the entire treatment period (gestation days 6-21) was evaluated and lower mean body weights compared to the control group on gestation days 20 and 21; the differences were significant ($p<0.05$ or $p<0.01$). Mean gravid uterine weight in the 1000 mg/kg/day group was significantly ($p<0.01$) lower than the control group as a result of the test substance-related lower mean fetal weights observed in this group (see Section G). Mean net body weight and net body weight gain in the 1000 mg/kg/day group were similar to the control group values.

Mean gravid uterine weight in the 100 mg/kg/day group was significantly ($p<0.05$) lower than the control group value due to the test substance-related lower mean fetal weights observed in this group (see Section G). Mean body weights, body weight gains, net body weights and net body weight gains in the 10 and 100 mg/kg/day groups were similar to the control group. Mean gravid uterine weight in the 10 mg/kg/day group was similar to the control group value.

D. Food Consumption

Summary Data: Table 7, Table 8
Individual Data: Table A7, Table A8

Test substance-related, significantly ($p<0.05$ or $p<0.01$) lower mean food consumption, evaluated as g/animal/day and g/kg/day, was noted in the 1000 mg/kg/day group females compared to the control group during gestation days 6-9 and 9-12 and also 12-13 (g/animal/day only). Mean food consumption in the 1000 mg/kg/day group was similar to that in the control group for the gestation days 12-18 and 18-21 intervals. Significantly ($p<0.05$ or $p<0.01$) lower mean food consumption was observed in this group during gestation days 20-21 and when the entire treatment period (gestation days 6-21) was evaluated compared to the control group. The lower mean food consumption in the 1000 mg/kg/day group during gestation days 6-9, 20-21, and 6-21 corresponded to decrements in mean body weight gain. No correspondingly lower mean body weight gain was noted during gestation days 9-13 in this group.

No test substance-related effects on mean food consumption were observed in the 10 and 100 mg/kg/day groups. Differences from the control group were slight and not statistically significant.

E. Maternal Necropsy Data

Summary Data: Table 9
Individual Data: Table A9
Historical Control Data: Appendix F

Female no. 57328 in the 1000 mg/kg/day group was found dead on gestation day 20. At necropsy, this female had a pale liver, as well as 17 dead fetuses and 3 late resorptions in utero. Four and 9 females in the 100 and 1000 mg/kg/day groups, respectively, delivered early on gestation day 21. The death in the 1000 mg/kg/day group and the early deliveries in the 100 and 1000 mg/kg/day groups were considered test substance-related. Of the 1000 mg/kg/day group females that delivered early, female no. 57316 had a mass in the mammary gland (corresponding to the mass noted on the right forelimb at the daily examinations), dark red contents in the stomach, and an edematous pancreas, female no. 57359 had pale kidneys, and female no. 57382 had an edematous pancreas. The relationship of edematous pancreas to the test substance is uncertain. Of the 100 mg/kg/day group females that delivered early, female nos. 57354, 57357, and 57372 had dark red contents in the stomach. In addition, female no. 57357 had dark red contents in the jejunum, and female no. 57354 had a white area in the liver. The findings of red contents in the gastrointestinal tract and pale organs are not uncommon for females that deliver; no relationship to the test substance was evident.

The only internal findings noted at the schedule laparohysterectomy were depressed areas in the kidneys for female no. 57317 in the 10 mg/kg/day group and a white area in the liver for female no. 57409 in the 1000 mg/kg/day group. One female in each of the 10 and 100 mg/kg/day groups was nongravid.

F. Organ Weights

Summary Data: Table 10
Individual Data: Table A10

Test substance-related higher mean liver and kidney weights were noted in the 1000 mg/kg/day group, and a higher mean liver weight was noted in the 100 mg/kg/day group. The differences from the control group were significant ($p<0.01$). Mean liver weight in the 10 mg/kg/day group and mean kidney weights in the 10 and 100 mg/kg/day group were similar to the control group values.

G. Microscopic Evaluation

Pathology Report: Appendix E

There were no test substance-related microscopic findings in dams administered 10 mg/kg/day of the test material.

In the 1000 mg/kg/day female found dead on gestation day 20 (animal no. 57328), test substance-related microscopic changes were present in the liver and kidney. In the liver, moderate coagulative necrosis was present. Necrosis was multifocal in 1 lobe and locally extensive and coalescing in the other lobe. In the kidney, fibrin thrombi consistent with disseminated intravascular coagulation were observed in glomerular capillaries. Although microscopic examination of kidney was complicated by *post mortem* autolysis, the glomerular changes were considered to represent *ante mortem* findings. The test substance-related liver and kidney changes were considered the cause of death in this animal.

Test substance-related microscopic findings were present in the liver of dams administered 100 or 1000 mg/kg/day. Focal necrosis of the liver occurred in 2/22 and 5/22 dams in the 100 and 1000 mg/kg/day group, respectively. This finding was not observed in any animals in the control or 10 mg/kg/day group. Necrosis was graded as minimal in all but the early death dam in the 1000 mg/kg/day group and was usually characterized by 1 or 2 circumscribed foci of coagulative liver necrosis. While focal liver necrosis may occur in control animals, the finding in the 100 and 1000 mg/kg/day dams was considered to be related to administration of the test material based upon the dose-response. Hepatocellular hypertrophy was present in 19/22 dams in the 1000 mg/kg/day group but was not observed in any animals in the other treated groups or in controls. Hypertrophy was graded as minimal in all but one animal (where it was graded as mild) and was primarily characterized by increased hepatocyte cytoplasm which contained fine eosinophilic granules. These changes are consistent with PPARα agonism, and results of previous studies demonstrated that the test substance is a PPARα agonist.

There were no test substance-related microscopic changes in the kidneys at any of the dose levels tested. All microscopic changes in the kidneys were consistent with background changes commonly observed in rats of this strain.

H. Gestation Day 21 Laparohysterectomy Data

Summary Data: Table 11, Table 12
Individual Data: Table A11, Table A12, Table A13
Historical Control Data: Appendix F

Mean fetal weights were 8.8% and 28.1% lower in the 100 and 1000 mg/kg/day groups, respectively, when compared to the control group; the differences were significant ($p<0.01$). The lower mean fetal weights in these groups were attributed to the test substance. There were no effects on intrauterine survival in the 100 and 1000 mg/kg/day groups; parameters included postimplantation loss and viable fetuses.

A significantly ($p<0.05$) lower mean litter proportion of males (46.8% per litter) and subsequent higher mean litter proportion of females (53.2% per litter) was noted in the 1000 mg/kg/day group compared to the concurrent control group (55.0% and 45.0% per litter, respectively). However, the 1000 mg/kg/day group was skewed toward females, and the control group was also skewed toward males. The range of the percentage of males in the WIL historical control data is 42.1% to 54.3% per litter (45.7% to 57.9% per litter for females). The values for the 1000 mg/kg/day group were within the WIL historical control data ranges. Therefore, the differences in sex ratio were not considered test substance-related. Fetal sex ratio in the 100 mg/kg/day group was not significantly different from the control group.

Intrauterine growth and survival in the 10 mg/kg/day group was unaffected by test substance administration. Mean numbers of corpora lutea and implantation sites and the mean litter proportion of pre-implantation loss were similar across groups.

I. Fetal Morphological Data

Summary Data: Table 13, Table 14, Table 15, Table 16
Individual Data: Table A14
Historical Control Data: Appendix F

The numbers of fetuses (litters) available for morphological evaluation were 340(22), 324(21), 316(21), and 329(21) in the control, 10, 100, and 1000 mg/kg/day groups, respectively. Malformations were observed in 2 fetuses from 2 litters in the 10 mg/kg/day group. Because there were no malformations in the 100 and 1000 mg/kg/day groups, the malformations in the 10 mg/kg/day group were not considered test substance-related.

1. External Malformations and Variations

There were no external malformations or developmental variations observed in fetuses at any dosage level.

2. Visceral Malformations and Variations

Fetus no. 57307-14 in the 10 mg/kg/day group had a right-sided aorta (the aortic arch and descending aorta coursed to the right of the vertebral column, the right carotid and subclavian arteries arose independently from the aortic arch [no brachiocephalic trunk], and the left carotid and subclavian arteries arose from the aortic arch via a common vessel), persistent truncus arteriosus (the pulmonary arteries arose from the ascending aorta, the right pulmonary artery coursed retroesophageal, and an interventricular septal defect consisting of an opening in the anterior portion of the septum), and situs inversus (lateral transposition of the thoracic and abdominal organs). This fetus also had developmental variations of small lungs and a misshapen heart. These findings were not attributed to the test substance because no visceral malformations were observed at 10 or 1000 mg/kg/day. No other soft tissue malformations were noted at any dosage level.

No test substance-related developmental visceral variations were observed. Findings consisting of hemorrhagic ring around the iris, distended ureter(s), major blood vessel variation (the right carotid and subclavian arteries arose independently from the aortic arch; no brachiocephalic trunk), and accessory lobule of the liver were noted in single fetuses, did not occur in a dose-related manner, and/or were observed similarly in the control group.

Findings not recorded as malformations or developmental variations consisted of renal papilla(e) not fully developed (Woo and Hoar grade 1), noted in 4(3), 1(1), and 5(3) fetuses (litters) in the control, 10, and 1000 mg/kg/day groups, respectively, and a dark red area in the liver of 1 fetus in the control group. No relationship to the test substance was evident.

3. Skeletal Malformations and Variations

Fetus no. 57319-04 in the 10 mg/kg/day group had severely malaligned sternebrae. This finding was not attributed to the test substance because no skeletal malformations were observed at 100 or 1000 mg/kg/day. No other skeletal malformations were noted at any dosage level.

A higher mean litter proportion of 14^{th} rudimentary ribs (not statistically significant) was noted in the 1000 mg/kg/day group and was considered test substance-related. The higher mean litter proportion of this finding resulted in a significantly ($p<0.05$) higher mean litter proportion of skeletal variations and total variations. However, it has been suggested that 14^{th} rudimentary ribs resorb during the postnatal period (Holson et al., 2006; Wickramaratne, 1988); therefore, this finding was not considered to be adverse. No test substance-related skeletal developmental variations were observed in the 10 and 100 mg/kg/day groups.

4. Summary of External, Visceral, and Skeletal Examinations

The numbers of fetuses (litters) available for morphological evaluation were 340(22), 324(21), 316(21), and 329(21) in the control, 10, 100, and 1000 mg/kg/day groups, respectively. Malformations were observed in 2 fetuses from 2 litters in the 10 mg/kg/day group. Because there were no malformations in the 100 and 1000 mg/kg/day groups, the malformations in the 10 mg/kg/day group were not considered test substance-related. When the total malformations were evaluated on a proportional basis, no statistically significant differences from the control

group were noted. Fetal malformations, when observed in the test article-treated groups, occurred infrequently or at a frequency similar to that in the control group, did not occur in a dose-related manner, and/or were within the WIL historical control data ranges. Based on these data, no fetal malformations were attributed to the test substance.

Significantly higher mean litter proportions of skeletal developmental variations and total variations were observed in the 1000 mg/kg/day group because of a higher mean litter proportion (not statistically significant) of 14th rudimentary ribs. This finding was considered test substance-related, but not adverse because it has been suggested that these ribs are resorbed during the postnatal period (Holson et al., 2006; Wickramaratne, 1988). No test substance-related developmental variations were observed in the 10 and 100 mg/kg/day groups.

CONCLUSIONS

The no-observed-adverse-effect level (NOAEL) for maternal and developmental toxicity was considered to be 10 mg/kg/day based on mortality and lower mean body weight gains and food consumption at 1000 mg/kg/day and early deliveries, microscopic findings in the liver (focal necrosis), and lower mean fetal weights at 100 and 1000 mg/kg/day. At 1000 mg/kg/day, there were additional test substance-related effects that were not considered adverse and consisted of higher kidney and liver weights and hepatocellular hypertrophy.

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TABLES 1-16

TABLE 1

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT SUMMARY OF MATERNAL SURVIVAL AND PREGNANCY STATUS
SPONSOR NO.:18405-841

DOSE GROUP :	1		2		3		4	
	NO.	%	NO.	%	NO.	%	NO.	%
FEMALES ON STUDY	22		22		22		22	
FEMALES THAT ABORTED OR DELIVERED	0	0.0	0	0.0	0	0.0	0	0.0
FEMALES THAT DIED	0	0.0	0	0.0	0	0.0	1	4.5
FEMALES THAT ABORTED	0	0.0	0	0.0	0	0.0	0	0.0
NONGRAVID	0	0.0	0	0.0	0	0.0	0	0.0
GRAVID	0	0.0	0	0.0	0	0.0	1	100.0
FEMALES THAT WERE EUTHANIZED	0	0.0	0	0.0	0	0.0	0	0.0
NONGRAVID	0	0.0	0	0.0	0	0.0	0	0.0
GRAVID	0	0.0	0	0.0	0	0.0	0	0.0
FEMALES EXAMINED AT SCHEDULED NECROPSY	22	100.0	22	100.0	22	100.0-A	21	95.5-B
NONGRAVID	0	0.0	1	4.5	1	4.5	0	0.0
GRAVID	22	100.0	21	95.5	21	95.5	21	100.0
WITH RESORPTIONS ONLY	0	0.0	0	0.0	0	0.0	0	0.0
WITH VIABLE FETUSES	22	100.0	21	100.0	21	100.0	21	100.0
TOTAL FEMALES GRAVID	22	100.0	21	95.5	21	95.5	22	100.0

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY
A = INCLUDES 4 FEMALES THAT DELIVERED ON GESTATION DAY 21
B = INCLUDES 9 FEMALES THAT DELIVERED ON GESTATION DAY 21

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TABLE 2 (DAILY EXAMINATIONS)

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS
SPONSOR NO.:18405-841

----- F E M A L E -----

TABLE RANGE:	10-27-09 TO 11-22-09			
GROUP:	1	2	3	4
NORMAL				
-NO SIGNIFICANT CLINICAL OBSERVATIONS	478/22	478/22	475/22	445/22
DISPOSITION				
-SCHEDULED EUTHANASIA; GESTATION DAY 21	22/22	22/22	18/18	12/12
-DELIVERED; SENT TO NECROPSY	0/ 0	0/ 0	4/ 4	9/ 9
-FOUND DEAD	0/ 0	0/ 0	0/ 0	1/ 1
BODY/INTEGUMENT				
-SCABBING DORSAL THORACIC AREA	1/ 1	1/ 1	0/ 0	0/ 0
-WET YELLOW MATERIAL VENTRAL ABDOMINAL AREA	0/ 0	0/ 0	1/ 1	7/ 6
-WET YELLOW MATERIAL UROGENITAL AREA	0/ 0	0/ 0	1/ 1	7/ 6
-WET YELLOW MATERIAL ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	3/ 3
-WET YELLOW MATERIAL VENTRAL THORACIC AREA	0/ 0	0/ 0	0/ 0	1/ 1
-DRIED YELLOW MATERIAL VENTRAL ABDOMINAL AREA	0/ 0	0/ 0	0/ 0	6/ 3
-DRIED YELLOW MATERIAL UROGENITAL AREA	0/ 0	0/ 0	0/ 0	4/ 3
-HARD MOVABLE MASS RIGHT FORELIMB 20mm x 15mm x 10mm	0/ 0	0/ 0	0/ 0	4/ 1
-HAIR LOSS RIGHT FORELIMB	2/ 1	4/ 1	2/ 1	5/ 1

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY

TABLE 2 (DAILY EXAMINATIONS)

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 2
SPONSOR:E.I. DUPONT SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS
SPONSOR NO.:18405-841

----- F E M A L E -----

TABLE RANGE:	10-27-09 TO 11-22-09			
GROUP:	1	2	3	4
BODY/INTEGUMENT				
-HAIR LOSS LEFT FORELIMB	0/ 0	2/ 1	1/ 1	5/ 1
-HARD MOVABLE MASS RIGHT FORELIMB 26mm x 20mm x 10mm	0/ 0	0/ 0	0/ 0	3/ 1
EYES/EARS/NOSE				
-DRIED RED MATERIAL AROUND NOSE	3/ 3	0/ 0	1/ 1	1/ 1
EXCRETA				
-DECREASED DEFECATION	0/ 0	0/ 0	0/ 0	1/ 1
ORAL/DENTAL				
-DRIED RED MATERIAL AROUND MOUTH	0/ 0	1/ 1	0/ 0	0/ 0
-SALIVATION	0/ 0	0/ 0	0/ 0	1/ 1

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY

PCSUv4.07
12/16/2009

TABLE 3

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT SUMMARY OF POST-DOSE FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS
SPONSOR NO.:18405-841

----- F E M A L E -----

	TABLE RANGE: 11-02-09 TO 11-21-09 GROUP: 1	2	3	4
NORMAL				
1 - 2 HOUR POST DOSING				
-NO SIGNIFICANT CLINICAL OBSERVATIONS	330/22	328/22	328/22	265/22
BODY/INTEGUMENT				
1 - 2 HOUR POST DOSING				
-WET YELLOW MATERIAL VENTRAL ABDOMINAL AREA	0/0	0/0	1/1	18/10
-WET YELLOW MATERIAL UROGENITAL AREA	0/0	0/0	1/1	29/15
-WET YELLOW MATERIAL ANOGENITAL AREA	0/0	0/0	0/0	10/6
-WET YELLOW MATERIAL RIGHT HINDLIMB	0/0	0/0	1/1	8/7
-WET YELLOW MATERIAL LEFT HINDLIMB	0/0	0/0	1/1	8/7
-WET YELLOW MATERIAL VENTRAL THORACIC AREA	0/0	0/0	0/0	3/2
-WET YELLOW MATERIAL RIGHT INGUINAL AREA	0/0	0/0	0/0	5/5
-WET YELLOW MATERIAL LEFT INGUINAL AREA	0/0	0/0	0/0	5/4
-WET YELLOW MATERIAL RIGHT FORELIMB	0/0	0/0	0/0	2/1
-WET YELLOW MATERIAL LEFT FORELIMB	0/0	0/0	0/0	2/2
-WET RED MATERIAL UROGENITAL AREA	0/0	0/0	0/0	1/1
CARDIO-PULMONARY				
1 - 2 HOUR POST DOSING				
-RALES	0/0	0/0	0/0	1/1
EYES/EARS/NOSE				
1 - 2 HOUR POST DOSING				
-DRIED RED MATERIAL AROUND NOSE	0/0	2/2	1/1	1/1
-WET CLEAR MATERIAL AROUND NOSE	0/0	0/0	0/0	2/2

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY

TABLE 3

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 2
SPONSOR:E.I. DUPONT SUMMARY OF POST-DOSE FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS
SPONSOR NO.:18405-841

----- F E M A L E -----

TABLE RANGE: 11-02-09 TO 11-21-09 GROUP:	1	2	3	4
ORAL/DENTAL				
TIME OF DOSE				
-SALIVATION PRIOR TO DOSE	0/0	0/0	0/0	16/9
-WET CLEAR MATERIAL AROUND MOUTH	0/0	0/0	0/0	1/1
1 - 2 HOUR POST DOSING				
-DRIED RED MATERIAL AROUND MOUTH	0/0	0/0	0/0	2/2
-WET CLEAR MATERIAL AROUND MOUTH	0/0	0/0	0/0	32/13
-SALIVATION	0/0	0/0	0/0	10/8

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY

PPDTSUv1.46
12/03/2009

TABLE 4

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT SUMMARY OF BODY WEIGHTS DURING GESTATION [G]
SPONSOR NO.:18405-841

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	100 MG/KG/DAY	1000 MG/KG/DAY
DAY 0				
MEAN	254.	256.	252.	256.
% DIFFERENCE		0.8	-0.8	0.8
S.D.	13.8	13.9	13.5	14.1
S.E.	2.9	3.0	2.9	3.0
N	22	21	21	22
DAY 6				
MEAN	286.	287.	287.	288.
% DIFFERENCE		0.3	0.3	0.7
S.D.	18.2	13.6	12.8	15.2
S.E.	3.9	3.0	2.8	3.2
N	22	21	21	22
DAY 7				
MEAN	290.	291.	289.	283.
% DIFFERENCE		0.3	-0.3	-2.4
S.D.	18.2	12.8	14.5	14.9
S.E.	3.9	2.8	3.2	3.2
N	22	21	21	22
DAY 8				
MEAN	295.	294.	293.	286.
% DIFFERENCE		-0.3	-0.7	-3.1
S.D.	17.5	13.3	13.9	17.2
S.E.	3.7	2.9	3.0	3.7
N	22	21	21	22
DAY 9				
MEAN	299.	299.	298.	290.
% DIFFERENCE		0.0	-0.3	-3.0
S.D.	18.9	12.7	13.9	19.8
S.E.	4.0	2.8	3.0	4.2
N	22	21	21	22

None significantly different from control group
NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 4

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 2
SPONSOR:E.I. DUPONT SUMMARY OF BODY WEIGHTS DURING GESTATION [G]
SPONSOR NO.:18405-841

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	100 MG/KG/DAY	1000 MG/KG/DAY
DAY 10				
MEAN	304.	304.	304.	295.
% DIFFERENCE		0.0	0.0	-3.0
S.D.	19.1	14.0	15.0	17.4
S.E.	4.1	3.1	3.3	3.7
N	22	21	21	22
DAY 11				
MEAN	311.	310.	309.	302.
% DIFFERENCE		-0.3	-0.6	-2.9
S.D.	19.5	13.5	14.0	16.0
S.E.	4.2	2.9	3.0	3.4
N	22	21	21	22
DAY 12				
MEAN	314.	314.	312.	304.
% DIFFERENCE		0.0	-0.6	-3.2
S.D.	19.3	13.0	15.4	17.1
S.E.	4.1	2.8	3.4	3.7
N	22	21	21	22
DAY 13				
MEAN	319.	319.	316.	309.
% DIFFERENCE		0.0	-0.9	-3.1
S.D.	20.0	13.7	15.3	18.0
S.E.	4.3	3.0	3.3	3.8
N	22	21	21	22
DAY 14				
MEAN	326.	324.	322.	316.
% DIFFERENCE		-0.6	-1.2	-3.1
S.D.	21.2	13.5	16.3	17.9
S.E.	4.5	2.9	3.6	3.8
N	22	21	21	22

None significantly different from control group
NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 4

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 3

SPONSOR:E.I. DUPONT SUMMARY OF BODY WEIGHTS DURING GESTATION [G]

SPONSOR NO.:18405-841

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	100 MG/KG/DAY	1000 MG/KG/DAY
DAY 15				
MEAN	333.	333.	330.	324.
% DIFFERENCE		0.0	-0.9	-2.7
S.D.	21.2	14.3	15.7	18.1
S.E.	4.5	3.1	3.4	3.9
N	22	21	21	22
DAY 16				
MEAN	344.	343.	342.	335.
% DIFFERENCE		-0.3	-0.6	-2.6
S.D.	22.9	14.8	18.2	17.8
S.E.	4.9	3.2	4.0	3.8
N	22	21	21	22
DAY 17				
MEAN	359.	357.	357.	350.
% DIFFERENCE		-0.6	-0.6	-2.5
S.D.	24.5	14.6	18.3	18.4
S.E.	5.2	3.2	4.0	3.9
N	22	21	21	22
DAY 18				
MEAN	376.	374.	374.	367.
% DIFFERENCE		-0.5	-0.5	-2.4
S.D.	25.3	15.8	18.4	19.5
S.E.	5.4	3.5	4.0	4.2
N	22	21	21	22
DAY 19				
MEAN	392.	392.	392.	382.
% DIFFERENCE		0.0	0.0	-2.6
S.D.	26.5	16.8	18.7	19.7
S.E.	5.6	3.7	4.1	4.2
N	22	21	21	22

None significantly different from control group

NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 4

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 4
SPONSOR:E.I. DUPONT SUMMARY OF BODY WEIGHTS DURING GESTATION [G]
SPONSOR NO.:18405-841

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	100 MG/KG/DAY	1000 MG/KG/DAY
DAY 20				
MEAN	411.	409.	410.	392.*
% DIFFERENCE		-0.5	-0.2	-4.6
S.D.	28.6	17.3	20.7	20.3
S.E.	6.1	3.8	4.5	4.4
N	22	21	21	21
DAY 21				
MEAN	431.	428.	426.	395.**
% DIFFERENCE		-0.7	-1.2	-8.4
S.D.	31.6	19.0	19.0	22.3
S.E.	6.7	4.2	4.6	6.0
N	22	21	17	14

* = Significantly different from the control group at 0.05 using Dunnett's test
** = Significantly different from the control group at 0.01 using Dunnett's test
NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

PGBWSUv5.10
12/03/2009

TABLE 5

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT SUMMARY OF BODY WEIGHT CHANGES DURING GESTATION [G]
SPONSOR NO.:18405-841

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	100 MG/KG/DAY	1000 MG/KG/DAY
DAY 0- 6				
MEAN	32.	31.	35.	32.
S.D.	10.1	6.7	7.1	6.6
S.E.	2.1	1.5	1.5	1.4
N	22	21	21	22
DAY 6- 7				
MEAN	4.	4.	2.	-5.**
S.D.	3.4	3.7	4.2	7.1
S.E.	0.7	0.8	0.9	1.5
N	22	21	21	22
DAY 7- 8				
MEAN	6.	3.	4.	3.
S.D.	2.6	3.7	4.0	6.7
S.E.	0.6	0.8	0.9	1.4
N	22	21	21	22
DAY 8- 9				
MEAN	3.	4.	5.	3.
S.D.	3.5	3.2	3.9	4.9
S.E.	0.7	0.7	0.9	1.0
N	22	21	21	22
DAY 9- 10				
MEAN	6.	5.	6.	6.
S.D.	3.2	3.8	3.6	4.2
S.E.	0.7	0.8	0.8	0.9
N	22	21	21	22

** = Significantly different from the control group at 0.01 using Dunnett's test
MEAN DIFFERENCES CALCULATED FROM INDIVIDUAL DIFFERENCES
NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 5

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS
SPONSOR:E.I. DUPONT SUMMARY OF BODY WEIGHT CHANGES DURING GESTATION [G]
SPONSOR NO.:18405-841

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	100 MG/KG/DAY	1000 MG/KG/DAY
DAY 10- 11				
MEAN	7.	6.	6.	7.
S.D.	3.6	3.5	3.6	5.6
S.E.	0.8	0.8	0.8	1.2
N	22	21	21	22
DAY 11- 12				
MEAN	3.	4.	3.	2.
S.D.	3.5	3.3	3.8	6.0
S.E.	0.7	0.7	0.8	1.3
N	22	21	21	22
DAY 12- 13				
MEAN	5.	5.	4.	4.
S.D.	3.5	2.4	4.3	4.1
S.E.	0.7	0.5	0.9	0.9
N	22	21	21	22
DAY 13- 14				
MEAN	8.	5.	5.	8.
S.D.	4.4	3.5	3.9	3.1
S.E.	0.9	0.8	0.8	0.7
N	22	21	21	22
DAY 14- 15				
MEAN	7.	8.	8.	8.
S.D.	3.7	4.4	4.3	4.2
S.E.	0.8	1.0	0.9	0.9
N	22	21	21	22

None significantly different from control group
MEAN DIFFERENCES CALCULATED FROM INDIVIDUAL DIFFERENCES
NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 5

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 3
SPONSOR:E.I. DUPONT SUMMARY OF BODY WEIGHT CHANGES DURING GESTATION [G]
SPONSOR NO.:18405-841

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	100 MG/KG/DAY	1000 MG/KG/DAY
DAY 15- 16				
MEAN	11.	10.	12.	11.
S.D.	4.6	4.0	3.4	4.7
S.E.	1.0	0.9	0.7	1.0
N	22	21	21	22
DAY 16- 17				
MEAN	15.	14.	15.	15.
S.D.	4.4	3.7	4.5	5.0
S.E.	0.9	0.8	1.0	1.1
N	22	21	21	22
DAY 17- 18				
MEAN	17.	17.	17.	18.
S.D.	4.1	5.0	4.9	3.6
S.E.	0.9	1.1	1.1	0.8
N	22	21	21	22
DAY 18- 19				
MEAN	16.	17.	18.	15.
S.D.	4.3	4.8	4.9	5.1
S.E.	0.9	1.1	1.1	1.1
N	22	21	21	22
DAY 19- 20				
MEAN	18.	18.	18.	9.**
S.D.	3.5	3.7	4.1	5.5
S.E.	0.7	0.8	0.9	1.2
N	22	21	21	21

** = Significantly different from the control group at 0.01 using Dunnett's test
MEAN DIFFERENCES CALCULATED FROM INDIVIDUAL DIFFERENCES
NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 5

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 4
SPONSOR:E.I. DUPONT SUMMARY OF BODY WEIGHT CHANGES DURING GESTATION [G]
SPONSOR NO.:18405-841

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	100 MG/KG/DAY	1000 MG/KG/DAY
DAY 20- 21				
MEAN	20.	19.	17.	4.**
S.D.	6.0	5.2	6.2	9.8
S.E.	1.3	1.1	1.5	2.6
N	22	21	17	14
DAY 6- 9				
MEAN	13.	12.	11.	2.**
S.D.	4.8	4.2	4.5	13.4
S.E.	1.0	0.9	1.0	2.9
N	22	21	21	22
DAY 9- 12				
MEAN	15.	16.	14.	15.
S.D.	3.8	4.2	5.5	10.2
S.E.	0.8	0.9	1.2	2.2
N	22	21	21	22
DAY 12- 18				
MEAN	62.	60.	62.	63.
S.D.	8.6	9.8	11.5	11.5
S.E.	1.8	2.1	2.5	2.4
N	22	21	21	22
DAY 18- 21				
MEAN	55.	54.	53.	29.**
S.D.	9.5	7.8	7.6	10.9
S.E.	2.0	1.7	1.8	2.9
N	22	21	17	14

** = Significantly different from the control group at 0.01 using Dunnett's test
MEAN DIFFERENCES CALCULATED FROM INDIVIDUAL DIFFERENCES
NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 5

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 5
SPONSOR:E.I. DUPONT SUMMARY OF BODY WEIGHT CHANGES DURING GESTATION [G]
SPONSOR NO.:18405-841

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	100 MG/KG/DAY	1000 MG/KG/DAY
DAY 6- 21				
MEAN	145.	141.	139.	109.**
S.D.	18.4	13.1	13.9	17.7
S.E.	3.9	2.9	3.4	4.7
N	22	21	17	14

** = Significantly different from the control group at 0.01 using Dunnett's test
MEAN DIFFERENCES CALCULATED FROM INDIVIDUAL DIFFERENCES
NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

PGBWSUv5.10
12/03/2009

TABLE 6

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT SUMMARY OF GRAVID UTERINE WTS. AND NET BODY WT. CHANGES [G]
SPONSOR NO.:18405-841

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	100 MG/KG/DAY	1000 MG/KG/DAY
INITIAL BODY WT.				
MEAN	254.	256.	250.	254.
S.D.	13.8	13.9	13.2	11.4
S.E.	2.9	3.0	3.2	3.1
N	22	21	17	14
TERMINAL BODY WT.				
MEAN	431.	428.	426.	395.**
S.D.	31.6	19.0	19.0	22.3
S.E.	6.7	4.2	4.6	6.0
N	22	21	17	14
GRAVID UTERINE WT.				
MEAN	116.3	114.7	104.4*	87.1**
S.D.	20.22	9.22	13.30	6.60
S.E.	4.31	2.01	3.23	1.90
N	22	21	17	12-A
NET BODY WT.				
MEAN	314.2	313.5	321.2	308.9
S.D.	23.38	15.71	19.93	20.51
S.E.	4.98	3.43	4.83	5.92
N	22	21	17	12-A
NET BODY WT. CHANGE				
MEAN	60.3	57.8	70.7	52.3
S.D.	16.82	10.79	13.54	15.14
S.E.	3.59	2.35	3.28	4.37
N	22	21	17	12-A

* = Significantly different from the control group at 0.05 using Dunnett's test
** = Significantly different from the control group at 0.01 using Dunnett's test
A = EXCLUDES 2 FEMALES THAT DELIVERED AFTER COLLECTION OF BODY WEIGHTS ON GESTATION DAY 21

PUTSUv5.07
12/03/2009
R:12/15/2009

TABLE 7

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT SUMMARY OF FOOD CONSUMPTION DURING GESTATION [G/ANIMAL/DAY]
SPONSOR NO.:18405-841

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	100 MG/KG/DAY	1000 MG/KG/DAY
DAY 0- 6				
MEAN	21.	21.	22.	21.
S.D.	2.2	1.9	1.9	2.2
S.E.	0.5	0.4	0.4	0.5
N	21	21	21	22
DAY 6- 7				
MEAN	21.	21.	20.	14.**
S.D.	2.6	2.0	3.4	4.9
S.E.	0.6	0.4	0.7	1.1
N	22	21	21	22
DAY 7- 8				
MEAN	22.	21.	21.	17.**
S.D.	3.3	2.8	3.2	5.1
S.E.	0.7	0.6	0.7	1.1
N	22	21	21	22
DAY 8- 9				
MEAN	22.	21.	22.	17.**
S.D.	3.9	2.8	2.8	4.9
S.E.	0.8	0.6	0.6	1.0
N	22	21	21	22
DAY 9- 10				
MEAN	22.	22.	22.	18.**
S.D.	3.8	2.4	2.9	2.4
S.E.	0.8	0.5	0.6	0.5
N	22	21	21	22

** = Significantly different from the control group at 0.01 using Dunnett's test
NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 7

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 2
SPONSOR:E.I. DUPONT SUMMARY OF FOOD CONSUMPTION DURING GESTATION [G/ANIMAL/DAY]
SPONSOR NO.:18405-841

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	100 MG/KG/DAY	1000 MG/KG/DAY
DAY 10- 11				
MEAN	23.	23.	23.	20.*
S.D.	4.0	2.7	2.8	4.7
S.E.	0.8	0.6	0.6	1.0
N	22	21	21	22
DAY 11- 12				
MEAN	23.	23.	23.	21.
S.D.	3.3	3.7	3.4	4.6
S.E.	0.7	0.8	0.7	1.0
N	22	21	21	22
DAY 12- 13				
MEAN	22.	23.	24.	20.*
S.D.	3.3	2.4	2.8	4.0
S.E.	0.7	0.5	0.6	0.9
N	21	21	21	22
DAY 13- 14				
MEAN	23.	23.	22.	21.
S.D.	3.6	3.4	3.2	4.9
S.E.	0.8	0.8	0.7	1.0
N	22	21	21	22
DAY 14- 15				
MEAN	22.	23.	23.	20.
S.D.	3.3	2.3	2.9	2.6
S.E.	0.7	0.5	0.6	0.6
N	22	21	21	22

* = Significantly different from the control group at 0.05 using Dunnett's test
NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 7

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 3
SPONSOR:E.I. DUPONT SUMMARY OF FOOD CONSUMPTION DURING GESTATION [G/ANIMAL/DAY]
SPONSOR NO.:18405-841

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	100 MG/KG/DAY	1000 MG/KG/DAY
DAY 15- 16				
MEAN	24.	24.	24.	23.
S.D.	3.0	3.7	3.1	3.1
S.E.	0.7	0.8	0.7	0.7
N	21	21	21	22
DAY 16- 17				
MEAN	25.	25.	26.	23.
S.D.	3.5	2.9	3.9	4.2
S.E.	0.7	0.6	0.9	0.9
N	22	21	21	22
DAY 17- 18				
MEAN	24.	25.	26.	26.
S.D.	3.6	4.0	3.2	4.0
S.E.	0.8	0.9	0.7	0.9
N	22	21	21	22
DAY 18- 19				
MEAN	25.	26.	27.	25.
S.D.	3.5	4.3	2.4	4.6
S.E.	0.7	0.9	0.5	1.0
N	22	21	21	22
DAY 19- 20				
MEAN	25.	25.	25.	22.
S.D.	4.0	2.9	5.5	4.6
S.E.	0.9	0.6	1.2	1.0
N	22	21	21	21

None significantly different from control group
NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 7

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 4
SPONSOR:E.I. DUPONT SUMMARY OF FOOD CONSUMPTION DURING GESTATION [G/ANIMAL/DAY]
SPONSOR NO.:18405-841

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	100 MG/KG/DAY	1000 MG/KG/DAY
DAY 20- 21				
MEAN	26.	25.	26.	21.**
S.D.	3.8	4.0	3.4	5.5
S.E.	0.8	0.9	0.8	1.5
N	22	21	17	14
DAY 6- 9				
MEAN	22.	21.	21.	16.**
S.D.	2.7	1.8	2.1	4.5
S.E.	0.6	0.4	0.5	1.0
N	22	21	21	22
DAY 9- 12				
MEAN	23.	22.	23.	19.**
S.D.	2.8	1.9	2.4	2.5
S.E.	0.6	0.4	0.5	0.5
N	22	21	21	22
DAY 12- 18				
MEAN	23.	24.	24.	22.
S.D.	2.6	2.3	2.3	2.5
S.E.	0.5	0.5	0.5	0.5
N	22	21	21	22
DAY 18- 21				
MEAN	25.	25.	26.	23.
S.D.	3.2	2.6	2.4	3.6
S.E.	0.7	0.6	0.5	0.8
N	22	21	21	21

** = Significantly different from the control group at 0.01 using Dunnett's test
NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 7

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 5
SPONSOR:E.I. DUPONT SUMMARY OF FOOD CONSUMPTION DURING GESTATION [G/ANIMAL/DAY]
SPONSOR NO.:18405-841

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	100 MG/KG/DAY	1000 MG/KG/DAY
DAY 6- 21				
MEAN	23.	23.	24.	21.**
S.D.	2.4	1.8	1.9	1.8
S.E.	0.5	0.4	0.4	0.4
N	22	21	21	21

** = Significantly different from the control group at 0.01 using Dunnett's test
NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

PGFWSUv5.16
12/03/2009

TABLE 8

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT SUMMARY OF FOOD CONSUMPTION DURING GESTATION [G/KG/DAY]
SPONSOR NO.:18405-841

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	100 MG/KG/DAY	1000 MG/KG/DAY
DAY 0- 6				
MEAN	76.	78.	81.	77.
S.D.	5.7	6.7	6.6	6.0
S.E.	1.2	1.5	1.4	1.3
N	21	21	21	22
DAY 6- 7				
MEAN	74.	73.	70.	50.**
S.D.	7.3	7.0	11.1	17.0
S.E.	1.6	1.5	2.4	3.6
N	22	21	21	22
DAY 7- 8				
MEAN	74.	71.	73.	58.**
S.D.	9.5	8.6	9.9	17.2
S.E.	2.0	1.9	2.2	3.7
N	22	21	21	22
DAY 8- 9				
MEAN	74.	72.	74.	60.**
S.D.	10.5	9.9	9.3	16.2
S.E.	2.2	2.2	2.0	3.5
N	22	21	21	22
DAY 9- 10				
MEAN	73.	72.	73.	60.**
S.D.	10.2	6.4	8.3	6.6
S.E.	2.2	1.4	1.8	1.4
N	22	21	21	22

** = Significantly different from the control group at 0.01 using Dunnett's test
NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 8

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 2
SPONSOR:E.I. DUPONT SUMMARY OF FOOD CONSUMPTION DURING GESTATION [G/KG/DAY]
SPONSOR NO.:18405-841

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	100 MG/KG/DAY	1000 MG/KG/DAY
DAY 10- 11				
MEAN	75.	74.	74.	68.
S.D.	9.7	8.2	7.8	18.1
S.E.	2.1	1.8	1.7	3.9
N	22	21	21	22
DAY 11- 12				
MEAN	73.	73.	73.	68.
S.D.	9.5	11.1	9.9	15.0
S.E.	2.0	2.4	2.2	3.2
N	22	21	21	22
DAY 12- 13				
MEAN	70.	73.	75.	64.
S.D.	8.2	8.0	8.7	11.9
S.E.	1.8	1.7	1.9	2.5
N	21	21	21	22
DAY 13- 14				
MEAN	71.	71.	68.	68.
S.D.	9.0	10.0	8.1	13.0
S.E.	1.9	2.2	1.8	2.8
N	22	21	21	22
DAY 14- 15				
MEAN	66.	70.	70.	64.
S.D.	8.6	5.7	6.4	7.3
S.E.	1.8	1.3	1.4	1.6
N	22	21	21	22

None significantly different from control group
NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 8

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 3
SPONSOR:E.I. DUPONT SUMMARY OF FOOD CONSUMPTION DURING GESTATION [G/KG/DAY]
SPONSOR NO.:18405-841

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	100 MG/KG/DAY	1000 MG/KG/DAY
DAY 15- 16				
MEAN	72.	70.	71.	70.
S.D.	7.8	9.9	8.5	9.1
S.E.	1.7	2.2	1.9	1.9
N	21	21	21	22
DAY 16- 17				
MEAN	72.	72.	74.	66.
S.D.	7.7	7.7	10.0	11.4
S.E.	1.6	1.7	2.2	2.4
N	22	21	21	22
DAY 17- 18				
MEAN	65.	70.	72.	72.
S.D.	9.6	10.5	7.2	10.9
S.E.	2.0	2.3	1.6	2.3
N	22	21	21	22
DAY 18- 19				
MEAN	66.	67.	70.	67.
S.D.	6.5	10.1	5.7	11.5
S.E.	1.4	2.2	1.2	2.5
N	22	21	21	22
DAY 19- 20				
MEAN	61.	63.	62.	57.
S.D.	8.3	8.0	13.0	11.3
S.E.	1.8	1.7	2.8	2.5
N	22	21	21	21

None significantly different from control group
NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 8

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 4
SPONSOR:E.I. DUPONT SUMMARY OF FOOD CONSUMPTION DURING GESTATION [G/KG/DAY]
SPONSOR NO.:18405-841

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	100 MG/KG/DAY	1000 MG/KG/DAY
DAY 20- 21				
MEAN	61.	61.	63.	53.*
S.D.	7.0	8.6	7.5	12.6
S.E.	1.5	1.9	1.8	3.4
N	22	21	17	14
DAY 6- 9				
MEAN	74.	72.	73.	56.**
S.D.	6.3	5.9	6.4	14.9
S.E.	1.3	1.3	1.4	3.2
N	22	21	21	22
DAY 9- 12				
MEAN	74.	73.	74.	65.**
S.D.	5.9	5.4	6.2	9.0
S.E.	1.3	1.2	1.4	1.9
N	22	21	21	22
DAY 12- 18				
MEAN	69.	71.	72.	68.
S.D.	5.9	6.0	4.9	6.1
S.E.	1.3	1.3	1.1	1.3
N	22	21	21	22
DAY 18- 21				
MEAN	63.	63.	66.	61.
S.D.	5.0	5.4	5.5	7.9
S.E.	1.1	1.2	1.3	2.1
N	22	21	17	14

* = Significantly different from the control group at 0.05 using Dunnett's test
** = Significantly different from the control group at 0.01 using Dunnett's test
NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 8

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 5
SPONSOR:E.I. DUPONT SUMMARY OF FOOD CONSUMPTION DURING GESTATION [G/KG/DAY]
SPONSOR NO.:18405-841

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	100 MG/KG/DAY	1000 MG/KG/DAY
DAY 6- 21				
MEAN	69.	70.	71.	63.**
S.D.	4.3	4.4	3.7	3.4
S.E.	0.9	1.0	0.9	0.9
N	22	21	17	14

** = Significantly different from the control group at 0.01 using Dunnett's test
NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

PGFWSUv5.16
12/03/2009

TABLE 9

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT SUMMARY OF MATERNAL MACROSCOPIC FINDINGS
SPONSOR NO.:18405-841

GROUP :	1	2	3	4
NUMBER EXAMINED	22	22	22	22
NO SIGNIFICANT CHANGES OBSERVED	22	20	17	11
NONGRAVID -- AMMONIUM SULFIDE NEGATIVE	0	1	1	0
KIDNEYS: AREA(S), DEPRESSED	0	1	0	0
DELIVERED GESTATION DAY 21	0	0	4	9
STOMACH: CONTENTS, DARK RED	0	0	3	1
PANCREAS: EDEMATOUS	0	0	0	2
LIVER: AREA(S), WHITE	0	0	1	1
JEJUNUM: CONTENTS, DARK RED	0	0	1	0
MAMMARY GLAND: MASS	0	0	0	1
LIVER: PALE	0	0	0	1
DIED GESTATION DAY 20	0	0	0	1
KIDNEYS: PALE	0	0	0	1

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY

PMGSIv4.04
01/25/2010

TABLE 10

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT SUMMARY OF ORGAN WEIGHTS [G]
SPONSOR NO.:18405-841

	----- F E M A L E -----			
GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	100 MG/KG/DAY	1000 MG/KG/DAY
LIVER				
MEAN	14.82	14.93	16.61**	19.88**
% DIFFERENCE		0.7	12.1	34.1
S.D.	1.552	1.308	1.946	1.689
S.E.	0.331	0.285	0.425	0.369
N	22	21	21	21
KIDNEYS				
MEAN	2.07	2.10	2.15	2.28**
% DIFFERENCE		1.4	3.9	10.1
S.D.	0.225	0.118	0.187	0.173
S.E.	0.048	0.026	0.041	0.038
N	22	21	21	21

** = Significantly different from the control group at 0.01 using Dunnett's test
NONGRAVID WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

POFBSRv5.05
12/15/2009

TABLE 11

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT SUMMARY OF FETAL DATA AT SCHEDULED NECROPSY
SPONSOR NO.:18405-841

GROUP	SEX M	SEX F	VIABLE FETUSES	DEAD FETUSES	RESORPTIONS EARLY	RESORPTIONS LATE	POST IMPLANTATION LOSS	IMPLANTATION SITES	CORPORA LUTEA	PRE IMPLANTATION LOSS	FETAL WEIGHTS IN GRAMS	NO. OF GRAVID FEMALES
1 TOTAL	191	149	340	0	16	0	16	356	376	20	NA	22
MEAN	8.7	6.8	15.5	0.0	0.7	0.0	0.7	16.2	17.1	0.9	5.7	
S.D.	2.66	1.97	2.67	0.00	0.98	0.00	0.98	2.67	2.33	1.77	0.38	
S.E.	0.57	0.42	0.57	0.00	0.21	0.00	0.21	0.57	0.50	0.38	0.08	
2 TOTAL	157	167	324	0	19	0	19	343	361	18	NA	21
MEAN	7.5	8.0	15.4	0.0	0.9	0.0	0.9	16.3	17.2	0.9	5.6	
S.D.	2.06	2.20	1.40	0.00	1.18	0.00	1.18	1.65	1.75	0.91	0.24	
S.E.	0.45	0.48	0.31	0.00	0.26	0.00	0.26	0.36	0.38	0.20	0.05	
3 TOTAL	155	161	316	0	19	0	19	335	342	7	NA	21
MEAN	7.4	7.7	15.0	0.0	0.9	0.0	0.9	16.0	16.3	0.3	5.2**	
S.D.	1.94	1.91	2.29	0.00	1.76	0.00	1.76	1.75	1.82	0.58	0.24	
S.E.	0.42	0.42	0.50	0.00	0.38	0.00	0.38	0.38	0.40	0.13	0.05	
4 TOTAL	154	175	329	0	10	0	10	339	359	20	NA	21
MEAN	7.3	8.3	15.7	0.0	0.5	0.0	0.5	16.1	17.1	1.0	4.1**	
S.D.	1.68	1.68	1.74	0.00	0.60	0.00	0.60	1.65	2.10	1.36	0.29	
S.E.	0.37	0.37	0.38	0.00	0.13	0.00	0.13	0.36	0.46	0.30	0.06	

** = Significantly different from the control group at 0.01
NA = NOT APPLICABLE
MEAN NUMBER OF VIABLE FETUSES, MEAN NUMBER OF IMPLANTATION SITES, MEAN NUMBER OF CORPORA LUTEA,
FETAL WEIGHTS COMPARED USING DUNNETT'S TEST

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY

PLSUv5.12
12/15/2009

TABLE 12

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT SUMMARY OF FETAL DATA AT SCHEDULED NECROPSY [% PER LITTER]
SPONSOR NO.:18405-841

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	100 MG/KG/DAY	1000 MG/KG/DAY
CORPORA LUTEA				
MEAN	17.1	17.2	16.3	17.1
S.D.	2.33	1.75	1.82	2.10
S.E.	0.50	0.38	0.40	0.46
N	22	21	21	21
IMPLANTATION SITES				
MEAN	16.2	16.3	16.0	16.1
S.D.	2.67	1.65	1.75	1.65
S.E.	0.57	0.36	0.38	0.36
N	22	21	21	21
VIABLE FETUSES (%)				
MEAN	95.5	94.8	94.4	97.0
S.D.	5.82	6.66	10.65	3.94
S.E.	1.24	1.45	2.33	0.86
N	22	21	21	21
DEAD FETUSES (%)				
MEAN	0.0	0.0	0.0	0.0
S.D.	0.00	0.00	0.00	0.00
S.E.	0.00	0.00	0.00	0.00
N	22	21	21	21
EARLY RESORPTIONS (%)				
MEAN	4.6	5.2	5.6	3.0
S.D.	5.82	6.66	10.66	3.95
S.E.	1.24	1.45	2.33	0.86
N	22	21	21	21

PROPORTIONAL (%) DATA COMPARED USING DUNN'S TEST
CORPORA LUTEA AND IMPLANTATION SITES COMPARED USING DUNNETT'S TEST
MODIFIED STATISTICS USED. * INDICATES PARAMETRIC ANALYSIS AND + INDICATES NON-PARAMETRIC ANALYSIS.
None significantly different from control group

TABLE 12

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 2
SPONSOR:E.I. DUPONT SUMMARY OF FETAL DATA AT SCHEDULED NECROPSY [% PER LITTER]
SPONSOR NO.:18405-841

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	100 MG/KG/DAY	1000 MG/KG/DAY
LATE RESORPTIONS (%)				
MEAN	0.0	0.0	0.0	0.0
S.D.	0.00	0.00	0.00	0.00
S.E.	0.00	0.00	0.00	0.00
N	22	21	21	21
TOTAL RESORPTIONS (%)				
MEAN	4.6	5.2	5.6	3.0
S.D.	5.82	6.66	10.66	3.95
S.E.	1.24	1.45	2.33	0.86
N	22	21	21	21
PRE-IMPLANTATION LOSS (%)				
MEAN	5.2	4.8	2.0	5.2
S.D.	10.75	5.14	3.40	6.70
S.E.	2.29	1.12	0.74	1.46
N	22	21	21	21
POST-IMPLANTATION LOSS (%)				
MEAN	4.6	5.2	5.6	3.0
S.D.	5.82	6.66	10.66	3.95
S.E.	1.24	1.45	2.33	0.86
N	22	21	21	21
MALES (%)				
MEAN	55.0	48.5	48.9	46.8*
S.D.	16.19	13.56	10.52	9.57
S.E.	3.45	2.96	2.30	2.09
N	22	21	21	21

PROPORTIONAL (%) DATA COMPARED USING DUNN'S TEST
MODIFIED STATISTICS USED. * INDICATES PARAMETRIC ANALYSIS AND + INDICATES NON-PARAMETRIC ANALYSIS.
* = Significantly different from the control group at 0.05

TABLE 12

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 3
SPONSOR:E.I. DUPONT SUMMARY OF FETAL DATA AT SCHEDULED NECROPSY [% PER LITTER]
SPONSOR NO.:18405-841

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	100 MG/KG/DAY	1000 MG/KG/DAY
FEMALES (%)				
MEAN	45.0	51.5	51.1	53.2*
S.D.	16.19	13.56	10.52	9.57
S.E.	3.45	2.96	2.30	2.09
N	22	21	21	21
MALE FETAL WEIGHTS (g)				
MEAN	5.9	5.8	5.3**	4.2**
% DIFFERENCE		-1.7	-10.2	-28.8
S.D.	0.30	0.28	0.21	0.31
S.E.	0.07	0.06	0.05	0.07
N	21	21	21	21
FEMALE FETAL WEIGHTS (g)				
MEAN	5.5	5.5	5.1**	4.0**
% DIFFERENCE		0.0	-7.3	-27.3
S.D.	0.41	0.22	0.28	0.27
S.E.	0.09	0.05	0.06	0.06
N	22	21	21	21
COMBINED FETAL WEIGHTS (g)				
MEAN	5.7	5.6	5.2**	4.1**
% DIFFERENCE		-1.8	-8.8	-28.1
S.D.	0.38	0.24	0.24	0.29
S.E.	0.08	0.05	0.05	0.06
N	22	21	21	21

PROPORTIONAL (%) DATA COMPARED USING DUNN'S TEST
FETAL WEIGHTS COMPARED USING DUNNETT'S TEST
MODIFIED STATISTICS USED. * INDICATES PARAMETRIC ANALYSIS AND + INDICATES NON-PARAMETRIC ANALYSIS.
* = Significantly different from the control group at 0.05
** = Significantly different from the control group at 0.01

PLPSUv5.10
12/15/2009
R:12/15/2009

TABLE 13

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT SUMMARY OF FETUSES AND LITTERS WITH MALFORMATIONS [ABSOLUTE NO.]
SPONSOR NO.:18405-841 DAY 21

	FETUSES				LITTERS			
DOSE GROUP:	1	2	3	4	1	2	3	4
NUMBER EXAMINED EXTERNALLY	340	324	316	329	22	21	21	21
NUMBER WITH FINDINGS	0	0	0	0	0	0	0	0
NUMBER EXAMINED VISCERALLY	340	324	316	329	22	21	21	21
RIGHT-SIDED AORTIC ARCH	0	1	0	0	0	1	0	0
PERSISTENT TRUNCUS ARTERIOSUS	0	1	0	0	0	1	0	0
SITUS INVERSUS	0	1	0	0	0	1	0	0
NUMBER EXAMINED SKELETALLY	340	324	316	329	22	21	21	21
STERNEBRA(E) MALALIGNED (SEVERE)	0	1	0	0	0	1	0	0
TOTAL NUMBER WITH MALFORMATIONS								
EXTERNAL :	0	0	0	0	0	0	0	0
SOFT TISSUE :	0	1	0	0	0	1	0	0
SKELETAL :	0	1	0	0	0	1	0	0
COMBINED :	0	2	0	0	0	2	0	0

