FINAL REPORT

PROTOCOL 418-011

ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS

SPONSOR'S STUDY NUMBER: T-6316.7

FINAL REPORT DATE: 17 DECEMBER 1998

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ARGUS RESEARCH LABORATORIES, INC.
PROTOCOL NUMBER: 418-011
SPONSOR'S STUDY NUMBER: T-6316.7

I. SUMMARY AND CONCLUSION

A. Methods[a]

Twenty-five Crl:CD®BR VAF/Plus® (Sprague-Dawley) presumed pregnant female rats were assigned to each of five dosage groups (Groups I through V). Nineteen additional female rats were assigned to one of five dosage groups for the satellite study (three, five, three, three and five rats assigned to Groups I through V, respectively). The test article, N-EtFOSE, or vehicle, 2% Tween® 80 in Reverse Osmosis Membrane Processed Deionized Water (R.O. Deionized Water), was administered via gavage once daily to female rats on days 6 through 17 of presumed gestation (DGs 6 through 17). Dosages of 0 (Vehicle), 1, 5, 10 and 20 mg/kg/day were administered at a dosage volume of 5 mL/kg, adjusted daily on the basis of individual body weights.

The female rats were observed for viability at least twice each day of the study. The rats were also examined for clinical observations of effects of the test article, abortions, premature deliveries and deaths before and approximately one hour after dosage (DGs 6 through 17), and once daily during the postdosage period.

a. Detailed descriptions of all procedures used in the conduct of this study are provided in the appropriate sections of this report and in APPENDIX C (PROTOCOL AND AMENDMENT).

Body weights were recorded on DGs 0 and 4 and daily during the dosage and postdosage periods. Feed consumption values were recorded on DGs 0, 4, 6, 8, 10, 12, 14, 16, 18 and 20.

All rats in the main study were sacrificed by carbon dioxide asphyxiation on DG 20 and a gross necropsy of the thoracic, abdominal and pelvic viscera was performed. The number of corpora lutea in each ovary was recorded. The uterus of each rat was examined for pregnancy, number and distribution of implantations, live and dead fetuses and early and late resorptions. Each fetus was identified, weighed and examined for sex and gross external alterations. Approximately one-half of the fetuses in each litter were examined for soft tissue alterations and the remaining fetuses in each litter were examined for skeletal alterations.

Rats in the satellite study were sacrificed on DG 18. Blood samples were collected and centrifuged. The liver was excised, weighed and sectioned. Fetuses were examined grossly to the extent possible as described for rats assigned to the main study. Fetuses and placentae were pooled per litter. After completion of sample collection, serum, liver section, fetal and placental samples were shipped to the Sponsor for analysis.

B. Results

No deaths, abortions or premature deliveries occurred during the study. All rats survived until scheduled sacrifice on gestation day 20 (DG 20).

All clinical and necropsy observations were considered unrelated to the test article.

Maternal body weight gains were significantly reduced in groups administered 5 mg/kg/day and higher dosages of the test article. The effect was minimal and transient in the 5 mg/kg/day dosage group, occurring only on DGs 8 to 10. In the 10 mg/kg/day dosage group, significant reductions in maternal body weight gains occurred on DGs 6 to 8 and 10 to 12, followed by a significant increase in weight gain on DGs 14 to 16. The 20 mg/kg/day dosage group had significant weight loss followed by significant reductions in maternal body weight gain on DGs 8 to 14 and 16 to 18. These effects of the test article resulted in a tendency for reduced weight gain in the 10 mg/kg/day dosage group and significant reductions in the 20 mg/kg/day dosage group for the entire treatment period (DGs 6 to 10), the entire interval after initiation of treatment (DGs 6 to 20) and the entire gestation period (DGs 0 to 20). Maternal body weights were

significantly reduced in the 10 and 20 mg/kg/day dosage groups on DGs 11 through 13 and 8 through 20, respectively.

Body weights and body weight gains were unaffected by the 1 mg/kg/day dosage of the test article.

The absolute feed consumption value was significantly reduced in the 10 mg/kg/day dosage group on DGs 6 to 8 and absolute and relative feed consumption values were significantly reduced in the 20 mg/kg/day dosage group for the entire dosage period and at all intervals within this period. The absolute feed consumption value continued to be significantly reduced and the relative feed consumption value tended to be reduced in the 20 mg/kg/day dosage group during the postdosage interval. These effects of the 20 mg/kg/day dosage of the test article resulted in significantly reduced absolute and relative feed consumption values on DGs 6 to 20 and DGs 0 to 20.

Absolute and relative feed consumption values were unaffected by dosages of the test article as high as 5 mg/kg/day.

Fetal body weights (total, male and/or female) were significantly reduced in the 10 and 20 mg/kg/day dosage groups, as compared to the control group values. Dosages of N-EtFOSE as high as 20 mg/kg/day did not affect any other Caesarean-sectioning or litter parameters. The litter averages for corpora lutea, implantations, litter sizes, live fetuses, early resorptions, percent resorbed conceptuses and percent male fetuses, as well as the numbers of dams with any resorptions or with viable fetuses were comparable in the five dosage groups and did not significantly differ. No dams had litters with all conceptuses resorbed, and there were no dead fetuses or late resorptions. All placentae appeared normal. All of these values were within the ranges observed historically at the Testing Facility.

Reversible delays in fetal ossification associated with the significantly reduced fetal body weights in the 10 and 20 mg/kg/day dosage groups, were evident as significant reductions in the litter averages for ossified caudal vertebrae in the 10 and 20 mg/kg/day dosage groups and a significant increase in the fetal incidence of wavy ribs in the 20 mg/kg/day dosage group.

All other fetal gross external, soft tissue and skeletal alterations (malformations and variations) were considered unrelated to the test article because: 1) the incidences were not dosage-dependent; and/or 2) the incidences were within ranges observed historically at the Testing Facility.

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C. Conclusion

On the basis of these data, the maternal no-observable-effect-level (NOEL) of N-EtFOSE is 5 mg/kg/day (the 10 and 20 mg/kg/day dosages caused biologically important and statistically significant reductions in body weight gains or weight losses, and the 20 mg/kg/day dosage also persistently reduced the absolute and relative feed consumption values). The developmental NOEL is also 5 mg/kg/day (the 10 and 20 mg/kg/day dosages significantly reduced fetal body weights and caused minimal, but statistically significant reversible delays in ossification of the caudal vertebrae; the 20 mg/kg/day dosage also significantly increased the incidence of wavy ribs, an additional reversible delay in ossification associated with the reduced fetal body weights).

Mildred S. Christian, Ph.D., Fellow, ATS — Date
Executive Director of Research

17 Dec 98

Alan M. Hoberman, Ph.D., DABT. — Date
Director of Research

17-DEC-98

Raymond G. York, Ph.D., DABT — Date
Associate Director of Research
and Study Director

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II. DESCRIPTION OF TEST PROCEDURES

A. Conduct of Study:

A.1. Sponsor:

3M CorporateToxicology, 3M Center, Building 220-2E-02, St. Paul, Minnesota 55144-1000

A.2. Testing Facility:

Argus Research Laboratories, Inc., 905 Sheehy Drive, Building A, Horsham, Pennsylvania 19044-1297

A.3. Study Number:

418-011

A.4. Sponsor's Study Number:

T-6316.7

A.5. Purpose of the Study:

The purpose of this study was to detect adverse effects of N-EtFOSE on Crl:CD®BR VAF/Plus® presumed pregnant female rats and development of the embryo and fetus consequent to exposure of the dam from implantation to closure of the hard palate. This study evaluated ICH Harmonised Tripartite Guideline stages C and D of the reproductive process.

A.6. Study Design:

The requirements of the International Conference on Harmonisation (ICH) Harmonised Tripartite Guideline[1] were used as the basis of study design.

A.7. Regulatory Compliance:

The study was conducted in compliance with Good Laboratory Practice (GLP) regulations of the U.S. Food and Drug Administration (FDA)[2], the Japanese Ministry of Health and Welfare (MHW)[3] and the European Economic Community (EEC)[4]. There were no significant deviations from the GLP regulations that affected the quality or integrity of the study. Quality Assurance Unit findings derived from the inspections during the conduct of this study are documented

and have been provided to the Study Director and the Testing Facility Management.

A.8. Ownership of the Study:

The Sponsor owns the study. All raw data, analyses, reports and preserved tissues are the property of the Sponsor.

A.9. Study Monitor:

Marvin T. Case, D.V.M., Ph.D.

A.10. Alternate Study Monitor:

Andrew M. Seacat, Ph.D.

A.11. Study Director:

Raymond G. York, Ph.D., DABT (Associate Director of Research)

A.12. Technical Performance:

John F. Barnett, B.S. (Director of Laboratory Operations)
Kristen Iandola Sherer, B.S. (Research Associate/Fetal Evaluation)
Sharon Adamski (Laboratory Technician)

A.13. Report Preparation:

Raymond G. York, Ph.D., DABT
Jo Ann Frazee, M.S. (Study Coordinator)
Susan K. Bradshaw, B.S. (Data Management Specialist)
Karen G. Parker, A.A. (Administrative Assistant)

A.14. Report Review:

Alan M. Hoberman, Ph.D, DABT (Director of Research)
Mildred S. Christian, Ph.D., Fellow, ATS (Executive Director of Research)

A.15. Date Protocol Signed:

29 July 1998

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A.16. Dates of Technical Performance:

Rat Arrival Date	11 AUG 98
Cohabitation Period	18 AUG 98 PM - 23 AUG 98 AM
Day 0 of Presumed Gestation (DG 0)	19 AUG 98 - 23 AUG 98
Dosage Period (DGs 6 through 17)	25 AUG 98 - 09 SEP 98
Toxicokinetic Sample Collection and Caesarean-Sectioning Period (DG 18) - Satellite Study	10 SEP 98
Caesarean-Sectioning Period - Main Study (DG 20)	08 SEP 98 - 12 SEP 98

A.17. Records Maintained:

The original report, raw data and reserve samples of the test article and vehicle are retained in the archives of Argus Research Laboratories, Inc. Any preserved tissues are retained in the archives of the Testing Facility for one year after the mailing of the draft final report, after which time the Sponsor will decide their final disposition. Prepared formulations were discarded at the Testing Facility. Unused bulk test article will remain at the Testing Facility until its disposition is decided by the Sponsor.

B. Test Article Information:

B.1. Description:

N-EtFOSE - a waxy solid

B.2. Lot/Batch Number:

FM-3929 [30035, 30037, 30039 (Expiration date: May 2000)]

B.3. Date Received and Storage Conditions:

The test article was received on 20 May 1998, and stored at room temperature. Prepared formulations were stored refrigerated.

B.4. Special Handling Instructions:

Standard safety precautions (use of protective clothing, gloves, dust-mist respirator, safety goggles or safety glasses and a face-shield) were taken when handling the bulk test article and prepared formulations.

B.5. Analysis of Purity:

Information regarding the identity, composition, strength, and purity of the test article is on file with the Sponsor.

C. Vehicle Information:

C.1. Description:

2% Tween® 80 in Reverse Osmosis Membrane Processed Deionized Water (R.O. Deionized Water).

C.2. Lot Number:

M03H05

C.3. Date Received and Storage Conditions:

The vehicle was received on 8 July 1998 from J.T. Baker, Phillipsburg, New Jersey, and stored at room temperature. R.O. Deionized Water is available from a continuous source at the Testing Facility and is maintained at room temperature.

C.4. Special Handling Instructions:

Standard safety precautions (use of protective clothing, gloves, dust-mist respirator, safety goggles or safety glasses and a face-shield) were taken when handling the vehicle.

C.5. Analysis of Purity:

Neither the Sponsor nor the Study Director was aware of any potential contaminants likely to be present in the vehicle that would interfere with the results of this study.

D. Test Article Preparation:

Suspensions of N-EtFOSE were prepared daily at concentrations of 0, 0.2, 1, 2 and 4 mg/mL. The test article was considered 100% pure for the purpose of dosage calculations.

D.1. Sample Information:

Sample Type	Components	Size	Date Retained	Storage Conditions	Shipped To	Date Shipped
Concentration (all levels)	N/A	2 mL[a]	25 AUG 98[b] 09 SEP 98[c]	Frozen	Sponsor	26 AUG 98 10 SEP 98
Bulk Test Article Reserve	N/A	1 g	25 AUG 98	Room Temperature	Testing Facility Archives	01 OCT 98
Vehicle Reserve	Tween ® 80	5 mL	25 AUG 98	Room Temperature	Testing Facility Archives	01 OCT 98
	R.O. Deionized Water	5 mL	25 AUG 98	Room Temperature	Testing Facility Archives	01 OCT 98

a. Duplicate samples were taken from the first and last preparation on the day prepared. One sample of each set was shipped to the Sponsor for analysis. The remaining samples were retained at the Testing Facility as backup samples.
b. First day of preparation.
c. Last day of preparation.

Homogeneity and stability of prepared formulations are on file with the Sponsor.

D.2. Analytical Results:

Concentration samples (2 mL) were taken on the first and last days of preparation for analyses by 3M Environmental Technology and Safety Services. The results of these analyses were not available at the time of this report.

E. Test System:

E.1. Species:

Rat

E.2. Strain:

Crl:CD®BR VAF/Plus® (Sprague-Dawley)

E.3. Supplier (Source):

Charles River Laboratories, Inc., Raleigh, North Carolina

E.4. Sex:

Female (Note: Male rats were used only for the purposes of breeding and are not considered part of the Test System.)

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E.5. Rationale for Test System:

The Crl:CD®BR VAF/Plus® (Sprague-Dawley) rat was selected as the Test System because: 1) it is one mammalian species accepted and widely used throughout industry for nonclinical studies of developmental toxicity (embryo-fetal toxicity/teratogenicity); 2) this strain has been demonstrated to be sensitive to developmental toxins; 3) historical data and experience exist at the Testing Facility[5-7]; and 4) the test article is biologically active in this species and strain.

E.6. Test System Data:

Number of Rats	190
Approximate Date of Birth	08 AUG 98
Approximate Age at Arrival	64 days
Weight (g) on the Day after Arrival	195 - 234
Weight (g) at Study Assignment	210 - 251

E.7. Breeder Male Rat Data:

	Shipment 1	Shipment 2
Number of Rats	110	120
Approximate Date of Birth	13 JAN 98	26 JAN 98
Approximate Age at Arrival	87 days	75 days
Weight (g) on the Day after Arrival	300 - 356	300 - 356
Weight (g) at Study Assignment	498 - 784	

E.8. Method of Randomization:

Upon arrival, rats were assigned to individual housing on the basis of computer-generated random units. Female rats were assigned to one of five dosage groups (Groups I through V), 25 rats per dosage group, using a computer-generated (weight-ordered) randomization procedure based on body weights recorded on DG 0. Nineteen additional female rats were assigned to one of five dosage groups for the satellite study (three, five, three, three and five rats assigned to Groups I through V, respectively) using a computer-generated randomization based on body weights recorded on DG 0.

E.9. System of Identification:

Each rat was individually identified with a Monel® self-piercing ear tag (Gey Band and Tag Co., Inc., No. MSPT 20101) inscribed with the rat's designated unique permanent number. Cage tags were marked with the study number and permanent rat number.

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F. Husbandry:

F.1. Research Facility Registration:

USDA Registration No. 23-R-099 under the Animal Welfare Act, 7 U.S.C. 2131 *et seq.*

F.2. Study Rooms:

The study rooms were maintained under conditions of positive airflow relative to a hallway and independently supplied with a minimum of ten changes per hour of 100% fresh air that had been passed through 99.97% HEPA filters (Airo Clean® room). Room temperature and humidity were monitored constantly throughout the study. Room temperature was targeted at 64°F to 79°F (18°C to 26°C); relative humidity was targeted at 30% to 70%. See APPENDIX E (TEMPERATURE AND RELATIVE HUMIDITY REPORT).

F.3. Housing:

Rats were individually housed except during the cohabitation period. During cohabitation, each pair of male and female rats was housed in the male rat's cage. All cage sizes and housing conditions were in compliance with the *Guide for the Care and Use of Laboratory Animals* [8].

F.4. Lighting:

An automatically-controlled fluorescent light cycle was maintained at 12-hours light: 12-hours dark, with each dark period beginning at 1900 hours EST.

F.5. Sanitization:

Cage pan liners were changed approximately three times each week. Cages were changed approximately every other week.

F.6. Feed:

Rats were given *ad libitum* access to Certified Rodent Diet® #5002 (PMI Nutrition International, St. Louis, Missouri) in individual feeders.

F.7. Feed Analysis:

Analyses were routinely performed by the feed supplier. No contaminants at levels exceeding the maximum concentration for certified feed or deviations from

expected nutritional requirements were detected by these analyses. Copies of the results of the feed analyses are available in the raw data.

Neither the Study Director nor the Sponsor was aware of any agent present in the feed that was known to interfere with the results of this study.

F.8. Water:

Local water that had been processed by passage through a reverse osmosis membrane (R.O. water) was available to the rats *ad libitum* from individual water bottles attached to the cages and/or from an automatic watering system. Chlorine was added to the processed water as a bacteriostat.

F.9. Water Analysis:

The processed water is analyzed twice annually for possible chemical contamination (Lancaster Laboratories, Lancaster, Pennsylvania) and monthly for possible bacterial contamination (Analytical Laboratories, Inc., Chalfont, Pennsylvania). Copies of the results of the water analyses are available in the raw data.

Neither the Study Director nor the Sponsor was aware of any agent present in the water that was known to interfere with the results of this study.

G. Methods:

G.1. Dosage Administration:

Dosage Group	Number of Rats	Dosage (mg/kg/day)	Concentration (mg/mL)	Dosage Volume (mL/kg)	Assigned Numbers	
					Main Study	Satellite Study[a]
I	25 + 3[a]	0 (Vehicle)	0	5	12801 - 12825	12573 - 12575
II	25 + 5[a]	1	0.2	5	12826 - 12850	12576 - 12580
III	25 + 3[a]	5	1	5	12851 - 12875	12581 - 12583
IV	25 + 3[a]	10	2	5	12876 - 12900	12584 - 12586
V	25 + 5[a]	20	4	5	12901 - 19295	12587 - 12591

The test article was considered 100% pure for the purpose of dosage calculations.

a. Rats assigned to the satellite group for blood collection.

The test article was considered 100% pure for the purpose of dosage calculations.

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G.2. Rationale for Dosage Selection:

Dosages were selected on the basis of a dosage-range study (Argus Research Laboratories, Inc., Protocol 418-011P) that tested 0, 1, 5, 10, 25 and 35 mg/kg/day. In that study, body weight gain was decreased at 10 mg/kg/day and higher dosages, and feed consumption values were reduced at all dosages tested.

G.3. Route of Administration:

Oral (gavage)

G.4. Rationale for Route of Administration:

The oral (gavage) route was selected for use because: 1) in comparison with the dietary route, the exact dosage can be accurately administered; and 2) it is a proposed route of human exposure.

G.5. Frequency of Administration:

Appropriate dosages of the test article were administered orally (via gavage) once daily to female rats on DGs 6 through 17. Dosages of 0 (Vehicle), 1, 5, 10 and 20 mg/kg/day of the test article were administered at a dosage volume of 5 mL/kg, adjusted daily on the basis of the individual body weights recorded before dosage. The rats were dosed at approximately the same time each day.

G.6. Length of Study:

Approximately 4 weeks

G.7. Method of Study Performance:

After acclimation, 190 healthy virgin female rats were placed into cohabitation with 190 breeder male rats (one male rat per female rat in the male rat's cage). Female rats with spermatozoa observed in a smear of the vaginal contents and/or a copulatory plug *in situ* were considered to be at DG 0 and returned to individual housing.

The female rats were observed for viability at least twice each day of the study and for general appearance weekly during acclimation and on DG 0. The rats were also examined for clinical observations of effects of the test article,

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abortions, premature deliveries and deaths before and approximately one hour after dosage (DGs 6 through 17[a]), and once daily during the postdosage period.

Body weights were recorded weekly during acclimation, on DGs 0 and 4 and daily during the dosage and postdosage periods (DGs 6 through 20). Feed consumption values were recorded on DGs 0, 4, 6, 8, 10, 12, 14, 16, 18 and 20.

G.8. **Gross Necropsy**[b]:

Rats Assigned to the Main Study:

All rats were sacrificed by carbon dioxide asphyxiation on DG 20, Caesarean-sectioned and a gross necropsy of the thoracic, abdominal and pelvic viscera was performed. Uteri of apparently nonpregnant rats were stained with 10% ammonium sulfide to confirm the absence of implantation sites[9]. Tissues with gross lesions were preserved in neutral buffered 10% formalin for possible future evaluation; all other maternal tissues were discarded.

The number of corpora lutea in each ovary was recorded. The uterus of each rat was excised and examined for pregnancy, number and distribution of implantations, live and dead fetuses and early and late resorptions. An early resorption was defined as one in which organogenesis was not grossly evident. A late resorption was defined as one in which the occurrence of organogenesis was grossly evident. A live fetus was defined as a term fetus that responded to stimuli. Nonresponding term fetuses are considered to be dead (there were no dead fetuses). Dead fetuses and late resorptions are differentiated by the degree of autolysis present; marked to extreme autolysis indicated that the fetus was a late resorption.

Each fetus was removed from the uterus, placed in an individual container and identified with a tag noting the study number, litter number, uterine distribution and fixative. Each fetus was subsequently weighed and examined for sex and gross external alterations. Live fetuses were sacrificed by an intraperitoneal

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a. See APPENDIX D (DEVIATIONS FROM THE PROTOCOL AND STANDARD OPERATING PROCEDURES OF THE TESTING FACILITY), item 1.

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

injection of Beuthanasia®-D Special (Schering-Plough Animal Health). Photographs of gross external fetal alterations are available in the raw data.

Approximately one-half of the fetuses in each litter were examined for soft tissue alterations using an adaptation of Wilson's sectioning technique[10]. The fetuses were initially fixed in Bouin's solution; sections were stored in alcohol. The remaining fetuses in each litter were eviscerated, cleared, stained with alizarin red S[11], fixed in alcohol and examined for skeletal alterations. Skeletal preparations were retained in glycerin with thymol added as a preservative.

Rats Assigned to the Satellite Study:

On DG 18, rats assigned to the toxicokinetic evaluation were sacrificed and the following samples collected. Blood samples (approximately 4 mL per rat) were collected from the inferior vena cava into serum separator tubes and centrifuged. The resulting serum (approximately 2 mL) was immediately frozen on dry ice and maintained frozen (-70°C) until shipment to the Sponsor for analysis. The liver was excised, weighed, and a sample section (lateral lobe) was frozen and retained at -70°C until shipment to the Sponsor for analysis.

Rats were Caesarean-sectioned and fetuses were examined grossly to the extent possible as described above for rats assigned to the main study. Fetuses and placentae were pooled per litter and retained frozen (-70°C) until shipment to the Sponsor for analysis. After completion of sample collection, serum, liver section (lateral lobe), fetal and placental samples were shipped (frozen on dry ice) to the Sponsor for analysis.

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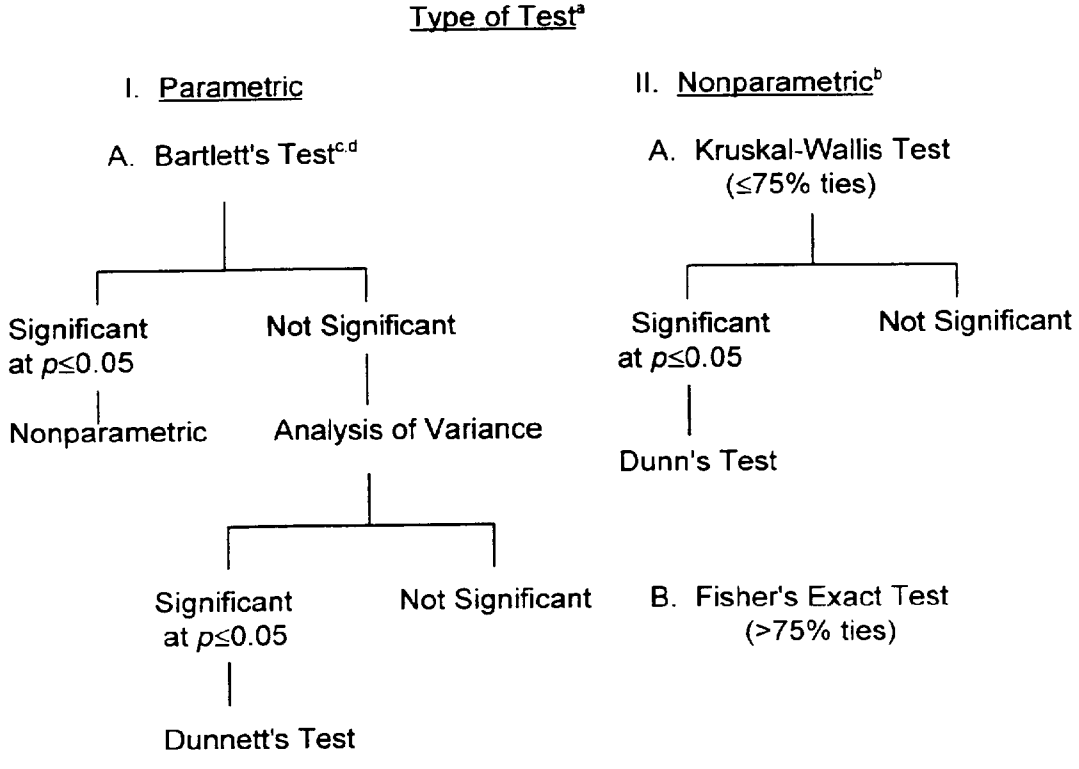
G.9. Statistical Analyses:

The following schematic represents the statistical analyses of data:



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a. Statistically significant probabilities are reported as either $p \leq 0.05$ or $p \leq 0.01$.
b. Proportion data are not included in this category.
c. Used only to analyze data with homogeneity of variance.
d. Test for homogeneity of variance.

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Clinical observation and other proportion data were analyzed using the Variance Test for Homogeneity of the Binomial Distribution[12].

Continuous data (e.g., maternal body weights, body weight changes, feed consumption values and litter averages for percent male fetuses, percent resorbed conceptuses, fetal body weights, fetal anomaly data and fetal ossification site data) were analyzed using Bartlett's Test of Homogeneity of Variances[13] and the Analysis of Variance[14], when appropriate [i.e., Bartlett's Test was not significant ($p>0.05$)]. If the Analysis of Variance was significant ($p\leq0.05$), Dunnett's Test[15] was used to identify the statistical significance of the individual groups. If the Analysis of Variance was not appropriate [i.e., Bartlett's Test was significant ($p\leq0.05$)], the Kruskal-Wallis Test[16] was used, when less than or equal to 75% ties were present. In cases where the Kruskal-Wallis Test was statistically significant ($p\leq0.05$), Dunn's Method of Multiple Comparisons[17] was used to identify the statistical significance of the individual groups. If there were greater than 75% ties, Fisher's Exact Test[18] was used to analyze the data.

Count data obtained at Caesarean-sectioning of the dams were evaluated using the procedures described above for the Kruskal-Wallis Test[16].

Dam 12868 (5 mg/kg/day dosage group) had a litter consisting of five live fetuses and two early resorptions and dam 12889 (10 mg/kg/day dosage group) had a litter consisting of three live fetuses. Because such occurrences can abnormally skew the distribution of data[19], statistical analyses were made with and without the values for these rats and litters. Maternal body weights, feed consumption values and Caesarean-section data for these dams and litters were excluded from summarization and statistical analyses; all values are presented on the individual tables.

III. RESULTS

A. Mortality, Clinical and Necropsy Observations (Summaries - Tables 1 and 2; Individual Data - Tables 14 and 15)

A.1. Mortality

No deaths, abortions or premature deliveries occurred during the study. All rats survived until scheduled sacrifice on gestation day 20 (DG 20).

A.2. Clinical Observations

All clinical observations were considered unrelated to the test article because: 1) the incidences were not dosage-dependent; 2) the observations occurred in only one rat; and/or 3) the observations are common events in the laboratory environment. Clinical observations included localized alopecia on the underside, limbs and/or neck, ungroomed coat, cold to touch and fused second and third digits on the right forepaw.

A.3. Necropsy Observations

The only necropsy finding was a tan area (0.6 cm x 0.8 cm) on the median lobe of the liver in one 20 mg/kg/day dosage group dam (12913). This observation was considered unrelated to the test article because it occurred in only one rat.

B. Maternal Body Weights and Body Weight Changes (Figure 1; Summaries - Tables 3 and 4; Individual Data - Table 16)

Maternal body weight gains were significantly reduced ($p \leq 0.05$ or $p \leq 0.01$) in groups administered 5 mg/kg/day and higher dosages of the test article. The effect was minimal and transient in the 5 mg/kg/day dosage group, occurring only on DGs 8 to 10. In the 10 mg/kg/day dosage group, significant reductions ($p \leq 0.05$) in maternal body weight gains occurred on DGs 6 to 8 and 10 to 12, followed by a significant increase ($p \leq 0.05$) in weight gain on DGs 14 to 16. The 20 mg/kg/day dosage group had significant weight loss ($p \leq 0.01$) on DGs 6 to 8 followed by significant reductions ($p \leq 0.05$ or $p \leq 0.01$) in maternal body weight gain on DGs 8 to 14 and 16 to 18. These effects of the test article resulted in a tendency for reduced weight gain in the 10 mg/kg/day dosage group and significant reductions ($p \leq 0.01$) in the 20 mg/kg/day dosage group for the entire treatment period (calculated as DGs 6 to 18), the entire interval after initiation of treatment (DGs 6 to 20) and the entire gestation period (DGs 0 to 20). Maternal

body weights were significantly reduced ($p \leq 0.05$ or $p \leq 0.01$) in the 10 and 20 mg/kg/day dosage groups on DGs 11 through 14 and 8 through 20, respectively.

Body weights and body weight gains were unaffected by the 1 mg/kg/day dosage of the test article.

C. Maternal Absolute (g/day) and Relative (g/kg/day) Feed Consumption Values (Summaries - Tables 5 and 6; Individual Data - Table 17)

The absolute (g/kg/day) feed consumption value was significantly reduced ($p \leq 0.05$) in the 10 mg/kg/day dosage group on DGs 6 to 8 and absolute (g/day) and relative (g/kg/day) feed consumption values were significantly reduced ($p \leq 0.01$) in the 20 mg/kg/day dosage group for the entire dosage period (calculated as DGs 6 to 18) and at all intervals within this period. The absolute feed consumption value continued to be significantly reduced ($p \leq 0.01$) and the relative feed consumption value tended to be reduced in the 20 mg/kg/day dosage group during the postdosage interval (DGs 18 to 20). These effects of the 20 mg/kg/day dosage of the test article resulted in significantly reduced ($p \leq 0.01$) absolute and relative feed consumption values on DGs 6 to 20 (the entire interval after the first dosage was administered) and DGs 0 to 20 (the entire gestation period).

Absolute and relative feed consumption values were unaffected by dosages of the test article as high as 5 mg/kg/day. The significant reduction ($p \leq 0.05$) in the relative feed consumption value in the 1 mg/kg/day dosage group on DGs 6 to 8 was considered unrelated to the test article because the value was not dosage-dependent.

D. Caesarean-Sectioning and Litter Observations (Summaries -Tables 7 and 8; Individual Data - Tables 18 through 20)

Pregnancy occurred in 24 (96%), 23 (92%), 24 (96%), 25 (100%) and 24 (96%) of the rats in the 0 (Vehicle), 1, 5, 10 and 20 mg/kg/day dosage groups, respectively. One 5 mg/kg/day dosage group litter consisted of five live fetuses and two early resorptions, and one 10 mg/kg/day dosage group litter consisted of three live fetuses. Because such occurrences can abnormally skew the distribution of the data[19], values for these dams and litters were excluded from data summarization and statistical analyses. As a result, Caesarean-sectioning observations were based on 24, 23, 23, 24 and 24 pregnant dams.

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Fetal body weights (total, male and/or female) were significantly reduced ($p \leq 0.05$ or $p \leq 0.01$) in the 10 and 20 mg/kg/day dosage groups, as compared to the control group values. The reduced fetal body weights in the 10 and 20mg/kg/day dosage groups were a reflection of body weight reduction of the dams at these higher dosage levels. Dosages of N-EtFOSE as high as 20 mg/kg/day did not affect any other Caesarean-sectioning or litter parameters. The litter averages for corpora lutea, implantations, litter sizes, live fetuses, early resorptions, percent resorbed conceptuses and percent male fetuses, as well as the numbers of dams with any resorptions or with viable fetuses were comparable in the five dosage groups and did not significantly differ. No dams had litters with all conceptuses resorbed, and there were no dead fetuses or late resorptions. All placentae appeared normal. All of these values were within the ranges observed historically at the Testing Facility[a].

E. Fetal Alterations (Summaries - Tables 9 through 13; Individual Data - Table 21)

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

Fetal evaluations were based on 342, 349, 347, 354 and 326 DG 20 Caesarean-delivered live fetuses in 24, 23, 24, 25 and 24 litters in the 0 (Vehicle), 1, 5, 10 and 20 mg/kg/day dosage groups, respectively. Each fetus was examined for gross external alterations. Of these respective fetuses 166, 167, 169, 170 and 158 were examined for soft tissue alterations and 176, 182, 178, 184 and 168 were examined for skeletal alterations and fetal ossification site averages.

E.1. Summary of Fetal Alterations (Summary - Table 9; Individual Data - Table 21)

In the five respective dosage groups, litters with fetuses with alterations present numbered 6 (25.0%), 8 (34.8%), 4 (16.7%), 7 (28.0%) and 8 (33.3%). The numbers of fetuses with any alteration observed were 15 (4.4%), 10 (2.9%), 6 (1.7%), 8 (2.2%) and 12 (3.7%), and the percentages of fetuses with any alteration were 4.4%, 2.8%, 1.6%, 2.1% and 4.0%, in these same respective dosage groups.

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a. See APPENDIX G (HISTORICAL CONTROL DATA).

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Reversible delays in fetal ossification[20,21] associated with the significantly reduced ($p \leq 0.05$ or $p \leq 0.01$) fetal body weights in the 10 and 20 mg/kg/day dosage groups, were evident as significant reductions ($p \leq 0.05$) in the litter averages for ossified caudal vertebrae in the 10 and 20 mg/kg/day dosage groups and a significant increase ($p \leq 0.05$) in the fetal incidence of wavy ribs in the 20 mg/kg/day dosage group.

All other fetal gross external, soft tissue and skeletal alterations (malformations and variations) were considered unrelated to the test article because: 1) the incidences were not dosage-dependent; and/or 2) the incidences were within ranges observed historically at the Testing Facility.

E.2. Fetal Gross External Alterations (Summary - Table 10; Individual Data - Table 21)

E.2.a. Malformations

One 10 mg/kg/day dosage group fetus (12885-15) had a short trunk and absent tail. Subsequent skeletal examination of this fetus revealed that only four cervical vertebrae were present and that there were no thoracic, lumbar, sacral or caudal vertebrae, or ribs. This fetus also had a variation in pelvic ossification (the pubes were not ossified).

E.2.b. Variations

No gross external variations occurred in the fetuses in this study.

E.3. Fetal Soft Tissue Alterations (Summary - Table 11; Individual Data - Table 21)

E.3.a. Malformations

No fetal malformations were identified at visceral examination.

E.3.b. Variations

E.3.b.1. Vessels

Three control group fetuses (12801-10; 12810-10; 12821-6), one 1 mg/kg/day dosage group fetus (12834-14) and two 5 mg/kg/day dosage group littermates

(12860-5, -9) had the umbilical artery descending to the left of the bladder. These fetuses had no external findings and no other soft tissue alterations. Two 1 mg/kg/day dosage group fetuses (12826-12; 12837-9) had an absent innominate artery. No additional alterations occurred in these fetuses.

E.3.b.2. Lungs

One control group fetus (12822-4) had an absent apical lung lobe, and one 1 mg/kg/day dosage group fetus (12850-16) had an absent diaphragmatic lung lobe. No additional alterations occurred in these fetuses.

E.3.b.3. Kidneys

Two control group fetuses (12802-11; 12803-2) and one 10 mg/kg/day dosage group fetus (12877-14) had slight or moderate dilation of the pelvis of one or both kidneys, a reversible developmental delay[22]. No additional alterations occurred in these fetuses.

E.4. Fetal Skeletal Alterations (Summaries - Tables 12 and 13; Individual Data - Table 21)

E.4.a. Malformations

Externally malformed 10 mg/kg/day dosage group fetus 12885-15 had only four cervical vertebrae and no thoracic, lumbar, sacral or caudal vertebrae or ribs, as well as a variation in pelvic ossification (not ossified pubes), as previously described.

E.4.b. Variations

E.4.b.1. Skull

A large nasal-frontal suture occurred in one 10 mg/kg/day dosage group fetus (12893-13). No additional alterations occurred in this fetus.

E.4.b.2. Ribs

A cervical rib at the 7th cervical vertebra, a common variation in this strain of rat [23], occurred in 0, 3, 1, 3 and 4 fetuses from 0, 2, 1, 3 and 4 litters in the 0 (Vehicle), 1, 5, 10 and 20 mg/kg/day dosage groups, respectively. These fetuses had no other external or skeletal alterations.

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Wavy ribs, a reversible delay in ossification[21], occurred in one 1 mg/kg/day dosage group fetus (12848-1) and seven ($p \leq 0.05$) 20 mg/kg/day group fetuses (12904-1; 12909-5, -7, -10, -12; 12919-3, -9). One 20 mg/kg/day dosage group fetus (12909-7) also had incompletely ossified ribs. The significant increase in the fetal incidence of wavy ribs in the 20 mg/kg/day dosage group was considered a treatment-related developmental delay, associated with the significantly reduced ($p \leq 0.05$ or $p \leq 0.01$) fetal body weights in this dosage group.

E.4.b.3. Sternum

Delayed sternal ossification (incompletely ossified or not ossified 1st sternebra) occurred in 7, 2**, 1**, 1** and 1** fetuses from 3, 2, 1, 1 and 1 litters in the 0 (Vehicle), 1, 5, 10 and 20 mg/kg/day dosage groups, respectively. Of these fetuses, one control group fetus (12802-1) had incompletely ossified pubes in addition to an unossified 1st sternal centrum.

E.4.b.4. Pelvis

The ischia and/or pubes were incompletely or not ossified in 3, 0, 2, 2 and 0 fetuses from 1, 0, 1, 2 and 0 litters in the 0 (Vehicle), 1, 5, 10 and 20 mg/kg/day dosage groups, respectively. One fetus in the control group (12802-1) and one 10 mg/kg/day dosage group fetus (12885-15) had additional skeletal alterations, as previously described.

E.4.b.5. Fetal Ossification Site Averages

The litter averages for ossified caudal vertebrae per fetus were significantly reduced ($p \leq 0.05$) in the 10 and 20 mg/kg/day dosage groups. These delays in caudal vertebral ossification were considered effects of the test article associated with the significantly reduced ($p \leq 0.05$ or $p \leq 0.01$) fetal body weights in these dosage groups.

Analyses of the average numbers of fetal ossification sites per fetus did not reveal any other statistically significant differences among the five dosage groups. Ossification of the hyoid, vertebrae (cervical, thoracic, lumbar and sacral), ribs, sternum (manubrium, sternal centers and xiphoid), forelimbs (carpals, metacarpals and phalanges) and hindlimbs (tarsals, metatarsals and phalanges) occurred at similar incidences in litters in all dosage groups. All values were within the ranges observed historically at the Testing Facility.

** Significantly different from the vehicle control group ($p \leq 0.01$).

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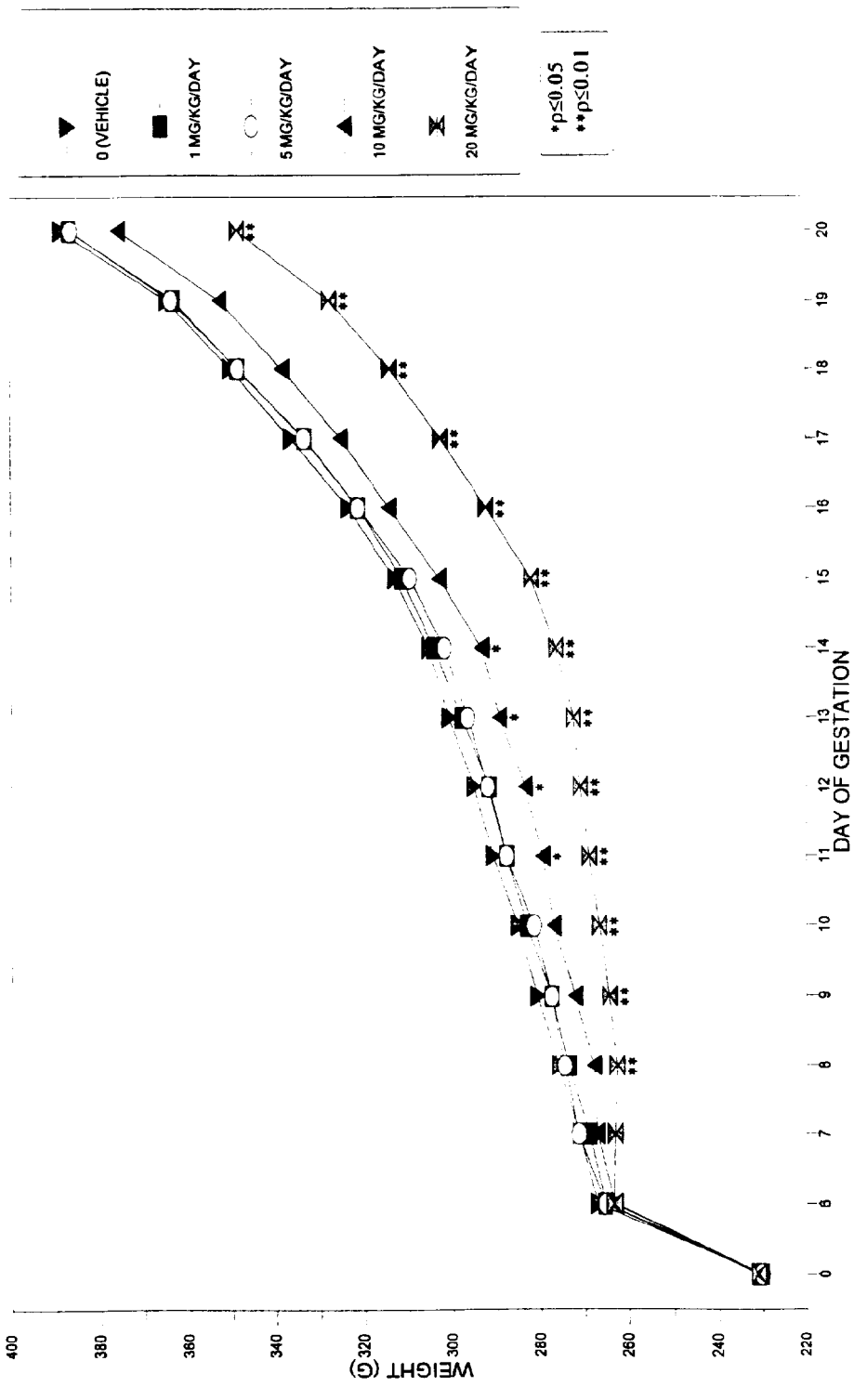
APPENDIX A

REPORT FIGURE

MATERNAL BODY WEIGHTS

Figure 1



APPENDIX B

REPORT TABLES

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PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 1 (PAGE 1): CLINICAL OBSERVATIONS - SUMMARY

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)a		0 (VEHICLE)	1	5	10	20
MAXIMUM POSSIBLE INCIDENCE		375/ 25	375/ 25	375/ 25	375/ 25	375/ 25
MORTALITY		0	0	0	0	0
LOCALIZED ALOPECIA:	TOTAL	12/ 1	29/ 3	9/ 3	15/ 2	33/ 5
	UNDERSIDE	0/ 0	28/ 3	7/ 2	11/ 1	18/ 3
	LIMBS	12/ 1	2/ 1	0/ 0	7/ 2	15/ 2
	NECK	0/ 0	0/ 0	2/ 1	0/ 0	0/ 0
UNGROOMED COAT		0/ 0	0/ 0	0/ 0	0/ 0	3/ 1
COLD TO TOUCH		0/ 0	0/ 0	0/ 0	0/ 0	3/ 1
RIGHT FOREPAW: SECOND AND THIRD DIGITS FUSED		0/ 0	0/ 0	4/ 1	0/ 0	0/ 0

STATISTICAL ANALYSES OF CLINICAL OBSERVATION DATA WERE RESTRICTED TO THE NUMBER OF RATS WITH OBSERVATIONS.
MAXIMUM POSSIBLE INCIDENCE = (DAYS x RATS)/NUMBER OF RATS EXAMINED PER GROUP ON DAYS 6 THROUGH 20 OF PRESUMED GESTATION.
N/N = TOTAL NUMBER OF OBSERVATIONS/NUMBER OF RATS WITH OBSERVATION.
a. Dosage occurred on days 6 through 17 of presumed gestation.

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 2 (PAGE 1): NECROPSY OBSERVATIONS - SUMMARY

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)a		0 (VEHICLE)	1	5	10	20
RATS EXAMINED	N	25	25	25	25	25
MORTALITY	N	0	0	0	0	0
APPEARED NORMAL	N	25	25	25	25	24
LIVER:						
MEDIAN LOBE, TAN AREA	N	0	0	0	0	1

a. Dosage occurred on days 6 through 17 of presumed gestation.

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ELFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 3 (PAGE 1): MATERNAL BODY WEIGHTS - SUMMARY

DOSAGE GROUP DOSAGE (MG/KG/DAY)a		I 0 (VEHICLE)	II 1	III 5	IV 10	V 20
RATS TESTED	N	25	25	25	25	25
PREGNANT	N	24	23	24	25	24
INCLUDED IN ANALYSES	N	24	23	23b	24c	24
MATERNAL BODY WEIGHT (G)						
DAY 0	MEAN±S.D.	230.8 ± 9.9	231.0 ± 9.6	230.1 ± 10.5	230.5 ± 10.0	231.0 ± 9.5
DAY 6	MEAN±S.D.	267.1 ± 12.1	265.4 ± 14.0	265.4 ± 15.4	263.2 ± 12.5	263.4 ± 8.1
DAY 7	MEAN±S.D.	271.3 ± 12.7	269.0 ± 14.2	271.5 ± 15.0	267.3 ± 12.2	263.2 ± 9.6
DAY 8	MEAN±S.D.	276.1 ± 12.6	273.8 ± 14.4	274.6 ± 16.1 [22]d	268.1 ± 14.7	262.7 ± 9.3**
DAY 9	MEAN±S.D.	280.8 ± 13.1	277.5 ± 13.8	277.6 ± 17.0	272.2 ± 14.1	264.4 ± 10.8**
DAY 10	MEAN±S.D.	285.2 ± 13.6	283.2 ± 15.4	281.6 ± 18.2	277.1 ± 13.6	266.7 ± 9.8**
DAY 11	MEAN±S.D.	290.8 ± 14.8	287.8 ± 15.8	287.9 ± 17.3	279.6 ± 13.4*	269.0 ± 10.8**
DAY 12	MEAN±S.D.	295.1 ± 15.3	291.6 ± 16.0	291.9 ± 17.7	283.5 ± 14.4*	271.0 ± 12.8**
DAY 13	MEAN±S.D.	300.7 ± 16.2	297.8 ± 17.1	296.5 ± 20.2	289.2 ± 17.1*	272.4 ± 13.1**
DAY 14	MEAN±S.D.	305.4 ± 17.1	304.0 ± 17.7	301.8 ± 21.0	293.3 ± 18.0*	276.4 ± 14.3**
DAY 15	MEAN±S.D.	313.0 ± 17.6	311.4 ± 17.8	309.5 ± 22.1	302.9 ± 16.5	282.1 ± 17.1**

DAY = DAY OF GESTATION
[ ] = NUMBER OF VALUES AVERAGED
a. Dosage occurred on days 6 through 17 of gestation.
b. Excludes values for dam 12868, which had a litter consisting of 7 conceptuses.
c. Excludes values for dam 12889, which had a litter consisting of 3 conceptuses.
d. Excludes a value that was not recorded.
* Significantly different from the vehicle control group value ($p \leq 0.05$).
** Significantly different from the vehicle control group value ($p \leq 0.01$).

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 3 (PAGE 2): MATERNAL BODY WEIGHTS - SUMMARY

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)a		0 (VEHICLE)	1	5	10	20
RATS TESTED	N	25	25	25	25	25
PREGNANT	N	24	23	24	25	24
INCLUDED IN ANALYSES	N	24	23	23b	24c	24
MATERNAL BODY WEIGHT (G)						
DAY 16	MEAN±S.D.	323.5 ± 19.3	321.3 ± 18.5	321.3 ± 22.7	314.4 ± 18.4	292.4 ± 18.5**
DAY 17	MEAN±S.D.	336.5 ± 19.6	333.3 ± 17.8	333.6 ± 23.4	325.2 ± 19.1	302.7 ± 17.7**
DAY 18	MEAN±S.D.	350.3 ± 19.9	348.6 ± 19.3	348.5 ± 24.7	338.4 ± 20.9	314.2 ± 15.9**
DAY 19	MEAN±S.D.	364.8 ± 19.5	363.3 ± 20.6	363.9 ± 27.5	352.8 ± 20.3	327.8 ± 17.3**
DAY 20	MEAN±S.D.	388.7 ± 21.6	386.7 ± 23.2	386.6 ± 29.4	375.7 ± 23.0	348.7 ± 19.6**

DAY = DAY OF GESTATION
a. Dosage occurred on days 6 through 17 of gestation.
b. Excludes values for dam 12868, which had a litter consisting of 7 conceptuses.
c. Excludes values for dam 12889, which had a litter consisting of 3 conceptuses.
** Significantly different from the vehicle control group value ($p \leq 0.01$).

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 4 (PAGE 1): MATERNAL BODY WEIGHT CHANGES - SUMMARY

DOSAGE GROUP DOSAGE (MG/KG/DAY)a		I 0 (VEHICLE)	II 1	III 5	IV 10	V 20
RATS TESTED	N	25	25	25	25	25
PREGNANT	N	24	23	24	25	24
INCLUDED IN ANALYSES	N	24	23	23b	24c	24
MATERNAL BODY WEIGHT CHANGE (G)						
DAYS 0 - 6	MEAN±S.D.	+36.3 ± 8.7	+34.4 ± 12.0	+35.3 ± 10.9	+32.6 ± 8.2	+32.5 ± 8.0
DAYS 6 - 8	MEAN±S.D.	+9.0 ± 4.3	+8.4 ± 3.0	+9.9 ± 6.8 [22]d	+4.9 ± 5.4*	-0.8 ± 8.0**
DAYS 8 - 10	MEAN±S.D.	+9.1 ± 4.0	+9.4 ± 3.4	+6.0 ± 4.6* [22]d	+9.0 ± 5.3	+4.0 ± 4.4**
DAYS 10 - 12	MEAN±S.D.	+9.9 ± 4.2	+8.4 ± 5.0	+10.3 ± 5.6	+6.4 ± 4.5*	+4.3 ± 9.0*
DAYS 12 - 14	MEAN±S.D.	+10.3 ± 4.4	+12.3 ± 4.8	+9.9 ± 5.3	+9.8 ± 5.6	+5.3 ± 8.6*
DAYS 14 - 16	MEAN±S.D.	+18.1 ± 6.6	+17.3 ± 4.7	+19.5 ± 4.5	+21.1 ± 3.9*	+16.1 ± 6.9
DAYS 16 - 18	MEAN±S.D.	+26.8 ± 3.8	+27.3 ± 5.7	+27.3 ± 5.2	+24.0 ± 6.2	+21.7 ± 7.5**
DAYS 6 - 18	MEAN±S.D.	+83.2 ± 11.4	+83.3 ± 11.2	+83.1 ± 11.9	+75.2 ± 12.0	+50.7 ± 15.8**
DAYS 18 - 20	MEAN±S.D.	+38.3 ± 6.3	+38.1 ± 7.3	+38.0 ± 7.9	+37.2 ± 6.0	+34.5 ± 6.7
DAYS 6 - 20	MEAN±S.D.	+121.5 ± 13.2	+121.3 ± 15.9	+121.1 ± 16.0	+112.5 ± 15.1	+85.2 ± 19.2**
DAYS 0 - 20	MEAN±S.D.	+157.9 ± 17.9	+155.7 ± 20.3	+156.5 ± 24.3	+145.1 ± 18.9	+117.7 ± 22.6**

DAYS = DAYS OF GESTATION
[ ] = NUMBER OF VALUES AVERAGED
a. Dosage occurred on days 6 through 17 of gestation.
b. Excludes values for dam 12868, which had a litter consisting of 7 conceptuses.
c. Excludes values for dam 12889, which had a litter consisting of 3 conceptuses.
d. Excludes values that were not recorded.
* Significantly different from the vehicle control group value ($p \leq 0.05$).
** Significantly different from the vehicle control group value ($p \leq 0.01$).

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 5 (PAGE 1): MATERNAL ABSOLUTE FEED CONSUMPTION VALUES (G/DAY) - SUMMARY

DOSAGE GROUP DOSAGE (MG/KG/DAY)a		I 0 (VEHICLE)	II 1	III 5	IV 10	V 20
RATS TESTED	N	25	25	25	25	25
PREGNANT	N	24	23	24	25	24
INCLUDED IN ANALYSES	N	24	23	23b	24c	24
MATERNAL FEED CONSUMPTION (G/DAY)						
DAYS 0 - 6	MEAN±S.D.	21.5 ± 3.0 [23]d	21.1 ± 3.3	21.6 ± 3.0	21.1 ± 3.3	21.2 ± 2.1
DAYS 6 - 8	MEAN±S.D.	24.6 ± 3.1	23.0 ± 2.0	24.1 ± 3.6	22.4 ± 2.8*	19.4 ± 3.0**
DAYS 8 - 10	MEAN±S.D.	23.9 ± 2.3	22.9 ± 1.9	22.6 ± 3.0	22.6 ± 2.4	19.2 ± 3.2**
DAYS 10 - 12	MEAN±S.D.	24.6 ± 3.2	23.5 ± 2.4	24.0 ± 2.5	23.6 ± 2.3 [23]d	19.8 ± 4.4**
DAYS 12 - 14	MEAN±S.D.	25.7 ± 2.8	24.5 ± 2.8	24.7 ± 3.4	23.9 ± 3.0	20.5 ± 4.2**
DAYS 14 - 16	MEAN±S.D.	26.0 ± 3.4	25.2 ± 3.0	25.7 ± 3.6	26.1 ± 2.8	21.3 ± 4.3**
DAYS 16 - 18	MEAN±S.D.	27.6 ± 2.3	26.6 ± 2.8	27.2 ± 3.3	26.2 ± 2.7	22.5 ± 2.5**
DAYS 6 - 18	MEAN±S.D.	25.4 ± 2.3	24.3 ± 1.9	24.7 ± 2.7	24.2 ± 1.9	20.4 ± 2.6**
DAYS 18 - 20	MEAN±S.D.	26.4 ± 2.4	25.2 ± 2.8	25.9 ± 3.1	24.9 ± 2.7	22.5 ± 2.4**
DAYS 6 - 20	MEAN±S.D.	25.5 ± 2.2	24.4 ± 1.9	24.9 ± 2.7	24.2 ± 1.9	20.7 ± 2.4**
DAYS 0 - 20	MEAN±S.D.	24.6 ± 2.4	23.4 ± 2.1	23.9 ± 2.7	23.3 ± 2.1	20.9 ± 2.0**

DAYS = DAYS OF GESTATION
[ ] = NUMBER OF VALUES AVERAGED
a. Dosage occurred on days 6 through 17 of gestation.
b. Excludes values for dam 12868, which had a litter consisting of 7 conceptuses.
c. Excludes values for dam 12889, which had a litter consisting of 3 conceptuses.
d. Excludes values that were incorrectly recorded, as well as those associated with spillage.
* Significantly different from the vehicle control group value ($p \leq 0.05$).
** Significantly different from the vehicle control group value ($p \leq 0.01$).

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 6 (PAGE 1): MATERNAL RELATIVE FEED CONSUMPTION VALUES (G/KG/DAY) - SUMMARY

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)a		0 (VEHICLE)	1	5	10	20
RATS TESTED	N	25	25	25	25	25
PREGNANT	N	24	23	24	25	24
INCLUDED IN ANALYSES	N	24	23	23b	24c	24
MATERNAL FEED CONSUMPTION (G/KG/DAY)						
DAYS 0 - 6	MEAN±S.D.	85.5 ± 10.1 [23]d	84.4 ± 11.4	86.4 ± 9.8	85.1 ± 12.1	85.3 ± 7.6
DAYS 6 - 8	MEAN±S.D.	90.3 ± 8.4	85.3 ± 5.5*	89.0 ± 10.2	83.9 ± 8.5	73.7 ± 10.7**
DAYS 8 - 10	MEAN±S.D.	85.1 ± 6.4	82.3 ± 5.0	81.3 ± 8.5	82.9 ± 7.3	72.4 ± 10.2**
DAYS 10 - 12	MEAN±S.D.	84.4 ± 8.7	81.8 ± 6.5	83.5 ± 6.9	84.3 ± 6.2 [23]d	73.2 ± 15.0**
DAYS 12 - 14	MEAN±S.D.	85.4 ± 6.3	82.3 ± 6.9	83.1 ± 8.6	82.5 ± 8.0	74.6 ± 14.0**
DAYS 14 - 16	MEAN±S.D.	82.7 ± 8.6	80.6 ± 7.2	82.7 ± 8.9	86.0 ± 8.6	74.6 ± 12.9**
DAYS 16 - 18	MEAN±S.D.	82.0 ± 6.0	79.6 ± 8.2	81.5 ± 8.3	80.5 ± 7.7	74.3 ± 6.5**
DAYS 6 - 18	MEAN±S.D.	84.6 ± 4.5	81.7 ± 4.2	83.0 ± 5.8	83.1 ± 4.1	73.6 ± 7.5**
DAYS 18 - 20	MEAN±S.D.	71.6 ± 5.6	68.8 ± 6.2	70.6 ± 6.3	70.0 ± 6.1	68.2 ± 5.3
DAYS 6 - 20	MEAN±S.D.	82.2 ± 4.2	79.3 ± 4.2	80.8 ± 5.6	80.7 ± 4.2	72.6 ± 6.5**
DAYS 0 - 20	MEAN±S.D.	80.2 ± 4.3	77.8 ± 4.4	79.4 ± 5.8	79.0 ± 4.9	74.3 ± 4.8**

DAYS = DAYS OF GESTATION
[ ] = NUMBER OF VALUES AVERAGED
a. Dosage occurred on days 6 through 17 of gestation.
b. Excludes values for dam 12868, which had a litter consisting of 7 conceptuses.
c. Excludes values for dam 12889, which had a litter consisting of 3 conceptuses.
d. Excludes values were incorrectly recorded, as well as those associated with spillage.
* Significantly different from the vehicle control group value ($p \leq 0.05$).
** Significantly different from the vehicle control group value ($p \leq 0.01$).

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TABLE 7 (PAGE 1): CAESAREAN-SECTIONING OBSERVATIONS - SUMMARY

DOSAGE GROUP DOSAGE (MG/KG/DAY)a		I 0 (VEHICLE)	II 1	III 5	IV 10	V 20
RATS TESTED	N	25	25	25	25	25
PREGNANT	N(%)	24(96.0)	23(92.0)	24(96.0)	25(100.0)	24(96.0)
RATS PREGNANT AND CAESAREAN-SECTIONED ON DAY 20 OF GESTATION	N	24	23	24	25	24
INCLUDED IN ANALYSES	N	24	23	23b	24c	24
CORPORA LUTEA	MEAN±S.D.	17.1 ± 1.8	17.2 ± 1.9	17.2 ± 2.1	16.8 ± 2.0	16.5 ± 1.8
IMPLANTATIONS	MEAN±S.D.	15.1 ± 1.8	15.6 ± 2.0	15.6 ± 1.4	15.1 ± 1.3	14.5 ± 1.7
LITTER SIZES	MEAN±S.D.	14.2 ± 1.8	15.2 ± 2.1	14.9 ± 1.9	14.6 ± 1.6	13.6 ± 1.9
LIVE FETUSES	N	342	349	342	351	327
	MEAN±S.D.	14.2 ± 1.8	15.2 ± 2.1	14.9 ± 1.9	14.6 ± 1.6	13.6 ± 1.9
DEAD FETUSES	N	0	0	0	0	0
RESORPTIONS	MEAN±S.D.	0.9 ± 1.2	0.4 ± 0.6	0.8 ± 1.2	0.5 ± 0.8	0.9 ± 1.0
EARLY RESORPTIONS	N	21	10	18	12	21
	MEAN±S.D.	0.9 ± 1.2	0.4 ± 0.6	0.8 ± 1.2	0.5 ± 0.8	0.9 ± 1.0
LATE RESORPTIONS	N	0	0	0	0	0
DAMS WITH ANY RESORPTIONS	N(%)	12(50.0)	9(39.1)	11(47.8)	9(37.5)	14(58.3)
DAMS WITH ALL CONCEPTUSES RESORBED	N(%)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
DAMS WITH VIABLE FETUSES	N(%)	24(100.0)	23(100.0)	23(100.0)	24(100.0)	24(100.0)
PLACENTAE APPEARED NORMAL	N(%)	24(100.0)	23(100.0)	23(100.0)	24(100.0)	24(100.0)

a. Dosage occurred on days 6 through 17 of gestation.
b. Excludes values for dam 12868, which had a litter consisting of 7 conceptuses.
c. Excludes values for dam 12889, which had a litter consisting of 3 conceptuses.

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TABLE 8 (PAGE 1): LITTER OBSERVATIONS (CAESAREAN-DELIVERED FETUSES) - SUMMARY

DOSAGE GROUP DOSAGE (MG/KG/DAY)a		I 0 (VEHICLE)	II 1	III 5	IV 10	V 20
LITTERS WITH ONE OR MORE LIVE FETUSES	N	24	23	24	25	24
INCLUDED IN ANALYSES	N	24	23	23b	24c	24
IMPLANTATIONS	MEAN±S.D.	15.1 ± 1.8	15.6 ± 2.0	15.6 ± 1.4	15.1 ± 1.3	14.5 ± 1.7
LIVE FETUSES	N	342	349	342	351	327
	MEAN±S.D.	14.2 ± 1.8	15.2 ± 2.1	14.9 ± 1.9	14.6 ± 1.6	13.6 ± 1.9
LIVE MALE FETUSES	N	166	171	165	180	172
% LIVE MALE FETUSES/LITTER	MEAN±S.D.	48.8 ± 13.1	48.8 ± 12.2	48.6 ± 11.8	51.7 ± 10.6	52.4 ± 13.0
LIVE FETAL BODY WEIGHTS (GRAMS)/LITTER	MEAN±S.D.	3.50 ± 0.50	3.36 ± 0.22	3.39 ± 0.20	3.32 ± 0.20*	3.16 ± 0.17**
MALE FETUSES	MEAN±S.D.	3.61 ± 0.50	3.48 ± 0.23	3.50 ± 0.22	3.38 ± 0.20**	3.26 ± 0.19**
FEMALE FETUSES	MEAN±S.D.	3.38 ± 0.52	3.25 ± 0.24	3.30 ± 0.19	3.25 ± 0.23	3.05 ± 0.16**
% RESORBED CONCEPTUSES/LITTER	MEAN±S.D.	5.5 ± 7.2	2.8 ± 3.7	5.1 ± 7.7	3.4 ± 5.0	6.0 ± 6.8

a. Dosage occurred on days 6 through 17 of gestation.
b. Excludes values for dam 12868, which had a litter consisting of 7 conceptuses.
c. Excludes values for dam 12889, which had a litter consisting of 3 concpetuses.
* Significantly different from the vehicle control group value ($p \leq 0.05$).
** Significantly different from the vehicle control group value ($p \leq 0.01$).

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TABLE 9 (PAGE 1): FETAL ALTERATIONS - SUMMARY

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)a		0 (VEHICLE)	1	5	10	20
LITTERS EVALUATED	N	24	23	24	25	24
FETUSES EVALUATED	N	342	349	347	354	326
LIVE	N	342	349	347	354	326
LITTERS WITH FETUSES WITH ANY ALTERATION OBSERVED	N(%)	6(25.0)	8(34.8)	4(16.7)	7(28.0)	8(33.3)
FETUSES WITH ANY ALTERATION OBSERVED	N(%)	15(4.4)	10(2.9)	6(1.7)	8(2.2)	12(3.7)
% FETUSES WITH ANY ALTERATION/LITTER	MEAN±S.D.	4.4 ± 10.3	2.8 ± 4.4	1.6 ± 3.9	2.1 ± 3.9	4.0 ± 7.6

a. Dosage occurred on days 6 through 17 of gestation.

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TABLE 10 (PAGE 1): FETAL GROSS EXTERNAL ALTERATIONS - SUMMARY

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)a		0 (VEHICLE)	1	5	10	20
LITTERS EVALUATED	N	24	23	24	25	24
FETUSES EVALUATED	N	342	349	347	354	326
LIVE	N	342	349	347	354	326
BODY: TRUNK SHORT						
LITTER INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(4.0)	0(0.0)
FETAL INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(0.3)	0(0.0)
TAIL: ABSENT						
LITTER INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(4.0)	0(0.0)
FETAL INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(0.3)	0(0.0)

a. Dosage occurred on days 6 through 17 of gestation.

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TABLE 11 (PAGE 1): FETAL SOFT TISSUE ALTERATIONS - SUMMARY

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY) a		0 (VEHICLE)	1	5	10	20
LITTERS EVALUATED	N	24	23	24	25	24
FETUSES EVALUATED	N	166	167	169	170	158
LIVE	N	166	167	169	170	158
VESSELS: UMBILICAL ARTERY DESCENDS TO THE LEFT OF URINARY BLADDER						
LITTER INCIDENCE	N(%)	3(12.5)	1(4.3)	1(4.2)	0(0.0)	0(0.0)
FETAL INCIDENCE	N(%)	3(1.8)	1(0.6)	2(1.2)	0(0.0)	0(0.0)
VESSELS: INNOMINATE, ABSENT						
LITTER INCIDENCE	N(%)	0(0.0)	2(8.7)	0(0.0)	0(0.0)	0(0.0)
FETAL INCIDENCE	N(%)	0(0.0)	2(1.2)	0(0.0)	0(0.0)	0(0.0)
LUNGS: DIAPHRAGMATIC LOBE, ABSENT						
LITTER INCIDENCE	N(%)	0(0.0)	1(4.3)	0(0.0)	0(0.0)	0(0.0)
FETAL INCIDENCE	N(%)	0(0.0)	1(0.6)	0(0.0)	0(0.0)	0(0.0)
LUNGS: APICAL LOBE, ABSENT						
LITTER INCIDENCE	N(%)	1(4.2)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
FETAL INCIDENCE	N(%)	1(0.6)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
KIDNEYS: PELVIS, SLIGHT DILATION						
LITTER INCIDENCE	N(%)	2(8.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
FETAL INCIDENCE	N(%)	2(1.2)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
KIDNEYS: PELVIS, MODERATE DILATION						
LITTER INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(4.0)	0(0.0)
FETAL INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(0.6)	0(0.0)

a. Dosage occurred on days 6 through 17 of gestation.

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TABLE 12 (PAGE 1): FETAL SKELETAL ALTERATIONS - SUMMARY
(See footnotes on the last page of this table.)

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)a		0 (VEHICLE)	1	5	10	20
LITTERS EVALUATED	N	24	23	24	25	24
FETUSES EVALUATED	N	176	182	178	184	168
LIVE	N	176	182	178	184	168
SKULL: NASAL - FRONTAL, SUTURE LARGE						
LITTER INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(4.0)	0(0.0)
FETAL INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(0.5)	0(0.0)
CERVICAL VERTEBRAE: CERVICAL RIB PRESENT AT 7TH CERVICAL VERTEBRA						
LITTER INCIDENCE	N(%)	0(0.0)	2(8.7)	1(4.2)	3(12.0)	4(16.7)
FETAL INCIDENCE	N(%)	0(0.0)	3(1.6)	1(0.6)	3(1.6)	4(2.4)
CERVICAL VERTEBRAE: 4 PRESENT						
LITTER INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(4.0)	0(0.0)
FETAL INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(0.5)b	0(0.0)
THORACIC VERTEBRAE: 0 PRESENT						
LITTER INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(4.0)	0(0.0)
FETAL INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(0.5)b	0(0.0)
THORACIC VERTEBRAE: ARCH, NOT OSSIFIED						
LITTER INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(4.0)	0(0.0)
FETAL INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(0.5)b	0(0.0)
THORACIC VERTEBRAE: CENTRUM, NOT OSSIFIED						
LITTER INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(4.0)	0(0.0)
FETAL INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(0.5)b	0(0.0)
LUMBAR VERTEBRAE: 0 PRESENT						
LITTER INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(4.0)	0(0.0)
FETAL INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(0.5)b	0(0.0)
LUMBAR VERTEBRAE: ARCH, NOT OSSIFIED						
LITTER INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(4.0)	0(0.0)
FETAL INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(0.5)b	0(0.0)
LUMBAR VERTEBRAE: CENTRUM, NOT OSSIFIED						
LITTER INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(4.0)	0(0.0)
FETAL INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(0.5)b	0(0.0)

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TABLE 12 (PAGE 2): FETAL SKELETAL ALTERATIONS - SUMMARY
(See footnotes on the last page of this table.)

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)a		0 (VEHICLE)	1	5	10	20
LITTERS EVALUATED	N	24	23	24	25	24
FETUSES EVALUATED	N	176	182	178	184	168
LIVE	N	176	182	178	184	168
SACRAL VERTEBRAE: 0 PRESENT						
LITTER INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(4.0)	0(0.0)
FETAL INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(0.5)b	0(0.0)
SACRAL VERTEBRAE: ARCH, NOT OSSIFIED						
LITTER INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(4.0)	0(0.0)
FETAL INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(0.5)b	0(0.0)
SACRAL VERTEBRAE: CENTRUM, NOT OSSIFIED						
LITTER INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(4.0)	0(0.0)
FETAL INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(0.5)b	0(0.0)
CAUDAL VERTEBRAE: 0 PRESENT						
LITTER INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(4.0)	0(0.0)
FETAL INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(0.5)b	0(0.0)
RIBS: WAVY						
LITTER INCIDENCE	N(%)	0(0.0)	1(4.3)	0(0.0)	0(0.0)	3(12.5)
FETAL INCIDENCE	N(%)	0(0.0)	1(0.5)	0(0.0)	0(0.0)	7(4.2)**c
RIBS: 0 PRESENT						
LITTER INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(4.0)	0(0.0)
FETAL INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(0.5)b	0(0.0)
RIBS: NOT OSSIFIED						
LITTER INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(4.0)	0(0.0)
FETAL INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(0.5)b	0(0.0)
RIBS: INCOMPLETELY OSSIFIED (HYPOPLASTIC)						
LITTER INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(4.2)
FETAL INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(0.6)c

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TABLE 12 (PAGE 3): FETAL SKELETAL ALTERATIONS - SUMMARY

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)a		0 (VEHICLE)	1	5	10	20
LITTERS EVALUATED	N	24	23	24	25	24
FETUSES EVALUATED	N	176	182	178	184	168
LIVE	N	176	182	178	184	168
STERNAL CENTRA: SUMMARIZATION (Includes incompletely ossified and not ossified sternal centra)						
LITTER INCIDENCE	N(%)	3(12.5)	2(8.7)	1(4.2)	1(4.0)	1(4.2)
FETAL INCIDENCE	N(%)	7(4.0)	2(1.1)**	1(0.6)**	1(0.5)**	1(0.6)**
STERNAL CENTRA: 1ST, INCOMPLETELY OSSIFIED						
LITTER INCIDENCE	N(%)	2(8.3)	1(4.3)	1(4.2)	1(4.0)	0(0.0)
FETAL INCIDENCE	N(%)	4(2.3)	1(0.5)	1(0.6)	1(0.5)	0(0.0)
STERNAL CENTRA: 1ST, NOT OSSIFIED						
LITTER INCIDENCE	N(%)	1(4.2)	1(4.3)	0(0.0)	0(0.0)	1(4.2)
FETAL INCIDENCE	N(%)	3(1.7)d	1(0.5)	0(0.0)	0(0.0)	1(0.6)
PELVIS: SUMMARIZATION (Includes incompletely ossified pubes and ischia, and not ossified pubes)						
LITTER INCIDENCE	N(%)	1(4.2)	0(0.0)	1(4.2)	2(8.0)	0(0.0)
FETAL INCIDENCE	N(%)	3(1.7)	0(0.0)	2(1.1)	2(1.1)	0(0.0)
PELVIS: PUBIS, INCOMPLETELY OSSIFIED						
LITTER INCIDENCE	N(%)	1(4.2)	0(0.0)	0(0.0)	1(4.0)	0(0.0)
FETAL INCIDENCE	N(%)	3(1.7)d	0(0.0)	0(0.0)	1(0.5)	0(0.0)
PELVIS: PUBIS, NOT OSSIFIED						
LITTER INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(4.0)	0(0.0)
FETAL INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	1(0.5)b	0(0.0)
PELVIS: ISCHIUM, INCOMPLETELY OSSIFIED						
LITTER INCIDENCE	N(%)	0(0.0)	0(0.0)	1(4.2)	0(0.0)	0(0.0)
FETAL INCIDENCE	N(%)	0(0.0)	0(0.0)	2(1.1)	0(0.0)	0(0.0)

a. Dosage occurred on days 6 through 17 of gestation.
b. Fetus 12885-15 had other skeletal alterations.
c. Fetus 12909-7 had other skeletal alterations.
d. Fetus 12802-1 had other skeletal alterations.
** Significantly different from the control group value ($p \leq 0.01$).

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TABLE 13 (PAGE 1): FETAL OSSIFICATION SITES - CAESAREAN-DELIVERED LIVE FETUSES (DAY 20 OF GESTATION) - SUMMARY

DOSAGE GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)a		0 (VEHICLE)	1	5	10	20
LITTERS EXAMINED	N	24	23	23	24	24
FETUSES EXAMINED	N	176	182	178	184	168
LIVE	N	176	182	178	184	168
OSSIFICATION SITES PER FETUS PER LITTER						
HYOID	MEAN±S.D.	0.97 ± 0.08	0.98 ± 0.06	0.98 ± 0.06	0.97 ± 0.06	1.00 ± 0.02
VERTEBRAE						
CERVICAL	MEAN±S.D.	7.00 ± 0.00	7.00 ± 0.00	7.00 ± 0.00	7.00 ± 0.00	7.00 ± 0.00
THORACIC	MEAN±S.D.	13.08 ± 0.14	13.05 ± 0.09	13.07 ± 0.17	13.10 ± 0.19	13.13 ± 0.16
LUMBAR	MEAN±S.D.	5.91 ± 0.14	5.95 ± 0.09	5.92 ± 0.17	5.89 ± 0.20	5.84 ± 0.16
SACRAL	MEAN±S.D.	3.00 ± 0.00	3.00 ± 0.00	3.00 ± 0.00	3.00 ± 0.00	3.00 ± 0.00
CAUDAL	MEAN±S.D.	4.96 ± 1.08	4.89 ± 0.41	4.74 ± 0.37	4.70 ± 0.23*	4.59 ± 0.43*
RIBS (PAIRS)	MEAN±S.D.	13.06 ± 0.10	13.03 ± 0.06	13.04 ± 0.10	13.09 ± 0.17	13.12 ± 0.14
STERNUM						
MANUBRIUM	MEAN±S.D.	0.99 ± 0.04	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.02	1.00 ± 0.00
STERNAL CENTERS	MEAN±S.D.	3.70 ± 0.55	3.56 ± 0.33	3.80 ± 0.24	3.68 ± 0.25	3.74 ± 0.32
XIPHOID	MEAN±S.D.	0.98 ± 0.08	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.02	1.00 ± 0.00
FORELIMB b						
CARPALS	MEAN±S.D.	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
METACARPALS	MEAN±S.D.	3.72 ± 0.27	3.73 ± 0.29	3.68 ± 0.31	3.72 ± 0.27	3.69 ± 0.28
DIGITS	MEAN±S.D.	5.00 ± 0.00	5.00 ± 0.00	5.00 ± 0.00	5.00 ± 0.00	5.00 ± 0.00
PHALANGES	MEAN±S.D.	5.20 ± 0.73	5.12 ± 0.30	5.04 ± 0.18	5.09 ± 0.28	5.01 ± 0.03
HINDLIMB b						
TARSALS	MEAN±S.D.	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
METATARSALS	MEAN±S.D.	3.99 ± 0.28	4.00 ± 0.00	4.00 ± 0.00	4.00 ± 0.02	3.99 ± 0.04
DIGITS	MEAN±S.D.	5.00 ± 0.00	5.00 ± 0.00	5.00 ± 0.00	5.00 ± 0.00	5.00 ± 0.00
PHALANGES	MEAN±S.D.	4.82 ± 0.90	5.00 ± 0.00	5.00 ± 0.00	4.98 ± 0.12	4.96 ± 0.20

a. Dosage occurred on days 6 through 17 of gestation.
b. Calculated as average per limb.
* Significantly different from the vehicle control group value ($p \leq 0.05$).

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 14 (PAGE 1): CLINICAL OBSERVATIONS - INDIVIDUAL DATA

RAT #		DESCRIPTION
DOSAGE GROUP I		0 (VEHICLE) MG/KG/DAY
12801		NO ADVERSE FINDINGS
12802		NO ADVERSE FINDINGS
12803		NO ADVERSE FINDINGS
12804		NO ADVERSE FINDINGS
12805		NO ADVERSE FINDINGS
12806		NO ADVERSE FINDINGS
12807		NO ADVERSE FINDINGS
12808		NO ADVERSE FINDINGS
12809		NO ADVERSE FINDINGS
12810		NO ADVERSE FINDINGS
12811		NO ADVERSE FINDINGS
12812		NO ADVERSE FINDINGS
12813		NO ADVERSE FINDINGS
12814		NO ADVERSE FINDINGS
12815		NO ADVERSE FINDINGS
12816		NO ADVERSE FINDINGS
12817		NO ADVERSE FINDINGS
12818		NO ADVERSE FINDINGS
12819		NO ADVERSE FINDINGS
12820		NO ADVERSE FINDINGS
12821		NO ADVERSE FINDINGS
12822	DG(8- 19)	LOCALIZED ALOPECIA: LIMBS
	DG(20)	ALOPECIA NO LONGER APPARENT
12823		NO ADVERSE FINDINGS
12824		NO ADVERSE FINDINGS
12825		NO ADVERSE FINDINGS

DG = DAY OF PRESUMED GESTATION

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ELFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 14 (PAGE 2): CLINICAL OBSERVATIONS - INDIVIDUAL DATA

RAT #		DESCRIPTION
DOSAGE GROUP II		1 MG/KG/DAY
12826		NO ADVERSE FINDINGS
12827		NO ADVERSE FINDINGS
12828		NO ADVERSE FINDINGS
12829		NO ADVERSE FINDINGS
12830		NO ADVERSE FINDINGS
12831	DG(9- 19)	LOCALIZED ALOPECIA: UNDERSIDE
	DG(19 20)	LOCALIZED ALOPECIA: LIMBS a
12832		NO ADVERSE FINDINGS
12833		NO ADVERSE FINDINGS
12834	DG(14- 19)	LOCALIZED ALOPECIA: UNDERSIDE
	DG(20)	ALOPECIA NO LONGER APPARENT
12835		NO ADVERSE FINDINGS
12836		NO ADVERSE FINDINGS
12837		NO ADVERSE FINDINGS
12838		NO ADVERSE FINDINGS
12839		NO ADVERSE FINDINGS
12840		NO ADVERSE FINDINGS
12841		NO ADVERSE FINDINGS
12842		NO ADVERSE FINDINGS
12843		NO ADVERSE FINDINGS
12844		NO ADVERSE FINDINGS
12845		NO ADVERSE FINDINGS
12846		NO ADVERSE FINDINGS
12847		NO ADVERSE FINDINGS
12848		NO ADVERSE FINDINGS
12849	DG(10- 20)	LOCALIZED ALOPECIA: UNDERSIDE a
12850		NO ADVERSE FINDINGS

DG = DAY OF PRESUMED GESTATION
a. Observation confirmed at necropsy.

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 14 (PAGE 3): CLINICAL OBSERVATIONS - INDIVIDUAL DATA

RAT #		DESCRIPTION
DOSAGE GROUP III		5 MG/KG/DAY
12851		NO ADVERSE FINDINGS
12852		NO ADVERSE FINDINGS
12853		NO ADVERSE FINDINGS
12854		NO ADVERSE FINDINGS
12855		NO ADVERSE FINDINGS
12856		NO ADVERSE FINDINGS
12857		NO ADVERSE FINDINGS
12858	DG(18- 20)	LOCALIZED ALOPECIA: UNDERSIDE a
12859		NO ADVERSE FINDINGS
12860		NO ADVERSE FINDINGS
12861		NO ADVERSE FINDINGS
12862		NO ADVERSE FINDINGS
12863	DG(17- 20)	LOCALIZED ALOPECIA: UNDERSIDE a
12864		NO ADVERSE FINDINGS
12865		NO ADVERSE FINDINGS
12866	DG(19- 20)	LOCALIZED ALOPECIA: NECK a
12867		NO ADVERSE FINDINGS
12868	DG(17- 20)	RIGHT FOREPAW: SECOND AND THIRD DIGITS FUSED a
12869		NO ADVERSE FINDINGS
12870		NO ADVERSE FINDINGS
12871		NO ADVERSE FINDINGS
12872		NO ADVERSE FINDINGS
12873		NO ADVERSE FINDINGS
12874		NO ADVERSE FINDINGS
12875		NO ADVERSE FINDINGS

DG = DAY OF PRESUMED GESTATION
a. Observation confirmed at necropsy.

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 14 (PAGE 4): CLINICAL OBSERVATIONS - INDIVIDUAL DATA

RAT #		DESCRIPTION	
DOSAGE GROUP IV		10 MG/KG/DAY	
12876		NO ADVERSE FINDINGS	
12877		NO ADVERSE FINDINGS	
12878		NO ADVERSE FINDINGS	
12879		NO ADVERSE FINDINGS	
12880		NO ADVERSE FINDINGS	
12881		NO ADVERSE FINDINGS	
12882		NO ADVERSE FINDINGS	
12883		NO ADVERSE FINDINGS	
12884		NO ADVERSE FINDINGS	
12885		NO ADVERSE FINDINGS	
12886		NO ADVERSE FINDINGS	
12887		NO ADVERSE FINDINGS	
12888		NO ADVERSE FINDINGS	
12889		NO ADVERSE FINDINGS	
12890		NO ADVERSE FINDINGS	
12891	DG(10- 20)	LOCALIZED ALOPECIA:	UNDERSIDE a
	DG(18- 20)	LOCALIZED ALOPECIA:	LIMBS a
12892		NO ADVERSE FINDINGS	
12893		NO ADVERSE FINDINGS	
12894	DG(17- 20)	LOCALIZED ALOPECIA:	LIMBS a
12895		NO ADVERSE FINDINGS	
12896		NO ADVERSE FINDINGS	
12897		NO ADVERSE FINDINGS	
12898		NO ADVERSE FINDINGS	
12899		NO ADVERSE FINDINGS	
12900		NO ADVERSE FINDINGS	

DG = DAY OF PRESUMED GESTATION
a. Observation confirmed at necropsy.

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 14 (PAGE 5): CLINICAL OBSERVATIONS - INDIVIDUAL DATA

RAT #		DESCRIPTION
DOSAGE GROUP V		20 MG/KG/DAY
12901		NO ADVERSE FINDINGS
12902		NO ADVERSE FINDINGS
12903		NO ADVERSE FINDINGS
12904		NO ADVERSE FINDINGS
12905		NO ADVERSE FINDINGS
12906		NO ADVERSE FINDINGS
12907		NO ADVERSE FINDINGS
12908		LOCALIZED ALOPECIA: LIMBS a
12909	DG(10- 20)	NO ADVERSE FINDINGS
12910		NO ADVERSE FINDINGS
12911		NO ADVERSE FINDINGS
12912		LOCALIZED ALOPECIA: UNDERSIDE a
12913	DG(13- 20)	NO ADVERSE FINDINGS
12914		NO ADVERSE FINDINGS
12915		NO ADVERSE FINDINGS
12916		NO ADVERSE FINDINGS
12917		LOCALIZED ALOPECIA: UNDERSIDE a
12918	DG(16- 20)	LOCALIZED ALOPECIA: UNDERSIDE
12919	DG(16- 20)	NO ADVERSE FINDINGS
12920		NO ADVERSE FINDINGS
12921		NO ADVERSE FINDINGS
12922		NO ADVERSE FINDINGS
12923		LOCALIZED ALOPECIA: LIMBS a
12924	DG(17- 20)	COLD TO TOUCH
12925	DG(15- 17)	UNGROOMED COAT
	DG(15- 17)	

DG = DAY OF PRESUMED GESTATION
a. Observation confirmed at necropsy.

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 14 (PAGE 6): CLINICAL OBSERVATIONS - INDIVIDUAL DATA

RAT #	DESCRIPTION	0 (VEHICLE) MG/KG/DAY
SATELLITE DOSAGE GROUP I		
12573	NO ADVERSE FINDINGS	
12574	NO ADVERSE FINDINGS	
12575	NO ADVERSE FINDINGS	1 MG/KG/DAY
SATELLITE DOSAGE GROUP II		
12576	NO ADVERSE FINDINGS	
12577	NO ADVERSE FINDINGS	
12578	NO ADVERSE FINDINGS	
12579	NO ADVERSE FINDINGS	
12580	NO ADVERSE FINDINGS	5 MG/KG/DAY
SATELLITE DOSAGE GROUP III		
12581	NO ADVERSE FINDINGS	UNDERSIDE a
12582	LOCALIZED ALOPECIA:	
12583	DG(17- 18) NO ADVERSE FINDINGS	10 MG/KG/DAY
SATELLITE DOSAGE GROUP IV		
12584	NO ADVERSE FINDINGS	
12585	NO ADVERSE FINDINGS	
12586	NO ADVERSE FINDINGS	20 MG/KG/DAY
SATELLITE DOSAGE GROUP V		
12587	NO ADVERSE FINDINGS	
12588	NO ADVERSE FINDINGS	
12589	NO ADVERSE FINDINGS	
12590	NO ADVERSE FINDINGS	
12591	NO ADVERSE FINDINGS	

DG = DAY OF PRESUMED GESTATION

a. Observation confirmed at necropsy.

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 15 (PAGE 1): NECROPSY OBSERVATIONS - INDIVIDUAL DATA

DOSAGE GROUP DOSAGE (MG/KG/DAY)	RAT NUMBER	DAY OF NECROPSY	PREGNANCY STATUS	DOSAGES ADMINISTERED	OBSERVATIONS
I 0 (VEHICLE)	12801	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12802	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12803	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12804	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12805	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12806	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12807	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12808	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12809	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12810	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12811	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12812	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12813	DG 20	NP	12	ALL TISSUES APPEARED NORMAL.
	12814	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12815	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12816	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12817	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12818	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12819	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12820	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12820	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12821	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12822	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12823	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12824	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12825	DG 20	P	12	ALL TISSUES APPEARED NORMAL.

P = PREGNANT NP = NOT PREGNANT
DG = DAY OF GESTATION

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T 6316.7)

TABLE 15 (PAGE 2): NECROPSY OBSERVATIONS - INDIVIDUAL DATA

DOSAGE GROUP DOSAGE (MG/KG/DAY)	RAT NUMBER	DAY OF NECROPSY	PREGNANCY STATUS	DOSAGES ADMINISTERED	OBSERVATIONS
II					
1	12826	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12827	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12828	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12829	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12830	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12831	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12832	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12833	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12834	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12835	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12836	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12837	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12838	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12839	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12840	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12841	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12842	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12843	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12844	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12845	DG 20	NP	12	ALL TISSUES APPEARED NORMAL.
	12846	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12847	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12848	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12849	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12850	DG 20	P	12	ALL TISSUES APPEARED NORMAL.