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY

PMALv5.08
01/25/2010

TABLE 14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT SUMMARY OF LITTER PROPORTIONS OF MALFORMATIONS
SPONSOR NO.:18405-841 % PER LITTER DAY 21

DOSE GROUP:	1	2	3	4
NUMBER OF LITTERS EXAMINED EXTERNALLY	22	21	21	21
NUMBER OF LITTERS WITH FINDINGS	0	0	0	0

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY
MODIFIED STATISTICS USED.
None significantly different from control group

TABLE 14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 2
SPONSOR:E.I. DUPONT SUMMARY OF LITTER PROPORTIONS OF MALFORMATIONS
SPONSOR NO.:18405-841 % PER LITTER DAY 21

DOSE GROUP:		1	2	3	4
NUMBER OF LITTERS EXAMINED VISCERALLY		22	21	21	21
RIGHT-SIDED AORTIC ARCH	MEAN	0.0	0.3	0.0	0.0
	S.D.	0.00	1.56	0.00	0.00
	S.E.	0.00	0.34	0.00	0.00
PERSISTENT TRUNCUS ARTERIOSUS	MEAN	0.0	0.3	0.0	0.0
	S.D.	0.00	1.56	0.00	0.00
	S.E.	0.00	0.34	0.00	0.00
SITUS INVERSUS	MEAN	0.0	0.3	0.0	0.0
	S.D.	0.00	1.56	0.00	0.00
	S.E.	0.00	0.34	0.00	0.00

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY
MODIFIED STATISTICS USED.
None significantly different from control group

TABLE 14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 3
SPONSOR:E.I. DUPONT SUMMARY OF LITTER PROPORTIONS OF MALFORMATIONS
SPONSOR NO.:18405-841 % PER LITTER DAY 21

DOSE GROUP:		1	2	3	4
NUMBER OF LITTERS EXAMINED SKELETALLY		22	21	21	21
STERNEBRA(E) MALALIGNED (SEVERE)	MEAN	0.0	0.3	0.0	0.0
	S.D.	0.00	1.56	0.00	0.00
	S.E.	0.00	0.34	0.00	0.00

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY
MODIFIED STATISTICS USED.
None significantly different from control group

TABLE 14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 4
SPONSOR:E.I. DUPONT SUMMARY OF LITTER PROPORTIONS OF MALFORMATIONS
SPONSOR NO.:18405-841 % PER LITTER DAY 21

DOSE GROUP:		1	2	3	4
NUMBER OF LITTERS EXAMINED		22	21	21	21
TOTAL MALFORMATIONS					
PERCENT PER LITTER WITH EXTERNAL MALFORMATIONS	MEAN	0.0	0.0	0.0	0.0
	S.D.	0.00	0.00	0.00	0.00
	S.E.	0.00	0.00	0.00	0.00
PERCENT PER LITTER WITH SOFT TISSUE MALFORMATIONS	MEAN	0.0	0.3	0.0	0.0
	S.D.	0.00	1.56	0.00	0.00
	S.E.	0.00	0.34	0.00	0.00
PERCENT PER LITTER WITH SKELETAL MALFORMATIONS	MEAN	0.0	0.3	0.0	0.0
	S.D.	0.00	1.56	0.00	0.00
	S.E.	0.00	0.34	0.00	0.00
TOTAL PERCENT PER LITTER WITH MALFORMATIONS	MEAN	0.0	0.7	0.0	0.0
	S.D.	0.00	2.15	0.00	0.00
	S.E.	0.00	0.47	0.00	0.00

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY
MODIFIED STATISTICS USED.
None significantly different from control group

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TABLE 15

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT SUMMARY OF FETUSES AND LITTERS WITH VARIATIONS [ABSOLUTE NO.]
SPONSOR NO.:18405-841 DAY 21

	FETUSES				LITTERS			
DOSE GROUP:	1	2	3	4	1	2	3	4
NUMBER EXAMINED EXTERNALLY	340	324	316	329	22	21	21	21
NUMBER WITH FINDINGS	0	0	0	0	0	0	0	0
NUMBER EXAMINED VISCERALLY	340	324	316	329	22	21	21	21
HEMORRHAGIC RING AROUND THE IRIS	0	0	1	0	0	0	1	0
RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S)	5	5	1	0	4	4	1	0
MAJOR BLOOD VESSEL VARIATION	1	1	0	0	1	1	0	0
LUNGS- SMALL	0	1	0	0	0	1	0	0
HEART- MISSHAPEN	0	1	0	0	0	1	0	0
LIVER- ACCESSORY LOBULE(S)	0	0	0	1	0	0	0	1
NUMBER EXAMINED SKELETALLY	340	324	316	329	22	21	21	21
14TH RUDIMENTARY RIB(S)	31	33	38	90	10	16	15	17
7TH CERVICAL RIB(S)	2	1	5	5	1	1	3	3
STERNEBRA(E) MALALIGNED(SLIGHT OR MODERATE)	2	3	2	3	2	1	2	2
REDUCED OSSIFICATION OF THE 13TH RIB(S)	1	0	0	1	1	0	0	1
25 PRESACRAL VERTEBRAE	1	1	1	1	1	1	1	1
VERTEBRAL CENTRA NOT FULLY OSSIFIED	0	0	1	1	0	0	1	1
STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED	0	0	0	2	0	0	0	1
REDUCED OSSIFICATION OF THE VERTEBRAL ARCHES	1	0	0	0	1	0	0	0

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY

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TABLE 16

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT SUMMARY OF LITTER PROPORTIONS OF VARIATIONS
SPONSOR NO.:18405-841 % PER LITTER DAY 21

DOSE GROUP:	1	2	3	4
NUMBER OF LITTERS EXAMINED EXTERNALLY	22	21	21	21
NUMBER OF LITTERS WITH FINDINGS	0	0	0	0

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY
MODIFIED STATISTICS USED.
None significantly different from control group

TABLE 16

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 2
SPONSOR:E.I. DUPONT SUMMARY OF LITTER PROPORTIONS OF VARIATIONS
SPONSOR NO.:18405-841 % PER LITTER DAY 21

DOSE GROUP:		1	2	3	4
NUMBER OF LITTERS EXAMINED VISCERALLY		22	21	21	21
HEMORRHAGIC RING AROUND THE IRIS	MEAN	0.0	0.0	0.3	0.0
	S.D.	0.00	0.00	1.45	0.00
	S.E.	0.00	0.00	0.32	0.00
RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S)	MEAN	1.4	1.5	0.3	0.0
	S.D.	3.24	3.46	1.36	0.00
	S.E.	0.69	0.75	0.30	0.00
MAJOR BLOOD VESSEL VARIATION	MEAN	0.3	0.3	0.0	0.0
	S.D.	1.18	1.28	0.00	0.00
	S.E.	0.25	0.28	0.00	0.00
LUNGS- SMALL	MEAN	0.0	0.3	0.0	0.0
	S.D.	0.00	1.56	0.00	0.00
	S.E.	0.00	0.34	0.00	0.00
HEART- MISSHAPEN	MEAN	0.0	0.3	0.0	0.0
	S.D.	0.00	1.56	0.00	0.00
	S.E.	0.00	0.34	0.00	0.00
LIVER- ACCESSORY LOBULE(S)	MEAN	0.0	0.0	0.0	0.3
	S.D.	0.00	0.00	0.00	1.15
	S.E.	0.00	0.00	0.00	0.25

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY
MODIFIED STATISTICS USED.
None significantly different from control group

TABLE 16

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 3
SPONSOR:E.I. DUPONT SUMMARY OF LITTER PROPORTIONS OF VARIATIONS
SPONSOR NO.:18405-841 % PER LITTER DAY 21

DOSE GROUP:		1	2	3	4
NUMBER OF LITTERS EXAMINED SKELETALLY		22	21	21	21
14TH RUDIMENTARY RIB(S)	MEAN	9.1	10.2	12.3	27.4
	S.D.	14.03	9.85	11.02	28.44
	S.E.	2.99	2.15	2.41	6.21
7TH CERVICAL RIB(S)	MEAN	0.6	0.3	1.5	1.5
	S.D.	3.05	1.45	4.47	4.07
	S.E.	0.65	0.32	0.97	0.89
STERNEBRA(E) MALALIGNED(SLIGHT OR MODERATE)	MEAN	0.6	0.8	0.6	0.9
	S.D.	1.85	3.64	1.81	2.89
	S.E.	0.39	0.79	0.39	0.63
REDUCED OSSIFICATION OF THE 13TH RIB(S)	MEAN	0.3	0.0	0.0	0.3
	S.D.	1.42	0.00	0.00	1.56
	S.E.	0.30	0.00	0.00	0.34
25 PRESACRAL VERTEBRAE	MEAN	0.3	0.3	0.3	0.3
	S.D.	1.25	1.36	1.36	1.56
	S.E.	0.27	0.30	0.30	0.34
VERTEBRAL CENTRA NOT FULLY OSSIFIED	MEAN	0.0	0.0	0.3	0.3
	S.D.	0.00	0.00	1.36	1.36
	S.E.	0.00	0.00	0.30	0.30
STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED	MEAN	0.0	0.0	0.0	0.6
	S.D.	0.00	0.00	0.00	2.57
	S.E.	0.00	0.00	0.00	0.56
REDUCED OSSIFICATION OF THE VERTEBRAL ARCHES	MEAN	0.3	0.0	0.0	0.0
	S.D.	1.18	0.00	0.00	0.00
	S.E.	0.25	0.00	0.00	0.00

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY
MODIFIED STATISTICS USED.
None significantly different from control group

TABLE 16

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 4
SPONSOR:E.I. DUPONT SUMMARY OF LITTER PROPORTIONS OF VARIATIONS
SPONSOR NO.:18405-841 % PER LITTER DAY 21

DOSE GROUP:		1	2	3	4
NUMBER OF LITTERS EXAMINED		22	21	21	21
TOTAL VARIATIONS					
PERCENT PER LITTER WITH EXTERNAL VARIATIONS	MEAN	0.0	0.0	0.0	0.0
	S.D.	0.00	0.00	0.00	0.00
	S.E.	0.00	0.00	0.00	0.00
PERCENT PER LITTER WITH SOFT TISSUE VARIATIONS	MEAN	1.6	2.1	0.6	0.3
	S.D.	3.34	3.73	1.94	1.15
	S.E.	0.71	0.81	0.42	0.25
PERCENT PER LITTER WITH SKELETAL VARIATIONS	MEAN	10.6	11.6	14.7	30.3*
	S.D.	14.17	10.90	10.42	27.49
	S.E.	3.02	2.38	2.27	6.00
TOTAL PERCENT PER LITTER WITH VARIATIONS	MEAN	11.9	12.8	15.3	30.6*
	S.D.	14.31	10.92	9.86	27.22
	S.E.	3.05	2.38	2.15	5.94

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY
MODIFIED STATISTICS USED.
* = Significantly different from the control group at 0.05

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APPENDIX A

Individual Animal Data

TABLE A1 (DAILY EXAMINATIONS)

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT INDIVIDUAL CLINICAL OBSERVATIONS
SPONSOR NO.:18405-841

OBSERVATION	ANIMAL	GROUP	GESTATIONAL DAY 0 1 2 3 4 5 6 7 8 9	1 0	1 1	1 2	1 3	1 4	1 5	1 6	1 7	1 8	1 9	2 0	2 1
NO SIGNIFICANT CLINICAL OBSERVATIONS	57352	1	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P
	57381	1	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P
	57364	1	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P
	57379	1	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P
	57360	1	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P
	57356	1	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P
	57333	1	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P
	57320	1	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P
	57392	1	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P
	57369	1	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P
	57326	1	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P
	57371	1	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P
	57397	1	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P
	57406	1	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P
	57385	1	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P
	57312	1	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P
	57325	1	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P
	57370	1	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P
	57322	1	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P
	57380	1	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P
	57329	1	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	
	57398	1	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P
	57319	2	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P
	57317	2	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P
	57376	2	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P
	57307	2	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P
	57308	2	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY

TABLE A1 (DAILY EXAMINATIONS)

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 2
SPONSOR:E.I. DUPONT INDIVIDUAL CLINICAL OBSERVATIONS
SPONSOR NO.:18405-841

OBSERVATION	ANIMAL	GROUP	GESTATIONAL DAY 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
NO SIGNIFICANT CLINICAL OBSERVATIONS	57339	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57373	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57343	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57332	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57335	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57337	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57405	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57367	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57324	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57403	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57358	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57347	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57334	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P				
	57353	2	P			P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57350	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57340	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57393	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57386	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57368	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57372	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	
	57354	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	
	57383	3	P	P	P	P	P		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	
	57361	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P		P
	57314	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57345	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57348	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P		P	P	P	P	P	P
	57375	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY

TABLE A1 (DAILY EXAMINATIONS)

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 3
SPONSOR:E.I. DUPONT INDIVIDUAL CLINICAL OBSERVATIONS
SPONSOR NO.:18405-841

OBSERVATION	ANIMAL	GROUP	GESTATIONAL DAY 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
NO SIGNIFICANT CLINICAL OBSERVATIONS	57357	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	
	57404	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57387	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57344	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57365	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P			P	P
	57321	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57389	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57331	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57318	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57327	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57390	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57394	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57349	4	P	P	P	P	P	P	P	P	P	P	P	P	P	P		P					P	P
	57366	4	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57382	4	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	
	57363	4	P	P	P	P	P	P	P	P	P		P	P		P	P	P	P	P	P	P	P	P
	57388	4	P	P	P	P	P	P	P	P	P	P	P	P		P	P	P	P	P	P	P	P	
	57378	4	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P		
	57330	4	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P		P	
	57391	4	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P		
	57310	4	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P		
	57316	4	P	P	P	P	P	P	P	P	P	P	P	P	P			P						
	57315	4	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P		
	57362	4	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57359	4	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57336	4	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57351	4	P	P	P	P	P	P	P	P	P	P	P	P	P	P		P	P	P		P	P	P

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY

TABLE A1 (DAILY EXAMINATIONS)

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 4
SPONSOR:E.I. DUPONT INDIVIDUAL CLINICAL OBSERVATIONS
SPONSOR NO.:18405-841

OBSERVATION	ANIMAL	GROUP	GESTATIONAL DAY 0 1 2 3 4 5 6 7 8 9	1 0	1 1	1 2	1 3	1 4	1 5	1 6	1 7	1 8	1 9	2 0	2 1
NO SIGNIFICANT CLINICAL OBSERVATIONS	57338	4	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P
	57328	4	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P		
	57374	4	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	
	57309	4	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	
	57323	4	P P P P P P P P P P	P	P	P	P	P	P	P	P	P	P	P	P
	57342	4	P P P P P P P P P P	P	P	P	P	P	P	P		P		P	P
	57409	4	P P P P P P P P P P	P	P	P	P	P	P	P					
SCHEDULED EUTHANASIA; GESTATION DAY 21	57352	1													P
	57381	1													P
	57364	1													P
	57379	1													P
	57360	1													P
	57356	1													P
	57333	1													P
	57320	1													P
	57392	1													P
	57369	1													P
	57326	1													P
	57371	1													P
	57397	1													P
	57406	1													P
	57385	1													P
	57312	1													P
	57325	1													P
	57370	1													P
	57322	1													P

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY

TABLE A1 (DAILY EXAMINATIONS)

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 5
SPONSOR:E.I. DUPONT INDIVIDUAL CLINICAL OBSERVATIONS
SPONSOR NO.:18405-841

OBSERVATION	ANIMAL	GROUP	GESTATIONAL DAY 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
SCHEDULED EUTHANASIA; GESTATION DAY 21	57380	1	P
	57329	1	P
	57398	1	P
	57319	2	P
	57317	2	P
	57376	2	P
	57307	2	P
	57308	2	P
	57339	2	P
	57373	2	P
	57343	2	P
	57332	2	P
	57335	2	P
	57337	2	P
	57405	2	P
	57367	2	P
	57324	2	P
	57403	2	P
	57358	2	P
	57347	2	P
	57334	2	P
	57353	2	P
	57350	2	P
	57340	2	P
	57393	2	P
	57386	3	P
	57368	3	P

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY

TABLE A1 (DAILY EXAMINATIONS)

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 6
SPONSOR:E.I. DUPONT INDIVIDUAL CLINICAL OBSERVATIONS
SPONSOR NO.:18405-841

OBSERVATION	ANIMAL	GROUP	GESTATIONAL DAY 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
SCHEDULED EUTHANASIA; GESTATION DAY 21	57361	3	P
	57314	3	P
	57345	3	P
	57348	3	P
	57375	3	P
	57404	3	P
	57387	3	P
	57344	3	P
	57365	3	P
	57321	3	P
	57389	3	P
	57331	3	P
	57318	3	P
	57327	3	P
	57390	3	P
	57394	3	P
	57349	4	P
	57366	4	P
	57363	4	P
	57378	4	P
	57330	4	P
	57362	4	P
	57336	4	P
	57351	4	P
	57338	4	P
	57323	4	P
	57342	4	P

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY

TABLE A1 (DAILY EXAMINATIONS)

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 7
SPONSOR:E.I. DUPONT INDIVIDUAL CLINICAL OBSERVATIONS
SPONSOR NO.:18405-841

OBSERVATION	ANIMAL	GROUP	GESTATIONAL DAY 0 1 2 3 4 5 6 7 8 9	1 0	1 1 2 3 4 5 6 7 8 9	2 0	2 1
SCHEDULED EUTHANASIA; GESTATION DAY 21	57409	4					P
DELIVERED; SENT TO NECROPSY	57372	3					P
	57354	3					P
	57383	3					P
	57357	3					P
	57382	4					P
	57388	4					P
	57391	4					P
	57310	4					P
	57316	4					P
	57315	4					P
	57359	4					P
	57374	4					P
	57309	4					P
FOUND DEAD	57328	4				P	
SCABBING DORSAL THORACIC AREA	57326	1	P				
	57353	2	P				
WET YELLOW MATERIAL VENTRAL ABDOMINAL AREA	57361	3					1
	57349	4				2	
	57330	4					1
	57316	4					1
	57338	4			1		
	57328	4		1			

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY

TABLE A1 (DAILY EXAMINATIONS)

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 8
SPONSOR:E.I. DUPONT INDIVIDUAL CLINICAL OBSERVATIONS
SPONSOR NO.:18405-841

OBSERVATION	ANIMAL	GROUP	GESTATIONAL DAY 0 1 2 3 4 5 6 7 8 9	1 0	1 1 2	1 3	1 4	1 5	1 6	1 7	1 8	1 9	2 0	2 1
WET YELLOW MATERIAL VENTRAL ABDOMINAL AREA	57342	4								1		1		
WET YELLOW MATERIAL UROGENITAL AREA	57348	3						1						
	57388	4			1									
	57378	4										1		
	57351	4									1			
	57338	4								3				
	57328	4				1								
	57342	4								1		1		
WET YELLOW MATERIAL ANOGENITAL AREA	57388	4			1									
	57378	4										1		
	57342	4								1				
WET YELLOW MATERIAL VENTRAL THORACIC AREA	57328	4				1								
DRIED YELLOW MATERIAL VENTRAL ABDOMINAL AREA	57349	4					1	1		1	2			
	57378	4											1	
	57351	4					1							
DRIED YELLOW MATERIAL UROGENITAL AREA	57349	4					1	1						
	57378	4											1	
	57351	4					1							
HARD MOVABLE MASS RIGHT FORELIMB 20mm x 15mm x 10mm	57316	4					P	P		P	P			
HAIR LOSS RIGHT FORELIMB	57329	1											1	2

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY

TABLE A1 (DAILY EXAMINATIONS)

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 9
SPONSOR:E.I. DUPONT INDIVIDUAL CLINICAL OBSERVATIONS
SPONSOR NO.:18405-841

OBSERVATION	ANIMAL	GROUP	GESTATIONAL DAY 0 1 2 3 4 5 6 7 8 9	1 0 1 2 3 4 5 6 7 8 9	1 2 0 1
HAIR LOSS RIGHT FORELIMB	57334	2		1 1 1 1	
	57365	3		1 1	
	57409	4		1 1 1 1 1	
HAIR LOSS LEFT FORELIMB	57334	2		1	1
	57365	3		1	
	57409	4		1 1 1 1 1	
HARD MOVABLE MASS RIGHT FORELIMB 26mm x 20mm x 10mm	57316	4		P P P	
DRIED RED MATERIAL AROUND NOSE	57364	1	1		
	57360	1	1		
	57333	1	1		
	57383	3	1		
	57363	4	1		
DECREASED DEFECATION	57363	4	P		
DRIED RED MATERIAL AROUND MOUTH	57353	2	1		
SALIVATION	57330	4		1	

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY

PCOv3.13
12/16/2009

TABLE A2 (AT TIME OF DOSING)

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT INDIVIDUAL POST-DOSE OBSERVATIONS
SPONSOR NO.:18405-841

- - - F E M A L E S - - -

OBSERVATION	ANIMAL	GD GP	1 1 1 1 1 1 1 1 1 1 2 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0
ORAL/DENTAL			
SALIVATION PRIOR	57349	4	2
TO DOSE	57382	4	1 1
	57330	4	1 1
	57391	4	1 1
	57315	4	1 1 1
	57362	4	1
	57338	4	1
	57309	4	1 1
	57323	4	1 1
WET CLEAR MATERIAL AROUND MOUTH	57349	4	1

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE

PCOPDv1.04
12/03/2009

TABLE A3 (1-2 HOURS POST-DOSING)

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1

SPONSOR:E.I. DUPONT INDIVIDUAL POST-DOSE OBSERVATIONS

SPONSOR NO.:18405-841

- - - F E M A L E S - - -

OBSERVATION	ANIMAL	GD GP	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
NORMAL																	
NO SIGNIFICANT CLINICAL OBSERVATIONS	57352	1	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57381	1	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57364	1	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57379	1	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57360	1	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57356	1	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57333	1	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57320	1	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57392	1	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57369	1	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57326	1	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57371	1	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57397	1	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57406	1	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57385	1	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57312	1	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57325	1	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57370	1	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57322	1	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57380	1	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57329	1	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57398	1	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57319	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57317	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57376	2	P	P	P	P		P	P	P	P	P	P	P	P	P	P
	57307	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57308	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57339	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57373	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57343	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE

TABLE A3 (1-2 HOURS POST-DOSING)

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 2
SPONSOR:E.I. DUPONT INDIVIDUAL POST-DOSE OBSERVATIONS
SPONSOR NO.:18405-841

- - - F E M A L E S - - -

OBSERVATION	ANIMAL	GD GP	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
NO SIGNIFICANT CLINICAL OBSERVATIONS	57332	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57335	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57337	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57405	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57367	2	P	P		P	P	P	P	P	P	P	P	P	P	P	P
	57324	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57403	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57358	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57347	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57334	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57353	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57350	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57340	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57393	2	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57386	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57368	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57372	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57354	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57383	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57361	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57314	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57345	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57348	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57375	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57357	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57404	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57387	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57344	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57365	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57321	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57389	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57331	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE

TABLE A3 (1-2 HOURS POST-DOSING)

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 3
SPONSOR:E.I. DUPONT INDIVIDUAL POST-DOSE OBSERVATIONS
SPONSOR NO.:18405-841

- - - F E M A L E S - - -

OBSERVATION	ANIMAL	GD GP	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
NO SIGNIFICANT CLINICAL OBSERVATIONS	57318	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57327	3	P		P	P	P	P	P	P	P	P	P	P	P	P	P
	57390	3	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57394	3	P	P	P		P	P	P	P	P	P	P	P	P	P	P
	57349	4	P	P	P		P	P	P	P	P	P	P	P	P	P	P
	57366	4	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57382	4	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57363	4	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57388	4	P	P	P	P	P	P	P	P			P	P	P	P	P
	57378	4	P		P	P	P	P	P	P	P	P	P	P			
	57330	4	P	P	P	P	P	P	P		P		P	P	P	P	P
	57391	4	P	P	P	P	P	P	P	P	P		P	P	P		
	57310	4	P	P	P	P	P			P	P	P	P	P	P	P	P
	57316	4	P	P	P	P	P	P	P	P	P	P	P	P	P		
	57315	4	P	P	P	P	P	P	P		P		P				P
	57362	4	P	P	P	P	P	P	P	P	P	P	P	P	P		
	57359	4	P	P	P	P	P	P	P	P	P	P			P	P	P
	57336	4	P	P	P		P	P	P		P	P	P	P	P		P
	57351	4	P	P	P	P	P			P		P	P	P	P	P	P
	57338	4	P	P	P	P	P	P		P	P	P	P				
	57328	4	P	P	P	P	P			P				P			
	57374	4	P	P	P	P		P	P	P	P	P	P	P			
	57309	4	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
	57323	4	P	P	P	P		P	P						P	P	
	57342	4	P	P	P	P	P		P	P	P		P		P		P
	57409	4	P	P		P	P	P	P	P		P		P			
BODY/INTEGUMENT																	
WET YELLOW MATERIAL VENTRAL ABDOMINAL AREA	57394	3				1											
	57388	4										1					
	57378	4													3	1	1

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE

TABLE A3 (1-2 HOURS POST-DOSING)

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 4
SPONSOR:E.I. DUPONT INDIVIDUAL POST-DOSE OBSERVATIONS
SPONSOR NO.:18405-841

- - - F E M A L E S - - -

OBSERVATION	ANIMAL	GD GP	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
WET YELLOW MATERIAL VENTRAL ABDOMINAL AREA	57330	4										1					
	57316	4														1	
	57336	4				1											
	57351	4						1	1								
	57328	4						1								1	
	57374	4				1								1	1	1	
	57323	4															1
	57409	4														1	1
WET YELLOW MATERIAL UROGENITAL AREA	57394	3				1											
	57388	4									1	1					
	57378	4														1	1
	57330	4										1					
	57391	4										1				1	
	57310	4						1	1								
	57316	4														1	
	57362	4														1	1
	57336	4				1				1							
	57351	4						1	1								
	57338	4														1	
	57328	4						1	1							1	
	57374	4				1								1	1	1	
	57323	4				1											
	57342	4						1									
	57409	4			1											1	1
WET YELLOW MATERIAL ANOGENITAL AREA	57391	4										1				1	2
	57310	4						1	1								
	57362	4														1	1
	57328	4						1									
	57374	4				1											
	57409	4														1	

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE

TABLE A3 (1-2 HOURS POST-DOSING)

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 5
SPONSOR:E.I. DUPONT INDIVIDUAL POST-DOSE OBSERVATIONS
SPONSOR NO.:18405-841

- - - F E M A L E S - - -

OBSERVATION	ANIMAL	GD GP	1 1 1 1 1 1 1 1 1 2 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0
WET YELLOW MATERIAL RIGHT HINDLIMB	57394	3	1
	57388	4	1
	57378	4	1
	57391	4	1 1
	57310	4	1
	57362	4	1
	57328	4	1
	57342	4	1
WET YELLOW MATERIAL LEFT HINDLIMB	57394	3	1
	57391	4	1 1
	57310	4	1
	57362	4	1
	57328	4	1
	57374	4	1
	57323	4	1
	57342	4	1
WET YELLOW MATERIAL VENTRAL THORACIC AREA	57328	4	1 1
	57374	4	1
WET YELLOW MATERIAL RIGHT INGUINAL AREA	57388	4	1
	57378	4	1
	57362	4	1
	57328	4	1
	57342	4	1
WET YELLOW MATERIAL LEFT INGUINAL AREA	57362	4	1
	57328	4	1
	57374	4	1 1

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE

TABLE A3 (1-2 HOURS POST-DOSING)

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 6
SPONSOR:E.I. DUPONT INDIVIDUAL POST-DOSE OBSERVATIONS
SPONSOR NO.:18405-841

- - - F E M A L E S - - -

OBSERVATION	ANIMAL	GD GP	6	7	8	9	1 0	1 1	1 2	1 3	1 4	1 5	1 6	1 7	1 8	1 9	2 0
WET YELLOW MATERIAL LEFT INGUINAL AREA	57342	4						1									
WET YELLOW MATERIAL RIGHT FORELIMB	57374	4							1								1
WET YELLOW MATERIAL LEFT FORELIMB	57374	4							1								
	57323	4															1
WET RED MATERIAL UROGENITAL AREA	57342	4										1					
CARDIO-PULMONARY																	
RALES	57323	4									P						
EYES/EARS/NOSE																	
DRIED RED MATERIAL AROUND NOSE	57376	2							1								
	57367	2				1											
	57327	3		1													
	57378	4		1													
WET CLEAR MATERIAL AROUND NOSE	57362	4															1
	57338	4														1	
ORAL/DENTAL																	
DRIED RED MATERIAL AROUND MOUTH	57349	4			1												
	57330	4								1							
WET CLEAR MATERIAL AROUND MOUTH	57378	4														1	
	57391	4														1	
	57316	4															2
	57315	4								2		1		2	2	1	
	57362	4															1
	57359	4											1	1			

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE

TABLE A3 (1-2 HOURS POST-DOSING)

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 7
SPONSOR:E.I. DUPONT INDIVIDUAL POST-DOSE OBSERVATIONS
SPONSOR NO.:18405-841

- - - F E M A L E S - - -

OBSERVATION	ANIMAL	GD GP	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
WET CLEAR MATERIAL AROUND MOUTH	57336	4														1	
	57351	4								1							
	57338	4					1						3	1	2	1	
	57328	4					1		1	2	2		1				
	57323	4						1		1	1	2				1	
	57342	4											1		1		
	57409	4								1				1			
SALIVATION	57330	4									1						
	57391	4														1	
	57316	4															1
	57315	4									2					2	
	57338	4														2	
	57328	4					1										
	57323	4											1				
	57409	4										1		1			

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 100 MG/KG/DAY 4- 1000 MG/KG/DAY

GRADE CODE: P = PRESENT 1 = SLIGHT 2 = MODERATE 3 = SEVERE

PCOPDv1.04
12/03/2009

TABLE A4

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT INDIVIDUAL BODY WEIGHTS DURING GESTATION [G]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 0	6	7	8	9	10	11	12	13
DAMS FROM GROUP 1: 0 MG/KG/DAY										
57312	G	261.	304.	307.	311.	319.	327.	333.	336.	341.
57320	G	245.	267.	272.	279.	278.	283.	294.	297.	303.
57322	G	276.	310.	310.	315.	318.	327.	329.	334.	338.
57325	G	267.	314.	322.	326.	331.	337.	341.	342.	346.
57326	G	228.	262.	265.	276.	279.	285.	287.	287.	294.
57329	G	250.	275.	278.	284.	283.	285.	292.	296.	302.
57333	G	249.	273.	282.	287.	291.	299.	312.	308.	317.
57352	G	246.	276.	276.	283.	286.	288.	295.	299.	299.
57356	G	257.	281.	285.	290.	295.	298.	303.	306.	307.
57360	G	260.	277.	284.	291.	293.	295.	303.	302.	309.
57364	G	268.	303.	308.	308.	312.	316.	332.	329.	330.
57369	G	236.	268.	275.	283.	283.	291.	297.	296.	303.
57370	G	269.	289.	294.	303.	303.	308.	316.	321.	324.
57371	G	238.	254.	253.	255.	258.	266.	269.	272.	276.
57379	G	265.	292.	300.	309.	310.	321.	329.	332.	348.
57380	G	250.	308.	306.	309.	317.	323.	325.	331.	340.
57381	G	250.	278.	282.	288.	291.	297.	303.	313.	316.
57385	G	254.	293.	302.	305.	317.	317.	321.	328.	331.
57392	G	240.	274.	275.	284.	290.	291.	299.	306.	310.
57397	G	243.	280.	283.	291.	288.	300.	306.	307.	313.
57398	G	284.	323.	323.	329.	333.	337.	348.	347.	353.
57406	G	251.	287.	287.	294.	294.	301.	307.	312.	313.
MEAN		254.	286.	290.	295.	299.	304.	311.	314.	319.
S.D.		13.8	18.2	18.2	17.5	18.9	19.1	19.5	19.3	20.0
S.E.		2.9	3.9	3.9	3.7	4.0	4.1	4.2	4.1	4.3
N		22	22	22	22	22	22	22	22	22

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE A4

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 2
SPONSOR:E.I. DUPONT INDIVIDUAL BODY WEIGHTS DURING GESTATION [G]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 14	15	16	17	18	19	20	21	
DAMS FROM GROUP 1: 0 MG/KG/DAY										
57312	G	350.	356.	367.	379.	401.	418.	437.	462.	SCHEDULED NECROPSY DAY 21
57320	G	313.	319.	329.	343.	355.	372.	387.	406.	SCHEDULED NECROPSY DAY 21
57322	G	347.	356.	375.	396.	413.	436.	458.	483.	SCHEDULED NECROPSY DAY 21
57325	G	357.	360.	376.	387.	405.	416.	437.	458.	SCHEDULED NECROPSY DAY 21
57326	G	297.	304.	316.	323.	336.	361.	380.	400.	SCHEDULED NECROPSY DAY 21
57329	G	305.	315.	325.	341.	354.	368.	390.	393.	SCHEDULED NECROPSY DAY 21
57333	G	320.	335.	337.	350.	359.	369.	382.	393.	SCHEDULED NECROPSY DAY 21
57352	G	310.	313.	325.	332.	350.	364.	379.	396.	SCHEDULED NECROPSY DAY 21
57356	G	313.	321.	328.	347.	366.	381.	397.	427.	SCHEDULED NECROPSY DAY 21
57360	G	312.	317.	328.	340.	358.	372.	384.	404.	SCHEDULED NECROPSY DAY 21
57364	G	338.	343.	352.	366.	378.	388.	406.	421.	SCHEDULED NECROPSY DAY 21
57369	G	306.	319.	326.	337.	357.	365.	385.	405.	SCHEDULED NECROPSY DAY 21
57370	G	335.	343.	355.	368.	397.	413.	433.	458.	SCHEDULED NECROPSY DAY 21
57371	G	285.	288.	299.	315.	333.	349.	369.	381.	SCHEDULED NECROPSY DAY 21
57379	G	344.	352.	364.	387.	402.	418.	443.	466.	SCHEDULED NECROPSY DAY 21
57380	G	347.	354.	365.	381.	398.	417.	437.	454.	SCHEDULED NECROPSY DAY 21
57381	G	322.	327.	344.	355.	371.	391.	409.	435.	SCHEDULED NECROPSY DAY 21
57385	G	346.	343.	365.	383.	399.	422.	444.	462.	SCHEDULED NECROPSY DAY 21
57392	G	318.	322.	337.	349.	369.	387.	404.	425.	SCHEDULED NECROPSY DAY 21
57397	G	323.	329.	333.	351.	368.	382.	394.	418.	SCHEDULED NECROPSY DAY 21
57398	G	368.	377.	391.	407.	423.	441.	463.	487.	SCHEDULED NECROPSY DAY 21
57406	G	323.	329.	337.	360.	379.	396.	414.	439.	SCHEDULED NECROPSY DAY 21
MEAN		326.	333.	344.	359.	376.	392.	411.	431.	
S.D.		21.2	21.2	22.9	24.5	25.3	26.5	28.6	31.6	
S.E.		4.5	4.5	4.9	5.2	5.4	5.6	6.1	6.7	
N		22	22	22	22	22	22	22	22	

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE A4

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 3
SPONSOR:E.I. DUPONT INDIVIDUAL BODY WEIGHTS DURING GESTATION [G]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 0	6	7	8	9	10	11	12	13
DAMS FROM GROUP 2: 10 MG/KG/DAY										
57307	G	267.	301.	309.	311.	317.	322.	331.	331.	336.
57308	G	261.	294.	306.	302.	310.	314.	325.	327.	334.
57317	G	262.	289.	292.	299.	299.	306.	315.	325.	327.
57319	G	246.	268.	271.	280.	281.	284.	289.	297.	301.
57324	G	252.	282.	282.	283.	288.	290.	296.	297.	299.
57332	G	241.	274.	282.	285.	290.	294.	303.	304.	306.
57334	G	276.	311.	312.	316.	314.	326.	327.	329.	329.
57335	G	238.	286.	292.	297.	300.	304.	314.	315.	321.
57337	G	229.	261.	271.	269.	273.	278.	284.	291.	295.
57339	G	252.	277.	286.	286.	296.	303.	312.	312.	321.
57340	G	246.	279.	282.	283.	292.	291.	299.	309.	312.
57343	G	244.	271.	279.	280.	286.	292.	298.	297.	306.
57347	G	267.	300.	299.	308.	310.	317.	324.	326.	332.
57350	G	255.	296.	296.	300.	308.	308.	318.	324.	332.
57353	G	276.	297.	301.	300.	302.	305.	309.	313.	319.
57358	G	265.	303.	308.	310.	312.	326.	323.	325.	331.
57367	G	240.	268.	270.	274.	276.	282.	291.	293.	295.
57373	G	249.	282.	286.	290.	296.	307.	312.	319.	325.
57376	G	267.	291.	296.	307.	307.	314.	323.	328.	334.
57393	G	280.	302.	301.	305.	309.	311.	315.	320.	326.
57403	G	256.	291.	296.	299.	304.	306.	308.	314.	319.
57405	NG	228.	264.	263.	265.	270.	273.	273.	276.	273.
MEAN		256.	287.	291.	294.	299.	304.	310.	314.	319.
S.D.		13.9	13.6	12.8	13.3	12.7	14.0	13.5	13.0	13.7
S.E.		3.0	3.0	2.8	2.9	2.8	3.1	2.9	2.8	3.0
N		21	21	21	21	21	21	21	21	21

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE A4

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 4
SPONSOR:E.I. DUPONT INDIVIDUAL BODY WEIGHTS DURING GESTATION [G]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 14	15	16	17	18	19	20	21	
DAMS FROM GROUP 2: 10 MG/KG/DAY										
57307	G	344.	352.	365.	376.	396.	414.	426.	451.	SCHEDULED NECROPSY DAY 21
57308	G	337.	351.	357.	367.	382.	411.	423.	455.	SCHEDULED NECROPSY DAY 21
57317	G	325.	329.	342.	353.	360.	380.	401.	420.	SCHEDULED NECROPSY DAY 21
57319	G	308.	312.	326.	337.	350.	370.	385.	404.	SCHEDULED NECROPSY DAY 21
57324	G	308.	312.	322.	335.	359.	377.	389.	408.	SCHEDULED NECROPSY DAY 21
57332	G	310.	326.	333.	345.	362.	377.	392.	405.	SCHEDULED NECROPSY DAY 21
57334	G	338.	344.	353.	365.	380.	392.	408.	427.	SCHEDULED NECROPSY DAY 21
57335	G	325.	333.	346.	358.	374.	393.	407.	427.	SCHEDULED NECROPSY DAY 21
57337	G	295.	308.	317.	335.	350.	368.	386.	406.	SCHEDULED NECROPSY DAY 21
57339	G	328.	334.	343.	363.	381.	402.	421.	440.	SCHEDULED NECROPSY DAY 21
57340	G	317.	329.	341.	352.	369.	385.	406.	425.	SCHEDULED NECROPSY DAY 21
57343	G	312.	320.	323.	344.	365.	377.	396.	400.	SCHEDULED NECROPSY DAY 21
57347	G	334.	341.	347.	361.	380.	394.	411.	432.	SCHEDULED NECROPSY DAY 21
57350	G	339.	347.	361.	377.	404.	420.	441.	456.	SCHEDULED NECROPSY DAY 21
57353	G	329.	338.	353.	369.	391.	410.	434.	449.	SCHEDULED NECROPSY DAY 21
57358	G	339.	341.	357.	371.	387.	408.	428.	449.	SCHEDULED NECROPSY DAY 21
57367	G	306.	307.	316.	330.	348.	360.	380.	397.	SCHEDULED NECROPSY DAY 21
57373	G	327.	338.	353.	361.	387.	392.	415.	433.	SCHEDULED NECROPSY DAY 21
57376	G	337.	354.	356.	378.	391.	409.	429.	446.	SCHEDULED NECROPSY DAY 21
57393	G	328.	335.	348.	360.	370.	387.	406.	430.	SCHEDULED NECROPSY DAY 21
57403	G	328.	339.	348.	363.	376.	398.	411.	431.	SCHEDULED NECROPSY DAY 21
57405	NG	279.	276.	275.	270.	274.	276.	269.	266.	SCHEDULED NECROPSY DAY 21
MEAN		324.	333.	343.	357.	374.	392.	409.	428.	
S.D.		13.5	14.3	14.8	14.6	15.8	16.8	17.3	19.0	
S.E.		2.9	3.1	3.2	3.2	3.5	3.7	3.8	4.2	
N		21	21	21	21	21	21	21	21	

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE A4

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 5

SPONSOR:E.I. DUPONT INDIVIDUAL BODY WEIGHTS DURING GESTATION [G]

SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 0	6	7	8	9	10	11	12	13
DAMS FROM GROUP 3: 100 MG/KG/DAY										
57314	G	247.	282.	287.	289.	299.	301.	307.	314.	314.
57318	NG	255.	298.	295.	308.	308.	302.	308.	308.	301.
57321	G	263.	301.	302.	305.	310.	323.	322.	324.	337.
57327	G	251.	275.	278.	280.	285.	286.	292.	294.	301.
57331	G	271.	300.	304.	307.	311.	314.	317.	319.	319.
57344	G	244.	290.	295.	294.	294.	306.	307.	311.	315.
57345	G	245.	285.	285.	289.	299.	304.	315.	322.	324.
57348	G	240.	273.	279.	285.	289.	295.	305.	304.	314.
57354	G	265.	296.	289.	306.	304.	313.	313.	310.	314.
57357	G	236.	269.	266.	271.	272.	281.	292.	291.	289.
57361	G	252.	288.	290.	294.	301.	307.	314.	314.	318.
57365	G	259.	303.	304.	305.	314.	321.	324.	326.	332.
57368	G	266.	296.	296.	301.	304.	308.	315.	314.	318.
57372	G	269.	297.	307.	304.	313.	314.	322.	329.	336.
57375	G	238.	261.	259.	265.	266.	271.	279.	276.	286.
57383	G	261.	295.	302.	308.	315.	321.	325.	323.	332.
57386	G	240.	281.	278.	282.	290.	293.	303.	305.	302.
57387	G	242.	277.	283.	286.	292.	293.	298.	301.	305.
57389	G	266.	292.	298.	302.	307.	313.	315.	321.	323.
57390	G	231.	278.	276.	287.	289.	291.	296.	305.	310.
57394	G	271.	311.	317.	322.	318.	329.	339.	348.	346.
57404	G	232.	276.	278.	281.	289.	293.	297.	301.	308.
MEAN		252.	287.	289.	293.	298.	304.	309.	312.	316.
S.D.		13.5	12.8	14.5	13.9	13.9	15.0	14.0	15.4	15.3
S.E.		2.9	2.8	3.2	3.0	3.0	3.3	3.0	3.4	3.3
N		21	21	21	21	21	21	21	21	21

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE A4

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 6
SPONSOR:E.I. DUPONT INDIVIDUAL BODY WEIGHTS DURING GESTATION [G]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 14	15	16	17	18	19	20	21	
DAMS FROM GROUP 3: 100 MG/KG/DAY										
57314	G	314.	320.	334.	343.	356.	374.	391.	417.	SCHEDULED NECROPSY DAY 21
57318	NG	289.	294.	295.	285.	275.	285.	292.	293.	SCHEDULED NECROPSY DAY 21
57321	G	339.	350.	366.	381.	402.	421.	439.	457.	SCHEDULED NECROPSY DAY 21
57327	G	307.	317.	327.	340.	360.	379.	393.	411.	SCHEDULED NECROPSY DAY 21
57331	G	327.	333.	347.	356.	369.	385.	401.	427.	SCHEDULED NECROPSY DAY 21
57344	G	330.	338.	350.	371.	391.	416.	435.	453.	SCHEDULED NECROPSY DAY 21
57345	G	329.	337.	351.	370.	385.	406.	421.	447.	SCHEDULED NECROPSY DAY 21
57348	G	315.	327.	341.	355.	374.	392.	409.	425.	SCHEDULED NECROPSY DAY 21
57354	G	316.	331.	341.	346.	368.	388.	409.	NA	SCHEDULED NECROPSY DAY 21
57357	G	297.	301.	309.	332.	348.	363.	374.	NA	SCHEDULED NECROPSY DAY 21
57361	G	317.	327.	334.	349.	368.	384.	405.	422.	SCHEDULED NECROPSY DAY 21
57365	G	338.	344.	359.	378.	389.	411.	424.	439.	SCHEDULED NECROPSY DAY 21
57368	G	326.	327.	335.	346.	362.	379.	392.	415.	SCHEDULED NECROPSY DAY 21
57372	G	344.	356.	377.	391.	414.	425.	442.	NA	SCHEDULED NECROPSY DAY 21
57375	G	288.	301.	310.	328.	345.	362.	379.	399.	SCHEDULED NECROPSY DAY 21
57383	G	336.	348.	359.	378.	382.	414.	439.	NA	SCHEDULED NECROPSY DAY 21
57386	G	307.	317.	326.	340.	364.	387.	410.	427.	SCHEDULED NECROPSY DAY 21
57387	G	310.	314.	322.	341.	353.	376.	391.	397.	SCHEDULED NECROPSY DAY 21
57389	G	332.	343.	357.	373.	391.	407.	429.	443.	SCHEDULED NECROPSY DAY 21
57390	G	312.	320.	332.	344.	362.	378.	391.	399.	SCHEDULED NECROPSY DAY 21
57394	G	356.	353.	366.	377.	395.	406.	432.	443.	SCHEDULED NECROPSY DAY 21
57404	G	316.	324.	336.	349.	374.	387.	404.	413.	SCHEDULED NECROPSY DAY 21
MEAN		322.	330.	342.	357.	374.	392.	410.	426.	
S.D.		16.3	15.7	18.2	18.3	18.4	18.7	20.7	19.0	
S.E.		3.6	3.4	4.0	4.0	4.0	4.1	4.5	4.6	
N		21	21	21	21	21	21	21	17	

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN
NA = NOT APPLICABLE

TABLE A4

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 7
SPONSOR:E.I. DUPONT INDIVIDUAL BODY WEIGHTS DURING GESTATION [G]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 0	6	7	8	9	10	11	12	13
DAMS FROM GROUP 4: 1000 MG/KG/DAY										
57309	G	267.	301.	298.	308.	309.	309.	323.	328.	335.
57310	G	244.	268.	272.	277.	280.	287.	285.	292.	293.
57315	G	230.	266.	270.	266.	270.	276.	283.	285.	285.
57316	G	238.	271.	269.	279.	279.	281.	291.	296.	295.
57323	G	255.	298.	294.	301.	305.	308.	309.	310.	320.
57328	G	269.	314.	308.	311.	319.	327.	331.	334.	340.
57330	G	248.	271.	264.	267.	276.	280.	289.	287.	296.
57336	G	247.	289.	286.	292.	295.	304.	304.	306.	306.
57338	G	261.	294.	291.	293.	296.	301.	302.	302.	310.
57342	G	265.	289.	276.	278.	280.	286.	292.	292.	295.
57349	G	247.	284.	269.	279.	284.	292.	301.	305.	303.
57351	G	253.	281.	281.	281.	287.	297.	300.	309.	307.
57359	G	241.	276.	272.	278.	288.	296.	298.	302.	309.
57362	G	240.	266.	269.	274.	273.	279.	282.	283.	290.
57363	G	262.	290.	265.	249.	238.	257.	280.	287.	295.
57366	G	277.	303.	309.	312.	319.	322.	333.	331.	335.
57374	G	285.	318.	309.	309.	322.	321.	325.	331.	342.
57378	G	257.	282.	283.	271.	274.	282.	291.	292.	300.
57382	G	274.	299.	293.	305.	308.	309.	318.	323.	323.
57388	G	260.	288.	277.	283.	288.	294.	300.	279.	282.
57391	G	245.	277.	273.	280.	278.	280.	293.	300.	302.
57409	G	267.	305.	300.	305.	305.	310.	315.	321.	325.
MEAN		256.	288.	283.	286.	290.	295.	302.	304.	309.
S.D.		14.1	15.2	14.9	17.2	19.8	17.4	16.0	17.1	18.0
S.E.		3.0	3.2	3.2	3.7	4.2	3.7	3.4	3.7	3.8
N		22	22	22	22	22	22	22	22	22

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE A4

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 8
SPONSOR:E.I. DUPONT INDIVIDUAL BODY WEIGHTS DURING GESTATION [G]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 14	15	16	17	18	19	20	21	
DAMS FROM GROUP 4: 1000 MG/KG/DAY										
57309	G	345.	355.	371.	388.	411.	425.	438.	NA	SCHEDULED NECROPSY DAY 21
57310	G	299.	305.	316.	333.	350.	362.	374.	NA	SCHEDULED NECROPSY DAY 21
57315	G	294.	301.	312.	319.	340.	359.	360.	NA	SCHEDULED NECROPSY DAY 21
57316	G	304.	304.	320.	334.	348.	363.	372.	375.	SCHEDULED NECROPSY DAY 21
57323	G	324.	333.	346.	363.	378.	399.	409.	416.	SCHEDULED NECROPSY DAY 21
57328	G	354.	358.	359.	359.	370.	371.	NA	NA	GRAVID, DIED DAY 20
57330	G	300.	309.	317.	333.	351.	365.	376.	381.	SCHEDULED NECROPSY DAY 21
57336	G	311.	317.	326.	343.	357.	369.	376.	370.	SCHEDULED NECROPSY DAY 21
57338	G	313.	321.	327.	338.	348.	362.	371.	373.	SCHEDULED NECROPSY DAY 21
57342	G	303.	316.	326.	340.	360.	385.	399.	404.	SCHEDULED NECROPSY DAY 21
57349	G	311.	316.	333.	346.	364.	381.	398.	401.	SCHEDULED NECROPSY DAY 21
57351	G	317.	325.	340.	359.	384.	401.	413.	424.	SCHEDULED NECROPSY DAY 21
57359	G	316.	326.	336.	353.	375.	384.	400.	402.	SCHEDULED NECROPSY DAY 21
57362	G	301.	305.	316.	332.	348.	363.	377.	353.	SCHEDULED NECROPSY DAY 21
57363	G	305.	324.	329.	349.	365.	383.	391.	406.	SCHEDULED NECROPSY DAY 21
57366	G	340.	351.	358.	379.	398.	406.	418.	425.	SCHEDULED NECROPSY DAY 21
57374	G	344.	351.	358.	370.	386.	398.	398.	NA	SCHEDULED NECROPSY DAY 21
57378	G	306.	317.	327.	341.	360.	374.	382.	384.	SCHEDULED NECROPSY DAY 21
57382	G	332.	343.	361.	380.	400.	417.	426.	NA	SCHEDULED NECROPSY DAY 21
57388	G	294.	306.	312.	334.	351.	368.	382.	NA	SCHEDULED NECROPSY DAY 21
57391	G	309.	310.	329.	337.	355.	369.	378.	NA	SCHEDULED NECROPSY DAY 21
57409	G	335.	340.	349.	365.	382.	404.	398.	415.	SCHEDULED NECROPSY DAY 21
MEAN		316.	324.	335.	350.	367.	382.	392.	395.	
S.D.		17.9	18.1	17.8	18.4	19.5	19.7	20.3	22.3	
S.E.		3.8	3.9	3.8	3.9	4.2	4.2	4.4	6.0	
N		22	22	22	22	22	22	21	14	

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN
NA = NOT APPLICABLE

PGBWv4.07
12/03/2009

TABLE A5

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT INDIVIDUAL BODY WEIGHT CHANGES DURING GESTATION [G]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 0- 6	6- 7	7- 8	8- 9	9-10	10-11	11-12	12-13	13-14
DAMS FROM GROUP 1: 0 MG/KG/DAY										
57312	G	43.	3.	4.	8.	8.	6.	3.	5.	9.
57320	G	22.	5.	7.	-1.	5.	11.	3.	6.	10.
57322	G	34.	0.	5.	3.	9.	2.	5.	4.	9.
57325	G	47.	8.	4.	5.	6.	4.	1.	4.	11.
57326	G	34.	3.	11.	3.	6.	2.	0.	7.	3.
57329	G	25.	3.	6.	-1.	2.	7.	4.	6.	3.
57333	G	24.	9.	5.	4.	8.	13.	-4.	9.	3.
57352	G	30.	0.	7.	3.	2.	7.	4.	0.	11.
57356	G	24.	4.	5.	5.	3.	5.	3.	1.	6.
57360	G	17.	7.	7.	2.	2.	8.	-1.	7.	3.
57364	G	35.	5.	0.	4.	4.	16.	-3.	1.	8.
57369	G	32.	7.	8.	0.	8.	6.	-1.	7.	3.
57370	G	20.	5.	9.	0.	5.	8.	5.	3.	11.
57371	G	16.	-1.	2.	3.	8.	3.	3.	4.	9.
57379	G	27.	8.	9.	1.	11.	8.	3.	16.	-4.
57380	G	58.	-2.	3.	8.	6.	2.	6.	9.	7.
57381	G	28.	4.	6.	3.	6.	6.	10.	3.	6.
57385	G	39.	9.	3.	12.	0.	4.	7.	3.	15.
57392	G	34.	1.	9.	6.	1.	8.	7.	4.	8.
57397	G	37.	3.	8.	-3.	12.	6.	1.	6.	10.
57398	G	39.	0.	6.	4.	4.	11.	-1.	6.	15.
57406	G	36.	0.	7.	0.	7.	6.	5.	1.	10.
MEAN		32.	4.	6.	3.	6.	7.	3.	5.	8.
S.D.		10.1	3.4	2.6	3.5	3.2	3.6	3.5	3.5	4.4
S.E.		2.1	0.7	0.6	0.7	0.7	0.8	0.7	0.7	0.9
N		22	22	22	22	22	22	22	22	22