P = PREGNANT NP = NOT PREGNANT
DG = DAY OF GESTATION

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 15 (PAGE 3): NECROPSY OBSERVATIONS - INDIVIDUAL DATA

DOSAGE GROUP DOSAGE (MG/KG/DAY)	RAT NUMBER	DAY OF NECROPSY	PREGNANCY STATUS	DOSAGES ADMINISTERED	OBSERVATIONS
III					
5	12851	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12852	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12853	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12854	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12855	DG 20	NP	12	ALL TISSUES APPEARED NORMAL.
	12856	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12857	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12858	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12859	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12860	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12861	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12862	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12863	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12864	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12865	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12866	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12867	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12868	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12869	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12870	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12871	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12872	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12873	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12874	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12875	DG 20	P	12	ALL TISSUES APPEARED NORMAL.

P = PREGNANT NP = NOT PREGNANT
DG = DAY OF GESTATION

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 15 (PAGE 4): NECROPSY OBSERVATIONS - INDIVIDUAL DATA

DOSAGE GROUP DOSAGE (MG/KG/DAY)	RAT NUMBER	DAY OF NECROPSY	PREGNANCY STATUS	DOSAGES ADMINISTERED	OBSERVATIONS
IV 10	12876	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12877	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12878	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12879	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12880	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12881	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12882	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12883	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12884	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12885	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12886	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12887	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12888	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12889	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12890	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12891	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12892	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12893	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12894	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12895	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12896	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12897	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12898	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12899	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12900	DG 20	P	12	ALL TISSUES APPEARED NORMAL.

P = PREGNANT NP = NOT PREGNANT
DG = DAY OF GESTATION

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 15 (PAGE 5): NECROPSY OBSERVATIONS - INDIVIDUAL DATA

DOSAGE GROUP DOSAGE (MG/KG/DAY)	RAT NUMBER	DAY OF NECROPSY	PREGNANCY STATUS	DOSAGES ADMINISTERED	OBSERVATIONS
V 20	12901	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12902	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12903	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12904	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12905	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12906	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12907	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12908	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12909	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12910	DG 20	NP	12	ALL TISSUES APPEARED NORMAL.
	12911	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12912	DG 20	P	12	LIVER: MEDIAN LOBE, TAN AREA (0.6 CM X 0.8 CM). ALL OTHER TISSUES APPEARED NORMAL.
	12913	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12914	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12915	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12916	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12917	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12918	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12919	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12920	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12921	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12922	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12923	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12924	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	12925	DG 20	P	12	ALL TISSUES APPEARED NORMAL.

P = PREGNANT NP = NOT PREGNANT
DG = DAY OF GESTATION

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 15 (PAGE 6): NECROPSY OBSERVATIONS - INDIVIDUAL DATA

SATELLITE DOSAGE GROUP DOSAGE (MG/KG/DAY)	RAT NUMBER	DAY OF NECROPSY	PREGNANCY STATUS	DOSAGES ADMINISTERED	OBSERVATIONS
I 0 (VEHICLE)	12573	DG 18	P	12	ALL TISSUES APPEARED NORMAL.
	12574	DG 18	P	12	ALL TISSUES APPEARED NORMAL.
	12575	DG 18	P	12	ALL TISSUES APPEARED NORMAL.
II 1	12576	DG 18	P	12	ALL TISSUES APPEARED NORMAL.
	12577	DG 18	P	12	ALL TISSUES APPEARED NORMAL.
	12578	DG 18	P	12	ALL TISSUES APPEARED NORMAL.
	12579	DG 18	P	12	ALL TISSUES APPEARED NORMAL.
	12580	DG 18	P	12	ALL TISSUES APPEARED NORMAL.
III 5	12581	DG 18	P	12	ALL TISSUES APPEARED NORMAL.
	12582	DG 18	P	12	ALL TISSUES APPEARED NORMAL.
	12583	DG 18	P	12	ALL TISSUES APPEARED NORMAL.
IV 10	12584	DG 18	P	12	ALL TISSUES APPEARED NORMAL.
	12585	DG 18	P	12	ALL TISSUES APPEARED NORMAL.
	12586	DG 18	P	12	ALL TISSUES APPEARED NORMAL.
V 20	12587	DG 18	P	12	ALL TISSUES APPEARED NORMAL.
	12588	DG 18	P	12	ALL TISSUES APPEARED NORMAL.
	12589	DG 18	P	12	ALL TISSUES APPEARED NORMAL.
	12590	DG 18	P	12	ALL TISSUES APPEARED NORMAL.
	12591	DG 18	P	12	ALL TISSUES APPEARED NORMAL.

P = PREGNANT NP = NOT PREGNANT
DG = DAY OF GESTATION

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TABLE 16 (PAGE 1): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

PREGNANCY STATUS	DAY 0	4	6	7	8	9	10	11	12	13	14	15	16
RAT #	DOSAGE GROUP I					0 (VEHICLE) MG/KG/DAY							
12801 P	226.	261.	272.	277.	284.	286.	297.	304.	312.	316.	325.	329.	335.
12802 P	212.	242.	250.	254.	262.	263.	270.	274.	280.	282.	288.	297.	303.
12803 P	236.	267.	285.	292.	292.	301.	310.	317.	319.	327.	331.	345.	357.
12804 P	221.	245.	255.	256.	261.	262.	269.	273.	269.	279.	281.	289.	300.
12805 P	242.	256.	276.	278.	281.	286.	288.	294.	299.	310.	316.	315.	333.
12806 P	229.	252.	256.	266.	270.	275.	283.	285.	288.	292.	299.	302.	314.
12807 P	224.	263.	273.	284.	285.	290.	293.	300.	304.	309.	314.	314.	326.
12808 P	244.	267.	277.	290.	293.	299.	299.	308.	317.	317.	321.	333.	345.
12809 P	228.	262.	276.	280.	287.	288.	297.	301.	308.	308.	318.	332.	357.
12810 P	247.	273.	283.	284.	291.	295.	292.	298.	307.	316.	320.	323.	328.
12811 P	238.	253.	257.	265.	276.	281.	289.	289.	291.	295.	303.	308.	314.
12812 P	232.	254.	266.	270.	273.	277.	278.	289.	291.	298.	294.	308	313.
12813 NP	228.	257.	267.	273.	279.	283.	285.	290.	287.	286.	288.	288.	289.
12814 P	240.	274.	288.	284.	292.	293.	299.	303.	312.	316.	325.	330.	344.
12815 P	226.	259.	271.	274.	279.	286.	287.	294.	298.	303.	310.	317.	327.
12816 P	230.	a	275.	277.	279.	285.	292.	297.	301.	307.	304.	316.	323.
12817 P	220.	a	249.	256.	259.	262.	266.	272.	281.	288.	289.	298.	306.
12818 P	237.	a	277.	280.	283.	295.	296.	309.	309.	316.	323.	331.	338.
12819 P	234.	a	256.	261.	266.	268.	268.	273.	279.	283.	287.	292.	300.
12820 P	242.	a	265.	272.	274.	276.	281.	287.	288.	295.	299.	306.	317.
12821 P	222.	a	260.	266.	271.	277.	283.	285.	287.	299.	302.	309.	318.
12822 P	245.	a	280.	283.	291.	298.	299.	305.	309.	322.	322.	334.	352.
12823 P	215.	a	249.	248.	249.	258.	259.	266.	268.	270.	276.	280.	296.
12824 P	219.	a	253.	249.	256.	264.	262.	261.	270.	268.	270.	281.	289.
12825 P	230.	246.	262.	265.	272.	273.	287.	294.	295.	301.	312.	322.	329.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Value was not recorded.

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TABLE 16 (PAGE 2): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

PREGNANCY STATUS	DAY 17	18	19	20
RAT #	DOSAGE GROUP I			0 (VEHICLE) MG/KG/DAY
12801 P	354.	367.	379.	400.
12802 P	309.	323.	340.	356.
12803 P	373.	387.	401.	429.
12804 P	312.	323.	337.	367.
12805 P	345.	366.	374.	393.
12806 P	326.	338.	350.	376.
12807 P	333.	353.	365.	385.
12808 P	354.	367.	378.	402.
12809 P	367.	383.	387.	421.
12810 P	342.	350.	366.	391.
12811 P	325.	343.	354.	382.
12812 P	322.	341.	351.	378.
12813 NP	292.	293.	295.	311.
12814 P	360.	366.	387.	420.
12815 P	343.	357.	373.	402.
12816 P	341.	353.	365.	388.
12817 P	323.	336.	350.	375.
12818 P	354.	370.	382.	399.
12819 P	313.	329.	347.	367.
12820 P	328.	340.	357.	382.
12821 P	334.	346.	363.	394.
12822 P	360.	374.	396.	419.
12823 P	308.	323.	334.	355.
12824 P	306.	315.	336.	347.
12825 P	344.	358.	384.	400.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

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TABLE 16 (PAGE 3): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

PREGNANCY STATUS	DAY 0	4	6	7	8	9	10	11	12	13	14	15	16
RAT #	DOSAGE GROUP II					1 MG/KG/DAY							
12826 P	224.	258.	273.	280.	284.	288.	293.	295.	309.	314.	322.	330.	340.
12827 P	236.	248.	261.	264.	264.	272.	274.	279.	286.	291.	291.	304.	303.
12828 P	212.	249.	269.	277.	276.	286.	284.	293.	302.	298.	312.	314.	331.
12829 P	212.	224.	234.	245.	243.	241.	244.	248.	257.	257.	259.	272.	278.
12830 P	228.	256.	260.	264.	275.	275.	277.	280.	287.	291.	292.	305.	315.
12831 P	238.	252.	268.	273.	274.	284.	286.	296.	292.	302.	311.	316.	323.
12832 P	227.	244.	254.	260.	264.	268.	277.	279.	284.	287.	295.	299.	312.
12833 P	239.	261.	274.	275.	281.	284.	292.	290.	289.	292.	298.	302.	306.
12834 P	225.	236.	249.	252.	253.	257.	265.	267.	274.	279.	284.	292.	305.
12835 P	230.	274.	293.	298.	302.	291.	310.	311.	316.	326.	333.	338.	347.
12836 P	220.	247.	259.	265.	264.	273.	275.	281.	282.	292.	296.	303.	306.
12837 P	240.	248.	255.	249.	268.	269.	275.	282.	282.	284.	296.	298.	315.
12838 P	228.	239.	253.	253.	261.	266.	267.	270.	274.	288.	290.	297.	306.
12839 P	243.	a	281.	286.	292.	292.	300.	308.	315.	321.	325.	332.	341.
12840 P	230.	a	263.	268.	270.	278.	283.	288.	292.	302.	309.	319.	329.
12841 P	222.	a	272.	273.	279.	285.	292.	295.	303.	312.	320.	330.	342.
12842 P	234.	a	278.	280.	289.	293.	302.	304.	303.	308.	314.	325.	339.
12843 P	222.	a	241.	246.	252.	256.	262.	266.	264.	270.	276.	278.	291.
12844 P	242.	a	281.	282.	287.	290.	294.	304.	303.	311.	314.	326.	340.
12845 NP	217.	a	233.	232.	228.	227.	232.	234.	234.	230.	239.	239.	238.
12846 NP	230.	a	257.	258.	263.	266.	269.	268.	269.	272.	277.	267.	266.
12847 P	236.	a	263.	261.	270.	275.	277.	284.	285.	289.	303.	306.	318.
12848 P	240.	256.	267.	268.	272.	274.	284.	288.	288.	298.	305.	314.	327.
12849 P	237.	260.	274.	282.	284.	290.	298.	301.	303.	317.	322.	333.	335.
12850 P	248.	272.	282.	287.	293.	296.	302.	310.	317.	320.	324.	330.	341.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Value was not recorded.

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TABLE 16 (PAGE 4): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

PREGNANCY STATUS	DAY 17	18	19	20
RAT #	DOSAGE GROUP II			1 MG/KG/DAY
12826 P	352.	364.	371.	396.
12827 P	317.	323.	340.	362.
12828 P	350.	366.	383.	402.
12829 P	293.	306.	324.	331.
12830 P	323.	346.	360.	378.
12831 P	340.	356.	370.	394.
12832 P	322.	340.	343.	373.
12833 P	318.	335.	340.	357.
12834 P	323.	337.	354.	381.
12835 P	354.	362.	376.	391.
12836 P	313.	327.	342.	359.
12837 P	327.	341.	353.	383.
12838 P	319.	333.	344.	372.
12839 P	357.	377.	396.	418.
12840 P	343.	362.	378.	408.
12841 P	351.	364.	374.	402.
12842 P	346.	368.	382.	414.
12843 P	306.	313.	333.	352.
12844 P	342.	358.	372.	412.
12845 NP	235.	239.	240.	245.
12846 NP	265.	266.	261.	265.
12847 P	326.	346.	359.	387.
12848 P	340.	363.	384.	405.
12849 P	350.	365.	388.	407.
12850 P	354.	367.	391.	411.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

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TABLE 16 (PAGE 5): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

PREGNANCY STATUS	DAY 0	4	6	7	8	9	10	11	12	13	14	15	16
RAT #	DOSAGE GROUP III					5 MG/KG/DAY							
12851 P	225.	268.	278.	288.	292.	295.	303.	310.	314.	325.	330.	340.	350.
12852 P	223.	253.	265.	267.	276.	281.	278.	283.	285.	292.	298.	305.	315.
12853 P	222.	259.	274.	273.	278.	280.	288.	290.	299.	302.	308.	318.	328.
12854 P	232.	267.	267.	289.	290.	294.	302.	300.	299.	300.	312.	317.	329.
12855 NP	244.	259.	269.	275.	282.	283.	285.	285.	286.	280.	271.	279.	280.
12856 P	228.	249.	256.	259.	256.	266.	271.	279.	278.	279.	283.	288.	305.
12857 P	246.	264.	276.	281.	282.	287.	291.	300.	306.	312.	320.	329.	344.
12858 P	219.	236.	235.	244.	260.	260.	263.	273.	269.	268.	273.	273.	287.
12859 P	233.	254.	281.	286.	292.	297.	296.	303.	301.	316.	320.	333.	344.
12860 P	230.	262.	275.	282.	291.	281.	296.	300.	306.	312.	317.	328.	339.
12861 P	227.	238.	236.	254.	255.	260.	267.	268.	268.	274.	273.	281.	290.
12862 P	210.	238.	248.	251.	254.	258.	258.	265.	269.	276.	282.	286.	301.
12863 P	221.	247.	260.	265.	270.	273.	275.	283.	290.	288.	290.	289.	307.
12864 P	228.	a	272.	275.	279.	284.	283.	297.	300.	303.	316.	320.	331.
12865 P	220.	a	246.	256.	255.	246.	250.	251.	273.	266.	271.	289.	299.
12866 P	247.	a	289.	296.	301.	301.	307.	311.	321.	326.	333.	348.	359.
12867 P	214.	a	245.	247.	246.	246.	249.	256.	258.	265.	266.	275.	284.
12868 P b	240.	a	278.	279.	279.	281.	287.	291.	292.	289.	297.	309.	315.
12869 P	236.	a	270.	268.	281.	281.	283.	292.	296.	302.	307.	312.	325.
12870 P	238.	264.	278.	284.	285.	284.	290.	298.	299.	310.	311.	322.	335.
12871 P	230.	249.	252.	261.	258.	261.	261.	272.	275.	274.	279.	290.	294.
12872 P	252.	271.	281.	286.	a	302.	304.	310.	318.	327.	327.	326.	348.
12873 P	233.	258.	274.	278.	284.	286.	290.	294.	298.	301.	314.	317.	324.
12874 P	242.	269.	282.	287.	293.	297.	305.	304.	311.	318.	321.	334.	347.
12875 P	236.	252.	265.	267.	263.	265.	266.	282.	281.	284.	290.	299.	304.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Value was not recorded.
b. Dam 12868 had a litter consisting of 7 conceptuses; values excluded from group averages and statistical analyses.

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TABLE 16 (PAGE 6): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

PREGNANCY STATUS	DAY 17	18	19	20
RAT #	DOSAGE GROUP III		5 MG/KG/DAY	
12851 P	364.	381.	397.	416.
12852 P	333.	353.	367.	393.
12853 P	346.	362.	378.	400.
12854 P	347.	368.	384.	399.
12855 NP	274.	268.	272.	282.
12856 P	320.	333.	348.	376.
12857 P	358.	374.	389.	420.
12858 P	296.	313.	320.	341.
12859 P	361.	374.	388.	421.
12860 P	350.	361.	380.	409.
12861 P	300.	309.	318.	341.
12862 P	315.	330.	338.	363.
12863 P	314.	331.	342.	357.
12864 P	338.	357.	368.	400.
12865 P	310.	324.	338.	358.
12866 P	368.	388.	403.	429.
12867 P	294.	308.	317.	344.
12868 P a	315.	330.	333.	349.
12869 P	337.	352.	368.	394.
12870 P	346.	355.	387.	405.
12871 P	307.	320.	331.	342.
12872 P	355.	372.	372.	400.
12873 P	339.	355.	383.	400.
12874 P	359.	373.	402.	422.
12875 P	315.	323.	352.	361.

(VALUES EXCLUDED FROM AVERAGES)

P = PREGNANT NP = NOT PREGNANT
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Dam 12868 had a litter consisting of 7 conceptuses; values excluded from group averages and statistical analyses.

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TABLE 16 (PAGE 7): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

PREGNANCY STATUS	DAY 0	4	6	7	8	9	10	11	12	13	14	15	16
RAT #	DOSAGE GROUP IV					10 MG/KG/DAY							
12876 P	219.	266.	278.	286.	290.	297.	300.	296.	300.	312.	324.	324.	341.
12877 P	230.	262.	273.	274.	276.	282.	289.	290.	294.	298.	306.	313.	326.
12878 P	212.	242.	247.	253.	258.	264.	268.	270.	266.	275.	277.	291.	300.
12879 P	228.	244.	254.	258.	260.	262.	268.	270.	275.	274.	276.	290.	300.
12880 P	230.	248.	258.	258.	259.	267.	268.	272.	274.	279.	282.	291.	304.
12881 P	211.	235.	236.	242.	231.	239.	247.	250.	250.	246.	246.	263.	268.
12882 P	244.	254.	274.	277.	282.	288.	291.	294.	306.	313.	318.	327.	339.
12883 P	244.	a	276.	284.	286.	288.	295.	296.	298.	308.	311.	321.	335.
12884 P	224.	a	254.	270.	262.	273.	282.	280.	283.	298.	292.	304.	312.
12885 P	237.	a	270.	274.	274.	284.	286.	291.	290.	297.	300.	310.	327.
12886 P	235.	a	266.	273.	273.	277.	279.	284.	286.	288.	294.	301.	311.
12887 P	247.	a	279.	279.	289.	288.	291.	296.	301.	308.	314.	323.	337.
12888 P	239.	a	270.	272.	273.	278.	283.	284.	290.	297.	301.	310.	317.
12889 P b	228.	a	263.	272.	271.	272.	271.	271.	278.	281.	283.	286.	285.
12890 P	242.	a	274.	271.	273.	280.	282.	281.	293.	297.	297.	303.	317.
12891 P	236.	a	256.	262.	262.	265.	269.	272.	274.	280.	286.	295.	300.
12892 P	226.	a	256.	265.	263.	260.	263.	265.	275.	282.	289.	292.	304.
12893 P	232.	a	278.	276.	278.	286.	294.	295.	303.	313.	313.	330.	339.
12894 P	221.	a	253.	251.	242.	256.	259.	267.	271.	273.	270.	284.	296.
12895 P	221.	a	244.	252.	254.	257.	267.	266.	267.	269.	279.	283.	293.
12896 P	236.	a	271.	275.	273.	268.	279.	284.	288.	297.	301.	305.	323.
12897 P	233.	a	269.	278.	275.	275.	281.	282.	284.	291.	292.	302.	314.
12898 P	240.	265.	276.	279.	287.	284.	286.	297.	297.	301.	310.	322.	336.
12899 P	220.	244.	256.	261.	260.	266.	262.	270.	274.	277.	285.	296.	307.
12900 P	226.	237.	248.	246.	254.	250.	261.	259.	265.	268.	276.	290.	300.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Value was not recorded.
b. Dam 12889 had a litter consisting of 3 conceptuses; values excluded from group averages and statistical analyses.

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TABLE 16 (PAGE 8): MATERNAL BODY WEIGHTS INDIVIDUAL DATA

PREGNANCY STATUS	DAY 17	18	19	20
RAT #	DOSAGE GROUP IV			10 MG/KG/DAY
12876 P	358.	360.	375.	390.
12877 P	329.	344.	354.	378.
12878 P	313.	329.	346.	374.
12879 P	309.	326.	342.	367.
12880 P	314.	333.	341.	372.
12881 P	280.	282.	298.	310.
12882 P	358.	378.	385.	420.
12883 P	348.	365.	373.	392.
12884 P	320.	334.	344.	371.
12885 P	330.	344.	358.	378.
12886 P	315.	332.	344.	379.
12887 P	349.	360.	373.	396.
12888 P	329.	337.	351.	369.
12889 P a	289.	301.	309.	321.
12890 P	328.	339.	354.	374.
12891 P	306.	318.	331.	349.
12892 P	319.	328.	347.	371.
12893 P	348.	369.	383.	412.
12894 P	309.	321.	341.	364.
12895 P	307.	313.	328.	343.
12896 P	331.	345.	355.	380.
12897 P	326.	335.	344.	374.
12898 P	350.	365.	390.	414.
12899 P	314.	327.	352.	364.
12900 P	314.	338.	359.	375.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Dam 12889 had a litter consisting of 3 conceptuses; values excluded from group averages and statistical analyses.

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TABLE 16 (PAGE 9): MATERNAL BODY WEIGHTS INDIVIDUAL DATA

PREGNANCY STATUS	DAY 0	4	6	7	8	9	10	11	12	13	14	15	16
RAT #	DOSAGE GROUP V					20 MG/KG/DAY							
12901 P	219.	243.	254.	254.	264.	269.	266.	273.	277.	282.	286.	292.	306.
12902 P	229.	244.	251.	252.	259.	256.	258.	264.	265.	271.	274.	275.	284.
12903 P	211.	249.	260.	260.	263.	258.	267.	271.	276.	267.	282.	283.	295.
12904 P	227.	255.	261.	263.	259.	265.	264.	266.	260.	264.	256.	270.	273.
12905 P	222.	242.	259.	258.	261.	261.	269.	272.	269.	277.	279.	285.	294.
12906 P	228.	242.	254.	253.	257.	259.	263.	266.	274.	269.	280.	282.	298.
12907 P	230.	251.	271.	278.	276.	276.	272.	267.	283.	290.	286.	294.	302.
12908 P	238.	254.	268.	268.	276.	275.	272.	283.	285.	284.	285.	288.	303.
12909 P	239.	257.	268.	265.	267.	275.	271.	271.	274.	268.	278.	275.	289.
12910 NP	212.	243.	253.	254.	259.	251.	256.	260.	247.	243.	246.	246.	240.
12911 P	215.	241.	253.	251.	252.	253.	258.	259.	260.	263.	268.	275.	286.
12912 P	224.	a	256.	258.	262.	259.	264.	266.	274.	287.	287.	287.	298.
12913 P	243.	a	272.	274.	274.	278.	282.	280.	284.	286.	292.	300.	308.
12914 P	225.	a	274.	279.	274.	284.	285.	290.	295.	300.	301.	315.	325.
12915 P	237.	a	267.	279.	275.	278.	282.	289.	292.	287.	290.	300.	314.
12916 P	248.	a	275.	260.	256.	264.	263.	245.	238.	250.	264.	271.	289.
12917 P	236.	a	254.	252.	250.	251.	252.	252.	257.	263.	266.	269.	282.
12918 P	245.	a	265.	266.	245.	248.	258.	263.	264.	266.	264.	266.	280.
12919 P	228.	a	269.	257.	271.	279.	277.	272.	268.	276.	276.	293.	304.
12920 P	222.	a	255.	250.	253.	254.	250.	256.	272.	266.	281.	284.	285.
12921 P	230.	a	268.	271.	273.	273.	277.	280.	278.	278.	281.	293.	304.
12922 P	233.	a	259.	258.	251.	251.	255.	259.	260.	260.	258.	263.	273.
12923 P	240.	268.	278.	279.	269.	271.	277.	276.	281.	280.	292.	304.	311.
12924 P	234.	250.	259.	262.	255.	257.	256.	266.	261.	258.	272.	276.	285.
12925 P	240.	260.	273.	270.	262.	253.	263.	270.	258.	247.	235.	230.	231.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Value was not recorded.

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TABLE 16 (PAGE 10): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

PREGNANCY STATUS	DAY 17	18	19	20
RAT #	DOSAGE GROUP V			20 MG/KG/DAY
12901 P	313.	320.	333.	360.
12902 P	295.	310.	320.	337.
12903 P	309.	322.	329.	353.
12904 P	279.	292.	301.	309.
12905 P	294.	310.	323.	350.
12906 P	306.	320.	337.	352.
12907 P	301.	310.	328.	352.
12908 P	313.	323.	330.	352.
12909 P	303.	315.	323.	343.
12910 NP	239.	240.	245.	252.
12911 P	296.	303.	321.	345.
12912 P	309.	322.	338.	364.
12913 P	310.	317.	333.	354.
12914 P	336.	337.	355.	384.
12915 P	325.	338.	350.	379.
12916 P	304.	317.	330.	352.
12917 P	294.	305.	322.	343.
12918 P	294.	302.	325.	335.
12919 P	311.	322.	335.	347.
12920 P	298.	313.	322.	347.
12921 P	313.	325.	339.	358.
12922 P	283.	292.	298.	323.
12923 P	328.	346.	366.	385.
12924 P	303.	307.	325.	341.
12925 P	247.	272.	284.	303.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ELFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 16 (PAGE 11): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

PREGNANCY STATUS	DAY 0	4	6	7	8	9	10	11	12	13	14	15	16
						0 (VEHICLE) MG/KG/DAY							
SATELLITE DOSAGE GROUP I													
RAT #													
12573 P	236.	254.	266.	271.	271.	279.	283.	293.	296.	301.	305.	310.	317.
12574 P	233.	259.	273.	280.	280.	290.	295.	299.	304.	309.	318.	328.	333.
12575 P	248.	269.	283.	288.	293.	296.	299.	305.	309.	314.	320.	328.	334.
DAY 17		18											
12573 P	332.	347.											
12574 P	348.	367.											
12575 P	350.	366.											

(VALUES EXCLUDED FROM AVERAGES)

NP = NOT PREGNANT

P = PREGNANT

DAY = DAY OF PRESUMED GESTATION

ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N Et FOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 16 (PAGE 12): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

PREGNANCY STATUS	DAY 0	4	6	7	8	9	10	11	12	13	14	15	16
						1 MG/KG/DAY							
RAT #				SATELLITE DOSAGE GROUP II									
12576 P	227.	244.	253.	259.	260.	260.	267.	272.	280.	285.	290.	296.	310.
12577 P	245.	259.	280.	282.	284.	290.	296.	301.	306.	308.	318.	328.	337.
12578 P	221.	232.	258.	257.	260.	265.	271.	271.	278.	278.	286.	293.	305.
12579 P	232.	253.	269.	271.	282.	282.	288.	292.	294.	302.	309.	317.	325.
12580 P	248.	261.	273.	272.	277.	280.	291.	296.	302.	305.	312.	319.	333.
	DAY 17	18											
12576 P	312.	339.											
12577 P	358.	382.											
12578 P	314.	343.											
12579 P	343.	367.											
12580 P	353.	370.											

NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
P = PREGNANT
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 16 (PAGE 13): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

PREGNANCY STATUS	DAY 0	4	6	7	8	9	10	11	12	13	14	15	16
RAT #	SATELLITE DOSAGE GROUP III					5 MG/KG/DAY							
12581 P	228.	244.	257.	258.	258.	256.	258.	267.	272.	282.	287.	297.	301.
12582 P	243.	260.	271.	274.	279.	283.	290.	291.	295.	306.	305.	314.	325.
12583 P	251.	275.	296.	306.	309.	313.	319.	322.	328.	338.	344.	356.	373.

	DAY 17	18
12581 P	316.	334.
12582 P	338.	360.
12583 P	389.	412.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 16 (PAGE 14): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

PREGNANCY STATUS	DAY 0	4	6	7	8	9	10	11	12	13	14	15	16
RAT #	SATELLITE DOSAGE GROUP IV					10 MG/KG/DAY							
12584 P	228.	252.	265.	269.	272.	270.	274.	275.	281.	290.	290.	297.	309.
12585 P	242.	265.	276.	273.	277.	283.	287.	290.	296.	303.	308.	310.	322.
12586 P	250.	262.	273.	275.	277.	282.	283.	290.	289.	294.	296.	306.	316.

	DAY 17	18
12584 P	318.	340.
12585 P	334.	351.
12586 P	323.	339.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 16 (PAGE 15): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

PREGNANCY STATUS	DAY 0	4	6	7	8	9	10	11	12	13	14	15	16
RAT #	SATELLITE DOSAGE GROUP V					20 MG/KG/DAY							
12587 P	228.	232.	249.	232.	243.	241.	243.	258.	260.	249.	255.	266.	285.
12588 P	243.	262.	282.	286.	289.	288.	287.	291.	289.	294.	305.	318.	328.
12589 P	221.	240.	252.	258.	262.	267.	256.	246.	254.	267.	268.	283.	284.
12590 P	236.	256.	270.	266.	268.	268.	268.	274.	279.	280.	284.	292.	304.
12591 P	249.	267.	288.	292.	293.	295.	300.	306.	302.	297.	295.	316.	327.

	DAY 17	18
12587 P	294.	319.
12588 P	346.	360.
12589 P	299.	321.
12590 P	314.	336.
12591 P	345.	362.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T 6316.7)

TABLE 17 (PAGE 1): MATERNAL FEED CONSUMPTION VALUES - INDIVIDUAL DATA

PREGNANCY STATUS	DAYS 0 - 4	4 - 6	6 - 8	8 - 10	10 - 12	12 - 14	14 - 16	16 - 18	18 - 20
RAT #	DOSAGE GROUP I					0 (VEHICLE) MG/KG/DAY			
12801 P	56.	48.	52.	50.	58.	60.	50.	60.	59.
12802 P	54.	40.	43.	44.	47.	49.	50.	49.	52.
12803 P	82.	51.	55.	53.	57.	59.	62.	63.	60.
12804 P	86.	44.	42.	41.	32.	44.	50.	58.	52.
12805 P	79.	47.	51.	49.	55.	52.	46.	55.	54.
12806 P	53.	41.	49.	48.	47.	51.	45.	54.	53.
12807 P	71.	51.	52.	50.	49.	51.	45.	50.	53.
12808 P	96.	45.	61.	49.	51.	47.	52.	63.	56.
12809 P	91.	47.	57.	49.	53.	61.	64.	50.	51.
12810 P	103.	45.	53.	47.	50.	56.	46.	58.	58.
12811 P	88.	35.	51.	44.	40.	44.	40.	52.	48.
12812 P	190.a	a	48.	48.	49.	47.	46.	48.	48.
12813 NP	89.	45.	49.	53.	41.	44.	51.	54.	43.
12814 P	102.	54.	48.	50.	50.	54.	58.	61.	59.
12815 P	94.	49.	50.	47.	49.	49.	53.	60.	56.
12816 P	97.	56.	56.	53.	57.	53.	58.	59.	53.
12817 P	74.	43.	45.	45.	46.	48.	53.	52.	45.
12818 P	104.	61.	58.	62.	62.	63.	65.	61.	60.
12819 P	85.	39.	43.	41.	44.	47.	46.	49.	45.
12820 P	81.	42.	44.	42.	48.	50.	54.	55.	57.
12821 P	84.	44.	49.	51.	48.	52.	54.	51.	53.
12822 P	85.	47.	53.	52.	54.	55.	62.	55.	51.
12823 P	71.	45.	41.	44.	42.	43.	47.	54.	48.
12824 P	81.	46.	35.	45.	47.	45.	48.	54.	50.
12825 P	80.	44.	44.	44.	44.	54.	53.	53.	44.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAYS = DAYS OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Value appeared incorrectly recorded and was excluded from group averages and statistical analyses.

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TABLE 17 (PAGE 2): MATERNAL FEED CONSUMPTION VALUES - INDIVIDUAL DATA

PREGNANCY STATUS	DAYS 0 - 4	4 - 6	6 - 8	8 - 10	10 - 12	12 - 14	14 - 16	16 - 18	18 - 20
RAT #	DOSAGE GROUP II					1 MG/KG/DAY			
12826 P	82.	49.	49.	47.	48.	56.	55.	57.	55.
12827 P	71.	41.	42.	43.	45.	47.	41.	50.	45.
12828 P	91.	47.	49.	45.	50.	47.	45.	58.	57.
12829 P	14.	41.	44.	33.	40.	43.	47.	51.	44.
12830 P	90.	38.	48.	45.	43.	45.	46.	55.	52.
12831 P	89.	48.	49.	50.	50.	54.	52.	60.	57.
12832 P	87.	43.	48.	46.	44.	48.	46.	46.	46.
12833 P	90.	45.	45.	47.	36.	43.	40.	50.	40.
12834 P	73.	44.	40.	43.	44.	45.	47.	60.	55.
12835 P	101.	57.	55.	47.	52.	62.	64.	60.	55.
12836 P	91.	47.	46.	50.	49.	52.	49.	50.	40.
12837 P	87.	30.	39.	47.	46.	40.	49.	58.	55.
12838 P	70.	40.	43.	43.	41.	50.	44.	50.	48.
12839 P	95.	47.	50.	48.	50.	51.	54.	55.	52.
12840 P	80.	49.	49.	50.	55.	56.	62.	62.	60.
12841 P	86.	47.	45.	48.	50.	55.	56.	42.	47.
12842 P	93.	50.	51.	51.	47.	52.	54.	58.	54.
12843 P	76.	36.	41.	43.	45.	42.	47.	48.	46.
12844 P	94.	52.	48.	47.	56.	49.	57.	54.	57.
12845 NP	69.	35.	77.	47.	42.	66.	a	40.	43.
12846 NP	64.	40.	45.	46.	45.	45.	32.	33.	30.
12847 P	77.	39.	40.	44.	45.	43.	51.	52.	49.
12848 P	82.	43.	44.	42.	44.	45.	50.	49.	44.
12849 P	82.	45.	49.	47.	51.	56.	52.	54.	52.
12850 P	86.	46.	44.	48.	52.	48.	52.	43.	51.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAYS = DAYS OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Spilled feed precluded the calculation of this value.

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TABLE 17 (PAGE 3): MATERNAL FEED CONSUMPTION VALUES - INDIVIDUAL DATA

PREGNANCY STATUS	DAYS 0 - 4	4 - 6	6 - 8	8 - 10	10 - 12	12 - 14	14 - 16	16 - 18	18 - 20
RAT #	DOSAGE GROUP III					5 MG/KG/DAY			
12851 P	97.	48.	53.	52.	55.	55.	59.	61.	54.
12852 P	48.	45.	47.	44.	43.	49.	48.	53.	51.
12853 P	69.	49.	49.	48.	50.	54.	46.	57.	59.
12854 P	103.	39.	60.	51.	41.	48.	48.	69.	57.
12855 NP	81.	40.	47.	41.	38.	32.	37.	31.	34.
12856 P	88.	38.	39.	47.	41.	47.	50.	58.	52.
12857 P	103.	49.	50.	49.	50.	55.	56.	52.	57.
12858 P	78.	32.	42.	41.	43.	39.	40.	45.	45.
12859 P	101.	57.	63.	55.	52.	58.	58.	65.	61.
12860 P	103.	57.	58.	49.	56.	63.	67.	62.	59.
12861 P	78.	33.	47.	47.	45.	47.	43.	52.	53.
12862 P	82.	44.	47.	47.	47.	48.	46.	59.	51.
12863 P	80.	42.	46.	45.	48.	42.	40.	46.	44.
12864 P	96.	54.	53.	46.	58.	58.	61.	63.	60.
12865 P	56.	54.	41.	29.	39.	37.	53.	51.	46.
12866 P	95.	52.	57.	51.	52.	53.	60.	57.	52.
12867 P	76.	43.	36.	38.	45.	45.	49.	48.	44.
12868 P a	87.	50.	48.	48.	49.	46.	58.	54.	52.
12869 P	76.	43.	48.	46.	53.	46.	51.	50.	49.
12870 P	87.	44.	45.	42.	44.	52.	54.	53.	54.
12871 P	71.	35.	40.	37.	46.	38.	45.	43.	35.
12872 P	90.	44.	46.	45.	49.	50.	43.	48.	52.
12873 P	83.	52.	52.	42.	50.	59.	55.	56.	53.
12874 P	96.	46.	51.	52.	50.	50.	59.	54.	54.
12875 P	81.	46.	37.	36.	46.	44.	53.	51.	48.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAYS = DAYS OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Dam 12868 had a litter consisting of 7 conceptuses; values excluded from group averages and statistical analyses.

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TABLE 17 (PAGE 4): MATERNAL FEED CONSUMPTION VALUES - INDIVIDUAL DATA

PREGNANCY STATUS	DAYS 0 - 4	4 - 6	6 - 8	8 - 10	10 - 12	12 - 14	14 - 16	16 - 18	18 - 20
RAT #	DOSAGE GROUP IV					10 MG/KG/DAY			
12876 P	101.	56.	54.	52.	50.	54.	56.	46.	50.
12877 P	88.	47.	49.	50.	50.	50.	50.	47.	48.
12878 P	20.	36.	42.	46.	41.	40.	48.	56.	54.
12879 P	94.	45.	49.	43.	53.	41.	46.	56.	55.
12880 P	90.	43.	43.	45.	44.	47.	48.	54.	48.
12881 P	77.	26.	35.	38.	37.	31.	43.	43.	38.
12882 P	86.	48.	51.	49.	54.	53.	45.	57.	54.
12883 P	88.	52.	47.	47.	48.	50.	56.	52.	49.
12884 P	84.	43.	49.	52.	46.	48.	53.	55.	54.
12885 P	70.	43.	45.	47.	47.	47.	52.	50.	44.
12886 P	100.	50.	50.	54.	53.	50.	55.	55.	59.
12887 P	86.	47.	53.	50.	53.	54.	59.	56.	52.
12888 P	85.	51.	46.	46.	50.	54.	56.	57.	49.
12889 P a	74.	48.	45.	42.	41.	46.	43.	50.	48.
12890 P	84.	48.	40.	45.	51.	49.	53.	55.	48.
12891 P	94.	44.	46.	46.	48.	50.	48.	52.	45.
12892 P	91.	40.	42.	39.	47.	55.	49.	56.	55.
12893 P	87.	51.	45.	49.	b	54.	59.	62.	56.
12894 P	74.	47.	32.	43.	44.	35.	55.	53.	51.
12895 P	67.	35.	37.	45.	39.	44.	45.	43.	39.
12896 P	77.	46.	37.	37.	49.	47.	50.	52.	48.
12897 P	78.	43.	46.	44.	45.	44.	47.	40.	45.
12898 P	92.	51.	48.	39.	46.	52.	60.	60.	57.
12899 P	77.	47.	47.	43.	48.	47.	54.	49.	46.
12900 P	77.	38.	41.	36.	41.	50.	66.	53.	51.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAYS = DAYS OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Dam 12889 had a litter consisting of 3 conceptuses; values excluded from group averages and statistical analyses.
b. Spilled feed precluded the calculation of this value.

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T 6316.7)

TABLE 17 (PAGE 5): MATERNAL FEED CONSUMPTION VALUES - INDIVIDUAL DATA

PREGNANCY STATUS	DAYS	0 - 4	4 - 6	6 - 8	8 - 10	10 - 12	12 - 14	14 - 16	16 - 18	18 - 20
RAT #	DOSAGE GROUP V					20 MG/KG/DAY				
12901	P	49.	45.	46.	42.	44.	50.	49.	45.	46.
12902	P	83.	43.	41.	37.	41.	44.	40.	50.	40.
12903	P	71.	48.	45.	43.	46.	42.	35.	46.	52.
12904	P	68.	44.	38.	41.	34.	31.	35.	37.	39.
12905	P	83.	45.	39.	43.	40.	46.	45.	48.	49.
12906	P	81.	42.	38.	37.	45.	47.	40.	48.	46.
12907	P	97.	52.	49.	40.	39.	49.	43.	40.	49.
12908	P	98.	49.	50.	47.	47.	49.	45.	41.	42.
12909	P	92.	46.	38.	47.	40.	33.	33.	47.	48.
12910	NP	84.	44.	38.	37.	36.	31.	32.	31.	41.
12911	P	84.	46.	39.	39.	39.	43.	48.	46.	40.
12912	P	81.	43.	41.	41.	47.	50.	49.	51.	51.
12913	P	87.	45.	39.	47.	40.	46.	49.	40.	46.
12914	P	90.	51.	42.	45.	55.	50.	53.	45.	49.
12915	P	101.	44.	45.	44.	51.	46.	53.	56.	54.
12916	P	80.	44.	29.	31.	9.	42.	53.	52.	47.
12917	P	76.	40.	37.	30.	33.	39.	39.	44.	45.
12918	P	68.	52.	26.	30.	39.	37.	34.	40.	46.
12919	P	79.	44.	39.	45.	31.	41.	52.	48.	43.
12920	P	74.	43.	34.	29.	45.	42.	38.	41.	40.
12921	P	85.	46.	43.	39.	39.	35.	48.	48.	44.
12922	P	76.	42.	33.	33.	37.	35.	37.	42.	41.
12923	P	89.	49.	35.	34.	39.	41.	48.	49.	50.
12924	P	75.	42.	34.	30.	37.	33.	41.	42.	37.
12925	P	90.	48.	31.	28.	32.	12.	16.	36.	38.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAYS = DAYS OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 17 (PAGE 6): MATERNAL FEED CONSUMPTION VALUES - INDIVIDUAL DATA

PREGNANCY STATUS	DAYS	0 - 4	4 - 6	6 - 8	8 - 10	10 - 12	12 - 14	14 - 16	16 - 18
RAT #	SATELLITE DOSAGE GROUP I						0 (VEHICLE) MG/KG/DAY		
12573 P		87.	48.	44.	48.	50.	48.	42.	45.
12574 P		89.	48.	49.	50.	52.	52.	44.	45.
12575 P		97.	53.	56.	50.	57.	59.	64.	62.
RAT #	SATELLITE DOSAGE GROUP II						1 MG/KG/DAY		
12576 P		85.	42.	47.	43.	48.	46.	53.	43.
12577 P		92.	56.	53.	52.	52.	50.	55.	54.
12578 P		71.	40.	42.	43.	44.	42.	50.	48.
12579 P		86.	47.	53.	48.	46.	49.	53.	51.
12580 P		78.	41.	39.	45.	48.	49.	57.	52.
RAT #	SATELLITE DOSAGE GROUP III						5 MG/KG/DAY		
12581 P		82.	52.	42.	40.	53.	57.	52.	55.
12582 P		85.	43.	41.	46.	45.	47.	51.	48.
12583 P		92.	49.	54.	50.	49.	56.	60.	55.
RAT #	SATELLITE DOSAGE GROUP IV						10 MG/KG/DAY		
12584 P		83.	48.	46.	45.	46.	48.	54.	46.
12585 P		90.	42.	40.	49.	53.	55.	53.	48.
12586 P		85.	43.	42.	43.	40.	41.	51.	32.
RAT #	SATELLITE DOSAGE GROUP V						20 MG/KG/DAY		
12587 P		74.	37.	23.	34.	42.	32.	53.	46.
12588 P		85.	50.	48.	41.	42.	50.	51.	44.
12589 P		76.	42.	44.	33.	24.	44.	40.	39.
12590 P		90.	46.	43.	40.	42.	44.	55.	47.
12591 P		100.	57.	54.	44.	43.	32.	61.	52.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAYS = DAYS OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 18 (PAGE 1): CAESAREAN-SECTIONING OBSERVATIONS - INDIVIDUAL DATA

			VIABLE FETUSES			DEAD FETUSES			EARLY RESORPTIONS			LATE RESORPTIONS			IMPLANTATION SITES			CORPORA LUTEA		
RAT #	SEX M	SEX F	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT OVARY	LEFT OVARY	TOTAL
DOSAGE GROUP I			0 (VEHICLE) MG/KG/DAY																	
12801	9	4	8	5	13	0	0	0	0	1	1	0	0	0	8	6	14	8	9	17
12802	9	5	9	5	14	0	0	0	1	0	1	0	0	0	10	5	15	10	9	19
12803	9	7	8	8	16	0	0	0	0	0	0	0	0	0	8	8	16	9	8	17
12804	5	8	5	8	13	0	0	0	0	0	0	0	0	0	5	8	13	6	11	17
12805	7	8	8	7	15	0	0	0	0	0	0	0	0	0	8	7	15	10	7	17
12806	9	6	9	6	15	0	0	0	0	0	0	0	0	0	9	6	15	9	7	16
12807	6	8	4	10	14	0	0	0	1	1	2	0	0	0	5	11	16	5	12	17
12808	7	5	6	6	12	0	0	0	2	3	5	0	0	0	8	9	17	9	11	20
12809	8	10	10	8	18	0	0	0	0	0	0	0	0	0	10	8	18	10	9	19
12810	6	4	0	10	10	0	0	0	0	0	0	0	0	0	0	10	10	5	10	15
12811	4	10	5	9	14	0	0	0	1	0	1	0	0	0	5	9	14	7	9	16
12812	7	7	8	6	14										9	6	15	10	6	16
12813	NOT PREGNANT																			
12814	7	9	7	9	16	0	0	0	2	1	3	0	0	0	8	10	18	9	10	19
12815	6	9	8	7	15	0	0	0	2	0	2	0	0	0	10	7	17	10	9	19
12816	7	5	5	7	12	0	0	0	2	0	2	0	0	0	7	7	14	7	7	14
12817	8	7	6	9	15	0	0	0	0	0	0	0	0	0	6	9	15	6	9	15
12818	3	10	9	4	13	0	0	0	1	1	2	0	0	0	10	5	15	12	6	18
12819	5	10	10	5	15	0	0	0	0	1	1	0	0	0	10	6	16	11	6	17
12820	6	8	8	6	14	0	0	0	0	1	1	0	0	0	8	7	15	8	7	15
12821	10	5	7	8	15	0	0	0	0	0	0	0	0	0	7	8	15	11	10	21
12822	10	5	7	8	15	0	0	0	0	0	0	0	0	0	7	8	15	7	10	17
12823	8	6	11	3	14	0	0	0	0	1	1	0	0	0	11	4	15	12	5	17
12824	4	8	6	6	12	0	0	0	0	0	0	0	0	0	6	6	12	7	7	14
12825	7	11	8	10	18	0	0	0	0	0	0	0	0	0	8	10	18	8	10	18

M = MALE F = FEMALE
PLACENTAE APPEARED NORMAL UNLESS NOTED OTHERWISE.

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ELFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 18 (PAGE 2): CAESAREAN-SECTIONING OBSERVATIONS - INDIVIDUAL DATA

		VIABLE FETUSES			DEAD FETUSES			EARLY RESORPTIONS			LATE RESORPTIONS			IMPLANTATION SITES			CORPORA LUTEA		
		RIGHT LEFT HORN		TOTAL	RIGHT LEFT HORN		TOTAL	RIGHT LEFT HORN		TOTAL	RIGHT LEFT HORN		TOTAL	RIGHT LEFT HORN		TOTAL	RIGHT LEFT OVARY		TOTAL
RAT #	SEX M F																		
1 MG/KG/DAY																			
DOSAGE GROUP II																			
12826	8 6	9	5	14	0	0	0	0	1	1	0	0	0	0	0	0	9	5	14	12	5	17
12827	5 8	7	6	13	0	0	0	0	0	0	1	0	1	0	0	0	7	7	14	8	9	17
12828	10 8	11	7	18	0	0	0	1	0	1	0	0	0	0	0	0	11	7	18	11	8	19
12829	8 6	7	7	14	0	0	0	0	0	0	1	0	1	0	0	0	7	8	15	8	7	16
12830	7 8	8	7	15	0	0	0	0	1	1	1	0	1	0	0	0	8	6	14	8	7	16
12831	6 10	11	5	16	0	0	0	1	0	1	0	0	0	0	0	0	5	10	15	9	5	17
12832	7 7	6	8	14	0	0	0	0	0	0	0	0	0	0	0	0	2	7	9	8	8	17
12833	10 3	7	6	13	0	0	0	0	0	0	0	0	0	0	0	0	8	8	16	8	8	16
12834	9 6	5	10	15	0	0	0	0	1	1	0	0	0	0	0	0	8	7	15	8	6	15
12835	3 6	2	7	9	0	0	0	1	0	1	0	0	0	0	0	0	9	6	15	7	11	18
12836	6 9	7	8	15	0	0	0	0	0	0	0	0	0	0	0	0	7	10	17	7	10	19
12837	4 10	7	7	14	0	0	0	0	0	0	0	0	0	0	0	0	9	8	17	9	8	17
12838	8 7	9	6	15	0	0	0	0	0	0	0	0	0	0	0	0	9	8	17	9	8	17
12839	6 11	7	10	17	0	0	0	0	0	0	0	0	0	0	0	0	8	8	16	10	6	16
12840	11 6	9	8	17	0	0	0	0	0	0	0	0	0	0	0	0	10	6	16	8	8	16
12841	9 8	9	8	17	0	0	0	0	0	0	1	0	1	0	0	0	7	7	14	7	8	15
12842	9 7	10	6	16	0	0	0	0	0	0	0	0	0	0	0	0	10	6	16	10	6	16
12843	5 8	7	6	13	0	0	0	0	0	0	0	0	0	0	0	0	7	7	14	7	8	15
12844	6 11	11	6	17	0	0	0	0	0	0	0	0	0	0	0	0	11	6	17	11	8	19
12845	NOT PREGNANT																					
12846	NOT PREGNANT																					
12847	11 7	14	4	18	0	0	0	0	0	0	0	0	0	0	0	0	14	4	18	15	6	21
12848	7 11	13	5	18	0	0	0	0	0	0	0	0	0	0	0	0	13	5	18	13	7	20
12849	9 6	9	6	15	0	0	0	0	0	0	2	0	2	0	0	0	9	6	15	9	6	15
12850	7 9	7	9	16	0	0	0	0	0	0	0	0	0	0	0	0	7	11	18	7	12	19

M = MALE F = FEMALE

PLACENTAE APPEARED NORMAL UNLESS NOTED OTHERWISE.

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 18 (PAGE 3): CAESAREAN-SECTIONING OBSERVATIONS - INDIVIDUAL DATA

			VIABLE FETUSES			DEAD FETUSES			EARLY RESORPTIONS			LATE RESORPTIONS			IMPLANTATION SITES			CORPORA LUTEA		
	SEX		RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT OVARY	LEFT OVARY	TOTAL
RAT #	M	F																		
DOSAGE GROUP III					5 MG/KG/DAY															
12851	7	8	4	11	15	0	0	0	1	0	1	0	0	0	5	11	16	6	12	18
12852	8	8	6	10	16	0	0	0	0	0	0	0	0	0	6	10	16	6	11	17
12853	5	9	10	4	14	0	0	0	0	1	1	0	0	0	10	5	15	10	7	17
12854	6	10	7	9	16	0	0	0	0	0	0	0	0	0	7	9	16	8	10	18
12855	NOT PREGNANT																			
12856	5	9	5	9	14	0	0	0	0	0	0	0	0	0	5	9	14	5	9	14
12857	11	8	9	10	19	0	0	0	0	0	0	0	0	0	9	10	19	12	11	23
12858	7	7	5	9	14	0	0	0	1	0	1	0	0	0	6	9	15	6	11	17
12859	10	7	10	7	17	0	0	0	0	0	0	0	0	0	10	7	17	10	7	17
12860	7	8	6	9	15	0	0	0	1	0	1	0	0	0	7	9	16	9	11	20
12861	6	6	8	4	12	0	0	0	1	1	2	0	0	0	9	5	14	10	8	18
12862	7	8	8	7	15	0	0	0	0	0	0	0	0	0	8	7	15	8	7	15
12863	5	9	4	10	14	0	0	0	1	0	1	0	0	0	5	10	15	5	10	15
12864	6	8	10	4	14	0	0	0	0	0	0	0	0	0	10	4	14	12	5	17
12865	5	10	7	8	15	0	0	0	1	1	2	0	0	0	8	9	17	8	9	17
12866	9	10	11	8	19	0	0	0	0	0	0	0	0	0	11	8	19	11	11	22
12867	9	5	4	10	14	0	0	0	0	0	0	0	0	0	4	10	14	5	10	15
12868	1	4	2	3	5	0	0	0	0	2	2	0	0	0	2	5	7	7	6	13
12869	9	6	7	8	15	0	0	0	0	0	0	0	0	0	7	8	15	7	8	15
12870	6	10	6	10	16	0	0	0	0	0	0	0	0	0	6	10	16	6	11	17
12871	8	6	6	8	14	0	0	0	0	2	2	0	0	0	6	10	16	6	11	17
12872	9	5	9	5	14	0	0	0	0	0	0	0	0	0	9	5	14	10	6	16
12873	5	9	4	10	14	0	0	0	1	0	1	0	0	0	5	10	15	5	13	18
12874	7	9	7	9	16	0	0	0	0	1	1	0	0	0	7	10	17	7	10	17
12875	8	2	2	8	10	0	0	0	4	1	5	0	0	0	6	9	15	7	9	16

M = MALE F = FEMALE
PLACENTAE APPEARED NORMAL UNLESS NOTED OTHERWISE.

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 18 (PAGE 4): CAESAREAN-SECTIONING OBSERVATIONS - INDIVIDUAL DATA

			VIABLE FETUSES			DEAD FETUSES			EARLY RESORPTIONS			LATE RESORPTIONS			IMPLANTATION SITES			CORPORA LUTEA		
	SEX		RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT OVARY	LEFT OVARY	TOTAL
RAT #	M	F																		
DOSAGE GROUP IV						10 MG/KG/DAY														
12876	9	6	8	7	15	0	0	0	0	0	0	0	0	0	8	7	15	9	8	17
12877	6	8	9	5	14	0	0	0	0	0	0	0	0	0	9	5	14	11	6	17
12878	7	8	3	12	15	0	0	0	0	0	0	0	0	0	3	12	15	4	12	16
12879	9	6	8	7	15	0	0	0	0	0	0	0	0	0	8	7	15	10	9	19
12880	8	7	9	6	15	0	0	0	0	0	0	0	0	0	9	6	15	11	9	20
12881	6	6	8	4	12	0	0	0	1	1	2	0	0	0	9	5	14	10	5	15
12882	6	11	7	10	17	0	0	0	0	0	0	0	0	0	7	10	17	8	11	19
12883	8	6	5	9	14	0	0	0	1	2	3	0	0	0	6	11	17	6	11	17
12884	6	6	9	3	12	0	0	0	0	1	1	0	0	0	9	4	13	9	6	15
12885	9	8	9	8	17	0	0	0	0	0	0	0	0	0	9	8	17	10	9	19
12886	9	4	8	5	13	0	0	0	1	0	1	0	0	0	9	5	14	10	7	17
12887	8	8	6	10	16	0	0	0	0	0	0	0	0	0	6	10	16	6	10	16
12888	6	7	7	6	13	0	0	0	0	1	1	0	0	0	7	7	14	8	10	18
12889	1	2	2	1	3	0	0	0	0	0	0	0	0	0	2	1	3	11	4	15
12890	7	8	4	11	15	0	0	0	1	0	1	0	0	0	5	11	16	5	11	16
12891	8	5	6	7	13	0	0	0	0	0	0	0	0	0	6	7	13	6	7	13
12892	5	10	8	7	15	0	0	0	0	0	0	0	0	0	8	7	15	8	7	15
12893	10	6	11	5	16	0	0	0	0	0	0	0	0	0	11	5	16	14	7	21
12894	7	7	8	6	14	0	0	0	0	1	1	0	0	0	8	7	15	8	7	15
12895	8	6	6	8	14	0	0	0	1	0	1	0	0	0	7	8	15	7	8	15
12896	6	8	5	9	14	0	0	0	0	0	0	0	0	0	5	9	14	5	10	15
12897	7	8	6	9	15	0	0	0	0	0	0	0	0	0	6	9	15	9	9	18
12898	6	12	11	7	18	0	0	0	0	0	0	0	0	0	11	7	18	11	8	19
12899	10	3	7	6	13	0	0	0	1	0	1	0	0	0	8	6	14	8	7	15
12900	9	7	10	6	16	0	0	0	0	0	0	0	0	0	10	6	16	11	6	17

M = MALE F = FEMALE
PLACENTAE APPEARED NORMAL UNLESS NOTED OTHERWISE.

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T 6316.7)

TABLE 18 (PAGE 5): CAESAREAN-SECTIONING OBSERVATIONS - INDIVIDUAL DATA

			VIABLE FETUSES			DEAD FETUSES			EARLY RESORPTIONS			LATE RESORPTIONS			IMPLANTATION SITES			CORPORA LUTEA		
RAT #	SEX M	SEX F	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT OVARY	LEFT OVARY	TOTAL
DOSAGE GROUP V					20 MG/KG/DAY															
12901	11	6	9	8	17	0	0	0	0	0	0	0	0	0	9	8	17	9	8	17
12902	4	8	7	5	12	0	0	0	1	0	1	0	0	0	9	5	14	11	6	17
12903	8	6	8	6	14	0	0	0	1	0	1	0	0	0	9	6	15	10	7	17
12904	2	8	6	4	10	0	0	0	1	2	3	0	0	0	7	6	13	8	7	15
12905	5	7	6	6	12	0	0	0	0	0	0	0	0	0	6	6	12	7	8	15
12906	6	7	7	6	13	0	0	0	1	0	1	0	0	0	8	6	14	8	6	14
12907	6	3	0	9	9	0	0	0	0	1	1	0	0	0	0	10	10	8	10	18
12908	6	8	3	11	14	0	0	0	0	2	2	0	0	0	3	13	16	4	14	18
12909	8	4	7	5	12	0	0	0	0	1	1	0	0	0	7	6	13	9	8	17
12910	NOT PREGNANT																			
12911	9	4	5	8	13	0	0	0	1	0	1	0	0	0	6	8	14	6	8	14
12912	7	6	9	4	13	0	0	0	0	0	0	0	0	0	9	4	13	11	4	15
12913	7	5	5	7	12	0	0	0	1	0	1	0	0	0	6	7	13	9	8	17
12914	8	7	12	3	15	0	0	0	0	0	0	0	0	0	12	3	15	12	4	16
12915	8	6	8	6	14	0	0	0	1	2	3	0	0	0	9	8	17	9	13	22
12916	8	8	8	8	16	0	0	0	0	1	1	0	0	0	8	9	17	8	9	17
12917	10	4	9	5	14	0	0	0	1	0	1	0	0	0	10	5	15	11	6	17
12918	5	10	12	3	15	0	0	0	0	1	1	0	0	0	12	4	16	12	5	17
12919	8	6	6	8	14	0	0	0	0	0	0	0	0	0	6	8	14	6	8	14
12920	8	8	9	7	16	0	0	0	0	0	0	0	0	0	9	7	16	10	9	19
12921	6	8	7	7	14	0	0	0	0	0	0	0	0	0	7	7	14	7	10	17
12922	7	5	7	5	12	0	0	0	1	2	3	0	0	0	8	7	15	8	8	16
12923	7	7	8	6	14	0	0	0	0	0	0	0	0	0	8	6	14	8	6	14
12924	7	8	8	7	15	0	0	0	0	0	0	0	0	0	8	7	15	8	8	16
12925	11	5	9	7	16	0	0	0	0	0	0	0	0	0	9	7	16	9	9	18

M = MALE F = FEMALE
PLACENTAE APPEARED NORMAL UNLESS NOTED OTHERWISE.

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ELFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 18 (PAGE 6): CAESAREAN-SECTIONING OBSERVATIONS - INDIVIDUAL DATA

RAT #	VIABLE FETUSES RIGHT HORN	VIABLE FETUSES LEFT HORN	VIABLE FETUSES TOTAL	DEAD FETUSES RIGHT HORN	DEAD FETUSES LEFT HORN	DEAD FETUSES TOTAL	EARLY RESORPTIONS RIGHT HORN	EARLY RESORPTIONS LEFT HORN	EARLY RESORPTIONS TOTAL	LATE RESORPTIONS RIGHT HORN	LATE RESORPTIONS LEFT HORN	LATE RESORPTIONS TOTAL	IMPLANTATION SITES RIGHT HORN	IMPLANTATION SITES LEFT HORN	IMPLANTATION SITES TOTAL	CORPORA LUTEA RIGHT OVARY	CORPORA LUTEA LEFT OVARY	CORPORA LUTEA TOTAL
SATELLITE DOSAGE GROUP I							0 (VEHICLE) MG/KG/DAY											
12573	12	3	15	0	0	0	1	0	1	0	0	0	13	3	16	13	3	16
12574	9	9	18	0	0	0	0	0	0	0	0	0	9	9	18	12	12	24
12575	6	1	7	0	0	0	0	0	0	0	0	0	6	1	7	6	6	12
SATELLITE DOSAGE GROUP II							1 MG/KG/DAY											
12576	11	3	14	0	0	0	1	0	1	0	0	0	12	3	15	15	5	20
12577	7	11	18	0	0	0	0	0	0	0	0	0	7	11	18	8	12	20
12578	6	10	16	0	0	0	0	1	1	0	0	0	6	11	17	8	11	19
12579	10	5	15	0	0	0	0	0	0	0	0	0	10	5	15	10	5	15
12580	10	4	14	0	0	0	0	1	1	0	0	0	10	5	15	11	5	16
SATELLITE DOSAGE GROUP III							5 MG/KG/DAY											
12581	6	7	13	0	0	0	0	2	2	0	0	0	6	9	15	6	9	15
12582	13	5	18	0	0	0	0	0	0	0	0	0	13	5	18	14	7	21
12583	13	7	20	0	0	0	0	0	0	0	0	0	13	7	20	13	11	24
SATELLITE DOSAGE GROUP IV							10 MG/KG/DAY											
12584	9	6	15	0	0	0	2	0	2	0	0	0	11	6	17	14	8	22
12585	6	10	16	0	0	0	0	0	0	0	0	0	6	10	16	6	10	16
12586	8	5	13	0	0	0	0	1	1	0	0	0	8	6	14	9	7	16
SATELLITE DOSAGE GROUP V							20 MG/KG/DAY											
12587	9	5	14	0	0	0	0	0	0	0	0	0	9	5	14	9	5	14
12588	9	6	15	0	0	0	0	0	0	0	0	0	9	6	15	9	6	15
12589	7	7	14	0	0	0	0	0	0	0	0	0	7	7	14	7	7	14
12590	11	3	14	0	0	0	0	1	1	0	0	0	12	4	16	12	4	16
12591	9	7	16	0	0	0	0	1	1	0	0	0	10	7	17	10	9	19

PLACENTAE APPEARED NORMAL UNLESS NOTED OTHERWISE.

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T 6316.7)

TABLE 19 (PAGE 1): LITTER OBSERVATIONS (CAESAREAN-DELIVERED FETUSES) - INDIVIDUAL DATA

	NUMBER OF LIVE FETUSES			AVERAGE FETAL BODY WEIGHT (G)			CONCEPTUSES RESORBED		
RAT #	MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL a	N	N	%
DOSAGE GROUP 1				0 (VEHICLE) MG/KG/DAY					
12801	9	4	13	3.62	3.37	3.54	14	1	7.1
12802	9	5	14	2.03	1.89	1.98	15	1	6.7
12803	9	7	16	3.49	3.46	3.48	16	0	0.0
12804	5	8	13	3.63	3.44	3.51	13	0	0.0
12805	7	8	15	3.64	3.55	3.59	15	0	0.0
12806	9	6	15	3.64	3.36	3.53	15	2	12.5
12807	6	8	14	3.39	3.51	3.46	16	5	29.4
12808	7	5	12	3.70	3.42	3.58	17	0	0.0
12809	8	10	18	5.25	5.11	5.17	18	0	0.0
12810	6	4	10	3.58	3.14	3.40	10	0	0.0
12811	4	10	14	3.78	3.51	3.59	14	1	6.7
12812	7	7	14	3.54	3.24	3.39	15		
12813	NOT PREGNANT	9	16	3.77	3.45	3.59	18	2	11.1
12814	7	9	15	3.56	3.43	3.48	17	2	11.8
12815	6	5	12	3.62	3.35	3.51	14	2	14.3
12816	7	7	15	3.44	2.85	3.17	15	0	0.0
12817	8	7	15	3.76	3.49	3.55	15	2	13.3
12818	3	10	13	3.27	3.01	3.10	16	1	6.2
12819	5	10	15	3.52	3.38	3.44	15	1	6.7
12820	6	8	14	3.31	3.14	3.25	15	0	0.0
12821	10	5	15	3.54	3.16	3.41	15	0	0.0
12822	10	6	15	3.84	3.87	3.85	15	1	6.7
12823	8	8	14	3.87	3.42	3.57	12	0	0.0
12824	4	11	12	3.96	3.66	3.78	18	0	0.0
12825	7		18						

a. TOTAL = SUM OF FETAL WEIGHTS/NUMBER OF LIVE FETUSES.

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ELFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 19 (PAGE 2): LITTER OBSERVATIONS (CAESAREAN-DELIVERED FETUSES) - INDIVIDUAL DATA

RAT #	NUMBER OF LIVE FETUSES			AVERAGE FETAL BODY WEIGHT (G)			CONCEPTUSES	RESORBED	
	MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL a	N	N	%
DOSAGE GROUP II					1 MG/KG/DAY				
12826	8	6	14	3.33	2.94	3.16	14	0	0.0
12827	5	8	13	3.39	3.21	3.28	14	1	7.1
12828	10	8	18	3.53	3.27	3.41	18	0	0.0
12829	8	6	14	3.00	3.03	3.01	15	1	6.7
12830	7	8	15	3.77	3.60	3.68	15	0	0.0
12831	6	10	16	3.48	3.18	3.30	17	1	5.9
12832	7	7	14	3.12	2.98	3.05	15	1	6.7
12833	10	3	13	3.30	3.27	3.30	14	1	7.1
12834	9	6	15	3.48	3.35	3.43	15	0	0.0
12835	3	6	9	3.68	3.49	3.55	9	0	0.0
12836	6	9	15	3.48	3.20	3.32	16	1	6.2
12837	4	10	14	3.85	3.67	3.72	15	1	6.7
12838	8	7	15	3.48	3.21	3.35	15	0	0.0
12839	6	11	17	3.42	3.22	3.29	17	0	0.0
12840	11	6	17	3.23	2.85	3.10	17	0	0.0
12841	9	8	17	3.46	3.18	3.33	17	0	0.0
12842	9	7	16	3.78	3.56	3.68	16	1	7.1
12843	5	8	13	3.74	3.58	3.64	14	0	0.0
12844	6	11	17	3.90	3.63	3.72	17		
12845	NOT PREGNANT								
12846	NOT PREGNANT								
12847	11	7	18	3.29	2.96	3.16	18	0	0.0
12848	7	11	18	3.36	3.08	3.19	18	0	0.0
12849	9	6	15	3.52	3.24	3.41	15	0	0.0
12850	7	9	16	3.34	3.05	3.18	18	2	11.1

a. TOTAL = SUM OF FETAL WEIGHTS/NUMBER OF LIVE FETUSES.

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 19 (PAGE 3): LITTER OBSERVATIONS (CAESAREAN DELIVERED FETUSES) - INDIVIDUAL DATA

	NUMBER OF LIVE FETUSES			AVERAGE FETAL BODY WEIGHT (G)			CONCEPTUSES	RESORBED	
RAT #	MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL a	N	N	%
DOSAGE GROUP III					5 MG/KG/DAY				
12851	7	8	15	3.69	3.36	3.51	16	1	6.2
12852	8	8	16	3.34	3.20	3.27	16	0	0.0
12853	5	9	14	3.78	3.65	3.70	15	1	6.7
12854	6	10	16	3.52	3.07	3.24	16	0	0.0
12855	NOT PREGNANT								
12856	5	9	14	3.55	3.24	3.35	14	0	0.0
12857	11	8	19	3.34	3.16	3.26	19	0	0.0
12858	7	7	14	3.55	3.43	3.49	15	1	6.7
12859	10	7	17	3.20	3.20	3.20	17	0	0.0
12860	7	8	15	3.82	3.55	3.67	16	1	6.2
12861	6	6	12	3.12	2.98	3.04	14	2	14.3
12862	7	8	15	2.95	2.91	2.93	15	0	0.0
12863	5	9	14	3.67	3.37	3.48	15	1	6.7
12864	6	8	14	3.76	3.52	3.62	14	0	0.0
12865	5	10	15	3.67	3.44	3.52	17	2	11.8
12866	9	10	19	3.42	3.21	3.31	19	0	0.0
12867	9	5	14	3.44	3.15	3.34	14	0	0.0
12868	1	4	5	3.35	3.16	3.19	7	2	28.6
12869	9	6	15	3.35	3.20	3.29	15	0	0.0
12870	6	10	16	3.69	3.40	3.51	16	0	0.0
12871	8	6	14	3.46	3.26	3.37	16	2	12.5
12872	9	5	14	3.32	3.19	3.27	14	0	0.0
12873	5	9	14	3.54	3.41	3.45	15	1	6.7
12874	7	9	16	3.66	3.54	3.59	17	1	5.9
12875	8	2	10	3.68	3.38	3.62	15	5	33.3

a. TOTAL = SUM OF FETAL WEIGHTS/NUMBER OF LIVE FETUSES.

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 19 (PAGE 4): LITTER OBSERVATIONS (CAESAREAN-DELIVERED FETUSES) - INDIVIDUAL DATA

	NUMBER OF LIVE FETUSES			AVERAGE FETAL BODY WEIGHT (G)			---- CONCEPTUSES ---- RESORBED		
RAT #	MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL a	N	N	%
DOSAGE GROUP IV					10 MG/KG/DAY				
12876	9	6	15	3.67	3.59	3.64	15	0	0.0
12877	6	8	14	3.27	3.08	3.16	14	0	0.0
12878	7	8	15	3.53	3.34	3.43	15	0	0.0
12879	9	6	15	3.39	3.46	3.42	15	0	0.0
12880	8	7	15	3.32	3.08	3.21	15	0	0.0
12881	6	6	12	3.12	2.82	2.97	14	2	14.3
12882	6	11	17	3.69	3.43	3.52	17	0	0.0
12883	8	6	14	3.40	3.30	3.36	17	3	17.6
12884	6	6	12	3.18	3.14	3.16	13	1	7.7
12885	9	8	17	3.26	2.86	3.07	17	0	0.0
12886	9	4	13	3.60	3.45	3.55	14	1	7.1
12887	8	8	16	3.21	2.95	3.08	16	0	0.0
12888	6	7	13	3.01	2.98	3.00	14	1	7.1
12889	1	2	3	3.47	3.66	3.60	3	0	0.0
12890	7	8	15	3.24	3.04	3.14	16	1	6.2
12891	8	5	13	3.82	3.52	3.70	13	0	0.0
12892	5	10	15	3.60	3.43	3.49	15	0	0.0
12893	10	6	16	3.39	3.26	3.34	16	0	0.0
12894	7	7	14	3.55	3.69	3.62	15	1	6.7
12895	8	6	14	3.25	3.18	3.22	15	1	6.7
12896	6	8	14	3.48	3.34	3.40	14	0	0.0
12897	7	8	15	3.38	3.41	3.40	15	0	0.0
12898	6	12	18	3.22	3.23	3.22	18	0	0.0
12899	10	3	13	3.31	3.24	3.29	14	1	7.1
12900	9	7	16	3.22	3.25	3.24	16	0	0.0

a. TOTAL = SUM OF FETAL WEIGHTS/NUMBER OF LIVE FETUSES.

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 19 (PAGE 5): LITTER OBSERVATIONS (CAESAREAN-DELIVERED FETUSES) - INDIVIDUAL DATA

	NUMBER OF LIVE FETUSES			AVERAGE FETAL BODY WEIGHT (G)			CONCEPTUSES RESORBED		
RAT #	MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL a	N	N	%
DOSAGE GROUP V					20 MG/KG/DAY				
12901	11	6	17	3.28	3.07	3.21	17	0	0.0
12902	4	8	12	3.23	3.05	3.11	14	2	14.3
12903	8	6	14	3.21	3.00	3.12	15	1	6.7
12904	2	8	10	3.20	3.01	3.04	13	3	23.1
12905	5	7	12	3.34	3.28	3.31	12	0	0.0
12906	6	7	13	3.41	3.24	3.32	14	1	7.1
12907	6	3	9	2.96	2.86	2.93	10	1	10.0
12908	6	8	14	3.15	2.98	3.05	16	2	12.5
12909	8	4	12	3.12	2.68	2.97	13	1	7.7
12910	NOT PREGNANT								
12911	9	4	13	3.27	2.95	3.17	14	1	7.1
12912	7	6	13	3.74	3.34	3.55	13	0	0.0
12913	7	5	12	2.97	2.99	2.98	13	1	7.7
12914	8	7	15	3.43	3.20	3.32	15	0	0.0
12915	8	6	14	3.59	3.20	3.42	17	3	17.6
12916	8	8	16	3.05	2.85	2.95	17	1	5.9
12917	10	4	14	3.18	2.82	3.07	15	1	6.7
12918	5	10	15	3.27	3.05	3.12	16	1	6.2
12919	8	6	14	3.24	2.99	3.13	14	0	0.0
12920	8	8	16	3.35	3.09	3.22	16	0	0.0
12921	6	8	14	3.36	3.27	3.31	14	0	0.0
12922	7	5	12	3.18	3.07	3.14	15	3	20.0
12923	7	7	14	3.44	3.25	3.35	14	0	0.0
12924	7	8	15	3.39	3.13	3.25	15	0	0.0
12925	11	5	16	2.91	2.91	2.91	16	0	0.0

a. TOTAL = SUM OF FETAL WEIGHTS/NUMBER OF LIVE FETUSES.

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 19 (PAGE 6): LITTER OBSERVATIONS (CAESAREAN-DELIVERED FETUSES) - INDIVIDUAL DATA

	NUMBER OF LIVE FETUSES	AVERAGE FETAL BODY WEIGHT (G)	CONCEPTUSES RESORBED		
RAT #	TOTAL	TOTAL a	N	N	%
SATELLITE DOSAGE GROUP I		0 (VEHICLE) MG/KG/DAY			
12573	15	1.15	16	1	6.2
12574	18	1.19	18	0	0.0
12575	7	1.43	7	0	0.0
SATELLITE DOSAGE GROUP II		1 MG/KG/DAY			
12576	14	1.31	15	1	6.7
12577	18	1.38	18	0	0.0
12578	16	1.28	17	1	5.9
12579	15	1.37	15	0	0.0
12580	14	1.46	15	1	6.7
SATELLITE DOSAGE GROUP III		5 MG/KG/DAY			
12581	13	1.43	15	2	13.3
12582	18	1.30	18	0	0.0
12583	20	1.34	20	0	0.0
SATELLITE DOSAGE GROUP IV		10 MG/KG/DAY			
12584	15	1.22	17	2	11.8
12585	16	1.17	16	0	0.0
12586	13	1.26	14	1	7.1
SATELLITE DOSAGE GROUP V		20 MG/KG/DAY			
12587	14	1.16	14	0	0.0
12588	15	1.35	15	0	0.0
12589	14	1.32	14	0	0.0
12590	14	1.41	16	2	12.5
12591	16	1.32	17	1	5.9

a. TOTAL = SUM OF FETAL WEIGHTS/NUMBER OF LIVE FETUSES.

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 20 (PAGE 1): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
DOSAGE GROUP I	0 (VEHICLE) MG/KG/DAY																						
RAT # CLs																							
12801 8/ 9	MA	MA	FA	FA	MA	MA	MA	MA / MA	FA	MA	E	FA	MA										
	3.54	3.90	3.31	3.15	3.41	3.58	3.64	3.84	3.48	3.51	3.36		3.51	3.80									
12802 10/ 9	MA	FA	FA	FA	MA	MA	E	FA	MA	MA / MA	MA	MA	FA	MA									
	2.01	1.70	1.94	1.83	1.89	2.01		1.82	2.06	2.14	1.95	2.12	2.05	2.15	2.08								
12803 9/ 8	MA	MA	MA	FA	FA	MA	FA	MA / MA	FA	FA	FA	MA	MA	MA	FA								
	3.28	3.60	3.72	3.44	3.66	3.82	3.24	3.40	3.26	3.88	3.51	3.08	3.39	3.30	3.65	3.43							
12804 6/11	MA	FA	MA	FA	FA / FA	FA	FA	FA	MA	MA	FA	MA											
	3.44	3.50	3.72	3.43	3.18	3.53	3.46	3.41	3.53	3.59	3.51	3.45	3.88										
12805 10/ 7	FA	MA	FA	FA	FA	FA	FA	FA / MA	MA	MA	MA	FA	MA	MA									
	3.47	3.84	3.62	3.48	3.30	3.49	3.59	3.91	3.42	3.99	3.41	3.51	3.52	3.63	3.72								
12806 9/ 7	MA	FA	MA	MA	MA	MA	FA	FA	FA / MA	FA	MA	MA	MA	FA									
	3.65	3.36	3.67	3.62	3.81	3.31	3.18	3.27	3.49	3.62	3.50	3.46	3.76	3.85	3.34								
12807 5/12	MA	FA	FA	E	MA / MA	FA	FA	FA	MA	MA	FA	MA	E	FA	FA								
	3.41	3.64	3.62		3.02	3.63	3.81	3.30	3.09	3.60	3.27	3.68	3.41		3.50	3.47							
12808 9/11	FA	E	E	FA	MA	FA	MA	MA / FA	FA	E	MA	MA	MA	E	E	MA							
	3.43			3.75	3.91	3.35	3.58	3.82	3.18	3.38		3.57	3.80	3.65		3.57							
12809 10/ 9	FA	FA	FA	FA	FA	MA	FA	FA	MA	MA / FA	FA	FA	MA	MA	MA	MA	MA						
	5.33	5.24	4.95	5.36	5.03	5.52	4.86	5.06	5.08	5.47	4.83	5.05	5.41	4.91	5.32	4.84	5.43	5.43					
12810 5/10	/ FA	FA	FA	MA	MA	MA	MA	MA	MA	FA													
	2.95	3.21	2.96	3.84	3.81	3.34	3.55	3.54	3.39	3.46													
12811 7/ 9	FA	FA	FA	FA	MA / FA	FA	FA	FA	FA	MA	FA	MA	MA										
	3.46	3.38	3.72	3.30	3.81	3.61	3.75	3.56	3.45	3.46	3.86	3.43	3.77	3.68									
12812 10/ 6	FA	MA	MA	MA	FA	E	MA	MA	FA / FA	MA	FA	FA	FA	MA									
	3.61	3.40	3.33	3.47	3.41		3.40	3.56	3.23	3.32	3.66	2.68	3.19	3.26	4.00								
12813	NOT PREGNANT																						

M = MALE F = FEMALE A = ALIVE E = EARLY RESORPTION "/" DENOTES POSITION OF CERVIX
CLs = CORPORA LUTEA/OVARY FETAL BODY WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ELFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 20 (PAGE 2): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
DOSAGE GROUP 1	0 (VEHICLE) MG/KG/DAY																						
RAT # CLS																							
12814 9/10	FA	E	MA	FA	MA	FA	FA	MA / MA	FA	FA	FA	E	FA	MA	MA	MA	FA						
	3.37		3.77	3.65	3.80	3.55	3.44	4.03	3.61	3.22	3.36	3.46		3.62	3.76	3.78	3.39	3.65					
12815 10/ 9	E	E	FA	FA	MA	MA	FA	FA	MA / FA	FA	FA	FA	FA	FA	MA	MA	MA	FA					
			3.32	3.78	3.52	3.35	3.36	3.45	3.57	3.43	3.57	3.04	3.41	3.80	3.62	3.65	3.36						
12816 7/ 7	E	MA	FA	MA	FA	MA		E / FA	FA	FA	3.28	3.38	3.81	3.76	3.64	3.54							
		3.85	3.53	3.40	3.45	3.36		3.09	FA	MA	MA	MA	MA	FA	2.63	3.16	3.31						
12817 6/ 9	MA	MA	MA	FA	FA	FA / FA	FA	FA	3.22	3.35	3.29	3.73	FA	FA	FA	FA							
	3.67	3.78	3.25	2.99	1.82	3.25	3.13	2.93	MA	MA	FA /	E	3.54	3.35	3.56	3.77							
12818 12/ 6	FA	FA	FA	MA	FA		E	FA	MA	MA	3.71	MA / FA	MA	FA	FA	E	MA						
	3.14	3.29	3.80	3.60	3.43		3.30	3.90	3.77	3.71			3.07	3.53	3.02	3.21	3.41						
12819 11/ 6	FA	FA	FA	MA	FA	FA	MA	FA	2.70	2.85	3.29	3.07	3.53	E	MA	FA	MA						
	2.91	3.30	2.77	3.13	3.37	2.90	3.01	FA / MA	FA	FA	FA		3.72	3.31	3.60								
12820 8/ 7	FA	MA	FA	MA	FA	MA	FA	3.27	3.42	3.22	3.22		FA	MA	FA								
	3.36	3.46	3.80	3.27	3.55	3.63	3.30	MA / MA	MA	MA	3.40	3.06	3.18	3.09	3.32	3.13							
12821 11/10	MA	MA	MA	FA	MA	MA	3.27	3.19	3.32	MA	MA	MA	FA	FA	MA	MA							
	3.13	3.15	3.43	3.22	3.80	3.08	FA / MA		3.38	3.34	3.31	3.27	3.48	3.80									
12822 7/10	MA	FA	FA	MA	MA	3.58	3.34	3.45	3.19	MA	MA / MA	FA	E	FA	4.09								
	3.46	3.17	2.71	3.78	3.89	3.58	MA	FA	FA	3.52	4.28	3.97	3.68	3.65									
12823 12/ 5	MA	MA	FA	MA	MA	3.86	4.40	3.97	3.52	FA	FA	FA	FA										
	3.68	3.45	3.60	3.56	4.20	3.86	MA / FA	FA	FA	3.20	3.38	3.40	3.52	3.37									
12824 7/ 7	FA	MA	MA	FA	MA	MA	MA / FA		3.63	2.99	3.20	3.38	MA	MA	FA	FA	FA	MA	FA	MA	FA		
	3.59	4.00	3.86	3.91	4.00	3.63	2.99	3.20	3.38	3.40	3.52	3.37											
12825 8/10	FA	FA	MA	FA	FA	MA	MA	FA / FA		MA	MA	MA	FA	FA	FA	MA	FA						
	3.67	3.59	3.97	3.74	3.54	4.08	4.05	3.59	3.61	3.98	3.75	3.69	3.58	3.69	3.80	3.78	4.12	3.75					

"/" DENOTES POSITION OF CERVIX

M = MALE F = FEMALE A = ALIVE E = EARLY RESORPTION

CLS = CORPORA LUTEA/OVARY FETAL BODY WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 20 (PAGE 3): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
DOSAGE GROUP II												1 MG/KG/DAY											
RAT # CLs																							
12826 12/ 5	FA	MA	FA	MA	MA	MA	MA	MA	FA / FA		MA	MA	FA	FA									
	2.26	3.30	3.22	3.42	3.14	3.31	3.46	3.56	3.16	2.89	3.33	3.12	2.95	3.19									
12827 8/ 9	FA	MA	FA	FA	FA	FA	MA / MA		MA	FA	MA	FA	E	FA									
	2.95	3.39	3.12	3.55	3.21	3.16	3.30	3.60	3.40	3.09	3.24	3.30		3.32									
12828 11/ 8	FA	MA	MA	MA	MA	MA	FA	MA	MA	MA	FA / FA		FA	MA	FA	FA	MA	FA					
	3.29	3.57	3.53	3.26	3.59	3.50	3.47	3.65	3.35	3.23	3.23	3.08	3.05	3.63	3.49	3.12	3.98	3.44					
12829 8/ 8	MA	E	FA	MA	FA	MA	MA	FA / MA		MA	FA	FA	FA	MA	MA								
	2.88		3.13	3.05	3.16	3.45	3.03	3.14	2.79	2.72	2.99	2.86	2.89	3.07	3.01								
12830 9/ 7	MA	FA	FA	FA	FA	FA	FA	MA / FA		FA	MA	MA	MA	MA	MA								
	3.85	3.60	3.58	3.76	3.63	3.77	3.59	3.80	3.19	3.65	3.33	3.48	4.14	3.88	3.92								
12831 12/ 5	FA	MA	FA	FA	FA	MA	E	FA	FA	FA	FA	FA / MA		MA	FA	MA	MA						
	3.32	3.22	3.25	2.89	3.26	3.22		3.29	3.23	2.95	3.07	3.41	3.34	3.49	3.18	3.76	3.85						
12832 10/10	MA	FA	E	FA	MA	FA	MA / FA		MA	MA	FA	FA	MA	MA	FA								
	3.24	3.00		2.79	3.13	3.20	3.16	3.03	3.36	2.93	2.91	2.98	3.04	3.02	2.93								
12833 8/ 6	FA	MA	MA	E	MA	MA	MA	MA / MA		MA	MA	FA	MA	FA									
	3.46	3.40	3.42		3.07	3.20	3.45	3.09	3.56	2.95	3.33	3.08	3.56	3.27									
12834 5/10	FA	FA	FA	MA	FA / FA		MA	MA	MA	MA	MA	MA	FA	MA	MA								
	3.49	3.41	3.14	3.41	3.40	3.42	3.38	3.34	3.70	3.72	3.57	3.52	3.25	3.18	3.49								
12835 9/ 8	MA	FA / FA		FA	FA	MA	FA	MA	FA														
	3.52	3.60	3.73	3.80	2.36	3.77	3.92	3.76	3.52														
12836 8/10	FA	E	FA	FA	FA	MA	FA	FA / MA		MA	MA	FA	MA	FA	MA	FA							
	2.84		3.06	3.19	3.18	3.47	3.63	3.30	3.39	3.20	3.91	3.36	3.64	3.06	3.29	3.23							
12837 8/ 8	FA	FA	MA	E	FA	FA	FA	FA / FA		FA	MA	MA	FA	FA	MA								
	3.54	3.49	3.74		3.80	3.69	3.78	3.64	3.58	3.74	3.84	3.91	4.26	3.14	3.92								
12838 9/ 6	MA	FA	FA	MA	MA	FA	MA	MA	FA / FA		MA	MA	FA	FA	MA								
	3.12	3.25	3.43	3.60	3.46	3.51	3.67	3.23	2.40	3.26	3.84	3.51	3.17	3.46	3.39								

M = MALE F = FEMALE A = ALIVE E = EARLY RESORPTION "/" DENOTES POSITION OF CERVIX
CLs = CORPORA LUTEA/OVARY FETAL BODY WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 20 (PAGE 4): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