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE A5

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 2
SPONSOR:E.I. DUPONT INDIVIDUAL BODY WEIGHT CHANGES DURING GESTATION [G]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY14-15	15-16	16-17	17-18	18-19	19-20	20-21	6- 9	9-12
DAMS FROM GROUP 1: 0 MG/KG/DAY										
57312	G	6.	11.	12.	22.	17.	19.	25.	15.	17.
57320	G	6.	10.	14.	12.	17.	15.	19.	11.	19.
57322	G	9.	19.	21.	17.	23.	22.	25.	8.	16.
57325	G	3.	16.	11.	18.	11.	21.	21.	17.	11.
57326	G	7.	12.	7.	13.	25.	19.	20.	17.	8.
57329	G	10.	10.	16.	13.	14.	22.	3.	8.	13.
57333	G	15.	2.	13.	9.	10.	13.	11.	18.	17.
57352	G	3.	12.	7.	18.	14.	15.	17.	10.	13.
57356	G	8.	7.	19.	19.	15.	16.	30.	14.	11.
57360	G	5.	11.	12.	18.	14.	12.	20.	16.	9.
57364	G	5.	9.	14.	12.	10.	18.	15.	9.	17.
57369	G	13.	7.	11.	20.	8.	20.	20.	15.	13.
57370	G	8.	12.	13.	29.	16.	20.	25.	14.	18.
57371	G	3.	11.	16.	18.	16.	20.	12.	4.	14.
57379	G	8.	12.	23.	15.	16.	25.	23.	18.	22.
57380	G	7.	11.	16.	17.	19.	20.	17.	9.	14.
57381	G	5.	17.	11.	16.	20.	18.	26.	13.	22.
57385	G	-3.	22.	18.	16.	23.	22.	18.	24.	11.
57392	G	4.	15.	12.	20.	18.	17.	21.	16.	16.
57397	G	6.	4.	18.	17.	14.	12.	24.	8.	19.
57398	G	9.	14.	16.	16.	18.	22.	24.	10.	14.
57406	G	6.	8.	23.	19.	17.	18.	25.	7.	18.
MEAN		7.	11.	15.	17.	16.	18.	20.	13.	15.
S.D.		3.7	4.6	4.4	4.1	4.3	3.5	6.0	4.8	3.8
S.E.		0.8	1.0	0.9	0.9	0.9	0.7	1.3	1.0	0.8
N		22	22	22	22	22	22	22	22	22

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE A5

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 3
SPONSOR:E.I. DUPONT INDIVIDUAL BODY WEIGHT CHANGES DURING GESTATION [G]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY12-18	18-21	6-21	
DAMS FROM GROUP 1: 0 MG/KG/DAY					
57312	G	65.	61.	158.	SCHEDULED NECROPSY DAY 21
57320	G	58.	51.	139.	SCHEDULED NECROPSY DAY 21
57322	G	79.	70.	173.	SCHEDULED NECROPSY DAY 21
57325	G	63.	53.	144.	SCHEDULED NECROPSY DAY 21
57326	G	49.	64.	138.	SCHEDULED NECROPSY DAY 21
57329	G	58.	39.	118.	SCHEDULED NECROPSY DAY 21
57333	G	51.	34.	120.	SCHEDULED NECROPSY DAY 21
57352	G	51.	46.	120.	SCHEDULED NECROPSY DAY 21
57356	G	60.	61.	146.	SCHEDULED NECROPSY DAY 21
57360	G	56.	46.	127.	SCHEDULED NECROPSY DAY 21
57364	G	49.	43.	118.	SCHEDULED NECROPSY DAY 21
57369	G	61.	48.	137.	SCHEDULED NECROPSY DAY 21
57370	G	76.	61.	169.	SCHEDULED NECROPSY DAY 21
57371	G	61.	48.	127.	SCHEDULED NECROPSY DAY 21
57379	G	70.	64.	174.	SCHEDULED NECROPSY DAY 21
57380	G	67.	56.	146.	SCHEDULED NECROPSY DAY 21
57381	G	58.	64.	157.	SCHEDULED NECROPSY DAY 21
57385	G	71.	63.	169.	SCHEDULED NECROPSY DAY 21
57392	G	63.	56.	151.	SCHEDULED NECROPSY DAY 21
57397	G	61.	50.	138.	SCHEDULED NECROPSY DAY 21
57398	G	76.	64.	164.	SCHEDULED NECROPSY DAY 21
57406	G	67.	60.	152.	SCHEDULED NECROPSY DAY 21
MEAN		62.	55.	145.	
S.D.		8.6	9.5	18.4	
S.E.		1.8	2.0	3.9	
N		22	22	22	

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE A5

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 4

SPONSOR:E.I. DUPONT INDIVIDUAL BODY WEIGHT CHANGES DURING GESTATION [G]

SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 0- 6	6- 7	7- 8	8- 9	9-10	10-11	11-12	12-13	13-14
DAMS FROM GROUP 2: 10 MG/KG/DAY										
57307	G	34.	8.	2.	6.	5.	9.	0.	5.	8.
57308	G	33.	12.	-4.	8.	4.	11.	2.	7.	3.
57317	G	27.	3.	7.	0.	7.	9.	10.	2.	-2.
57319	G	22.	3.	9.	1.	3.	5.	8.	4.	7.
57324	G	30.	0.	1.	5.	2.	6.	1.	2.	9.
57332	G	33.	8.	3.	5.	4.	9.	1.	2.	4.
57334	G	35.	1.	4.	-2.	12.	1.	2.	0.	9.
57335	G	48.	6.	5.	3.	4.	10.	1.	6.	4.
57337	G	32.	10.	-2.	4.	5.	6.	7.	4.	0.
57339	G	25.	9.	0.	10.	7.	9.	0.	9.	7.
57340	G	33.	3.	1.	9.	-1.	8.	10.	3.	5.
57343	G	27.	8.	1.	6.	6.	6.	-1.	9.	6.
57347	G	33.	-1.	9.	2.	7.	7.	2.	6.	2.
57350	G	41.	0.	4.	8.	0.	10.	6.	8.	7.
57353	G	21.	4.	-1.	2.	3.	4.	4.	6.	10.
57358	G	38.	5.	2.	2.	14.	-3.	2.	6.	8.
57367	G	28.	2.	4.	2.	6.	9.	2.	2.	11.
57373	G	33.	4.	4.	6.	11.	5.	7.	6.	2.
57376	G	24.	5.	11.	0.	7.	9.	5.	6.	3.
57393	G	22.	-1.	4.	4.	2.	4.	5.	6.	2.
57403	G	35.	5.	3.	5.	2.	2.	6.	5.	9.
57405	NG	36.	-1.	2.	5.	3.	0.	3.	-3.	6.
MEAN		31.	4.	3.	4.	5.	6.	4.	5.	5.
S.D.		6.7	3.7	3.7	3.2	3.8	3.5	3.3	2.4	3.5
S.E.		1.5	0.8	0.8	0.7	0.8	0.8	0.7	0.5	0.8
N		21	21	21	21	21	21	21	21	21

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE A5

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 5
SPONSOR:E.I. DUPONT INDIVIDUAL BODY WEIGHT CHANGES DURING GESTATION [G]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY14-15	15-16	16-17	17-18	18-19	19-20	20-21	6- 9	9-12
DAMS FROM GROUP 2: 10 MG/KG/DAY										
57307	G	8.	13.	11.	20.	18.	12.	25.	16.	14.
57308	G	14.	6.	10.	15.	29.	12.	32.	16.	17.
57317	G	4.	13.	11.	7.	20.	21.	19.	10.	26.
57319	G	4.	14.	11.	13.	20.	15.	19.	13.	16.
57324	G	4.	10.	13.	24.	18.	12.	19.	6.	9.
57332	G	16.	7.	12.	17.	15.	15.	13.	16.	14.
57334	G	6.	9.	12.	15.	12.	16.	19.	3.	15.
57335	G	8.	13.	12.	16.	19.	14.	20.	14.	15.
57337	G	13.	9.	18.	15.	18.	18.	20.	12.	18.
57339	G	6.	9.	20.	18.	21.	19.	19.	19.	16.
57340	G	12.	12.	11.	17.	16.	21.	19.	13.	17.
57343	G	8.	3.	21.	21.	12.	19.	4.	15.	11.
57347	G	7.	6.	14.	19.	14.	17.	21.	10.	16.
57350	G	8.	14.	16.	27.	16.	21.	15.	12.	16.
57353	G	9.	15.	16.	22.	19.	24.	15.	5.	11.
57358	G	2.	16.	14.	16.	21.	20.	21.	9.	13.
57367	G	1.	9.	14.	18.	12.	20.	17.	8.	17.
57373	G	11.	15.	8.	26.	5.	23.	18.	14.	23.
57376	G	17.	2.	22.	13.	18.	20.	17.	16.	21.
57393	G	7.	13.	12.	10.	17.	19.	24.	7.	11.
57403	G	11.	9.	15.	13.	22.	13.	20.	13.	10.
57405	NG	-3.	-1.	-5.	4.	2.	-7.	-3.	6.	6.
MEAN		8.	10.	14.	17.	17.	18.	19.	12.	16.
S.D.		4.4	4.0	3.7	5.0	4.8	3.7	5.2	4.2	4.2
S.E.		1.0	0.9	0.8	1.1	1.1	0.8	1.1	0.9	0.9
N		21	21	21	21	21	21	21	21	21

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE A5

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 6
SPONSOR:E.I. DUPONT INDIVIDUAL BODY WEIGHT CHANGES DURING GESTATION [G]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY12-18	18-21	6-21	
DAMS FROM GROUP 2: 10 MG/KG/DAY					
57307	G	65.	55.	150.	SCHEDULED NECROPSY DAY 21
57308	G	55.	73.	161.	SCHEDULED NECROPSY DAY 21
57317	G	35.	60.	131.	SCHEDULED NECROPSY DAY 21
57319	G	53.	54.	136.	SCHEDULED NECROPSY DAY 21
57324	G	62.	49.	126.	SCHEDULED NECROPSY DAY 21
57332	G	58.	43.	131.	SCHEDULED NECROPSY DAY 21
57334	G	51.	47.	116.	SCHEDULED NECROPSY DAY 21
57335	G	59.	53.	141.	SCHEDULED NECROPSY DAY 21
57337	G	59.	56.	145.	SCHEDULED NECROPSY DAY 21
57339	G	69.	59.	163.	SCHEDULED NECROPSY DAY 21
57340	G	60.	56.	146.	SCHEDULED NECROPSY DAY 21
57343	G	68.	35.	129.	SCHEDULED NECROPSY DAY 21
57347	G	54.	52.	132.	SCHEDULED NECROPSY DAY 21
57350	G	80.	52.	160.	SCHEDULED NECROPSY DAY 21
57353	G	78.	58.	152.	SCHEDULED NECROPSY DAY 21
57358	G	62.	62.	146.	SCHEDULED NECROPSY DAY 21
57367	G	55.	49.	129.	SCHEDULED NECROPSY DAY 21
57373	G	68.	46.	151.	SCHEDULED NECROPSY DAY 21
57376	G	63.	55.	155.	SCHEDULED NECROPSY DAY 21
57393	G	50.	60.	128.	SCHEDULED NECROPSY DAY 21
57403	G	62.	55.	140.	SCHEDULED NECROPSY DAY 21
57405	NG	-2.	-8.	2.	SCHEDULED NECROPSY DAY 21
MEAN		60.	54.	141.	
S.D.		9.8	7.8	13.1	
S.E.		2.1	1.7	2.9	
N		21	21	21	

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE A5

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 7
SPONSOR:E.I. DUPONT INDIVIDUAL BODY WEIGHT CHANGES DURING GESTATION [G]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 0- 6	6- 7	7- 8	8- 9	9-10	10-11	11-12	12-13	13-14
DAMS FROM GROUP 3: 100 MG/KG/DAY										
57314	G	35.	5.	2.	10.	2.	6.	7.	0.	0.
57318	NG	43.	-3.	13.	0.	-6.	6.	0.	-7.	-12.
57321	G	38.	1.	3.	5.	13.	-1.	2.	13.	2.
57327	G	24.	3.	2.	5.	1.	6.	2.	7.	6.
57331	G	29.	4.	3.	4.	3.	3.	2.	0.	8.
57344	G	46.	5.	-1.	0.	12.	1.	4.	4.	15.
57345	G	40.	0.	4.	10.	5.	11.	7.	2.	5.
57348	G	33.	6.	6.	4.	6.	10.	-1.	10.	1.
57354	G	31.	-7.	17.	-2.	9.	0.	-3.	4.	2.
57357	G	33.	-3.	5.	1.	9.	11.	-1.	-2.	8.
57361	G	36.	2.	4.	7.	6.	7.	0.	4.	-1.
57365	G	44.	1.	1.	9.	7.	3.	2.	6.	6.
57368	G	30.	0.	5.	3.	4.	7.	-1.	4.	8.
57372	G	28.	10.	-3.	9.	1.	8.	7.	7.	8.
57375	G	23.	-2.	6.	1.	5.	8.	-3.	10.	2.
57383	G	34.	7.	6.	7.	6.	4.	-2.	9.	4.
57386	G	41.	-3.	4.	8.	3.	10.	2.	-3.	5.
57387	G	35.	6.	3.	6.	1.	5.	3.	4.	5.
57389	G	26.	6.	4.	5.	6.	2.	6.	2.	9.
57390	G	47.	-2.	11.	2.	2.	5.	9.	5.	2.
57394	G	40.	6.	5.	-4.	11.	10.	9.	-2.	10.
57404	G	44.	2.	3.	8.	4.	4.	4.	7.	8.
MEAN		35.	2.	4.	5.	6.	6.	3.	4.	5.
S.D.		7.1	4.2	4.0	3.9	3.6	3.6	3.8	4.3	3.9
S.E.		1.5	0.9	0.9	0.9	0.8	0.8	0.8	0.9	0.8
N		21	21	21	21	21	21	21	21	21

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE A5

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 8
SPONSOR:E.I. DUPONT INDIVIDUAL BODY WEIGHT CHANGES DURING GESTATION [G]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY14-15	15-16	16-17	17-18	18-19	19-20	20-21	6- 9	9-12
DAMS FROM GROUP 3: 100 MG/KG/DAY										
57314	G	6.	14.	9.	13.	18.	17.	26.	17.	15.
57318	NG	5.	1.	-10.	-10.	10.	7.	1.	10.	0.
57321	G	11.	16.	15.	21.	19.	18.	18.	9.	14.
57327	G	10.	10.	13.	20.	19.	14.	18.	10.	9.
57331	G	6.	14.	9.	13.	16.	16.	26.	11.	8.
57344	G	8.	12.	21.	20.	25.	19.	18.	4.	17.
57345	G	8.	14.	19.	15.	21.	15.	26.	14.	23.
57348	G	12.	14.	14.	19.	18.	17.	16.	16.	15.
57354	G	15.	10.	5.	22.	20.	21.	NA	8.	6.
57357	G	4.	8.	23.	16.	15.	11.	NA	3.	19.
57361	G	10.	7.	15.	19.	16.	21.	17.	13.	13.
57365	G	6.	15.	19.	11.	22.	13.	15.	11.	12.
57368	G	1.	8.	11.	16.	17.	13.	23.	8.	10.
57372	G	12.	21.	14.	23.	11.	17.	NA	16.	16.
57375	G	13.	9.	18.	17.	17.	17.	20.	5.	10.
57383	G	12.	11.	19.	4.	32.	25.	NA	20.	8.
57386	G	10.	9.	14.	24.	23.	23.	17.	9.	15.
57387	G	4.	8.	19.	12.	23.	15.	6.	15.	9.
57389	G	11.	14.	16.	18.	16.	22.	14.	15.	14.
57390	G	8.	12.	12.	18.	16.	13.	8.	11.	16.
57394	G	-3.	13.	11.	18.	11.	26.	11.	7.	30.
57404	G	8.	12.	13.	25.	13.	17.	9.	13.	12.
MEAN		8.	12.	15.	17.	18.	18.	17.	11.	14.
S.D.		4.3	3.4	4.5	4.9	4.9	4.1	6.2	4.5	5.5
S.E.		0.9	0.7	1.0	1.1	1.1	0.9	1.5	1.0	1.2
N		21	21	21	21	21	21	17	21	21

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN
NA = NOT APPLICABLE

TABLE A5

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 9
SPONSOR:E.I. DUPONT INDIVIDUAL BODY WEIGHT CHANGES DURING GESTATION [G]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY12-18	18-21	6-21	
DAMS FROM GROUP 3: 100 MG/KG/DAY					
57314	G	42.	61.	135.	SCHEDULED NECROPSY DAY 21
57318	NG	-33.	18.	-5.	SCHEDULED NECROPSY DAY 21
57321	G	78.	55.	156.	SCHEDULED NECROPSY DAY 21
57327	G	66.	51.	136.	SCHEDULED NECROPSY DAY 21
57331	G	50.	58.	127.	SCHEDULED NECROPSY DAY 21
57344	G	80.	62.	163.	SCHEDULED NECROPSY DAY 21
57345	G	63.	62.	162.	SCHEDULED NECROPSY DAY 21
57348	G	70.	51.	152.	SCHEDULED NECROPSY DAY 21
57354	G	58.	NA	NA	SCHEDULED NECROPSY DAY 21
57357	G	57.	NA	NA	SCHEDULED NECROPSY DAY 21
57361	G	54.	54.	134.	SCHEDULED NECROPSY DAY 21
57365	G	63.	50.	136.	SCHEDULED NECROPSY DAY 21
57368	G	48.	53.	119.	SCHEDULED NECROPSY DAY 21
57372	G	85.	NA	NA	SCHEDULED NECROPSY DAY 21
57375	G	69.	54.	138.	SCHEDULED NECROPSY DAY 21
57383	G	59.	NA	NA	SCHEDULED NECROPSY DAY 21
57386	G	59.	63.	146.	SCHEDULED NECROPSY DAY 21
57387	G	52.	44.	120.	SCHEDULED NECROPSY DAY 21
57389	G	70.	52.	151.	SCHEDULED NECROPSY DAY 21
57390	G	57.	37.	121.	SCHEDULED NECROPSY DAY 21
57394	G	47.	48.	132.	SCHEDULED NECROPSY DAY 21
57404	G	73.	39.	137.	SCHEDULED NECROPSY DAY 21
MEAN		62.	53.	139.	
S.D.		11.5	7.6	13.9	
S.E.		2.5	1.8	3.4	
N		21	17	17	

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN
NA = NOT APPLICABLE

TABLE A5

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 10
SPONSOR:E.I. DUPONT INDIVIDUAL BODY WEIGHT CHANGES DURING GESTATION [G]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 0- 6	6- 7	7- 8	8- 9	9-10	10-11	11-12	12-13	13-14
DAMS FROM GROUP 4: 1000 MG/KG/DAY										
57309	G	34.	-3.	10.	1.	0.	14.	5.	7.	10.
57310	G	24.	4.	5.	3.	7.	-2.	7.	1.	6.
57315	G	36.	4.	-4.	4.	6.	7.	2.	0.	9.
57316	G	33.	-2.	10.	0.	2.	10.	5.	-1.	9.
57323	G	43.	-4.	7.	4.	3.	1.	1.	10.	4.
57328	G	45.	-6.	3.	8.	8.	4.	3.	6.	14.
57330	G	23.	-7.	3.	9.	4.	9.	-2.	9.	4.
57336	G	42.	-3.	6.	3.	9.	0.	2.	0.	5.
57338	G	33.	-3.	2.	3.	5.	1.	0.	8.	3.
57342	G	24.	-13.	2.	2.	6.	6.	0.	3.	8.
57349	G	37.	-15.	10.	5.	8.	9.	4.	-2.	8.
57351	G	28.	0.	0.	6.	10.	3.	9.	-2.	10.
57359	G	35.	-4.	6.	10.	8.	2.	4.	7.	7.
57362	G	26.	3.	5.	-1.	6.	3.	1.	7.	11.
57363	G	28.	-25.	-16.	-11.	19.	23.	7.	8.	10.
57366	G	26.	6.	3.	7.	3.	11.	-2.	4.	5.
57374	G	33.	-9.	0.	13.	-1.	4.	6.	11.	2.
57378	G	25.	1.	-12.	3.	8.	9.	1.	8.	6.
57382	G	25.	-6.	12.	3.	1.	9.	5.	0.	9.
57388	G	28.	-11.	6.	5.	6.	6.	-21.	3.	12.
57391	G	32.	-4.	7.	-2.	2.	13.	7.	2.	7.
57409	G	38.	-5.	5.	0.	5.	5.	6.	4.	10.
MEAN		32.	-5.	3.	3.	6.	7.	2.	4.	8.
S.D.		6.6	7.1	6.7	4.9	4.2	5.6	6.0	4.1	3.1
S.E.		1.4	1.5	1.4	1.0	0.9	1.2	1.3	0.9	0.7
N		22	22	22	22	22	22	22	22	22

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE A5

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 11
SPONSOR:E.I. DUPONT INDIVIDUAL BODY WEIGHT CHANGES DURING GESTATION [G]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY14-15	15-16	16-17	17-18	18-19	19-20	20-21	6- 9	9-12
DAMS FROM GROUP 4: 1000 MG/KG/DAY										
57309	G	10.	16.	17.	23.	14.	13.	NA	8.	19.
57310	G	6.	11.	17.	17.	12.	12.	NA	12.	12.
57315	G	7.	11.	7.	21.	19.	1.	NA	4.	15.
57316	G	0.	16.	14.	14.	15.	9.	3.	8.	17.
57323	G	9.	13.	17.	15.	21.	10.	7.	7.	5.
57328	G	4.	1.	0.	11.	1.	NA	NA	5.	15.
57330	G	9.	8.	16.	18.	14.	11.	5.	5.	11.
57336	G	6.	9.	17.	14.	12.	7.	-6.	6.	11.
57338	G	8.	6.	11.	10.	14.	9.	2.	2.	6.
57342	G	13.	10.	14.	20.	25.	14.	5.	-9.	12.
57349	G	5.	17.	13.	18.	17.	17.	3.	0.	21.
57351	G	8.	15.	19.	25.	17.	12.	11.	6.	22.
57359	G	10.	10.	17.	22.	9.	16.	2.	12.	14.
57362	G	4.	11.	16.	16.	15.	14.	-24.	7.	10.
57363	G	19.	5.	20.	16.	18.	8.	15.	-52.	49.
57366	G	11.	7.	21.	19.	8.	12.	7.	16.	12.
57374	G	7.	7.	12.	16.	12.	0.	NA	4.	9.
57378	G	11.	10.	14.	19.	14.	8.	2.	-8.	18.
57382	G	11.	18.	19.	20.	17.	9.	NA	9.	15.
57388	G	12.	6.	22.	17.	17.	14.	NA	0.	-9.
57391	G	1.	19.	8.	18.	14.	9.	NA	1.	22.
57409	G	5.	9.	16.	17.	22.	-6.	17.	0.	16.
MEAN		8.	11.	15.	18.	15.	9.	4.	2.	15.
S.D.		4.2	4.7	5.0	3.6	5.1	5.5	9.8	13.4	10.2
S.E.		0.9	1.0	1.1	0.8	1.1	1.2	2.6	2.9	2.2
N		22	22	22	22	22	21	14	22	22

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN
NA = NOT APPLICABLE

TABLE A5

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 12
SPONSOR:E.I. DUPONT INDIVIDUAL BODY WEIGHT CHANGES DURING GESTATION [G]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY12-18	18-21	6-21	
DAMS FROM GROUP 4: 1000 MG/KG/DAY					
57309	G	83.	NA	NA	SCHEDULED NECROPSY DAY 21
57310	G	58.	NA	NA	SCHEDULED NECROPSY DAY 21
57315	G	55.	NA	NA	SCHEDULED NECROPSY DAY 21
57316	G	52.	27.	104.	SCHEDULED NECROPSY DAY 21
57323	G	68.	38.	118.	SCHEDULED NECROPSY DAY 21
57328	G	36.	NA	NA	GRAVID, DIED DAY 20
57330	G	64.	30.	110.	SCHEDULED NECROPSY DAY 21
57336	G	51.	13.	81.	SCHEDULED NECROPSY DAY 21
57338	G	46.	25.	79.	SCHEDULED NECROPSY DAY 21
57342	G	68.	44.	115.	SCHEDULED NECROPSY DAY 21
57349	G	59.	37.	117.	SCHEDULED NECROPSY DAY 21
57351	G	75.	40.	143.	SCHEDULED NECROPSY DAY 21
57359	G	73.	27.	126.	SCHEDULED NECROPSY DAY 21
57362	G	65.	5.	87.	SCHEDULED NECROPSY DAY 21
57363	G	78.	41.	116.	SCHEDULED NECROPSY DAY 21
57366	G	67.	27.	122.	SCHEDULED NECROPSY DAY 21
57374	G	55.	NA	NA	SCHEDULED NECROPSY DAY 21
57378	G	68.	24.	102.	SCHEDULED NECROPSY DAY 21
57382	G	77.	NA	NA	SCHEDULED NECROPSY DAY 21
57388	G	72.	NA	NA	SCHEDULED NECROPSY DAY 21
57391	G	55.	NA	NA	SCHEDULED NECROPSY DAY 21
57409	G	61.	33.	110.	SCHEDULED NECROPSY DAY 21
MEAN		63.	29.	109.	
S.D.		11.5	10.9	17.7	
S.E.		2.4	2.9	4.7	
N		22	14	14	

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN
NA = NOT APPLICABLE

PGBWv4.07
12/03/2009

TABLE A6

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT INDIVIDUAL GRAVID UTERINE WTS. AND NET BODY WT. CHANGES [G]
SPONSOR NO.:18405-841

DAM #	PREGNANCY STATUS	INITIAL BODY WT.	TERMINAL BODY WT.	GRAVID UTERINE WT.	NET BODY WT.	NET BODY WT. CHANGE
GROUP 1: 0 MG/KG/DAY						
57312	G	261.	462.	116.5	345.5	84.5
57320	G	245.	406.	115.5	290.5	45.5
57322	G	276.	483.	142.5	340.5	64.5
57325	G	267.	458.	114.6	343.4	76.4
57326	G	228.	400.	123.7	276.3	48.3
57329	G	250.	393.	100.1	292.9	42.9
57333	G	249.	393.	47.9	345.1	96.1
57352	G	246.	396.	110.6	285.4	39.4
57356	G	257.	427.	125.4	301.6	44.6
57360	G	260.	404.	108.6	295.4	35.4
57364	G	268.	421.	98.2	322.8	54.8
57369	G	236.	405.	100.7	304.3	68.3
57370	G	269.	458.	139.8	318.2	49.2
57371	G	238.	381.	110.9	270.1	32.1
57379	G	265.	466.	136.4	329.6	64.6
57380	G	250.	454.	123.3	330.7	80.7
57381	G	250.	435.	127.1	307.9	57.9
57385	G	254.	462.	135.3	326.7	72.7
57392	G	240.	425.	121.7	303.3	63.3
57397	G	243.	418.	104.6	313.4	70.4
57398	G	284.	487.	138.1	348.9	64.9
57406	G	251.	439.	118.1	320.9	69.9
MEAN		254.	431.	116.3	314.2	60.3
S.D.		13.8	31.6	20.22	23.38	16.82
S.E.		2.9	6.7	4.31	4.98	3.59
N		22	22	22	22	22

G = GRAVID

TABLE A6

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 2
SPONSOR:E.I. DUPONT INDIVIDUAL GRAVID UTERINE WTS. AND NET BODY WT. CHANGES [G]
SPONSOR NO.:18405-841

DAM #	PREGNANCY STATUS	INITIAL BODY WT.	TERMINAL BODY WT.	GRAVID UTERINE WT.	NET BODY WT.	NET BODY WT. CHANGE
GROUP 2: 10 MG/KG/DAY						
57307	G	267.	451.	110.8	340.2	73.2
57308	G	261.	455.	125.7	329.3	68.3
57317	G	262.	420.	101.9	318.1	56.1
57319	G	246.	404.	99.3	304.7	58.7
57324	G	252.	408.	115.1	292.9	40.9
57332	G	241.	405.	114.6	290.4	49.4
57334	G	276.	427.	104.7	322.3	46.3
57335	G	238.	427.	122.9	304.1	66.1
57337	G	229.	406.	117.3	288.7	59.7
57339	G	252.	440.	128.9	311.1	59.1
57340	G	246.	425.	117.5	307.5	61.5
57343	G	244.	400.	104.7	295.3	51.3
57347	G	267.	432.	102.9	329.1	62.1
57350	G	255.	456.	116.6	339.4	84.4
57353	G	276.	449.	124.0	325.0	49.0
57358	G	265.	449.	131.6	317.4	52.4
57367	G	240.	397.	106.8	290.2	50.2
57373	G	249.	433.	117.0	316.0	67.0
57376	G	267.	446.	123.2	322.8	55.8
57393	G	280.	430.	110.9	319.1	39.1
57403	G	256.	431.	111.7	319.3	63.3
57405	NG	228.	266.	NA	NA	NA
MEAN		256.	428.	114.7	313.5	57.8
S.D.		13.9	19.0	9.22	15.71	10.79
S.E.		3.0	4.2	2.01	3.43	2.35
N		21	21	21	21	21

G = GRAVID, NG = NONGRAVID, NOT INCLUDED IN CALCULATION OF THE MEAN
NA = NOT APPLICABLE

TABLE A6

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 3
SPONSOR:E.I. DUPONT INDIVIDUAL GRAVID UTERINE WTS. AND NET BODY WT. CHANGES [G]
SPONSOR NO.:18405-841

DAM #	PREGNANCY STATUS	INITIAL BODY WT.	TERMINAL BODY WT.	GRAVID UTERINE WT.	NET BODY WT.	NET BODY WT. CHANGE
GROUP 3: 100 MG/KG/DAY						
57314	G	247.	417.	92.5	324.5	77.5
57318	NG	255.	293.	NA	NA	NA
57321	G	263.	457.	110.7	346.3	83.3
57327	G	251.	411.	108.7	302.3	51.3
57331	G	271.	427.	92.9	334.1	63.1
57344	G	244.	453.	126.2	326.8	82.8
57345	G	245.	447.	110.7	336.3	91.3
57348	G	240.	425.	108.5	316.5	76.5
57361	G	252.	422.	101.7	320.3	68.3
57365	G	259.	439.	110.7	328.3	69.3
57368	G	266.	415.	82.2	332.8	66.8
57375	G	238.	399.	108.9	290.1	52.1
57386	G	240.	427.	108.1	318.9	78.9
57387	G	242.	397.	100.0	297.0	55.0
57389	G	266.	443.	123.5	319.5	53.5
57390	G	231.	399.	98.7	300.3	69.3
57394	G	271.	443.	75.1	367.9	96.9
57404	G	232.	413.	115.2	297.8	65.8
MEAN		250.	426.	104.4	321.2	70.7
S.D.		13.2	19.0	13.30	19.93	13.54
S.E.		3.2	4.6	3.23	4.83	3.28
N		17	17	17	17	17

G = GRAVID, NG = NONGRAVID, NOT INCLUDED IN CALCULATION OF THE MEAN
NA = NOT APPLICABLE

TABLE A6

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 4
SPONSOR:E.I. DUPONT INDIVIDUAL GRAVID UTERINE WTS. AND NET BODY WT. CHANGES [G]
SPONSOR NO.:18405-841

DAM #	PREGNANCY STATUS	INITIAL BODY WT.	TERMINAL BODY WT.	GRAVID UTERINE WT.	NET BODY WT.	NET BODY WT. CHANGE
GROUP 4: 1000 MG/KG/DAY						
57316	G	238.	375.	NA	NA	NA
57323	G	255.	416.	91.4	324.6	69.6
57330	G	248.	381.	87.2	293.8	45.8
57336	G	247.	370.	84.9	285.1	38.1
57338	G	261.	373.	74.7	298.3	37.3
57342	G	265.	404.	96.2	307.8	42.8
57349	G	247.	401.	82.8	318.2	71.2
57351	G	253.	424.	98.1	325.9	72.9
57359	G	241.	402.	NA	NA	NA
57362	G	240.	353.	85.8	267.2	27.2
57363	G	262.	406.	82.7	323.3	61.3
57366	G	277.	425.	85.7	339.3	62.3
57378	G	257.	384.	82.6	301.4	44.4
57409	G	267.	415.	93.1	321.9	54.9
MEAN		254.	395.	87.1	308.9	52.3
S.D.		11.4	22.3	6.60	20.51	15.14
S.E.		3.1	6.0	1.90	5.92	4.37
N		14	14	12	12	12

G = GRAVID
NA = NOT APPLICABLE

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TABLE A7

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT INDIVIDUAL FOOD CONSUMPTION DURING GESTATION [G/ANIMAL/DAY]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY	0- 6	6- 7	7- 8	8- 9	9-10	10-11	11-12	12-13	13-14
DAMS FROM GROUP 1: 0 MG/KG/DAY											
57312	G		23.	24.	24.	24.	27.	27.	22.	27.	25.
57320	G		18.	18.	18.	18.	21.	20.	19.	25.	24.
57322	G		23.	24.	25.	26.	27.	22.	28.	23.	29.
57325	G		25.	27.	28.	25.	29.	31.	23.	29.	33.
57326	G		20.	19.	21.	21.	18.	21.	22.	20.	20.
57329	G		21.	23.	21.	20.	20.	18.	22.	21.	22.
57333	G		18.	26.	24.	24.	26.	28.	23.	22.	26.
57352	G		21.	19.	20.	20.	21.	18.	21.	19.	20.
57356	G		18.	20.	21.	23.	17.	22.	22.	18.	23.
57360	G		21.	19.	21.	20.	18.	21.	21.	16.	17.
57364	G		NA	21.	13.	26.	16.	32.	29.	19.	19.
57369	G		18.	21.	19.	21.	21.	20.	24.	21.	18.
57370	G		21.	22.	27.	19.	22.	24.	20.	22.	22.
57371	G		17.	18.	18.	18.	18.	19.	18.	20.	20.
57379	G		21.	21.	23.	23.	26.	26.	27.	NA	22.
57380	G		24.	24.	24.	34.	29.	22.	28.	27.	25.
57381	G		20.	20.	19.	21.	21.	20.	26.	23.	21.
57385	G		19.	24.	22.	22.	22.	22.	24.	22.	23.
57392	G		21.	19.	23.	23.	20.	22.	26.	22.	24.
57397	G		20.	21.	22.	17.	24.	24.	19.	24.	21.
57398	G		23.	20.	25.	26.	23.	28.	20.	27.	26.
57406	G		19.	19.	21.	17.	21.	22.	18.	21.	23.
MEAN			21.	21.	22.	22.	22.	23.	23.	22.	23.
S.D.			2.2	2.6	3.3	3.9	3.8	4.0	3.3	3.3	3.6
S.E.			0.5	0.6	0.7	0.8	0.8	0.8	0.7	0.7	0.8
N			21	22	22	22	22	22	22	21	22

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN
NA = NOT APPLICABLE

TABLE A7

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 2
SPONSOR:E.I. DUPONT INDIVIDUAL FOOD CONSUMPTION DURING GESTATION [G/ANIMAL/DAY]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 14-15	15-16	16-17	17-18	18-19	19-20	20-21	6- 9	9-12
DAMS FROM GROUP 1: 0 MG/KG/DAY										
57312	G	27.	25.	28.	31.	28.	34.	28.	24.	25.
57320	G	19.	24.	24.	26.	23.	19.	22.	18.	20.
57322	G	22.	29.	33.	27.	32.	26.	29.	25.	26.
57325	G	29.	26.	32.	26.	27.	31.	28.	27.	28.
57326	G	20.	24.	22.	21.	25.	21.	26.	20.	20.
57329	G	20.	25.	24.	22.	22.	21.	20.	21.	20.
57333	G	26.	27.	25.	26.	24.	27.	27.	25.	26.
57352	G	20.	22.	24.	22.	23.	22.	21.	20.	20.
57356	G	21.	24.	25.	27.	21.	20.	29.	21.	20.
57360	G	18.	21.	19.	18.	26.	17.	22.	20.	20.
57364	G	17.	29.	20.	18.	25.	28.	29.	20.	26.
57369	G	18.	21.	21.	21.	19.	22.	21.	20.	22.
57370	G	25.	22.	26.	29.	25.	26.	26.	23.	22.
57371	G	19.	21.	22.	23.	20.	26.	18.	18.	18.
57379	G	26.	NA	26.	19.	32.	29.	34.	22.	26.
57380	G	23.	25.	27.	23.	27.	27.	24.	27.	26.
57381	G	25.	24.	27.	26.	28.	23.	27.	20.	22.
57385	G	18.	29.	27.	24.	31.	26.	26.	23.	23.
57392	G	20.	29.	26.	29.	26.	24.	25.	22.	23.
57397	G	22.	19.	26.	24.	23.	24.	25.	20.	22.
57398	G	20.	25.	24.	23.	25.	25.	30.	24.	24.
57406	G	22.	21.	29.	21.	26.	23.	28.	19.	20.
MEAN		22.	24.	25.	24.	25.	25.	26.	22.	23.
S.D.		3.3	3.0	3.5	3.6	3.5	4.0	3.8	2.7	2.8
S.E.		0.7	0.7	0.7	0.8	0.7	0.9	0.8	0.6	0.6
N		22	21	22	22	22	22	22	22	22

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN
NA = NOT APPLICABLE

TABLE A7

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 3
SPONSOR:E.I. DUPONT INDIVIDUAL FOOD CONSUMPTION DURING GESTATION [G/ANIMAL/DAY]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 12-18	18-21	6-21	
DAMS FROM GROUP 1: 0 MG/KG/DAY					
57312	G	27.	30.	27.	SCHEDULED NECROPSY DAY 21
57320	G	24.	21.	21.	SCHEDULED NECROPSY DAY 21
57322	G	27.	29.	27.	SCHEDULED NECROPSY DAY 21
57325	G	29.	29.	28.	SCHEDULED NECROPSY DAY 21
57326	G	21.	24.	21.	SCHEDULED NECROPSY DAY 21
57329	G	22.	21.	21.	SCHEDULED NECROPSY DAY 21
57333	G	25.	26.	25.	SCHEDULED NECROPSY DAY 21
57352	G	21.	22.	21.	SCHEDULED NECROPSY DAY 21
57356	G	23.	23.	22.	SCHEDULED NECROPSY DAY 21
57360	G	18.	22.	20.	SCHEDULED NECROPSY DAY 21
57364	G	20.	27.	23.	SCHEDULED NECROPSY DAY 21
57369	G	20.	21.	21.	SCHEDULED NECROPSY DAY 21
57370	G	24.	26.	24.	SCHEDULED NECROPSY DAY 21
57371	G	21.	21.	20.	SCHEDULED NECROPSY DAY 21
57379	G	23.	32.	26.	SCHEDULED NECROPSY DAY 21
57380	G	25.	26.	26.	SCHEDULED NECROPSY DAY 21
57381	G	24.	26.	23.	SCHEDULED NECROPSY DAY 21
57385	G	24.	28.	24.	SCHEDULED NECROPSY DAY 21
57392	G	25.	25.	24.	SCHEDULED NECROPSY DAY 21
57397	G	23.	24.	22.	SCHEDULED NECROPSY DAY 21
57398	G	24.	27.	24.	SCHEDULED NECROPSY DAY 21
57406	G	23.	26.	22.	SCHEDULED NECROPSY DAY 21
MEAN		23.	25.	23.	
S.D.		2.6	3.2	2.4	
S.E.		0.5	0.7	0.5	
N		22	22	22	

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE A7

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 4
SPONSOR:E.I. DUPONT INDIVIDUAL FOOD CONSUMPTION DURING GESTATION [G/ANIMAL/DAY]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY	0- 6	6- 7	7- 8	8- 9	9-10	10-11	11-12	12-13	13-14
DAMS FROM GROUP 2: 10 MG/KG/DAY											
57307	G		23.	25.	23.	25.	24.	27.	27.	23.	30.
57308	G		22.	25.	23.	25.	23.	25.	25.	25.	25.
57317	G		19.	21.	21.	20.	24.	19.	25.	24.	15.
57319	G		19.	19.	20.	19.	20.	19.	20.	23.	23.
57324	G		21.	19.	20.	19.	22.	23.	17.	20.	20.
57332	G		22.	24.	23.	25.	21.	26.	26.	22.	26.
57334	G		21.	19.	22.	15.	25.	22.	17.	21.	21.
57335	G		24.	24.	24.	24.	20.	25.	25.	22.	25.
57337	G		18.	22.	17.	21.	19.	19.	24.	19.	19.
57339	G		20.	21.	16.	23.	19.	23.	24.	21.	21.
57340	G		20.	22.	20.	25.	22.	21.	25.	22.	24.
57343	G		21.	21.	18.	24.	18.	21.	22.	23.	24.
57347	G		24.	20.	28.	21.	24.	28.	23.	24.	20.
57350	G		20.	22.	20.	23.	24.	23.	27.	24.	25.
57353	G		20.	22.	18.	20.	20.	21.	21.	22.	23.
57358	G		23.	21.	20.	19.	27.	21.	19.	25.	19.
57367	G		22.	18.	22.	17.	21.	26.	18.	30.	21.
57373	G		18.	19.	17.	21.	21.	21.	22.	22.	24.
57376	G		24.	20.	23.	23.	23.	25.	31.	27.	29.
57393	G		21.	20.	22.	22.	18.	22.	22.	23.	21.
57403	G		20.	22.	22.	19.	21.	21.	18.	24.	23.
57405	NG		19.	18.	19.	20.	20.	19.	18.	17.	20.
MEAN			21.	21.	21.	21.	22.	23.	23.	23.	23.
S.D.			1.9	2.0	2.8	2.8	2.4	2.7	3.7	2.4	3.4
S.E.			0.4	0.4	0.6	0.6	0.5	0.6	0.8	0.5	0.8
N			21	21	21	21	21	21	21	21	21

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE A7

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 5
SPONSOR:E.I. DUPONT INDIVIDUAL FOOD CONSUMPTION DURING GESTATION [G/ANIMAL/DAY]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 14-15	15-16	16-17	17-18	18-19	19-20	20-21	6- 9	9-12
DAMS FROM GROUP 2: 10 MG/KG/DAY										
57307	G	24.	28.	27.	31.	30.	26.	33.	24.	26.
57308	G	25.	25.	21.	26.	28.	23.	30.	24.	24.
57317	G	23.	19.	22.	13.	20.	35.	19.	21.	23.
57319	G	22.	23.	24.	22.	26.	25.	22.	19.	20.
57324	G	21.	20.	21.	28.	24.	26.	26.	19.	21.
57332	G	24.	27.	27.	27.	24.	23.	22.	24.	24.
57334	G	23.	20.	26.	25.	23.	23.	22.	19.	21.
57335	G	23.	31.	26.	26.	28.	21.	29.	24.	23.
57337	G	21.	23.	23.	23.	25.	22.	26.	20.	21.
57339	G	22.	25.	27.	26.	30.	25.	29.	20.	22.
57340	G	23.	27.	26.	28.	27.	24.	26.	22.	23.
57343	G	21.	21.	24.	29.	26.	24.	25.	21.	20.
57347	G	26.	19.	29.	26.	26.	26.	25.	23.	25.
57350	G	25.	27.	29.	29.	32.	24.	30.	22.	25.
57353	G	21.	27.	27.	28.	29.	27.	19.	20.	21.
57358	G	20.	20.	26.	21.	24.	24.	23.	20.	22.
57367	G	20.	18.	24.	24.	20.	26.	23.	19.	22.
57373	G	22.	25.	19.	24.	14.	21.	21.	19.	21.
57376	G	29.	28.	30.	31.	33.	27.	31.	22.	26.
57393	G	21.	25.	22.	22.	25.	26.	26.	21.	21.
57403	G	26.	22.	27.	26.	26.	27.	28.	21.	20.
57405	NG	17.	18.	16.	20.	20.	22.	14.	19.	19.
MEAN		23.	24.	25.	25.	26.	25.	25.	21.	22.
S.D.		2.3	3.7	2.9	4.0	4.3	2.9	4.0	1.8	1.9
S.E.		0.5	0.8	0.6	0.9	0.9	0.6	0.9	0.4	0.4
N		21	21	21	21	21	21	21	21	21

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE A7

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 6
SPONSOR:E.I. DUPONT INDIVIDUAL FOOD CONSUMPTION DURING GESTATION [G/ANIMAL/DAY]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 12-18	18-21	6-21	
DAMS FROM GROUP 2: 10 MG/KG/DAY					
57307	G	27.	30.	27.	SCHEDULED NECROPSY DAY 21
57308	G	25.	27.	25.	SCHEDULED NECROPSY DAY 21
57317	G	19.	25.	21.	SCHEDULED NECROPSY DAY 21
57319	G	23.	24.	22.	SCHEDULED NECROPSY DAY 21
57324	G	22.	25.	22.	SCHEDULED NECROPSY DAY 21
57332	G	26.	23.	24.	SCHEDULED NECROPSY DAY 21
57334	G	23.	23.	22.	SCHEDULED NECROPSY DAY 21
57335	G	26.	26.	25.	SCHEDULED NECROPSY DAY 21
57337	G	21.	24.	22.	SCHEDULED NECROPSY DAY 21
57339	G	24.	28.	23.	SCHEDULED NECROPSY DAY 21
57340	G	25.	26.	24.	SCHEDULED NECROPSY DAY 21
57343	G	24.	25.	23.	SCHEDULED NECROPSY DAY 21
57347	G	24.	26.	24.	SCHEDULED NECROPSY DAY 21
57350	G	27.	29.	26.	SCHEDULED NECROPSY DAY 21
57353	G	25.	25.	23.	SCHEDULED NECROPSY DAY 21
57358	G	22.	24.	22.	SCHEDULED NECROPSY DAY 21
57367	G	23.	23.	22.	SCHEDULED NECROPSY DAY 21
57373	G	23.	19.	21.	SCHEDULED NECROPSY DAY 21
57376	G	29.	30.	27.	SCHEDULED NECROPSY DAY 21
57393	G	22.	26.	22.	SCHEDULED NECROPSY DAY 21
57403	G	25.	27.	23.	SCHEDULED NECROPSY DAY 21
57405	NG	18.	19.	19.	SCHEDULED NECROPSY DAY 21
MEAN		24.	25.	23.	
S.D.		2.3	2.6	1.8	
S.E.		0.5	0.6	0.4	
N		21	21	21	

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE A7

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 7
SPONSOR:E.I. DUPONT INDIVIDUAL FOOD CONSUMPTION DURING GESTATION [G/ANIMAL/DAY]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY	0- 6	6- 7	7- 8	8- 9	9-10	10-11	11-12	12-13	13-14
DAMS FROM GROUP 3: 100 MG/KG/DAY											
57314	G		21.	21.	21.	24.	20.	22.	24.	21.	21.
57318	NG		22.	20.	21.	24.	21.	19.	23.	17.	15.
57321	G		23.	21.	24.	22.	27.	24.	23.	29.	21.
57327	G		21.	24.	21.	23.	24.	19.	24.	24.	25.
57331	G		23.	21.	24.	19.	21.	24.	19.	22.	21.
57344	G		22.	20.	23.	17.	25.	21.	19.	24.	23.
57345	G		19.	15.	15.	23.	17.	24.	26.	27.	20.
57348	G		24.	22.	23.	24.	22.	26.	26.	26.	23.
57354	G		23.	12.	25.	24.	22.	18.	23.	19.	19.
57357	G		18.	15.	17.	21.	19.	22.	20.	18.	20.
57361	G		25.	22.	20.	26.	21.	26.	25.	21.	21.
57365	G		23.	19.	24.	22.	25.	25.	20.	27.	23.
57368	G		23.	21.	22.	21.	21.	19.	21.	25.	20.
57372	G		24.	25.	18.	29.	21.	29.	30.	25.	27.
57375	G		18.	16.	14.	18.	16.	20.	16.	21.	18.
57383	G		21.	22.	22.	24.	23.	23.	22.	23.	24.
57386	G		22.	18.	20.	21.	22.	21.	23.	24.	16.
57387	G		20.	22.	23.	21.	20.	21.	21.	25.	18.
57389	G		21.	23.	22.	22.	23.	25.	22.	23.	22.
57390	G		24.	23.	26.	23.	25.	21.	28.	25.	24.
57394	G		22.	24.	25.	18.	27.	26.	27.	21.	30.
57404	G		21.	19.	22.	20.	23.	23.	20.	27.	21.
MEAN			22.	20.	21.	22.	22.	23.	23.	24.	22.
S.D.			1.9	3.4	3.2	2.8	2.9	2.8	3.4	2.8	3.2
S.E.			0.4	0.7	0.7	0.6	0.6	0.6	0.7	0.6	0.7
N			21	21	21	21	21	21	21	21	21

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE A7

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 8
SPONSOR:E.I. DUPONT INDIVIDUAL FOOD CONSUMPTION DURING GESTATION [G/ANIMAL/DAY]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 14-15	15-16	16-17	17-18	18-19	19-20	20-21	6- 9	9-12
DAMS FROM GROUP 3: 100 MG/KG/DAY										
57314	G	21.	24.	19.	25.	27.	25.	30.	22.	22.
57318	NG	15.	20.	19.	8.	20.	19.	20.	22.	21.
57321	G	27.	23.	29.	32.	29.	26.	29.	22.	25.
57327	G	20.	26.	28.	25.	29.	22.	29.	23.	22.
57331	G	24.	22.	24.	28.	25.	27.	26.	21.	21.
57344	G	27.	20.	31.	31.	26.	30.	27.	20.	22.
57345	G	23.	25.	29.	29.	32.	27.	31.	18.	22.
57348	G	24.	28.	23.	30.	28.	25.	27.	23.	25.
57354	G	24.	26.	21.	24.	24.	24.	NA	20.	21.
57357	G	16.	24.	24.	23.	25.	20.	NA	18.	20.
57361	G	21.	25.	24.	28.	27.	24.	24.	23.	24.
57365	G	27.	21.	32.	25.	29.	7.	28.	22.	23.
57368	G	21.	21.	22.	23.	27.	25.	30.	21.	20.
57372	G	26.	32.	27.	28.	31.	26.	NA	24.	27.
57375	G	19.	19.	18.	21.	26.	20.	25.	16.	17.
57383	G	23.	24.	25.	24.	27.	25.	NA	23.	23.
57386	G	22.	20.	25.	27.	27.	32.	22.	20.	22.
57387	G	21.	21.	30.	21.	25.	27.	19.	22.	21.
57389	G	23.	24.	28.	28.	22.	28.	25.	22.	23.
57390	G	20.	27.	29.	26.	27.	24.	24.	24.	25.
57394	G	25.	25.	30.	27.	28.	36.	30.	22.	27.
57404	G	24.	24.	26.	31.	24.	27.	22.	20.	22.
MEAN		23.	24.	26.	26.	27.	25.	26.	21.	23.
S.D.		2.9	3.1	3.9	3.2	2.4	5.5	3.4	2.1	2.4
S.E.		0.6	0.7	0.9	0.7	0.5	1.2	0.8	0.5	0.5
N		21	21	21	21	21	21	17	21	21

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN
NA = NOT APPLICABLE

TABLE A7

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 9
SPONSOR:E.I. DUPONT INDIVIDUAL FOOD CONSUMPTION DURING GESTATION [G/ANIMAL/DAY]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 12-18	18-21	6-21	
DAMS FROM GROUP 3: 100 MG/KG/DAY					
57314	G	22.	27.	23.	SCHEDULED NECROPSY DAY 21
57318	NG	16.	20.	19.	SCHEDULED NECROPSY DAY 21
57321	G	27.	28.	26.	SCHEDULED NECROPSY DAY 21
57327	G	25.	27.	24.	SCHEDULED NECROPSY DAY 21
57331	G	24.	26.	23.	SCHEDULED NECROPSY DAY 21
57344	G	26.	28.	24.	SCHEDULED NECROPSY DAY 21
57345	G	26.	30.	24.	SCHEDULED NECROPSY DAY 21
57348	G	26.	27.	25.	SCHEDULED NECROPSY DAY 21
57354	G	22.	24.	22.	SCHEDULED NECROPSY DAY 21
57357	G	21.	23.	20.	SCHEDULED NECROPSY DAY 21
57361	G	23.	25.	24.	SCHEDULED NECROPSY DAY 21
57365	G	26.	21.	24.	SCHEDULED NECROPSY DAY 21
57368	G	22.	27.	23.	SCHEDULED NECROPSY DAY 21
57372	G	28.	29.	27.	SCHEDULED NECROPSY DAY 21
57375	G	19.	24.	19.	SCHEDULED NECROPSY DAY 21
57383	G	24.	26.	24.	SCHEDULED NECROPSY DAY 21
57386	G	22.	27.	23.	SCHEDULED NECROPSY DAY 21
57387	G	23.	24.	22.	SCHEDULED NECROPSY DAY 21
57389	G	25.	25.	24.	SCHEDULED NECROPSY DAY 21
57390	G	25.	25.	25.	SCHEDULED NECROPSY DAY 21
57394	G	26.	31.	27.	SCHEDULED NECROPSY DAY 21
57404	G	26.	24.	24.	SCHEDULED NECROPSY DAY 21
MEAN		24.	26.	24.	
S.D.		2.3	2.4	1.9	
S.E.		0.5	0.5	0.4	
N		21	21	21	