FETUS #		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
DOSAGE GROUP II											1 MG/KG/DAY													
RAT #	CLs																							
12839	7/11	FA	FA	MA	FA	FA	MA	FA / MA	FA	MA	FA	FA	FA	MA	FA	FA	MA							
		2.69	3.32	3.40	2.91	3.16	3.37	3.23	3.49	3.27	3.09	3.11	3.33	3.23	3.63	3.36	3.87	3.51						
12840	9/10	FA	MA	MA	MA	MA	FA	MA	MA	FA / MA	MA	FA	FA	FA	MA	MA	MA							
		2.90	3.19	3.33	3.11	3.68	2.96	3.19	3.13	3.03	3.31	3.07	2.56	2.86	2.79	3.24	3.17	3.12						
12841	9/ 8	FA	MA	FA	MA	MA	FA	MA	FA	MA / MA	MA	FA	FA	MA	FA	FA	MA							
		3.39	3.69	3.14	3.56	3.25	3.13	3.31	2.62	3.53	3.60	3.13	3.29	3.32	3.43	3.11	3.44	3.68						
12842	10/ 6	FA	MA	MA	MA	MA	FA	MA	MA	FA	FA / MA	MA	FA	MA	FA	FA								
		3.18	3.54	3.81	4.17	3.97	3.60	3.84	3.70	3.82	3.66	3.51	3.81	3.52	3.65	3.77	3.39							
12843	7/ 8	FA	MA	FA	FA	MA	FA	MA / FA	FA	FA	FA	MA	E	MA										
		3.66	3.34	3.57	3.51	3.99	3.40	3.39	3.58	3.41	3.62	3.91	3.98	4.02										
12844	11/ 8	MA	FA	FA	FA	FA	FA	MA	MA	MA	FA	MA / FA	FA	FA	FA	MA	FA	FA						
		3.70	3.94	3.49	3.75	3.65	3.74	3.73	3.93	3.88	3.55	4.22	3.36	3.58	3.43	3.93	3.92	3.51						
12845		NOT PREGNANT																						
12846		NOT PREGNANT																						
12847	15/ 6	MA	MA	MA	MA	MA	MA	MA	FA	MA	FA	FA	FA	FA	FA / MA	MA	MA	FA						
		3.63	2.80	3.07	2.97	3.28	3.62	2.80	3.03	3.28	3.24	2.74	2.92	2.92	2.65	3.78	3.45	3.52	3.21					
12848	13/ 7	MA	MA	FA	MA	FA	MA	FA	MA	FA	FA	FA	FA	FA / MA	FA	MA	FA	FA						
		3.19	3.31	2.99	3.78	3.08	3.40	3.18	3.27	3.26	2.86	3.09	3.15	3.06	3.16	3.01	3.43	3.04	3.12					
12849	9/ 6	MA	FA	MA	MA	FA	FA	FA	MA	MA / MA	FA	FA	MA	MA	MA									
		3.72	3.31	3.45	3.60	3.40	3.07	3.36	3.58	3.49	3.35	3.30	3.03	3.65	3.46	3.39								
12850	7/12	FA	MA	MA	FA	MA	FA	MA / MA	FA	FA	E	E	FA	FA	FA	MA	FA	MA						
		3.39	3.66	3.32	3.45	3.14	3.14	3.37	3.25	2.95	2.91		3.23	3.00	3.07	3.46	2.33	3.18						

M = MALE F = FEMALE A = ALIVE E = EARLY RESORPTION "/" DENOTES POSITION OF CERVIX
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PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 20 (PAGE 5): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
DOSAGE GROUP III										5 MG/KG/DAY													
RAT # CLs																							
12851 6/12	FA	MA	E	MA	MA / FA	FA	MA	FA	FA	FA	MA	MA	FA	FA	MA								
	3.42	3.57		3.55	3.80	3.25	3.13	3.77	3.34	3.20	3.54	3.84	3.48	3.52	3.48	3.82							
12852 6/11	FA	FA	MA	FA	MA	MA / MA	MA	FA	FA	MA	FA	MA	MA	FA	FA								
	3.09	3.31	3.29	3.22	3.23	3.58	3.12	3.44	3.10	2.98	3.36	3.21	3.30	3.39	3.29	3.38							
12853 10/ 7	MA	FA	MA	FA	FA	FA	FA	FA	MA	FA / MA	MA	E	FA	FA									
	3.26	3.52	3.87	3.65	3.48	3.76	3.82	3.50	3.66	3.35	4.00	4.09		4.03	3.75								
12854 8/10	MA	FA	FA	MA	FA	MA	MA / FA	FA	FA	FA	MA	FA	MA	FA	FA								
	3.57	2.90	3.21	3.44	2.98	3.43	3.50	2.96	2.29	3.24	3.24	3.59	3.50	3.56	3.18	3.24							
12855	NOT PREGNANT																						
12856 5/ 9	FA	MA	FA	FA	MA / FA	MA	FA	FA	FA	FA	MA	FA	MA										
	3.35	3.57	3.10	3.56	3.61	3.16	3.47	3.47	2.68	3.43	3.16	3.61	3.21	3.49									
12857 12/11	MA	MA	FA	MA	MA	MA	MA	MA	FA / MA	FA	MA	MA	MA	FA	FA	FA	FA	FA					
	3.31	3.30	3.34	3.50	3.28	3.49	3.40	3.31	3.45	3.18	3.13	3.19	3.21	3.56	3.14	2.61	3.24	2.93	3.44				
12858 6/11	MA	FA	MA	E	FA	FA / MA	MA	FA	FA	MA	FA	MA	FA	MA									
	3.59	3.83	3.88		3.50	3.73	3.25	3.73	3.13	3.34	3.38	3.47	3.32	2.99	3.70								
12859 10/ 7	MA	MA	FA	FA	FA	MA	MA	MA	MA	FA / MA	MA	FA	FA	MA	MA	FA							
	3.21	3.19	3.15	3.26	3.24	3.31	3.29	3.21	3.22	3.28	2.97	3.22	3.21	3.12	3.26	3.15	3.17						
12860 9/11	MA	E	MA	MA	FA	MA	MA / FA	MA	FA	FA	MA	FA	FA	FA	FA								
	3.54		3.43	3.64	3.70	4.31	4.00	3.50	3.85	3.47	3.55	3.95	3.51	3.53	3.36	3.76							
12861 10/ 8	MA	MA	E	FA	FA	MA	FA	MA	MA / MA	FA	E	FA	FA										
	2.84	3.13		2.91	2.92	3.26	2.89	3.07	3.40	2.99	2.87		3.06	3.20									
12862 8/ 7	MA	FA	FA	FA	MA	MA	FA	MA / FA	MA	MA	FA	FA	MA	FA									
	2.93	2.77	3.02	3.13	2.96	3.13	2.81	2.70	2.77	3.04	2.89	2.99	3.00	3.02	2.76								
12863 5/10	MA	MA	FA	FA	E / FA	MA	MA	FA	FA	FA	FA	FA	MA										
	3.65	3.48	3.40	3.37		3.64	3.78	3.75	3.19	3.24	3.47	3.56	3.14	3.29	3.69								

M = MALE F = FEMALE A = ALIVE E = EARLY RESORPTION "/" DENOTES POSITION OF CERVIX
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PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 20 (PAGE 6): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
DOSAGE GROUP III										5 MG/KG/DAY													
RAT # CLs																							
12864 12/ 5	FA	FA	MA	MA	FA	FA	FA	FA	MA	MA / FA		MA	MA	FA									
	3.51	3.46	3.54	3.77	3.60	3.49	3.67	3.73	3.97	3.91	3.36	3.48	3.90	3.37									
12865 8/ 9	FA	FA	FA	E	MA	FA	FA	MA / FA		FA	MA	FA	FA	MA	FA	E	MA						
	3.32	3.22	3.86		3.87	3.42	3.30	3.28	3.49	3.50	3.65	3.77	3.38	3.84	3.18		3.72						
12866 11/11	FA	FA	FA	FA	FA	FA	MA	MA	FA	FA	FA / MA		FA	MA	MA	MA	MA	MA	MA				
	2.70	3.08	3.15	2.84	3.18	3.38	3.30	3.41	3.46	3.35	3.43	3.39	3.57	3.34	3.52	3.44	3.30	3.44	3.68				
12867 5/10	MA	MA	FA	MA / MA		MA	MA	MA	FA	MA	FA	FA	MA	FA									
	4.00	3.53	3.25	3.46	3.21	3.10	3.53	3.16	3.03	3.53	3.00	3.38	3.44	3.08									
12868 7/ 6	FA	FA / FA		FA	MA	E	E																
	3.22	3.46	3.13	2.81	3.35																		
12869 7/ 8	MA	FA	MA	FA	MA	FA	MA / FA		MA	FA	MA	MA	MA	MA	FA								
	3.50	3.38	3.30	3.30	3.22	3.20	3.35	3.01	3.19	3.21	3.44	3.41	3.55	3.20	3.07								
12870 6/11	FA	MA	MA	FA	FA	FA / MA		MA	MA	MA	FA	FA	MA	FA	FA	FA	FA						
	3.48	3.92	3.91	3.28	3.32	3.09	3.64	3.61	3.37	3.63	3.22	3.68	3.49	3.75	3.33	3.45							
12871 6/11	MA	FA	FA	MA	MA	FA / FA		FA	E	MA	FA	MA	MA	E	MA	MA							
	3.26	3.46	3.33	3.62	3.72	3.55	2.66	3.34		3.29	3.21	3.58	3.19		3.54	3.46							
12872 10/ 6	FA	MA	MA	MA	FA	MA	FA	MA	FA / MA		FA	MA	MA	MA									
	3.21	3.36	3.34	3.45	3.15	3.25	3.29	3.50	3.16	3.11	3.12	3.37	3.44	3.07									
12873 5/13	FA	E	FA	MA	FA / FA		FA	FA	FA	FA	MA	MA	MA	MA	FA								
	3.55		3.78	3.71	3.26	3.34	3.02	2.90	3.59	3.57	3.56	3.57	3.18	3.68	3.65								
12874 7/10	MA	MA	MA	MA	MA	FA	MA / FA		E	FA	FA	FA	FA	MA	FA	FA	FA						
	3.67	3.53	3.75	3.67	3.79	3.62	3.66	3.43		3.36	3.53	3.39	3.77	3.58	3.28	3.54	3.92						
12875 7/ 9	E	E	E	MA	FA	E / MA		FA	MA	E	MA	MA	MA	MA	MA								
				4.04	3.51		3.73	3.25	3.76		3.56	3.71	3.43	3.62	3.57								

M = MALE F = FEMALE A = ALIVE E = EARLY RESORPTION "/" DENOTES POSITION OF CERVIX
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PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 20 (PAGE 7): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

FETUS #		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
DOSAGE GROUP IV											10 MG/KG/DAY													
RAT #	CLs																							
12876	9/ 8	MA	FA	FA	MA	FA	MA	MA	MA / FA		MA	MA	MA	FA	MA	FA								
		3.48	3.62	3.64	3.79	3.21	3.55	3.49	3.91	3.63	3.46	3.62	3.84	3.62	3.89	3.81								
12877	11/ 6	FA	MA	FA	MA	MA	FA	FA	FA	FA / MA		MA	MA	FA	FA									
		2.93	3.13	3.07	3.28	3.23	2.88	3.28	2.95	3.27	3.40	3.44	3.14	3.08	3.16									
12878	4/12	MA	FA	MA / MA		MA	FA	FA	FA	MA	MA	MA	FA	FA	FA	FA								
		3.80	3.88	3.82	3.36	3.44	3.20	3.30	3.63	3.31	3.40	3.60	3.34	3.15	3.00	3.18								
12879	10/ 9	FA	FA	MA	FA	FA	FA	MA	MA / MA		MA	MA	MA	MA	MA	FA								
		3.21	3.83	3.61	3.34	3.49	3.44	3.08	3.60	3.41	3.20	3.55	3.10	3.62	3.31	3.45								
12880	11/ 9	FA	MA	MA	FA	FA	MA	FA	FA	MA / FA		MA	MA	MA	FA	MA								
		3.01	3.40	3.65	3.01	3.19	3.30	3.16	3.25	3.21	2.83	3.17	3.35	3.23	3.11	3.28								
12881	10/ 5	FA	E	MA	FA	MA	MA	MA	FA	FA / MA		FA	FA	E	MA									
		2.31		3.03	2.91	3.03	3.07	3.27	2.88	2.93	2.95	2.89	3.00		3.39									
12882	8/11	MA	FA	FA	FA	MA	FA	FA / MA		MA	FA	MA	FA	FA	FA	FA	FA	MA						
		3.39	3.64	3.86	3.57	3.60	3.61	3.15	3.85	3.56	3.23	3.79	3.19	3.06	3.66	3.44	3.28	3.93						
12883	6/11	FA	FA	MA	MA	MA	E / MA		FA	MA	FA	MA	MA	FA	E	FA	E	MA						
		3.38	3.23	3.89	3.20	3.28		3.46	3.42	3.69	3.34	3.31	3.19	3.12		3.29		3.18						
12884	9/ 6	FA	MA	FA	MA	FA	MA	MA	FA	MA / MA		FA	E	FA										
		3.02	3.41	3.23	2.97	3.02	3.24	3.09	3.00	3.52	2.84	3.19		3.40										
12885	10/ 9	FA	FA	MA	MA	MA	MA	FA	MA	FA / FA		MA	MA	MA	MA	FA	FA	FA						
		3.02	3.15	3.52	3.38	3.22	3.24	3.17	3.44	3.01	2.87	3.36	2.10	3.76	3.32	1.67	3.00	3.03						
12886	10/ 7	MA	FA	FA	MA	MA	MA	E	MA	FA / MA		FA	MA	MA	MA									
		3.61	3.21	3.61	3.71	3.53	3.47		3.80	3.82	3.16	3.15	3.41	4.00	3.72									
12887	6/10	FA	FA	MA	MA	MA	MA / MA		FA	FA	MA	FA	FA	MA	FA	FA	MA							
		3.08	2.88	3.28	2.95	3.26	3.16	3.38	3.04	3.19	3.17	2.71	2.91	3.27	2.90	2.90	3.23							
12888	8/10	MA	FA	FA	FA	MA	MA	MA / FA		FA	E	FA	FA	MA	MA									
		3.03	3.01	3.16	2.88	3.05	2.90	2.85	2.83	3.07		2.99	2.95	2.96	3.27									

M = MALE F = FEMALE A = ALIVE E = EARLY RESORPTION "/" DENOTES POSITION OF CERVIX
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PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 20 (PAGE 8): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
DOSAGE GROUP IV	10 MG/KG/DAY																						
RAT # CLs																							
12889 11/ 4	FA	MA	/	FA																			
	3.54	3.47	3.79																				
12890 5/11	MA	MA	FA	FA	E	/	MA	MA	FA	MA	FA	FA	FA	FA	MA	MA	FA						
	3.25	3.55	3.44	2.99			3.04	3.18	3.20	3.34	2.15	3.39	3.09	3.26	3.20	3.16	2.84						
12891 6/ 7	MA	FA	MA	MA	FA	FA	/	MA	MA	MA	MA	MA	FA	FA									
	3.46	3.49	3.88	3.87	3.82	3.39	3.74	3.98	4.06	3.93	3.63	3.29	3.59										
12892 8/ 7	FA	FA	FA	FA	FA	FA	FA	MA	/	FA	MA	FA	MA	MA	MA	FA							
	3.31	3.41	3.56	3.43	3.38	3.41	3.21	3.75	3.71	3.52	3.50	3.63	3.58	3.52	3.42								
12893 14/ 7	FA	MA	FA	FA	MA	FA	FA	MA	FA	MA	MA	/	MA	MA	MA	MA	MA						
	3.24	3.27	3.30	3.42	3.48	3.34	3.16	3.48	3.08	3.51	3.37	3.31	3.02	3.52	3.45	3.49							
12894 8/ 7	FA	FA	FA	MA	MA	FA	FA	MA	/	MA	MA	FA	E	MA	FA	MA							
	3.24	3.74	3.72	3.55	3.58	3.72	3.60	3.66	3.32	3.52	4.16		3.50	3.68	3.73								
12895 7/ 8	MA	MA	MA	MA	MA	MA	E	/	MA	MA	FA	FA	FA	FA	FA								
	3.00	3.17	3.43	3.16	3.27	3.35			3.35	3.26	3.04	3.25	3.20	2.92	3.11	3.55							
12896 5/10	FA	MA	FA	MA	MA	/	FA	FA	MA	FA	FA	MA	MA	FA	FA								
	3.07	3.65	3.41	3.53	3.12	3.39	3.19	3.56	3.40	3.44	3.36	3.69	3.54	3.29									
12897 9/ 9	MA	FA	FA	FA	MA	FA	/	MA	FA	FA	FA	MA	MA	MA	MA								
	3.19	3.53	3.51	3.63	3.59	3.54	3.53	3.29	3.08	3.30	3.18	3.65	3.18	3.41	3.33								
12898 11/ 8	FA	MA	MA	FA	FA	FA	FA	FA	MA	MA	FA	/	MA	FA	FA	FA	FA	MA	FA				
	3.00	3.18	2.77	3.15	3.03	3.19	3.24	3.14	3.46	3.26	3.25	3.16	3.19	3.44	3.38	3.36	3.47	3.36					
12899 8/ 7	MA	FA	FA	MA	FA	MA	MA	E	/	MA	MA	MA	MA	MA	MA								
	3.34	3.12	3.23	3.47	3.36	3.44	3.18			3.20	3.03	3.37	3.68	3.11	3.29								
12900 11/ 6	MA	MA	MA	FA	MA	FA	FA	FA	FA	MA	/	MA	MA	MA	FA	FA	MA						
	2.96	2.95	3.47	3.39	3.00	3.05	3.35	3.59	3.37	3.31	3.56	3.12	3.22	2.66	3.33	3.43							

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PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 20 (PAGE 9): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
DOSAGE GROUP V											20 MG/KG/DAY												
RAT # CLs																							
12901 9/ 8	MA	MA	MA	MA	MA	FA	FA	FA	MA / FA		FA	FA	MA	MA	MA	MA	MA						
	3.17	3.37	3.23	3.11	3.06	2.94	3.03	2.82	3.16	3.25	3.12	3.27	3.40	3.59	3.40	3.26	3.38						
12902 11/ 6	FA	E	FA	FA	MA	MA	FA	E	FA / MA		MA	FA	FA	FA									
	2.93		3.01	3.00	3.31	3.07	2.70		3.07	3.16	3.37	3.18	3.41	3.09									
12903 10/ 7	FA	MA	MA	E	MA	MA	FA	MA	FA / FA		MA	MA	FA	FA	MA								
	3.08	3.48	3.37		3.27	3.32	2.85	2.80	3.12	3.04	3.16	3.09	2.84	3.07	3.18								
12904 8/ 7	FA	FA	MA	FA	E	FA	FA / FA		E	E	MA	FA	FA										
	3.01	3.16	3.10	2.99		2.92	2.86	3.09			3.30	3.13	2.89										
12905 7/ 8	MA	FA	FA	MA	FA	MA / FA		FA	FA	FA	MA	MA											
	3.37	3.10	3.37	3.76	3.37	3.24	3.04	3.44	3.22	3.46	3.12	3.19											
12906 8/ 6	FA	MA	MA	FA	MA	FA	E	MA / MA		FA	FA	FA	MA	FA									
	3.10	3.44	3.48	3.11	3.49	3.37		3.38	2.96	3.17	3.34	3.24	3.71	3.37									
12907 8/10	/ MA	FA	MA	MA	FA	MA	E	MA	MA	FA													
	2.50	2.43	2.85	3.20	2.90	3.17		3.11	2.94	3.25													
12908 4/14	FA	MA	FA / MA		FA	MA	FA	FA	MA	FA	FA	MA	E	MA	FA	E							
	3.09	3.49	3.01	3.02	3.05	3.08	2.80	2.61	3.16	3.22	3.12	3.17		2.99	2.92								
12909 9/ 8	FA	FA	MA	MA	MA	FA	MA / MA		E	MA	MA	FA	MA										
	2.47	3.13	3.31	3.18	3.01	2.38	2.88	3.32		3.23	2.97	2.76	3.03										
12910	NOT PREGNANT																						
12911 6/ 8	E	FA	MA	MA	MA	FA / MA		MA	FA	MA	FA	MA	MA	MA									
		3.15	3.12	3.29	2.97	3.07	3.37	3.40	2.54	3.22	3.05	3.25	3.47	3.32									
12912 11/ 4	FA	FA	FA	MA	FA	FA	MA	MA	MA / MA		MA	FA	MA										
	3.06	3.34	3.15	3.82	3.98	3.49	3.62	3.57	4.10	3.52	3.64	2.99	3.89										
12913 9/ 8	MA	MA	E	MA	FA	FA / MA		MA	FA	MA	MA	FA	FA										
	2.94	3.26		3.39	3.08	3.06	2.41	2.98	3.11	2.93	2.91	2.72	2.98										

M = MALE F = FEMALE A = ALIVE E = EARLY RESORPTION "/" DENOTES POSITION OF CERVIX
CLs = CORPORA LUTEA/OVARY FETAL BODY WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 20 (PAGE 10): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
DOSAGE GROUP V												20 MG/KG/DAY											
RAT # CLs																							
12914 12/ 4	FA	MA	MA	FA	FA	FA	MA	FA	MA	MA	MA	FA / FA		MA	MA								
	3.06	3.16	3.59	3.37	2.79	3.27	3.40	3.35	3.32	3.35	3.71	3.32	3.24	3.37	3.53								
12915 9/13	FA	MA	FA	E	MA	MA	FA	FA	MA / MA		FA	E	E	MA	MA	MA	FA						
	2.94	3.58	3.41		3.43	3.65	2.98	2.99	3.72	3.27	3.21			3.87	3.38	3.81	3.66						
12916 8/ 9	FA	MA	MA	FA	MA	MA	MA	MA / FA		E	FA	MA	FA	FA	FA	FA	MA						
	2.58	3.03	3.11	2.94	3.33	3.16	2.76	3.02	2.64		2.90	3.15	3.34	3.05	2.63	2.75	2.86						
12917 11/ 6	MA	MA	MA	E	MA	MA	MA	FA	FA	MA / FA		FA	MA	MA	MA								
	3.13	3.07	3.07		3.39	3.22	3.24	2.79	2.77	3.12	2.76	2.94	3.14	3.37	3.02								
12918 12/ 5	FA	FA	FA	FA	MA	FA	MA	FA	FA	MA	FA	MA / E		FA	MA	FA							
	2.57	3.22	2.89	3.08	3.10	2.87	3.34	3.25	3.26	3.30	3.02	3.11		2.99	3.50	3.35							
12919 6/ 8	MA	FA	MA	MA	MA	MA / MA		FA	MA	FA	MA	FA	FA	FA									
	3.05	2.87	3.15	3.61	3.26	3.17	3.22	3.07	3.28	2.97	3.14	3.00	3.05	2.97									
12920 10/ 9	FA	MA	MA	MA	MA	MA	FA	FA	MA / FA		MA	FA	MA	FA	FA	FA							
	3.25	3.52	3.31	3.32	3.43	3.23	2.91	3.17	3.43	3.03	3.28	3.16	3.26	2.93	3.15	3.14							
12921 7/10	MA	FA	FA	FA	MA	MA	MA / FA		MA	FA	FA	MA	FA	FA									
	3.66	3.26	3.14	3.28	3.39	2.71	3.44	3.20	3.23	3.31	3.34	3.73	3.34	3.27									
12922 8/ 8	MA	FA	MA	E	MA	FA	FA	MA / E		E	MA	MA	FA	MA	FA								
	2.80	2.95	3.36		3.58	3.35	2.96	2.96			3.16	3.06	3.07	3.38	3.01								
12923 8/ 6	MA	MA	MA	FA	FA	FA	FA	FA / FA		MA	MA	MA	MA	FA									
	3.54	3.39	3.16	3.08	3.58	3.24	3.38	2.94	3.12	3.55	3.55	3.31	3.58	3.44									
12924 8/ 8	MA	MA	FA	MA	MA	FA	FA	MA / FA		FA	FA	MA	MA	FA	FA								
	3.27	2.92	3.45	3.68	3.61	2.98	2.93	3.59	3.10	3.03	3.26	3.04	3.63	3.47	2.85								
12925 9/ 9	MA	FA	FA	FA	MA	MA	MA	MA	FA / MA		MA	FA	MA	MA	MA	MA							
	2.45	2.65	3.04	3.17	3.17	2.79	2.74	2.93	2.93	2.86	3.06	2.76	2.82	3.08	3.06	3.06							

M = MALE F = FEMALE A = ALIVE E = EARLY RESORPTION "/" DENOTES POSITION OF CERVIX
CLs = CORPORA LUTEA/OVARY FETAL BODY WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 20 (PAGE 11): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
SATELLITE DOSAGE GROUP I									0 (VEHICLE) MG/KG/DAY														
RAT # CLs																							
12573 13/ 3	E	A	A	A	A	A	A	A	A	A	A	A	A /	A	A	A							
		0.80	1.08	1.15	1.07	1.16	1.34	1.23	1.28	1.11	1.32	1.26	1.09	0.08a	1.22	1.05							
12574 12/12	A	A	A	A	A	A	A	A	A /	A	A	A	A	A	A	A	A	A					
	1.12	1.21	1.27	1.17	1.29	1.20	1.12	1.20	1.19	1.09	1.24	1.31	1.32	1.10	1.18	1.19	1.12	1.18					
12575 6/ 6	A	A	A	A	A	A /	A																
	1.36	1.49	1.43	1.27	1.45	1.44	1.57																
SATELLITE DOSAGE GROUP II									1 MG/KG/DAY														
12576 15/ 5	A	A	A	A	A	A	A	A	A	A	A	E /	A	A	A								
	1.17	1.05	1.17	1.21	1.30	1.29	1.36	1.36	1.38	1.32	1.42		1.46	1.42	1.46								
12577 8/12	A	A	A	A	A	A	A /	A	A	A	A	A	A	A	A	A	A	A					
	1.08	1.38	1.51	1.40	1.45	1.39	1.47	1.36	1.45	1.39	1.42	1.49	1.31	1.44	1.45	1.30	1.29	1.29					
12578 8/11	A	A	A	A	A	A /	A	A	A	A	A	E	A	A	A	A	A						
	1.17	1.35	1.28	1.27	1.28	1.29	1.23	1.24	1.28	1.30	1.36		1.23	1.30	1.30	1.18	1.38						
12579 10/ 5	A	A	A	A	A	A	A	A	A	A /	A	A	A	A	A								
	1.32	1.32	1.23	1.39	1.34	1.46	1.50	1.36	1.26	1.26	1.52	1.51	1.34	1.28	1.50								
12580 11/ 5	A	A	A	A	A	A	A	A	A	A /	A	A	E	A	A								
	1.23	1.39	1.49	1.50	1.51	1.46	1.52	1.49	1.39	1.54	1.48	1.36		1.55	1.54								
SATELLITE DOSAGE GROUP III									5 MG/KG/DAY														
12581 6/ 9	A	A	A	A	A	A /	A	A	A	A	A	E	E	A	A								
	1.24	1.42	1.55	1.54	1.37	1.47	1.32	1.31	1.47	1.51	1.45			1.44	1.52								
12582 14/ 7	A	A	A	A	A	A	A	A	A	A	A	A	A	A /	A	A	A	A					
	1.10	1.12	1.34	1.21	1.37	1.23	1.40	1.43	1.50	1.29	1.26	1.22	1.32	1.29	1.43	1.32	1.02	1.49					
12583 13/11	A	A	A	A	A	A	A	A	A	A	A	A	A /	A	A	A	A	A	A	A			
	1.49	1.26	1.27	1.48	1.26	1.45	1.30	1.35	1.19	1.30	1.52	1.29	1.05	1.30	1.43	1.44	1.38	1.45	1.34	1.31			

A = ALIVE E = EARLY RESORPTION "/" DENOTES POSITION OF CERVIX
CLs = CORPORA LUTEA/OVARY FETAL BODY WEIGHTS WERE RECORDED IN GRAMS (G).
a. Value presumed incorrectly recorded; value excluded from group averages.

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 20 (PAGE 12): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
SATELLITE DOSAGE GROUP IV										10 MG/KG/DAY													
RAT # CLs																							
12584 14/ 8	E	A	A	E	A	A	A	A	A	A	A /	A	A	A	A	A	A						
		1.28	1.18		1.29	1.17	1.39	1.30	1.26	1.17	1.24	1.04	1.12	1.26	1.18	1.15	1.21						
12585 6/10	A	A	A	A	A	A /	A	A	A	A	A	A	A	A	A	A							
	1.18	1.32	1.25	1.30	1.19	1.07	1.17	1.10	0.71	1.21	1.17	1.30	1.20	1.13	1.24	1.17							
12586 9/ 7	A	A	A	A	A	A	A	A /	A	E	A	A	A	A									
	1.25	1.25	1.35	0.99	1.44	1.30	1.26	1.13	1.27		1.27	1.23	1.35	1.35									
SATELLITE DOSAGE GROUP V										20 MG/KG/DAY													
12587 9/ 5	A	A	A	A	A	A	A	A	A /	A	A	A	A	A									
	1.03	1.15	1.16	1.25	1.17	1.07	1.13	1.12	1.19	1.05	1.23	1.32	1.17	1.26									
12588 9/ 6	A	A	A	A	A	A	A	A	A /	A	A	A	A	A	A								
	1.25	1.27	1.32	1.28	1.47	1.11	1.42	1.35	1.28	1.40	1.36	1.37	1.47	1.47	1.38								
12589 7/ 7	A	A	A	A	A	A	A /	A	A	A	A	A	A	A									
	1.25	1.26	1.30	1.31	1.34	1.30	1.32	1.11	1.35	1.29	1.40	1.32	1.49	1.38									
12590 12/ 4	A	A	A	A	A	A	A	E	A	A	A	A /	E	A	A	A							
	1.25	1.37	1.56	1.38	1.38	1.43	1.31		1.25	1.41	1.32	1.52		1.65	1.50	1.46							
12591 10/ 9	A	A	A	A	A	A	A	A	A	E /	A	A	A	A	A	A	A						
	1.20	1.28	1.36	1.36	1.37	1.17	1.22	1.35	1.36		1.31	1.41	1.30	1.40	1.34	1.29	1.32						

A = ALIVE E = EARLY RESORPTION "/" DENOTES POSITION OF CERVIX
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PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 21 (PAGE 1): FETAL ALTERATIONS - INDIVIDUAL DATA

DOSAGE GROUP I — 0 (VEHICLE) MG/KG/DAY

RAT NUMBER	SPECIMENS WITH ANY ALTERATIONS N(%)	GROSS EXTERNAL EXAMINATION N/N	GROSS EXTERNAL EXAMINATION DESCRIPTION	SOFT TISSUE EXAMINATION N/N	SOFT TISSUE EXAMINATION DESCRIPTION	SKELETAL EXAMINATION N/N	SKELETAL EXAMINATION DESCRIPTION
12801	1(7.7)	0/13		1/ 6	FETUS 10 VESSELS: UMBILICAL ARTERY DESCENDS TO THE LEFT OF URINARY BLADDER	0/ 7	
12802	6(42.8)	0/14		1/ 7	FETUS 11 KIDNEYS: PELVIS, SLIGHT DILATION, right	5/ 7	FETUS 1 STERNAL CENTRA: 1ST, NOT OSSIFIED PELVIS: PUBIS, INCOMPLETELY OSSIFIED, bilateral FETUS 3 PELVIS: PUBIS, INCOMPLETELY OSSIFIED, left FETUS 5 STERNAL CENTRA: 1ST, NOT OSSIFIED FETUS 8 PELVIS: PUBIS, INCOMPLETELY OSSIFIED, bilateral FETUS 10 STERNAL CENTRA: 1ST, NOT OSSIFIED
12803	1(6.2)	0/16		1/ 8	FETUS 2 KIDNEYS: PELVIS, SLIGHT DILATION, bilateral	0/ 8	

N/N = NUMBER OF SPECIMENS WITH ALTERATIONS/NUMBER OF SPECIMENS EXAMINED

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 21 (PAGE 2): FETAL ALTERATIONS - INDIVIDUAL DATA

DOSAGE GROUP I 0 (VEHICLE) MG/KG/DAY

RAT NUMBER	SPECIMENS WITH ANY ALTERATIONS N(%)	GROSS EXTERNAL EXAMINATION N/N	DESCRIPTION	SOFT TISSUE EXAMINATION N/N	DESCRIPTION	SKELETAL EXAMINATION N/N	DESCRIPTION
12804	0(0.0)	0/13		0/ 6		0/ 7	
12805	0(0.0)	0/15		0/ 7		0/ 8	
12806	0(0.0)	0/15		0/ 7		0/ 8	
12807	0(0.0)	0/14		0/ 7		0/ 7	
12808	0(0.0)	0/12		0/ 6		0/ 6	
12809	0(0.0)	0/18		0/ 9		0/ 9	
12810	1(10.0)	0/10		1/ 5	FETUS 10 VESSELS: UMBILICAL ARTERY DESCENDS TO THE LEFT OF URINARY BLADDER	0/ 5	
12811	0(0.0)	0/14		0/ 7		0/ 7	
12812	0(0.0)	0/14		0/ 7		0/ 7	
12813	NOT PREGNANT						
12814	0(0.0)	0/16		0/ 8		0/ 8	
12815	0(0.0)	0/15		0/ 7		0/ 8	
12816	0(0.0)	0/12		0/ 6		0/ 6	
12817	0(0.0)	0/15		0/ 7		0/ 8	
12818	0(0.0)	0/13		0/ 6		0/ 7	
12819	0(0.0)	0/15		0/ 7		0/ 8	

N/N = NUMBER OF SPECIMENS WITH ALTERATIONS/NUMBER OF SPECIMENS EXAMINED

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 21 (PAGE 3): FETAL ALTERATIONS - INDIVIDUAL DATA

DOSAGE GROUP I — 0 (VEHICLE) MG/KG/DAY

RAT NUMBER	SPECIMENS WITH ANY ALTERATIONS N(%)	GROSS EXTERNAL EXAMINATION N/N	GROSS EXTERNAL EXAMINATION DESCRIPTION	SOFT TISSUE EXAMINATION N/N	SOFT TISSUE EXAMINATION DESCRIPTION	SKELETAL EXAMINATION N/N	SKELETAL EXAMINATION DESCRIPTION
12820	0(0.0)	0/14		0/ 7		0/ 7	
12821	4(26.7)	0/15		1/ 7	FETUS 6 VESSELS: UMBILICAL ARTERY DESCENDS TO THE LEFT OF URINARY BLADDER	3/ 8	FETUS 7 STERNAL CENTRA: 1ST, INCOMPLETELY OSSIFIED FETUS 11 STERNAL CENTRA: 1ST, INCOMPLETELY OSSIFIED FETUS 15 STERNAL CENTRA: 1ST, INCOMPLETELY OSSIFIED
12822	2(13.3)	0/15		1/ 7	FETUS 4 LUNGS: APICAL LOBE, ABSENT	1/ 8	FETUS 9 STERNAL CENTRA: 1ST, INCOMPLETELY OSSIFIED
12823	0(0.0)	0/14		0/ 7		0/ 7	
12824	0(0.0)	0/12		0/ 6		0/ 6	
12825	0(0.0)	0/18		0/ 9		0/ 9	

N/N = NUMBER OF SPECIMENS WITH ALTERATIONS/NUMBER OF SPECIMENS EXAMINED

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 21 (PAGE 4): FETAL ALTERATIONS - INDIVIDUAL DATA

DOSAGE GROUP II — 1 MG/KG/DAY

RAT NUMBER	SPECIMENS WITH ANY ALTERATIONS N(%)	GROSS EXTERNAL EXAMINATION N/N	GROSS EXTERNAL EXAMINATION DESCRIPTION	SOFT TISSUE EXAMINATION N/N	SOFT TISSUE EXAMINATION DESCRIPTION	SKELETAL EXAMINATION N/N	SKELETAL EXAMINATION DESCRIPTION
12826	1(7.1)	0/14		1/ 7	FETUS 12 VESSELS: INNOMINATE, ABSENT	0/ 7	
12827	0(0.0)	0/13		0/ 6		0/ 7	
12828	0(0.0)	0/18		0/ 8		0/10	
12829	0(0.0)	0/14		0/ 7		0/ 7	
12830	0(0.0)	0/15		0/ 7		0/ 8	
12831	0(0.0)	0/16		0/ 8		0/ 8	
12832	2(14.3)	0/14		0/ 7		2/ 7	FETUS 4 CERVICAL VERTEBRAE: CERVICAL RIB PRESENT AT 7TH CERVICAL VERTEBRA, right FETUS 6 CERVICAL VERTEBRAE: CERVICAL RIB PRESENT AT 7TH CERVICAL VERTEBRA, right
12833	0(0.0)	0/13		0/ 6		0/ 7	
12834	1(6.7)	0/15		1/ 7	FETUS 14 VESSELS: UMBILICAL ARTERY DESCENDS TO THE LEFT OF URINARY BLADDER	0/ 8	

N/N = NUMBER OF SPECIMENS WITH ALTERATIONS/NUMBER OF SPECIMENS EXAMINED

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 21 (PAGE 5): FETAL ALTERATIONS - INDIVIDUAL DATA

DOSAGE GROUP II — 1 MG/KG/DAY

RAT NUMBER	SPECIMENS WITH ANY ALTERATIONS N(%)	GROSS EXTERNAL EXAMINATION N/N	GROSS EXTERNAL EXAMINATION DESCRIPTION	SOFT TISSUE EXAMINATION N/N	SOFT TISSUE EXAMINATION DESCRIPTION	SKELETAL EXAMINATION N/N	SKELETAL EXAMINATION DESCRIPTION
12835	0(0.0)	0/ 9		0/ 4		0/ 5	
12836	0(0.0)	0/15		0/ 7		0/ 8	
12837	1(7.1)	0/14		1/ 7	FETUS 9 VESSELS: INNOMINATE, ABSENT	0/ 7	
12838	0(0.0)	0/15		0/ 7		0/ 8	
12839	0(0.0)	0/17		0/ 8		0/ 9	
12840	1(5.9)	0/17		0/ 8		1/ 9	FETUS 13 STERNAL CENTRA: 1ST, INCOMPLETELY OSSIFIED
12841	0(0.0)	0/17		0/ 8		0/ 9	
12842	1(6.2)	0/16		0/ 8		1/ 8	FETUS 15 CERVICAL VERTEBRAE: CERVICAL RIB PRESENT AT 7TH CERVICAL VERTEBRA, right
12843	0(0.0)	0/13		0/ 6		0/ 7	
12844	0(0.0)	0/17		0/ 8		0/ 9	
12845	NOT PREGNANT						

N/N = NUMBER OF SPECIMENS WITH ALTERATIONS/NUMBER OF SPECIMENS EXAMINED

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 21 (PAGE 6): FETAL ALTERATIONS - INDIVIDUAL DATA

DOSAGE GROUP II 1 MG/KG/DAY

RAT NUMBER	SPECIMENS WITH ANY ALTERATIONS N(%)	GROSS EXTERNAL EXAMINATION N/N	GROSS EXTERNAL EXAMINATION DESCRIPTION	SOFT TISSUE EXAMINATION N/N	SOFT TISSUE EXAMINATION DESCRIPTION	SKELETAL EXAMINATION N/N	SKELETAL EXAMINATION DESCRIPTION
12846	NOT PREGNANT						
12847	0(0.0)	0/18		0/ 9		0/ 9	
12848	1(5.6)	0/18		0/ 9		1/ 9	FETUS 1 RIBS: WAVY, right 7th - 10th
12849	0(0.0)	0/15		0/ 7		0/ 8	
12850	2(12.5)	0/16		1/ 8	FETUS 16 LUNGS: DIAPHRAGMATIC LOBE, ABSENT	1/ 8	FETUS 17 STERNAL CENTRA: 1ST, NOT OSSIFIED

N/N = NUMBER OF SPECIMENS WITH ALTERATIONS/NUMBER OF SPECIMENS EXAMINED

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 21 (PAGE 7): FETAL ALTERATIONS - INDIVIDUAL DATA

DOSAGE GROUP III 5 MG/KG/DAY

RAT NUMBER	SPECIMENS WITH ANY ALTERATIONS N(%)	GROSS EXTERNAL EXAMINATION N/N	DESCRIPTION	SOFT TISSUE EXAMINATION N/N	DESCRIPTION	SKELETAL EXAMINATION N/N	DESCRIPTION
12851	0(0.0)	0/15		0/ 7		0/ 8	
12852	0(0.0)	0/16		0/ 8		0/ 8	
12853	0(0.0)	0/14		0/ 7		0/ 7	
12854	0(0.0)	0/16		0/ 8		0/ 8	
12855	NOT PREGNANT						
12856	0(0.0)	0/14		0/ 6		0/ 8	
12857	0(0.0)	0/19		0/ 9		0/10	
12858	0(0.0)	0/14		0/ 7		0/ 7	
12859	2(11.8)	0/17		0/ 8		2/ 9	FETUS 11 PELVIS: ISCHIUM, INCOMPLETELY OSSIFIED, right FETUS 15 PELVIS: ISCHIUM, INCOMPLETELY OSSIFIED, right
12860	2(13.3)	0/15		2/ 7	FETUS 5 VESSELS: UMBILICAL ARTERY DESCENDS TO THE LEFT OF URINARY BLADDER FETUS 9 VESSELS: UMBILICAL ARTERY DESCENDS TO THE LEFT OF URINARY BLADDER	0/ 8	

N/N = NUMBER OF SPECIMENS WITH ALTERATIONS/NUMBER OF SPECIMENS EXAMINED

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 21 (PAGE 8): FETAL ALTERATIONS - INDIVIDUAL DATA

DOSAGE GROUP III 5 MG/KG/DAY

RAT NUMBER	SPECIMENS WITH ANY ALTERATIONS N(%)	GROSS EXTERNAL EXAMINATION N/N	GROSS EXTERNAL EXAMINATION DESCRIPTION	SOFT TISSUE EXAMINATION N/N	SOFT TISSUE EXAMINATION DESCRIPTION	SKELETAL EXAMINATION N/N	SKELETAL EXAMINATION DESCRIPTION
12861	0(0.0)	0/12		0/ 6		0/ 6	
12862	0(0.0)	0/15		0/ 7		0/ 8	
12863	1(7.1)	0/14		0/ 8		1/ 6	FETUS 14 STERNAL CENTRA: 1ST, INCOMPLETELY OSSIFIED
12864	0(0.0)	0/14		0/ 7		0/ 7	
12865	1(6.7)	0/15		0/ 7		1/ 8	FETUS 6 CERVICAL VERTEBRAE: CERVICAL RIB PRESENT AT 7TH CERVICAL VERTEBRA, left
12866	0(0.0)	0/19		0/ 9		0/10	
12867	0(0.0)	0/14		0/ 7		0/ 7	
12868	0(0.0)	0/ 5		0/ 2		0/ 3	
12869	0(0.0)	0/15		0/ 7		0/ 8	
12870	0(0.0)	0/16		0/ 8		0/ 8	
12871	0(0.0)	0/14		0/ 7		0/ 7	
12872	0(0.0)	0/14		0/ 7		0/ 7	
12873	0(0.0)	0/14		0/ 7		0/ 7	
12874	0(0.0)	0/16		0/ 8		0/ 8	
12875	0(0.0)	0/10		0/ 5		0/ 5	

N/N = NUMBER OF SPECIMENS WITH ALTERATIONS/NUMBER OF SPECIMENS EXAMINED

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 21 (PAGE 9): FETAL ALTERATIONS - INDIVIDUAL DATA

DOSAGE GROUP IV 10 MG/KG/DAY

RAT NUMBER	SPECIMENS WITH ANY ALTERATIONS N(%)	GROSS EXTERNAL EXAMINATION N/N	DESCRIPTION	SOFT TISSUE EXAMINATION N/N	DESCRIPTION	SKELETAL EXAMINATION N/N	DESCRIPTION
12876	0(0.0)	0/15		0/ 7		0/ 8	
12877	1(7.1)	0/14		1/ 7	FETUS 14 KIDNEYS: PELVIS, MODERATE DILATION, right	0/ 7	
12878	0(0.0)	0/15		0/ 7		0/ 8	
12879	0(0.0)	0/15		0/ 7		0/ 8	
12880	0(0.0)	0/15		0/ 7		0/ 8	
12881	0(0.0)	0/12		0/ 6		0/ 6	
12882	1(5.9)	0/17		0/ 8		1/ 9	FETUS 3 CERVICAL VERTEBRAE: CERVICAL RIB PRESENT AT 7TH CERVICAL VERTEBRA, left
12883	0(0.0)	0/14		0/ 7		0/ 7	
12884	0(0.0)	0/12		0/ 6		0/ 6	

N/N = NUMBER OF SPECIMENS WITH ALTERATIONS/NUMBER OF SPECIMENS EXAMINED

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 21 (PAGE 10): FETAL ALTERATIONS - INDIVIDUAL DATA

DOSAGE GROUP IV — 10 MG/KG/DAY

RAT NUMBER	SPECIMENS WITH ANY ALTERATIONS N(%)	GROSS EXTERNAL EXAMINATION N/N	GROSS EXTERNAL EXAMINATION DESCRIPTION	SOFT TISSUE EXAMINATION N/N	SOFT TISSUE EXAMINATION DESCRIPTION	SKELETAL EXAMINATION N/N	SKELETAL EXAMINATION DESCRIPTION
12885	1(5.9)	1/17	FETUS 15 BODY: TRUNK SHORT TAIL: ABSENT	0/ 8		1/ 9	FETUS 15 CERVICAL VERTEBRAE: 4 PRESENT a THORACIC VERTEBRAE: 0 PRESENT a ARCH, NOT OSSIFIED, bilateral 1st - 13th; CENTRUM, NOT OSSIFIED, 1st - 13th LUMBAR VERTEBRAE: 0 PRESENT a ARCH, NOT OSSIFIED, bilateral 1st - 6th; CENTRUM, NOT OSSIFIED, 1st - 6th SACRAL VERTEBRAE: 0 PRESENT a ARCH, NOT OSSIFIED, bilateral 1st - 3rd; CENTRUM, NOT OSSIFIED, 1st - 3rd CAUDAL VERTEBRAE: 0 PRESENT a PELVIS: PUBIS, NOT OSSIFIED, bilateral RIBS: 0 PRESENT a, NOT OSSIFIED, bilateral 1st - 13th

N/N = NUMBER OF SPECIMENS WITH ALTERATIONS/NUMBER OF SPECIMENS EXAMINED
a. Excluded from ossification site group averages and statistical analyses.

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 21 (PAGE 11): FETAL ALTERATIONS - INDIVIDUAL DATA

DOSAGE GROUP IV 10 MG/KG/DAY

RAT NUMBER	SPECIMENS WITH ANY ALTERATIONS N(%)	GROSS EXTERNAL EXAMINATION N/N	GROSS EXTERNAL EXAMINATION DESCRIPTION	SOFT TISSUE EXAMINATION N/N	SOFT TISSUE EXAMINATION DESCRIPTION	SKELETAL EXAMINATION N/N	SKELETAL EXAMINATION DESCRIPTION
12886	0(0.0)	0/13		0/ 6		0/ 7	
12887	0(0.0)	0/16		0/ 8		0/ 8	
12888	2(15.4)	0/13		0/ 6		2/ 7	FETUS 1 PELVIS: PUBIS, INCOMPLETELY OSSIFIED, left FETUS 14 STERNAL CENTRA: 1ST, INCOMPLETELY OSSIFIED
12889	0(0.0)	0/ 3		0/ 1		0/ 2	
12890	1(6.7)	0/15		0/ 7		1/ 8	FETUS 10 CERVICAL VERTEBRAE: CERVICAL RIB PRESENT AT 7TH CERVICAL VERTEBRA, left
12891	0(0.0)	0/13		0/ 6		0/ 7	
12892	0(0.0)	0/15		0/ 7		0/ 8	

N/N = NUMBER OF SPECIMENS WITH ALTERATIONS/NUMBER OF SPECIMENS EXAMINED

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 21 (PAGE 12): FETAL ALTERATIONS - INDIVIDUAL DATA

DOSAGE GROUP IV — 10 MG/KG/DAY

RAT NUMBER	SPECIMENS WITH ANY ALTERATIONS N(%)	GROSS EXTERNAL EXAMINATION N/N	GROSS EXTERNAL EXAMINATION DESCRIPTION	SOFT TISSUE EXAMINATION N/N	SOFT TISSUE EXAMINATION DESCRIPTION	SKELETAL EXAMINATION N/N	SKELETAL EXAMINATION DESCRIPTION
12893	1(6.2)	0/16		0/ 8		1/ 8	FETUS 13 SKULL: NASAL - FRONTAL, SUTURE LARGE
12894	0(0.0)	0/14		0/ 7		0/ 7	
12895	0(0.0)	0/14		0/ 7		0/ 7	
12896	0(0.0)	0/14		0/ 7		0/ 7	
12897	0(0.0)	0/15		0/ 7		0/ 8	
12898	1(5.6)	0/18		0/ 9		1/ 9	FETUS 15 CERVICAL VERTEBRAE: CERVICAL RIB PRESENT AT 7TH CERVICAL VERTEBRA, right
12899	0(0.0)	0/13		0/ 6		0/ 7	
12900	0(0.0)	0/16		0/ 8		0/ 8	

N/N = NUMBER OF SPECIMENS WITH ALTERATIONS/NUMBER OF SPECIMENS EXAMINED

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 21 (PAGE 13): FETAL ALTERATIONS - INDIVIDUAL DATA

DOSAGE GROUP V — 20 MG/KG/DAY

RAT NUMBER	SPECIMENS WITH ANY ALTERATIONS N(%)	GROSS EXTERNAL EXAMINATION N/N	GROSS EXTERNAL EXAMINATION DESCRIPTION	SOFT TISSUE EXAMINATION N/N	SOFT TISSUE EXAMINATION DESCRIPTION	SKELETAL EXAMINATION N/N	SKELETAL EXAMINATION DESCRIPTION
12901	0(0.0)	0/17		0/ 7		0/10	
12902	0(0.0)	0/12		0/ 6		0/ 6	
12903	0(0.0)	0/14		0/ 7		0/ 7	
12904	1(10.0)	0/10		0/ 5		1/ 5	FETUS 1 RIBS: WAVY, right 5th - 7th and 10th
12905	0(0.0)	0/12		0/ 6		0/ 6	
12906	0(0.0)	0/13		0/ 6		0/ 7	
12907	1(11.1)	0/ 9		0/ 4		1/ 5	FETUS 1 STERNAL CENTRA: 1ST, NOT OSSIFIED
12908	1(7.1)	0/14		0/ 7		1/ 7	FETUS 5 CERVICAL VERTEBRAE: CERVICAL RIB PRESENT AT 7TH CERVICAL VERTEBRA, left
12909	4(33.3)	0/12		0/ 6		4/ 6	FETUS 5 RIBS: WAVY, bilateral 4th - 11th

N/N = NUMBER OF SPECIMENS WITH ALTERATIONS/NUMBER OF SPECIMENS EXAMINED

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 21 (PAGE 14): FETAL ALTERATIONS - INDIVIDUAL DATA

DOSAGE GROUP V — 20 MG/KG/DAY

RAT NUMBER	SPECIMENS WITH ANY ALTERATIONS N(%)	GROSS EXTERNAL EXAMINATION N/N	GROSS EXTERNAL EXAMINATION DESCRIPTION	SOFT TISSUE EXAMINATION N/N	SOFT TISSUE EXAMINATION DESCRIPTION	SKELETAL EXAMINATION N/N	SKELETAL EXAMINATION DESCRIPTION
12909 (CONT)							FETUS 7 RIBS: WAVY, right 4th - 12th, left 3rd - 12th; INCOMPLETELY OSSIFIED (HYPOPLASTIC), right 9th - 12th, left 10th - 12th FETUS 10 RIBS: WAVY, right 6th - 11th, left 6th, 7th and 10th FETUS 12 RIBS: WAVY, right 4th - 11th, left 6th - 9th
12910	NOT PREGNANT						
12911	0(0.0)	0/13		0/ 6		0/ 7	
12912	1(7.7)	0/13		0/ 6		1/ 7	FETUS 5 CERVICAL VERTEBRAE: CERVICAL RIB PRESENT AT 7TH CERVICAL VERTEBRA, left
12913	0(0.0)	0/12		0/ 6		0/ 6	
12914	0(0.0)	0/15		0/ 7		0/ 8	
12915	0(0.0)	0/14		0/ 7		0/ 7	
12916	0(0.0)	0/16		0/ 8		0/ 8	

N/N = NUMBER OF SPECIMENS WITH ALTERATIONS/NUMBER OF SPECIMENS EXAMINED

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 21 (PAGE 15): FETAL ALTERATIONS - INDIVIDUAL DATA

DOSAGE GROUP V — 20 MG/KG/DAY

RAT NUMBER	SPECIMENS WITH ANY ALTERATIONS N(%)	GROSS EXTERNAL EXAMINATION N/N	GROSS EXTERNAL EXAMINATION DESCRIPTION	SOFT TISSUE EXAMINATION N/N	SOFT TISSUE EXAMINATION DESCRIPTION	SKELETAL EXAMINATION N/N	SKELETAL EXAMINATION DESCRIPTION
12917	0(0.0)	0/14		0/ 7		0/ 7	
12918	0(0.0)	0/15		0/ 7		0/ 8	
12919	2(14.3)	0/14		0/ 7		2/ 7	FETUS 3 RIBS: WAVY, bilateral 4th 12th FETUS 9 RIBS: WAVY, bilateral 4th - 12th
12920	1(6.2)	0/16		0/ 8		1/ 8	FETUS 1 CERVICAL VERTEBRAE: CERVICAL RIB PRESENT AT 7TH CERVICAL VERTEBRA, left
12921	0(0.0)	0/14		0/ 7		0/ 7	
12922	0(0.0)	0/12		0/ 6		0/ 6	
12923	1(7.1)	0/14		0/ 7		1/ 7	FETUS 7 CERVICAL VERTEBRAE: CERVICAL RIB PRESENT AT 7TH CERVICAL VERTEBRA, bilateral
12924	0(0.0)	0/15		0/ 7		0/ 8	
12925	0(0.0)	0/16		0/ 8		0/ 8	

N/N = NUMBER OF SPECIMENS WITH ALTERATIONS/NUMBER OF SPECIMENS EXAMINED

APPENDIX C

PROTOCOL AND AMENDMENTS

PRIMEDICA

Argus Research Laboratories, Inc.
905 Sheehy Drive, Building A
Horsham, PA 19044
Telephone: (215) 443-8710
Telefax: (215) 443-8587

PROTOCOL 418-011

SPONSOR'S STUDY NUMBER: T-6316.7

STUDY TITLE: Oral (Gavage) Developmental Toxicity Study of N-EtFOSE in Rats

PURPOSE: The purpose of this study is to detect adverse effects of N-EtFOSE on Crl:CD®BR VAF/Plus® presumed pregnant female rats and development of the embryo and fetus consequent to exposure of the dam from implantation to closure of the hard palate. This study evaluates ICH Harmonised Tripartite Guideline stages C and D of the reproductive process.

TESTING FACILITY: Argus Research Laboratories, Inc.
905 Sheehy Drive, Building A
Horsham, Pennsylvania 19044-1297
Telephone: (215) 443-8710
Telefax: (215) 443-8587

STUDY DIRECTOR: Raymond G. York, Ph.D.,DABT
Associate Director of Research

SPONSOR: 3M Toxicology Services
3M Center, Building 220-2E-02
St. Paul, Minnesota 55144-1000

STUDY MONITOR: Marvin T. Case, D.V.M., Ph.D.
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Telefax: (651) 733-1773

ALTERNATE STUDY MONITOR: Andrew M. Seacat, Ph.D.
Telephone: (651) 575-3161
Telefax: (651) 733-1773

10 171306

REGULATORY CITATIONS:

U.S. Food and Drug Administration (1994). International Conference on Harmonisation; Guideline on detection of toxicity to reproduction for medicinal products. *Federal Register*, September 22, 1994, Vol. 59, No. 183.

U.S. Food and Drug Administration. Good Laboratory Practice Regulations; Final Rule. 21 CFR Part 58.

Japanese Ministry of Health and Welfare (1997). *Good Laboratory Practice Standard for Safety Studies on Drugs*, MHW Ordinance Number 21, March 26, 1997.

European Economic Community (1989). *Council decision on 28 July 1989 on the acceptance by the European Economic Community of an OECD decision/recommendation on compliance with principles of good laboratory practice*. Official Journal of the European Communities: Legislation. 32(No. L 315; 28 October): 1-17.

REGULATORY COMPLIANCE:

This study will be conducted in compliance with the Good Laboratory Practice (GLP) regulations cited above.

All changes or revisions of this protocol shall be documented, signed by the Study Director and the Sponsor, dated and maintained with the protocol.

The Quality Assurance Unit (QAU) will audit the protocol, the raw data and the report, and will inspect critical phases of the study in accordance with the Standard Operating Procedures of Argus Research Laboratories, Inc.

The final report will include a statement signed by the Study Director that the report accurately reflects the raw data obtained during the performance of the study and that all applicable GLP regulations were followed in the conduct of the study. Should significant deviations from GLP regulations occur, each will be described in detail, together with how the deviation might affect the quality or integrity of the study.

SCHEMATIC OF STUDY DESIGN AND STUDY SCHEDULE:

See ATTACHMENT 1 to the protocol.

10 171307

TEST ARTICLE AND VEHICLE:

Identification:

Test Article:

Name:	N-EtFOSE.
Physical Description:	Waxy solid.
Lot/Batch Number:	FM-3929 (30035, 30037, 30039).
Specific Gravity:	~1.7.
Purity:	99.1%.
Expiration Date:	May, 2000.

Information on the identity, composition, strength and purity of the test article is on file with the Sponsor.

Vehicle:

2% Tween® 80 in Reverse Osmosis Membrane Processed Deionized Water (R.O. Deionized Water). Supplier and lot identification of Tween® 80 will be documented in the raw data.

Neither the Sponsor nor the Study Director is aware of any potential contaminants likely to be present in the vehicle that would interfere with the results of this study. Therefore, no analyses other than those mentioned in this protocol will be conducted.

Safety Precautions:

Gloves, mask, appropriate eye protection and a uniform/lab coat are to be worn during formulation preparation and administration. The Material Safety Data Sheet (MSDS) is attached to the protocol (see ATTACHMENT 2).

Storage:

Bulk Test Article:	Room Temperature.
Vehicle Components:	Room Temperature.
Prepared Vehicle:	Room Temperature.
Prepared Formulations:	Refrigerated (samples to be frozen).

All test article shipments to the Testing Facility should be addressed to the attention of Julian Gulbinski, Manager of Formulations, at the previously cited address and telephone number.

10 171308

Shipments should include information concerning storage conditions and shipping cartons should be labeled appropriately. The recipient should be notified in advance of shipment.

FORMULATION:

Frequency of Preparation:

Formulations suspensions will be prepared weekly at the Testing Facility.

Detailed preparation procedures are attached to this protocol (ATTACHMENT 3).

Adjustment for Purity:

The test article will be considered 100% pure for the purpose of dosage calculations.

Testing Facility Reserve Samples:

The Testing Facility will reserve a sample (1 g) of each lot of bulk test article used during the course of this study. The Testing Facility will reserve a sample (5 ml) of each lot of vehicle components used during the course of the study. Samples will be stored under the previously cited conditions.

ANALYSES:

Samples additional to those described below may be taken if deemed necessary during the course of the study.

Bulk Test Article Sampling:

No analyses of the bulk test article will be conducted during the course of this study. Information on the stability of the bulk test article is on file with the Sponsor.

Analyses of Prepared Formulations:

At the request of the Sponsor, no analyses of prepared test article formulations will be conducted during the course of the study. Homogeneity and stability information is on file with the Sponsor. However, records will be maintained to document how the test article formulations were prepared.

Concentration of Test Article Formulations:

Concentration of the prepared formulations will be verified during the course of this study. Duplicate samples (2 mL each) will be taken from the first and last preparation on the day prepared. One sample of each set will be shipped for analysis; the remaining samples will be retained at the Testing Facility as backup samples. Backup samples will be stored under the previously cited conditions and discarded at the Testing Facility upon request of the Sponsor.

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Shipping Instructions:

Samples to be analyzed will be shipped (frozen on dry ice) to:

Kris J. Hansen, Ph.D.
3M Environmental Technology and Safety Services
935 Bush Avenue
Building 2-3E-09
St. Paul, Minnesota 55133-3331
Telephone: (612) 778-6018
Telefax: (612) 778-6176

The recipient will be notified in advance of sample shipment.

DISPOSITION:

Prepared formulations will be discarded at the Testing Facility. All remaining bulk test article will be returned to the Study Monitor at the previously cited address.

TEST SYSTEM:

Species/Strain and Reason for Selection:

The Crl:CD®BR VAF/Plus® (Sprague-Dawley) rat was selected as the Test System because: 1) it is one mammalian species accepted and widely used throughout industry for nonclinical studies of developmental toxicity (embryo-fetal toxicity/teratogenicity); 2) this strain has been demonstrated to be sensitive to developmental toxins; 3) historical data and experience exist at the Testing Facility[1-3]; and 4) the test article is pharmacologically active in this species and strain.

Number:

Initial population acclimated:	190 virgin female rats.
Population selected for study:	125 mated female rats (25 per dosage group).
Population assigned to satellite study:	19 mated female rats (five per Groups II and V and three per Groups I, III and IV) assigned to toxicokinetic evaluation.

Body Weight and Age:

Female rats will be ordered to have body weights of 200 g to 225 g each at receipt, at which time they will be expected to be at least 60 days of age. Actual body weights will be recorded the day after receipt and will be documented in the raw data. The weight range will be included in the final report.

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Sex:

Female rats will be given the test article. Male rats of the same source and strain will be used only as breeders and are not considered part of the Test System.

Source:

Charles River Laboratories, Inc.

The rats will be shipped in filtered cartons by air freight and/or truck from Charles River Laboratories, Inc., to the Testing Facility.

Identification:

Rats are permanently identified using Monel® self-piercing ear tags (Gey Band and Tag Co., Inc., No. MSPT 20101). Male rats are given unique permanent identification numbers upon assignment to the Testing Facility's breeder male rat population. Female rats are assigned temporary numbers at receipt and given unique permanent identification numbers when assigned to the study on the basis of day 0 of presumed gestation body weights.

ANIMAL HUSBANDRY:

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

Housing:

The rats will be individually housed in stainless steel, wire-bottomed cages except during the cohabitation period. During cohabitation, each pair of rats will be housed in the male rat's cage. No nesting materials will be supplied because the female rats will be sacrificed before parturition is expected.

Room Air, Temperature and Humidity:

The animal room is independently supplied with at least ten changes per hour of 100% fresh air that has been passed through 99.97% HEPA filters (Airo Clean® room). Room temperature will be maintained at 64°F (18°C) to 79°F (26°C) and monitored constantly. Room humidity will also be monitored constantly and maintained at 30% to 70%.

Light:

An automatically controlled 12-hour light:12-hour dark fluorescent light cycle will be maintained. Each dark period will begin at 1900 hours EST.

10 171311

Diet:

Rats will be given Certified Rodent Diet® #5002 (PMI Nutrition International) available *ad libitum* from individual feeders.

Water:

Water will be available *ad libitum* from individual bottles attached to the cages or from an automatic watering access system. All water will be from a local source and passed through a reverse osmosis membrane before use. Chlorine will be added to the processed water as a bacteriostat; processed water is expected to contain no more than 1.2 ppm chlorine at the time of analysis. Water is analyzed monthly for possible bacterial contamination and twice annually for possible chemical contamination.

Contaminants:

Neither the Sponsor nor the Study Director is aware of any potential contaminants likely to be present in the certified diet or in the drinking water at levels that would interfere with the results of this study. Therefore, no analyses other than those routinely performed by the feed supplier or those mentioned in this protocol will be conducted.

RANDOMIZATION AND COHABITATION:

Upon arrival, male and female rats will be assigned to individual housing on the basis of computer-generated random units. After acclimation, virgin female rats will be cohabited with breeder male rats, one male rat per female rat. The cohabitation period will consist of a maximum of five days. Female rats with spermatozoa observed in a smear of the vaginal contents and/or a copulatory plug observed *in situ* will be considered to be at day 0 of presumed gestation and assigned to individual housing.

Healthy mated female rats will be assigned to dosage groups based on computer-generated (weight-ordered) randomization procedures.

ADMINISTRATION:

Route and Reason for Choice:

The oral (gavage) route was selected for use because: 1) in comparison with the dietary route, the exact dosage can be accurately administered; and 2) it is one of the proposed routes for clinical use.

10 171312

Method and Frequency:

Female rats will be given the test article once daily on days 6 through 17 of presumed gestation, the period of organogenesis. Dosages will be adjusted for the most recently recorded body weight and given at approximately the same time each day.

Rationale for Dosage Selection:

Dosages were selected on the basis of a dosage-range study (Argus Research Laboratories, Inc., Protocol 418-011P) that tested 0, 1, 5, 10, 25 and 35 mg/kg/day. In that study, body weight gain was decreased at 10 mg/kg/day and higher dosages, and feed consumption values were reduced at all dosages tested.

Dosage Levels, Concentrations and Volumes:

Dosage Group	Number of Rats	Dosage (mg/kg/day)	Concentration (mg/mL)	Dosage Volume (mL/kg)	Argus Batch Number
I	25 + 3*	0 (Vehicle)	0	5	B-418-011-A(Day.Month.Year)
II	25 + 5*	1	0.2	5	B-418-011-B(Day.Month.Year)
III	25 + 3*	5	1	5	B-418-011-B(Day.Month.Tear)
IV	25 + 3*	10	2	5	B-418-011-C(Day.Month.Year)
V	25 + 5*	20	4	5	B-418-011-D(Day.Month.Year)

The test article will be considered 100% pure for the purpose of dosage calculations.
*. Rats assigned to the satellite group for blood collection.

TESTS, ANALYSES AND MEASUREMENTS:

Viability:

All Periods: At least twice daily.

Clinical Observations and/or General Appearance:

Acclimation Period: Weekly.

Predosage Period: Day 0 of presumed gestation.

Dosage Period: Twice daily. Prior to dosage administration and once approximately one hour postdosage.

Postdosage Period: Once daily.

Clinical observations may be recorded more frequently than cited above, if deemed appropriate by the Study Director and/or Study Monitor.

Body Weights:

Acclimation Period: Weekly.

Predosage Period: Day 0 and 4 of presumed gestation.

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Dosage Period: Daily.

Postdosage Period: Daily.

Feed Consumption Values (recorded and tabulated):

Predosage Period: Day 0 and 4 of presumed gestation.

Dosage Period: Days 6, 8, 10, 12, 14 and 16 of presumed gestation.

Postdosage Period: Days 18 and 20 of presumed gestation.

Feed consumption values may be recorded more frequently if it is necessary to replenish the feed. These intervals will not be tabulated.

Mating Performance:

Mating will be evaluated daily during the cohabitation period and confirmed by observation of spermatozoa in a smear of the vaginal contents and/or a copulatory plug observed *in situ*.

Caesarean-Sectioning Observations:

Rats will be Caesarean-sectioned on day 20 of presumed gestation. The fetuses will be removed from the uterus and placed in individual containers. The rats will be examined for number and distribution of:

Corpora Lutea.

Implantation Sites.
[Placentae appearance (size, color or shape if abnormal) will be noted in the raw data].

Live and Dead Fetuses.
(A live fetus is defined as one that responds to stimuli; a dead fetus is defined as a term fetus that does not respond to stimuli and that is not markedly autolyzed; dead fetuses demonstrating marked to extreme autolysis are considered to be late resorptions.)

Early and Late Resorptions.
(A conceptus is defined as a late resorption if it is grossly evident that organogenesis has occurred; if this is not the case, the conceptus is defined as an early resorption.)

10 171314

Fetal Observations:

Gross External Alterations and Sex:

Fetuses will be examined for sex and for gross external alterations. Late resorptions and dead fetuses also will be examined for sex and for gross external alterations to the extent possible but such observations will not be included in either data summarization or statistical analyses.

Body Weights and Identification:

The body weight of each fetus will be recorded. Only body weights of live fetuses will be used to determine litter fetal body weight averages. Fetuses will be tagged with identification noting study number, litter number, uterine distribution and fixative.

Soft Tissue Examination:

Approximately one-half of the fetuses in each litter will be examined for soft tissue alterations by using an adaptation of Wilson's sectioning technique[5]. The fetuses will be initially fixed in Bouin's solution; sections will be retained in alcohol.

Skeletal Examination:

The remaining fetuses (approximately one-half of the fetuses in each litter) will be examined for skeletal alterations after staining with alizarin red S[6]. The fetuses will be initially fixed in alcohol; skeletal preparations will be retained in glycerin with thymol added as a preservative.

Representative photographs of fetal gross, soft tissue and skeletal alterations will be taken.

METHOD OF SACRIFICE:

Rats will be sacrificed by carbon dioxide asphyxiation. Live fetuses will be sacrificed by an intraperitoneal injection of euthanasia solution (Beuthanasia®-D Special, manufactured by Schering-Plough Animal Health).

NECROPSY:

Gross lesions will be retained in neutral buffered 10% formalin for possible future evaluation (a table of random units will be used to select one control group rat from which all tissues examined at necropsy will be retained, in order to provide control tissues for any possible histopathological evaluations of gross lesions). Unless specifically cited below, all other tissues will be discarded.

10 171315

Satellite Rats Assigned to Toxicokinetic Sample Collection:

On day 18 of presumed gestation (the day following the last dosage), rats assigned to the toxicokinetic evaluation will be sacrificed and the following samples collected. Blood samples (approximately 4 mL per rat) will be collected from the inferior vena cava into serum separator tubes and centrifuged. The resulting serum (approximately 2 mL) will be immediately frozen on dry ice and maintained frozen (-70°C) until shipment to the Sponsor for analysis. The liver will be excised, weighed, and a sample section (lateral lobe) will be frozen and retained at -70°C until shipment to the Sponsor for analysis.

Rats will be Caesarean-sectioned and fetuses will be examined grossly to the extent possible as described above for rats assigned to the main study. Fetuses and placentae will be pooled per litter and retained frozen (-70°C) until shipment to the Sponsor for analysis

After completion of sample collection, serum, liver section (lateral lobe), fetal and placental samples will be shipped (frozen on dry ice) to Kris J. Hansen, Ph.D., at the previously cited address for analysis. Both the recipient and the Study Monitor will be notified in advance of sample shipment.

Scheduled Sacrifice:

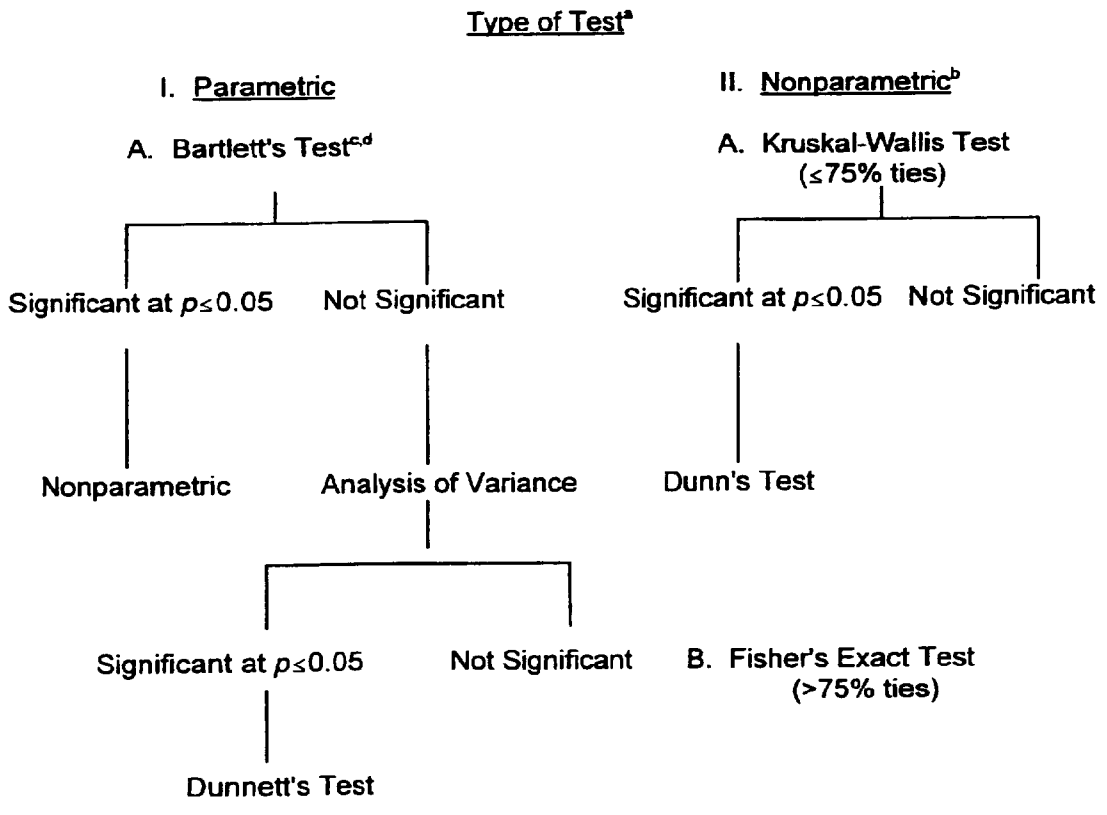
On day 20 of presumed gestation, female rats will be Caesarean-sectioned, and a gross necropsy of the thoracic, abdominal and pelvic viscera will be performed. Uteri of apparently nonpregnant rats will be stained with 10% ammonium sulfide to confirm the absence of implantation sites[7].

Rats Found Dead or Moribund:

Rats that die or are sacrificed because of moribund condition, abortion or premature delivery will be examined for the cause of death or moribund condition on the day the observation is made. The rats will be examined for gross lesions. Pregnancy status and uterine contents of female rats will be recorded. Aborted fetuses and/or delivered pups will be examined to the extent possible, using the same methods described for fetuses. Uteri of apparently nonpregnant rats will be stained with 10% ammonium sulfide to confirm the absence of implantation sites[7].

PROPOSED STATISTICAL METHODS[6-14]:

Averages and percentages will be calculated. Litter values will be used where appropriate. Additional procedures and/or analyses may be performed, if appropriate.



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a. Statistically significant probabilities are reported as either $p \leq 0.05$ or $p \leq 0.01$.
b. Proportion data are not included in this category.
c. Used only to analyze data with homogeneity of variance.
d. Test for homogeneity of variance.

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DATA ACQUISITION, VERIFICATION AND STORAGE:

Data will be hand- and/or computer-recorded. Records will be reviewed by the Study Director and/or appropriate management personnel within 21 days after generation. All original records will be stored in the archives of the Testing Facility. All original data will be bound and indexed. A copy of all raw data will be supplied to the Sponsor upon request. Preserved tissues will be stored at the Testing Facility at no charge for one year after mailing of the draft final report, after which time the Sponsor will be contacted to determine the disposition of these materials.

RECORDS TO BE MAINTAINED:

Protocol and Amendments.
Test Article, Vehicle and/or Reagent Receipt, Preparation and Use.
Animal Acquisition.
Randomization Schedules.
Mating History.
Treatment (if prescribed by Staff Veterinarian).
General Comments.
Clinical Observations and/or General Appearance.
Blood and Tissue Sample Collection, Processing and Shipment.
Body Weights.
Feed Consumption Values.
Caesarean-Sectioning and Fetal Observations.
Gross Necropsy Observations.
Organ Weights.
Photographs (if required).
Study Maintenance (room and environmental records).
Feed and Water Analyses.
Packing and/or Shipment Lists.

KEY PERSONNEL:

Executive Director of Research: Mildred S. Christian, Ph.D., Fellow, ATS
Director of Research: Alan M. Hoberman, Ph.D., DABT
Associate Director of Research and Study Director: Raymond G. York, Ph.D., DABT
Director of Laboratory Operations: John F. Barnett, B.S.
Manager of Study Coordination: Valerie A. Sharper, M.S.
Manager of Animal Operations and Member, Institutional Animal Care and Use Committee: Dena C. Lebo, V.M.D.
Manager of Regulatory Compliance: Kathleen A. Moran, M.S.
Consultant, Veterinary Pathology: W. Ray Brown, D.V.M., Ph.D., ACVP

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FINAL REPORT:

A comprehensive draft final report will be prepared on completion of the study and will be finalized following consultation with the Sponsor. The report will include the following:

Summary and Conclusion.
Experimental Design and Method.
Evaluation of Test Results.
Appendices: Figures, Summary and Individual Tables Summarizing the Above Data, Protocol and Associated Amendments and Deviations, Study Director's GLP Compliance Statement, Reports of Supporting Data (if appropriate) and QAU Statement.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE STATEMENT:

The procedures described in this protocol have been reviewed by the Testing Facility's Institutional Animal Care and Use Committee. All procedures described in this protocol that involve study animals will be conducted in a manner to avoid or minimize discomfort, distress or pain to the animals.

The Sponsor's signature below documents the fact that information concerning the necessity for conducting this study and the fact that this is not an unnecessarily duplicative study may be obtained from the Sponsor. No alternative (*in vitro*) procedures were available for meeting the stated purposes of the study.

REFERENCES:

1. Christian, M.S. and Voytek, P.E. (1982). *In Vivo Reproductive and Mutagenicity Tests*. Environmental Protection Agency, Washington, D.C. National Technical Information Service, U.S. Department of Commerce, Springfield, VA 22161.

2. Christian, M.S. (1984). Reproductive toxicity and teratology evaluations of naltrexone (Proceedings of Naltrexone Symposium, New York Academy of Sciences, November 7, 1983), J. Clin. Psychiat. 45(9):7-10.

3. Lang, P.L. (1988). *Embryo and Fetal Developmental Toxicity (Teratology) Control Data in the Charles River Crl:CD®BR Rat*. Charles River Laboratories, Inc., Wilmington, MA 01887-0630. (Data base provided by Argus Research Laboratories, Inc.)

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10 171319

5. Wilson, J.G. (1965). Methods for administering agents and detecting malformations in experimental animals. *Teratology: Principles and Techniques* (Wilson, J.G. and Warkany, J., eds.), University of Chicago Press, pp. 262-277.

6. Staples, R.E. and Schnell, V.L. (1964). Refinement in rapid clearing technique in the KOH-alizarin red S method for fetal bone. Stain Technol. 39:61-63.

7. Salewski, E. (1964). Färbemethode zum makroskopischen Nachweis von Implantationsstellen am Uterus der Ratte. Arch. Pathol. Exp. Pharmakol. 247:367.

8. Snedecor, G.W. and Cochran, W.G. (1967). Variance test for homogeneity of the binomial distribution. *Statistical Methods*, 6th Edition, Iowa State University Press, Ames, pp. 240-241.

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11. Dunnett, C.W. (1955). A multiple comparison procedure for comparing several treatments with a control. J. Amer. Stat. Assoc. 50:1096-1129.

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13. Dunn, O.J. (1964). Multiple comparisons using rank sums. Technometrics 6(3):241-252.

14. Siegel, S. (1956). *Nonparametric Statistics for the Behavioral Sciences*, McGraw-Hill, New York, pp. 96-104.

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PROTOCOL APPROVAL:

FOR THE TESTING FACILITY

Alan M. Hoberman, Ph.D.,DABT
Director of Research

29 JUL -98
Date

Raymond G. York, Ph.D., DABT
Associate Director of Research
Study Director

31-JUL-98
Date

Dena C. Lebo, V.M.D.
Member, Institutional Animal Care and
Use Committee

29 Jul 98
Date

FOR THE SPONSOR

Marvin T. Case, D.V.M., Ph.D.
Study Monitor

3 Aug 1998
Date

10 171321

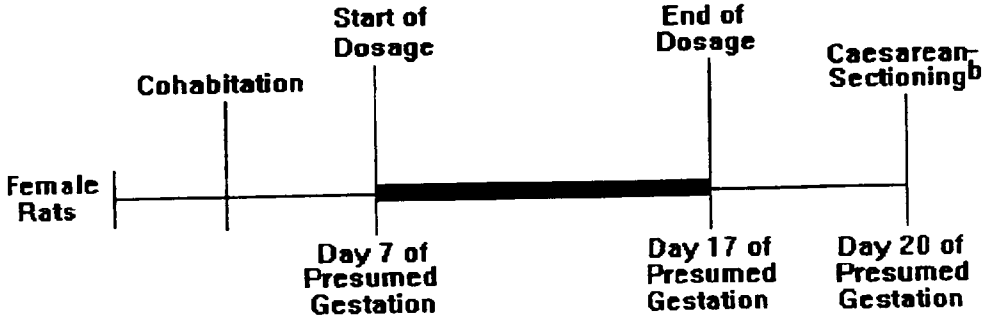
ATTACHMENT 1

SCHEMATIC OF STUDY DESIGN AND STUDY SCHEDULE

ATTACHMENT 1

STUDY SCHEMATIC

DEVELOPMENTAL TOXICITY STUDY [a]



▬ = Dosage Period

a = For additional details see "Tests, Analyses and Measurements" section of the protocol

b = Fetal evaluations (all - external, 1/2 per litter - soft tissue or skeletal)

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ATTACHMENT 2

MATERIAL SAFETY DATA SHEET

10 171324

N-ETFOSE

MATERIAL SAFETY DATA SHEET

3M
3M Center
St. Paul, Minnesota
55144-1000
1-800-364-3577 or (612) 737-6501 (24 hours)

DIVISION: 3M CHEMICALS
TRADE NAME:
FC-10 FLUORAD Brand Fluorochemical Alcohol
ID NUMBER/U.P.C.:
98-0211-1113-7 00-51135-09495-2 98-0211-1183-0 00-51135-09542-3
98-0211-1575-7 00-51135-02145-3 98-0211-6620-6 00-51135-10439-2
ZF-0002-0572-2 - - -
ISSUED: January 29, 1998
SUPERSEDES: November 05, 1997
DOCUMENT: 10-3778-7

1. INGREDIENT	C.A.S. NO.	PERCENT	
PERFLUOROOCTANESULFONAMIDO ALCOHOL.....	1691-99-2	80.0	- 90.0
PERFLUOROHEXANESULFONAMIDO ALCOHOL.....	34455-03-3	3.0	- 7.0
PERFLUOROHEPTANESULFONAMIDO ALCOHOL.....	68555-73-7	2.0	- 6.0
PERFLUOROBUTANESULFONAMIDO ALCOHOL.....	34449-89-3	2.0	- 6.0
PERFLUOROPENTANESULFONAMIDO ALCOHOL.....	68555-72-6	1.0	- 3.0

2. PHYSICAL DATA

BOILING POINT:.....	ca. 118 C @ 1 mm Hg
VAPOR PRESSURE:.....	< 10 mmHg Calc @ 20 C
VAPOR DENSITY:.....	> 1.0 Air=1 Calc @ 20 C.
EVAPORATION RATE:.....	< 1.0 BuOAc=1
SOLUBILITY IN WATER:.....	neglig.
SPECIFIC GRAVITY:.....	ca. 1.7 Water=1 (of melt)
PERCENT VOLATILE:.....	0 %
pH:.....	N/A
VISCOSITY:.....	N/D
MELTING POINT:.....	N/D

10 171325

2. PHYSICAL DATA (continued)

APPEARANCE AND ODOR:
Amber waxy solid

3. FIRE AND EXPLOSION HAZARD DATA

FLASH POINT:..... > 148 C Setaflash
FLAMMABLE LIMITS - LEL:..... N/A
FLAMMABLE LIMITS - UEL:..... N/A
AUTOIGNITION TEMPERATURE:..... N/A

EXTINGUISHING MEDIA:
Water, Carbon dioxide, Dry chemical, Foam

SPECIAL FIRE FIGHTING PROCEDURES:
Wear full protective clothing, including helmet, self-contained, positive pressure or pressure demand breathing apparatus, bunker coat and pants, bands around arms, waist and legs, face mask, and protective covering for exposed areas of the head.

UNUSUAL FIRE AND EXPLOSION HAZARDS:
See Hazardous Decomposition section for products of combustion.

4. REACTIVITY DATA

STABILITY: Stable

INCOMPATIBILITY - MATERIALS/CONDITIONS TO AVOID:
Not applicable.

HAZARDOUS POLYMERIZATION: Hazardous polymerization will not occur.

HAZARDOUS DECOMPOSITION PRODUCTS:
Carbon Monoxide and Carbon Dioxide, Oxides of Nitrogen, Oxides of Sulfur, Hydrogen Fluoride, Toxic Vapors, Gases or Particulates.

5. ENVIRONMENTAL INFORMATION

SPILL RESPONSE:
Refer to other sections of this MSDS for information regarding physical and health hazards, respiratory protection, ventilation, and personal protective equipment. Collect spilled material. Clean up residue. Place in a U.S. DOT-approved container.

10 171326

5. ENVIRONMENTAL INFORMATION (continued)

RECOMMENDED DISPOSAL:
Incinerate in a permitted hazardous waste incinerator in the presence of a combustible material. Combustion products will include HF. Dispose of waste product in a facility permitted to accept chemical waste.

ENVIRONMENTAL DATA:
Laboratory tests showed no biodegradation. 96-Hr. LD50 Fathead Minnow (Pimephales promelas) - No mortality at water saturation. No statistically significant effect on % hatch, % survival, weight, and length in 30 day Fathead Minnow egg fry study. Lab tests showed 200 fold bioconcentration of FC-10 into muscle fillets of channel catfish.

REGULATORY INFORMATION:
Volatile Organic Compounds: N/A.
VOC Less H2O & Exempt Solvents: N/A.

This product complies with the chemical registration requirements of TSCA, EINECS, CDSL, AICS and Korea.

EPCRA HAZARD CLASS:
FIRE HAZARD: No PRESSURE: No REACTIVITY: No ACUTE: Yes CHRONIC: Yes

6. SUGGESTED FIRST AID

EYE CONTACT:
Immediately flush eyes with large amounts of water. Get immediate medical attention.

SKIN CONTACT:
Immediately wash skin with soap and large amounts of water. Remove contaminated clothing. If signs/symptoms occur, call a physician. Wash contaminated clothing before reuse and dispose of contaminated shoes.

INHALATION:
If signs/symptoms occur, remove person to fresh air. If signs/symptoms continue, call a physician.

IF SWALLOWED:
Call a physician IMMEDIATELY. If swallowed, induce vomiting immediately as directed by medical personnel. Never give anything by mouth to an unconscious person.

10 171327

7. PRECAUTIONARY INFORMATION

EYE PROTECTION:
Avoid eye contact. Wear safety glasses with side shields.

SKIN PROTECTION:
Avoid skin contact. Wear appropriate gloves when handling this material. A pair of gloves made from the following material(s) are recommended: butyl rubber. Use one or more of the following personal protection items as necessary to prevent skin contact: coveralls.

RECOMMENDED VENTILATION:
Use with appropriate local exhaust ventilation. Provide sufficient ventilation to maintain emissions below recommended exposure limits. If exhaust ventilation is not adequate, use appropriate respiratory protection.

RESPIRATORY PROTECTION:
Avoid breathing of airborne material. Select one of the following NIOSH approved respirators based on airborne concentration of contaminants and in accordance with OSHA regulations: half-mask dust respirator, full-face supplied air respirator.

PREVENTION OF ACCIDENTAL INGESTION:
Do not eat, drink or smoke when using this product. Wash exposed areas thoroughly with soap and water. Wash hands after handling and before eating.

RECOMMENDED STORAGE:
Store away from heat. Keep container closed when not in use.

FIRE AND EXPLOSION AVOIDANCE:
Nonflammable.

OTHER PRECAUTIONARY INFORMATION:
No smoking: Smoking while using this product can result in contamination of the tobacco and/or smoke and lead to the formation of the hazardous decomposition products mentioned in section 4 of this MSDS.

HMIS HAZARD RATINGS: HEALTH: 1 FLAMMABILITY: 1 REACTIVITY: 0
PERSONAL PROTECTION: X (See precautions, section 7.)

EXPOSURE LIMITS

10 171328

INGREDIENT	VALUE	UNIT	TYPE	AUTH	SKIN*
PERFLUOROOCTANESULFONAMIDO ALCOHOL...	0.1	MG/M3	TWA	3M	Y
PERFLUOROHEXANESULFONAMIDO ALCOHOL...	0.1	MG/M3	TWA	3M	Y
PERFLUOROHEPTANESULFONAMIDO ALCOHOL.....	0.1	MG/M3	TWA	3M	Y

EXPOSURE LIMITS (continued)

INGREDIENT	VALUE	UNIT	TYPE	AUTH	SKIN*
PERFLUOROBUTANESULFONAMIDO ALCOHOL...	0.1	MG/M3	TWA	3M	Y
PERFLUOROPENTANESULFONAMIDO ALCOHOL.....	0.1	MG/M3	TWA	3M	Y

* SKIN NOTATION: Listed substances indicated with 'Y' under SKIN refer to the potential contribution to the overall exposure by the cutaneous route including mucous membrane and eye, either by airborne or, more particularly, by direct contact with the substance. Vehicles can alter skin absorption.

SOURCE OF EXPOSURE LIMIT DATA:
- 3M: 3M Recommended Exposure Guidelines

8. HEALTH HAZARD DATA

EYE CONTACT:
No adverse health effects are expected from eye contact.