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE A7

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 10
SPONSOR:E.I. DUPONT INDIVIDUAL FOOD CONSUMPTION DURING GESTATION [G/ANIMAL/DAY]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY	0- 6	6- 7	7- 8	8- 9	9-10	10-11	11-12	12-13	13-14
DAMS FROM GROUP 4: 1000 MG/KG/DAY											
57309	G		21.	16.	20.	17.	20.	19.	27.	22.	39.
57310	G		19.	17.	18.	21.	18.	18.	19.	19.	21.
57315	G		18.	16.	12.	15.	14.	38.	27.	14.	18.
57316	G		18.	14.	19.	18.	14.	18.	24.	17.	22.
57323	G		22.	19.	20.	19.	19.	17.	23.	22.	21.
57328	G		24.	17.	22.	18.	23.	18.	21.	26.	26.
57330	G		18.	10.	13.	18.	15.	21.	20.	18.	20.
57336	G		20.	13.	19.	16.	19.	21.	17.	21.	19.
57338	G		22.	15.	19.	19.	18.	16.	14.	20.	17.
57342	G		19.	11.	12.	13.	15.	17.	16.	16.	19.
57349	G		22.	5.	18.	18.	18.	17.	22.	22.	18.
57351	G		23.	18.	16.	16.	18.	18.	21.	20.	18.
57359	G		20.	18.	20.	21.	22.	19.	19.	22.	21.
57362	G		20.	19.	22.	18.	18.	20.	17.	23.	19.
57363	G		23.	2.	0.	0.	15.	25.	26.	24.	23.
57366	G		22.	21.	19.	22.	17.	22.	23.	20.	23.
57374	G		21.	15.	15.	20.	16.	16.	23.	21.	20.
57378	G		18.	16.	12.	13.	15.	17.	18.	19.	19.
57382	G		25.	12.	20.	24.	19.	22.	24.	19.	26.
57388	G		23.	11.	17.	22.	18.	20.	7.	8.	14.
57391	G		19.	7.	11.	13.	15.	23.	20.	17.	22.
57409	G		24.	20.	22.	21.	19.	24.	23.	26.	25.
MEAN			21.	14.	17.	17.	18.	20.	21.	20.	21.
S.D.			2.2	4.9	5.1	4.9	2.4	4.7	4.6	4.0	4.9
S.E.			0.5	1.1	1.1	1.0	0.5	1.0	1.0	0.9	1.0
N			22	22	22	22	22	22	22	22	22

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE A7

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 11
SPONSOR:E.I. DUPONT INDIVIDUAL FOOD CONSUMPTION DURING GESTATION [G/ANIMAL/DAY]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 14-15	15-16	16-17	17-18	18-19	19-20	20-21	6- 9	9-12
DAMS FROM GROUP 4: 1000 MG/KG/DAY										
57309	G	23.	28.	27.	28.	27.	24.	NA	18.	22.
57310	G	19.	23.	19.	27.	26.	21.	NA	19.	18.
57315	G	16.	21.	16.	23.	22.	14.	NA	14.	26.
57316	G	16.	25.	23.	24.	19.	19.	22.	17.	19.
57323	G	21.	22.	27.	23.	30.	21.	22.	19.	20.
57328	G	22.	15.	11.	17.	12.	NA	NA	19.	21.
57330	G	20.	22.	21.	27.	28.	24.	22.	14.	19.
57336	G	18.	24.	25.	25.	21.	19.	13.	16.	19.
57338	G	20.	20.	19.	17.	21.	18.	19.	18.	16.
57342	G	19.	23.	22.	26.	25.	27.	22.	12.	16.
57349	G	21.	24.	27.	25.	27.	32.	24.	14.	19.
57351	G	21.	22.	28.	33.	28.	26.	27.	17.	19.
57359	G	23.	23.	23.	27.	24.	24.	17.	20.	20.
57362	G	21.	20.	26.	26.	24.	26.	8.	20.	18.
57363	G	26.	23.	23.	28.	33.	25.	28.	1.	22.
57366	G	21.	22.	24.	24.	27.	24.	27.	21.	21.
57374	G	22.	22.	21.	20.	22.	11.	NA	17.	18.
57378	G	19.	24.	21.	28.	26.	22.	21.	14.	17.
57382	G	24.	30.	27.	32.	31.	25.	NA	19.	22.
57388	G	21.	21.	24.	26.	26.	24.	NA	17.	15.
57391	G	15.	27.	19.	29.	29.	21.	NA	10.	19.
57409	G	20.	26.	27.	29.	29.	20.	20.	21.	22.
MEAN		20.	23.	23.	26.	25.	22.	21.	16.	19.
S.D.		2.6	3.1	4.2	4.0	4.6	4.6	5.5	4.5	2.5
S.E.		0.6	0.7	0.9	0.9	1.0	1.0	1.5	1.0	0.5
N		22	22	22	22	22	21	14	22	22

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN
NA = NOT APPLICABLE

TABLE A7

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 12
SPONSOR:E.I. DUPONT INDIVIDUAL FOOD CONSUMPTION DURING GESTATION [G/ANIMAL/DAY]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 12-18	18-21	6-21	
DAMS FROM GROUP 4: 1000 MG/KG/DAY					
57309	G	28.	26.	24.	SCHEDULED NECROPSY DAY 21
57310	G	21.	24.	20.	SCHEDULED NECROPSY DAY 21
57315	G	18.	18.	19.	SCHEDULED NECROPSY DAY 21
57316	G	21.	20.	20.	SCHEDULED NECROPSY DAY 21
57323	G	23.	24.	22.	SCHEDULED NECROPSY DAY 21
57328	G	20.	NA	NA	GRAVID, DIED DAY 20
57330	G	21.	25.	20.	SCHEDULED NECROPSY DAY 21
57336	G	22.	18.	19.	SCHEDULED NECROPSY DAY 21
57338	G	19.	19.	18.	SCHEDULED NECROPSY DAY 21
57342	G	21.	25.	19.	SCHEDULED NECROPSY DAY 21
57349	G	23.	28.	21.	SCHEDULED NECROPSY DAY 21
57351	G	24.	27.	22.	SCHEDULED NECROPSY DAY 21
57359	G	23.	22.	22.	SCHEDULED NECROPSY DAY 21
57362	G	23.	19.	20.	SCHEDULED NECROPSY DAY 21
57363	G	25.	29.	20.	SCHEDULED NECROPSY DAY 21
57366	G	22.	26.	22.	SCHEDULED NECROPSY DAY 21
57374	G	21.	17.	19.	SCHEDULED NECROPSY DAY 21
57378	G	22.	23.	19.	SCHEDULED NECROPSY DAY 21
57382	G	26.	28.	24.	SCHEDULED NECROPSY DAY 21
57388	G	19.	25.	19.	SCHEDULED NECROPSY DAY 21
57391	G	22.	25.	19.	SCHEDULED NECROPSY DAY 21
57409	G	26.	23.	23.	SCHEDULED NECROPSY DAY 21
MEAN		22.	23.	21.	
S.D.		2.5	3.6	1.8	
S.E.		0.5	0.8	0.4	
N		22	21	21	

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN
NA = NOT APPLICABLE

PGFWv4.11
12/03/2009

TABLE A8

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT INDIVIDUAL FOOD CONSUMPTION DURING GESTATION [G/KG/DAY]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY	0- 6	6- 7	7- 8	8- 9	9-10	10-11	11-12	12-13	13-14
DAMS FROM GROUP 1: 0 MG/KG/DAY											
57312	G		81.	78.	78.	76.	84.	82.	66.	80.	72.
57320	G		70.	67.	65.	65.	75.	69.	64.	83.	78.
57322	G		78.	77.	80.	82.	84.	67.	84.	68.	85.
57325	G		86.	85.	86.	76.	87.	91.	67.	84.	94.
57326	G		82.	72.	77.	76.	64.	73.	77.	69.	68.
57329	G		80.	83.	75.	70.	70.	62.	75.	70.	72.
57333	G		69.	94.	84.	83.	88.	92.	74.	70.	82.
57352	G		80.	69.	71.	70.	73.	62.	71.	64.	66.
57356	G		67.	71.	73.	78.	57.	73.	72.	59.	74.
57360	G		78.	68.	73.	68.	61.	70.	69.	52.	55.
57364	G		NA	69.	42.	84.	51.	99.	88.	58.	57.
57369	G		71.	77.	68.	74.	73.	68.	81.	70.	59.
57370	G		75.	75.	90.	63.	72.	77.	63.	68.	67.
57371	G		69.	71.	71.	70.	69.	71.	66.	73.	71.
57379	G		75.	71.	75.	74.	82.	80.	82.	NA	64.
57380	G		86.	78.	78.	109.	91.	68.	85.	80.	73.
57381	G		76.	71.	67.	72.	71.	67.	84.	73.	66.
57385	G		69.	81.	72.	71.	69.	69.	74.	67.	68.
57392	G		82.	69.	82.	80.	69.	75.	86.	71.	76.
57397	G		76.	74.	77.	59.	82.	79.	62.	77.	66.
57398	G		76.	62.	77.	79.	69.	82.	57.	77.	72.
57406	G		71.	66.	72.	58.	70.	72.	58.	67.	72.
MEAN			76.	74.	74.	74.	73.	75.	73.	70.	71.
S.D.			5.7	7.3	9.5	10.5	10.2	9.7	9.5	8.2	9.0
S.E.			1.2	1.6	2.0	2.2	2.2	2.1	2.0	1.8	1.9
N			21	22	22	22	22	22	22	21	22

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN
NA = NOT APPLICABLE

TABLE A8

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 2
SPONSOR:E.I. DUPONT INDIVIDUAL FOOD CONSUMPTION DURING GESTATION [G/KG/DAY]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 14-15	15-16	16-17	17-18	18-19	19-20	20-21	6- 9	9-12
DAMS FROM GROUP 1: 0 MG/KG/DAY										
57312	G	76.	69.	75.	79.	68.	79.	62.	77.	76.
57320	G	60.	74.	71.	74.	63.	50.	55.	66.	69.
57322	G	63.	79.	85.	67.	75.	58.	62.	80.	80.
57325	G	81.	71.	84.	66.	66.	73.	63.	84.	83.
57326	G	66.	77.	69.	64.	72.	57.	67.	74.	70.
57329	G	65.	78.	72.	63.	61.	55.	51.	75.	69.
57333	G	79.	80.	73.	73.	66.	72.	70.	88.	86.
57352	G	64.	69.	73.	65.	64.	59.	54.	71.	68.
57356	G	66.	74.	74.	76.	56.	51.	70.	73.	66.
57360	G	57.	65.	57.	52.	71.	45.	56.	70.	67.
57364	G	50.	83.	56.	48.	65.	71.	70.	65.	81.
57369	G	58.	65.	63.	61.	53.	59.	53.	72.	75.
57370	G	74.	63.	72.	76.	62.	61.	58.	77.	71.
57371	G	66.	71.	72.	71.	59.	72.	48.	71.	68.
57379	G	75.	NA	69.	48.	78.	67.	75.	73.	80.
57380	G	66.	69.	72.	59.	66.	63.	54.	87.	80.
57381	G	77.	71.	77.	72.	73.	58.	64.	70.	73.
57385	G	52.	82.	72.	61.	75.	60.	57.	76.	72.
57392	G	63.	88.	76.	81.	69.	61.	60.	78.	77.
57397	G	67.	57.	76.	67.	61.	62.	62.	70.	73.
57398	G	54.	65.	60.	55.	58.	55.	63.	73.	70.
57406	G	67.	63.	83.	57.	67.	57.	66.	65.	66.
MEAN		66.	72.	72.	65.	66.	61.	61.	74.	74.
S.D.		8.6	7.8	7.7	9.6	6.5	8.3	7.0	6.3	5.9
S.E.		1.8	1.7	1.6	2.0	1.4	1.8	1.5	1.3	1.3
N		22	21	22	22	22	22	22	22	22

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN
NA = NOT APPLICABLE

TABLE A8

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 3
SPONSOR:E.I. DUPONT INDIVIDUAL FOOD CONSUMPTION DURING GESTATION [G/KG/DAY]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 12-18	18-21	6-21	
DAMS FROM GROUP 1: 0 MG/KG/DAY					
57312	G	75.	70.	75.	SCHEDULED NECROPSY DAY 21
57320	G	74.	55.	66.	SCHEDULED NECROPSY DAY 21
57322	G	74.	65.	74.	SCHEDULED NECROPSY DAY 21
57325	G	79.	68.	77.	SCHEDULED NECROPSY DAY 21
57326	G	68.	65.	68.	SCHEDULED NECROPSY DAY 21
57329	G	69.	56.	66.	SCHEDULED NECROPSY DAY 21
57333	G	75.	69.	77.	SCHEDULED NECROPSY DAY 21
57352	G	66.	59.	66.	SCHEDULED NECROPSY DAY 21
57356	G	70.	59.	67.	SCHEDULED NECROPSY DAY 21
57360	G	56.	58.	62.	SCHEDULED NECROPSY DAY 21
57364	G	57.	68.	66.	SCHEDULED NECROPSY DAY 21
57369	G	62.	56.	66.	SCHEDULED NECROPSY DAY 21
57370	G	69.	61.	69.	SCHEDULED NECROPSY DAY 21
57371	G	71.	59.	68.	SCHEDULED NECROPSY DAY 21
57379	G	64.	74.	73.	SCHEDULED NECROPSY DAY 21
57380	G	70.	61.	73.	SCHEDULED NECROPSY DAY 21
57381	G	72.	65.	69.	SCHEDULED NECROPSY DAY 21
57385	G	67.	65.	68.	SCHEDULED NECROPSY DAY 21
57392	G	76.	63.	73.	SCHEDULED NECROPSY DAY 21
57397	G	69.	61.	67.	SCHEDULED NECROPSY DAY 21
57398	G	63.	59.	63.	SCHEDULED NECROPSY DAY 21
57406	G	68.	64.	65.	SCHEDULED NECROPSY DAY 21
MEAN		69.	63.	69.	
S.D.		5.9	5.0	4.3	
S.E.		1.3	1.1	0.9	
N		22	22	22	

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE A8

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 4
SPONSOR:E.I. DUPONT INDIVIDUAL FOOD CONSUMPTION DURING GESTATION [G/KG/DAY]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY	0- 6	6- 7	7- 8	8- 9	9-10	10-11	11-12	12-13	13-14
DAMS FROM GROUP 2: 10 MG/KG/DAY											
57307	G		81.	82.	74.	80.	75.	83.	82.	69.	88.
57308	G		79.	83.	76.	82.	74.	78.	77.	76.	74.
57317	G		69.	72.	71.	67.	79.	61.	78.	74.	46.
57319	G		74.	70.	72.	68.	71.	66.	68.	77.	75.
57324	G		79.	67.	71.	66.	76.	78.	57.	67.	66.
57332	G		85.	86.	81.	87.	72.	87.	86.	72.	84.
57334	G		71.	61.	70.	48.	78.	67.	52.	64.	63.
57335	G		92.	83.	81.	80.	66.	81.	79.	69.	77.
57337	G		73.	83.	63.	77.	69.	68.	83.	65.	64.
57339	G		75.	74.	56.	79.	63.	75.	77.	66.	65.
57340	G		76.	78.	71.	87.	75.	71.	82.	71.	76.
57343	G		81.	76.	64.	85.	62.	71.	74.	76.	78.
57347	G		85.	67.	92.	68.	76.	87.	71.	73.	60.
57350	G		72.	74.	67.	76.	78.	73.	84.	73.	74.
57353	G		70.	74.	60.	66.	66.	68.	68.	70.	71.
57358	G		81.	69.	65.	61.	85.	65.	59.	76.	57.
57367	G		87.	67.	81.	62.	75.	91.	62.	102.	70.
57373	G		68.	67.	59.	72.	70.	68.	70.	68.	74.
57376	G		86.	68.	76.	75.	74.	78.	95.	82.	86.
57393	G		72.	66.	73.	72.	58.	70.	69.	71.	64.
57403	G		73.	75.	74.	63.	69.	68.	58.	76.	71.
57405	NG		77.	68.	72.	75.	74.	70.	65.	62.	72.
MEAN			78.	73.	71.	72.	72.	74.	73.	73.	71.
S.D.			6.7	7.0	8.6	9.9	6.4	8.2	11.1	8.0	10.0
S.E.			1.5	1.5	1.9	2.2	1.4	1.8	2.4	1.7	2.2
N			21	21	21	21	21	21	21	21	21

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE A8

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 5
SPONSOR:E.I. DUPONT INDIVIDUAL FOOD CONSUMPTION DURING GESTATION [G/KG/DAY]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 14-15	15-16	16-17	17-18	18-19	19-20	20-21	6- 9	9-12
DAMS FROM GROUP 2: 10 MG/KG/DAY										
57307	G	69.	78.	73.	80.	74.	62.	75.	77.	80.
57308	G	73.	71.	58.	69.	71.	55.	68.	79.	75.
57317	G	70.	57.	63.	36.	54.	90.	46.	71.	74.
57319	G	71.	72.	72.	64.	72.	66.	56.	69.	69.
57324	G	68.	63.	64.	81.	65.	68.	65.	67.	72.
57332	G	75.	82.	80.	76.	65.	60.	55.	85.	81.
57334	G	67.	57.	72.	67.	60.	58.	53.	61.	65.
57335	G	70.	91.	74.	71.	73.	53.	70.	82.	75.
57337	G	70.	73.	71.	67.	70.	58.	66.	74.	74.
57339	G	66.	74.	76.	70.	77.	61.	67.	70.	72.
57340	G	71.	81.	75.	78.	72.	61.	63.	77.	77.
57343	G	66.	65.	72.	82.	70.	62.	63.	75.	68.
57347	G	77.	55.	82.	70.	67.	65.	59.	76.	78.
57350	G	73.	76.	79.	74.	78.	56.	67.	73.	79.
57353	G	63.	78.	75.	74.	72.	64.	43.	67.	68.
57358	G	59.	57.	71.	55.	60.	57.	52.	65.	68.
57367	G	65.	58.	74.	71.	56.	70.	59.	70.	77.
57373	G	66.	72.	53.	64.	36.	52.	50.	66.	68.
57376	G	84.	79.	82.	81.	83.	64.	71.	73.	82.
57393	G	63.	73.	62.	60.	66.	65.	62.	69.	67.
57403	G	78.	64.	76.	70.	67.	67.	67.	70.	65.
57405	NG	61.	65.	59.	74.	73.	81.	52.	71.	70.
MEAN		70.	70.	72.	70.	67.	63.	61.	72.	73.
S.D.		5.7	9.9	7.7	10.5	10.1	8.0	8.6	5.9	5.4
S.E.		1.3	2.2	1.7	2.3	2.2	1.7	1.9	1.3	1.2
N		21	21	21	21	21	21	21	21	21

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE A8

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 6
SPONSOR:E.I. DUPONT INDIVIDUAL FOOD CONSUMPTION DURING GESTATION [G/KG/DAY]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 12-18	18-21	6-21	
DAMS FROM GROUP 2: 10 MG/KG/DAY					
57307	G	76.	71.	76.	SCHEDULED NECROPSY DAY 21
57308	G	71.	65.	71.	SCHEDULED NECROPSY DAY 21
57317	G	56.	64.	63.	SCHEDULED NECROPSY DAY 21
57319	G	72.	64.	70.	SCHEDULED NECROPSY DAY 21
57324	G	69.	65.	69.	SCHEDULED NECROPSY DAY 21
57332	G	80.	60.	74.	SCHEDULED NECROPSY DAY 21
57334	G	66.	57.	63.	SCHEDULED NECROPSY DAY 21
57335	G	77.	65.	74.	SCHEDULED NECROPSY DAY 21
57337	G	67.	63.	71.	SCHEDULED NECROPSY DAY 21
57339	G	71.	68.	68.	SCHEDULED NECROPSY DAY 21
57340	G	75.	66.	73.	SCHEDULED NECROPSY DAY 21
57343	G	74.	65.	71.	SCHEDULED NECROPSY DAY 21
57347	G	69.	64.	70.	SCHEDULED NECROPSY DAY 21
57350	G	76.	67.	74.	SCHEDULED NECROPSY DAY 21
57353	G	72.	59.	67.	SCHEDULED NECROPSY DAY 21
57358	G	63.	57.	63.	SCHEDULED NECROPSY DAY 21
57367	G	73.	62.	71.	SCHEDULED NECROPSY DAY 21
57373	G	67.	47.	62.	SCHEDULED NECROPSY DAY 21
57376	G	82.	72.	77.	SCHEDULED NECROPSY DAY 21
57393	G	65.	65.	65.	SCHEDULED NECROPSY DAY 21
57403	G	73.	67.	68.	SCHEDULED NECROPSY DAY 21
57405	NG	65.	70.	70.	SCHEDULED NECROPSY DAY 21
MEAN		71.	63.	70.	
S.D.		6.0	5.4	4.4	
S.E.		1.3	1.2	1.0	
N		21	21	21	

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE A8

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 7
SPONSOR:E.I. DUPONT INDIVIDUAL FOOD CONSUMPTION DURING GESTATION [G/KG/DAY]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY	0- 6	6- 7	7- 8	8- 9	9-10	10-11	11-12	12-13	13-14
DAMS FROM GROUP 3: 100 MG/KG/DAY											
57314	G		79.	74.	73.	82.	67.	72.	77.	67.	67.
57318	NG		79.	67.	70.	78.	69.	62.	75.	56.	51.
57321	G		82.	70.	79.	71.	85.	74.	71.	88.	62.
57327	G		80.	87.	75.	81.	84.	66.	82.	81.	82.
57331	G		80.	70.	78.	61.	67.	76.	60.	69.	65.
57344	G		82.	68.	78.	58.	83.	68.	61.	77.	71.
57345	G		72.	53.	52.	78.	56.	77.	82.	84.	61.
57348	G		93.	80.	82.	84.	75.	87.	85.	84.	73.
57354	G		82.	41.	84.	79.	71.	58.	74.	61.	60.
57357	G		71.	56.	63.	77.	69.	77.	68.	62.	68.
57361	G		93.	76.	68.	87.	69.	84.	80.	66.	66.
57365	G		82.	63.	79.	71.	79.	77.	62.	82.	69.
57368	G		82.	71.	74.	69.	69.	61.	67.	79.	62.
57372	G		85.	83.	59.	94.	67.	91.	92.	75.	79.
57375	G		72.	62.	53.	68.	59.	73.	58.	75.	63.
57383	G		76.	74.	72.	77.	72.	71.	68.	70.	72.
57386	G		84.	64.	71.	73.	75.	70.	76.	79.	52.
57387	G		77.	79.	81.	73.	68.	71.	70.	83.	58.
57389	G		75.	78.	73.	72.	74.	80.	69.	71.	67.
57390	G		94.	83.	92.	80.	86.	71.	93.	81.	77.
57394	G		76.	76.	78.	56.	83.	78.	78.	61.	85.
57404	G		83.	69.	79.	70.	79.	78.	67.	89.	67.
MEAN			81.	70.	73.	74.	73.	74.	73.	75.	68.
S.D.			6.6	11.1	9.9	9.3	8.3	7.8	9.9	8.7	8.1
S.E.			1.4	2.4	2.2	2.0	1.8	1.7	2.2	1.9	1.8
N			21	21	21	21	21	21	21	21	21

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE A8

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 8
SPONSOR:E.I. DUPONT INDIVIDUAL FOOD CONSUMPTION DURING GESTATION [G/KG/DAY]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 14-15	15-16	16-17	17-18	18-19	19-20	20-21	6- 9	9-12
DAMS FROM GROUP 3: 100 MG/KG/DAY										
57314	G	66.	73.	56.	71.	74.	65.	74.	76.	72.
57318	NG	51.	68.	66.	29.	71.	66.	68.	73.	68.
57321	G	78.	64.	78.	82.	70.	60.	65.	72.	78.
57327	G	64.	81.	84.	71.	78.	57.	72.	82.	76.
57331	G	73.	65.	68.	77.	66.	69.	63.	69.	67.
57344	G	81.	58.	86.	81.	64.	70.	61.	68.	72.
57345	G	69.	73.	80.	77.	81.	65.	71.	62.	71.
57348	G	75.	84.	66.	82.	73.	62.	65.	82.	84.
57354	G	74.	77.	61.	67.	63.	60.	NA	67.	68.
57357	G	54.	79.	75.	68.	70.	54.	NA	67.	70.
57361	G	65.	76.	70.	78.	72.	61.	58.	78.	78.
57365	G	79.	60.	87.	65.	73.	17.	65.	72.	72.
57368	G	64.	63.	65.	65.	73.	65.	74.	70.	65.
57372	G	74.	87.	70.	69.	74.	60.	NA	79.	84.
57375	G	64.	62.	56.	62.	73.	54.	64.	61.	62.
57383	G	67.	68.	68.	63.	68.	59.	NA	75.	72.
57386	G	71.	62.	75.	77.	72.	80.	53.	71.	74.
57387	G	67.	66.	90.	61.	68.	70.	48.	77.	71.
57389	G	68.	69.	77.	73.	55.	67.	57.	73.	73.
57390	G	63.	83.	86.	74.	73.	62.	61.	85.	85.
57394	G	70.	69.	81.	70.	70.	86.	68.	69.	81.
57404	G	75.	73.	76.	86.	63.	68.	54.	71.	75.
MEAN		70.	71.	74.	72.	70.	62.	63.	73.	74.
S.D.		6.4	8.5	10.0	7.2	5.7	13.0	7.5	6.4	6.2
S.E.		1.4	1.9	2.2	1.6	1.2	2.8	1.8	1.4	1.4
N		21	21	21	21	21	21	17	21	21

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN
NA = NOT APPLICABLE

TABLE A8

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 9
SPONSOR:E.I. DUPONT INDIVIDUAL FOOD CONSUMPTION DURING GESTATION [G/KG/DAY]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 12-18	18-21	6-21	
DAMS FROM GROUP 3: 100 MG/KG/DAY					
57314	G	67.	70.	70.	SCHEDULED NECROPSY DAY 21
57318	NG	55.	70.	64.	SCHEDULED NECROPSY DAY 21
57321	G	76.	65.	73.	SCHEDULED NECROPSY DAY 21
57327	G	78.	70.	75.	SCHEDULED NECROPSY DAY 21
57331	G	71.	66.	68.	SCHEDULED NECROPSY DAY 21
57344	G	76.	66.	70.	SCHEDULED NECROPSY DAY 21
57345	G	75.	72.	70.	SCHEDULED NECROPSY DAY 21
57348	G	78.	68.	76.	SCHEDULED NECROPSY DAY 21
57354	G	66.	NA	NA	SCHEDULED NECROPSY DAY 21
57357	G	68.	NA	NA	SCHEDULED NECROPSY DAY 21
57361	G	69.	63.	72.	SCHEDULED NECROPSY DAY 21
57365	G	74.	50.	68.	SCHEDULED NECROPSY DAY 21
57368	G	66.	70.	69.	SCHEDULED NECROPSY DAY 21
57372	G	77.	NA	NA	SCHEDULED NECROPSY DAY 21
57375	G	62.	65.	62.	SCHEDULED NECROPSY DAY 21
57383	G	68.	NA	NA	SCHEDULED NECROPSY DAY 21
57386	G	68.	68.	71.	SCHEDULED NECROPSY DAY 21
57387	G	72.	63.	69.	SCHEDULED NECROPSY DAY 21
57389	G	72.	60.	69.	SCHEDULED NECROPSY DAY 21
57390	G	77.	65.	77.	SCHEDULED NECROPSY DAY 21
57394	G	72.	74.	75.	SCHEDULED NECROPSY DAY 21
57404	G	79.	61.	73.	SCHEDULED NECROPSY DAY 21
MEAN		72.	66.	71.	
S.D.		4.9	5.5	3.7	
S.E.		1.1	1.3	0.9	
N		21	17	17	

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN
NA = NOT APPLICABLE

TABLE A8

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 10
SPONSOR:E.I. DUPONT INDIVIDUAL FOOD CONSUMPTION DURING GESTATION [G/KG/DAY]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY	0- 6	6- 7	7- 8	8- 9	9-10	10-11	11-12	12-13	13-14
DAMS FROM GROUP 4: 1000 MG/KG/DAY											
57309	G		74.	53.	66.	55.	65.	60.	83.	66.	115.
57310	G		74.	63.	65.	75.	63.	63.	66.	65.	71.
57315	G		73.	60.	45.	56.	51.	136.	95.	49.	62.
57316	G		71.	52.	69.	65.	50.	63.	82.	57.	73.
57323	G		79.	64.	67.	63.	62.	55.	74.	70.	65.
57328	G		82.	55.	71.	57.	71.	55.	63.	77.	75.
57330	G		69.	37.	49.	66.	54.	74.	69.	62.	67.
57336	G		75.	45.	66.	54.	63.	69.	56.	69.	61.
57338	G		79.	51.	65.	64.	60.	53.	46.	65.	54.
57342	G		69.	39.	43.	47.	53.	59.	55.	54.	64.
57349	G		83.	18.	66.	64.	63.	57.	73.	72.	59.
57351	G		86.	64.	57.	56.	62.	60.	69.	65.	58.
57359	G		77.	66.	73.	74.	75.	64.	63.	72.	67.
57362	G		79.	71.	81.	66.	65.	71.	60.	80.	64.
57363	G		83.	7.	0.	0.	60.	93.	92.	82.	77.
57366	G		76.	69.	61.	70.	53.	67.	69.	60.	68.
57374	G		70.	48.	49.	63.	50.	50.	70.	62.	58.
57378	G		67.	57.	43.	48.	54.	59.	62.	64.	63.
57382	G		87.	41.	67.	78.	61.	70.	75.	59.	79.
57388	G		84.	39.	61.	77.	62.	67.	24.	28.	49.
57391	G		73.	25.	40.	47.	54.	80.	67.	56.	72.
57409	G		84.	66.	73.	69.	62.	77.	72.	80.	76.
MEAN			77.	50.	58.	60.	60.	68.	68.	64.	68.
S.D.			6.0	17.0	17.2	16.2	6.6	18.1	15.0	11.9	13.0
S.E.			1.3	3.6	3.7	3.5	1.4	3.9	3.2	2.5	2.8
N			22	22	22	22	22	22	22	22	22

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE A8

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 11
SPONSOR:E.I. DUPONT INDIVIDUAL FOOD CONSUMPTION DURING GESTATION [G/KG/DAY]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 14-15	15-16	16-17	17-18	18-19	19-20	20-21	6- 9	9-12
DAMS FROM GROUP 4: 1000 MG/KG/DAY										
57309	G	66.	77.	71.	70.	65.	56.	NA	59.	69.
57310	G	63.	74.	58.	79.	73.	57.	NA	69.	63.
57315	G	54.	68.	51.	70.	63.	39.	NA	52.	93.
57316	G	53.	80.	70.	70.	53.	52.	59.	62.	66.
57323	G	64.	65.	76.	62.	77.	52.	53.	63.	65.
57328	G	62.	42.	31.	47.	32.	NA	NA	61.	64.
57330	G	66.	70.	65.	79.	78.	65.	58.	52.	67.
57336	G	57.	75.	75.	71.	58.	51.	35.	55.	63.
57338	G	63.	62.	57.	50.	59.	49.	51.	61.	53.
57342	G	61.	72.	66.	74.	67.	69.	55.	43.	56.
57349	G	67.	74.	79.	70.	72.	82.	60.	50.	64.
57351	G	65.	66.	80.	89.	71.	64.	64.	60.	64.
57359	G	72.	69.	67.	74.	63.	61.	42.	72.	68.
57362	G	69.	64.	80.	76.	67.	70.	22.	74.	65.
57363	G	83.	70.	68.	78.	88.	65.	70.	4.	83.
57366	G	61.	62.	65.	62.	67.	58.	64.	68.	64.
57374	G	63.	62.	58.	53.	56.	28.	NA	54.	55.
57378	G	61.	75.	63.	80.	71.	58.	55.	50.	60.
57382	G	71.	85.	73.	82.	76.	59.	NA	63.	70.
57388	G	70.	68.	74.	76.	72.	64.	NA	60.	52.
57391	G	48.	84.	57.	84.	80.	56.	NA	36.	66.
57409	G	59.	75.	76.	78.	74.	50.	49.	69.	70.
MEAN		64.	70.	66.	72.	67.	57.	53.	56.	65.
S.D.		7.3	9.1	11.4	10.9	11.5	11.3	12.6	14.9	9.0
S.E.		1.6	1.9	2.4	2.3	2.5	2.5	3.4	3.2	1.9
N		22	22	22	22	22	21	14	22	22

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN
NA = NOT APPLICABLE

TABLE A8

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 12
SPONSOR:E.I. DUPONT INDIVIDUAL FOOD CONSUMPTION DURING GESTATION [G/KG/DAY]
SPONSOR NO.:18405-841

	PREGNANCY STATUS	DAY 12-18	18-21	6-21	
DAMS FROM GROUP 4: 1000 MG/KG/DAY					
57309	G	77.	NA	NA	SCHEDULED NECROPSY DAY 21
57310	G	67.	NA	NA	SCHEDULED NECROPSY DAY 21
57315	G	59.	NA	NA	SCHEDULED NECROPSY DAY 21
57316	G	67.	55.	64.	SCHEDULED NECROPSY DAY 21
57323	G	68.	60.	65.	SCHEDULED NECROPSY DAY 21
57328	G	57.	NA	NA	GRAVID, DIED DAY 20
57330	G	67.	68.	65.	SCHEDULED NECROPSY DAY 21
57336	G	68.	49.	59.	SCHEDULED NECROPSY DAY 21
57338	G	59.	52.	56.	SCHEDULED NECROPSY DAY 21
57342	G	66.	65.	59.	SCHEDULED NECROPSY DAY 21
57349	G	71.	73.	65.	SCHEDULED NECROPSY DAY 21
57351	G	72.	67.	66.	SCHEDULED NECROPSY DAY 21
57359	G	69.	56.	67.	SCHEDULED NECROPSY DAY 21
57362	G	74.	53.	65.	SCHEDULED NECROPSY DAY 21
57363	G	78.	75.	64.	SCHEDULED NECROPSY DAY 21
57366	G	62.	63.	63.	SCHEDULED NECROPSY DAY 21
57374	G	59.	NA	NA	SCHEDULED NECROPSY DAY 21
57378	G	69.	61.	60.	SCHEDULED NECROPSY DAY 21
57382	G	74.	NA	NA	SCHEDULED NECROPSY DAY 21
57388	G	62.	NA	NA	SCHEDULED NECROPSY DAY 21
57391	G	69.	NA	NA	SCHEDULED NECROPSY DAY 21
57409	G	75.	58.	67.	SCHEDULED NECROPSY DAY 21
MEAN		68.	61.	63.	
S.D.		6.1	7.9	3.4	
S.E.		1.3	2.1	0.9	
N		22	14	14	

G = GRAVID NG = NONGRAVID - WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN
NA = NOT APPLICABLE

PGFWv4.11
12/03/2009

TABLE A9

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT INDIVIDUAL MATERNAL MACROSCOPIC FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 1: 0 MG/KG/DAY	MATERNAL GROSS OBSERVATION
57312	NO SIGNIFICANT CHANGES OBSERVED
57320	NO SIGNIFICANT CHANGES OBSERVED
57322	NO SIGNIFICANT CHANGES OBSERVED
57325	NO SIGNIFICANT CHANGES OBSERVED
57326	NO SIGNIFICANT CHANGES OBSERVED
57329	NO SIGNIFICANT CHANGES OBSERVED
57333	NO SIGNIFICANT CHANGES OBSERVED
57352	NO SIGNIFICANT CHANGES OBSERVED
57356	NO SIGNIFICANT CHANGES OBSERVED
57360	NO SIGNIFICANT CHANGES OBSERVED
57364	NO SIGNIFICANT CHANGES OBSERVED
57369	NO SIGNIFICANT CHANGES OBSERVED
57370	NO SIGNIFICANT CHANGES OBSERVED
57371	NO SIGNIFICANT CHANGES OBSERVED
57379	NO SIGNIFICANT CHANGES OBSERVED
57380	NO SIGNIFICANT CHANGES OBSERVED
57381	NO SIGNIFICANT CHANGES OBSERVED
57385	NO SIGNIFICANT CHANGES OBSERVED
57392	NO SIGNIFICANT CHANGES OBSERVED
57397	NO SIGNIFICANT CHANGES OBSERVED
57398	NO SIGNIFICANT CHANGES OBSERVED
57406	NO SIGNIFICANT CHANGES OBSERVED

TABLE A9

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 2
SPONSOR:E.I. DUPONT INDIVIDUAL MATERNAL MACROSCOPIC FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 2: 10 MG/KG/DAY	MATERNAL GROSS OBSERVATION
57307	NO SIGNIFICANT CHANGES OBSERVED
57308	NO SIGNIFICANT CHANGES OBSERVED
57317	KIDNEYS: AREA(S), DEPRESSED FEW, IRREGULARLY SHAPED, IN CORTEX, BILATERAL
57319	NO SIGNIFICANT CHANGES OBSERVED
57324	NO SIGNIFICANT CHANGES OBSERVED
57332	NO SIGNIFICANT CHANGES OBSERVED
57334	NO SIGNIFICANT CHANGES OBSERVED
57335	NO SIGNIFICANT CHANGES OBSERVED
57337	NO SIGNIFICANT CHANGES OBSERVED
57339	NO SIGNIFICANT CHANGES OBSERVED
57340	NO SIGNIFICANT CHANGES OBSERVED
57343	NO SIGNIFICANT CHANGES OBSERVED
57347	NO SIGNIFICANT CHANGES OBSERVED
57350	NO SIGNIFICANT CHANGES OBSERVED
57353	NO SIGNIFICANT CHANGES OBSERVED
57358	NO SIGNIFICANT CHANGES OBSERVED
57367	NO SIGNIFICANT CHANGES OBSERVED
57373	NO SIGNIFICANT CHANGES OBSERVED
57376	NO SIGNIFICANT CHANGES OBSERVED
57393	NO SIGNIFICANT CHANGES OBSERVED
57403	NO SIGNIFICANT CHANGES OBSERVED
57405	NONGRAVID -- AMMONIUM SULFIDE NEGATIVE

TABLE A9

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 3
SPONSOR:E.I. DUPONT INDIVIDUAL MATERNAL MACROSCOPIC FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 3: 100 MG/KG/DAY	MATERNAL GROSS OBSERVATION
57314	NO SIGNIFICANT CHANGES OBSERVED
57318	NONGRAVID -- AMMONIUM SULFIDE NEGATIVE
57321	NO SIGNIFICANT CHANGES OBSERVED
57327	NO SIGNIFICANT CHANGES OBSERVED
57331	NO SIGNIFICANT CHANGES OBSERVED
57344	NO SIGNIFICANT CHANGES OBSERVED
57345	NO SIGNIFICANT CHANGES OBSERVED
57348	NO SIGNIFICANT CHANGES OBSERVED
57354	LIVER: AREA(S), WHITE ONE, IRREGULARLY SHAPED, MEDIAN LOBE DELIVERED GESTATION DAY 21 STOMACH: CONTENTS, DARK RED
57357	JEJUNUM: CONTENTS, DARK RED STOMACH: CONTENTS, DARK RED DELIVERED GESTATION DAY 21
57361	NO SIGNIFICANT CHANGES OBSERVED
57365	NO SIGNIFICANT CHANGES OBSERVED
57368	NO SIGNIFICANT CHANGES OBSERVED
57372	DELIVERED GESTATION DAY 21 SITES ARBITRARILY ASSIGNED STOMACH: CONTENTS, DARK RED
57375	NO SIGNIFICANT CHANGES OBSERVED
57383	DELIVERED GESTATION DAY 21
57386	NO SIGNIFICANT CHANGES OBSERVED
57387	NO SIGNIFICANT CHANGES OBSERVED
57389	NO SIGNIFICANT CHANGES OBSERVED
57390	NO SIGNIFICANT CHANGES OBSERVED
57394	NO SIGNIFICANT CHANGES OBSERVED
57404	NO SIGNIFICANT CHANGES OBSERVED

TABLE A9

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 4
SPONSOR:E.I. DUPONT INDIVIDUAL MATERNAL MACROSCOPIC FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 4: 1000 MG/KG/DAY	MATERNAL GROSS OBSERVATION
57309	DELIVERED GESTATION DAY 21 SITES ARBITRARILY ASSIGNED
57310	DELIVERED GESTATION DAY 21
57315	DELIVERED GESTATION DAY 21
57316	MAMMARY GLAND: MASS 20 X 20 X 10 MM, TAN, RIGHT LATERAL THORACIC, FIRM, MASS #1 PANCREAS: EDEMATOUS STOMACH: CONTENTS, DARK RED DELIVERED GESTATION DAY 21 SITES ARBITRARILY ASSIGNED
57323	NO SIGNIFICANT CHANGES OBSERVED
57328	LIVER: PALE ALL LOBES DIED GESTATION DAY 20 UTERUS: LEFT- 9 FETUSES; RIGHT- 11 FETUSES OVARIES: CORPORA LUTEA- 10, LEFT; 11, RIGHT FETAL GROSS OBSERVATIONS IN UTERO: 17 DEAD FETUSES WITH NO APPARENT MALFORMATIONS; CROWN-RUMP LENGTHS: 2.5 TO 3.0 CM; 10 FEMALES, 7 MALES; 3 LATE RESORPTIONS WITH NO APPARENT MALFORMATIONS, CROWN-RUMP LENGTHS: 2.5 CM, SLIGHT AUTOLYSIS
57330	NO SIGNIFICANT CHANGES OBSERVED
57336	NO SIGNIFICANT CHANGES OBSERVED
57338	NO SIGNIFICANT CHANGES OBSERVED
57342	NO SIGNIFICANT CHANGES OBSERVED
57349	NO SIGNIFICANT CHANGES OBSERVED
57351	NO SIGNIFICANT CHANGES OBSERVED
57359	KIDNEYS: PALE BILATERAL DELIVERED GESTATION DAY 21
57362	NO SIGNIFICANT CHANGES OBSERVED
57363	NO SIGNIFICANT CHANGES OBSERVED

TABLE A9

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 5
SPONSOR:E.I. DUPONT INDIVIDUAL MATERNAL MACROSCOPIC FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 4: 1000 MG/KG/DAY	MATERNAL GROSS OBSERVATION
57366	NO SIGNIFICANT CHANGES OBSERVED
57374	DELIVERED GESTATION DAY 21 SITE #10 DELIVERED
57378	NO SIGNIFICANT CHANGES OBSERVED
57382	PANCREAS: EDEMATOUS DELIVERED GESTATION DAY 21 SITES ARBITRARILY ASSIGNED
57388	DELIVERED GESTATION DAY 21 SITES ARBITRARILY ASSIGNED
57391	DELIVERED GESTATION DAY 21 SITES ARBITRARILY ASSIGNED
57409	LIVER: AREA(S), WHITE ONE, IRREGULARLY SHAPED, MEDIAN LOBE

PMFGRDv4.16
01/25/2010

TABLE A10

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT INDIVIDUAL ORGAN WEIGHTS [G]
SPONSOR NO.:18405-841

FEMALE GROUP: 0 MG/KG/DAY

ANIMAL	PREGNANCY STATUS	LIVER	KIDNEYS
57312	G	17.06	2.42
57320	G	15.00	1.91
57322	G	17.74	2.47
57325	G	16.60	2.18
57326	G	13.88	1.84
57329	G	13.56	1.89
57333	G	17.55	2.51
57352	G	13.51	1.78
57356	G	14.46	1.89
57360	G	12.30	1.92
57364	G	15.18	2.01
57369	G	12.64	1.77
57370	G	15.85	2.30
57371	G	12.01	1.91
57379	G	15.18	1.99
57380	G	14.05	1.95
57381	G	15.20	2.36
57385	G	15.40	2.10
57392	G	14.30	2.13
57397	G	14.77	1.93
57398	G	15.30	2.22
57406	G	14.41	2.11
MEAN		14.82	2.07
S.D.		1.552	0.225
S.E.		0.331	0.048
N		22	22

G = GRAVID NG = NONGRAVID - WEIGHTS NOT INCLUDED IN THE CALCULATION OF THE MEAN

TABLE A10

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 2
SPONSOR:E.I. DUPONT INDIVIDUAL ORGAN WEIGHTS [G]
SPONSOR NO.:18405-841

FEMALE GROUP: 10 MG/KG/DAY

ANIMAL	PREGNANCY STATUS	LIVER	KIDNEYS
57307	G	17.89	2.30
57308	G	15.80	2.16
57317	G	14.63	2.19
57319	G	17.06	2.15
57324	G	13.13	2.21
57332	G	13.32	2.09
57334	G	14.83	2.23
57335	G	15.19	2.00
57337	G	12.83	2.03
57339	G	15.69	1.98
57340	G	15.51	2.05
57343	G	12.93	2.08
57347	G	15.16	2.13
57350	G	14.96	1.92
57353	G	15.13	2.25
57358	G	14.61	2.12
57367	G	13.76	1.89
57373	G	15.15	2.18
57376	G	16.64	2.26
57393	G	14.89	1.99
57403	G	14.38	1.96
57405	NG	11.09	2.14
MEAN		14.93	2.10
S.D.		1.308	0.118
S.E.		0.285	0.026
N		21	21

G = GRAVID NG = NONGRAVID - WEIGHTS NOT INCLUDED IN THE CALCULATION OF THE MEAN

TABLE A10

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 3
SPONSOR:E.I. DUPONT INDIVIDUAL ORGAN WEIGHTS [G]
SPONSOR NO.:18405-841

FEMALE GROUP: 100 MG/KG/DAY

ANIMAL	PREGNANCY STATUS	LIVER	KIDNEYS
57314	G	17.79	2.23
57318	NG	13.59	2.29
57321	G	18.03	2.27
57327	G	16.19	2.11
57331	G	16.17	2.10
57344	G	19.06	2.32
57345	G	20.65	2.44
57348	G	15.67	2.10
57354	G	15.98	2.03
57357	G	13.29	1.77
57361	G	15.05	2.15
57365	G	16.16	2.52
57368	G	16.45	2.20
57372	G	17.68	2.22
57375	G	15.31	1.86
57383	G	16.62	2.38
57386	G	17.88	2.04
57387	G	16.15	1.99
57389	G	16.62	2.25
57390	G	13.69	2.03
57394	G	20.40	2.25
57404	G	13.94	1.93
MEAN		16.61	2.15
S.D.		1.946	0.187
S.E.		0.425	0.041
N		21	21

G = GRAVID NG = NONGRAVID - WEIGHTS NOT INCLUDED IN THE CALCULATION OF THE MEAN

TABLE A10

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 4
SPONSOR:E.I. DUPONT INDIVIDUAL ORGAN WEIGHTS [G]
SPONSOR NO.:18405-841

FEMALE GROUP: 1000 MG/KG/DAY

ANIMAL	PREGNANCY STATUS	LIVER	KIDNEYS
57309	G	22.80	2.66
57310	G	19.40	2.26
57315	G	17.72	2.10
57316	G	20.19	2.29
57323	G	20.23	2.16
57330	G	18.14	2.01
57336	G	19.08	2.29
57338	G	18.14	2.15
57342	G	20.53	2.28
57349	G	21.02	2.29
57351	G	21.23	2.23
57359	G	19.19	2.46
57362	G	16.67	1.94
57363	G	22.27	2.40
57366	G	19.79	2.59
57374	G	18.61	2.13
57378	G	20.64	2.32
57382	G	19.68	2.23
57388	G	17.87	2.38
57391	G	21.80	2.29
57409	G	22.47	2.41
MEAN		19.88	2.28
S.D.		1.689	0.173
S.E.		0.369	0.038
N		21	21

G = GRAVID NG = NONGRAVID - WEIGHTS NOT INCLUDED IN THE CALCULATION OF THE MEAN

POFBWRv4.07
12/15/2009

TABLE A11

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL DATA AT SCHEDULED NECROPSY
SPONSOR NO.:18405-841

DAMS FROM GROUP 1: 0 MG/KG/DAY

			VIABLE FETUSES			DEAD FETUSES			EARLY RESORPTIONS			LATE RESORPTIONS			IMPLANTATION SITES			CORPORA LUTEA		
	SEX		LEFT	RIGHT		LEFT	RIGHT		LEFT	RIGHT		LEFT	RIGHT		LEFT	RIGHT		LEFT	RIGHT	
DAM#	M	F	HORN	HORN	TOTAL	HORN	HORN	TOTAL	HORN	HORN	TOTAL	HORN	HORN	TOTAL	HORN	HORN	TOTAL	OVARY		TOTAL
57312	8	7	6	9	15	0	0	0	1	3	4	0	0	0	7	12	19	7	12	19
57320	11	5	9	7	16	0	0	0	0	0	0	0	0	0	9	7	16	9	7	16
57322	8	11	9	10	19	0	0	0	0	1	1	0	0	0	9	11	20	11	11	22
57325	7	7	10	4	14	0	0	0	1	0	1	0	0	0	11	4	15	11	4	15
57326	9	7	6	10	16	0	0	0	0	0	0	0	0	0	6	10	16	6	10	16
57329	11	3	5	9	14	0	0	0	0	0	0	0	0	0	5	9	14	5	10	15
57333	0	7	3	4	7	0	0	0	0	1	1	0	0	0	3	5	8	6	10	16
57352	8	8	9	7	16	0	0	0	0	0	0	0	0	0	9	7	16	10	7	17
57356	8	8	6	10	16	0	0	0	0	0	0	0	0	0	6	10	16	6	10	16
57360	10	5	7	8	15	0	0	0	0	1	1	0	0	0	7	9	16	7	9	16
57364	8	4	6	6	12	0	0	0	0	2	2	0	0	0	6	8	14	6	9	15
57369	9	4	7	6	13	0	0	0	0	0	0	0	0	0	7	6	13	7	6	13
57370	12	7	9	10	19	0	0	0	0	0	0	0	0	0	9	10	19	9	11	20
57371	6	9	10	5	15	0	0	0	0	0	0	0	0	0	10	5	15	10	6	16
57379	7	10	9	8	17	0	0	0	1	1	2	0	0	0	10	9	19	10	9	19
57380	13	5	9	9	18	0	0	0	1	0	1	0	0	0	10	9	19	11	9	20
57381	11	6	6	11	17	0	0	0	0	0	0	0	0	0	6	11	17	6	11	17
57385	9	8	11	6	17	0	0	0	1	0	1	0	0	0	12	6	18	12	6	18
57392	10	6	5	11	16	0	0	0	0	0	0	0	0	0	5	11	16	5	11	16
57397	8	6	6	8	14	0	0	0	1	0	1	0	0	0	7	8	15	7	9	16
57398	11	8	8	11	19	0	0	0	0	0	0	0	0	0	8	11	19	9	13	22
57406	7	8	4	11	15	0	0	0	1	0	1	0	0	0	5	11	16	5	11	16
TOTAL	191	149	160	180	340	0	0	0	7	9	16	0	0	0	167	189	356	175	201	376
MEAN	8.7	6.8	7.3	8.2	15.5	0.0	0.0	0.0	0.3	0.4	0.7	0.0	0.0	0.0	7.6	8.6	16.2	8.0	9.1	17.1
S.D.	2.66	1.97	2.14	2.28	2.67	0.00	0.00	0.00	0.48	0.80	0.98	0.00	0.00	0.00	2.28	2.32	2.67	2.28	2.27	2.33
S.E.	0.57	0.42	0.46	0.49	0.57	0.00	0.00	0.00	0.10	0.17	0.21	0.00	0.00	0.00	0.49	0.50	0.57	0.49	0.48	0.50
N =	22																			

TABLE A11

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 2
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL DATA AT SCHEDULED NECROPSY
SPONSOR NO.:18405-841

DAMS FROM GROUP 2: 10 MG/KG/DAY

			VIABLE FETUSES			DEAD FETUSES			EARLY RESORPTIONS			LATE RESORPTIONS			IMPLANTATION SITES			CORPORA LUTEA		
	SEX		LEFT	RIGHT		LEFT	RIGHT		LEFT	RIGHT		LEFT	RIGHT		LEFT	RIGHT		LEFT	RIGHT	
DAM#	M	F	HORN	HORN	TOTAL	HORN	HORN	TOTAL	HORN	HORN	TOTAL	HORN	HORN	TOTAL	HORN	HORN	TOTAL	OVARY		TOTAL
57307	9	5	6	8	14	0	0	0	0	1	1	0	0	0	6	9	15	6	9	15
57308	9	8	5	12	17	0	0	0	1	0	1	0	0	0	6	12	18	7	12	19
57317	7	7	5	9	14	0	0	0	0	1	1	0	0	0	5	10	15	6	11	17
57319	3	11	8	6	14	0	0	0	2	2	4	0	0	0	10	8	18	10	8	18
57324	6	10	7	9	16	0	0	0	1	0	1	0	0	0	8	9	17	8	9	17
57332	8	7	8	7	15	0	0	0	0	0	0	0	0	0	8	7	15	8	7	15
57334	7	7	6	8	14	0	0	0	0	0	0	0	0	0	6	8	14	6	10	16
57335	9	7	6	10	16	0	0	0	0	0	0	0	0	0	6	10	16	6	11	17
57337	8	7	10	5	15	0	0	0	0	0	0	0	0	0	10	5	15	10	5	15
57339	6	11	8	9	17	0	0	0	0	0	0	0	0	0	8	9	17	10	9	19
57340	7	10	5	12	17	0	0	0	0	0	0	0	0	0	5	12	17	5	13	18
57343	7	6	7	6	13	0	0	0	0	0	0	0	0	0	7	6	13	7	6	13
57347	8	6	3	11	14	0	0	0	0	3	3	0	0	0	3	14	17	3	15	18
57350	9	8	9	8	17	0	0	0	1	1	2	0	0	0	10	9	19	10	10	20
57353	8	9	10	7	17	0	0	0	0	0	0	0	0	0	10	7	17	11	7	18
57358	7	11	10	8	18	0	0	0	0	0	0	0	0	0	10	8	18	10	8	18
57367	3	11	6	8	14	0	0	0	0	0	0	0	0	0	6	8	14	6	9	15
57373	8	8	11	5	16	0	0	0	1	1	2	0	0	0	12	6	18	12	6	18
57376	10	6	6	10	16	0	0	0	1	1	2	0	0	0	7	11	18	7	11	18
57393	12	3	8	7	15	0	0	0	1	1	2	0	0	0	9	8	17	9	10	19
57403	6	9	8	7	15	0	0	0	0	0	0	0	0	0	8	7	15	8	10	18
57405	NONGRAVID																			
TOTAL	157	167	152	172	324	0	0	0	8	11	19	0	0	0	160	183	343	165	196	361
MEAN	7.5	8.0	7.2	8.2	15.4	0.0	0.0	0.0	0.4	0.5	0.9	0.0	0.0	0.0	7.6	8.7	16.3	7.9	9.3	17.2
S.D.	2.06	2.20	2.05	2.02	1.40	0.00	0.00	0.00	0.59	0.81	1.18	0.00	0.00	0.00	2.22	2.22	1.65	2.26	2.44	1.75
S.E.	0.45	0.48	0.45	0.44	0.31	0.00	0.00	0.00	0.13	0.18	0.26	0.00	0.00	0.00	0.49	0.48	0.36	0.49	0.53	0.38
N =	21																			