SKIN CONTACT:
Product is not expected to be irritating to the skin.

May be absorbed through the skin and persist in the body for an extended time.

INHALATION:
May be absorbed by inhalation and persist in the body for an extended time.

IF SWALLOWED:
Ingestion is not a likely route of exposure to this product.

Illness may occur after a single swallowing of relatively large quantities of this material.

MUTAGENICITY:
Not mutagenic in in-vitro assays.

REPRODUCTIVE/DEVELOPMENTAL TOXINS:
Substance was not teratogenic in the rat at doses as high as 30 milligrams per kilogram per day via oral route.

OTHER HEALTH HAZARD INFORMATION:
This product is not known to contain any substances regulated under California Proposition 65.

A Product Toxicity Summary Sheet is available.

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SECTION CHANGE DATES

HEADING	SECTION CHANGED SINCE November 05, 1997 ISSUE

Abbreviations: N/D - Not Determined N/A - Not Applicable CA - Approximately

The information in this Material Safety Data Sheet (MSDS) is believed to be correct as of the date issued. 3M MAKES NO WARRANTIES, EXPRESSED OR IMPLIED, INCLUDING, BUT NOT LIMITED TO, ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE OR COURSE OF PERFORMANCE OR USAGE OF TRADE. User is responsible for determining whether the 3M product is fit for a particular purpose and suitable for user's method of use or application. Given the variety of factors that can affect the use and application of a 3M product, some of which are uniquely within the user's knowledge and control, it is essential that the user evaluate the 3M product to determine whether it is fit for a particular purpose and suitable for user's method of use or application.

3M provides information in electronic form as a service to its customers. Due to the remote possibility that electronic transfer may have resulted in errors, omissions or alterations in this information, 3M makes no representations as to its completeness or accuracy. In addition, information obtained from a database may not be as current as the

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ATTACHMENT 3

TEST ARTICLE PREPARATION PROCEDURE

ATTACHMENT 3

TEST ARTICLE AND CONTROL ARTICLE PREPARATION PROCEDURE

Test Article: N-EtFOSE

Vehicle: 2% Tween® 80, in R.O. Water

A. Purpose: The purpose of this procedure is to provide a method for the preparation of dosage suspensions of N-EtFOSE and the control article for oral administration to rats on Argus Study 418-011.

B. General Information:

1. All suspension containers will be labeled and color coded. Each label will specify the protocol number, test article identification, Argus batch number, concentration, dosage level, preparation date, expiration date and storage conditions.

2a. Suspensions will be prepared:
___ Daily ___X___ Weekly ___ For____ days of use

2b. Vehicle will be prepared:
___ Daily ___X___ Weekly ___ For____ days of use

3. Suspensions will be prepared at a final dosage volume of 5 mL/kg.

4. Safety:
___X___ Gloves, lab coat, goggles or safety glasses and faceshield
___X___ Dust-Mist Respirator
___ Half-Face Respirator
___ Full-Face Respirator/Positive Pressure Hood
___ Tyvek Suit/Apron

5. Dosage suspensions adjusted for Free base and % Purity.
___ Yes ___X___ No (Calculations based on 100%)
___ Free Base ___ Purity

6. Sampling requirements: Cited in protocol.

7. Storage: Cited in protocol.

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TEST ARTICLE AND CONTROL ARTICLE PREPARATION PROCEDURE

NOTE: Test article will be prepared as a serial dilution from the high dosage to the low dosage. Once the final volumes are achieved, stir bars are to be added to the containers; mixing should occur during sampling and/or administration.

C. Preparation of Vehicle

1. Add the required amount of R.O. deionized water to an appropriately labeled container. Heat the water to 50 ±5°C, add the required amount of Tween® 80 and mix until uniform (See TEST ARTICLE CALCULATIONS).

D. Test Article Suspension Preparation:

1. To prepare the 4.0-mg/mL, Group V suspension, add the required amount of test article (See TEST ARTICLE CALCULATIONS) into an appropriately sized, labeled container. Add the required amount of vehicle and heat the mixture to 80 ±5°C for approximately 30 minutes.

2. Once the test article has dissolved; spin over night while the solution cools. (Be sure there is a visible vortex, this will achieve the desired emulsion.)

3. To prepare the 2.0-mg/mL, Group IV suspension, remove the required amount of stock suspension (Group V) (See TEST ARTICLE CALCULATIONS), add the required amount of vehicle and mix.

4. To prepare the 1.0-mg/mL, Group III suspension, remove the required amount of stock suspension (Group IV) (See TEST ARTICLE CALCULATIONS), add the required amount of vehicle and mix.

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ATTACHMENT 3

TEST ARTICLE AND CONTROL ARTICLE PREPARATION PROCEDURE

5. To prepare the 0.2-mg/mL, Group II suspension, remove the required amount of stock suspension (Group III) (See TEST ARTICLE CALCULATIONS), add the required amount of vehicle and mix.

Written by: _____

Approved by: _____ Date: 31-JUL-98

Clarification: X No ___ Yes (See attached clarification form.)

Initials/Date : MC 9-21-98

10 171334

PRIMEDICA

Argus Research Laboratories, Inc.
905 Sheehy Drive, Building A
Horsham, PA 19044
Telephone: (215) 443-8710
Telefax: (215) 443-8587

PROTOCOL 418-011

ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS

SPONSOR'S STUDY NUMBER: T-6316.7

Amendment 1 - 12 August 1998

1. Frequency of Preparation (page 4 and page 1 of Attachment 3 to the protocol):

Formulations (suspensions) will be prepared daily at the Testing Facility, rather than weekly.

Reason for Change:

This change corrects the protocol.

for Alan M. Hoberman, Ph.D., DABT Date
Director of Research

Raymond G. York, Ph.D., DABT Date
Associate Director of Research
Study Director

Dena C. Lebo, V.M.D. Date
Member, Institutional Animal Care and Use Committee

Marvin T. Case, D.V.M., Ph.D. Date
Study Monitor

10 171335

PRIMEDICA

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PROTOCOL 418-011

ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS

SPONSOR'S STUDY NUMBER: T-6316.7

Amendment 2 - 11 December 1998

---

1. Sponsor (page 1 of the protocol):

   The Sponsor is 3M Corporate Toxicology, rather than 3M Toxicology Services.

   Reason for Change:

   This change was made at the request of the Sponsor.

2. Species/Strain and Reason for Selection (page 5 of the protocol):

   The test article is biologically active, rather than pharmacologically active in this strain.

   Reason for Change:

   This change was made at the request of the Sponsor to correct the protocol.

3. Route and Reason for Choice (page 7 of the protocol):

   The oral (gavage) route is a possible route of human exposure, rather than the one proposed for clinical use.

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Reason for Change:

This change was made at the request of the Sponsor to correct the protocol.

11-DEC-98

Alan M. Hoberman, Ph.D., DABT Date
Director of Research

11-DEC-98

Raymond G. York, Ph.D., DABT Date
Associate Director of Research
Study Director

Theresa A Worland for 11-Dec 98

Dena C. Lebo, V.M.D. Date
Member, Institutional Animal Care and
Use Committee

Marvin T Case 14 Dec 98

Marvin T. Case, D.V.M., Ph.D. Date
Study Monitor

10 171337

APPENDIX D

DEVIATIONS FROM THE PROTOCOL AND THE STANDARD OPERATING PROCEDURES OF THE TESTING FACILITY

DEVIATIONS FROM THE PROTOCOL AND STANDARD OPERATING PROCEDURES OF THE TESTING FACILITY

1. 26 AUG 98 (Day 4 of presumed gestation): Clinical observations and body weights were not recorded for the following rats:

Dosage Group	Dosage (mg/kg/day)	Assigned Numbers
I	0 (Vehicle)	12814 - 12816
II	1	12839 - 12847
III	5	12864 - 12872
IV	10	12883 - 12897
V	20	12912 - 12922

This deviation did not adversely affect the outcome of the study because it occurred before initiation of the dosage period and represents a small loss of data across all dosage groups.

All deviations are documented in the raw data.

17-Dec-98

Raymond G. York, Ph.D., DABT Date
Associate Director of Research
and Study Director

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APPENDIX E

TEMPERATURE AND RELATIVE HUMIDITY REPORTS

10 171340

ARGUS

Temperature and Relative Humidity Report
Location: Room 04

Protocol Number: 418-011

Range of Dates: 11-Aug-1998 13:45 to 12-Sep-1998 10:26

	Temperature 64°F to 79°F		Relative Humidity 30% to 70%	
Target Range:				
Species: Rat				
Total Number of Days:	33		33	
Total Number of Hours:	764.49		764.49	
Total Number of Data Points:	766		766	
Mean (± SD):	69.3	(± 0.4)	47.7	(± 2.4)
Maximum:	70.2		54.1	
Median:	69.3		47.7	
Minimum:	67.7		41.3	
Number of Points in Range (%):	766	(100.0)	766	(100.0)
Number of Points High (%):	0	(0.0)	0	(0.0)
Number of Points Low (%):	0	(0.0)	0	(0.0)

Report Generated: 23-Oct-1998 at 09:15

COMMENTS: _____

REVIEWED BY: _____ **DATE:** 11/23/98

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Cumulative by Location (v04.01.97)

APPENDIX F

PILOT REPORT

10 171342

FINAL PILOT REPORT

Study Title

Oral (Gavage) Dosage-Range Developmental Toxicity Study of N-EtFOSE in Rats

Sponsor's Study Number: T-6316.7

Author

Raymond G. York, Ph.D., DABT
(Study Director)

Study Completed On

10 December 1998
(Final Pilot Report)

Performing Laboratory

Argus Research Laboratories, Inc.
905 Sheehy Drive, Building A
Horsham, Pennsylvania 19044-1297

Laboratory Project ID

Argus Research Laboratories, Inc., Protocol Number: 418-011P

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS

TABLE OF CONTENTS

10 171345

TITLE: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS

ARGUS RESEARCH LABORATORIES, INC.
PROTOCOL NUMBER: 418-011P
SPONSOR'S STUDY NUMBER: T-6316.7

ABSTRACT

Fifty-six presumed pregnant Crl:CD®BR VAF/Plus® (Sprague-Dawley) rats were randomly assigned to seven dosage groups [eight per group (Groups I through VII)]. Suspensions of the N-EtFOSE were administered orally via gavage once daily to these naturally-bred female rats on days 6 through 17 of presumed gestation (DGs 6 to 17) at dosages of 0 (Vehicle), 1, 5, 10, 20, 25 and 35 mg/kg/day. The dosage volume was 5 mL/kg, adjusted daily on the basis of the individual body weights recorded immediately before administration of the test article.

Checks for viability were made twice daily. Clinical observations were recorded daily before dosage, approximately one hour after administration and then four to six hours later. These observations were also recorded once daily during the postdosage period. Body weights were recorded daily during the dosage and postdosage periods and feed consumption values were recorded on DGs 0, 4, 6, 8, 10, 12, 14, 16, 18 and 20.

All rats were sacrificed on DG 20 and examined for the number and distribution of corpora lutea, implantation sites and uterine contents. A gross necropsy of the thoracic, abdominal and pelvic viscera was performed. Fetuses were weighed and examined for gross external alterations and sex.

All rats survived until scheduled sacrifice. Clinical observations during gestation considered treatment-related were limited to single rats with chromorhinorrhea, chromodacryorrhea or emaciation at the 20 and 35 mg/kg/day dosages. Clinical observations of localized alopecia and emaciation were confirmed at necropsy. No additional necropsy observations occurred.

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Body weight gains and absolute and relative feed consumption values for the entire dosage period (calculated as DGs 6 to 18), the entire interval after initiation of treatment (DGs 6 to 20) and the entire gestation period (DGs 0 to 20) were reduced in the 10 mg/kg/day and higher dosage groups, compared to the control group.

Reduced fetal body weights occurred at the 25 and 35 mg/kg/day dosages, relative to the control group (-8.5% and -13.8%, respectively). No other Caesarean-sectioning or litter parameters were affected by dosages of the test article as high as 35 mg/kg/day. One litter in the 35 mg/kg/day dosage group consisted of two early resorptions and 13 fetuses with cleft palate (two also had whole body edema). These fetal findings were considered genetic in origin and not test article-related.

Based on the results of this dosage-range finding study, dosages of 0, 1, 5, 10 and 20 mg/kg/day were recommended for the full developmental toxicity study of N-EtFOSE in rats.

I. Purpose:

The purpose of this study was to provide information for the selection of dosages to be used in the developmental toxicity (embryo-fetal toxicity and teratogenic potential) study of N-EtFOSE administered orally via gavage to Crl:CD®BR VAF/Plus® presumed pregnant female rats.

II. Methods[1]:

The test article, N-EtFOSE [lot/batch number FM-3929 (30035, 30037, 30039)], was received on 20 May 1998, and stored at room temperature. The vehicle was 2% Tween® 80 in reverse osmosis membrane processed deionized water (R.O. deionized water). The Tween® 80 was received from J.T. Baker, Philipsburg, New Jersey, on 22 May 1998, and was stored at room temperature. The R.O. deionized water is available from a continuous source at the Testing Facility and is maintained at room temperature. The prepared vehicle was stored at room temperature. Test article formulations were prepared daily.

Fifty-six presumed pregnant Crl:CD®BR VAF/Plus® (Sprague-Dawley) rats were randomly assigned to seven dosage groups [eight per group (Groups I through VII)]. Suspensions of the test article were administered orally via gavage once daily to these naturally-bred female rats on days 6 through 17 of presumed gestation (DGs 6 to 17) at dosages of 0 (Vehicle), 1, 5, 10, 20, 25 and 35 mg/kg/day. The dosage volume was 5 mL/kg, adjusted daily on the basis of the individual body weights recorded immediately before administration of the test article.

Checks for viability were made twice daily. Clinical observations were recorded daily before dosage, approximately one hour after administration and then four to six hours later. These observations were also recorded once daily during the postdosage period. Body weights were recorded daily during the dosage and postdosage periods and feed consumption values were recorded on DGs 0, 4, 6, 8, 10, 12, 14, 16, 18 and 20.

---

a. Detailed descriptions of all procedures used in the conduct of this study are provided in the appropriate sections of this report and in the attached protocol and amendments. Deviations from the Protocol and Standard Operating Procedures of the Testing Facility are available in the raw data.

All rats were sacrificed on DG 20 and examined for the number and distribution of corpora lutea, implantation sites live and dead fetuses and early and late resorptions. A gross necropsy of the thoracic, abdominal and pelvic viscera was performed. Fetuses were weighed and examined for gross external alterations and sex.

III. Results:

A. Mortality, Clinical and Necropsy Observations (Summary - Table 1; Individual Data - Tables 9 and 10)

A.1. Mortality

All rats survived until scheduled sacrifice.

A.2. Clinical Observations

Clinical observations during gestation considered treatment-related were limited to single rats with chromorhinorrhea, chromodacryorrhea or emaciation at the 20 and 35 mg/kg/day dosages.

All other clinical observations were considered unrelated to the test article because: 1) the incidences were not dosage-dependent; and/or 2) they occurred in only one rat. These observations included localized alopecia on the limbs, underside, back and/or neck.

A.3. Necropsy Observations

Clinical observations of localized alopecia and emaciation were confirmed at necropsy. No additional necropsy observations occurred.

B. Maternal Body Weights and Body Weight Changes (Figure 1; Summaries - Tables 2 and 3; Individual Data - Table 11)

Maternal body weight gains in the 10 mg/kg/day and higher dosage groups were decreased, compared to the control group on gestation days (DGs) 6 to 8 and 8 to 10. Body weights were decreased for the 25 mg/kg/day and higher dosages on DGs 10 to 12, 12 to 14 and 14 to 16. Maternal body weight gains in the 1, 5, 10, 20, 25 and 35 mg/kg/day dosage groups were generally comparable to control values postdosage (DGs 18 to 20).

Reflecting these effects of the test article, weight gains for the entire dosage period (calculated as DGs 6 to 18), the entire interval after initiation of treatment (DGs 6 to 20) and the entire gestation period (DGs 0 to 20) were reduced in the 10 mg/kg/day and higher dosage groups, compared to the control group.

Maternal body weights and body weight gains for the 1 and 5 mg/kg/day dosage groups were generally comparable to control values over each interval tabulated.

C. **Maternal Absolute (g/day) and Relative (g/kg/day) Feed Consumption Values (Summaries - Tables 4 and 5; Individual Data - Table 12)**

Absolute and relative feed consumption values for the 10 mg/kg/day and higher dosage groups were decreased, compared to the control group at all tabulated intervals during the dosage period (DGs 6 to 8, 8 to 10, 10 to 12, 12 to 14, 14 to 16 and 16 to 18). Maternal feed consumption values for the 1, 5, 10, 20, 25 and 35 mg/kg/day dosage groups were generally comparable to control values postdosage (DGs 18 to 20).

Reflecting these effects of the test article, absolute and relative feed consumption values for the entire dosage period (calculated as DGs 6 to 18), the entire interval after initiation of treatment (DGs 6 to 20) and the entire gestation period (DGs 0 to 20) were reduced in the 10 mg/kg/day and higher dosage groups, compared to the control group.

Absolute and relative feed consumption values for the 1 and 5 mg/kg/day dosage groups were generally comparable to control values over each interval tabulated.

D. **Caesarean-Sectioning and Litter Observations (Summaries - Tables 6 through 8; Individual Data – Tables 13 through 15)**

Caesarean-sectioning observations were based on 8 (100%), 7 (87.5%), 8 (100%), 8 (100%), 8 (100%), 8 (100%) and 8 (100%) pregnant rats with live litters in the seven respective dosage groups.

Reduced fetal body weights occurred at the 25 and 35 mg/kg/day dosages, relative to the control group (-8.5% and -13.8%, respectively). This observation was considered an effect of the test article because it was dosage-dependent

and occurred at the dosages in which there was maternal toxicity observed (decreased body weight and feed consumption values).

No other Caesarean-sectioning or litter parameters were affected by dosages of the test article as high as 35 mg/kg/day. The litter averages for corpora lutea, implantations, litter size, live fetuses, resorptions (early and late), dams with any resorptions and percent live male fetuses were comparable among the 0 Vehicle), 1, 5, 10, 20, 25 and 35 mg/kg/day dosage groups. No dams had all resorbed conceptuses, there were no dead fetuses and all placentae appeared normal.

Totals of 109, 93, 116, 110, 118, 116 and 114 live fetuses were evaluated for external gross alterations in the seven respective dosage groups. No fetal gross external alterations were observed at dosages up to 25 mg/kg/day. One litter (10650) in the 35 mg/kg/day dosage group consisted of two early resorptions and 13 fetuses with cleft palate (two also had whole body edema). These fetal findings were considered genetic in origin and not test article-related.

IV. Conclusion:

Based on the results of this study, dosages of 0 (Vehicle), 1, 5, 10 and 20 mg/kg/day of N-EtFOSE are recommended for the developmental toxicity study in rats (418-011). The 1 mg/kg/day dosage is expected to be a no-observable-effect-level (NOEL) for both maternal and embryo-fetal toxicity, and the 20 mg/kg/day dosage is expected to produce maternal toxicity (decreased maternal body weight and feed consumption values) and minimal developmental toxicity (decreased fetal body weights and possibly delayed ossification).

for _____ 10DEC 98
Alan M. Hoberman, Ph.D., DABT Date
Director of Research

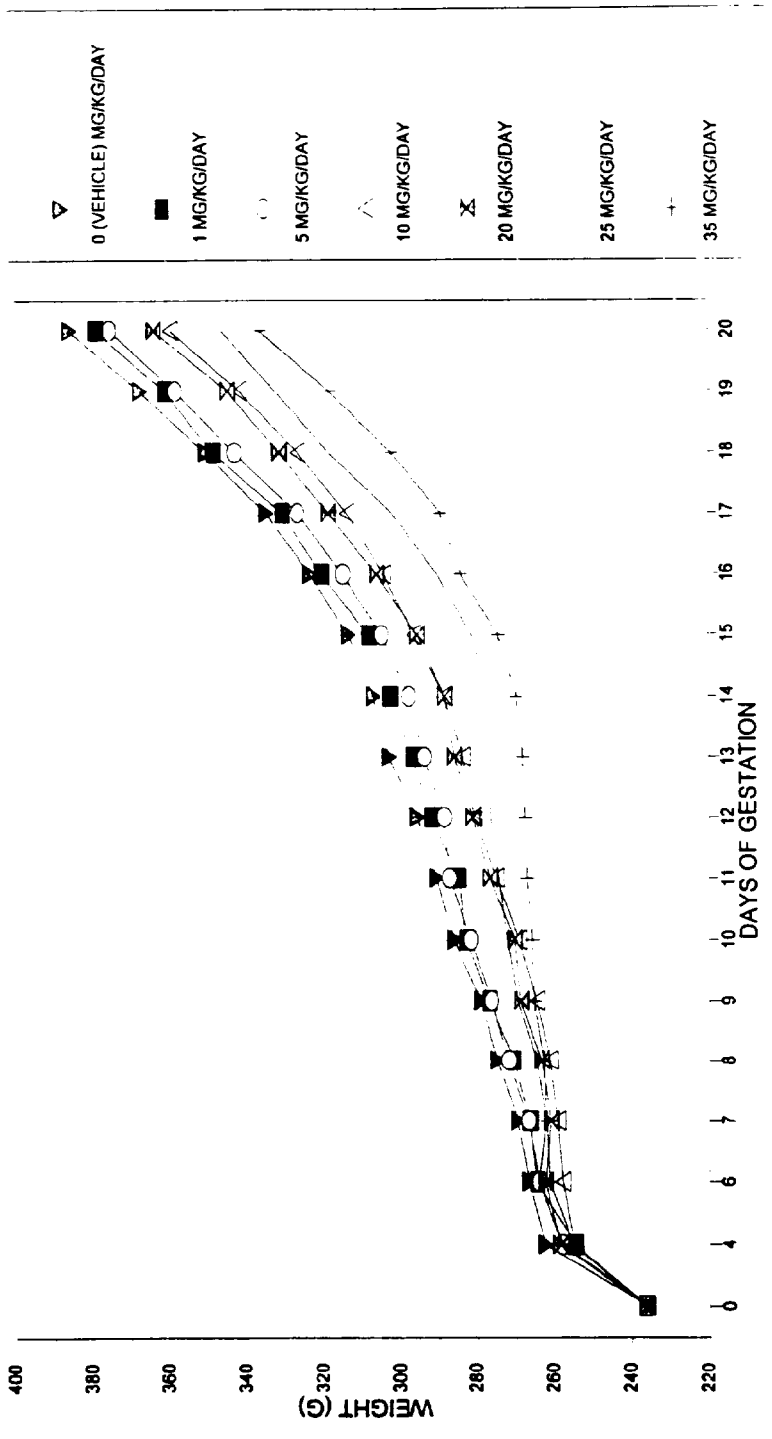
_____ 10-DEC-98
Raymond G. York, Ph.D., DABT Date
Associate Director of Research and
Study Director

10 171351

10 171352

MATERNAL BODY WEIGHTS

Figure 1



PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T 6316.7)

TABLE 1 (PAGE 1): CLINICAL AND NECROPSY OBSERVATIONS - SUMMARY

DOSAGE GROUP		I	II	III	IV
DOSAGE (MG/KG/DAY)a		0 (VEHICLE)	1	5	10
MAXIMUM POSSIBLE INCIDENCE		120/ 8	120/ 8	120/ 8	120/ 8
MORTALITY		0	0	0	0
LOCALIZED ALOPECIA:	TOTAL	0/ 0	0/ 0	15/ 2	0/ 0
	LIMBS	0/ 0	0/ 0	8/ 1	0/ 0
	UNDERSIDE	0/ 0	0/ 0	7/ 1	0/ 0
	BACK	0/ 0	0/ 0	0/ 0	0/ 0
	NECK	0/ 0	0/ 0	1/ 1	0/ 0
EMACIATION		0/ 0	0/ 0	0/ 0	0/ 0
CHROMORHINORRHEA		0/ 0	0/ 0	0/ 0	0/ 0
CHROMODACRYORRHEA		0/ 0	0/ 0	0/ 0	0/ 0

PERSISTENT ADVERSE CLINICAL OBSERVATIONS WERE CONFIRMED AT NECROPSY, NO ADDITIONAL GROSS LESIONS WERE IDENTIFIED

MAXIMUM POSSIBLE INCIDENCE = (DAYS x RATS)/NUMBER OF RATS EXAMINED PER GROUP ON DAYS 6 THROUGH 20 OF PRESUMED GESTATION.
N/N = TOTAL NUMBER OF OBSERVATIONS/NUMBER OF RATS WITH OBSERVATION.
a. Dosage occurred on days 6 through 17 of presumed gestation.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 1 (PAGE 2): CLINICAL AND NECROPSY OBSERVATIONS - SUMMARY

DOSAGE GROUP DOSAGE (MG/KG/DAY)a		V 20	VI 25	VII 35
MAXIMUM POSSIBLE INCIDENCE		120/ 8	120/ 8	120/ 8
MORTALITY		0	0	0
LOCALIZED ALOPECIA:	TOTAL	0/ 0	7/ 1	20/ 2
	LIMBS	0/ 0	0/ 0	12/ 1
	UNDERSIDE	0/ 0	7/ 1	8/ 1
	BACK	0/ 0	6/ 1	8/ 1
	NECK	0/ 0	0/ 0	0/ 0
EMACIATION		0/ 0	0/ 0	4/ 1
CHROMORHINORRHEA		0/ 0	0/ 0	1/ 1
CHROMODACRYORRHEA		3/ 1	0/ 0	0/ 0

PERSISTENT ADVERSE CLINICAL OBSERVATIONS WERE CONFIRMED AT NECROPSY. NO ADDITIONAL GROSS LESIONS WERE IDENTIFIED

MAXIMUM POSSIBLE INCIDENCE = (DAYS x RATS)/NUMBER OF RATS EXAMINED PER GROUP ON DAYS 6 THROUGH 20 OF PRESUMED GESTATION.
N/N = TOTAL NUMBER OF OBSERVATIONS/NUMBER OF RATS WITH OBSERVATION.
a. Dosage occurred on days 6 through 17 of presumed gestation.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 2 (PAGE 1): MATERNAL BODY WEIGHTS - SUMMARY

DOSAGE GROUP DOSAGE (MG/KG/DAY)a		I 0 (VEHICLE)	II 1	III 5	IV 10
RATS TESTED	N	8	8	8	8
PREGNANT	N	8	7	8	8
BODY WEIGHT (G)					
DAY 0	MEAN±S.D.	235.9 ± 10.3	236.4 ± 12.6	236.4 ± 8.4	236.0 ± 8.1
DAY 4	MEAN±S.D.	262.4 ± 15.2	254.7 ± 10.3	258.0 ± 9.0	255.0 ± 11.8
DAY 6	MEAN±S.D.	266.4 ± 13.9	264.4 ± 16.3	263.9 ± 10.2	257.8 ± 12.9
DAY 7	MEAN±S.D.	269.4 ± 16.6	266.3 ± 14.9	266.5 ± 9.4	259.0 ± 14.3
DAY 8	MEAN±S.D.	274.6 ± 17.0	270.4 ± 16.6	271.8 ± 8.7	260.9 ± 18.6
DAY 9	MEAN±S.D.	278.9 ± 17.2	276.6 ± 16.2	276.1 ± 9.8	264.4 ± 16.5
DAY 10	MEAN±S.D.	285.8 ± 19.0	282.7 ± 15.5	281.4 ± 9.8	268.9 ± 17.2
DAY 11	MEAN±S.D.	290.4 ± 19.4	284.4 ± 17.9	286.9 ± 11.0	274.8 ± 18.7
DAY 12	MEAN±S.D.	295.4 ± 18.2	291.7 ± 18.6	288.4 ± 8.5	280.4 ± 18.0
DAY 13	MEAN±S.D.	302.6 ± 20.5	296.6 ± 16.5	293.4 ± 9.9	283.4 ± 20.4
DAY 14	MEAN±S.D.	306.8 ± 21.9	302.4 ± 16.5	297.5 ± 8.9	288.2 ± 19.6
DAY 15	MEAN±S.D.	313.1 ± 21.9	307.8 ± 17.8	304.4 ± 9.6	296.1 ± 21.8
DAY 16	MEAN±S.D.	323.0 ± 24.0	320.0 ± 21.6	314.5 ± 9.5	303.8 ± 20.7
DAY 17	MEAN±S.D.	334.4 ± 24.0	330.1 ± 22.8	326.1 ± 10.0	313.4 ± 22.6
DAY 18	MEAN±S.D.	350.1 ± 29.0	348.0 ± 23.6	342.5 ± 8.5	326.2 ± 22.1
DAY 19	MEAN±S.D.	367.2 ± 29.0	360.6 ± 26.6	357.8 ± 11.2	341.2 ± 25.5
DAY 20	MEAN±S.D.	385.6 ± 31.8	378.7 ± 32.3	375.0 ± 9.9	359.1 ± 27.6

DAY = DAY OF GESTATION
a. Dosage occurred on days 6 through 17 of gestation.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 2 (PAGE 2): MATERNAL BODY WEIGHTS - SUMMARY

DOSAGE GROUP DOSAGE (MG/KG/DAY)a		V 20	VI 25	VII 35
RATS TESTED	N	8	8	8
PREGNANT	N	8	8	8
BODY WEIGHT (G)				
DAY 0	MEAN±S.D.	236.2 ± 8.0	236.0 ± 8.5	236.5 ± 9.2
DAY 4	MEAN±S.D.	258.5 ± 8.2	257.9 ± 12.6	255.2 ± 11.3
DAY 6	MEAN±S.D.	262.1 ± 8.2	264.0 ± 14.2	261.1 ± 10.5
DAY 7	MEAN±S.D.	260.8 ± 8.1	262.0 ± 15.8	261.9 ± 9.4
DAY 8	MEAN±S.D.	263.1 ± 9.0	264.4 ± 16.5	262.6 ± 7.2
DAY 9	MEAN±S.D.	268.5 ± 12.5	269.2 ± 16.3	265.0 ± 9.3
DAY 10	MEAN±S.D.	270.1 ± 12.6	272.1 ± 15.2	265.6 ± 11.4
DAY 11	MEAN±S.D.	276.5 ± 13.7	274.1 ± 15.0	266.9 ± 10.9
DAY 12	MEAN±S.D.	280.9 ± 12.5	276.0 ± 17.8	267.2 ± 12.2
DAY 13	MEAN±S.D.	285.6 ± 15.3	277.0 ± 16.7	267.8 ± 16.9
DAY 14	MEAN±S.D.	288.1 ± 12.9	276.8 ± 18.7	269.4 ± 20.7
DAY 15	MEAN±S.D.	295.1 ± 17.1	281.0 ± 19.2	274.0 ± 25.8
DAY 16	MEAN±S.D.	305.6 ± 18.2	289.9 ± 21.6	283.8 ± 30.1
DAY 17	MEAN±S.D.	318.2 ± 18.6	301.6 ± 23.5	289.0 ± 34.6
DAY 18	MEAN±S.D.	330.9 ± 21.3	318.0 ± 22.3	302.0 ± 39.7
DAY 19	MEAN±S.D.	344.2 ± 22.5	332.0 ± 22.4	318.1 ± 41.8
DAY 20	MEAN±S.D.	363.5 ± 22.1	345.8 ± 20.4	336.1 ± 41.6

DAY = DAY OF GESTATION
a. Dosage occurred on days 6 through 17 of gestation.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 3 (PAGE 1): MATERNAL BODY WEIGHT CHANGES - SUMMARY

DOSAGE GROUP DOSAGE (MG/KG/DAY)a		I 0 (VEHICLE)	II 1	III 5	IV 10
RATS TESTED	N	8	8	8	8
PREGNANT	N	8	7	8	8
BODY WEIGHT CHANGE (G)					
DAYS 0 - 6	MEAN±S.D.	+30.5 ± 10.3	+28.0 ± 7.2	+27.5 ± 5.8	+21.8 ± 6.4
DAYS 6 - 8	MEAN±S.D.	+8.2 ± 4.3	+6.0 ± 3.4	+7.9 ± 2.3	+3.1 ± 11.4
DAYS 8 - 10	MEAN±S.D.	+11.1 ± 2.9	+12.3 ± 1.5	+9.6 ± 3.1	+8.0 ± 5.0
DAYS 10 - 12	MEAN±S.D.	+9.6 ± 4.0	+9.0 ± 5.4	+7.0 ± 2.9	+11.5 ± 6.7
DAYS 12 - 14	MEAN±S.D.	+11.4 ± 5.0	+10.7 ± 5.8	+9.1 ± 3.1	+7.9 ± 3.2
DAYS 14 - 16	MEAN±S.D.	+16.2 ± 6.7	+17.6 ± 8.0	+17.0 ± 2.2	+15.5 ± 3.2
DAYS 16 - 18	MEAN±S.D.	+27.1 ± 7.4	+28.0 ± 4.7	+28.0 ± 4.5	+22.5 ± 4.0
DAYS 6 - 18	MEAN±S.D.	+83.8 ± 20.5	+83.6 ± 10.4	+78.6 ± 8.8	+68.5 ± 13.1
DAYS 18 - 20	MEAN±S.D.	+35.5 ± 7.0	+30.7 ± 11.4	+32.5 ± 5.1	+32.9 ± 6.8
DAYS 6 - 20	MEAN±S.D.	+119.2 ± 24.4	+114.3 ± 21.2	+111.1 ± 11.1	+101.4 ± 17.7
DAYS 0 - 20	MEAN±S.D.	+149.8 ± 33.1	+142.3 ± 26.4	+138.6 ± 12.2	+123.1 ± 20.5

DAYS = DAYS OF GESTATION
a. Dosage occurred on days 6 through 17 of gestation.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE RANGE DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 3 (PAGE 2): MATERNAL BODY WEIGHT CHANGES - SUMMARY

DOSAGE GROUP DOSAGE (MG/KG/DAY)a		V 20	VI 25	VII 35
RATS TESTED	N	8	8	8
PREGNANT	N	8	8	8
BODY WEIGHT CHANGE (G)				
DAYS 0 - 6	MEAN±S.D.	+25.9 ± 7.6	+28.0 ± 9.4	+24.6 ± 6.6
DAYS 6 - 8	MEAN±S.D.	+1.0 ± 4.8	+0.4 ± 4.5	+1.5 ± 6.7
DAYS 8 - 10	MEAN±S.D.	+7.0 ± 5.6	+7.8 ± 4.5	+3.0 ± 7.2
DAYS 10 - 12	MEAN±S.D.	+10.8 ± 3.6	+3.9 ± 7.6	+1.6 ± 10.5
DAYS 12 - 14	MEAN±S.D.	+7.2 ± 2.4	+0.8 ± 6.2	+2.1 ± 13.4
DAYS 14 - 16	MEAN±S.D.	+17.5 ± 7.9	+13.1 ± 11.3	+14.4 ± 11.1
DAYS 16 - 18	MEAN±S.D.	+25.2 ± 4.8	+28.1 ± 9.3	+18.2 ± 11.7
DAYS 6 - 18	MEAN±S.D.	+68.8 ± 15.4	+54.0 ± 13.9	+40.9 ± 42.3
DAYS 18 - 20	MEAN±S.D.	+32.6 ± 3.4	+27.8 ± 7.6	+34.1 ± 4.5
DAYS 6 - 20	MEAN±S.D.	+101.4 ± 16.1	+81.8 ± 11.9	+75.0 ± 44.6
DAYS 0 - 20	MEAN±S.D.	+127.2 ± 21.0	+109.8 ± 14.0	+99.6 ± 44.4

DAYS = DAYS OF GESTATION
a. Dosage occurred on days 6 through 17 of gestation.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 4 (PAGE 1): MATERNAL ABSOLUTE FEED CONSUMPTION VALUES (G/DAY) SUMMARY

DOSAGE GROUP		I	II	III	IV
DOSAGE (MG/KG/DAY)a		0 (VEHICLE)	1	5	10
RATS TESTED	N	8	8	8	8
PREGNANT	N	8	7	8	8
FEED CONSUMPTION (G/DAY)					
DAYS 0 - 6	MEAN±S.D.	23.6 ± 3.6	21.9 ± 2.9	23.5 ± 1.0	21.3 ± 2.4
DAYS 6 - 8	MEAN±S.D.	25.9 ± 5.4	23.5 ± 2.4	22.0 ± 4.6	19.1 ± 5.6
DAYS 8 - 10	MEAN±S.D.	25.4 ± 3.2	24.1 ± 2.5	24.2 ± 1.1	20.8 ± 2.7
DAYS 10 - 12	MEAN±S.D.	26.2 ± 3.7 [7]b	23.1 ± 2.0	24.4 ± 2.2	22.8 ± 2.0
DAYS 12 - 14	MEAN±S.D.	28.1 ± 8.2 [7]b	27.9 ± 5.2	23.5 ± 2.5	22.7 ± 3.3
DAYS 14 - 16	MEAN±S.D.	24.2 ± 2.3	25.1 ± 3.0	23.4 ± 2.5	21.1 ± 2.9
DAYS 16 - 18	MEAN±S.D.	25.9 ± 2.6	25.5 ± 4.4	25.4 ± 1.7	22.2 ± 2.6
DAYS 6 - 18	MEAN±S.D.	25.9 ± 3.4	24.8 ± 1.6	23.8 ± 1.4	21.4 ± 2.6
DAYS 18 - 20	MEAN±S.D.	26.2 ± 3.0	26.2 ± 2.0	24.8 ± 2.2	24.0 ± 3.1
DAYS 6 - 20	MEAN±S.D.	25.9 ± 3.2	25.0 ± 1.6	24.0 ± 1.3	21.8 ± 2.6
DAYS 0 - 20	MEAN±S.D.	25.2 ± 3.1	24.1 ± 1.8	23.8 ± 0.9	21.7 ± 2.3

DAYS = DAYS OF GESTATION
[ ] = NUMBER OF VALUES AVERAGED
a. Dosage occurred on days 6 through 17 of gestation.
b. Excludes values that were associated with spillage.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T 6316.7)

TABLE 4 (PAGE 2): MATERNAL ABSOLUTE FEED CONSUMPTION VALUES (G/DAY) - SUMMARY

DOSAGE GROUP		V	VI	VII
DOSAGE (MG/KG/DAY)a		20	25	35
RATS TESTED	N	8	8	8
PREGNANT	N	8	8	8
FEED CONSUMPTION (G/DAY)				
DAYS 0 - 6	MEAN±S.D.	24.8 ± 3.3	22.0 ± 2.7	22.6 ± 1.5
DAYS 6 - 8	MEAN±S.D.	21.2 ± 3.3	19.8 ± 3.7	21.1 ± 2.7
DAYS 8 - 10	MEAN±S.D.	22.2 ± 4.4	20.9 ± 2.4	20.1 ± 3.5
DAYS 10 - 12	MEAN±S.D.	23.1 ± 3.0	20.1 ± 2.4	18.9 ± 5.3
DAYS 12 - 14	MEAN±S.D.	23.1 ± 3.4	16.6 ± 3.3	20.1 ± 8.7
DAYS 14 - 16	MEAN±S.D.	22.6 ± 5.4	17.8 ± 5.8	18.1 ± 7.2
DAYS 16 - 18	MEAN±S.D.	23.4 ± 3.7	21.0 ± 3.3	18.6 ± 5.6
DAYS 6 - 18	MEAN±S.D.	22.6 ± 3.3	19.4 ± 2.6	19.5 ± 4.2
DAYS 18 - 20	MEAN±S.D.	23.8 ± 2.1	21.5 ± 1.6	24.2 ± 4.3
DAYS 6 - 20	MEAN±S.D.	22.8 ± 3.1	19.7 ± 2.3	20.2 ± 4.1
DAYS 0 - 20	MEAN±S.D.	23.4 ± 2.8	20.4 ± 2.1	20.9 ± 3.0

DAYS = DAYS OF GESTATION
a. Dosage occurred on days 6 through 17 of gestation.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 5 (PAGE 1): MATERNAL RELATIVE FEED CONSUMPTION VALUES (G/KG/DAY) - SUMMARY

DOSAGE GROUP		I	II	III	IV
DOSAGE (MG/KG/DAY)a		0 (VEHICLE)	1	5	10
RATS TESTED	N	8	8	8	8
PREGNANT	N	8	7	8	8
FEED CONSUMPTION (G/KG/DAY)					
DAYS 0 - 6	MEAN±S.D.	92.2 ± 11.2	86.7 ± 9.8	93.1 ± 2.7	85.1 ± 7.1
DAYS 6 - 8	MEAN±S.D.	95.5 ± 16.5	88.1 ± 8.3	82.5 ± 17.8	72.9 ± 19.5
DAYS 8 - 10	MEAN±S.D.	90.7 ± 7.5	87.2 ± 7.6	87.6 ± 4.5	78.4 ± 6.2
DAYS 10 - 12	MEAN±S.D.	90.0 ± 8.8 [7]b	80.5 ± 4.2	85.6 ± 7.8	82.8 ± 3.6
DAYS 12 - 14	MEAN±S.D.	93.4 ± 26.7 [7]b	95.1 ± 23.5	80.3 ± 9.2	79.7 ± 8.5
DAYS 14 - 16	MEAN±S.D.	77.1 ± 7.2	80.8 ± 7.6	76.5 ± 8.1	71.3 ± 7.6
DAYS 16 - 18	MEAN±S.D.	77.3 ± 5.8	76.3 ± 9.6	77.7 ± 5.6	70.4 ± 4.1
DAYS 6 - 18	MEAN±S.D.	86.4 ± 9.6	84.2 ± 5.0	81.4 ± 5.7	75.5 ± 5.3
DAYS 18 - 20	MEAN±S.D.	71.4 ± 7.8	72.4 ± 3.3	69.2 ± 5.5	69.9 ± 5.9
DAYS 6 - 20	MEAN±S.D.	83.8 ± 8.9	82.1 ± 4.5	79.1 ± 5.1	74.5 ± 4.7
DAYS 0 - 20	MEAN±S.D.	83.2 ± 7.6	80.8 ± 4.5	80.4 ± 3.6	75.5 ± 3.9

DAYS = DAYS OF GESTATION
[ ] = NUMBER OF VALUES AVERAGED
a. Dosage occurred on days 6 through 17 of gestation.
b. Excludes values that were associated with spillage.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE RANGE DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 5 (PAGE 2): MATERNAL RELATIVE FEED CONSUMPTION VALUES (G/KG/DAY) - SUMMARY

DOSAGE GROUP DOSAGE (MG/KG/DAY)a		V 20	VI 25	VII 35
RATS TESTED	N	8	8	8
PREGNANT	N	8	8	8
FEED CONSUMPTION (G/KG/DAY)				
DAYS 0 - 6	MEAN±S.D.	98.1 ± 13.5	86.8 ± 8.0	90.2 ± 6.1
DAYS 6 - 8	MEAN±S.D.	80.8 ± 10.5	74.5 ± 10.1	80.5 ± 10.4
DAYS 8 - 10	MEAN±S.D.	82.6 ± 13.8	77.7 ± 5.4	75.9 ± 11.8
DAYS 10 - 12	MEAN±S.D.	83.7 ± 9.1	73.1 ± 7.3	70.8 ± 19.3
DAYS 12 - 14	MEAN±S.D.	80.7 ± 9.8	59.8 ± 9.4	74.2 ± 32.8
DAYS 14 - 16	MEAN±S.D.	75.8 ± 16.0	62.3 ± 19.0	63.9 ± 25.3
DAYS 16 - 18	MEAN±S.D.	73.2 ± 9.1	69.2 ± 8.8	62.6 ± 15.4
DAYS 6 - 18	MEAN±S.D.	79.0 ± 8.9	69.2 ± 5.9	71.2 ± 13.4
DAYS 18 - 20	MEAN±S.D.	68.8 ± 4.1	64.9 ± 4.6	76.1 ± 9.3
DAYS 6 - 20	MEAN±S.D.	77.1 ± 7.6	68.4 ± 4.6	71.6 ± 11.9
DAYS 0 - 20	MEAN±S.D.	80.8 ± 7.1	72.0 ± 3.6	75.7 ± 7.9

DAYS = DAYS OF GESTATION
a. Dosage occurred on days 6 through 17 of gestation.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 6 (PAGE 1): CAESAREAN-SECTIONING OBSERVATIONS - SUMMARY