TABLE A11

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 3
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL DATA AT SCHEDULED NECROPSY
SPONSOR NO.:18405-841

DAMS FROM GROUP 3: 100 MG/KG/DAY

	VIABLE FETUSES					DEAD FETUSES			EARLY RESORPTIONS			LATE RESORPTIONS			IMPLANTATION SITES			CORPORA LUTEA		
	SEX		LEFT	RIGHT		LEFT	RIGHT		LEFT	RIGHT		LEFT	RIGHT		LEFT	RIGHT		LEFT	RIGHT	
DAM#	M	F	HORN	HORN	TOTAL	HORN	HORN	TOTAL	HORN	HORN	TOTAL	HORN	HORN	TOTAL	HORN	HORN	TOTAL	OVARY		TOTAL
57314	5	7	6	6	12	0	0	0	0	1	1	0	0	0	6	7	13	7	7	14
57318	NONGRAVID																			
57321	7	9	3	13	16	0	0	0	0	0	0	0	0	0	3	13	16	4	14	18
57327	7	10	8	9	17	0	0	0	0	1	1	0	0	0	8	10	18	8	10	18
57331	8	5	7	6	13	0	0	0	0	0	0	0	0	0	7	6	13	8	6	14
57344	10	9	9	10	19	0	0	0	1	0	1	0	0	0	10	10	20	10	11	21
57345	10	5	7	8	15	0	0	0	1	0	1	0	0	0	8	8	16	8	8	16
57348	9	7	7	9	16	0	0	0	0	0	0	0	0	0	7	9	16	8	9	17
57354	8	8	4	12	16	0	0	0	0	0	0	0	0	0	4	12	16	4	12	16
57357	9	5	10	4	14	0	0	0	0	0	0	0	0	0	10	4	14	10	4	14
57361	7	7	8	6	14	0	0	0	0	1	1	0	0	0	8	7	15	8	7	15
57365	9	6	10	5	15	0	0	0	0	0	0	0	0	0	10	5	15	10	5	15
57368	4	7	5	6	11	0	0	0	2	2	4	0	0	0	7	8	15	7	8	15
57372	10	7	10	7	17	0	0	0	0	0	0	0	0	0	10	7	17	10	7	17
57375	8	7	6	9	15	0	0	0	0	0	0	0	0	0	6	9	15	6	9	15
57383	8	11	11	8	19	0	0	0	0	0	0	0	0	0	11	8	19	11	8	19
57386	6	9	5	10	15	0	0	0	0	0	0	0	0	0	5	10	15	5	10	15
57387	4	10	5	9	14	0	0	0	2	1	3	0	0	0	7	10	17	7	10	17
57389	7	10	7	10	17	0	0	0	0	0	0	0	0	0	7	10	17	7	10	17
57390	5	10	6	9	15	0	0	0	0	0	0	0	0	0	6	9	15	6	9	15
57394	5	5	5	5	10	0	0	0	4	3	7	0	0	0	9	8	17	9	9	18
57404	9	7	8	8	16	0	0	0	0	0	0	0	0	0	8	8	16	8	8	16
TOTAL	155	161	147	169	316	0	0	0	10	9	19	0	0	0	157	178	335	161	181	342
MEAN	7.4	7.7	7.0	8.0	15.0	0.0	0.0	0.0	0.5	0.4	0.9	0.0	0.0	0.0	7.5	8.5	16.0	7.7	8.6	16.3
S.D.	1.94	1.91	2.17	2.33	2.29	0.00	0.00	0.00	1.03	0.81	1.76	0.00	0.00	0.00	2.09	2.14	1.75	1.96	2.29	1.82
S.E.	0.42	0.42	0.47	0.51	0.50	0.00	0.00	0.00	0.22	0.18	0.38	0.00	0.00	0.00	0.46	0.47	0.38	0.43	0.50	0.40
N =	21																			

TABLE A11

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 4
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL DATA AT SCHEDULED NECROPSY
SPONSOR NO.:18405-841

DAMS FROM GROUP 4: 1000 MG/KG/DAY

			VIABLE FETUSES			DEAD FETUSES			EARLY RESORPTIONS			LATE RESORPTIONS			IMPLANTATION SITES			CORPORA LUTEA		
	SEX		LEFT	RIGHT		LEFT	RIGHT		LEFT	RIGHT		LEFT	RIGHT		LEFT	RIGHT		LEFT	RIGHT	
DAM#	M	F	HORN	HORN	TOTAL	HORN	HORN	TOTAL	HORN	HORN	TOTAL	HORN	HORN	TOTAL	HORN	HORN	TOTAL	OVARY		TOTAL
57309	9	9	7	11	18	0	0	0	1	0	1	0	0	0	8	11	19	8	11	19
57310	7	8	8	7	15	0	0	0	0	1	1	0	0	0	8	8	16	8	8	16
57315	6	11	8	9	17	0	0	0	0	0	0	0	0	0	8	9	17	8	9	17
57316	6	10	8	8	16	0	0	0	0	0	0	0	0	0	8	8	16	8	8	16
57323	10	6	8	8	16	0	0	0	0	0	0	0	0	0	8	8	16	11	10	21
57328	GRAVID, DIED DAY 20																			
57330	5	10	7	8	15	0	0	0	0	0	0	0	0	0	7	8	15	7	9	16
57336	8	7	8	7	15	0	0	0	0	0	0	0	0	0	8	7	15	9	8	17
57338	8	5	5	8	13	0	0	0	0	0	0	0	0	0	5	8	13	6	8	14
57342	9	9	10	8	18	0	0	0	0	0	0	0	0	0	10	8	18	10	8	18
57349	6	8	6	8	14	0	0	0	0	0	0	0	0	0	6	8	14	6	9	15
57351	8	9	5	12	17	0	0	0	0	1	1	0	0	0	5	13	18	8	13	21
57359	7	9	8	8	16	0	0	0	0	1	1	0	0	0	8	9	17	8	9	17
57362	7	8	8	7	15	0	0	0	0	1	1	0	0	0	8	8	16	9	9	18
57363	4	10	6	8	14	0	0	0	0	1	1	0	0	0	6	9	15	6	9	15
57366	9	5	4	10	14	0	0	0	0	1	1	0	0	0	4	11	15	4	11	15
57374	10	9	10	9	19	0	0	0	0	0	0	0	0	0	10	9	19	10	9	19
57378	7	8	1	14	15	0	0	0	0	0	0	0	0	0	1	14	15	2	14	16
57382	9	8	9	8	17	0	0	0	0	0	0	0	0	0	9	8	17	9	8	17
57388	8	8	9	7	16	0	0	0	0	0	0	0	0	0	9	7	16	9	7	16
57391	5	7	6	6	12	0	0	0	2	0	2	0	0	0	8	6	14	9	6	15
57409	6	11	7	10	17	0	0	0	0	1	1	0	0	0	7	11	18	8	13	21
TOTAL	154	175	148	181	329	0	0	0	3	7	10	0	0	0	151	188	339	163	196	359
MEAN	7.3	8.3	7.0	8.6	15.7	0.0	0.0	0.0	0.1	0.3	0.5	0.0	0.0	0.0	7.2	9.0	16.1	7.8	9.3	17.1
S.D.	1.68	1.68	2.11	1.88	1.74	0.00	0.00	0.00	0.48	0.48	0.60	0.00	0.00	0.00	2.11	1.99	1.65	2.07	2.03	2.10
S.E.	0.37	0.37	0.46	0.41	0.38	0.00	0.00	0.00	0.10	0.11	0.13	0.00	0.00	0.00	0.46	0.43	0.36	0.45	0.44	0.46
N =	21																			

PLRDv4.08
12/15/2009

TABLE A12

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL DATA AT SCHEDULED NECROPSY [% PER LITTER]
SPONSOR NO.:18405-841

DAMS FROM GROUP 1: 0 MG/KG/DAY

DAM #	CORPORA LUTEA	IMPLANTATION SITES	FETUSES VIABLE	FETUSES DEAD	RESORPTIONS EARLY	RESORPTIONS LATE	RESORPTIONS TOTAL	PRE-IMPLANTATION LOSS	POST-IMPLANTATION LOSS	MALES	FEMALES
	#	#	%	%	%	%	%	%	%	%	%
57312	19.0	19.0	78.9	0.0	21.1	0.0	21.1	0.0	21.1	53.3	46.7
57320	16.0	16.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	68.8	31.3
57322	22.0	20.0	95.0	0.0	5.0	0.0	5.0	9.1	5.0	42.1	57.9
57325	15.0	15.0	93.3	0.0	6.7	0.0	6.7	0.0	6.7	50.0	50.0
57326	16.0	16.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	56.3	43.8
57329	15.0	14.0	100.0	0.0	0.0	0.0	0.0	6.7	0.0	78.6	21.4
57333	16.0	8.0	87.5	0.0	12.5	0.0	12.5	50.0	12.5	0.0	100.0
57352	17.0	16.0	100.0	0.0	0.0	0.0	0.0	5.9	0.0	50.0	50.0
57356	16.0	16.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	50.0	50.0
57360	16.0	16.0	93.8	0.0	6.3	0.0	6.3	0.0	6.3	66.7	33.3
57364	15.0	14.0	85.7	0.0	14.3	0.0	14.3	6.7	14.3	66.7	33.3
57369	13.0	13.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	69.2	30.8
57370	20.0	19.0	100.0	0.0	0.0	0.0	0.0	5.0	0.0	63.2	36.8
57371	16.0	15.0	100.0	0.0	0.0	0.0	0.0	6.3	0.0	40.0	60.0
57379	19.0	19.0	89.5	0.0	10.5	0.0	10.5	0.0	10.5	41.2	58.8
57380	20.0	19.0	94.7	0.0	5.3	0.0	5.3	5.0	5.3	72.2	27.8
57381	17.0	17.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	64.7	35.3
57385	18.0	18.0	94.4	0.0	5.6	0.0	5.6	0.0	5.6	52.9	47.1
57392	16.0	16.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	62.5	37.5
57397	16.0	15.0	93.3	0.0	6.7	0.0	6.7	6.3	6.7	57.1	42.9
57398	22.0	19.0	100.0	0.0	0.0	0.0	0.0	13.6	0.0	57.9	42.1
57406	16.0	16.0	93.8	0.0	6.3	0.0	6.3	0.0	6.3	46.7	53.3
MEAN	17.1	16.2	95.5	0.0	4.6	0.0	4.6	5.2	4.6	55.0	45.0
S.D.	2.33	2.67	5.82	0.00	5.82	0.00	5.82	10.75	5.82	16.19	16.19
S.E.	0.50	0.57	1.24	0.00	1.24	0.00	1.24	2.29	1.24	3.45	3.45
N	22	22	22	22	22	22	22	22	22	22	22

TABLE A12

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 2
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL DATA AT SCHEDULED NECROPSY [% PER LITTER]
SPONSOR NO.:18405-841

DAMS FROM GROUP 2: 10 MG/KG/DAY

DAM #	CORPORA LUTEA	IMPLANTATION SITES	FETUSES VIABLE	FETUSES DEAD	RESORPTIONS EARLY	RESORPTIONS LATE	RESORPTIONS TOTAL	PRE-IMPLANTATION LOSS	POST-IMPLANTATION LOSS	MALES	FEMALES
	#	#	%	%	%	%	%	%	%	%	%
57307	15.0	15.0	93.3	0.0	6.7	0.0	6.7	0.0	6.7	64.3	35.7
57308	19.0	18.0	94.4	0.0	5.6	0.0	5.6	5.3	5.6	52.9	47.1
57317	17.0	15.0	93.3	0.0	6.7	0.0	6.7	11.8	6.7	50.0	50.0
57319	18.0	18.0	77.8	0.0	22.2	0.0	22.2	0.0	22.2	21.4	78.6
57324	17.0	17.0	94.1	0.0	5.9	0.0	5.9	0.0	5.9	37.5	62.5
57332	15.0	15.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	53.3	46.7
57334	16.0	14.0	100.0	0.0	0.0	0.0	0.0	12.5	0.0	50.0	50.0
57335	17.0	16.0	100.0	0.0	0.0	0.0	0.0	5.9	0.0	56.3	43.8
57337	15.0	15.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	53.3	46.7
57339	19.0	17.0	100.0	0.0	0.0	0.0	0.0	10.5	0.0	35.3	64.7
57340	18.0	17.0	100.0	0.0	0.0	0.0	0.0	5.6	0.0	41.2	58.8
57343	13.0	13.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	53.8	46.2
57347	18.0	17.0	82.4	0.0	17.6	0.0	17.6	5.6	17.6	57.1	42.9
57350	20.0	19.0	89.5	0.0	10.5	0.0	10.5	5.0	10.5	52.9	47.1
57353	18.0	17.0	100.0	0.0	0.0	0.0	0.0	5.6	0.0	47.1	52.9
57358	18.0	18.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	38.9	61.1
57367	15.0	14.0	100.0	0.0	0.0	0.0	0.0	6.7	0.0	21.4	78.6
57373	18.0	18.0	88.9	0.0	11.1	0.0	11.1	0.0	11.1	50.0	50.0
57376	18.0	18.0	88.9	0.0	11.1	0.0	11.1	0.0	11.1	62.5	37.5
57393	19.0	17.0	88.2	0.0	11.8	0.0	11.8	10.5	11.8	80.0	20.0
57403	18.0	15.0	100.0	0.0	0.0	0.0	0.0	16.7	0.0	40.0	60.0
MEAN	17.2	16.3	94.8	0.0	5.2	0.0	5.2	4.8	5.2	48.5	51.5
S.D.	1.75	1.65	6.66	0.00	6.66	0.00	6.66	5.14	6.66	13.56	13.56
S.E.	0.38	0.36	1.45	0.00	1.45	0.00	1.45	1.12	1.45	2.96	2.96
N	21	21	21	21	21	21	21	21	21	21	21

TABLE A12

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 3
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL DATA AT SCHEDULED NECROPSY [% PER LITTER]
SPONSOR NO.:18405-841

DAMS FROM GROUP 3: 100 MG/KG/DAY

DAM #	CORPORA LUTEA	IMPLANTATION SITES	FETUSES VIABLE	FETUSES DEAD	RESORPTIONS EARLY	RESORPTIONS LATE	RESORPTIONS TOTAL	PRE-IMPLANTATION LOSS	POST-IMPLANTATION LOSS	MALES	FEMALES
	#	#	%	%	%	%	%	%	%	%	%
57314	14.0	13.0	92.3	0.0	7.7	0.0	7.7	7.1	7.7	41.7	58.3
57321	18.0	16.0	100.0	0.0	0.0	0.0	0.0	11.1	0.0	43.8	56.3
57327	18.0	18.0	94.4	0.0	5.6	0.0	5.6	0.0	5.6	41.2	58.8
57331	14.0	13.0	100.0	0.0	0.0	0.0	0.0	7.1	0.0	61.5	38.5
57344	21.0	20.0	95.0	0.0	5.0	0.0	5.0	4.8	5.0	52.6	47.4
57345	16.0	16.0	93.8	0.0	6.3	0.0	6.3	0.0	6.3	66.7	33.3
57348	17.0	16.0	100.0	0.0	0.0	0.0	0.0	5.9	0.0	56.3	43.8
57354	16.0	16.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	50.0	50.0
57357	14.0	14.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	64.3	35.7
57361	15.0	15.0	93.3	0.0	6.7	0.0	6.7	0.0	6.7	50.0	50.0
57365	15.0	15.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	60.0	40.0
57368	15.0	15.0	73.3	0.0	26.7	0.0	26.7	0.0	26.7	36.4	63.6
57372	17.0	17.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	58.8	41.2
57375	15.0	15.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	53.3	46.7
57383	19.0	19.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	42.1	57.9
57386	15.0	15.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	40.0	60.0
57387	17.0	17.0	82.4	0.0	17.6	0.0	17.6	0.0	17.6	28.6	71.4
57389	17.0	17.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	41.2	58.8
57390	15.0	15.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	33.3	66.7
57394	18.0	17.0	58.8	0.0	41.2	0.0	41.2	5.6	41.2	50.0	50.0
57404	16.0	16.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	56.3	43.8
MEAN	16.3	16.0	94.4	0.0	5.6	0.0	5.6	2.0	5.6	48.9	51.1
S.D.	1.82	1.75	10.65	0.00	10.66	0.00	10.66	3.40	10.66	10.52	10.52
S.E.	0.40	0.38	2.33	0.00	2.33	0.00	2.33	0.74	2.33	2.30	2.30
N	21	21	21	21	21	21	21	21	21	21	21

TABLE A12

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 4
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL DATA AT SCHEDULED NECROPSY [% PER LITTER]
SPONSOR NO.:18405-841

DAMS FROM GROUP 4: 1000 MG/KG/DAY

DAM #	CORPORA LUTEA	IMPLANTATION SITES	FETUSES VIABLE	FETUSES DEAD	RESORPTIONS EARLY	RESORPTIONS LATE	RESORPTIONS TOTAL	PRE-IMPLANTATION LOSS	POST-IMPLANTATION LOSS	MALES	FEMALES
	#	#	%	%	%	%	%	%	%	%	%
57309	19.0	19.0	94.7	0.0	5.3	0.0	5.3	0.0	5.3	50.0	50.0
57310	16.0	16.0	93.8	0.0	6.3	0.0	6.3	0.0	6.3	46.7	53.3
57315	17.0	17.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	35.3	64.7
57316	16.0	16.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	37.5	62.5
57323	21.0	16.0	100.0	0.0	0.0	0.0	0.0	23.8	0.0	62.5	37.5
57330	16.0	15.0	100.0	0.0	0.0	0.0	0.0	6.3	0.0	33.3	66.7
57336	17.0	15.0	100.0	0.0	0.0	0.0	0.0	11.8	0.0	53.3	46.7
57338	14.0	13.0	100.0	0.0	0.0	0.0	0.0	7.1	0.0	61.5	38.5
57342	18.0	18.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	50.0	50.0
57349	15.0	14.0	100.0	0.0	0.0	0.0	0.0	6.7	0.0	42.9	57.1
57351	21.0	18.0	94.4	0.0	5.6	0.0	5.6	14.3	5.6	47.1	52.9
57359	17.0	17.0	94.1	0.0	5.9	0.0	5.9	0.0	5.9	43.8	56.3
57362	18.0	16.0	93.8	0.0	6.3	0.0	6.3	11.1	6.3	46.7	53.3
57363	15.0	15.0	93.3	0.0	6.7	0.0	6.7	0.0	6.7	28.6	71.4
57366	15.0	15.0	93.3	0.0	6.7	0.0	6.7	0.0	6.7	64.3	35.7
57374	19.0	19.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	52.6	47.4
57378	16.0	15.0	100.0	0.0	0.0	0.0	0.0	6.3	0.0	46.7	53.3
57382	17.0	17.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	52.9	47.1
57388	16.0	16.0	100.0	0.0	0.0	0.0	0.0	0.0	0.0	50.0	50.0
57391	15.0	14.0	85.7	0.0	14.3	0.0	14.3	6.7	14.3	41.7	58.3
57409	21.0	18.0	94.4	0.0	5.6	0.0	5.6	14.3	5.6	35.3	64.7
MEAN	17.1	16.1	97.0	0.0	3.0	0.0	3.0	5.2	3.0	46.8	53.2
S.D.	2.10	1.65	3.94	0.00	3.95	0.00	3.95	6.70	3.95	9.57	9.57
S.E.	0.46	0.36	0.86	0.00	0.86	0.00	0.86	1.46	0.86	2.09	2.09
N	21	21	21	21	21	21	21	21	21	21	21

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TABLE A13

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL WEIGHTS [G]
SPONSOR NO.:18405-841

FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
DAM # MEAN	GROUP 1: 0 MG/KG/DAY																						
57312 5.6	5.6	5.6	5.9	5.8	E	5.8	5.6/	5.6	E	5.6	5.4	5.8	E	5.8	5.6	5.7	5.4	E	5.4				
57320 5.4	5.1	5.1	5.5	5.2	5.4	5.0	5.8	4.9	5.4/	5.4	5.9	5.2	5.6	5.5	5.9	5.1							
57322 5.6	5.5	5.4	5.4	5.3	6.1	5.4	5.0	5.5	5.7/	6.1	5.8	5.6	5.9	5.7	5.7	5.6	E	5.1	5.7	5.1			
57325 6.2	6.1	6.3	6.4	6.1	E	6.1	6.3	5.7	6.0	6.3	6.1/	6.2	6.7	6.2	6.8								
57326 6.1	6.3	6.2	6.2	6.3	6.1	5.9/	6.1	5.9	6.3	6.2	6.2	5.7	5.1	6.1	6.0	6.4							
57329 5.5	5.2	5.5	5.3	5.6	5.9/	5.5	5.2	5.6	5.5	5.3	5.7	5.6	5.4	5.4									
57333 4.4	3.1	4.3	4.7/	4.1	4.9	5.2	E	4.4															
57352 5.4	5.4	5.3	5.6	5.3	5.5	5.0	5.8	5.5	5.2/	5.3	5.4	5.5	5.4	4.9	5.3	5.2							
57356 5.9	5.5	5.9	6.3	6.1	5.8	5.7/	6.5	5.4	6.2	6.0	6.4	5.9	5.9	5.7	5.4	5.5							
57360 5.4	5.3	5.6	5.1	6.1	4.8	5.7	5.9/	5.8	5.3	4.8	5.1	5.2	5.5	E	5.9	5.6							
57364 6.1	6.6	6.7	6.3	5.7	6.3	6.7/	E	6.0	6.5	6.3	E	5.5	6.2	4.8									
57369 5.8	5.8	5.7	5.4	6.0	5.4	5.1	6.1/	6.2	5.7	6.1	6.0	5.9	6.2										
57370 5.6	5.6	5.5	5.6	5.8	5.8	5.7	5.5	6.0	5.9/	6.0	5.4	5.3	5.6	5.5	5.0	5.4	5.6	5.4	5.8				
57371 5.6	5.7	5.4	5.7	5.9	5.6	5.3	5.5	5.8	5.5	5.3/	5.6	5.6	5.7	5.4	5.5								
57379 5.9	5.5	6.4	5.8	5.9	6.2	6.0	5.5	E	6.0	5.8/	6.0	5.9	6.1	5.4	6.4	6.0	6.1	5.6	E				
57380 5.4	5.0	5.6	6.1	4.9	5.5	6.2	5.2	E	5.3	5.6/	5.6	5.6	1.8	5.4	6.1	6.1	5.7	6.0	5.8				
57381 5.6	4.8	5.8	5.7	5.8	5.6	6.2/	5.9	5.4	5.5	5.7	5.7	6.4	5.6	5.3	5.9	4.7	5.3						
57385 6.0	6.2	5.9	5.2	6.0	5.3	6.1	6.6	6.5	6.1	6.2	6.0	E /	5.6	6.4	6.2	6.6	6.0	5.8					
57392 5.9	6.0	6.0	5.9	6.4	6.4/	5.6	5.9	6.1	5.9	5.9	5.8	6.1	5.7	5.7	5.2	5.4							
57397 5.8	6.0	5.7	E	6.3	5.5	5.5	6.0/	6.7	6.2	5.7	5.8	6.2	5.4	5.7	5.1								
57398 5.5	5.5	5.7	5.9	5.5	5.3	5.5	5.6	5.9/	5.3	5.8	5.0	5.5	5.8	6.1	5.1	5.0	5.5	5.5	5.2				
57406 6.0	6.2	6.6	6.4	6.2	E /	6.3	5.4	5.8	5.7	5.7	6.2	5.6	5.5	6.2	5.8	5.8							
MEAN 5.7																							
S.D. 0.38																							
S.E. 0.08																							
N 22																							

E = EARLY RESORPTION L = LATE RESORPTION D = DEAD FETUS '/' DENOTES POSITION OF CERVIX

TABLE A13

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 2
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL WEIGHTS [G]
SPONSOR NO.:18405-841

FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
DAM # MEAN	GROUP 2: 10 MG/KG/DAY																						
57307 5.9	6.3	5.8	5.8	5.8	5.5	5.9/	E	6.0	5.9	6.0	6.1	5.5	6.4	5.2	5.8								
57308 5.5	5.7	5.7	E	5.8	5.6	5.6/	5.1	5.3	5.5	6.0	5.6	5.4	5.5	5.7	5.5	5.5	5.4	5.4					
57317 5.4	5.5	5.2	4.3	6.5	5.3/	5.3	5.6	5.5	5.5	E	5.5	5.2	5.5	5.4	5.2								
57319 5.2	5.3	E	5.4	5.0	E	5.5	5.0	4.8	5.2	6.0/	E	5.0	5.1	4.9	E	5.5	5.2	4.9					
57324 5.5	5.3	E	5.5	5.8	5.5	5.6	5.7	5.5/	5.7	5.0	5.4	5.2	5.7	5.6	5.5	5.4	5.2						
57332 5.9	5.8	5.3	5.9	5.5	5.6	5.9	5.7	7.1/	6.0	6.0	6.0	5.4	6.4	5.6	5.7								
57334 5.5	5.4	5.4	5.4	5.2	5.7	5.5/	5.7	5.3	5.2	5.8	5.5	5.3	5.8	5.4									
57335 5.9	5.9	6.0	6.1	5.6	5.8	6.4/	6.7	5.4	5.6	6.1	5.8	5.4	5.8	6.0	6.0	5.9							
57337 5.9	6.0	6.3	5.5	6.1	5.6	6.0	5.7	6.3	5.9	5.9/	6.0	6.6	5.8	5.8	5.7								
57339 5.7	5.6	5.6	5.5	5.5	6.2	5.9	5.5	6.2/	5.8	5.5	5.5	5.2	6.1	5.4	5.9	5.9	5.6						
57340 5.3	5.1	5.7	5.8	5.5	5.9/	5.8	5.3	5.3	5.0	4.9	5.6	5.1	5.3	5.4	5.1	4.9	4.9						
57343 6.1	5.7	6.2	5.8	6.5	5.5	6.1	6.0/	6.2	6.6	6.3	6.2	6.2	6.0										
57347 5.4	5.7	5.5	5.6/	5.8	5.5	5.5	5.1	5.7	5.3	5.2	E	5.3	5.5	E	5.1	5.2	E						
57350 5.3	4.9	5.4	5.5	E	5.2	5.3	5.4	5.0	5.4	5.1/	4.7	5.4	E	5.5	5.6	5.5	5.3	5.5	5.5				
57353 5.7	5.7	5.7	5.6	5.6	5.8	5.8	5.6	5.4	5.7	5.8/	5.5	6.0	5.9	5.7	5.9	5.4	6.0						
57358 5.4	5.8	5.3	5.3	5.3	5.7	5.4	5.1	5.2	5.7	5.1/	5.7	5.5	5.5	4.9	5.6	5.2	5.4	5.4					
57367 5.7	5.6	5.2	5.7	5.9	5.6	5.7/	5.8	5.9	5.9	6.1	5.9	5.3	5.4	5.4									
57373 5.6	5.7	6.0	5.4	5.3	5.8	6.0	5.9	5.7	5.0	5.1	5.4	E /	E	5.3	6.1	5.5	5.6	5.9					
57376 5.6	6.0	5.4	5.1	E	4.2	6.2	5.5/	5.6	5.6	5.8	5.8	6.1	5.7	5.7	6.0	5.5	E	5.8					
57393 5.5	6.0	5.7	5.3	E	5.7	5.5	5.4	5.6	6.1/	E	5.9	5.6	5.5	5.5	5.4	5.1	4.5						
57403 5.8	5.7	5.8	5.6	5.8	6.3	5.5	5.6	6.0/	6.5	5.7	5.7	5.7	5.5	5.7	5.6								

MEAN	5.6
S.D.	0.24
S.E.	0.05
N	21

E = EARLY RESORPTION L = LATE RESORPTION D = DEAD FETUS '/' DENOTES POSITION OF CERVIX

TABLE A13

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 3
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL WEIGHTS [G]
SPONSOR NO.:18405-841

FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
DAM # MEAN	GROUP 3: 100 MG/KG/DAY																						
57314 5.7	5.6	5.3	5.6	5.7	5.7	6.0/	6.2	E	5.7	5.5	6.2	5.6	5.7										
57321 5.2	5.4	5.3	6.2/	5.6	5.1	5.2	4.9	5.0	5.5	4.9	4.7	5.0	5.1	4.8	5.3	5.4							
57327 4.7	4.7	4.5	5.0	4.7	4.9	4.6	4.8	5.3/	5.0	4.9	4.8	E	4.0	4.0	4.8	4.9	4.8	4.6					
57331 5.3	5.3	5.7	5.1	5.5	5.3	5.1	5.3/	5.2	4.9	5.0	5.3	5.6	5.4										
57344 4.8	E	4.7	4.9	4.5	5.1	4.8	4.9	4.9	5.1	4.9/	5.2	4.8	4.5	4.6	4.5	4.2	4.6	4.7	4.7	4.7			
57345 5.4	E	4.8	5.4	5.7	5.8	5.2	5.8	5.4/	5.0	5.5	5.5	5.4	5.3	5.9	5.5	5.1							
57348 5.2	5.6	5.4	4.8	5.3	5.3	5.8	5.6/	5.3	5.2	4.5	4.9	4.8	5.2	5.0	4.9	5.0							
57354 5.2	5.6	4.8	4.7	5.5/	5.0	5.7	4.8	5.6	5.5	5.1	5.1	5.0	4.9	4.7	5.4	5.0							
57357 5.5	5.6	5.4	5.7	5.3	6.0	5.6	5.0	5.5	5.1	5.8/	5.8	5.5	5.0	5.3									
57361 5.4	5.7	5.5	4.9	5.4	5.4	5.1	5.6	5.5/	5.7	5.3	5.6	5.8	E	5.1	5.4								
57365 5.4	5.4	5.6	5.2	5.8	5.8	3.6	5.4	5.6	5.7	5.0/	4.0	6.0	5.7	5.8	5.7								
57368 5.3	5.5	E	E	5.5	5.6	5.1	5.5/	5.4	5.2	5.2	E	5.7	E	5.0	5.0								
57372 5.3	4.5	4.9	4.9	5.2	5.3	5.7	5.0	5.8	5.3	5.5/	5.1	5.3	5.4	5.7	5.4	5.1	5.4						
57375 5.3	5.6	5.4	5.2	5.6	5.5	5.5/	5.4	5.0	5.2	5.3	5.1	5.6	5.7	5.2	4.8								
57383 5.0	5.1	5.3	4.9	5.2	4.8	5.0	5.2	5.4	4.7	4.5	5.2/	4.8	5.1	5.1	4.8	4.9	5.2	5.1	5.3				
57386 5.3	5.5	5.1	5.5	5.8	5.8/	4.9	5.2	5.7	5.1	4.9	4.9	5.0	5.4	5.3	5.2								
57387 4.9	5.0	4.8	4.9	E	4.4	5.8	E /	E	5.6	4.5	4.9	5.4	5.1	4.8	4.4	3.9	4.9						
57389 5.3	5.6	5.2	5.0	5.1	5.5	5.5	5.9/	5.1	5.4	5.3	5.4	5.4	5.4	5.3	5.5	5.0	4.7						
57390 5.0	4.9	5.0	4.8	4.4	4.8	4.9/	5.4	5.6	4.9	5.1	4.9	5.2	4.8	5.0	4.9								
57394 5.4	5.4	5.2	5.8	5.7	E	E	E	E	5.5/	E	E	5.7	5.4	E	5.4	4.4	5.2						
57404 5.4	5.1	5.3	5.3	5.2	5.6	5.4	5.3	5.5/	5.3	5.3	5.5	5.5	5.0	6.0	5.7	5.3							

MEAN	5.2
S.D.	0.24
S.E.	0.05
N	21

E = EARLY RESORPTION L = LATE RESORPTION D = DEAD FETUS '/' DENOTES POSITION OF CERVIX

TABLE A13

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 4
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL WEIGHTS [G]
SPONSOR NO.:18405-841

FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
DAM # MEAN	GROUP 4: 1000 MG/KG/DAY																						
57309 4.0	4.5	3.5	E	4.2	3.8	3.8	3.7	3.8/	4.3	3.9	4.2	3.8	3.9	4.2	4.2	4.1	4.0	3.8	4.4				
57310 4.3	4.5	4.6	4.6	3.9	4.1	4.2	4.5	4.2/	4.3	3.9	4.0	4.5	4.3	4.1	4.4	E							
57315 3.8	4.0	3.7	3.5	4.1	3.7	3.6	3.7	3.4/	3.9	3.9	3.7	3.6	4.3	3.9	4.0	3.9	3.8						
57316 3.8	4.0	4.1	3.5	3.6	3.7	4.1	4.2	4.5/	3.7	3.9	3.2	3.5	3.5	3.7	3.7	3.6							
57323 4.0	3.7	4.0	3.9	3.9	3.6	3.5	4.6	4.5/	4.3	3.7	4.2	4.1	4.1	4.3	3.8	4.0							
57330 4.3	4.6	4.3	4.9	4.1	4.7	4.2	4.3/	3.1	4.3	4.4	4.1	4.4	4.2	4.5	4.5								
57336 4.1	4.0	4.2	4.3	4.2	3.9	4.2	4.3	4.2/	4.4	4.3	3.9	3.8	4.0	3.8	3.9								
57338 4.3	4.5	4.3	4.2	4.2	4.5/	4.6	4.2	4.5	4.2	4.4	4.1	4.1	3.6										
57342 3.9	4.2	4.2	3.6	3.8	4.0	3.9	4.0	3.9	3.4	3.8/	4.2	4.1	3.8	3.7	4.0	4.0	4.0	4.4					
57349 4.3	4.5	4.4	4.5	4.5	4.2	4.4/	4.4	4.7	4.4	3.8	4.1	4.2	3.8	4.2									
57351 4.3	4.6	4.7	4.1	4.5	4.5/	4.5	4.1	E	4.2	4.2	3.8	3.8	4.5	4.7	3.9	4.2	4.4	4.4					
57359 4.4	4.3	4.4	4.5	3.9	4.4	4.2	4.6	4.6/	4.6	4.5	4.3	4.4	4.6	4.3	4.6	E	4.6						
57362 4.1	3.8	3.8	4.2	4.2	3.5	4.0	4.4	4.5/	E	4.3	4.2	4.3	4.3	4.2	4.0	4.1							
57363 3.8	4.1	3.7	4.3	3.4	4.3	3.6/	3.8	3.9	3.8	E	4.2	4.2	3.6	3.3	3.5								
57366 4.5	4.7	4.5	4.8	4.9/	4.7	4.5	4.4	4.4	4.9	4.4	E	4.1	4.6	4.1	4.2								
57374 3.4	3.1	3.6	3.5	3.1	3.6	3.4	2.7	3.7	3.7	3.8/	3.6	3.4	3.4	3.4	3.4	3.0	3.2	3.5	3.3				
57378 3.9	4.6/	4.3	3.9	3.8	4.1	4.1	3.7	3.8	3.9	4.0	3.6	3.8	4.0	3.8	3.7								
57382 4.6	4.6	4.8	4.6	4.3	4.4	4.9	4.8	4.8	4.5/	4.4	4.4	4.5	4.4	4.9	4.6	4.4	4.5						
57388 3.8	3.7	3.7	3.5	3.7	3.8	3.9	3.8	4.0	3.9/	3.8	3.3	3.5	4.2	3.7	3.8	3.8							
57391 4.2	4.3	E	E	4.4	4.4	4.5	4.1	4.1/	4.1	4.0	3.9	4.5	3.9	3.9									
57409 4.1	3.8	4.3	3.9	4.3	4.1	3.7	4.5/	3.8	3.7	3.6	4.1	4.2	4.3	E	4.2	3.9	4.1	4.4					
MEAN 4.1																							
S.D. 0.29																							
S.E. 0.06																							
N 21																							

E = EARLY RESORPTION L = LATE RESORPTION D = DEAD FETUS '/' DENOTES POSITION OF CERVIX

PFWTv4.15
12/15/2009

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 1
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 1: 0 MG/KG/DAY	FETUS #	GRADE
57312	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19	
	A A A A E A A/ A E A A A E A A A A E A	
SEX:	F F M F - M F F - M F M - M M M F - M	
CEPHALIC:	1,3,8,11,14,16,19	
EXTERNAL	5 EARLY RESORPTION	
EXTERNAL	9 EARLY RESORPTION	
EXTERNAL	13 EARLY RESORPTION	
EXTERNAL	18 EARLY RESORPTION	
	NO REMARKABLE OBSERVATIONS	
EXTERNAL	1,2,3,4,6,7,8,10,11,12,14,15,16,17,19	
VISCERAL	1,2,3,4,6,7,8,10,11,12,14,15,16,17,19	
SKELETAL	1,2,3,4,6,7,8,10,11,12,14,15,16,17,19	
57320	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16	
	A A A A A A A A A/ A A A A A A A A	
SEX:	M F M M M F M F M F M F M M M M	
CEPHALIC:	1,3,5,7,9,11,13,15	
SKELETAL	5 V 14TH RUDIMENTARY RIB(S) RIGHT	P
	NO REMARKABLE OBSERVATIONS	
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16	
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16	
SKELETAL	1,2,3,4,6,7,8,9,10,11,12,13,14,15,16	
57322	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20	
	A A A A A A A A A/ A A A A A A E A A A	
SEX:	F F F F M F F F F M M F M M M M - F M F	
CEPHALIC:	1,3,5,7,9,11,13,15,18,20	

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 2
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 1: 0 MG/KG/DAY	FETUS #		GRADE
57322 (CONTINUED)			
VISCERAL	7	RENAL PAPILLA(E) NOT FULLY DEVELOPED (WOO AND HOAR GRADE 1)	P
SKELETAL	13	V 14TH RUDIMENTARY RIB(S) RIGHT	P
SKELETAL	16	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
EXTERNAL	17	EARLY RESORPTION	
SKELETAL	18	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
SKELETAL	20	V STERNEBRA(E) MALALIGNED(SLIGHT OR MODERATE) #5, MODERATE; #3 AND #4, SLIGHT	P
		V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,18,19,20		
VISCERAL	1,2,3,4,5,6,8,9,10,11,12,13,14,15,16,18,19,20		
SKELETAL	1,2,3,4,5,6,7,8,9,10,11,12,14,15,19		
57325	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15		
	A A A A E A A A A A A/ A A A A		
SEX:	M M F M - F M F F M F F M F M		
CEPHALIC:	2,4,7,9,11,13,15		
VISCERAL	3	RENAL PAPILLA(E) NOT FULLY DEVELOPED (WOO AND HOAR GRADE 1) BILATERAL	P
SKELETAL	4	V 7TH CERVICAL RIB(S) PINPOINT, LEFT	P
EXTERNAL	5	EARLY RESORPTION	
SKELETAL	6	V 7TH CERVICAL RIB(S) INTERMEDIATE, LEFT	P
		V 14TH RUDIMENTARY RIB(S)	P

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 3
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 1: 0 MG/KG/DAY	FETUS #		GRADE
57325 (CONTINUED)			
		BILATERAL	
SKELETAL	7	V 14TH RUDIMENTARY RIB(S)	P
		BILATERAL	
VISCERAL	12	RENAL PAPILLA(E) NOT FULLY DEVELOPED (WOO AND HOAR GRADE 1)	P
		RIGHT	
SKELETAL		V 14TH RUDIMENTARY RIB(S)	P
		BILATERAL	
SKELETAL	14	V 14TH RUDIMENTARY RIB(S)	P
		BILATERAL	
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,4,6,7,8,9,10,11,12,13,14,15		
VISCERAL	1,2,4,6,7,8,9,10,11,13,14,15		
SKELETAL	1,2,3,8,9,10,11,13,15		
57326	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16		
	A A A A A A/ A A A A A A A A A A		
SEX:	F F F M M F F M M M M F F M M M		
CEPHALIC:	1,3,5,7,9,11,13,15		
SKELETAL	4	V 14TH RUDIMENTARY RIB(S)	P
		BILATERAL	
VISCERAL	5	V RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S)	1
		URETER, BILATERAL	
SKELETAL	9	V 14TH RUDIMENTARY RIB(S)	P
		BILATERAL	
SKELETAL	10	V 14TH RUDIMENTARY RIB(S)	P
		BILATERAL	
SKELETAL	14	V 14TH RUDIMENTARY RIB(S)	P
		BILATERAL	
SKELETAL	15	V 14TH RUDIMENTARY RIB(S)	P

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 4
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 1: 0 MG/KG/DAY	FETUS #		GRADE
57326 (CONTINUED)			
		LEFT	
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16		
VISCERAL	1,2,3,4,6,7,8,9,10,11,12,13,14,15,16		
SKELETAL	1,2,3,5,6,7,8,11,12,13,16		
57329	1 2 3 4 5 6 7 8 9 10 11 12 13 14		
	A A A A A/ A A A A A A A A A		
SEX:	M M M M M M M F M M F M M F		
CEPHALIC:	2,4,6,8,10,12,14		
SKELETAL	1	V 14TH RUDIMENTARY RIB(S) RIGHT	P
SKELETAL	5	V 14TH RUDIMENTARY RIB(S) LEFT	P
SKELETAL	7	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
SKELETAL	8	V 14TH RUDIMENTARY RIB(S) LEFT	P
SKELETAL	9	V 14TH RUDIMENTARY RIB(S) RIGHT	P
SKELETAL	13	V 14TH RUDIMENTARY RIB(S) LEFT	P
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14		
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14		
SKELETAL	2,3,4,6,10,11,12,14		
57333	1 2 3 4 5 6 7 8		
	A A A/ A A A E A		
SEX:	F F F F F F - F		
CEPHALIC:	2,4,6		

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 5
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 1: 0 MG/KG/DAY	FETUS #		GRADE
57333 (CONTINUED)			
VISCERAL	5	LIVER- AREA(S) DARK RED ONE, IRREGULARLY SHAPED, MEDIAN LOBE	P
EXTERNAL	7	EARLY RESORPTION	
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,4,5,6,8		
VISCERAL	1,2,3,4,6,8		
SKELETAL	1,2,3,4,5,6,8		
57352	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16		
	A A A A A A A A A/ A A A A A A A		
SEX:	M M M F F F F M F F F M M F M M		
CEPHALIC:	1,3,5,7,9,11,13,15		
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16		
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16		
SKELETAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16		
57356	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16		
	A A A A A A/ A A A A A A A A A A		
SEX:	F F M F F F M F M M M F F M M M		
CEPHALIC:	1,3,5,7,9,11,13,15		
VISCERAL	2	V RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S) URETER, BILATERAL	1
VISCERAL	9	RENAL PAPILLA(E) NOT FULLY DEVELOPED (WOO AND HOAR GRADE 1) BILATERAL	P
VISCERAL	16	V RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S) URETER, BILATERAL	1

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 6
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 1: 0 MG/KG/DAY	FETUS #		GRADE
57356 (CONTINUED)			
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16		
VISCERAL	1,3,4,5,6,7,8,10,11,12,13,14,15		
SKELETAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16		
57360	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16		
	A A A A A A A/ A A A A A A E A A		
SEX:	M F F M M M M M M F F F M - M M		
CEPHALIC:	1,3,5,7,9,11,13,16		
SKELETAL	1	V 14TH RUDIMENTARY RIB(S) RIGHT	P
SKELETAL	4	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
SKELETAL	5	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
SKELETAL	7	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
SKELETAL	8	V 14TH RUDIMENTARY RIB(S) LEFT	P
SKELETAL	11	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
EXTERNAL	14	EARLY RESORPTION	
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,15,16		
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,15,16		
SKELETAL	2,3,6,9,10,12,13,15,16		
57364	1 2 3 4 5 6 7 8 9 10 11 12 13 14		
	A A A A A A/ E A A A E A A A		
SEX:	M M M F M M - F M F - F M M		
CEPHALIC:	1,3,5,8,10,13		

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 7
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 1: 0 MG/KG/DAY	FETUS #	GRADE
57364 (CONTINUED)		
EXTERNAL	7 EARLY RESORPTION	
EXTERNAL	11 EARLY RESORPTION	
	NO REMARKABLE OBSERVATIONS	
EXTERNAL	1,2,3,4,5,6,8,9,10,12,13,14	
VISCERAL	1,2,3,4,5,6,8,9,10,12,13,14	
SKELETAL	1,2,3,4,5,6,8,9,10,12,13,14	
57369	1 2 3 4 5 6 7 8 9 10 11 12 13	
	A A A A A A A/ A A A A A A	
SEX:	M F M M F F M M F M M M M	
CEPHALIC:	2,4,6,8,10,12	
	NO REMARKABLE OBSERVATIONS	
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13	
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13	
SKELETAL	1,2,3,4,5,6,7,8,9,10,11,12,13	
57370	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19	
	A A A A A A A A A/ A A A A A A A A A A	
SEX:	F M M M F F M M F M M M M M F F M F M	
CEPHALIC:	1,3,5,7,9,11,13,15,17,19	
	NO REMARKABLE OBSERVATIONS	
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19	
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19	
SKELETAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19	
57371	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15	
	A A A A A A A A A A/ A A A A A	
SEX:	F F M M F F F F F F M F M M M	
CEPHALIC:	2,4,6,8,10,12,14	

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 8
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 1: 0 MG/KG/DAY		FETUS #		GRADE
57371 (CONTINUED)				
	SKELETAL	14	V 14TH RUDIMENTARY RIB(S) RIGHT	P
			NO REMARKABLE OBSERVATIONS	
	EXTERNAL		1,2,3,4,5,6,7,8,9,10,11,12,13,14,15	
	VISCERAL		1,2,3,4,5,6,7,8,9,10,11,12,13,14,15	
	SKELETAL		1,2,3,4,5,6,7,8,9,10,11,12,13,15	
57379			1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19	
			A A A A A A A E A A/ A A A A A A A E	
		SEX:	F M F M M M F - M F F F M F M F F F -	
		CEPHALIC:	2,4,6,9,11,13,15,17	
	EXTERNAL	8	EARLY RESORPTION	
	EXTERNAL	19	EARLY RESORPTION	
			NO REMARKABLE OBSERVATIONS	
	EXTERNAL		1,2,3,4,5,6,7,9,10,11,12,13,14,15,16,17,18	
	VISCERAL		1,2,3,4,5,6,7,9,10,11,12,13,14,15,16,17,18	
	SKELETAL		1,2,3,4,5,6,7,9,10,11,12,13,14,15,16,17,18	
57380			1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19	
			A A A A A A A E A A/ A A A A A A A A A	
		SEX:	F M M F M M M - M F F M F M M M M M M	
		CEPHALIC:	1,3,5,7,10,12,14,16,18	
	EXTERNAL	8	EARLY RESORPTION	
	VISCERAL	13	V MAJOR BLOOD VESSEL VARIATION RIGHT CAROTID AND RIGHT SUBCLAVIAN ARISE INDEPENDENTLY FROM THE AORTIC ARCH (NO BRACHIOCEPHALIC TRUNK)	P
	SKELETAL		V REDUCED OSSIFICATION OF THE VERTEBRAL ARCHES CERVICAL #3, LEFT; CERVICAL #4 THROUGH #7 BILATERAL	1

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 9
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 1: 0 MG/KG/DAY	FETUS #	GRADE
57380 (CONTINUED)		
	NO REMARKABLE OBSERVATIONS	
EXTERNAL	1,2,3,4,5,6,7,9,10,11,12,13,14,15,16,17,18,19	
VISCERAL	1,2,3,4,5,6,7,9,10,11,12,14,15,16,17,18,19	
SKELETAL	1,2,3,4,5,6,7,9,10,11,12,14,15,16,17,18,19	
57381	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17	
	A A A A A A/ A A A A A A A A A A A	
SEX:	F F F M F M F M M M M M M F M M M	
CEPHALIC:	2,4,6,8,10,12,14,16	
SKELETAL	8 V 25 PRESACRAL VERTEBRAE	P
	NO REMARKABLE OBSERVATIONS	
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17	
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17	
SKELETAL	1,2,3,4,5,6,7,9,10,11,12,13,14,15,16,17	
57385	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	
	A A A A A A A A A A A E/ A A A A A A	
SEX:	M F M F F F M M M M M - F M F M F F	
CEPHALIC:	2,4,6,8,10,13,15,17	
EXTERNAL	12 EARLY RESORPTION	
SKELETAL	15 V 14TH RUDIMENTARY RIB(S) LEFT	P
	NO REMARKABLE OBSERVATIONS	
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,13,14,15,16,17,18	
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,13,14,15,16,17,18	
SKELETAL	1,2,3,4,5,6,7,8,9,10,11,13,14,16,17,18	
57392	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16	
	A A A A A/ A A A A A A A A A A A	
SEX:	M M F M M F M M M F F M M F F M	
CEPHALIC:	1,3,5,7,9,11,13,15	

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 10
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 1: 0 MG/KG/DAY		FETUS #		GRADE
57392 (CONTINUED)				
	VISCERAL	7	V RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S) URETER, LEFT	1
		NO REMARKABLE OBSERVATIONS		
	EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16		
	VISCERAL	1,2,3,4,5,6,8,9,10,11,12,13,14,15,16		
	SKELETAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16		
57397		1 2 3 4 5 6 7 8 9 10 11 12 13 14 15		
		A A E A A A A/ A A A A A A A A		
	SEX:	F M - M F F M M M M F M F M F		
	CEPHALIC:	2,5,7,9,11,13,15		
	EXTERNAL	3	EARLY RESORPTION	
	SKELETAL	9	V STERNEBRA(E) MALALIGNED(SLIGHT OR MODERATE) #4 AND #5	1
	SKELETAL	14	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
		NO REMARKABLE OBSERVATIONS		
	EXTERNAL	1,2,4,5,6,7,8,9,10,11,12,13,14,15		
	VISCERAL	1,2,4,5,6,7,8,9,10,11,12,13,14,15		
	SKELETAL	1,2,4,5,6,7,8,10,11,12,13,15		
57398		1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19		
		A A A A A A A A/ A A A A A A A A A A		
	SEX:	M M M F F F M M F M F M M M F F M F M		
	CEPHALIC:	1,3,5,7,9,11,13,15,17,19		
	VISCERAL	1	V RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S) URETER, BILATERAL	1
	SKELETAL	8	V 14TH RUDIMENTARY RIB(S)	P

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 11
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 1: 0 MG/KG/DAY	FETUS #		GRADE
57398 (CONTINUED)			
		RIGHT	
SKELETAL	16	V 14TH RUDIMENTARY RIB(S)	P
		LEFT	
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19		
VISCERAL	2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19		
SKELETAL	1,2,3,4,5,6,7,9,10,11,12,13,14,15,17,18,19		
57406	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16		
	A A A A E/ A A A A A A A A A A		
SEX:	M M M F - M F F M F M F F M F F		
CEPHALIC:	1,3,6,8,10,12,14,16		
EXTERNAL	5	EARLY RESORPTION	
SKELETAL	14	V REDUCED OSSIFICATION OF THE 13TH RIB(S)	2
		LEFT	
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,4,6,7,8,9,10,11,12,13,14,15,16		
VISCERAL	1,2,3,4,6,7,8,9,10,11,12,13,14,15,16		
SKELETAL	1,2,3,4,6,7,8,9,10,11,12,13,15,16		

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 12
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 2: 10 MG/KG/DAY	FETUS #			GRADE
57307	1	A	M	
	2	A	M	
	3	A	F	
	4	A	M	
	5	A	F	
	6	A/	M	
	7	E	-	
	8	A	M	
	9	A	M	
	10	A	M	
	11	A	F	
	12	A	F	
	13	A	M	
	14	A	F	
	15	A	M	
	CEPHALIC:	2,4,6,9,11,13,15		
SKELETAL	5	V	14TH RUDIMENTARY RIB(S) LEFT	P
EXTERNAL	7		EARLY RESORPTION	
SKELETAL	13	V	14TH RUDIMENTARY RIB(S) RIGHT	P
VISCERAL	14	V	LUNGS- SMALL BILATERAL	P
		V	HEART- MISSHAPEN	P
		M	RIGHT-SIDED AORTIC ARCH	P
			AORTIC ARCH AND DESCENDING AORTA COURSE TO THE RIGHT OF THE VERTEBRAL COLUMN; RIGHT CAROTID AND RIGHT SUBCLAVIAN ARISE INDEPENDENTLY FROM THE AORTIC ARCH (NO BRACHIOCEPHALIC TRUNK); LEFT CAROTID AND LEFT SUBCLAVIAN ARISE FROM A COMMON VESSEL FROM THE AORTIC ARCH	
		M	PERSISTENT TRUNCUS ARTERIOSUS	P
			PULMONARY ARTERIES ARISE FROM THE ASCENDING AORTA; RIGHT PULMONARY ARTERY COURSES RETROESOPHAGEAL; INTERVENTRICULAR SEPTAL DEFECT, A 2 MM IN DIAMETER OPENING IN ANTERIOR PORTION OF THE SEPTUM	
		M	SITUS INVERSUS	P
			TRACHEA, ESOPHAGUS, HEART, GREAT AND MAJOR VESSELS, LUNGS, LIVER, STOMACH, PANCREAS, SPLEEN, KIDNEYS, ADRENALS, AND INTESTINE LATERALLY TRANSPOSED	
SKELETAL		V	14TH RUDIMENTARY RIB(S)	P

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 13
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 2: 10 MG/KG/DAY	FETUS #			GRADE
57307 (CONTINUED)				
			RIGHT	
	NO REMARKABLE OBSERVATIONS			
EXTERNAL	1,2,3,4,5,6,8,9,10,11,12,13,14,15			
VISCERAL	1,2,3,4,5,6,8,9,10,11,12,13,15			
SKELETAL	1,2,3,4,6,8,9,10,11,12,15			
57308	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18			
	A A E A A A/ A A A A A A A A A A A A			
SEX:	M F - F F F F M F M F M M M M F M M			
CEPHALIC:	1,4,6,8,10,12,14,16,18			
EXTERNAL	3	EARLY RESORPTION		
SKELETAL	5	V 14TH RUDIMENTARY RIB(S)	LEFT	P
VISCERAL	18	V MAJOR BLOOD VESSEL VARIATION	RIGHT CAROTID AND RIGHT SUBCLAVIAN ARISE INDEPENDENTLY FROM THE AORTIC ARCH (NO BRACHIOCEPHALIC TRUNK)	P
	NO REMARKABLE OBSERVATIONS			
EXTERNAL	1,2,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18			
VISCERAL	1,2,4,5,6,7,8,9,10,11,12,13,14,15,16,17			
SKELETAL	1,2,4,6,7,8,9,10,11,12,13,14,15,16,17,18			
57317	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15			
	A A A A A/ A A A A E A A A A A			
SEX:	F F F M F F M M M - M F M F M			
CEPHALIC:	2,4,6,8,11,13,15			
EXTERNAL	10	EARLY RESORPTION		
SKELETAL	11	V 14TH RUDIMENTARY RIB(S)	LEFT	P

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 14
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 2: 10 MG/KG/DAY	FETUS #			GRADE
57317 (CONTINUED)				
	NO REMARKABLE OBSERVATIONS			
EXTERNAL	1,2,3,4,5,6,7,8,9,11,12,13,14,15			
VISCERAL	1,2,3,4,5,6,7,8,9,11,12,13,14,15			
SKELETAL	1,2,3,4,5,6,7,8,9,12,13,14,15			
57319	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18			
	A E A A E A A A A A/ E A A A E A A A			
SEX:	F - F F - M F F F F - M F F - M F F			
CEPHALIC:	3,6,8,10,13,16,18			
EXTERNAL	2		EARLY RESORPTION	
SKELETAL	4	M	STERNEBRA(E) MALALIGNED (SEVERE) #2 AND #4; #3 MODERATE; LEFT HALF OF #2 ATTACHED TO RIGHT HALF OF #3	P
EXTERNAL	5		EARLY RESORPTION	
EXTERNAL	11		EARLY RESORPTION	
EXTERNAL	15		EARLY RESORPTION	
	NO REMARKABLE OBSERVATIONS			
EXTERNAL	1,3,4,6,7,8,9,10,12,13,14,16,17,18			
VISCERAL	1,3,4,6,7,8,9,10,12,13,14,16,17,18			
SKELETAL	1,3,6,7,8,9,10,12,13,14,16,17,18			
57324	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17			
	A E A A A A A A/ A A A A A A A A			
SEX:	M - M F F M F F F F M F M M F F F			
CEPHALIC:	1,4,6,8,10,12,14,16			
SKELETAL	1	V	14TH RUDIMENTARY RIB(S) LEFT	P
EXTERNAL	2		EARLY RESORPTION	

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 15
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 2: 10 MG/KG/DAY	FETUS #	GRADE
57324 (CONTINUED)		
	NO REMARKABLE OBSERVATIONS	
EXTERNAL	1,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17	
VISCERAL	1,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17	
SKELETAL	3,4,5,6,7,8,9,10,11,12,13,14,15,16,17	
57332	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15	
	A A A A A A A A/ A A A A A A A	
SEX:	M F M F M F F M F M M F M F M	
CEPHALIC:	1,3,5,7,9,11,13,15	
SKELETAL	5 V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	NO REMARKABLE OBSERVATIONS	
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15	
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15	
SKELETAL	1,2,3,4,6,7,8,9,10,11,12,13,14,15	
57334	1 2 3 4 5 6 7 8 9 10 11 12 13 14	
	A A A A A A/ A A A A A A A A	
SEX:	F M F F M M F F F M F M M M	
CEPHALIC:	1,3,5,7,9,11,13	
SKELETAL	3 V 14TH RUDIMENTARY RIB(S) RIGHT	P
SKELETAL	6 V 14TH RUDIMENTARY RIB(S) BILATERAL	P
SKELETAL	12 V 14TH RUDIMENTARY RIB(S) LEFT	P
SKELETAL	13 V 14TH RUDIMENTARY RIB(S) LEFT	P

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 16
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 2: 10 MG/KG/DAY	FETUS #		GRADE
57334 (CONTINUED)			
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14		
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14		
SKELETAL	1,2,4,5,7,8,9,10,11,14		
57335	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16		
	A A A A A A/ A A A A A A A A A		
SEX:	M F M F M M M F M M F F F M M F		
CEPHALIC:	2,4,6,8,10,12,14,16		
SKELETAL	3	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
SKELETAL	6	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
SKELETAL	7	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
SKELETAL	9	V 14TH RUDIMENTARY RIB(S) RIGHT	P
VISCERAL	10	RENAL PAPILLA(E) NOT FULLY DEVELOPED (WOO AND HOAR GRADE 1) RIGHT	P
SKELETAL	13	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16		
VISCERAL	1,2,3,4,5,6,7,8,9,11,12,13,14,15,16		
SKELETAL	1,2,4,5,8,10,11,12,14,15,16		
57337	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15		
	A A A A A A A A A A/ A A A A A		
SEX:	M M F M F M M M M F F M F F F		
CEPHALIC:	2,4,6,8,10,12,14		

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 17
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 2: 10 MG/KG/DAY		FETUS #		GRADE
57337 (CONTINUED)				
	VISCERAL	3	V RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S) URETER, LEFT	1
	SKELETAL		V 7TH CERVICAL RIB(S) PINPOINT, LEFT	P
	SKELETAL	6	V 14TH RUDIMENTARY RIB(S) LEFT	P
	VISCERAL	8	V RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S) URETER, RIGHT	1
		NO REMARKABLE OBSERVATIONS		
	EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15		
	VISCERAL	1,2,4,5,6,7,9,10,11,12,13,14,15		
	SKELETAL	1,2,4,5,7,8,9,10,11,12,13,14,15		
57339		1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17		
		A A A A A A A A/ A A A A A A A A		
	SEX:	F M F F M M F M M M F F F F F F		
	CEPHALIC:	2,4,6,8,10,12,14,16		
	SKELETAL	1	V 14TH RUDIMENTARY RIB(S) LEFT	P
	SKELETAL	5	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	SKELETAL	10	V 14TH RUDIMENTARY RIB(S) LEFT	P
	SKELETAL	15	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
		NO REMARKABLE OBSERVATIONS		
	EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17		
	VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17		
	SKELETAL	2,3,4,6,7,8,9,11,12,13,14,16,17		

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 18
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 2: 10 MG/KG/DAY	FETUS #			GRADE
57340	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17			
	A A A A A/ A A A A A A A A A A A			
SEX:	F F M F M M M M F F M F F F M F F			
CEPHALIC:	1,3,5,7,9,11,13,15,17			
VISCERAL	4	V	RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S) URETER, BILATERAL	1
SKELETAL	10	V	14TH RUDIMENTARY RIB(S) LEFT	P
	NO REMARKABLE OBSERVATIONS			
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17			
VISCERAL	1,2,3,5,6,7,8,9,10,11,12,13,14,15,16,17			
SKELETAL	1,2,3,4,5,6,7,8,9,11,12,13,14,15,16,17			
57343	1 2 3 4 5 6 7 8 9 10 11 12 13			
	A A A A A A A/ A A A A A A			
SEX:	F M F M F M F M M M F M F			
CEPHALIC:	2,4,6,8,10,12			
SKELETAL	6	V	14TH RUDIMENTARY RIB(S) BILATERAL	P
SKELETAL	10	V	14TH RUDIMENTARY RIB(S) RIGHT	P
SKELETAL	13	V	14TH RUDIMENTARY RIB(S) BILATERAL	P
	NO REMARKABLE OBSERVATIONS			
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13			
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13			
SKELETAL	1,2,3,4,5,7,8,9,11,12			

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 19
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 2: 10 MG/KG/DAY	FETUS #		GRADE
57347	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17		
	A A A/ A A A A A A A E A A E A A E		
SEX:	F F M M M M F M M F - M M - F F -		
CEPHALIC:	2,4,6,8,10,13,16		
SKELETAL	10	V 14TH RUDIMENTARY RIB(S) LEFT	P
EXTERNAL	11	EARLY RESORPTION	
EXTERNAL	14	EARLY RESORPTION	
EXTERNAL	17	EARLY RESORPTION	
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,4,5,6,7,8,9,10,12,13,15,16		
VISCERAL	1,2,3,4,5,6,7,8,9,10,12,13,15,16		
SKELETAL	1,2,3,4,5,6,7,8,9,12,13,15,16		
57350	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19		
	A A A E A A A A A A/ A A E A A A A A A		
SEX:	F M M - F M M M M F F F - M F F F M M		
CEPHALIC:	1,3,6,8,10,12,15,17,19		
EXTERNAL	4	EARLY RESORPTION	
SKELETAL	5	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
VISCERAL	12	V RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S) URETER, RIGHT	1
EXTERNAL	13	EARLY RESORPTION	
SKELETAL	15	V 14TH RUDIMENTARY RIB(S) LEFT	P

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 20
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 2: 10 MG/KG/DAY	FETUS #	GRADE
57350 (CONTINUED)		
	NO REMARKABLE OBSERVATIONS	
EXTERNAL	1,2,3,5,6,7,8,9,10,11,12,14,15,16,17,18,19	
VISCERAL	1,2,3,5,6,7,8,9,10,11,14,15,16,17,18,19	
SKELETAL	1,2,3,6,7,8,9,10,11,12,14,16,17,18,19	
57353	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17	
	A A A A A A A A A A/ A A A A A A A	
SEX:	M M F M F M M F F F F F M F M F M	
CEPHALIC:	2,4,6,8,10,12,14,16	
	NO REMARKABLE OBSERVATIONS	
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17	
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17	
SKELETAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17	
57358	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	
	A A A A A A A A A A/ A A A A A A A A	
SEX:	M F F F M F F F M F F M M F M F M F	
CEPHALIC:	1,3,5,7,9,11,13,15,17	
SKELETAL	3 V 14TH RUDIMENTARY RIB(S) LEFT	P
SKELETAL	5 V 14TH RUDIMENTARY RIB(S) BILATERAL	P
SKELETAL	7 V 14TH RUDIMENTARY RIB(S) LEFT	P
SKELETAL	10 V STERNEBRA(E) MALALIGNED(SLIGHT OR MODERATE) #4 AND #5	1
SKELETAL	16 V STERNEBRA(E) MALALIGNED(SLIGHT OR MODERATE) #4 AND #5	1

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 21
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 2: 10 MG/KG/DAY	FETUS #			GRADE
57358 (CONTINUED)				
SKELETAL	17	V	STERNEBRA(E) MALALIGNED(SLIGHT OR MODERATE) #3 THROUGH #5	1
	NO REMARKABLE OBSERVATIONS			
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18			
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18			
SKELETAL	1,2,4,6,8,9,11,12,13,14,15,18			
57367	1 2 3 4 5 6 7 8 9 10 11 12 13 14			
	A A A A A A/ A A A A A A A A			
SEX:	F F F F F F F M F M M F F F			
CEPHALIC:	2,4,6,8,10,12,14			
	NO REMARKABLE OBSERVATIONS			
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14			
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14			
SKELETAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14			
57373	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18			
	A A A A A A A A A A A E/ E A A A A A			
SEX:	M M F F M M M M F F F - - F M F F M			
CEPHALIC:	2,4,6,8,10,14,16,18			
VISCERAL	3	V	RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S) URETER, RIGHT	1
SKELETAL		V	25 PRESACRAL VERTEBRAE	P
SKELETAL	8	V	14TH RUDIMENTARY RIB(S) BILATERAL	P
EXTERNAL	12		EARLY RESORPTION	
EXTERNAL	13		EARLY RESORPTION	

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 22
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 2: 10 MG/KG/DAY	FETUS #	GRADE
57373 (CONTINUED)		
	NO REMARKABLE OBSERVATIONS	
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,14,15,16,17,18	
VISCERAL	1,2,4,5,6,7,8,9,10,11,14,15,16,17,18	
SKELETAL	1,2,4,5,6,7,9,10,11,14,15,16,17,18	
57376	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	
	A A A E A A A/ A A A A A A A A E A	
SEX:	M F F - M M F F M M M M M F M F - M	
CEPHALIC:	1,3,6,8,10,12,14,16	
EXTERNAL	4 EARLY RESORPTION	
EXTERNAL	17 EARLY RESORPTION	
	NO REMARKABLE OBSERVATIONS	
EXTERNAL	1,2,3,5,6,7,8,9,10,11,12,13,14,15,16,18	
VISCERAL	1,2,3,5,6,7,8,9,10,11,12,13,14,15,16,18	
SKELETAL	1,2,3,5,6,7,8,9,10,11,12,13,14,15,16,18	
57393	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17	
	A A A E A A A A A/ E A A A A A A A	
SEX:	M M F - M M M M M - M M F M M F M	
CEPHALIC:	2,5,7,9,12,14,16	
EXTERNAL	4 EARLY RESORPTION	
EXTERNAL	10 EARLY RESORPTION	
	NO REMARKABLE OBSERVATIONS	
EXTERNAL	1,2,3,5,6,7,8,9,11,12,13,14,15,16,17	
VISCERAL	1,2,3,5,6,7,8,9,11,12,13,14,15,16,17	
SKELETAL	1,2,3,5,6,7,8,9,11,12,13,14,15,16,17	
57403	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15	
	A A A A A A A A/ A A A A A A A A	
SEX:	M F F F M F M M M F M F F F F	
CEPHALIC:	2,4,6,8,10,12,14	

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 23
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 2: 10 MG/KG/DAY	FETUS #			GRADE
57403 (CONTINUED)				
SKELETAL	3	V	14TH RUDIMENTARY RIB(S) BILATERAL	P
	NO REMARKABLE OBSERVATIONS			
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15			
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15			
SKELETAL	1,2,4,5,6,7,8,9,10,11,12,13,14,15			

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 24
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 3: 100 MG/KG/DAY	FETUS #			GRADE
57314	1 2 3 4 5 6 7 8 9 10 11 12 13			
	A A A A A A/ A E A A A A A			
SEX:	F F M M M F F - F F M F M			
CEPHALIC:	1,3,5,7,10,12			
SKELETAL	6	V	7TH CERVICAL RIB(S) INTERMEDIATE, LEFT	P
EXTERNAL	8		EARLY RESORPTION	
SKELETAL	13	V	14TH RUDIMENTARY RIB(S) BILATERAL	P
NO REMARKABLE OBSERVATIONS				
EXTERNAL	1,2,3,4,5,6,7,9,10,11,12,13			
VISCERAL	1,2,3,4,5,6,7,9,10,11,12,13			
SKELETAL	1,2,3,4,5,7,9,10,11,12			
57321	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16			
	A A A/ A A A A A A A A A A A A			
SEX:	F F M F F M F F M F F F M M M M			
CEPHALIC:	2,4,6,8,10,12,14,16			
SKELETAL	3	V	14TH RUDIMENTARY RIB(S) BILATERAL	P
		V	VERTEBRAL CENTRA NOT FULLY OSSIFIED THORACIC #12	P
SKELETAL	12	V	14TH RUDIMENTARY RIB(S) LEFT	P
SKELETAL	13	V	14TH RUDIMENTARY RIB(S) BILATERAL	P
SKELETAL	15	V	14TH RUDIMENTARY RIB(S)	P

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 25
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 3: 100 MG/KG/DAY	FETUS #	GRADE
57321 (CONTINUED)		
	LEFT	
SKELETAL	16 V 14TH RUDIMENTARY RIB(S)	P
	RIGHT	
	NO REMARKABLE OBSERVATIONS	
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16	
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16	
SKELETAL	1,2,4,5,6,7,8,9,10,11,14	
57327	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	
	A A A A A A A A/ A A A E A A A A A A	
SEX:	F F M F M F M M F F M - F F M M F F	
CEPHALIC:	2,4,6,8,10,13,15,17	
EXTERNAL	12 EARLY RESORPTION	
SKELETAL	13 V 14TH RUDIMENTARY RIB(S)	P
	LEFT	
	NO REMARKABLE OBSERVATIONS	
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,13,14,15,16,17,18	
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,13,14,15,16,17,18	
SKELETAL	1,2,3,4,5,6,7,8,9,10,11,14,15,16,17,18	
57331	1 2 3 4 5 6 7 8 9 10 11 12 13	
	A A A A A A A/ A A A A A A	
SEX:	M M M M M F M F M F F M F	
CEPHALIC:	2,4,6,8,10,12	
	NO REMARKABLE OBSERVATIONS	
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13	
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13	
SKELETAL	1,2,3,4,5,6,7,8,9,10,11,12,13	

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 26
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 3: 100 MG/KG/DAY	FETUS #																			GRADE
57344		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	
		E	A	A	A	A	A	A	A	A	A/	A	A	A	A	A	A	A	A	A	A	
	SEX:	-	M	F	F	M	M	M	M	M	F	M	F	M	F	F	F	F	M	F	M	
	CEPHALIC:	2,4,6,8,10,12,14,16,18,20																				
EXTERNAL		1		EARLY RESORPTION																		
SKELETAL		2		V 14TH RUDIMENTARY RIB(S) LEFT																		P
SKELETAL		20		V 14TH RUDIMENTARY RIB(S) LEFT																		P
	NO REMARKABLE OBSERVATIONS																					
EXTERNAL		2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20																				
VISCERAL		2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20																				
SKELETAL		3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19																				

																		GRADE
57345		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	
		E	A	A	A	A	A	A	A/	A	A	A	A	A	A	A	A	
	SEX:	-	M	M	F	M	M	M	M	F	M	M	M	F	M	F	F	
	CEPHALIC:	3,5,7,9,11,13,15																
EXTERNAL		1		EARLY RESORPTION														
SKELETAL		2		V STERNEBRA(E) MALALIGNED(SLIGHT OR MODERATE) #3 AND #4														1
SKELETAL		4		V 14TH RUDIMENTARY RIB(S) LEFT														P
SKELETAL		10		V 14TH RUDIMENTARY RIB(S) LEFT														P
SKELETAL		12		V 14TH RUDIMENTARY RIB(S) BILATERAL														P

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 27
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 3: 100 MG/KG/DAY	FETUS #	GRADE
57345 (CONTINUED)		
SKELETAL	15 V 14TH RUDIMENTARY RIB(S) LEFT	P
	NO REMARKABLE OBSERVATIONS	
EXTERNAL	2,3,4,5,6,7,8,9,10,11,12,13,14,15,16	
VISCERAL	2,3,4,5,6,7,8,9,10,11,12,13,14,15,16	
SKELETAL	3,5,6,7,8,9,11,13,14,16	
57348	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16	
	A A A A A A A/ A A A A A A A A A	
SEX:	M M M M M M F F F F M F F M M F	
CEPHALIC:	1,3,5,7,9,11,13,15	
SKELETAL	3 V 14TH RUDIMENTARY RIB(S) BILATERAL	P
SKELETAL	5 V 14TH RUDIMENTARY RIB(S) RIGHT	P
SKELETAL	6 V 14TH RUDIMENTARY RIB(S) BILATERAL	P
SKELETAL	16 V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	NO REMARKABLE OBSERVATIONS	
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16	
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16	
SKELETAL	1,2,4,7,8,9,10,11,12,13,14,15	
57354	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16	
	A A A A/ A A A A A A A A A A A A	
SEX:	M F F M M M F F F M F M F M M F	
CEPHALIC:	1,3,5,7,9,11,13,15	

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 28
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 3: 100 MG/KG/DAY		FETUS #		GRADE
57354 (CONTINUED)				
	SKELETAL	8	V 25 PRESACRAL VERTEBRAE	P
	VISCERAL	9	V RENAL PAPILLA(E) NOT DEVELOPED AND/OR DISTENDED URETER(S) URETER, BILATERAL	1
		NO REMARKABLE OBSERVATIONS		
	EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16		
	VISCERAL	1,2,3,4,5,6,7,8,10,11,12,13,14,15,16		
	SKELETAL	1,2,3,4,5,6,7,9,10,11,12,13,14,15,16		
57357		1 2 3 4 5 6 7 8 9 10 11 12 13 14		
		A A A A A A A A A A/ A A A A		
	SEX:	M M F M M M F F M M F F M M		
	CEPHALIC:	2,4,6,8,10,12,14		
	SKELETAL	10	V 14TH RUDIMENTARY RIB(S) RIGHT	P
	SKELETAL	11	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	SKELETAL	14	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
		NO REMARKABLE OBSERVATIONS		
	EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14		
	VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14		
	SKELETAL	1,2,3,4,5,6,7,8,9,12,13		
57361		1 2 3 4 5 6 7 8 9 10 11 12 13 14 15		
		A A A A A A A A/ A A A A E A A		
	SEX:	F M F M F M M M M F F F - M F		
	CEPHALIC:	2,4,6,8,10,12,15		
	EXTERNAL	13	EARLY RESORPTION	

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 29
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 3: 100 MG/KG/DAY	FETUS #		GRADE
57361 (CONTINUED)			
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,14,15		
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,14,15		
SKELETAL	1,2,3,4,5,6,7,8,9,10,11,12,14,15		
57365	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15		
	A A A A A A A A A A/ A A A A A		
SEX:	F M F M M M F M M F M M M F F		
CEPHALIC:	2,4,6,8,10,12,14		
SKELETAL	6	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
SKELETAL	10	V 14TH RUDIMENTARY RIB(S) LEFT	P
SKELETAL	12	V 14TH RUDIMENTARY RIB(S) LEFT	P
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15		
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15		
SKELETAL	1,2,3,4,5,7,8,9,11,13,14,15		
57368	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15		
	A E E A A A A/ A A A E A E A A		
SEX:	M - - F F F M F F F - M - M F		
CEPHALIC:	1,5,7,9,12,15		
EXTERNAL	2	EARLY RESORPTION	
EXTERNAL	3	EARLY RESORPTION	
SKELETAL	4	V 14TH RUDIMENTARY RIB(S) LEFT	P

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 30
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 3: 100 MG/KG/DAY	FETUS #		GRADE
57368 (CONTINUED)			
SKELETAL	5	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
EXTERNAL	11	EARLY RESORPTION	
EXTERNAL	13	EARLY RESORPTION	
SKELETAL	15	V 14TH RUDIMENTARY RIB(S) LEFT	P
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,4,5,6,7,8,9,10,12,14,15		
VISCERAL	1,4,5,6,7,8,9,10,12,14,15		
SKELETAL	1,6,7,8,9,10,12,14		
57372	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17		
	A A A A A A A A A A/ A A A A A A A		
SEX:	F F F M M M F M M M M F M M F F M		
CEPHALIC:	1,3,5,7,9,11,13,15,17		
SKELETAL	11	V 14TH RUDIMENTARY RIB(S) LEFT	P
SKELETAL	13	V 14TH RUDIMENTARY RIB(S) LEFT	P
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17		
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17		
SKELETAL	1,2,3,4,5,6,7,8,9,10,12,14,15,16,17		
57375	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15		
	A A A A A A/ A A A A A A A A A		
SEX:	F M M F M M F F F M M M M F F		
CEPHALIC:	2,4,6,8,10,12,14		

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 31
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 3: 100 MG/KG/DAY	FETUS #		GRADE
57375 (CONTINUED)			
SKELETAL	9	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15		
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15		
SKELETAL	1,2,3,4,5,6,7,8,10,11,12,13,14,15		
57383	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19		
	A A A A A A A A A A A/ A A A A A A A		
SEX:	M M M M F F F M M F F F F M F M F F F		
CEPHALIC:	2,4,6,8,10,12,14,16,18		
SKELETAL	6	V STERNEBRA(E) MALALIGNED(SLIGHT OR MODERATE) #3 THROUGH #5	1
SKELETAL	10	V 7TH CERVICAL RIB(S) PINPOINT, BILATERAL	P
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19		
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19		
SKELETAL	1,2,3,4,5,7,8,9,11,12,13,14,15,16,17,18,19		
57386	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15		
	A A A A A/ A A A A A A A A A A		
SEX:	F F M M F M M M F F F F F M F		
CEPHALIC:	1,3,5,7,9,11,13,15		
VISCERAL	8	V HEMORRHAGIC RING AROUND THE IRIS LEFT	P

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 32
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 3: 100 MG/KG/DAY	FETUS #		GRADE
57386 (CONTINUED)			
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15		
VISCERAL	1,2,3,4,5,6,7,9,10,11,12,13,14,15		
SKELETAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15		
57387	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17		
	A A A E A A E/ E A A A A A A A A		
SEX:	F F M - F M - - M F F M F F F F F		
CEPHALIC:	2,5,9,11,13,15,17		
SKELETAL	2	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
SKELETAL	3	V 14TH RUDIMENTARY RIB(S) RIGHT	P
EXTERNAL	4	EARLY RESORPTION	
EXTERNAL	7	EARLY RESORPTION	
EXTERNAL	8	EARLY RESORPTION	
SKELETAL	14	V 14TH RUDIMENTARY RIB(S) RIGHT	P
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,5,6,9,10,11,12,13,14,15,16,17		
VISCERAL	1,2,3,5,6,9,10,11,12,13,14,15,16,17		
SKELETAL	1,5,6,9,10,11,12,13,15,16,17		
57389	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17		
	A A A A A A A/ A A A A A A A A A		
SEX:	M F F F M M M F F F M M M F F F F		
CEPHALIC:	2,4,6,8,10,12,14,16		
SKELETAL	16	V 14TH RUDIMENTARY RIB(S)	P

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 33
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 3: 100 MG/KG/DAY	FETUS #		GRADE
57389 (CONTINUED)			
		RIGHT	
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17		
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17		
SKELETAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,17		
57390	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15		
	A A A A A A/ A A A A A A A A A		
SEX:	F M F F F F M M F F F F M F M		
CEPHALIC:	1,3,5,9,11,13,15		
SKELETAL	1	V 14TH RUDIMENTARY RIB(S) RIGHT	P
SKELETAL	6	V 14TH RUDIMENTARY RIB(S) LEFT	P
SKELETAL	12	V 14TH RUDIMENTARY RIB(S) LEFT	P
SKELETAL	15	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15		
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15		
SKELETAL	2,3,4,5,7,8,9,10,11,13,14		
57394	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17		
	A A A A E E E E A/ E E A A E A A A		
SEX:	M F M M - - - - F - - F F - M F M		
CEPHALIC:	1,3,9,13,16		
EXTERNAL	5	EARLY RESORPTION	

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 34
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 3: 100 MG/KG/DAY	FETUS #		GRADE
57394 (CONTINUED)			
EXTERNAL	6	EARLY RESORPTION	
EXTERNAL	7	EARLY RESORPTION	
EXTERNAL	8	EARLY RESORPTION	
EXTERNAL	10	EARLY RESORPTION	
EXTERNAL	11	EARLY RESORPTION	
SKELETAL	13	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
EXTERNAL	14	EARLY RESORPTION	
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,4,9,12,13,15,16,17		
VISCERAL	1,2,3,4,9,12,13,15,16,17		
SKELETAL	1,2,3,4,9,12,15,16,17		
57404	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16		
	A A A A A A A A/ A A A A A A A A		
SEX:	F F M F M M F M F M M F F M M M		
CEPHALIC:	1,3,5,7,9,11,13,15		
SKELETAL	11	V 7TH CERVICAL RIB(S) PINPOINT, RIGHT	P
SKELETAL	12	V 7TH CERVICAL RIB(S) PINPOINT, RIGHT	P
SKELETAL	13	V 7TH CERVICAL RIB(S) PINPOINT, RIGHT	P
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16		
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16		
SKELETAL	1,2,3,4,5,6,7,8,9,10,14,15,16		

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 35
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 4: 1000 MG/KG/DAY	FETUS #																			GRADE
57309		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	
		A	A	E	A	A	A	A	A/	A	A	A	A	A	A	A	A	A	A	A	
	SEX:	M	F	-	M	F	F	F	M	M	F	M	M	F	M	F	M	F	F	M	
	CEPHALIC:	2,5,7,9,11,13,15,17,19																			
EXTERNAL		3	EARLY RESORPTION																		
SKELETAL		8	V 14TH RUDIMENTARY RIB(S) BILATERAL																		P
SKELETAL		9	V 14TH RUDIMENTARY RIB(S) BILATERAL																		P
SKELETAL		10	V 14TH RUDIMENTARY RIB(S) RIGHT																		P
SKELETAL		12	V 14TH RUDIMENTARY RIB(S) BILATERAL																		P
SKELETAL		18	V 14TH RUDIMENTARY RIB(S) LEFT																		P
	NO REMARKABLE OBSERVATIONS																				
EXTERNAL		1,2,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19																			
VISCERAL		1,2,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19																			
SKELETAL		1,2,4,5,6,7,11,13,14,15,16,17,19																			
57310		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16				
		A	A	A	A	A	A	A	A/	A	A	A	A	A	A	A	E				
	SEX:	M	M	M	M	F	F	M	F	M	F	F	F	F	F	M	-				
	CEPHALIC:	1,3,5,7,9,11,13,15																			
SKELETAL		2	V 14TH RUDIMENTARY RIB(S) LEFT																		P
SKELETAL		3	V 14TH RUDIMENTARY RIB(S)																		P

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 36
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 4: 1000 MG/KG/DAY	FETUS #		GRADE
57310 (CONTINUED)			
		RIGHT	
SKELETAL	4	V 14TH RUDIMENTARY RIB(S)	P
		LEFT	
SKELETAL	5	V 14TH RUDIMENTARY RIB(S)	P
		BILATERAL	
SKELETAL	6	V 14TH RUDIMENTARY RIB(S)	P
		RIGHT	
SKELETAL	7	V 14TH RUDIMENTARY RIB(S)	P
		BILATERAL	
SKELETAL	8	V 14TH RUDIMENTARY RIB(S)	P
		LEFT	
SKELETAL	12	V 14TH RUDIMENTARY RIB(S)	P
		BILATERAL	
SKELETAL	13	V 14TH RUDIMENTARY RIB(S)	P
		LEFT	
EXTERNAL	16	EARLY RESORPTION	
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15		
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15		
SKELETAL	1,9,10,11,14,15		

57315	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
	A	A	A	A	A	A	A	A/	A	A	A	A	A	A	A	A	A
SEX:	M	F	F	F	F	M	M	F	M	F	F	F	M	F	F	M	F
CEPHALIC:	2,4,6,8,10,12,14,16																

SKELETAL	2	V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED	P
		#5	
SKELETAL	3	V STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED	P
		#5	

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 37
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 4: 1000 MG/KG/DAY		FETUS #		GRADE
57315 (CONTINUED)				
	SKELETAL	9	V 7TH CERVICAL RIB(S) PINPOINT, LEFT	P
	SKELETAL	10	V 7TH CERVICAL RIB(S) PINPOINT, BILATERAL	P
	SKELETAL	13	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
		NO REMARKABLE OBSERVATIONS		
	EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17		
	VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17		
	SKELETAL	1,4,5,6,7,8,11,12,14,15,16,17		
57316		1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16		
		A A A A A A A A/ A A A A A A A A		
	SEX:	F F F F M M F M F F M F M M F F		
	CEPHALIC:	3,5,7,9,11,13,15		
	SKELETAL	9	V 7TH CERVICAL RIB(S) PINPOINT, LEFT	P
		NO REMARKABLE OBSERVATIONS		
	EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16		
	VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16		
	SKELETAL	1,2,3,4,5,6,7,8,10,11,12,13,14,15,16		
57323		1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16		
		A A A A A A A A/ A A A A A A A A		
	SEX:	M F M M F F M M M F M M F M M F		
	CEPHALIC:	2,4,6,8,10,12,14,16		
	SKELETAL	2	V 14TH RUDIMENTARY RIB(S) LEFT	P

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 38
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 4: 1000 MG/KG/DAY		FETUS #		GRADE
57323 (CONTINUED)				
	SKELETAL	4	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	SKELETAL	5	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	SKELETAL	6	V VERTEBRAL CENTRA NOT FULLY OSSIFIED THORACIC #13	P
	SKELETAL	8	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	SKELETAL	9	V 14TH RUDIMENTARY RIB(S) LEFT	P
	SKELETAL	12	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	SKELETAL	14	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	SKELETAL	15	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	SKELETAL	16	V 14TH RUDIMENTARY RIB(S) LEFT	P
		NO REMARKABLE OBSERVATIONS		
	EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16		
	VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16		
	SKELETAL	1,3,7,10,11,13		
57330		1 2 3 4 5 6 7 8 9 10 11 12 13 14 15		
		A A A A A A A/ A A A A A A A A		
	SEX:	M M M F M F M F F F F F F F F		
	CEPHALIC:	1,3,5,7,9,11,13,15		
	SKELETAL	2	V 14TH RUDIMENTARY RIB(S) BILATERAL	P

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 39
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 4: 1000 MG/KG/DAY	FETUS #		GRADE
57330 (CONTINUED)			
SKELETAL	3	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
SKELETAL	8	V STERNEBRA(E) MALALIGNED(SLIGHT OR MODERATE) #2 THROUGH #4	2
SKELETAL	9	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
SKELETAL	10	V 14TH RUDIMENTARY RIB(S) RIGHT	P
SKELETAL	12	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
SKELETAL	14	V 14TH RUDIMENTARY RIB(S) LEFT	P
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15		
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15		
SKELETAL	1,4,5,6,7,11,13,15		
57336	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15		
	A A A A A A A A/ A A A A A A A		
SEX:	M M F M F F F M M M F F F M M		
CEPHALIC:	1,3,5,7,9,11,13,15		
SKELETAL	8	V 14TH RUDIMENTARY RIB(S) LEFT	P
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15		
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15		
SKELETAL	1,2,3,4,5,6,7,9,10,11,12,13,14,15		
57338	1 2 3 4 5 6 7 8 9 10 11 12 13		
	A A A A A/ A A A A A A A A		
SEX:	F M F F M M M M M M F M F		
CEPHALIC:	1,3,5,7,9,11,13		

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 40
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 4: 1000 MG/KG/DAY		FETUS #		GRADE
57338 (CONTINUED)				
	SKELETAL	6	V 14TH RUDIMENTARY RIB(S) LEFT	P
		NO REMARKABLE OBSERVATIONS		
	EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13		
	VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13		
	SKELETAL	1,2,3,4,5,7,8,9,10,11,12,13		
57342		1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18		
		A A A A A A A A A A/ A A A A A A A A		
	SEX:	M M F F M M F M F F F F M F F M M M		
	CEPHALIC:	1,3,5,7,9,11,13,15,17		
	SKELETAL	2	V 14TH RUDIMENTARY RIB(S) LEFT	P
	SKELETAL	5	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	SKELETAL	6	V 14TH RUDIMENTARY RIB(S) LEFT	P
	SKELETAL	16	V 14TH RUDIMENTARY RIB(S) RIGHT	P
		NO REMARKABLE OBSERVATIONS		
	EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18		
	VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18		
	SKELETAL	1,3,4,7,8,9,10,11,12,13,14,15,17,18		
57349		1 2 3 4 5 6 7 8 9 10 11 12 13 14		
		A A A A A A/ A A A A A A A A		
	SEX:	M F M M F F M M M F F F F F		
	CEPHALIC:	2,4,6,8,10,12,14		

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 41
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 4: 1000 MG/KG/DAY		FETUS #		GRADE
57349 (CONTINUED)				
	SKELETAL	1	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	SKELETAL	2	V 14TH RUDIMENTARY RIB(S) LEFT	P
	SKELETAL	3	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	SKELETAL	4	V 14TH RUDIMENTARY RIB(S) LEFT	P
	SKELETAL	5	V 14TH RUDIMENTARY RIB(S) LEFT	P
	SKELETAL	7	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	SKELETAL	8	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	SKELETAL	9	V 14TH RUDIMENTARY RIB(S) LEFT	P
	SKELETAL	10	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	SKELETAL	12	V 14TH RUDIMENTARY RIB(S) LEFT	P
	SKELETAL	13	V 14TH RUDIMENTARY RIB(S) LEFT	P
		NO REMARKABLE OBSERVATIONS		
	EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14		
	VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14		
	SKELETAL	6,11,14		

57351		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
		A	A	A	A	A/	A	A	E	A	A	A	A	A	A	A	A	A	A
	SEX:	F	M	F	M	F	M	F	-	M	M	M	F	M	M	F	F	F	F
	CEPHALIC:	2,4,6,9,11,13,15,17																	

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 42
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 4: 1000 MG/KG/DAY		FETUS #		GRADE
57351 (CONTINUED)				
	SKELETAL	3	V STERNEBRA(E) MALALIGNED(SLIGHT OR MODERATE) #4 AND #5	1
			V 14TH RUDIMENTARY RIB(S) RIGHT	P
	EXTERNAL	8	EARLY RESORPTION	
	SKELETAL	9	V 14TH RUDIMENTARY RIB(S) LEFT	P
	SKELETAL	13	V STERNEBRA(E) MALALIGNED(SLIGHT OR MODERATE) #3 THROUGH #5	1
		NO REMARKABLE OBSERVATIONS		
	EXTERNAL	1,2,3,4,5,6,7,9,10,11,12,13,14,15,16,17,18		
	VISCERAL	1,2,3,4,5,6,7,9,10,11,12,13,14,15,16,17,18		
	SKELETAL	1,2,4,5,6,7,10,11,12,14,15,16,17,18		
57359		1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17		
		A A A A A A A A/ A A A A A A A E A		
	SEX:	F M M F M F M F F M M F F F M - F		
	CEPHALIC:	2,4,6,8,10,12,14,17		
	VISCERAL	1	RENAL PAPILLA(E) NOT FULLY DEVELOPED (WOO AND HOAR GRADE 1) LEFT	P
	SKELETAL	3	V 14TH RUDIMENTARY RIB(S) LEFT	P
	SKELETAL	7	V 14TH RUDIMENTARY RIB(S) RIGHT	P
	EXTERNAL	16	EARLY RESORPTION	
		NO REMARKABLE OBSERVATIONS		
	EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,17		
	VISCERAL	2,3,4,5,6,7,8,9,10,11,12,13,14,15,17		
	SKELETAL	1,2,4,5,6,8,9,10,11,12,13,14,15,17		

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 43
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 4: 1000 MG/KG/DAY	FETUS #			GRADE
57362	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16			
	A A A A A A A A/ E A A A A A A A			
SEX:	M M M F F F M M - F F M F F F M			
CEPHALIC:	1,3,5,7,10,12,14,16			
SKELETAL	3	V	14TH RUDIMENTARY RIB(S) LEFT	P
SKELETAL	5	V	14TH RUDIMENTARY RIB(S) BILATERAL	P
SKELETAL	7	V	14TH RUDIMENTARY RIB(S) LEFT	P
SKELETAL	8	V	14TH RUDIMENTARY RIB(S) BILATERAL	P
EXTERNAL	9		EARLY RESORPTION	
SKELETAL	10	V	14TH RUDIMENTARY RIB(S) LEFT	P
SKELETAL	11	V	14TH RUDIMENTARY RIB(S) BILATERAL	P
SKELETAL	12	V	14TH RUDIMENTARY RIB(S) BILATERAL	P
SKELETAL	13	V	14TH RUDIMENTARY RIB(S) LEFT	P
SKELETAL	16	V	14TH RUDIMENTARY RIB(S) BILATERAL	P
NO REMARKABLE OBSERVATIONS				
EXTERNAL	1,2,3,4,5,6,7,8,10,11,12,13,14,15,16			
VISCERAL	1,2,3,4,5,6,7,8,10,11,12,13,14,15,16			
SKELETAL	1,2,4,6,14,15			
57363	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15			
	A A A A A A/ A A A E A A A A A			
SEX:	F F F F M F M M F - F M F F F			
CEPHALIC:	2,4,6,8,11,13,15			

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 44
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 4: 1000 MG/KG/DAY		FETUS #		GRADE
57363 (CONTINUED)				
	SKELETAL	5	V 7TH CERVICAL RIB(S) INTERMEDIATE, RIGHT	P
			V REDUCED OSSIFICATION OF THE 13TH RIB(S) SEVERE, LEFT; MODERATE, RIGHT	P
			V 25 PRESACRAL VERTEBRAE	P
	EXTERNAL	10	EARLY RESORPTION	
	SKELETAL	14	V 7TH CERVICAL RIB(S) PINPOINT, LEFT	P
		NO REMARKABLE OBSERVATIONS		
	EXTERNAL	1,2,3,4,5,6,7,8,9,11,12,13,14,15		
	VISCERAL	1,2,3,4,5,6,7,8,9,11,12,13,14,15		
	SKELETAL	1,2,3,4,6,7,8,9,11,12,13,15		
57366		1 2 3 4 5 6 7 8 9 10 11 12 13 14 15		
		A A A A/ A A A A A A E A A A A		
	SEX:	M F M M M M M M M M - F F F F		
	CEPHALIC:	1,3,5,7,9,12,14		
	SKELETAL	2	V 14TH RUDIMENTARY RIB(S) RIGHT	P
	SKELETAL	9	V 14TH RUDIMENTARY RIB(S) RIGHT	P
	EXTERNAL	11	EARLY RESORPTION	
	SKELETAL	14	V 14TH RUDIMENTARY RIB(S) RIGHT	P
		NO REMARKABLE OBSERVATIONS		
	EXTERNAL	1,2,3,4,5,6,7,8,9,10,12,13,14,15		
	VISCERAL	1,2,3,4,5,6,7,8,9,10,12,13,14,15		
	SKELETAL	1,3,4,5,6,7,8,10,12,13,15		
57374		1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19		
		A A A A A A A A A A/ A A A A A A A A A		
	SEX:	M M M F M M F M M M F F F F F M F M F		
	CEPHALIC:	1,3,5,7,9,11,13,15,17,19		

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 45
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 4: 1000 MG/KG/DAY	FETUS #			GRADE
57374 (CONTINUED)				
VISCERAL	2	V	LIVER- ACCESSORY LOBULE(S) ONE, 2 X 2 X 1, IN MEDIAN CLEFT	P
	NO REMARKABLE OBSERVATIONS			
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19			
VISCERAL	1,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19			
SKELETAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19			
57378	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15			
	A/ A A A A A A A A A A A A A A			
SEX:	M F F F M M M F M F M F M F F			
CEPHALIC:	1,3,5,7,9,11,13,15			
SKELETAL	3	V	14TH RUDIMENTARY RIB(S) RIGHT	P
	NO REMARKABLE OBSERVATIONS			
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15			
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15			
SKELETAL	1,2,4,5,6,7,8,9,10,11,12,13,14,15			
57382	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17			
	A A A A A A A A A/ A A A A A A A A			
SEX:	F M F F M M M M M F F F F M M F M			
CEPHALIC:	1,3,5,7,9,11,13,15,17			
SKELETAL	7	V	14TH RUDIMENTARY RIB(S) RIGHT	P
VISCERAL	12		RENAL PAPILLA(E) NOT FULLY DEVELOPED (WOO AND HOAR GRADE 1) RIGHT	P

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 46
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 4: 1000 MG/KG/DAY	FETUS #			GRADE
57382 (CONTINUED)				
	NO REMARKABLE OBSERVATIONS			
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17			
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,13,14,15,16,17			
SKELETAL	1,2,3,4,5,6,8,9,10,11,12,13,14,15,16,17			
57388	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16			
	A A A A A A A A A/ A A A A A A A			
SEX:	M F M F M M M M F M F F M F F F			
CEPHALIC:	1,3,5,7,9,11,13,15			
SKELETAL	1	V	14TH RUDIMENTARY RIB(S) LEFT	P
SKELETAL	5	V	14TH RUDIMENTARY RIB(S) BILATERAL	P
SKELETAL	6	V	14TH RUDIMENTARY RIB(S) LEFT	P
SKELETAL	8	V	14TH RUDIMENTARY RIB(S) BILATERAL	P
SKELETAL	10	V	14TH RUDIMENTARY RIB(S) LEFT	P
SKELETAL	11	V	14TH RUDIMENTARY RIB(S) BILATERAL	P
SKELETAL	12	V	14TH RUDIMENTARY RIB(S) BILATERAL	P
SKELETAL	13	V	14TH RUDIMENTARY RIB(S) LEFT	P
SKELETAL	14	V	14TH RUDIMENTARY RIB(S) LEFT	P
SKELETAL	15	V	14TH RUDIMENTARY RIB(S) BILATERAL	P

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 47
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 4: 1000 MG/KG/DAY	FETUS #		GRADE
57388 (CONTINUED)			
SKELETAL	16	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16		
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16		
SKELETAL	2,3,4,7,9		
57391	1 2 3 4 5 6 7 8 9 10 11 12 13 14		
	A E E A A A A A/ A A A A A A		
SEX:	F - - M M M F M F F F F M F		
CEPHALIC:	4,6,8,10,12,14		
EXTERNAL	2	EARLY RESORPTION	
EXTERNAL	3	EARLY RESORPTION	
VISCERAL	6	RENAL PAPILLA(E) NOT FULLY DEVELOPED (WOO AND HOAR GRADE 1) BILATERAL	P
VISCERAL	7	RENAL PAPILLA(E) NOT FULLY DEVELOPED (WOO AND HOAR GRADE 1) LEFT	P
VISCERAL	12	RENAL PAPILLA(E) NOT FULLY DEVELOPED (WOO AND HOAR GRADE 1) BILATERAL	P
	NO REMARKABLE OBSERVATIONS		
EXTERNAL	1,4,5,6,7,8,9,10,11,12,13,14		
VISCERAL	1,4,5,8,9,10,11,13,14		
SKELETAL	1,4,5,6,7,8,9,10,11,12,13,14		
57409	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18		
	A A A A A A A/ A A A A A A E A A A A		
SEX:	F M F M F F M F F F M M F - F F F M		
CEPHALIC:	2,4,6,8,10,12,15,17		

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 48
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 4: 1000 MG/KG/DAY		FETUS #		GRADE
57409 (CONTINUED)				
	SKELETAL	1	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	SKELETAL	2	V 14TH RUDIMENTARY RIB(S) LEFT	P
	SKELETAL	4	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	SKELETAL	5	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	SKELETAL	6	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	SKELETAL	7	V 14TH RUDIMENTARY RIB(S) LEFT	P
	SKELETAL	8	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	SKELETAL	10	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	SKELETAL	11	V 14TH RUDIMENTARY RIB(S) RIGHT	P
	SKELETAL	12	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	SKELETAL	13	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	EXTERNAL	14	EARLY RESORPTION	
	SKELETAL	15	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	SKELETAL	16	V 14TH RUDIMENTARY RIB(S) BILATERAL	P
	SKELETAL	18	V 14TH RUDIMENTARY RIB(S) BILATERAL	P

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

TABLE A14

PROJECT NO.:WIL-189223 AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS PAGE 49
SPONSOR:E.I. DUPONT INDIVIDUAL FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS
SPONSOR NO.:18405-841

DAMS FROM GROUP 4: 1000 MG/KG/DAY	FETUS #	GRADE
57409 (CONTINUED)		
	NO REMARKABLE OBSERVATIONS	
EXTERNAL	1,2,3,4,5,6,7,8,9,10,11,12,13,15,16,17,18	
VISCERAL	1,2,3,4,5,6,7,8,9,10,11,12,13,15,16,17,18	
SKELETAL	3,9,17	

A = VIABLE FETUS, E = EARLY RESORPTION, L = LATE RESORPTION, D = DEAD FETUS, "/" DENOTES CERVIX POSITION
OBSERVATION CODE: M = MALFORMATION, V = VARIATION GRADE CODE: 1 = SLIGHT, 2 = MODERATE, 3 = MARKED, P = PRESENT
SEX CODE: M = MALE, F = FEMALE, - = NOT APPLICABLE

PFETv4.14
01/25/2010

APPENDIX B

Certificate Of Analysis (Sponsor-Provided Data)

E. I. du Pont de Nemours and Company
Wilmington, DE 19898
USA

CERTIFICATE OF ANALYSIS

This Certificate of Analysis fulfills the requirement for characterization of a test substance prior to a study subject to GLP regulations. It documents the identity and content of the test substance. This work was conducted under EPA Good Laboratory Practice Standards (40 CFR 792).

Haskell Code Number	H-28548
Common Name	HFPO Dimer Acid Ammonium Salt
Purity Percent	84%
Other Components	Water – 12.7% Perfluorooctanoic acid – 150 ppm
Date of Analysis	June 13, 2008
Expiration Date	June 13, 2011
Instructions for storage	NRT&H
Reference	DuPont-25455
Analysis performed at	E. I. DuPont de Nemours and Company DuPont Haskell Laboratories Newark, Delaware USA

Approver:

Peter A. Bloxham, Ph.D.
Senior Research Chemist

24-JUN-2009
Date

Revision #1: Revised COA expiration date based on compound stability assessment. 6/23/09

APPENDIX C

Analyses Of Dosing Formulations (WIL Research Laboratories, LLC)

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats

Analyses of Dosing Formulations

Analytical Chemistry Department

WIL Research Laboratories, LLC

KEY STUDY PERSONNEL AND REPORT SUBMISSION

Report Submitted by: _____ 2 July 2010
Tammye L. Edwards, B.S., L.A.T. Date
Staff Toxicologist, Developmental and Reproductive Toxicology
Study Director

Report Prepared by: _____ 2 July 2010
Samantha T. Coffee, B.S. Date
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Daniel W. Sved, Ph.D. Date
Director, Metabolism and Analytical Chemistry

Study Personnel:

Michelle M. Flora, B.A. Publishing Specialist, Study Analysis and Reports

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SUMMARY

A high performance liquid chromatography tandem mass spectrometry method in the negative electrospray ionization mode for the determination of H-28548 (HFPO dimer acid ammonium salt) concentration in aqueous formulations containing DI water and test substance ranging in concentration from 0.00100 to 150 mg/mL was validated and extended-validated in previous studies (Haas, 2008; Haas, 2009). In the present study, formulations prepared at target concentrations of 1 and 100 mg H-28548/mL were evaluated for test substance homogeneity. Formulations prepared at target concentrations of 0, 1, 10, and 100 mg H-28548/mL were analyzed to assess test substance concentration acceptability.

Formulations prepared at target test substance concentrations of 1 and 100 mg/mL were analyzed to assess test substance homogeneity and concentration acceptability. The assessment met the WIL standard operating procedure (SOP) acceptance criteria for test substance homogeneity, i.e., the variability for the mean concentration was ≤10% relative standard deviation at a concentration within the acceptable limits (85% to 115% of target). Dosing formulations prepared at target test substance concentrations of 0, 1, 10, and 100 mg/mL were analyzed to confirm test substance concentration acceptability. The results of the mid stratum samples met the WIL SOP acceptance criteria for concentration acceptability in suspension formulations, i.e., the mean concentration was 85% to 115% of the target concentration. No quantifiable amounts test substance were detected in the analyzed vehicle formulations administered to the control group.

INTRODUCTION

This report provides a detailed description of a high performance liquid chromatography tandem mass spectrometry (HPLC/MS/MS) method in the negative electrospray ionization (ESI-) mode for the determination of H-28548 (HFPO dimer acid ammonium salt) concentration in aqueous formulations containing deionized (DI) water and test substance ranging in concentration from 0.00100 to 150 mg/mL. Method specificity/selectivity, ruggedness, calibration reproducibility, precision and accuracy were assessed, validated, and extended-validated in previous studies (Haas, 2008; Haas, 2009). In the present study, formulations prepared at target test substance concentrations of 1 and 100 mg/mL were analyzed to assess test substance homogeneity. Dosing formulations prepared at target test substance concentrations of 0, 1, 10, and 100 mg/mL were analyzed to confirm test substance concentration acceptability.

EXPERIMENTAL

A. Instruments

The HPLC/MS/MS system used was a Waters 2695 liquid chromatograph equipped with an autosampler and a Micromass Quattro Micro™ triple quadrupole mass spectrometer equipped with an ESI- interface. Data acquisition and analysis were performed using MassLynx™ software version 4.1 or equivalent. The retention time, run time, and mass spectrometer settings may have varied depending on column and mass spectrometer performance.

1. High Performance Liquid Chromatography

Instrument:	Waters 2695 liquid chromatograph equipped with an autosampler, Micromass tandem quadrupole Quattro Micro™ Mass Spectrometer, and MassLynx™ software, or equivalent system
Column:	Phenomenex Synergi Polar-RP, 4-µm, 75 × 2.0 mm
Column Temperature:	40ºC
Mobile Phase:	A: 90:10 (v/v) 5 mM ammonium acetate in DI water, pH 2.5:acetonitrile (ACN) B: 10:90 (v/v) 5 mM ammonium acetate in DI water, pH 2.5:ACN
Composition:	50:50 (v/v) A:B
Flow Rate:	0.4 mL/minute
Detector:	Mass spectrometer with conditions as described in Section A.2. (Mass Spectrometry)
Injection Volume:	10 µL
Retention Time:	Approximately 0.6 minutes for H-28548
Run Time:	1.0 minutes
Injector Wash:	90:10 (v/v) ACN:DI water

2. Mass Spectrometry

Ion Mode:	ESI-
Capillary Voltage:	1.50 kV
Cone:	9.00 V
Extractor:	3.00 V
RF Lens:	0.4 V
Source Temperature:	100°C
Desolvation Temperature:	400°C
Cone Gas Flow:	Approximately 100 L nitrogen/hour
Desolvation Gas Flow:	Approximately 700 L nitrogen/hour

Acquisition Parameters

Function Type:	Multiple reaction monitoring (MRM)
Precursor/Product Ion:	m/z 328.85/284.85 for H-28548
Collision Gas:	Argon
Collision Cell Pressure:	Approximately 3.28×10^{-3} mbar
Collision Energy:	5.0 V

B. Preparation of Diluent and Buffer (5 mM Ammonium Acetate in DI Water, pH 2.5)

Ammonium acetate (0.77 g) was dissolved in a final volume of 2 L of DI water, and the solution was vacuum-filtered through a 0.45-µm pore-size nylon filter. The solution was adjusted to pH 2.5 with the addition of glacial acetic acid. The solution was used as a buffer for preparation of mobile phase A and mobile phase B. In addition, the solution was used as the diluent in the preparation of the calibration and quality control (QC) stock solutions and the processing of the QC and formulation samples. The preparation was scaled as needed.

C. Mobile Phase A Preparation (90:10 [v/v] 5 mM Ammonium Acetate in DI Water, pH 2.5:ACN)

Ammonium acetate buffer (900 mL) and 100 mL of ACN were thoroughly mixed and degassed by sonication. The preparation was scaled as needed.

D. Mobile Phase B Preparation (10:90 [v/v] 5 mM Ammonium Acetate in DI Water, pH 2.5:ACN)

Ammonium acetate buffer (100 mL) and 900 mL of ACN were thoroughly mixed and degassed by sonication. The preparation was scaled as needed.

E. Preparation of Calibration Stock Solution

A calibration stock solution was prepared at a corrected concentration of 1.00 mg H-28548/mL as follows. Approximately 119 mg H-28548 (WIL ID no. 090123, purity 84.0%) was accurately weighed in a tared 100-mL volumetric flask. The flask was partially filled with diluent and stirred to achieve complete dissolution. Additional diluent was added to achieve desired concentration, and the solution was stirred to mix.

F. Preparation of Secondary Calibration Stock Solution

A secondary calibration stock solution was prepared at a concentration of 0.00100 mg H-28548/mL as follows. An aliquot of the calibration stock solution was diluted 1000-fold with diluent and stirred to mix.

G. Preparation of Calibration Standards

Calibration standards were prepared by diluting the secondary calibration stock solution with diluent in amber autosampler vials to yield calibration standards at 100, 250, 500, 750, and 1000 ng H-28548/mL. The vials were mixed with vortex action. Triplicate calibration standards were prepared at each concentration for each assay.

H. Preparation of Quality Control Stock Solution

The QC stock solution was prepared at 50.0 mg H-28548/mL by accurately weighing approximately 0.595 g of H-28548 (WIL ID no. 090123, purity 84.0%) in a tared 10-mL volumetric flask. The flask was partially filled with diluent and stirred to achieve complete dissolution. Additional diluent was added to obtain desired concentration, and the solution was stirred to mix.

I. Preparation of Secondary Quality Control Stock Solution

A secondary QC stock solution was prepared at a concentration of 5.00 mg H-28548/mL as follows. An aliquot of the QC stock solution was diluted 10-fold with diluent, and the solution was stirred to mix.

J. Preparation and Processing of Quality Control Samples

As detailed in the following table, QC samples were prepared to simulate the processing of formulations at concentrations of 1.00, 10.0, and 100 mg H-28548 (nominal QC concentrations) by combining aliquots of the QC stock solution, vehicle (DI water), and diluent in polypropylene tubes. The processed samples were mixed by vortex action. Secondary and tertiary dilutions were performed as necessary with diluent in polypropylene tubes to achieve theoretical final concentrations within the calibration range. Portions of the samples were transferred to amber autosampler vials for analysis as needed.

Nominal QC Concentration (mg/mL)	Stock Concentration (mg/mL)	Stock Volume (mL)	DI Water Volume (mL)	Diluent Volume (mL)	Secondary Dilution	Tertiary Dilution	Theoretical Final Concentration (µg/mL)
0	0	0	1.00	39.00	50-fold	NA	0
1.00	5.00	0.200	1.00	38.80	50-fold	NA	0.500
10.0	5.00	2.00	1.00	37.00	500-fold	NA	0.500
100	50.0	2.00	1.00	37.00	50-fold	100-fold	0.500

NA = Not applicable

K. Sample Processing

Quadruplicate formulation samples were collected using a syringe and dosing cannula and placed in polypropylene tubes. Two samples (from each quadruplicate set) were processed for analysis, and the remaining 2 samples were stored frozen (approximately -20°C) as back-up samples that were discarded once the Study Director approved the results. As detailed in the following table, formulation samples were processed by adding diluent and mixing by vortex action. Secondary and tertiary dilutions were performed as necessary with diluent in polypropylene tubes to achieve theoretical final concentrations within the calibration range. Portions of the diluted samples in tubes were transferred to amber autosampler vials for analysis as needed.

Groups	Target Test Article Concentration (mg/mL)	Sample Volume (mL)	Diluent Volume (mL)	Secondary Dilution	Tertiary Dilution	Theoretical Diluted Concentration (µg/mL)
1	0	1.0	39.0	50-fold	NA	0
2	1	1.0	39.0	50-fold	NA	0.500
3	10	1.0	39.0	500-fold	NA	0.500
4	100	1.0	39.0	50-fold	100-fold	0.500

NA = Not applicable

L. Concentration Quantitation

Single injections were made of each calibration standard and processed QC and formulation sample. A calibration curve was constructed for each set of analysis. Using MassLynx™, the H-28548 peak areas (y) and the theoretical concentrations of the calibration standards (x) were fit to the ln-quadratic function using least-squares regression analysis without weighting, excluding the origin:

$$\ln (y) = a \times [\ln (x)]^2 + b \times \ln (x) + c$$

Concentration and percent relative error (%RE) were calculated using MassLynx™. The concentration data were transferred to an Excel spreadsheet, where appropriate summary statistics, i.e., mean, standard deviation (SD), relative standard deviation (RSD), %RE, and percent of target, were calculated and presented in tabular form. The concentrations of the dosing formulations and QC samples were calculated by applying any necessary multiplication factors.

RESULTS AND DISCUSSION

Under the described chromatographic conditions, the retention time of the test substance was approximately 0.6 minutes. Figure 1, Figure 2, Figure 3, Figure 4, and Figure 5 are typical chromatograms of a processed calibration standard, a processed QC sample, a processed formulation sample, a processed vehicle (control formulation) sample, and a diluent sample. The total analysis time required for each run was 1.0 minute.

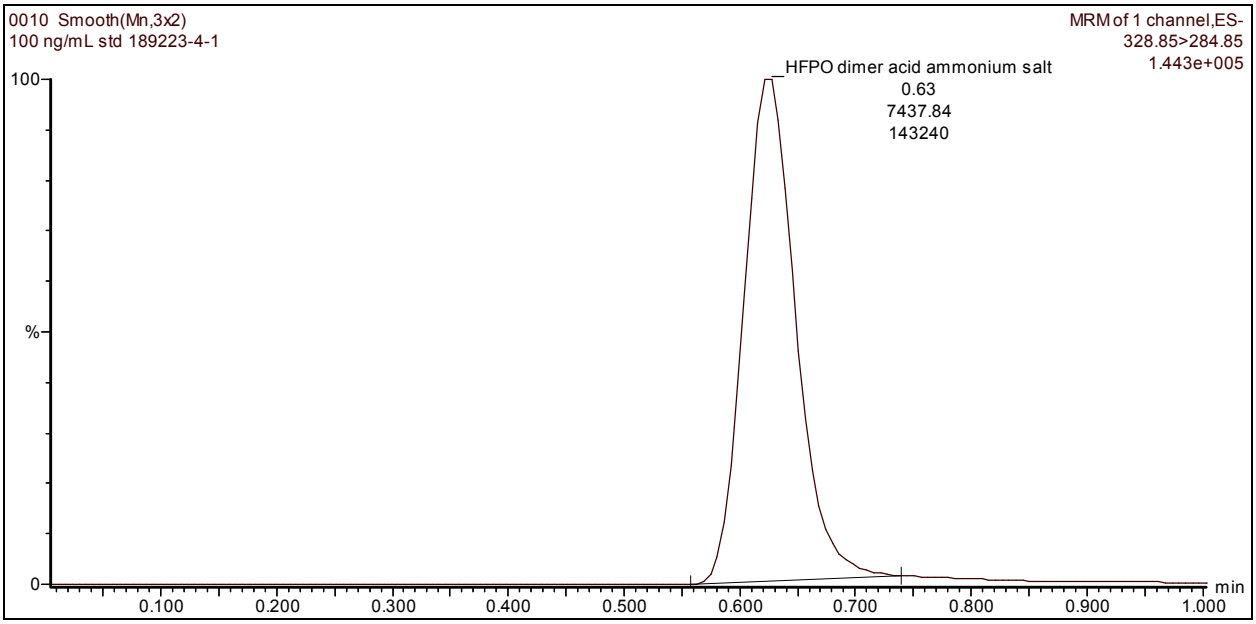

Figure 1: Representative Chromatogram of a 100 ng H-28548/mL Calibration Standard

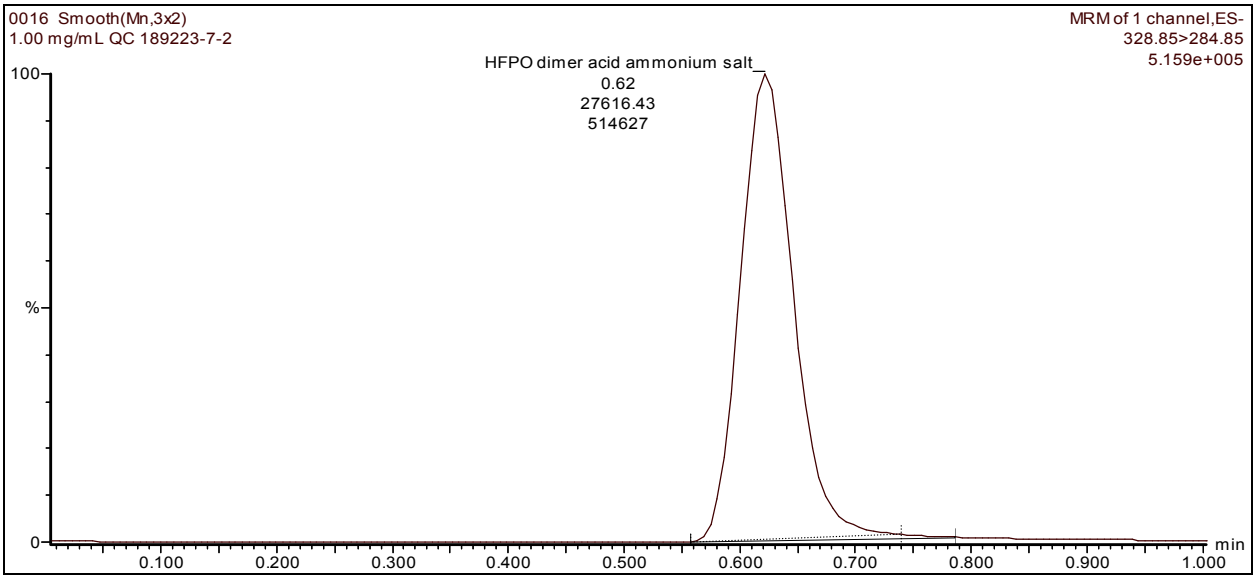

Figure 2: Representative Chromatogram of a Processed 1.00 mg H-28548/mL Quality Control Sample

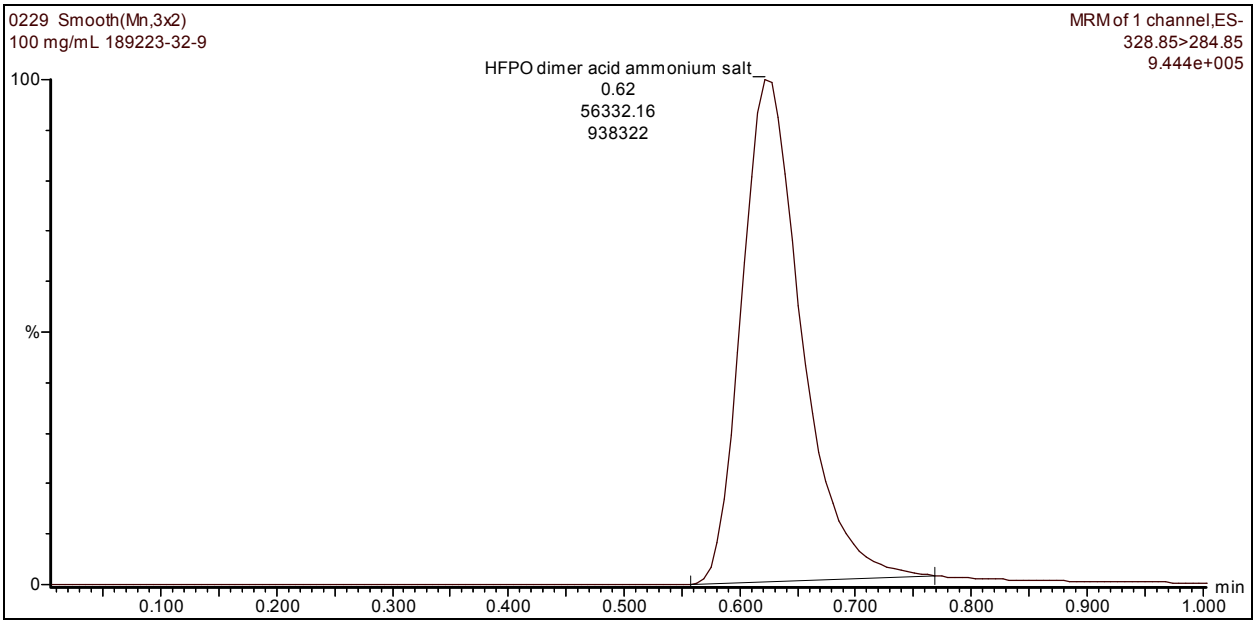

Figure 3: Representative Chromatogram of a Processed 100 mg H-28548/mL Formulation Sample

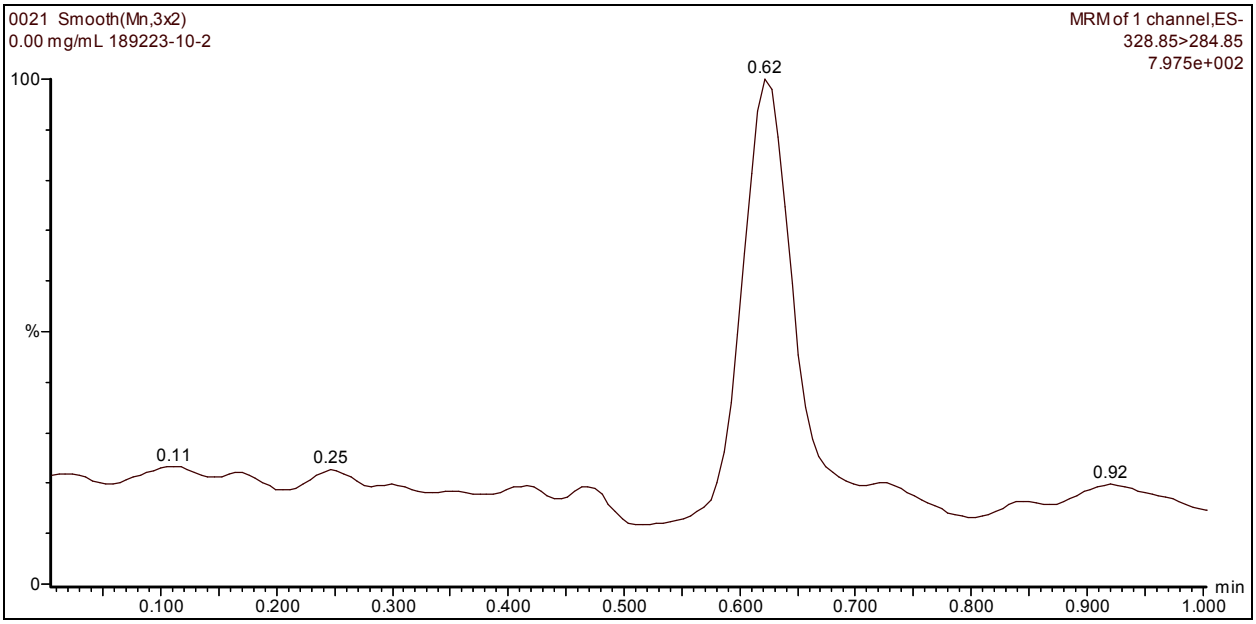

Figure 4: Representative Chromatogram of a Processed Control Formulation Sample

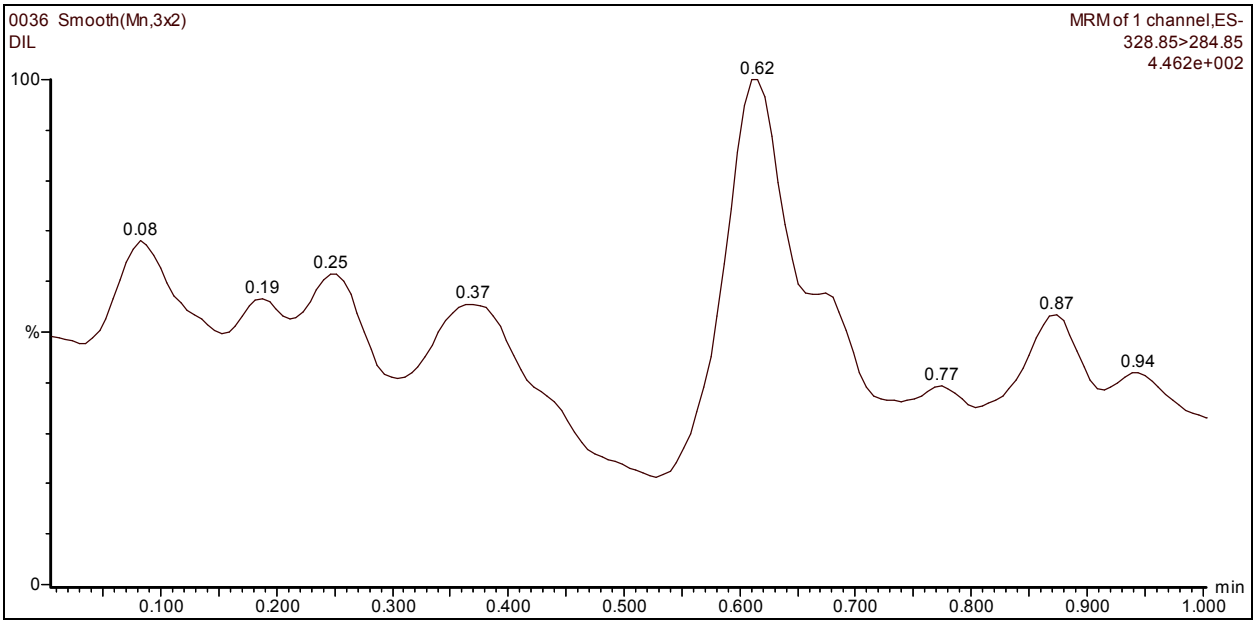

Figure 5: Representative Chromatogram of Diluent Sample

A. Specificity/Selectivity

As shown in Figure 4 and Figure 5, assay specificity/selectivity was confirmed when HPLC/MS/MS analysis of processed control samples revealed that there were no significant peaks (with signal to noise ratio [S/N] >10) at or near the retention time for the test article (approximately 0.6 minutes).

B. Assay Acceptability

In addition to the experimental samples, each analytical session consisted of (but was not limited to) calibration standards at 5 concentrations and triplicate QC samples at each of 3 concentrations. In this study, the formulations were prepared at target test substance concentrations of 0, 1, 10, and 100 mg/mL and the QC samples were prepared at nominal test substance concentrations of 1.00, 10.0, and 100 mg/mL. For an analytical session to be considered valid, at least two-thirds of the calculated QC concentrations with at least 1 sample at each concentration had to be 85% to 115% of the nominal QC concentration. All reported results were from analytical sessions that met the acceptance criteria.

C. Assessment of Test Substance Homogeneity

Duplicate samples from the top, middle, and bottom strata of formulations prepared on 29 October 2009 at target test substance concentrations of 1 and 100 mg H-28548/mL were analyzed to assess test substance homogeneity. The results of the homogeneity analysis are presented in Table 1, with the overall statistics summarized in the following tables.

Homogeneity Assessment of the 29 October 2009 Formulations		
	Group 2 (1 mg/mL)	Group 4 (100 mg/mL)
Mean Concentration (mg/mL)	0.866	86.8
SD	0.025	0.81
RSD (%)	2.9	0.94
Mean % of Target	86.6	86.8

The formulations analyzed met the WIL SOP acceptance criteria for test substance homogeneity, i.e., the RSD for the mean concentration was ≤10% at a concentration within the acceptable limits (85% to 115% of target concentration).

D. Test Substance Concentration in Aqueous Formulations

The results of the determination of test substance concentration in formulations prepared for dose administration are presented in Table 2 and Table 3. The mean concentration and percent of target values are summarized in the following table.

	Mean Concentration, mg/mL (% of Target)			
Date of Preparation	Group 1 (0 mg/mL)	Group 2 (1 mg/mL)	Group 3 (10 mg/mL)	Group 4 (100 mg/mL)
29 October 2009	ND	0.883 (88.3)	8.64 (86.4)	86.2 (86.2)
12 November 2009	ND	1.04 (104)	10.1 (101)	96.5 (96.5)

ND = Not detected. No test substance chromatographic peak was detected.

The analyzed formulations met the WIL standard operating procedure (SOP) requirement for concentration acceptability for suspension formulations, i.e., the analyzed concentration was 85% to 115% of the target concentration. No quantifiable amounts of test substance were detected in the analyzed vehicle formulations administered to the control group (Group 1).

CONCLUSION

A HPLC/MS/MS method in the ESI- mode for the determination of H-28548 (HFPO dimer acid ammonium salt) concentration in aqueous formulations was validated and extended-validated in previous studies (Haas, 2008; Haas, 2009). In the present study, aqueous formulations prepared at target test substance concentrations of 1 and 100 mg/mL were analyzed and met the WIL SOP acceptance criteria for test substance homogeneity. The analyzed formulations used for dose administration met the WIL SOP requirement for concentration acceptability for suspension formulations. No quantifiable amounts test substance were detected in the analyzed vehicle formulations administered to the control group.

REFERENCES

Haas, M.C., A 28-Day Oral (Gavage) Toxicity Study of H-28397 in Rats with a 28-Day Recovery (Study No. WIL-189205). WIL Research Laboratories, LLC, Ashland, OH, **2008**.

Haas, M.C., A 90-Day Oral (Gavage) Toxicity Study of H-28548 in Rats with a 28-Day Recovery (Study No. WIL-189216). WIL Research Laboratories, LLC, Ashland, OH, **2009**.

TABLES 1 - 3

AN ORAL (GAVAGE) PRENATAL
DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS

Table 1: Homogeneity Assessment of the 29 October 2009 Formulations

Dose Conc (mg/mL)	Group/ Strata	Ref # (189223 -)	Run #	Analyzed Conc (mg/mL)	Percent of Target (%)	Mean Conc (mg/mL)	SD	RSD (%)	Mean Conc % of Target (%)
1	2/Top	10 - 3	I2-0022	0.855	85.5	0.866	0.025	2.9	86.6
		10 - 4	I2-0023	0.850	85.0				
	2/Mid	10 - 5	I2-0024	0.914	91.4				
		10 - 6	I2-0025	0.851	85.1				
	2/Btm	10 - 7	I2-0026	0.874	87.4				
		10 - 8	I2-0027	0.851	85.1				
100	4/Top	10 - 17	I2-0030	88.3	88.3	86.8	0.81	0.94	86.8
		10 - 18	I2-0031	86.7	86.7				
	4/Mid	10 - 19	I2-0032	85.8	85.8				
		10 - 20	I2-0033	86.6	86.6				
	4/Btm	10 - 21	I2-0034	86.7	86.7				
		10 - 22	I2-0035	86.8	86.8				

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AN ORAL (GAVAGE) PRENATAL
DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS

Table 2: Concentration Assessment of the 29 October 2009 Formulations
(Analyzed 30 October 2009)

Dose Conc (mg/mL)	Group/ Strata	Ref # (189223 -)	Run #	Analyzed Conc (mg/mL)	Percent of Target (%)	Mean Conc (mg/mL)	SD	RSD (%)	Mean Conc % of Target (%)
0	1/Mid	10 - 1	I2-0020		---------- Not Quantifiable ----------				
		10 - 2	I2-0021		---------- Not Quantifiable ----------				
1	2/Mid	10 - 5	I2-0024	0.914	91.4	0.883	0.045	5.0	88.3
		10 - 6	I2-0025	0.851	85.1				
10	3/Mid	10 - 9	I2-0028	8.69	86.9	8.64	0.071	0.82	86.4
		10 - 10	I2-0029	8.59	85.9				
100	4/Mid	10 - 19	I2-0032	85.8	85.8	86.2	0.57	0.66	86.2
		10 - 20	I2-0033	86.6	86.6				

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AN ORAL (GAVAGE) PRENATAL
DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS

Table 3: Concentration Assessment of the 12 November 2009 Formulations
(Analyzed 13-15 November 2009)

Dose Conc (mg/mL)	Group/ Strata	Ref # (189223 -)	Run #	Analyzed Conc (mg/mL)	Percent of Target (%)	Mean Conc (mg/mL)	SD	RSD (%)	Mean Conc % of Target (%)
0	1/Mid	32 - 1	I2-0223		---------- Not Detected ----------				
		32 - 2	I2-0224		---------- Not Detected ----------				
1	2/Mid	32 - 3	I2-0225	1.05	105	1.04	0.014	1.4	104
		32 - 4	I2-0226	1.03	103				
10	3/Mid	32 - 5	I2-0227	10.1	101	10.1	0.071	0.70	101
		32 - 6	I2-0228	10.0	100				
100	4/Mid	32 - 9	I2-0229	98.3	98.3	96.5	2.6	2.7	96.5
		32 - 10	I2-0230	94.6	94.6				

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APPENDIX D

Animal Room Environmental Conditions

AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS

PROJECT NO.:WIL- 189223 TEMPERATURE/HUMIDITY - STUDY SUMMARY REPORT

SPONSOR: 189 - E.I. DUPONT

STUDY SPECIFICATIONS: 189223 DATE IN 10/13/09 TIME IN 10:00
DATE OUT 11/22/09 TIME OUT 08:00

ROOM SPECIFICATIONS: B ROOM 32 LOW TEMPERATURE °F: 66.0 HIGH TEMPERATURE °F: 76.0 LOW HUMIDITY %RH: 30.0

TEST SYSTEM: RAT LOW TEMPERATURE °C: 18.9 HIGH TEMPERATURE °C: 24.4 HIGH HUMIDITY %RH: 70.0

	PRIMARY TEMP		SECONDARY TEMP		PRIMARY HUM	SECONDARY HUM
DATE	MEAN (°F)	MEAN (°C)	MEAN (°F)	MEAN (°C)	MEAN (%RH)	MEAN (%RH)
10/13/09	71.6	22.0	72.5	22.5	45.4	44.1
10/14/09	71.0	21.7	72.2	22.3	45.4	44.7
10/15/09	70.6	21.4	70.8	21.6	45.7	46.1
10/16/09	70.4	21.3	70.0	21.1	46.3	48.2
10/17/09	70.6	21.4	70.2	21.2	45.7	47.8
10/18/09	70.9	21.6	70.5	21.4	44.8	47.3
10/19/09	70.9	21.6	70.4	21.3	45.5	47.9
10/20/09	70.6	21.4	70.2	21.2	46.2	47.6
10/21/09	70.7	21.5	70.9	21.6	46.3	46.7
10/22/09	70.9	21.6	71.8	22.1	46.9	46.3
10/23/09	71.0	21.7	72.1	22.3	49.2	48.1
10/24/09	70.8	21.6	72.0	22.2	46.8	45.7
10/25/09	71.0	21.7	72.2	22.3	44.9	43.9
10/26/09	70.9	21.6	72.0	22.2	46.0	45.9
10/27/09	71.2	21.8	72.2	22.3	45.7	44.9
10/28/09	71.1	21.7	72.2	22.3	49.1	48.7
10/29/09	71.1	21.7	72.2	22.3	48.5	47.6
10/30/09	71.0	21.7	72.0	22.2	51.1	50.7
10/31/09	71.1	21.7	72.2	22.3	47.4	46.9

AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS

PROJECT NO.:WIL- 189223 TEMPERATURE/HUMIDITY - STUDY SUMMARY REPORT

SPONSOR: 189 - E.I. DUPONT

	PRIMARY TEMP		SECONDARY TEMP		PRIMARY HUM	SECONDARY HUM
DATE	MEAN (°F)	MEAN (°C)	MEAN (°F)	MEAN (°C)	MEAN (%RH)	MEAN (%RH)
11/01/09	71.2	21.8	72.3	22.4	45.4	44.9
11/02/09	71.0	21.7	72.2	22.3	45.7	45.6
11/03/09	71.0	21.7	72.2	22.3	45.8	45.2
11/04/09	71.2	21.8	72.3	22.4	45.5	44.8
11/05/09	71.1	21.7	72.3	22.4	45.3	44.8
11/06/09	70.8	21.6	72.1	22.3	45.4	44.9
11/07/09	71.1	21.7	72.2	22.3	45.7	45.5
11/08/09	71.2	21.8	72.3	22.4	47.3	47.0
11/09/09	70.9	21.6	72.0	22.2	47.8	47.4
11/10/09	71.0	21.7	72.1	22.3	46.4	45.1
11/11/09	70.8	21.6	72.1	22.3	44.8	43.9
11/12/09	71.5	21.9	72.7	22.6	44.2	42.6
11/13/09	71.3	21.8	72.5	22.5	45.0	44.1
11/14/09	70.6	21.4	71.8	22.1	46.2	45.8
11/15/09	71.0	21.7	72.1	22.3	46.0	45.5
11/16/09	71.0	21.7	72.2	22.3	44.8	44.0
11/17/09	71.0	21.7	72.1	22.3	44.2	43.6
11/18/09	70.8	21.6	72.0	22.2	45.5	45.4
11/19/09	70.9	21.6	71.7	22.1	46.7	46.4
11/20/09	70.9	21.6	71.3	21.8	44.0	44.3
11/21/09	70.9	21.6	71.3	21.8	43.6	44.2
11/22/09	71.0	21.7	71.7	22.1	43.5	43.6

AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS

PROJECT NO.:WIL- 189223 TEMPERATURE/HUMIDITY - STUDY SUMMARY REPORT

SPONSOR: 189 - E.I. DUPONT

	PRIMARY TEMP		SECONDARY TEMP		PRIMARY HUM	SECONDARY HUM
DATE	MEAN (°F)	MEAN (°C)	MEAN (°F)	MEAN (°C)	MEAN (%RH)	MEAN (%RH)

SUMMARY OF DAILY MEANS	MEAN	MIN	MAX
PRIMARY TEMP °F:	71.0	70.4	71.6
PRIMARY TEMP °C:	21.7	21.3	22.0
SECONDARY TEMP °F:	71.8	70.0	72.7
SECONDARY TEMP °C:	22.1	21.1	22.6
PRIMARY HUM %RH:	46.0	43.5	51.1
SECONDARY HUM %RH:	45.9	42.6	50.7
N DAYS	41		

AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS

PROJECT NO.:WIL- 189223 TEMPERATURE/HUMIDITY - STUDY SUMMARY REPORT

SPONSOR: 189 - E.I. DUPONT

B ROOM 32 SUMMARY OF HOURLY VALUES

	PRIMARY TEMP				SECONDARY TEMP				PRIMARY HUM		SECONDARY HUM	
MEAN	71.0	°F	21.7	°C	71.8	°F	22.1	°C	46.0	%RH	45.9	%RH
MIN	68.2	°F	20.1	°C	69.1	°F	20.6	°C	40.3	%RH	37.8	%RH
MAX	75.1	°F	23.9	°C	75.5	°F	24.2	°C	56.0	%RH	61.0	%RH
SD	1.68		0.93		1.61		0.89		2.38		3.27	
SE	0.05		0.03		0.05		0.03		0.08		0.11	
N SAMPLES	958				958				958		958	
FIRST DAY	10/13/09											
LAST DAY	11/22/09											
N DAYS	41											

AN ORAL PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS

PROJECT NO.:WIL- 189223 TEMPERATURE/HUMIDITY - STUDY SUMMARY REPORT

SPONSOR: 189 - E.I. DUPONT

STUDY 189223 SUMMARY OF HOURLY VALUES

	PRIMARY TEMP				SECONDARY TEMP				PRIMARY HUM		SECONDARY HUM	
MEAN	71.0	°F	21.7	°C	71.8	°F	22.1	°C	46.0	%RH	45.9	%RH
MIN	68.2	°F	20.1	°C	69.1	°F	20.6	°C	40.3	%RH	37.8	%RH
MAX	75.1	°F	23.9	°C	75.5	°F	24.2	°C	56.0	%RH	61.0	%RH
SD	1.68		0.93		1.61		0.89		2.38		3.27	
SE	0.05		0.03		0.05		0.03		0.08		0.11	
N SAMPLES	958				958				958		958	
FIRST DAY	10/13/09											
LAST DAY	11/22/09											
N DAYS	41											

TRADE SECRET

FINAL REPORT
Volume 2 of 2 (Appendices E-G)

STUDY TITLE

AN ORAL (GAVAGE) PRENATAL
DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS

STUDY NUMBER

WIL-189223

DATA REQUIREMENT

OPPTS Guideline 870.3700
OECD Guideline 414

STUDY DIRECTOR

Tammye L. Edwards, B.S., L.A.T.

STUDY INITIATION DATE

12 October 2009

STUDY COMPLETION DATE

2 July 2010

PERFORMING LABORATORY

WIL Research Laboratories, LLC
1407 George Road
Ashland, Ohio 44805-8946
U.S.A.

SPONSOR STUDY NUMBER

18405-841

SPONSOR

E.I. du Pont de Nemours and Company
Wilmington, Delaware 19898
U.S.A.

APPENDIX E

Pathology Report (Sponsor-Provided Data)

DuPont-18405-841

TRADE SECRET

STUDY TITLE: Anatomic Pathology Report for
An Oral (Gavage) Prenatal Study of H-28548 in Rats

AUTHOR: Steven R. Frame, D.V.M., Ph.D., Diplomate ACVP

ANATOMIC PATHOLOGY REPORT COMPLETED ON: June 24, 2010

PERFORMING LABORATORY: E.I. du Pont de Nemours and Company
DuPont Haskell Global Centers for
Health & Environmental Sciences
P.O. Box 50
Newark, Delaware 19714
U.S.A.

LABORATORY PROJECT ID: DuPont-18405-841

WORK REQUEST NUMBER: 18405

SERVICE CODE NUMBER: 841

SPONSOR: E.I. du Pont de Nemours and Company
Wilmington, Delaware 19898
U.S.A.

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

This study was conducted in compliance with U.S. EPA TSCA (40 CFR part 792) Good Laboratory Practice Standards, which are compatible with current OECD Good Laboratory Practices.

Sponsor: E.I. du Pont de Nemours and Company
Wilmington, Delaware 19898
U.S.A.

Principal Investigator: _____ 24 June 2010
Steven R. Frame, D.V.M., Ph.D., Diplomate ACVP — Date
Manager

Sponsor: _____ _____
DuPont Representative — Date

QUALITY ASSURANCE STATEMENT

Work Request Number: 18405
Service Code Number: 841

Key inspections for DuPont work request 18405, service code 841, were completed by the Quality Assurance Unit of DuPont Haskell and the findings were submitted on the following dates.

Phase Audited	***Audit Dates***	***Date Reported to Principal Investigator (PI)/ PI Management***	***Date Reported to Study Director (SD)/ SD Management***
Report/Records:	June 16, 17 2010	June 17, 2010/ June 21, 2010	June 17, 2010/ June 21, 2010

Reported by: _____ 23 Jun 2010
Antonio Pedulla — Date
Quality Assurance Auditor

CERTIFICATION

We, the undersigned, declare that this report provides an accurate evaluation of data obtained from this study.

Anatomic Pathology Evaluation by: _____ 24 June 2010
Steven R. Frame, D.V.M., Ph.D., Diplomate ACVP — Date
Manager

Anatomic Pathology Evaluation Peer Review by: _____ 24 June 2010
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SUMMARY

An oral (gavage) prenatal developmental toxicity study in rats was conducted at WIL Research Laboratories, LLC, Ashland, Ohio. Time-mated female rats (22 per group) were dosed with 0, 10, 100, or 1000 mg/kg/day of H-28548 on days 6 to 20 of presumed gestation. Liver and kidney were examined grossly for all dams on study. Absolute weights for liver and kidneys were determined for all dams surviving to the final sacrifice. Formalin-fixed sections of liver and kidneys from all dams in all groups were processed to slides and shipped from WIL Research Laboratories to DuPont Haskell for selected microscopic evaluation and interpretation. Livers from all dams, and kidneys from dams in the control and 1000 mg/kg/day groups, were evaluated microscopically.

There were no adverse or test substance-related changes in the 10 mg/kg/day group.

One female in the 1000 mg/kg/day groups died on test day 20. Cause of death in this animal was likely related to microscopic findings of moderate coagulative necrosis in the liver and fibrin thrombi in renal glomerular capillaries consistent with disseminated intravascular coagulation. The death in this animal was considered to be test substance-related.

Test-substance related increases in absolute liver weight were present in the 100 and 1000 mg/kg/day groups. Microscopically, liver weight changes correlated with minimal hepatocellular hypertrophy in the 1000 mg/kg/day group. Hepatocellular hypertrophy was morphologically consistent with a PPARα mechanism. Absolute kidney weights were increased in the 1000 mg/kg/day group. Kidney weight changes were not associated with correlative microscopic findings and were considered test substance-related but nonadverse.

Microscopically, focal hepatocellular necrosis was present in 2/22 and 5/22 dams in the 100 and 1000 mg/kg/day groups, respectively. This finding was considered test substance-related and adverse.

There were no other adverse or treatment-related changes in anatomic pathology parameters in dams in any group. Under the conditions of this study, and for the anatomic pathology parameters measured, the no-observed-adverse-effect level (NOAEL) was 10 mg/kg/day based on focal liver necrosis observed in some dams administered 100 mg/kg/day and above of the test substance.

MATERIALS AND METHODS

A. Anatomic Pathology Evaluation

An oral (gavage) prenatal developmental toxicity study in rats was conducted at WIL Research Laboratories, LLC, Ashland, Ohio. Time-mated female rats (22 per group) were dosed with 0, 10, 100, or 1000 mg/kg/day of H-28548 beginning on days 6 to 20 of presumed gestation. An anatomic pathology evaluation, including interpretation of absolute organ weight changes and gross and microscopic findings in the liver and kidneys, was conducted at DuPont Haskell. Gross examination and organ weight determinations were conducted at WIL Research Laboratories. Hematoxylin and eosin stained slides of liver and kidney were received from WIL Research Laboratories for microscopic evaluation at DuPont Haskell. Liver from all dams, and kidneys from dams in the control and 1000 mg/kg/day groups, were evaluated microscopically.

RESULTS AND DISCUSSION

A. Mortality

(Appendix A)

In the 1000 mg/kg/day female found dead on gestation day 20 (animal number 57328), test substance-related microscopic changes were present in the liver and kidney. In the liver, moderate coagulative necrosis was present in the liver. Necrosis was multifocal in one lobe and locally extensive and coalescing in the other lobe. In the kidney, fibrin thrombi consistent with disseminated intravascular coagulation (DIC) were observed in glomerular capillaries. Although microscopic examination of kidney was complicated by post mortem autolysis, the glomerular changes were considered to represent ante mortem findings. The test substance related liver and kidney changes were considered the cause of death in this animal.

No other unscheduled deaths occurred in this study.

B. Gross Findings

(Appendix A)

A gross finding of pale liver (all lobes) was observed in the 1000 mg/kg/day dam found dead on gestation day 20. This finding correlated with test substance-related liver necrosis observed microscopically in this animal. An irregularly-shaped white area was noted in the liver of one dam in the 100 and 1000 mg/kg/day group (numbers 57354 and 57409, respectively). In animal number 57354 this finding likely correlated with test substance-related focal liver necrosis observed microscopically. No microscopic correlate was observed in the liver of animal number 57409.

All other gross findings occurred in low incidences and were considered incidental occurrences of gross findings common to rats of this strain.

C. Microscopic Findings

(Table 1, Appendix A)

There were no test substance-related microscopic findings in dams administered 10 mg/kg/day of the test material.

In the 1000 mg/kg/day female found dead on gestation day 20 (animal number 57328), test substance-related microscopic changes were present in the liver and kidney. In the liver, moderate coagulative necrosis was present in the liver. Necrosis was multifocal in one lobe and locally extensive and coalescing in the other lobe. In the kidney, fibrin thrombi consistent with disseminated intravascular coagulation (DIC) were observed in glomerular capillaries. Although microscopic examination of kidney was complicated by post mortem autolysis, the glomerular changes were considered to represent ante mortem findings. The test substance related liver and kidney changes were considered the cause of death in this animal.

Test substance related microscopic findings were present in the liver of dams administered 100 or 1000 mg/kg/day. Focal necrosis of the liver occurred in 2/22 and 5/22 dams in the 100 and 1000 mg/kg/day group, respectively. This finding was not observed in any animals in the control or 10 mg/kg/day group. Necrosis was graded as minimal in all but the early death dam in the 1000 mg/kg/day group and was usually characterized by one or 2 circumscribed foci of coagulative liver necrosis. While focal liver necrosis may occur in control animals, the finding in the 100 and 1000 mg/kg/day dams was considered to be related to administration of the test material based upon the dose-response. Hepatocellular hypertrophy was present in 19/22 dams in the 1000 mg/kg/day group but was not observed in any animals in the other treated groups or in controls. Hypertrophy was graded as minimal in all but one animal (where it was graded as mild) and was primarily characterized by increased hepatocyte cytoplasm which contained fine eosinophilic granules. These changes are consistent with PPARα agonism and results of previous studies demonstrated that the test material is a PPARα agonist.

There were no test substance related microscopic changes in the kidneys at any of the dose levels tested. All microscopic changes in the kidneys were consistent with background changes commonly observed in rats of this strain.

CONCLUSIONS

In conclusion, a test substance-related and adverse finding of focal liver necrosis was present in some dams in the 100 and 1000 mg/kg/day groups. A test substance related early death occurred in one dam in the 1000 mg/kg/day group. Other findings considered test substance related but nonadverse were increased liver weights in the 100 and 1000 mg/kg/day group, minimal hepatocellular hypertrophy in the 1000 mg/kg/day group, and increased kidney weights (without a microscopic correlate) in the 1000 mg/kg/day groups. No test substance related or adverse changes in the pathology parameters evaluated were observed in the 10 mg/kg/day group. Under the conditions of this study and for the anatomic pathology parameters measured, the no-observed-adverse-effect level (NOAEL) was 10 mg/kg/day based on focal liver necrosis observed in some dams administered 100 mg/kg/day and above of the test substance.

RECORDS AND SAMPLE STORAGE

For the work conducted at DuPont Haskell, specimens (if applicable), raw data, the anatomic pathology report will be retained at WIL Research Laboratories, LLC, Ashland, Ohio, DuPont Haskell, Newark, Delaware, Iron Mountain Records Management, Wilmington, Delaware, or Quality Associates Incorporated, Fulton, Maryland.

Data recorded and archived electronically will be retained at the facility where the work was done.

Laboratory-specific raw data such as personnel files, instrument, equipment, refrigerator and/or freezer raw data will be retained at the facility where the work was done.

TABLES

Table 1
Incidences and Lesion Grades of Microscopic Findings in Female Rats

Group:	1	2	3	4
Dosage (mg/kg/day):	0	10	100	1000
Number of Animals on Study :	22	22	22	22
KIDNEYS;				
Examined	(22)	(0)	(0)	(22)
Within Normal Limits	18	0	0	16
Chronic progressive nephropathy	(2)	(0)	(0)	(3)
minimal	2	0	0	2
mild	0	0	0	1
Dilatation; tubules; focal	(1)	(0)	(0)	(1)
minimal	1	0	0	1
Lymphoid aggregates	(3)	(0)	(0)	(1)
minimal	2	0	0	1
mild	1	0	0	0
Thrombi, glomeruli (dic)	(0)	(0)	(0)	(1)
moderate	0	0	0	1
LIVER;				
Examined	(22)	(22)	(22)	(22)
Within Normal Limits	16	16	14	3
Focus, eosinophilic	(0)	(0)	(1)	(0)
minimal	0	0	1	0
Hypertrophy, hepatocellular	(0)	(0)	(0)	(19)
minimal	0	0	0	18
mild	0	0	0	1
Inflammation, subacute/chronic	(6)	(6)	(6)	(3)
minimal	6	6	6	3
Necrosis, focal	(0)	(0)	(2)	(5)
minimal	0	0	2	4
moderate	0	0	0	1

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Appendix A
Individual Animal Pathology Data

INDIVIDUAL ANIMAL PATHOLOGY DATA

EXPLANATORY NOTES

LESION GRADING:

Histopathology changes are described according to their morphologic character, distribution and severity. The distribution (extent of tissue involvement) is indicated, where appropriate, by modifiers such as focal, multifocal, diffuse, unilateral, bilateral, etc. A severity score, if appropriate, is also assigned as follows:

PRESENT: Lesion present; severity not graded.

MINIMAL: The amount of change present barely exceeds that which is considered to be within normal limits.

MILD: In general, the lesion is easily identified but of limited severity. The lesion probably does not produce any functional impairment.

MODERATE: The lesion is prominent but there is significant potential for increased severity. Limited tissue or organ dysfunction is possible.

SEVERE: The degree of change is either as complete as considered possible or great enough in intensity or extent to expect significant tissue or organ dysfunction.

COMMENTS:

Grades minimal through severe represent progressive involvement/severity along a continuum with minimal lesions being the least severe and severe lesions being the most severe. While the grades refer to the morphologic characteristics of lesions, they also indicate their relative biologic significance.

Gross observations listing multiple masses for a tissue are distinguished with letters (i.e., a, b, c, d, etc.).

The microscopic correlate for selected gross observations, primarily masses, is provided to the right of the respective gross observation.

Individual Animal Pathology Data

Animal Ref.: 7312 Group: 1 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 0 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/19/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEYS LIVER

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Individual Animal Pathology Data

Animal Ref.: 7320 Group: 1 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 0 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

KIDNEYS;
Chronic progressive nephropathy; minimal
Lymphoid aggregates; minimal

The following tissues were within normal limits:

LIVER

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7322 Group: 1 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 0 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/20/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEYS LIVER

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7325 Group: 1 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 0 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/19/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEYS LIVER

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7326 Group: 1 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 0 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEYS LIVER

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7329 Group: 1 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 0 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/20/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Inflammation, subacute/chronic; minimal

The following tissues were within normal limits:

KIDNEYS

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7333 Group: 1 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 0 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Inflammation, subacute/chronic; minimal

The following tissues were within normal limits:

KIDNEYS

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7352 Group: 1 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 0 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/17/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEYS LIVER

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7356 Group: 1 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 0 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEYS LIVER

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7360 Group: 1 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 0 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Inflammation, subacute/chronic; minimal

The following tissues were within normal limits:

KIDNEYS

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7364 Group: 1 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 0 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEYS LIVER

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7369 Group: 1 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 0 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEYS LIVER

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7370 Group: 1 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 0 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/19/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Inflammation, subacute/chronic; minimal

The following tissues were within normal limits:

KIDNEYS

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7371 Group: 1 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 0 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/19/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEYS LIVER

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7379 Group: 1 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 0 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Inflammation, subacute/chronic; minimal

The following tissues were within normal limits:

KIDNEYS

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7380 Group: 1 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 0 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/20/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEYS LIVER

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7381 Group: 1 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 0 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/17/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

KIDNEYS;
Lymphoid aggregates; minimal

The following tissues were within normal limits:

LIVER

Individual Animal Pathology Data

Animal Ref.: 7385 Group: 1 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 0 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/19/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

KIDNEYS;
Chronic progressive nephropathy; minimal
Lymphoid aggregates; mild

The following tissues were within normal limits:

LIVER

Individual Animal Pathology Data

Animal Ref.: 7392 Group: 1 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 0 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

KIDNEYS;
Dilatation; tubules; focal; minimal

The following tissues were within normal limits:

LIVER

Individual Animal Pathology Data

Animal Ref.: 7397 Group: 1 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 0 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/19/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEYS LIVER

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7398 Group: 1 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 0 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/21/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEYS LIVER

Individual Animal Pathology Data

Animal Ref.: 7406 Group: 1 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 0 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/19/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Inflammation, subacute/chronic; minimal

The following tissues were within normal limits:

KIDNEYS

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7307 Group: 2 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 10 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

Individual Animal Pathology Data

Animal Ref.: 7308 Group: 2 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 10 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Inflammation, subacute/chronic; minimal

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Individual Animal Pathology Data

Animal Ref.: 7317 Group: 2 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 10 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/17/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Inflammation, subacute/chronic; minimal

Individual Animal Pathology Data

Animal Ref.: 7319 Group: 2 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 10 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/17/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

An Oral (Gavage) Prenatal Developmental
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Individual Animal Pathology Data

Animal Ref.: 7324 Group: 2 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 10 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/19/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Inflammation, subacute/chronic; minimal

Individual Animal Pathology Data

Animal Ref.: 7332 Group: 2 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 10 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

Individual Animal Pathology Data

Animal Ref.: 7334 Group: 2 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 10 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/19/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

An Oral (Gavage) Prenatal Developmental
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Individual Animal Pathology Data

Animal Ref.: 7335 Group: 2 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 10 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

An Oral (Gavage) Prenatal Developmental
Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7337 Group: 2 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 10 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

An Oral (Gavage) Prenatal Developmental
Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7339 Group: 2 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 10 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

An Oral (Gavage) Prenatal Developmental
Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7340 Group: 2 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 10 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/20/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

An Oral (Gavage) Prenatal Developmental
Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7343 Group: 2 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 10 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7347 Group: 2 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 10 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/19/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Inflammation, subacute/chronic; minimal

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7350 Group: 2 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 10 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/20/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Inflammation, subacute/chronic; minimal

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7353 Group: 2 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 10 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/20/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Inflammation, subacute/chronic; minimal

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7358 Group: 2 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 10 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/19/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7367 Group: 2 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 10 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/19/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

An Oral (Gavage) Prenatal Developmental
Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7373 Group: 2 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 10 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

An Oral (Gavage) Prenatal Developmental
Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7376 Group: 2 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 10 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

An Oral (Gavage) Prenatal Developmental
Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7393 Group: 2 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 10 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/21/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7403 Group: 2 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 10 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/19/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

An Oral (Gavage) Prenatal Developmental
Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7405 Group: 2 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 10 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/19/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7314 Group: 3 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 100 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

An Oral (Gavage) Prenatal Developmental
Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7318 Group: 3 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 100 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/20/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Inflammation, subacute/chronic; minimal

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7321 Group: 3 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 100 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/19/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

An Oral (Gavage) Prenatal Developmental
Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7327 Group: 3 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 100 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/20/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Focus, eosinophilic; minimal
Inflammation, subacute/chronic; minimal

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7331 Group: 3 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 100 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/19/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

An Oral (Gavage) Prenatal Developmental
Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7344 Group: 3 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 100 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/19/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

An Oral (Gavage) Prenatal Developmental
Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7345 Group: 3 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 100 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Necrosis, focal; minimal

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7348 Group: 3 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 100 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Inflammation, subacute/chronic; minimal

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7354 Group: 3 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 100 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Necrosis, focal; minimal

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7357 Group: 3 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 100 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7361 Group: 3 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 100 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Inflammation, subacute/chronic; minimal

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7365 Group: 3 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 100 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/19/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

Individual Animal Pathology Data

Animal Ref.: 7368 Group: 3 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 100 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/17/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Inflammation, subacute/chronic; minimal

Individual Animal Pathology Data

Animal Ref.: 7372 Group: 3 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 100 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

An Oral (Gavage) Prenatal Developmental
Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7375 Group: 3 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 100 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

Individual Animal Pathology Data

Animal Ref.: 7383 Group: 3 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 100 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

Individual Animal Pathology Data

Animal Ref.: 7386 Group: 3 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 100 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/17/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

An Oral (Gavage) Prenatal Developmental
Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7387 Group: 3 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 100 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/19/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

Individual Animal Pathology Data

Animal Ref.: 7389 Group: 3 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 100 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/19/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7390 Group: 3 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 100 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/20/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7394 Group: 3 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 100 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/22/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Inflammation, subacute/chronic; minimal

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7404 Group: 3 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 100 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/19/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

LIVER

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7309 Group: 4 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 1000 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/20/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Hypertrophy, hepatocellular; minimal
Necrosis, focal; minimal

The following tissues were within normal limits:

KIDNEYS

Individual Animal Pathology Data

Animal Ref.: 7310 Group: 4 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 1000 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

KIDNEYS;
Chronic progressive nephropathy; minimal

LIVER;
Hypertrophy, hepatocellular; minimal

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7315 Group: 4 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 1000 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEYS LIVER

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7316 Group: 4 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 1000 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Hypertrophy, hepatocellular; minimal
Inflammation, subacute/chronic; minimal

The following tissues were within normal limits:

KIDNEYS

Individual Animal Pathology Data

Animal Ref.: 7323 Group: 4 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 1000 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/20/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Hypertrophy, hepatocellular; minimal

The following tissues were within normal limits:

KIDNEYS

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7328 Group: 4 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 1000 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: FOUND DEAD
Date of Necropsy: 02/16/10

Histo Pathology Observations:

KIDNEYS;
AUTOLYSIS: NECRIPSY AND HISTOLOGY PERFORMED
Thrombi, glomeruli (dic); moderate: suggestive of disseminated intravascular coagulation (DIC)

LIVER;
Hypertrophy, hepatocellular; minimal
Necrosis, focal; moderate: locally extensive

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7330 Group: 4 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 1000 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Hypertrophy, hepatocellular; minimal

The following tissues were within normal limits:

KIDNEYS

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7336 Group: 4 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 1000 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/19/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEYS LIVER

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7338 Group: 4 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 1000 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/19/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

KIDNEYS;
Chronic progressive nephropathy; minimal

LIVER;
Hypertrophy, hepatocellular; minimal
Inflammation, subacute/chronic; minimal

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7342 Group: 4 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 1000 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/21/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Hypertrophy, hepatocellular; minimal

The following tissues were within normal limits:

KIDNEYS

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7349 Group: 4 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 1000 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/17/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Hypertrophy, hepatocellular; minimal

The following tissues were within normal limits:

KIDNEYS

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7351 Group: 4 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 1000 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/19/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

KIDNEYS;
Dilatation; tubules; focal; minimal

LIVER;
Hypertrophy, hepatocellular; minimal

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7359 Group: 4 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 1000 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/19/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations: None

The following tissues were within normal limits:

KIDNEYS LIVER

An Oral (Gavage) Prenatal Developmental
Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7362 Group: 4 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 1000 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/19/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Hypertrophy, hepatocellular; minimal

The following tissues were within normal limits:

KIDNEYS

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7363 Group: 4 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 1000 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

KIDNEYS;
Chronic progressive nephropathy; mild

LIVER;
Hypertrophy, hepatocellular; minimal

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7366 Group: 4 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 1000 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Hypertrophy, hepatocellular; minimal

The following tissues were within normal limits:

KIDNEYS

Individual Animal Pathology Data

Animal Ref.: 7374 Group: 4 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 1000 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/20/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Hypertrophy, hepatocellular; minimal

The following tissues were within normal limits:

KIDNEYS

Individual Animal Pathology Data

Animal Ref.: 7378 Group: 4 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 1000 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

KIDNEYS;
Lymphoid aggregates; minimal

LIVER;
Hypertrophy, hepatocellular; minimal
Inflammation, subacute/chronic; minimal

Individual Animal Pathology Data

Animal Ref.: 7382 Group: 4 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 1000 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Hypertrophy, hepatocellular; minimal
Necrosis, focal; minimal

The following tissues were within normal limits:

KIDNEYS

Individual Animal Pathology Data

Animal Ref.: 7388 Group: 4 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 1000 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Hypertrophy, hepatocellular; minimal
Necrosis, focal; minimal

The following tissues were within normal limits:

KIDNEYS

Individual Animal Pathology Data

Animal Ref.: 7391 Group: 4 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 1000 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/18/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Hypertrophy, hepatocellular; mild
Necrosis, focal; minimal

The following tissues were within normal limits:

KIDNEYS

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats DuPont-18405-841

Individual Animal Pathology Data

Animal Ref.: 7409 Group: 4 Sex: Female Species: Rat Strain: Crl:CD(SD)

Test Material: HFPODAAS Dose: 1000 mg/kg/day Route: Oral Study Type: Developmental Main
Date of Death : 11/21/09 Study Day No. (Week): 21 (3) Mode of Death: SACRIFICE BY DESIGN
Date of Necropsy: 02/16/10

Histo Pathology Observations:

LIVER;
Hypertrophy, hepatocellular; minimal

The following tissues were within normal limits:

KIDNEYS

APPENDIX F

WIL Developmental Historical Control Data Version 1.4 [Crl:CD(SD) Rats]

Mean of Study Means

Endpoint	Total	Mean	S.D.	SEM	Median	Min	Max	25th Quartile	75th Quartile
NO. OF DATASETS	**17**								
Total No. of Animals in the Control Group	395								
No. of Animals That Died	0								
No. of Animals That Aborted	0								
No. of Animals That Delivered	0								
Percent Pregnant		96.7	3.29	0.80	96.0	90.9	100.0	95.5	100.0
No. Gravid	382								
No. With Only Resorptions	1								
No. of Dams With Live Fetuses	381								
No. Nongravid	12								
No. of Animals Examined at Laparohysterectomy	394								
Mean Gravid Uterine Weight (g)		109.3	5.04	1.22	109.2	102.6	117.8	104.8	113.7
Mean No. Viable Fetuses/Dam		15.1	0.65	0.16	15.2	14.2	16.4	14.6	15.4
Total No. Viable Fetuses	5766								
Viable Fetuses (%/Litter)		94.9	2.65	0.64	952	86.5	97.8	94.6	96.2
Mean No. Postimplantation Loss/Dam		0.7	0.30	0.07	0.7	0.4	1.5	0.6	0.9
Total No. of Postimplantation Losses	280								
Postimplantation Loss (%/Litter)		5.1	2.65	0.64	4.8	2.2	13.5	3.8	5.4
Early Resorptions (%/Litter)		5.0	2.66	0.65	4.7	2.2	13.5	3.7	5.4
Late Resorptions (%/Litter)		0.1	0.14	0.03	0.0	0.0	0.5	0.0	0.0
Dead Fetuses (%/Litter)		0.0	0.00	0.00	0.0	0.0	0.0	0.0	0.0
Mean No. Implantations/Dam		15.8	0.58	0.14	15.8	14.6	16.8	15.6	16.1
Mean No. Corpora Lutea/Dam		17.0	0.56	0.14	16.9	16.4	18.2	16.6	17.5
Mean No. Preimplantation Loss/Dam		1.2	0.44	0.11	1.1	0.5	2.0	0.9	1.6
Total No. Preimplantation Losses	457								
Preimplantation Loss (%/Litter)		7.0	2.77	0.67	6.0	3.1	12.3	5.2	8.6
Total No. Male Fetuses	2914								
Total No. Female Fetuses	2852								
% Males/Litter		50.5	3.32	0.81	51.3	42.1	54.3	49.3	52.8
% Females/Litter		49.5	3.32	0.81	48.7	45.7	57.9	47.2	50.7
Mean Fetal Body Weight (g)		5.4	0.11	0.03	5.4	5.2	5.6	5.3	5.5
Mean Male Body Weight (g)		5.6	0.11	0.03	5.6	5.4	5.8	5.5	5.6
Mean Female Body Weight (g)		5.3	0.11	0.03	5.3	5.0	5.4	5.2	5.3

Mean of Study Means

NO. OF DATASETS	**17**	
Total No. of Fetuses/Litters Examined Externally	5766	381
Total No. of Fetuses/Litters Examined Viscerally	5766	381
Total No. of Fetuses/Litters Examined Skeletally	5765	381

MALFORMATIONS (% Per Litter)	**Mean**	**S.D.**	**SEM**	**Median**	**Min**	**Max**	**25th Quartile**	**75th Quartile**
TOTAL EXTERNAL MALFORMATIONS	0.1	0.21	0.05	0.0	0.0	0.6	0.0	0.3
TOTAL VISCERAL MALFORMATIONS	0.1	0.19	0.05	0.0	0.0	0.6	0.0	0.0
TOTAL SKELETAL MALFORMATIONS	0.2	0.28	0.07	0.3	0.0	0.9	0.0	0.3
EXTERNAL								
Astomia	0.0	0.07	0.02	0.0	0.0	0.3	0.0	0.0
Carpal and/or Tarsal Flexure	0.0	0.09	0.02	0.0	0.0	0.3	0.0	0.0
Cebocephaly	0.0	0.07	0.02	0.0	0.0	0.3	0.0	0.0
Exencephaly with or without Open Eyelid(s)	0.0	0.06	0.02	0.0	0.0	0.3	0.0	0.0
Fetal Anasarca	0.0	0.06	0.01	0.0	0.0	0.3	0.0	0.0
Gastroschisis	0.0	0.07	0.02	0.0	0.0	0.3	0.0	0.0
Mandibular Micrognathia	0.0	0.07	0.02	0.0	0.0	0.3	0.0	0.0
Microphthalmia and/or Anophthalmia	0.1	0.18	0.04	0.0	0.0	0.6	0.0	0.0
Tail- Curly	0.0	0.08	0.02	0.0	0.0	0.3	0.0	0.0
VISCERAL								
Hydrocephaly	0.0	0.08	0.02	0.0	0.0	0.3	0.0	0.0
Interventricular Septal Defect	0.0	0.06	0.02	0.0	0.0	0.3	0.0	0.0
Kidney(s) and/or Ureter(s) Absent	0.0	0.08	0.02	0.0	0.0	0.3	0.0	0.0
Retroesophageal Aortic Arch	0.0	0.06	0.01	0.0	0.0	0.2	0.0	0.0
Situs Inversus	0.0	0.11	0.03	0.0	0.0	0.3	0.0	0.0
Vessel(s)- Malpositioned	0.0	0.07	0.02	0.0	0.0	0.3	0.0	0.0
SKELETAL								
Costal Cartilage Anomaly	0.0	0.13	0.03	0.0	0.0	0.5	0.0	0.0
Rib Anomaly	0.0	0.14	0.04	0.0	0.0	0.6	0.0	0.0
Skull Anomaly	0.1	0.15	0.04	0.0	0.0	0.6	0.0	0.0

Mean of Study Means

NO. OF DATASETS	**17**	
Total No. of Fetuses/Litters Examined Externally	5766	381
Total No. of Fetuses/Litters Examined Viscerally	5766	381
Total No. of Fetuses/Litters Examined Skeletally	5765	381

MALFORMATIONS (% Per Litter)	**Mean**	**S.D.**	**SEM**	**Median**	**Min**	**Max**	**25th Quartile**	**75th Quartile**
SKELETAL								
Sternebra(e)- Malaligned (Severe)	0.0	0.06	0.02	0.0	0.0	0.3	0.0	0.0
Sternoschisis	0.0	0.10	0.03	0.0	0.0	0.3	0.0	0.0
Vertebral Anomaly with or without Associated Rib Anomaly	0.1	0.12	0.03	0.0	0.0	0.3	0.0	0.0
Vertebral Centra Anomaly	0.0	0.06	0.02	0.0	0.0	0.3	0.0	0.0

Mean of Study Means

NO. OF DATASETS	**17**	
Total No. of Fetuses/Litters Examined Externally	5766	381
Total No. of Fetuses/Litters Examined Viscerally	5766	381
Total No. of Fetuses/Litters Examined Skeletally	5765	381

VARIATIONS (% Per Litter)	**Mean**	**S.D.**	**SEM**	**Median**	**Min**	**Max**	**25th Quartile**	**75th Quartile**
TOTAL EXTERNAL VARIATIONS	0.0	0.00	0.00	0.0	0.0	0.0	0.0	0.0
TOTAL VISCERAL VARIATIONS	1.4	1.25	0.30	1.1	0.0	4.1	0.3	1.9
TOTAL SKELETAL VARIATIONS	12.4	3.41	0.83	12.8	5.9	19.3	9.7	14.2
VISCERAL								
Hemorrhagic Ring Around the Iris	0.0	0.07	0.02	0.0	0.0	0.3	0.0	0.0
Kidney(s)- Pale	0.0	0.07	0.02	0.0	0.0	0.3	0.0	0.0
Liver- Pale	0.1	0.21	0.05	0.0	0.0	0.7	0.0	0.0
Localized Depression of the Interventricular Septum	0.0	0.07	0.02	0.0	0.0	0.3	0.0	0.0
Major Blood Vessel Variation	0.2	0.25	0.06	0.0	0.0	0.9	0.0	0.3
Pulmonary Trunk- Cyst(s)	0.0	0.07	0.02	0.0	0.0	0.3	0.0	0.0
Renal Papilla(e) not Developed and/or Distended Ureter(s)	1.0	1.13	0.27	0.6	0.0	3.5	0.0	1.3
Spleen- Accessory	0.0	0.06	0.01	0.0	0.0	0.2	0.0	0.0
Spleen- Pale	0.0	0.06	0.01	0.0	0.0	0.3	0.0	0.0
Spleen- Small	0.0	0.07	0.02	0.0	0.0	0.3	0.0	0.0
SKELETAL								
14th Full Rib(s)	0.2	0.24	0.06	0.0	0.0	0.8	0.0	0.3
14th Rudimentary Rib(s)	9.2	2.97	0.72	9.8	2.8	13.9	7.6	11.5
25 Presacral Vertebrae	0.2	0.28	0.07	0.0	0.0	1.0	0.0	0.3
27 Presacral Vertebrae	0.1	0.13	0.03	0.0	0.0	0.3	0.0	0.2
7th Cervical Rib(s)	1.3	0.82	0.20	1.2	0.0	3.1	0.9	1.6
7th Sternebra	0.1	0.14	0.04	0.0	0.0	0.5	0.0	0.0
Bent Rib(s)	0.0	0.11	0.03	0.0	0.0	0.4	0.0	0.0
Hyoid Unossified	0.0	0.08	0.02	0.0	0.0	0.3	0.0	0.0
Reduced Ossification of the 13th Rib(s)	0.7	0.71	0.17	0.4	0.0	2.3	0.3	1.1
Reduced Ossification of the Rib(s)	0.1	0.32	0.08	0.0	0.0	1.3	0.0	0.0

Mean of Study Means

NO. OF DATASETS	**17**	
Total No. of Fetuses/Litters Examined Externally	5766	381
Total No. of Fetuses/Litters Examined Viscerally	5766	381
Total No. of Fetuses/Litters Examined Skeletally	5765	381

VARIATIONS (% Per Litter)	**Mean**	**S.D.**	**SEM**	**Median**	**Min**	**Max**	**25th Quartile**	**75th Quartile**
SKELETAL								
Reduced Ossification of the Skull	0.0	0.14	0.03	0.0	0.0	0.6	0.0	0.0
Reduced Ossification of the Vertebral Arches	0.1	0.31	0.08	0.0	0.0	1.3	0.0	0.0
Skull Bone(s)- Accessory	0.0	0.09	0.02	0.0	0.0	0.3	0.0	0.0
Sternebra(e) #5 and/or #6 Unossified	0.4	0.58	0.14	0.0	0.0	1.8	0.0	0.5
Sternebra(e)- Malaligned (Slight or Moderate)	0.2	0.23	0.06	0.0	0.0	0.6	0.0	0.3
Vertebral Centra Not Fully Ossified	0.5	1.27	0.31	0.0	0.0	5.1	0.0	0.0

Modal Distribution of Fetal Body Weights

No. of Datasets in Historical Control	**17**
Range of Study Dates	8/19/2003 - 5/23/2007
No. of Dams in Historical Control	395
No. of Dams with Live Fetuses	381
Mean Fetal Body Weight Range (g)	5.21 - 5.62

Mean Fetal Body Weight (g)	**5.2**	**5.3**	**5.4**	**5.5**	**5.6**
Total No. Datasets	1	4	4	6	2
Mean Litter Size	15.2	15.1	15.3	15.0	15.0
Litter Size Range	15.2 - 15.2	14.2 - 16.2	14.3 - 16.4	14.2 - 15.6	15.0 - 15.0

Summary Incidence Malformations and Variations

(Total Number Fetuses/Litters Affected)
Ranked Uppermost to Nethermost

NO. OF DATASETS	**17**	
Total No. of Fetuses/Litters Examined Externally	5766	381
Total No. of Fetuses/Litters Examined Viscerally	5766	381
Total No. of Fetuses/Litters Examined Skeletally	5765	381

MALFORMATIONS	**Number Fetuses**	**Litters**
EXTERNAL		
Microphthalmia and/or Anophthalmia	4	4
Carpal and/or Tarsal Flexure	2	2
Astomia	1	1
Cebocephaly	1	1
Exencephaly with or without Open Eyelid(s)	1	1
Fetal Anasarca	1	1
Gastroschisis	1	1
Mandibular Micrognathia	1	1
Tail- Curly	1	1
VISCERAL		
Situs Inversus	3	3
Hydrocephaly	1	1
Interventricular Septal Defect	1	1
Kidney(s) and/or Ureter(s) Absent	1	1
Retroesophageal Aortic Arch	1	1
Vessel(s)- Malpositioned	1	1
SKELETAL		
Sternoschisis	3	3
Vertebral Anomaly with or without Associated Rib Anomaly	3	3
Skull Anomaly	3	2
Costal Cartilage Anomaly	2	1
Rib Anomaly	2	1
Sternebra(e)- Malaligned (Severe)	1	1

Summary Incidence Malformations and Variations

(Total Number Fetuses/Litters Affected)

Ranked Uppermost to Nethermost

NO. OF DATASETS	**17**	
Total No. of Fetuses/Litters Examined Externally	5766	381
Total No. of Fetuses/Litters Examined Viscerally	5766	381
Total No. of Fetuses/Litters Examined Skeletally	5765	381

	Number	
MALFORMATIONS	**Fetuses**	**Litters**
SKELETAL		
Vertebral Centra Anomaly	1	1

Summary Incidence Malformations and Variations

(Total Number Fetuses/Litters Affected)
Ranked Uppermost to Nethermost

NO. OF DATASETS	**17**	
Total No. of Fetuses/Litters Examined Externally	5766	381
Total No. of Fetuses/Litters Examined Viscerally	5766	381
Total No. of Fetuses/Litters Examined Skeletally	5765	381

	Number	
VARIATIONS	**Fetuses**	**Litters**
VISCERAL		
Renal Papilla(e) not Developed and/or Distended Ureter(s)	53	26
Major Blood Vessel Variation	10	9
Liver- Pale	5	3
Hemorrhagic Ring Around the Iris	1	1
Kidney(s)- Pale	1	1
Localized Depression of the Interventricular Septum	1	1
Pulmonary Trunk- Cyst(s)	1	1
Spleen- Accessory	1	1
Spleen- Pale	1	1
Spleen- Small	1	1
SKELETAL		
14th Rudimentary Rib(s)	540	205
7th Cervical Rib(s)	75	50
Reduced Ossification of the 13th Rib(s)	41	30
Vertebral Centra Not Fully Ossified	29	16
Sternebra(e) #5 and/or #6 Unossified	18	15
Sternebra(e)- Malaligned (Slight or Moderate)	11	11
14th Full Rib(s)	10	8
25 Presacral Vertebrae	9	8
27 Presacral Vertebrae	5	5
Reduced Ossification of the Rib(s)	5	2
Reduced Ossification of the Vertebral Arches	4	1
7th Sternebra	3	3

Summary Incidence Malformations and Variations

(Total Number Fetuses/Litters Affected)

Ranked Uppermost to Nethermost

NO. OF DATASETS	**17**	
Total No. of Fetuses/Litters Examined Externally	5766	381
Total No. of Fetuses/Litters Examined Viscerally	5766	381
Total No. of Fetuses/Litters Examined Skeletally	5765	381

	Number	
VARIATIONS	**Fetuses**	**Litters**
SKELETAL		
Bent Rib(s)	2	2
Reduced Ossification of the Skull	2	2
Skull Bone(s)- Accessory	2	2
Hyoid Unossified	1	1

APPENDIX G

Study Protocol

Study Number: WIL-189223

PROTOCOL AMENDMENT V

Sponsor: E. I. du Pont de Nemours and Company
DuPont Work Request Number: 18405
DuPont Service Code: 841
DuPont Study Number: 18405-841

A. Title of Study:

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats

B. Protocol Modifications:

1) **7.9** **Microscopic Examination:**

The following is added to this section of the protocol:

The remaining wet tissues for all animals on this study will be shipped to Carolyn Lloyd (shipping address in Protocol Amendment II) in 10% neutral-buffered formalin.

WIL-189223
Protocol Amendment V
Page 2

C. Reasons for the Protocol Modification:

1) Sponsor requested shipment of remaining wet tissue.

Approval:

Sponsor approval received via email on March 10, 2010.

E. I. du Pont de Nemours and Company

Susan M. Munley, MA
Sponsor Representative — 12 March 2010 Date

WIL Research Laboratories, LLC

Tammye L. Edwards, BS, LAT
Study Director — 11 March 2010 Date

Donald G. Stump, PhD, DABT
Director, Developmental and
Reproductive Toxicology — 16 Mar 2010 Date

Study Number: WIL-189223

PROTOCOL AMENDMENT IV

Sponsor: E. I. du Pont de Nemours and Company
DuPont Work Request Number: 18405
DuPont Service Code: 841
DuPont Study Number: 18405-841

A. Title of Study:

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats

B. Protocol Modifications:

1) **2.4** **Principal Investigator, Pathology**

The Principal Investigator for Pathology is changed to the following:

Steven R. Frame, D.V.M., Ph.D., Diplomate ACVP
Stine-Haskell Research Center
1090 Elkton Rd.
Newark, DE 19711
Telephone (302)-366-5169
Fax (302)-451-4530
steven.r.frame@usa.dupont.com

2) **7.9** **Microscopic Examination:**

This first paragraph of this section is changed to the following:

Microscopic examination of hematoxylin-eosin stained paraffin sections will be performed on the following tissues from control and high dose females. If a treatment-related finding is noted in the high dose, those tissues demonstrating the treatment-related changes will be examined for the low and intermediate groups.

C. Reasons for the Protocol Modification:

1) Change in the Principal Investigator, Pathology at the Sponsor' request.

WIL-189223
Protocol Amendment IV
Page 2

2) Microscopic evaluation of tissues will only be performed in the control and high dose group unless there is a treatment-related effect.

Approval:

Sponsor approval received via email on 9 March 2010.

E. I. du Pont de Nemours and Company

Susan M. Munley, MA — 10 Mar 2010
Sponsor Representative — Date

WIL Research Laboratories, LLC

Tammye L. Edwards, BS, LAT — 9 Mar 2010
Study Director — Date

Donald G. Stump, PhD, DABT — 15 Mar 2010
Director, Developmental and Reproductive Toxicology — Date

Study Number: WIL-189223

PROTOCOL AMENDMENT III

Sponsor: E. I. du Pont de Nemours and Company
DuPont Work Request Number: 18405
DuPont Service Code: 841
DuPont Study Number: 18405-841

A. Title of Study:

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats

B. Protocol Modifications:

1) **7.6.2 Homogeneity, Resuspension Homogeneity, Stability and Concentration Determination of Test Article Formulations:**

The first paragraph is changed to the following:

Stability and resuspension homogeneity were established on a previous study (Haas, Draft; WIL-189216). Test article formulations were stable for 5 hours of room temperature storage or 12 days of refrigerated storage (2-8°C) at concentrations of 0.01 mg/mL and 100 mg/mL and homogenous following resuspension after 12 days of refrigerated storage (2-8°C). Stability and resuspension homogeneity will not be conducted on this study.

WIL-189223
Protocol Amendment III
Page 2

C. Reasons for the Protocol Modification:

1) Correction of room temperature stability to 5 hours as appropriate.

Approval:

Sponsor approval received via email on February 1, 2010.

E. I. du Pont de Nemours and Company

Susan M. Munley, MA
Sponsor Representative

3 Feb 2010
Date

whatever
3Feb2010

WIL Research Laboratories, LLC

Tammye L. Edwards, BS, LAT
Study Director

1 Feb 2010
Date

Donald G. Stump, PhD, DABT
Director, Developmental and
Reproductive Toxicology

1 Feb 2010
Date

Study Number: WIL-189223

PROTOCOL AMENDMENT II

Sponsor: E. I. du Pont de Nemours and Company
DuPont Work Request Number: 18405
DuPont Service Code: 841
DuPont Study Number: 18405-841

A. Title of Study:

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats

B. Protocol Modifications:

1) **2 PERSONNEL INVOLVED IN THE STUDY:**

The following Principal Investigator is added:

2.4 Principal Investigator, Pathology

Greg P. Sykes, VMD, DACVP, DACLAM, DABT
PharmPath, LLC.
105 Phillips Mill Rd.
West Grove, PA, 19390-9165
Tel: 302-451-3551
Cellular Tel: 484-678-4433
Email: greg.p.sykes@usa.dupont.com

2) This section is added to the protocol:

7.9 Microscopic Examination:

Microscopic examination of hematoxylin eosin stained paraffin sections will be performed on the following tissues from all females on study.

Kidneys (bilateral)
Liver

The slides will be prepared by WIL Research Laboratories, LLC and then shipped to Sponsor at the address and contact below for examination by the Principal Investigator, Pathology.

Carolyn Lloyd
DuPont Haskell Global Centers for Health & Environmental Sciences
Investigative Sciences, S320/531
1090 Elkton Road
Newark, DE 19714-0050
Tel: 302-366-5401
Fax: 302-451-4530
Email: carolyn.w.lloyd@usa.dupont.com

The examination of the slides will be performed by the Principal Investigator, Pathology. A final pathology report will be prepared and submitted to WIL Research for inclusion as an appendix in the main study final report. A Quality Assurance and GLP compliance statement signed by the performing laboratory will be provided to the WIL Study Director for inclusion in the Final Report. The Sponsor is responsible for archiving of raw data associated with the conduct of the pathological examination.

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C. Reasons for the Protocol Modification:

1) Addition of Principal Investigator, Pathology

2) Addition of microscopic examination of tissues at the Sponsors request.

Approval:

Sponsor approval received via email on 21 December 2009.

E. I. du Pont de Nemours and Company

Susan M. Munley, MA
Sponsor Representative — 8 Jan 2010 Date

WIL Research Laboratories, LLC

Tammye L. Edwards, BS, LAT
Study Director — 4 Jan 2010 Date

Donald G. Stump, PhD, DABT
Director, Developmental and
Reproductive Toxicology — 4 Jan 2010 Date

Study Number: WIL-189223

PROTOCOL AMENDMENT I

Sponsor: E. I. du Pont de Nemours and Company
DuPont Work Request Number: 18405
DuPont Service Code: 841
DuPont Study Number: 18405-841

A. Title of Study:

An Oral (Gavage) Prenatal Developmental Toxicity Study of H-28548 in Rats

B. Protocol Modifications:

1) **7.7.2 Body Weights:**

This section is changed to the following:

Individual body weights will be recorded on gestation days 0 and 6-21 (daily).

2) **7.7.3 Food Consumption:**

Individual food consumption will be recorded on gestation days 0 and 6-21 (daily). Food intake will be reported as g/animal/day and g/kg/day for each corresponding body weight interval of gestation.

3) **7.7.4 Deaths and Animals Euthanized *in Extremis:***

The following is added to this section:

Uteri which appear nongravid by macroscopic examination will be opened and placed in a 10% ammonium sulfide solution as described by Salewski (Salewski, 1964) for detection of early implantation loss.

4) **7.7.5 Premature Deliveries:**

The last sentence of this section is changed to the following:

Recognizable fetuses or pups that prematurely delivered on GD 21 will be examined according to Section 7.8.3, if possible.

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5) **7.8** **Scheduled Necropsy – Gestation Day 20:**

This heading of this section is changed to the following:
Scheduled Necropsy – Gestation Day 21:

6) **7.8.1** **Laparohysterectomy and Macroscopic Examination:**

The second sentence of the first paragraph is changed to the following:

All surviving rats will be euthanized by carbon dioxide inhalation on gestation day 21.

The first sentence of the 2nd paragraph is changed to the following:

The kidneys (bilateral), liver and any gross lesions will be preserved for possible future histopathological examination in 10% neutral-buffered formalin.

7) **7.8.2** **Organ Weights:**

The first sentence of this section is changed to the following:

The following organs will be weighed from all animals euthanized at the scheduled termination on Gestation Day 21.

8) **9.1** **Maternal In-life Data:**

This section is changed to the following:

Continuous data variables [mean body weights (absolute and net), body weight gains (absolute and net), food consumption of each interval] and absolute organ weight data will be subjected to a parametric one-way analysis of variance (ANOVA) (Snedecor, 1980) to determine intergroup difference. If the results of the ANOVA are significant ($p<0.05$), Dunnett's test (1964) will be applied to the data.

C. Reasons for the Protocol Modification:

1) Body weights will be collected on GD 21.

2) Food consumption will be collected on GD 21.

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Page 3

3) Addition of staining uteri with no macroscopic implantations.

4) The laparohysterectomy is changed to GD 21.

5) The scheduled necropsy is changed to GD 21.

6) The laparohysterectomy is changed to GD 21 and clarification that the tissues retained will be for possible histopathological examination.

7) The scheduled termination is changed to GD 21.

8) Addition of statistical evaluation of the organ weights.

Approval:

E. I. du Pont de Nemours and Company

Susan M. Munley, MA
Sponsor Representative

28 Oct 2009
Date

WIL Research Laboratories, LLC

Tammye L. Edwards, BS, LAT
Study Director

27 Octber 2009
Date

Donald G. Stump, PhD, DABT
Director, Developmental and
Reproductive Toxicology

27 Oct 2009
Date

PROTOCOL

AN ORAL (GAVAGE) PRENATAL DEVELOPMENTAL TOXICITY STUDY OF H-28548 IN RATS

(U.S. EPA OPPTS and OECD Guidelines)

Submitted To:

E.I. du Pont de Nemours and Company
Wilmington, Delaware 19898

DuPont Work Request Number: 18405
DuPont Service Code: 841
DuPont Study Number: 18405-841

WIL Research Laboratories, LLC
1407 George Road
Ashland, OH 44805-8946

1 OBJECTIVE:

The objective of this study is to determine the potential of H-28548 to induce developmental toxicity after maternal exposure during the critical period of organogenesis, to characterize maternal toxicity at the exposure levels tested and to determine a NOAEL (no-observed-adverse-effect level) for maternal toxicity and developmental toxicity.

This study is subject to the United States Environmental Protection Agency (EPA) Health Effects Test Guidelines OPPTS 870.3700, Prenatal Developmental Toxicity Study, August, 1998 and the Organisation of Economic Cooperation and Development Guidelines (OECD) for Testing of Chemicals Guideline 414, Prenatal Developmental Toxicity Study, January 2001, and will be conducted in accordance with the EPA (40 CFR Part 792 and 40 CFR Part 160) and OECD [C(97) 186/Final] Good Laboratory Practice Regulations.

2 PERSONNEL INVOLVED IN THE STUDY:

2.1 Sponsor Representative:

Susan M. Munley, MA
Research Toxicologist
Developmental, Reproductive and Neurobehavioral Toxicology
DuPont Haskell Laboratory for Health and Environmental Sciences
1090 Elkton Rd., PO Box 50
Newark, DE 19714
Tel: (302) 366-5240
Email: Susan.M.Munley@usa.dupont.com

2.2 WIL Study Director:

Tammye L. Edwards, BS, LAT
Staff Toxicologist, Developmental
and Reproductive Toxicology
WIL Research Laboratories, LLC
1407 George Road
Ashland, Ohio 44805-8946
Tel: (419) 289-8700 ext. 2105
Fax: (419) 289-3650
Email: tledwards@wilresearch.com

2.3 WIL Departmental Responsibilities:

Eddie D. Sloter, PhD
Senior Toxicologist, Developmental
and Reproductive Toxicology
Emergency Contact
Tel: (419) 289-8700
Fax: (419) 289-3650
Email: esloter@wilresearch.com

Mark D. Nemec, BS, DABT
President and Chief Operating Officer

Donald G. Stump, PhD, DABT
Director, Developmental and
Reproductive Toxicology

George A. Parker, DVM, PhD, DACVP, DABT
Director, Pathology

Melissa J. Beck, PhD
Assistant Director, Neurosciences

Daniel W. Sved, PhD
Director, Metabolism and Analytical Chemistry

Walter R. Miller, BS, DVM
Clinical Veterinarian,
Head of Surgery and Experimental Medicine

Ronald E. Wilson, BS
Director, Informational Systems

Carol A. Kopp, BS, LAT
Manager, Gross Pathology and
Developmental Toxicology Laboratory

Heather L. Johnson, BS, RQAP-GLP
Manager, Quality Assurance

Bennett J. Varsho, MPH, DABT
Operations Manager, Developmental and
Reproductive Toxicology and the Formulations Laboratory

Robert A. Wally, BS, RAC
Manager, Reporting and Regulatory
Technical Services

3 STUDY SCHEDULE:

Proposed Experimental Starting (Animal Receipt) Date:	13 October 2009
Proposed Experimental Start (First Day of Dosing) Date:	2 November 2009
Proposed Laparohysterectomy Dates:	17-21 November 2009
Proposed Experimental Completion/Termination Date (Completion of Skeletal Examinations):	11 December 2009
Proposed Audited Report Date:	20 January 2010

4 TEST ARTICLE DATA:

4.1 Test Substance Shipment:

Test article and applicable documentation, including a Certificate of Analysis, will be shipped under Sponsor's responsibility to:

Formulations Laboratory (WIL-189223; Tammye Edwards)
Attn: Larry Blessing
WIL Research Laboratories, LLC
1407 George Road
Ashland, Ohio 44805-8946

4.2 Identification:

H-28548 or HFPO Dimer Acid Ammonium Salt

4.3 Haskell Test Substance Number:

H-28548

4.4 Lot Number:

E109540-44A

4.5 Expiration/Retest Date:

13 June 2011

4.6 Purity:

84%

4.7 Storage Conditions:

Controlled room temperature and humidity (approximately 18° to 24°C and 20% to 70% relative humidity)

4.8 Stability:

The analysis was performed by the Sponsor and documented on the Certificate of Analysis.

4.9 Physical Description:

To be documented by WIL Research Laboratories, LLC.

4.10 Reserve Samples:

Reserve samples of the test article will be taken in accordance with WIL Standard Operating Procedures and stored in the Archives at WIL Research Laboratories, LLC indefinitely, unless otherwise specified.

4.11 Personnel Safety Data:

See the Material Safety Data Sheet (MSDS) provided by the Sponsor.

4.12 Test Article Disposition:

With the exception of the reserve sample for each batch of test article, which will be archived as described, all neat test article remaining at completion of the in-life phase of the study will be kept for subsequent studies.

5 TEST SYSTEM:

5.1 Species:

Rat

5.2 Strain:

Sprague-Dawley Crl:CD(SD)

5.3 Source:

Charles River Laboratories, Inc.
(Facility to be documented in the raw data)

5.4 Number of Study:

88 females (maximum of 110 purchased). A sufficient number of sexually mature untreated resident males of the same strain and source will be used to induce pregnancies. Animals not assigned to the study will be transferred to the stock animal colony or will be euthanized by carbon dioxide inhalation and the carcasses discarded.

The number of animals selected for this study is based on the US EPA Health Effects Test Guidelines OPPTS 870.3700, Prenatal Development Toxicity Study, August 1998 and the OECD Guidelines for Testing of Chemicals Guideline 414, Prenatal Developmental Toxicity Study, January 2001.

5.5 Body Weight Range:

A minimum of 220g at initiation of breeding.

5.6 Approximate Age:

80 to 120 days at the initiation of breeding.

5.7 Identification System:

The animals will be uniquely identified by a Monel® metal ear tag displaying the animal number. Individual cage cards will be affixed to each cage and will display the animal number, group number, study number, dosage level and sex of the animal.

5.8 Justification for Selection:

This species and strain of rat has been recognized as appropriate for developmental toxicity studies. WIL Research Laboratories, LLC has historical data on the background incidence of fetal malformations and developmental variations in the Crl:CD(SD) rat. This animal model has been proven to be susceptible to the effects of developmental toxicants.

6 SPECIFIC MAINTENANCE SCHEDULE:

6.1 Animal Housing:

The rats will be individually housed (except during mating) in solid bottom cages (plastic maternity cages) containing ground corncob nesting material (Bed-O' Cobs®) in an environmentally controlled room during the quarantine period and throughout the entire study until euthanasia. The cages will be subjected to routine cleaning at a frequency consistent with maintaining good animal health and WIL Standard Operating Procedures. The facilities at WIL Research Laboratories, LLC are fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC International).

6.2 Environmental Conditions:

Controls will be set to maintain temperature at 71 ± 5°F (22 ± 3°C) and relative humidity at 50 ± 20%. Temperature and relative humidity will be monitored continuously. Data for these two parameters will be scheduled for automatic collection on an hourly basis. Fluorescent lighting controlled by light timers will provide illumination for a 12-hour light/dark photoperiod. The ventilation rate will be set at a minimum of 10 room air changes per hour, 100% fresh air.

6.3 Drinking Water:

Reverse osmosis-purified water will be available *ad libitum*. Filters servicing the automatic watering system are changed regularly according to WIL Standard Operating Procedures. The municipal water supplying the laboratory is analyzed according to WIL Standard Operating Procedures on a routine basis to ensure that contaminants are not present in concentrations that would be expected to affect the outcome of the study.

6.4 Basal Diet:

PMI Nutrition International, LLC Certified Rodent LabDiet® 5002 will be offered *ad libitum* during the study. Periodic analyses of the certified feed are performed by the manufacturer to ensure that heavy metals and pesticides are not present at concentrations that would be expected to affect the outcome of the study. Results of the analyses are provided to WIL Research Laboratories, LLC by the manufacturer. Feeders will be changed and sanitized once per week.

6.5 Enrichment:

All animals will be offered Nestlets™ for enrichment that will be replaced as needed.

7 EXPERIMENTAL DESIGN:

7.1 Animal Receipt and Quarantine:

Each rat will be inspected by a qualified technician upon receipt. Rats judged to be in good health and suitable as test animals will be immediately placed in quarantine for a minimum of 10 days. All rats will be initially weighed, permanently identified with a metal ear tag and receive a clinical observation. During the quarantine period, each rat will be observed twice daily for changes in general appearance and behavior. Body weights may be recorded prior to the initiation of breeding. Prior to the start of the in-life phase, those rats judged to be suitable test subjects will be identified.

7.2 Breeding Procedure:

At the conclusion of the quarantine period, female rats judged to be suitable test subjects and meeting acceptable body weight requirements will be cohabitated with an untreated male (1:1) of the same source and strain. Detection of mating will be confirmed by evidence of a vaginal copulatory plug or by a vaginal lavage for sperm. After confirmation of mating, the female will be returned to an individual solid bottom cage (assigned to a group), and the day will be designated as day 0 of gestation.

7.3 Randomization:

Mated females will be assigned to groups using a WIL Toxicology Data Management System (WTDMS™) computer program which assigns animals based on stratification of gestation day 0 body weights into a block design to one control group and three test article groups of 22 rats each.

Any animal assigned to the study that is found dead, euthanized *in extremis* or exhibits abnormal clinical signs, reduced food consumption or body weight losses prior to the start of dosing may be replaced by an animal of appropriate gestation age when possible. Replacement animals will be arbitrarily assigned (not computer randomized) to the study based on comparable body weights (if possible) with respect to the animal that was replaced.

7.4 Route and Rationale of Test Article Administration:

The route of administration will be oral (gavage) as this is a potential route of exposure for humans. Historically, this route has been used extensively for studies of this nature. Appropriately sized flexible, Teflon®-shafted, stainless steel ball-tipped dosing cannulae will be used for the oral administration by gavage.

7.5 Organization of Test Groups, Dosage Levels and Treatment Regimen:

7.5.1 Organization of Test Groups:

The dosage levels will be determined from results of previous studies and will be provided by the Sponsor Representative after consultation with the WIL Study Director.

The following table presents the study group arrangement.

Group Number	Test Article	Dosage Level[a] (mg/kg/day)	Dosage Concentration[a] (mg/mL)	Dosage Volume (mL/kg)	Number of Females
1	Vehicle Control[b]	0	0	10	22
2	H-28548	10	1	10	22
3	H-28548	100	10	10	22
4	H-28548	1000	100	10	22

[a] Dosage levels will be corrected for the purity of 84%.
[b] Deionized Water

7.5.2 Vehicle Control Article:

Deionized Water

7.5.3 Treatment Regimen:

The test and control materials will be administered as a single daily dose during the period of major organogenesis, gestation days 6 through 20. All rats will be dosed at approximately the same time each day.

7.5.4 Adjustment of Doses:

Individual dosages will be calculated on the most recent body weight to provide the proper mg/kg/day dosage.

7.6 Preparation and Analysis of Test Article Formulations:

7.6.1 Method and Frequency of Preparation:

Based on the physical characteristics of the test article, appropriate methods will be used to ensure the best possible formulations of the test article in the vehicle. Dosing formulations will be stored refrigerated (2-8°C) for a maximum of 12 days. The Study Director or designee will visually inspect the formulations prior to the initiation of dosing. This visual inspection will be performed to ensure that the formulations are visibly homogeneous and acceptable for dosing. Any special procedures required for formulation will be documented according to Good Laboratory Practices and presented in the final report of this study. Test article formulations will be prepared weekly and divided into aliquots for daily dispensation. The test article and vehicle formulations will be stirred continuously during dosing.

7.6.2 Homogeneity, Resuspension Homogeneity, Stability and Concentration Determination of Test Article Formulations:

Stability and resuspension homogeneity were established on a previous study (Haas, Draft; WIL-189216). Test article formulations were stable and 12 days of room temperature storage or refrigerated storage (2-8°C) at concentrations of 0.01 mg/mL and 100 mg/mL and homogenous following resuspension after 12 days of refrigerated storage (2-8°C). Stability and resuspension homogeneity will not be conducted on this study.

Homogeneity will be conducted on the first formulations prepared for dosing. Four 1-mL samples will be collected from the top, middle and bottom of the test article formulations from the low and high dose groups and the samples analyzed to assess the homogeneity of the test article in the mixtures; the middle strata will serve as the measure of test article concentration. Four 1-mL samples will be taken from the middle on the control and the mid-dose groups and analyzed for concentration of the test substance.

Concentration will be assessed on the last weeks formulations prepared for dosing. Four 1-mL samples will be collected from the middle of each test article formulation and the control group and analyzed for test article content.

7.6.3 Sample Analysis:

Samples will be transferred to the Analytical Chemistry Department at WIL Research Laboratories, LLC for analysis. Analyses of test article formulations will be performed using a method developed and validated by WIL Research Laboratories, LLC. Initially, two of each set of four replicate, 1-mL samples will be analyzed; the remaining two 1-mL samples will be stored frozen (approximately -20°C) at WIL and will function as back-up samples. Back-up samples will be analyzed if requested by the Sponsor or Study Director or may be discarded following results that are within specifications and approval of the Study Director.

7.7 Maternal Observations During Gestation:

7.7.1 Appearance and Behavior:

Each rat will be observed twice daily for moribundity and mortality, once in the morning and once in the afternoon from gestation day 0 until euthanasia. Clinical observations will be recorded daily. Mortality and all signs of overt toxicity will be recorded on the day observed. The observations shall include, but are not limited to, evaluation for changes in appearance of skin and fur, eyes, mucous membranes, respiratory and circulatory system, autonomic and central nervous systems, somatomotor activity and behavior. All animals will also be observed on the day of necropsy and any findings will be recorded.

During the treatment period, each animal will be observed at approximately 1-2 hour(s) following each dose administration for findings that are potentially related to treatment or that might change before the next scheduled observation. Additional post-dosing observation periods may be necessary and will be documented in the study records.

7.7.2 Body Weights:

Individual body weights will be recorded on gestation days 0 and 6-20 (daily).

7.7.3 Food Consumption:

Individual food consumption will be recorded on gestation days 0 and 6-20 (daily). Food intake will be reported as g/animal/day and g/kg/day for each corresponding body weight interval of gestation.

7.7.4 Deaths and Animals Euthanized *in Extremis*:

Females not surviving until the scheduled euthanasia will be necropsied and cause of death recorded, if possible. Rats not expected to survive to the next observation period (moribund) will be euthanized by carbon dioxide inhalation. The cranial, thoracic, abdominal and pelvic cavities will be opened and the organs examined. The number and location of implantation sites and viable fetuses will be recorded. Corpora lutea will also be counted and recorded. The kidneys (bilateral), liver and any gross lesions will be preserved in 10% neutral-buffered formalin for possible future histopathological examination. Carcasses from adult animals will be discarded. Viable fetuses will be euthanized by hypothermia followed by an intrathoracic injection of sodium pentobarbital, if necessary. Recognizable fetuses will be examined externally and preserved in 10% neutral-buffered formalin.

7.7.5 Premature Deliveries:

Females that deliver prematurely will be euthanized by carbon dioxide inhalation that day. The thoracic, abdominal and pelvic cavities will be opened and the organs examined. The number and location of former implantation sites and viable fetuses will be recorded. Corpora lutea will also be counted and recorded. The kidneys (bilateral), liver and any gross lesions will be preserved in 10% neutral-buffered formalin for possible future histopathological examination. Carcasses from adult animals will be discarded. Viable fetuses will be euthanized by hypothermia followed by an intrathoracic injection of sodium pentobarbital (if needed). Viable pups will be euthanized by an intraperitoneal injection of sodium pentobarbital. Recognizable fetuses or pups will be examined externally and preserved in 10% neural buffered formalin. Recognizable fetuses or pups aborted on GD 20 will be examined according to Section 7.8.3, if possible.

7.8 Scheduled Necropsy – Gestation Day 20:

7.8.1 Laparohysterectomy and Macroscopic Examination:

Laparohysterectomy and macroscopic examinations will be performed blind to treatment group. All surviving rats will be euthanized by carbon dioxide inhalation on gestation day 20. The thoracic, abdominal and pelvic cavities will be opened and the organs examined. The uterus of each dam will be excised and its adnexa trimmed. Corpora lutea will be counted and recorded. Gravid uterine weights will be obtained and recorded. The uterus of each dam will be opened and the number of viable and nonviable fetuses, early and late resorptions and total number

of implantation sites will be recorded, and the placentae will be examined. The individual uterine distribution will be documented using the following procedure: all implantation sites, including early and late resorptions, will be numbered in consecutive fashion beginning with the left distal uterine horn, noting the position of the cervix and continuing from the proximal to the distal right uterine horn. Uteri which appear nongravid by macroscopic examination will be opened and placed in a 10% ammonium sulfide solution as described by Salewski (Salewski, 1964) for detection of early implantation loss.

The kidneys (bilateral), liver and any gross lesions will be preserved for future histopathological examination in 10% neutral-buffered formalin. Representative sections of corresponding organs of any gross lesions retained will be retained from a sufficient number of controls comparison, if possible. The carcasses will be discarded.

7.8.2 Organ Weights:

The following organs will be weighed from all animals euthanized at the scheduled termination on Gestation Day 20.

Kidneys (weighed paired)
Liver

7.8.3 Fetal Examination:

Fetal examinations will be conducted without knowledge of treatment group. External, internal and skeletal fetal findings will be recorded as developmental variations or malformations. Representative photographs of all malformations, as appropriate, will be included in the study records. Corresponding low magnification photographs, depicting both the malformed fetus and a comparison control fetus, or normal littermate, will also be included in the study records as needed and as appropriate for comparison, when possible. Prenatal data (viable and nonviable fetuses, early and late resorptions, pre- and post-implantation loss and the fetal sex distribution) will be presented on a group mean basis and additionally as proportional data (% per litter).

7.8.3.1 External:

Each viable fetus will be examined in detail, sexed, weighed, euthanized by hypothermia followed by an intrathoracic injection of sodium pentobarbital (if necessary), and tagged. Nonviable fetuses (the degree of autolysis is minimal or absent) will be

examined, crown-rump length measured, weighed, sexed and tagged individually. The crown-rump length of late resorptions (advanced degree of autolysis) will be measured, the degree of autolysis recorded, a gross external examination performed (if possible) and the tissue will be discarded.

7.8.3.2 Visceral (Internal):

Fetuses will be examined for visceral anomalies by dissection in the fresh (non-fixed) state. The thoracic and abdominal cavities will be opened and dissected using a technique described by Stuckhardt and Poppe (Stuckhardt, 1984). Fetal kidneys will be examined and graded for renal papillae development (Woo and Hoar, 1972). This examination will include the heart and major vessels. The sex of all fetuses will be confirmed by internal examination.

The heads will be removed from approximately one-half of the fetuses in each litter and placed in Bouin's solution for subsequent processing and soft tissue examination using the Wilson sectioning technique (1965).

The heads from the remaining one-half of the fetuses in each litter will be examined by a mid-coronal slice.

All carcasses, including the carcasses without heads, will be eviscerated and fixed in 100% ethyl alcohol for subsequent examination of skeletons.

7.8.3.3 Skeletal:

Each eviscerated viable and non-viable fetus, following fixation in alcohol, will be stained with Alizarin Red S by a method similar to that described by Dawson (1926). The skeletal examination will be made following this procedure.

8 DURATION OF STUDY:

The quarantine, breeding and gestation phases of the study will require approximately two months. The laparohysterectomy phase of the study and processing and evaluation of the fetal specimens will require approximately four weeks.

9 STATISTICAL METHODS:

All analyses will be two-tailed for significance levels of 5% and 1%. All statistical tests will be performed using a computer with appropriate programming as referenced below. The litter, rather than the fetus, will be considered as the experimental unit. Comparative statistics will not be performed on data from toxicokinetic phase animals.

9.1 Maternal In-Life Data:

Continuous data variables [mean body weights (absolute and net), body weight gains (absolute and net) and food consumption of each interval] will be subjected to a parametric one-way analysis of variance (ANOVA) (Snedecor, 1980) to determine intergroup difference. If the results of the ANOVA are significant ($p<0.05$), Dunnett's test (1964) will be applied to the data.

9.2 Laparohysterectomy Data:

The group mean numbers of corpora lutea, implantation sites, viable fetuses, maternal gravid uterine weights and mean fetal weight (separately by sex, and combined) will be subjected to a parametric one-way analysis of variance (ANOVA) (Snedecor, 1980) and Dunnett's test (1964) as described above. The mean litter proportions of prenatal data (% per litter of viable and nonviable fetuses, early and late resorptions, total resorptions, pre- and post-implantation loss and the fetal sex distribution) will be subjected to the Kruskal-Wallis nonparametric ANOVA test (1952) to determine intergroup difference. If the results of the ANOVA are significant ($p<0.05$), the Dunn's Test (1964) will be applied to the data.

9.3 Fetal Morphology Data:

The mean litter proportion (% per litter) of total fetal malformations and developmental variations (external, visceral, skeletal and combined) and of each particular external, visceral and skeletal malformation or variation will be tabulated. The mean litter proportions of fetal malformations and developmental variations will be subjected to the Kruskal-Wallis nonparametric ANOVA test (1952) followed by the Dunn's Test (1964) (if appropriate) as described above

10 QUALITY ASSURANCE:

The study will be audited by the WIL Quality Assurance Unit while in progress to assure compliance with the study protocol and protocol amendments, WIL Standard Operating Procedures and the appropriate provisions of the EPA TSCA and FIFRA

Good Laboratory Practice Standards published in the Federal Register (40 CFR Part 792 and 40 CFR Part 160) and the OECD Principles of Good Laboratory Practice, November 26, 1997 [C(97)186/Final]. The raw data and draft report will be audited by the WIL Quality Assurance Unit prior to submission to the Sponsor to assure that the final report accurately describes the conduct and the findings of the study.

This study will be included on the WIL master list of regulated studies.

11 RECORDS TO BE MAINTAINED:

All original raw data records, as defined by WIL SOPs and the applicable GLPs, will be stored as described in Section 12 in the Archives at WIL Research Laboratories, LLC.

12 WORK PRODUCT:

The Sponsor will have title to all documentation records, raw data, specimens or other work product generated during the performance of the study. All remaining formulation samples will not be archived, but will be discarded upon issuance of the Final Report. All work product, including raw paper data, pertinent electronic storage media and specimens, will be retained at no charge for six months following issuance of the final report in the Archives at WIL Research Laboratories, LLC. Thereafter, WIL Research Laboratories, LLC will charge a monthly archiving fee for retention of all work product. All work product will be stored in compliance with regulatory requirements.

Any work product, including documents, specimens, and samples, that are required by this protocol, its amendments, or other written instructions of the Sponsor, to be shipped by WIL Research Laboratories, LLC to another location will be appropriately packaged and labeled as defined by WIL's SOPs and delivered to a common carrier for shipment. WIL Research Laboratories, LLC will not be responsible for shipment following delivery to the common carrier.

All work product generated at a performing laboratory will be retained at an appropriate archive facility as designated by the SOPs of the performing laboratory.

13 REPORTS:

The final report will contain a summary, test article data, methods and procedures, maternal and fetal data, WIL Historical Control Data, the analytical chemistry report and an interpretation and discussion of the study results. The final report will be comprehensive and shall define level(s) inducing toxic effects as well as no effect level(s) under the condition of this investigation. The report will contain all information necessary to conform to current EPA OPPTS and OECD specifications.

WIL Research Laboratories, LLC will submit one copy of an audited draft report in a timely manner upon completion of data collection prior to issuance of the final report. One revision will be permitted as part of the cost of the study, from which the Sponsor's reasonable revisions and suggestions will be incorporated into the final report, as appropriate. Additional changes or revisions may be made, at extra cost. It is expected that the Sponsor will review the draft report and provide comments to WIL Research Laboratories, LLC within a two-month time frame following submission. WIL Research Laboratories, LLC will submit the final report within one month following receipt of comments. If the Sponsor's comments and/or authorization to finalize the report have not been received at WIL Research Laboratories, LLC within one year following submission of the draft report, WIL Research Laboratories, LLC may elect to finalize the report following appropriate written notification to the Sponsor. Two electronic copies (PDF) of the final report on CD-R will be provided. Requests for paper copies of the final report may result in additional charges.

14 ANIMAL WELFARE ACT COMPLIANCE:

This study will comply with all applicable sections of the Final Rules of the Animal Welfare Act (AWA) regulations (9 CFR Parts 1, 2 and 3). The Sponsor should make particular note of the following:

- The Sponsor Representative's signature on this protocol documents for the Study Director the Sponsor's assurance that the study described in this protocol does not unnecessarily duplicate previous experiments.

- Whenever possible, procedures used in this study have been designed to avoid or minimize discomfort, distress or pain to animals. All methods are described in this study protocol or in written laboratory Standard Operating Procedures.

- Animals that experience severe pain or distress that cannot be relieved will be painlessly euthanized as deemed appropriate by the veterinary staff and Study Director. The Sponsor will be advised by the Study Director of all circumstances which could lead to this action in as timely a manner as possible.

- Methods of euthanasia used during this study are in conformance with the above-referenced regulation.

- The Sponsor/Study Director has considered alternatives to procedures that may cause more than momentary or slight pain or distress to the animals and has provided a written narrative description (AWA covered species only) of the methods and sources used to determine that alternatives are not available.

15 PROTOCOL MODIFICATION:

Modification of the protocol may be accomplished during the course of this investigation. However, no changes will be made in the study design without the verbal or written permission of the Sponsor. In the event that the Sponsor verbally requests or approves a change in the protocol, such changes will be made by appropriate documentation in the form of a protocol amendment. All alterations of the protocol and reasons for the modification(s) will be signed by the Study Director and the Sponsor Representative.

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17 PROTOCOL APPROVAL:

E. I. du Pont de Nemours and Company

Susan M. Munley, MA
Sponsor Representative

14 wrong date entered 13 Oct 2009 Date

smm 14 Oct 2009

WIL Research Laboratories, LLC

Tammye L. Edwards, BS, LAT
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