DOSAGE GROUP DOSAGE (MG/KG/DAY)a		I 0 (VEHICLE)	II 1	III 5	IV 10
RATS TESTED	N	8	8	8	8
PREGNANT	N(%)	8(100.0)	7(87.5)	8(100.0)	8(100.0)
RATS PREGNANT AND CAESAREAN-SECTIONED ON DAY 20 OF GESTATION	N	8	7	8	8
CORPORA LUTEA	MEAN±S.D.	16.0 ± 2.6	15.7 ± 2.6	16.0 ± 1.8	16.0 ± 2.7
IMPLANTATIONS	MEAN±S.D.	14.0 ± 4.5	13.6 ± 3.2	15.2 ± 1.8	14.4 ± 1.7
LITTER SIZES	MEAN±S.D.	13.6 ± 4.6	13.3 ± 3.0	14.5 ± 1.7	13.8 ± 1.8
LIVE FETUSES	N	109	93	116	110
	MEAN±S.D.	13.6 ± 4.6	13.3 ± 3.0	14.5 ± 1.7	13.8 ± 1.8
DEAD FETUSES	N	0	0	0	0
RESORPTIONS	MEAN±S.D.	0.4 ± 0.7	0.3 ± 0.5	0.8 ± 1.2	0.6 ± 0.7
EARLY RESORPTIONS	N	3	2	6	4
	MEAN±S.D.	0.4 ± 0.7	0.3 ± 0.5	0.8 ± 1.2	0.5 ± 0.8
LATE RESORPTIONS	N	0	0	0	1
	MEAN±S.D.	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.1 ± 0.4
DAMS WITH ANY RESORPTIONS	N(%)	2(25.0)	2(28.6)	3(37.5)	4(50.0)
DAMS WITH ALL CONCEPTUSES RESORBED	N	0	0	0	0
DAMS WITH VIABLE FETUSES	N(%)	8(100.0)	7(100.0)	8(100.0)	8(100.0)
PLACENTAE APPEARED NORMAL	N(%)	8(100.0)	7(100.0)	8(100.0)	8(100.0)

a. Dosage occurred on days 6 through 17 of gestation.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 6 (PAGE 2): CAESAREAN-SECTIONING OBSERVATIONS - SUMMARY

DOSAGE GROUP DOSAGE (MG/KG/DAY)a		V 20	VI 25	VII 35
RATS TESTED	N	8	8	8
PREGNANT	N(%)	8(100.0)	8(100.0)	8(100.0)
RATS PREGNANT AND CAESAREAN-SECTIONED ON DAY 20 OF GESTATION	N	8	8	8
CORPORA LUTEA	MEAN±S.D.	15.5 ± 2.1	15.9 ± 2.8	16.2 ± 3.4
IMPLANTATIONS	MEAN±S.D.	15.1 ± 1.7	14.9 ± 2.8	15.1 ± 2.2
LITTER SIZES	MEAN±S.D.	14.8 ± 1.8	14.5 ± 2.6	14.2 ± 2.4
LIVE FETUSES	N	118	116	114
	MEAN±S.D.	14.8 ± 1.8	14.5 ± 2.6	14.2 ± 2.4
DEAD FETUSES	N	0	0	0
RESORPTIONS	MEAN±S.D.	0.4 ± 0.5	0.4 ± 0.7	0.9 ± 1.1
EARLY RESORPTIONS	N	3	3	7
	MEAN±S.D.	0.4 ± 0.5	0.4 ± 0.7	0.9 ± 1.1
LATE RESORPTIONS	N	0	0	0
	MEAN±S.D.	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
DAMS WITH ANY RESORPTIONS	N(%)	3(37.5)	2(25.0)	4(50.0)
DAMS WITH ALL CONCEPTUSES RESORBED	N	0	0	0
DAMS WITH VIABLE FETUSES	N(%)	8(100.0)	8(100.0)	8(100.0)
PLACENTAE APPEARED NORMAL	N(%)	8(100.0)	8(100.0)	8(100.0)

a. Dosage occurred on days 6 through 17 of gestation.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-EEFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 7 (PAGE 1): LITTER OBSERVATIONS (CAESAREAN DELIVERED FETUSES) - SUMMARY

DOSAGE GROUP DOSAGE (MG/KG/DAY)a		I 0 (VEHICLE)	II 1	III 5	IV 10
LITTERS WITH ONE OR MORE LIVE FETUSES	N	8	7	8	8
IMPLANTATIONS	MEAN±S.D.	14.0 ± 4.5	13.6 ± 3.2	15.2 ± 1.8	14.4 ± 1.7
LIVE FETUSES	N	109	93	116	110
	MEAN±S.D.	13.6 ± 4.6	13.3 ± 3.0	14.5 ± 1.7	13.8 ± 1.8
LIVE MALE FETUSES	N	49	42	59	50
% LIVE MALE FETUSES/LITTER	MEAN±S.D.	43.1 ± 14.3	42.8 ± 22.2	50.5 ± 13.0	46.7 ± 13.8
LIVE FETAL BODY WEIGHTS (GRAMS)/LITTER	MEAN±S.D.	3.40 ± 0.47	3.43 ± 0.22	3.28 ± 0.17	3.34 ± 0.16
MALE FETUSES	MEAN±S.D.	3.53 ± 0.47	3.56 ± 0.23	3.37 ± 0.21	3.42 ± 0.19
FEMALE FETUSES	MEAN±S.D.	3.30 ± 0.44	3.36 ± 0.21	3.18 ± 0.15	3.25 ± 0.16
% RESORBED CONCEPTUSES/LITTER	MEAN±S.D.	2.7 ± 5.6	1.8 ± 3.0	4.6 ± 6.9	4.4 ± 5.0

a. Dosage occurred on days 6 through 17 of gestation.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 7 (PAGE 2): LITTER OBSERVATIONS (CAESAREAN-DELIVERED FETUSES) - SUMMARY

DOSAGE GROUP DOSAGE (MG/KG/DAY)a		V 20	VI 25	VII 35
LITTERS WITH ONE OR MORE LIVE FETUSES	N	8	8	8
IMPLANTATIONS	MEAN±S.D.	15.1 ± 1.7	14.9 ± 2.8	15.1 ± 2.2
LIVE FETUSES	N	118	116	114
	MEAN±S.D.	14.8 ± 1.8	14.5 ± 2.6	14.2 ± 2.4
LIVE MALE FETUSES	N	66	59	58
% LIVE MALE FETUSES/LITTER	MEAN±S.D.	55.3 ± 9.1	49.2 ± 13.8	50.4 ± 15.3
LIVE FETAL BODY WEIGHTS (GRAMS)/LITTER	MEAN±S.D.	3.24 ± 0.15	3.11 ± 0.18	2.93 ± 0.46
MALE FETUSES	MEAN±S.D.	3.34 ± 0.17	3.21 ± 0.21	3.03 ± 0.45
FEMALE FETUSES	MEAN±S.D.	3.13 ± 0.14	3.03 ± 0.20	2.83 ± 0.44
% RESORBED CONCEPTUSES/LITTER	MEAN±S.D.	2.6 ± 3.6	2.4 ± 4.4	5.9 ± 7.5

a. Dosage occurred on days 6 through 17 of gestation.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 8 (PAGE 1): FETAL GROSS EXTERNAL ALTERATIONS - SUMMARY

DOSAGE GROUP		I	II	III	IV
DOSAGE (MG/KG/DAY)a		0 (VEHICLE)	1	5	10
LITTERS EVALUATED	N	8	7	8	8
FETUSES EVALUATED	N	109	93	116	110
LIVE	N	109	93	116	110
BODY: EDEMA					
LITTER INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
FETAL INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
PALATE: CLEFT					
LITTER INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
FETAL INCIDENCE	N(%)	0(0.0)	0(0.0)	0(0.0)	0(0.0)

a. Dosage occurred on days 6 through 17 of gestation.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 8 (PAGE 2): FETAL GROSS EXTERNAL ALTERATIONS - SUMMARY

DOSAGE GROUP		V	VI	VII
DOSAGE (MG/KG/DAY)a		20	25	35
LITTERS EVALUATED	N	8	8	8
FETUSES EVALUATED	N	118	116	114
LIVE	N	118	116	114
BODY: EDEMA				
LITTER INCIDENCE	N(%)	0(0.0)	0(0.0)	1(12.5)
FETAL INCIDENCE	N(%)	0(0.0)	0(0.0)	2(1.8)b,c
PALATE: CLEFT				
LITTER INCIDENCE	N(%)	0(0.0)	0(0.0)	1(12.5)
FETAL INCIDENCE	N(%)	0(0.0)	0(0.0)	13(11.4)b,c

a. Dosage occurred on days 6 through 17 of gestation.
b. Fetus 10650-1 had other gross external alterations.
c. Fetus 10650-10 had other gross external alterations.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 9 (PAGE 1): CLINICAL OBSERVATIONS - INDIVIDUAL DATA

RAT #	DESCRIPTION
DOSAGE GROUP I	0 (VEHICLE) MG/KG/DAY
10601	NO ADVERSE FINDINGS
10602	NO ADVERSE FINDINGS
10603	NO ADVERSE FINDINGS
10604	NO ADVERSE FINDINGS
10605	NO ADVERSE FINDINGS
10606	NO ADVERSE FINDINGS
10607	NO ADVERSE FINDINGS
10608	NO ADVERSE FINDINGS
DOSAGE GROUP II	1 MG/KG/DAY
10609	NO ADVERSE FINDINGS
10610	NO ADVERSE FINDINGS
10611	NO ADVERSE FINDINGS
10612	NO ADVERSE FINDINGS
10613	NO ADVERSE FINDINGS
10614	NO ADVERSE FINDINGS
10615	NO ADVERSE FINDINGS
10616	NO ADVERSE FINDINGS

DG = DAY OF PRESUMED GESTATION

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 9 (PAGE 2): CLINICAL OBSERVATIONS - INDIVIDUAL DATA

RAT #		DESCRIPTION
DOSAGE GROUP III		5 MG/KG/DAY
10617	DG(13- 20)	LOCALIZED ALOPECIA: LIMBS a
10618		NO ADVERSE FINDINGS
10619		NO ADVERSE FINDINGS
10620		NO ADVERSE FINDINGS
10621		NO ADVERSE FINDINGS
10622		NO ADVERSE FINDINGS
10623		NO ADVERSE FINDINGS
10624	DG(14- 20)	LOCALIZED ALOPECIA: UNDERSIDE a
	DG(20)	LOCALIZED ALOPECIA: NECK a
DOSAGE GROUP IV		10 MG/KG/DAY
10625		NO ADVERSE FINDINGS
10626		NO ADVERSE FINDINGS
10627		NO ADVERSE FINDINGS
10628		NO ADVERSE FINDINGS
10629		NO ADVERSE FINDINGS
10630		NO ADVERSE FINDINGS
10631		NO ADVERSE FINDINGS
10632		NO ADVERSE FINDINGS

DG = DAY OF PRESUMED GESTATION
a. Observation confirmed at necropsy.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-ETHOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 9 (PAGE 3): CLINICAL OBSERVATIONS - INDIVIDUAL DATA

RAT #		DESCRIPTION	
DOSAGE GROUP V		20 MG/KG/DAY	
10633		NO ADVERSE FINDINGS	
10634		NO ADVERSE FINDINGS	
10635		NO ADVERSE FINDINGS	
10636		NO ADVERSE FINDINGS	
10637	DG(15- 17)	CHROMODACRYORRHEA	
10638		NO ADVERSE FINDINGS	
10639		NO ADVERSE FINDINGS	
10640		NO ADVERSE FINDINGS	
DOSAGE GROUP VI		25 MG/KG/DAY	
10641		NO ADVERSE FINDINGS	
10642		NO ADVERSE FINDINGS	
10643	DG(14- 20)	LOCALIZED ALOPECIA:	UNDERSIDE a
	DG(15- 20)	LOCALIZED ALOPECIA:	BACK a
10644		NO ADVERSE FINDINGS	
10645		NO ADVERSE FINDINGS	
10646		NO ADVERSE FINDINGS	
10647		NO ADVERSE FINDINGS	
10648		NO ADVERSE FINDINGS	

DG = DAY OF PRESUMED GESTATION
a. Observation confirmed at necropsy.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE RANGE DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 9 (PAGE 4): CLINICAL OBSERVATIONS - INDIVIDUAL DATA

RAT #		DESCRIPTION
DOSAGE GROUP VII		35 MG/KG/DAY
10649		NO ADVERSE FINDINGS
10650	DG(13- 20)	LOCALIZED ALOPECIA: UNDERSIDE a
	DG(13- 20)	LOCALIZED ALOPECIA: BACK a
	DG(17- 20)	EMACIATION a
10651		NO ADVERSE FINDINGS
10652		NO ADVERSE FINDINGS
10653	DG(8- 19)	LOCALIZED ALOPECIA: LIMBS
	DG(20)	ALOPECIA NO LONGER APPARENT
10654		NO ADVERSE FINDINGS
10655		NO ADVERSE FINDINGS
10656	DG(12)	CHROMORHINORRHEA

DG = DAY OF PRESUMED GESTATION
a. Observation confirmed at necropsy.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 10 (PAGE 1): NECROPSY OBSERVATIONS - INDIVIDUAL DATA

DOSAGE GROUP (MG/KG/DAY)	RAT NUMBER	DAY OF NECROPSY	PREGNANCY STATUS	DOSAGES ADMINISTERED	OBSERVATIONS a
I					
0 (VEHICLE)	10601	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10602	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10603	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10604	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10605	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10606	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10607	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10608	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
II					
1	10609	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10610	DG 20	NP	12	ALL TISSUES APPEARED NORMAL.
	10611	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10612	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10613	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10614	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10615	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10616	DG 20	P	12	ALL TISSUES APPEARED NORMAL.

P = PREGNANT NP = NOT PREGNANT
DG = DAY OF PRESUMED GESTATION
a. Refer to the individual clinical observations table (Table 9) for external observations confirmed at necropsy.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 10 (PAGE 2): NECROPSY OBSERVATIONS - INDIVIDUAL DATA

DOSAGE GROUP (MG/KG/DAY)	RAT NUMBER	DAY OF NECROPSY	PREGNANCY STATUS	DOSAGES ADMINISTERED	OBSERVATIONS a
III					
5	10617	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10618	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10619	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10620	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10621	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10622	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10623	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10624	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
IV					
10	10625	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10626	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10627	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10628	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10629	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10630	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10631	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10632	DG 20	P	12	ALL TISSUES APPEARED NORMAL.

P = PREGNANT NP = NOT PREGNANT
DG = DAY OF PRESUMED GESTATION
a. Refer to the individual clinical observations table (Table 9) for external observations confirmed at necropsy.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 10 (PAGE 3): NECROPSY OBSERVATIONS - INDIVIDUAL DATA

DOSAGE GROUP (MG/KG/DAY)	RAT NUMBER	DAY OF NECROPSY	PREGNANCY STATUS	DOSAGES ADMINISTERED	OBSERVATIONS a
V					
20	10633	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10634	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10635	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10636	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10637	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10638	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10639	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10640	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
VI					
25	10641	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10642	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10643	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10644	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10645	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10646	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10647	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10648	DG 20	P	12	ALL TISSUES APPEARED NORMAL.

P = PREGNANT NP = NOT PREGNANT
DG = DAY OF PRESUMED GESTATION
a. Refer to the individual clinical observations table (Table 9) for external observations confirmed at necropsy.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE RANGE DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 10 (PAGE 4): NECROPSY OBSERVATIONS - INDIVIDUAL DATA

DOSAGE GROUP (MG/KG/DAY)	RAT NUMBER	DAY OF NECROPSY	PREGNANCY STATUS	DOSAGES ADMINISTERED	OBSERVATIONS a
VII 35	10649	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10650	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10651	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10652	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10653	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10654	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10655	DG 20	P	12	ALL TISSUES APPEARED NORMAL.
	10656	DG 20	P	12	ALL TISSUES APPEARED NORMAL.

P = PREGNANT NP = NOT PREGNANT
DG = DAY OF PRESUMED GESTATION
a. Refer to the individual clinical observations table (Table 9) for external observations confirmed at necropsy.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 11 (PAGE 1): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

RAT #	DOSAGE GROUP I	0 (VEHICLE) MG/KG/DAY											
	PREGNANCY STATUS	DAY 0	4	6	7	8	9	10	11	12	13	14	15	16
10601	P	218.	236.	244.	242.	247.	252.	257.	265.	270.	274.	274.	282.	295.
10602	P	227.	253.	263.	270.	273.	281.	287.	291.	295.	308.	311.	318.	331.
10603	P	242.	276.	286.	292.	300.	303.	314.	318.	321.	335.	341.	348.	364.
10604	P	245.	278.	280.	290.	293.	299.	306.	312.	315.	322.	325.	334.	344.
10605	P	238.	261.	260.	261.	263.	267.	270.	274.	282.	285.	289.	297.	301.
10606	P	232.	273.	275.	271.	280.	284.	294.	301.	310.	313.	321.	325.	333.
10607	P	250.	273.	269.	272.	277.	280.	285.	291.	288.	295.	301.	301.	304.
10608	P	235.	249.	254.	257.	264.	265.	273.	271.	282.	289.	292.	300.	312.

	DAY 17	18	19	20
10601 P	310.	319.	335.	361.
10602 P	338.	361.	371.	399.
10603 P	377.	400.	412.	432.
10604 P	353.	371.	390.	414.
10605 P	315.	329.	347.	362.
10606 P	348.	363.	392.	405.
10607 P	310.	315.	332.	338.
10608 P	324.	343.	359.	374.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE RANGE DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 11 (PAGE 2): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

RAT #	DOSAGE GROUP II	1 MG/KG/DAY											
	PREGNANCY STATUS	DAY 0	4	6	7	8	9	10	11	12	13	14	15	16
10609	P	241.	267.	276.	278.	286.	289.	296.	302.	309.	313.	321.	330.	342.
10610	NP	235.	247.	250.	251.	255.	248.	256.	260.	261.	268.	259.	263.	271.
10611	P	256.	250.	285.	282.	289.	295.	301.	306.	307.	313.	314.	321.	340.
10612	P	219.	246.	251.	255.	260.	265.	272.	276.	283.	290.	292.	298.	315.
10613	P	245.	270.	280.	282.	285.	291.	296.	297.	309.	310.	321.	324.	342.
10614	P	230.	256.	258.	262.	267.	274.	281.	276.	288.	291.	290.	300.	309.
10615	P	225.	243.	241.	243.	245.	250.	259.	256.	258.	268.	279.	280.	288.
10616	P	239.	251.	260.	262.	261.	272.	274.	278.	288.	291.	300.	302.	304.

	DAY 17	18	19	20
10609 P	351.	373.	386.	412.
10610 NP	266.	270.	265.	265.
10611 P	353.	374.	389.	409.
10612 P	325.	342.	357.	383.
10613 P	354.	369.	384.	408.
10614 P	311.	328.	331.	337.
10615 P	297.	318.	325.	344.
10616 P	320.	332.	352.	358.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 11 (PAGE 3): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

RAT #	DOSAGE GROUP III				5 MG/KG/DAY								
PREGNANCY STATUS	DAY 0	4	6	7	8	9	10	11	12	13	14	15	16
10617 P	242.	265.	270.	272.	277.	281.	286.	287.	291.	292.	295.	302.	312.
10618 P	244.	264.	273.	276.	280.	285.	291.	299.	300.	306.	310.	316.	327.
10619 P	223.	243.	249.	253.	260.	264.	274.	278.	283.	293.	294.	304.	316.
10620 P	229.	258.	265.	266.	272.	277.	280.	286.	290.	302.	300.	307.	317.
10621 P	230.	256.	251.	256.	263.	267.	270.	279.	276.	280.	289.	293.	305.
10622 P	236.	260.	268.	270.	274.	276.	280.	287.	288.	288.	294.	297.	309.
10623 P	240.	248.	258.	260.	264.	267.	272.	273.	280.	282.	287.	296.	302.
10624 P	247.	270.	277.	279.	284.	292.	298.	306.	299.	304.	311.	320.	328.

	DAY 17	18	19	20
10617 P	316.	334.	344.	371.
10618 P	339.	351.	366.	384.
10619 P	327.	341.	355.	380.
10620 P	324.	342.	352.	377.
10621 P	321.	339.	358.	373.
10622 P	328.	340.	365.	369.
10623 P	313.	334.	345.	357.
10624 P	341.	359.	377.	389.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 11 (PAGE 4): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

RAT #	DOSAGE GROUP IV					10 MG/KG/DAY						
PREGNANCY STATUS	DAY 0	4	6	7	8	9	10	11	12	13	14	15	16
10625 P	242.	268.	275.	275.	281.	285.	295.	298.	301.	309.	311.	317.	325.
10626 P	223.	234.	237.	239.	240.	243.	250.	252.	256.	259.	262.	264.	272.
10627 P	237.	258.	264.	266.	270.	273.	276.	279.	278.	285.	287.	292.	299.
10628 P	235.	254.	253.	256.	262.	265.	270.	278.	285.	289.	292.	302.	311.
10629 P	244.	270.	269.	276.	282.	286.	286.	299.	307.	308.	316.	322.	333.
10630 P	234.	254.	257.	244.	233.	246.	249.	256.	268.	260.	269.	276.	285.
10631 P	227.	244.	243.	248.	248.	252.	252.	255.	262.	264.	272.	279.	291.
10632 P	246.	258.	264.	268.	271.	265.	273.	281.	286.	293.	297.	317.	314.

	DAY 17	18	19	20
10625 P	341.	345.	365.	384.
10626 P	278.	289.	299.	312.
10627 P	311.	327.	332.	353.
10628 P	319.	330.	349.	364.
10629 P	340.	356.	377.	398.
10630 P	297.	306.	321.	342.
10631 P	294.	315.	330.	342.
10632 P	327.	342.	357.	378.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 11 (PAGE 5): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

RAT #	DOSAGE GROUP V				20 MG/KG/DAY								
PREGNANCY STATUS	DAY 0	4	6	7	8	9	10	11	12	13	14	15	16
10633 P	239.	259.	267.	268.	273.	277.	278.	282.	289.	295.	296.	304.	312.
10634 P	211.	260.	260.	256.	264.	269.	272.	280.	282.	290.	290.	303.	318.
10635 P	224.	244.	247.	248.	251.	251.	246.	249.	255.	255.	261.	257.	266.
10636 P	228.	260.	269.	268.	273.	283.	284.	290.	288.	299.	292.	308.	321.
10637 P	244.	259.	262.	260.	260.	266.	266.	275.	278.	281.	290.	294.	302.
10638 P	237.	250.	254.	254.	251.	255.	262.	270.	278.	281.	283.	295.	302.
10639 P	240.	266.	268.	272.	271.	285.	284.	293.	298.	304.	306.	311.	322.
10640 P	247.	270.	270.	260.	262.	262.	269.	273.	279.	280.	287.	289.	302.

	DAY 17	18	19	20
10633 P	326.	334.	351.	372.
10634 P	327.	342.	352.	376.
10635 P	277.	285.	293.	314.
10636 P	338.	356.	366.	387.
10637 P	318.	326.	340.	363.
10638 P	316.	326.	342.	358.
10639 P	331.	347.	362.	376.
10640 P	313.	331.	348.	362.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 11 (PAGE 6): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

RAT #	DOSAGE GROUP VI				25 MG/KG/DAY								
PREGNANCY STATUS	DAY 0	4	6	7	8	9	10	11	12	13	14	15	16
10641 P	240.	256.	264.	256.	262.	269.	265.	274.	273.	275.	274.	286.	299.
10642 P	221.	237.	240.	236.	239.	242.	247.	247.	244.	245.	248.	261.	272.
10643 P	247.	265.	270.	268.	269.	276.	281.	288.	288.	292.	291.	298.	311.
10644 P	236.	262.	270.	267.	264.	270.	278.	277.	281.	282.	270.	263.	260.
10645 P	244.	270.	275.	275.	278.	282.	283.	285.	301.	294.	301.	303.	313.
10646 P	233.	249.	249.	247.	246.	250.	255.	258.	261.	262.	256.	254.	267.
10647 P	228.	249.	260.	261.	266.	273.	276.	274.	272.	276.	279.	284.	286.
10648 P	239.	275.	284.	286.	291.	292.	292.	290.	288.	290.	295.	299.	311.

	DAY 17	18	19	20
10641 P	304.	314.	329.	349.
10642 P	281.	297.	304.	323.
10643 P	333.	345.	360.	377.
10644 P	273.	303.	324.	340.
10645 P	325.	337.	356.	359.
10646 P	276.	285.	302.	318.
10647 P	299.	320.	329.	336.
10648 P	322.	343.	352.	364.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 11 (PAGE 7): MATERNAL BODY WEIGHTS - INDIVIDUAL DATA

RAT #	DOSAGE GROUP VII				35 MG/KG/DAY								
PREGNANCY STATUS	DAY 0	4	6	7	8	9	10	11	12	13	14	15	16
10649 P	244.	252.	258.	260.	264.	264.	267.	268.	274.	278.	281.	286.	295.
10650 P	237.	253.	266.	264.	269.	261.	268.	260.	252.	235.	223.	216.	213.
10651 P	222.	245.	251.	254.	262.	267.	268.	275.	278.	279.	285.	292.	303.
10652 P	227.	243.	248.	250.	249.	251.	256.	258.	260.	266.	269.	275.	289.
10653 P	246.	269.	276.	275.	269.	276.	274.	281.	279.	280.	277.	289.	297.
10654 P	231.	256.	261.	268.	267.	273.	274.	276.	281.	259.	289.	297.	306.
10655 P	238.	249.	254.	252.	255.	254.	242.	248.	252.	258.	266.	271.	275.
10656 P	247.	275.	275.	272.	266.	274.	276.	269.	262.	287.	265.	266.	292.

	DAY 17	18	19	20
10649 P	291.	305.	316.	332.
10650 P	207.	208.	220.	239.
10651 P	316.	334.	350.	374.
10652 P	293.	304.	316.	343.
10653 P	300.	316.	331.	350.
10654 P	313.	327.	347.	364.
10655 P	289.	302.	324.	337.
10656 P	303.	320.	341.	350.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 12 (PAGE 1): MATERNAL FEED CONSUMPTION VALUES - INDIVIDUAL DATA

PREGNANCY STATUS	DAYS 0 - 4	4 - 6	6 - 8	8 - 10	10 - 12	12 - 14	14 - 16	16 - 18	18 - 20
RAT #	DOSAGE GROUP I			0 (VEHICLE) MG/KG/DAY					
10601 P	76.	45.	40.	44.	45.	44.	47.	54.	49.
10602 P	93.	56.	49.	49.	a	a	48.	53.	54.
10603 P	97.	56.	56.	54.	56.	61.	54.	61.	54.
10604 P	115.	62.	64.	61.	60.	55.	45.	53.	61.
10605 P	87.	44.	40.	43.	44.	46.	44.	50.	52.
10606 P	103.	51.	56.	53.	57.	55.	51.	54.	56.
10607 P	89.	47.	68.	57.	60.	90.	55.	46.	53.
10608 P	72.	37.	42.	46.	45.	43.	43.	44.	40.
RAT #	DOSAGE GROUP II			1 MG/KG/DAY					
10609 P	97.	50.	49.	50.	50.	51.	50.	53.	53.
10610 NP	88.	44.	44.	39.	43.	42.	37.	49.	36.
10611 P	77.	55.	51.	52.	49.	47.	50.	59.	57.
10612 P	94.	46.	51.	54.	47.	52.	52.	57.	54.
10613 P	93.	53.	46.	49.	46.	54.	60.	62.	57.
10614 P	94.	43.	51.	50.	48.	58.	53.	44.	47.
10615 P	61.	38.	41.	40.	38.	78.	41.	42.	51.
10616 P	76.	42.	40.	43.	45.	51.	45.	40.	48.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAYS = DAYS OF GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Spilled feed precluded the calculation of this value.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE RANGE DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 12 (PAGE 2): MATERNAL FEED CONSUMPTION VALUES - INDIVIDUAL DATA

PREGNANCY STATUS	DAYS 0 - 4	4 - 6	6 - 8	8 - 10	10 - 12	12 - 14	14 - 16	16 - 18	18 - 20
RAT #	DOSAGE GROUP III			5 MG/KG/DAY					
10617 P	90.	48.	45.	45.	45.	40.	45.	49.	49.
10618 P	94.	56.	22.	48.	50.	52.	51.	55.	53.
10619 P	86.	49.	49.	51.	56.	54.	53.	56.	56.
10620 P	95.	50.	50.	49.	54.	48.	46.	48.	44.
10621 P	90.	46.	44.	47.	46.	51.	48.	51.	52.
10622 P	95.	47.	47.	48.	46.	42.	36.	47.	50.
10623 P	90.	44.	45.	47.	44.	46.	48.	53.	43.
10624 P	103.	46.	50.	52.	50.	43.	47.	48.	50.
RAT #	DOSAGE GROUP IV			10 MG/KG/DAY					
10625 P	91.	50.	45.	48.	48.	46.	44.	48.	50.
10626 P	66.	33.	31.	38.	40.	35.	35.	37.	36.
10627 P	90.	56.	47.	43.	45.	40.	34.	46.	50.
10628 P	85.	42.	44.	45.	48.	50.	47.	46.	52.
10629 P	85.	45.	47.	49.	50.	55.	46.	51.	55.
10630 P	85.	46.	14.	35.	44.	40.	38.	39.	49.
10631 P	77.	40.	36.	38.	40.	47.	45.	39.	41.
10632 P	88.	43.	41.	37.	49.	50.	49.	49.	51.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAYS = DAYS OF GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 12 (PAGE 3): MATERNAL FEED CONSUMPTION VALUES - INDIVIDUAL DATA

PREGNANCY STATUS	DAYS 0 - 4	4 - 6	6 - 8	8 - 10	10 - 12	12 - 14	14 - 15	16 - 18	18 - 20
RAT #	DOSAGE GROUP V			20 MG/KG/DAY					
10633 P	88.	50.	47.	46.	47.	48.	46.	51.	48.
10634 P	89.	47.	41.	44.	46.	43.	47.	49.	44.
10635 P	78.	48.	31.	28.	33.	31.	21.	35.	41.
10636 P	105.	62.	45.	57.	44.	48.	59.	59.	53.
10637 P	87.	48.	41.	42.	50.	48.	48.	52.	51.
10638 P	140.	47.	40.	44.	51.	48.	46.	43.	44.
10639 P	95.	54.	54.	54.	52.	50.	46.	41.	51.
10640 P	103.	47.	41.	40.	47.	53.	49.	44.	49.
RAT #	DOSAGE GROUP VI			25 MG/KG/DAY					
10641 P	86.	48.	36.	40.	41.	33.	38.	37.	40.
10642 P	79.	42.	32.	34.	35.	25.	41.	41.	38.
10643 P	83.	47.	40.	45.	46.	38.	44.	53.	48.
10644 P	94.	51.	38.	45.	43.	25.	11.	40.	46.
10645 P	91.	54.	51.	45.	47.	40.	46.	39.	45.
10646 P	73.	38.	31.	35.	37.	27.	26.	32.	43.
10647 P	75.	38.	38.	45.	38.	39.	40.	48.	42.
10648 P	102.	54.	50.	46.	34.	39.	38.	46.	42.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAYS = DAYS OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-ELFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 12 (PAGE 4): MATERNAL FEED CONSUMPTION VALUES - INDIVIDUAL DATA

PREGNANCY STATUS DAYS	0 - 4	4 - 6	6 - 8	8 - 10	10 - 12	12 - 14	14 - 16	16 - 18	18 - 20
RAT #	DOSAGE GROUP VII			35 MG/KG/DAY					
10649 P	86.	48.	41.	41.	43.	41.	39.	38.	43.
10650 P	87.	49.	45.	39.	17.	2.	1.	13.	34.
10651 P	94.	53.	49.	48.	45.	42.	45.	51.	52.
10652 P	80.	43.	40.	38.	41.	39.	42.	44.	46.
10653 P	95.	55.	48.	43.	47.	46.	41.	35.	62.
10654 P	89.	46.	44.	46.	45.	46.	40.	36.	52.
10655 P	82.	47.	37.	25.	39.	64.	43.	43.	55.
10656 P	90.	42.	33.	42.	26.	42.	39.	38.	44.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAYS = DAYS OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-ELFOSE IN RATS (SPONSOR'S STUDY NUMBER: T 6316.7)

TABLE 13 (PAGE 1): CAESAREAN SECTIONING OBSERVATIONS - INDIVIDUAL DATA

			VIABLE FETUSES			DEAD FETUSES			EARLY RESORPTIONS			LATE RESORPTIONS			IMPLANTATION SITES			CORPORA LUTEA		
	SEX		RIGHT	LEFT		RIGHT	LEFT		RIGHT	LEFT		RIGHT	LEFT		RIGHT	LEFT		RIGHT	LEFT	
RAT #	M	F	HORN		TOTAL	HORN		TOTAL	HORN		TOTAL	HORN		TOTAL	HORN		TOTAL	OVARY		TOTAL
DOSAGE GROUP I					0 (VEHICLE) MG/KG/DAY															
10601	6	7	6	7	13	0	0	0	0	0	0	0	0	0	6	7	13	6	7	13
10602	5	10	11	4	15	0	0	0	1	0	1	0	0	0	12	4	16	12	5	17
10603	12	5	9	8	17	0	0	0	0	0	0	0	0	0	9	8	17	11	8	19
10604	5	10	3	12	15	0	0	0	0	0	0	0	0	0	3	12	15	4	12	16
10605	6	5	8	3	11	0	0	0	0	2	2	0	0	0	8	5	13	8	6	14
10606	6	9	5	10	15	0	0	0	0	0	0	0	0	0	5	10	15	5	11	16
10607	1	3	1	3	4	0	0	0	0	0	0	0	0	0	1	3	4	5	8	13
10608	8	11	10	9	19	0	0	0	0	0	0	0	0	0	10	9	19	10	10	20
DOSAGE GROUP II					1 MG/KG/DAY															
10609	11	5	7	9	16	0	0	0	0	0	0	0	0	0	7	9	16	7	11	18
10610	NOT PREGNANT																			
10611	2	13	8	7	15	0	0	0	0	1	1	0	0	0	8	8	16	9	9	18
10612	5	9	7	7	14	0	0	0	0	0	0	0	0	0	7	7	14	9	9	18
10613	9	6	9	6	15	0	0	0	0	1	1	0	0	0	9	7	16	10	7	17
10614	1	6	1	6	7	0	0	0	0	0	0	0	0	0	1	6	7	5	7	12
10615	7	6	4	9	13	0	0	0	0	0	0	0	0	0	4	9	13	5	9	14
10616	7	6	6	7	13	0	0	0	0	0	0	0	0	0	6	7	13	6	7	13

M = MALE F = FEMALE
PLACENTAE APPEARED NORMAL UNLESS NOTED OTHERWISE.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 13 (PAGE 2): CAESAREAN-SECTIONING OBSERVATIONS - INDIVIDUAL DATA

			VIABLE FETUSES			DEAD FETUSES			EARLY RESORPTIONS			LATE RESORPTIONS			IMPLANTATION SITES			CORPORA LUTEA		
	SEX		RIGHT	LEFT		RIGHT	LEFT		RIGHT	LEFT		RIGHT	LEFT		RIGHT	LEFT		RIGHT	LEFT	
RAT #	M	F	HORN		TOTAL	HORN		TOTAL	HORN		TOTAL	HORN		TOTAL	HORN		TOTAL	OVARY		TOTAL
DOSAGE GROUP III					**5 MG/KG/DAY**															
10617	7	6	7	6	13	0	0	0	0	1	1	0	0	0	7	7	14	7	7	14
10618	3	10	4	9	13	0	0	0	1	1	2	0	0	0	5	10	15	7	10	17
10619	7	9	10	6	16	0	0	0	0	0	0	0	0	0	10	6	16	10	7	17
10620	8	7	6	9	15	0	0	0	3	0	3	0	0	0	9	9	18	9	9	18
10621	9	6	9	6	15	0	0	0	0	0	0	0	0	0	9	6	15	10	6	16
10622	7	8	7	8	15	0	0	0	0	0	0	0	0	0	7	8	15	7	8	15
10623	7	5	4	8	12	0	0	0	0	0	0	0	0	0	4	8	12	4	9	13
10624	11	6	6	11	17	0	0	0	0	0	0	0	0	0	6	11	17	6	12	18
DOSAGE GROUP IV					**10 MG/KG/DAY**															
10625	5	10	11	4	15	0	0	0	1	0	1	0	0	0	12	4	16	13	8	21
10626	7	3	3	7	10	0	0	0	0	0	0	0	1	1	3	8	11	3	9	12
10627	6	7	9	4	13	0	0	0	0	1	1	0	0	0	9	5	14	9	5	14
10628	8	7	5	10	15	0	0	0	0	0	0	0	0	0	5	10	15	6	10	16
10629	6	9	8	7	15	0	0	0	0	0	0	0	0	0	8	7	15	8	7	15
10630	8	5	10	3	13	0	0	0	0	0	0	0	0	0	10	3	13	10	5	15
10631	5	10	11	4	15	0	0	0	0	0	0	0	0	0	11	4	15	12	6	18
10632	5	9	6	8	14	0	0	0	2	0	2	0	0	0	8	8	16	8	9	17

M = MALE F = FEMALE
PLACENTAE APPEARED NORMAL UNLESS NOTED OTHERWISE.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE RANGE DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 13 (PAGE 3): CAESAREAN SECTIONING OBSERVATIONS - INDIVIDUAL DATA

			VIABLE FETUSES			DEAD FETUSES			EARLY RESORPTIONS			LATE RESORPTIONS			IMPLANTATION SITES			CORPORA LUTEA		
	SEX		RIGHT	LEFT		RIGHT	LEFT		RIGHT	LEFT		RIGHT	LEFT		RIGHT	LEFT		RIGHT	LEFT	
RAT #	M	F	HORN		TOTAL	HORN		TOTAL	HORN		TOTAL	HORN		TOTAL	HORN		TOTAL	OVARY		TOTAL
DOSAGE GROUP V					20 MG/KG/DAY															
10633	9	5	4	10	14	0	0	0	0	0	0	0	0	0	4	10	14	4	11	15
10634	9	7	8	8	16	0	0	0	0	0	0	0	0	0	8	8	16	8	8	16
10635	5	6	7	4	11	0	0	0	0	1	1	0	0	0	7	5	12	7	5	12
10636	8	7	7	8	15	0	0	0	1	0	1	0	0	0	8	8	16	8	8	16
10637	8	7	9	6	15	0	0	0	0	0	0	0	0	0	9	6	15	9	6	15
10638	6	8	6	8	14	0	0	0	0	0	0	0	0	0	6	8	14	6	8	14
10639	9	7	8	8	16	0	0	0	0	1	1	0	0	0	8	9	17	8	9	17
10640	12	5	7	10	17	0	0	0	0	0	0	0	0	0	7	10	17	8	11	19
DOSAGE GROUP VI					25 MG/KG/DAY															
10641	4	9	7	6	13	0	0	0	0	0	0	0	0	0	7	6	13	7	6	13
10642	9	7	7	9	16	0	0	0	0	0	0	0	0	0	7	9	16	7	10	17
10643	8	7	9	6	15	0	0	0	0	0	0	0	0	0	9	6	15	9	8	17
10644	13	5	8	10	18	0	0	0	1	1	2	0	0	0	9	11	20	9	11	20
10645	7	7	6	8	14	0	0	0	0	0	0	0	0	0	6	8	14	8	8	16
10646	7	6	5	8	13	0	0	0	0	0	0	0	0	0	5	8	13	7	8	15
10647	3	7	2	8	10	0	0	0	1	0	1	0	0	0	3	8	11	3	8	11
10648	8	9	10	7	17	0	0	0	0	0	0	0	0	0	10	7	17	11	7	18

M = MALE F = FEMALE
PLACENTAE APPEARED NORMAL UNLESS NOTED OTHERWISE.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 13 (PAGE 4): CAESAREAN-SECTIONING OBSERVATIONS - INDIVIDUAL DATA

			VIABLE FETUSES			DEAD FETUSES			EARLY RESORPTIONS			LATE RESORPTIONS			IMPLANTATION SITES			CORPORA LUTEA		
	SEX		RIGHT	LEFT		RIGHT	LEFT		RIGHT	LEFT		RIGHT	LEFT		RIGHT	LEFT		RIGHT	LEFT	
RAT #	M	F	HORN		TOTAL	HORN		TOTAL	HORN		TOTAL	HORN		TOTAL	HORN		TOTAL	OVARY		TOTAL
DOSAGE GROUP VII					35 MG/KG/DAY															
10649	3	8	6	5	11	0	0	0	1	1	2	0	0	0	7	6	13	7	6	13
10650	5	8	5	8	13	0	0	0	2	1	3	0	0	0	7	9	16	8	9	17
10651	9	8	10	7	17	0	0	0	0	0	0	0	0	0	10	7	17	10	8	18
10652	8	6	7	7	14	0	0	0	0	0	0	0	0	0	7	7	14	7	8	15
10653	6	7	8	5	13	0	0	0	1	0	1	0	0	0	9	5	14	9	5	14
10654	7	10	9	8	17	0	0	0	0	1	1	0	0	0	9	9	18	9	13	22
10655	9	3	5	7	12	0	0	0	0	0	0	0	0	0	5	7	12	5	7	12
10656	11	6	9	8	17	0	0	0	0	0	0	0	0	0	9	8	17	9	10	19

M = MALE F = FEMALE
PLACENTAE APPEARED NORMAL UNLESS NOTED OTHERWISE.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 14 (PAGE 1): LITTER OBSERVATIONS (CAESAREAN DELIVERED FETUSES) INDIVIDUAL DATA

	NUMBER OF LIVE FETUSES			AVERAGE FETAL BODY WEIGHT (G)			---- CONCEPTUSES ------ RESORBED		
RAT #	MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL a	N	N	%
DOSAGE GROUP I			0 (VEHICLE) MG/KG/DAY						
10601	6	7	13	3.54	3.43	3.48	13	0	0.0
10602	5	10	15	3.71	3.50	3.57	16	1	6.2
10603	12	5	17	3.91	3.71	3.85	17	0	0.0
10604	5	10	15	3.68	3.44	3.52	15	0	0.0
10605	6	5	11	3.94	3.57	3.78	13	2	15.4
10606	6	9	15	3.62	3.42	3.50	15	0	0.0
10607	1	3	4	2.45	2.30	2.34	4	0	0.0
10608	8	11	19	3.38	3.06	3.20	19	0	0.0
DOSAGE GROUP II			1 MG/KG/DAY						
10609	11	5	16	3.37	3.29	3.35	16	0	0.0
10610	NOT PREGNANT								
10611	2	13	15	4.01	3.64	3.69	16	1	6.2
10612	5	9	14	3.53	3.48	3.50	14	0	0.0
10613	9	6	15	3.50	3.39	3.46	16	1	6.2
10614	1	6	7	3.31	2.96	3.01	7	0	0.0
10615	7	6	13	3.69	3.44	3.58	13	0	0.0
10616	7	6	13	3.50	3.33	3.42	13	0	0.0

a. TOTAL = SUM OF FETAL WEIGHTS/NUMBER OF LIVE FETUSES.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 14 (PAGE 2): LITTER OBSERVATIONS (CAESAREAN-DELIVERED FETUSES) - INDIVIDUAL DATA

	NUMBER OF LIVE FETUSES			AVERAGE FETAL BODY WEIGHT (G)			---- CONCEPTUSES ------ RESORBED		
RAT #	MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL a	N	N	%
DOSAGE GROUP III			5 MG/KG/DAY						
10617	7	6	13	3.63	3.32	3.49	14	1	7.1
10618	3	10	13	3.40	3.19	3.24	15	2	13.3
10619	7	9	16	3.18	2.91	3.03	16	0	0.0
10620	8	7	15	3.38	3.36	3.37	18	3	16.7
10621	9	6	15	3.62	3.29	3.48	15	0	0.0
10622	7	8	15	3.02	3.07	3.05	15	0	0.0
10623	7	5	12	3.44	3.08	3.29	12	0	0.0
10624	11	6	17	3.31	3.21	3.28	17	0	0.0
DOSAGE GROUP IV			10 MG/KG/DAY						
10625	5	10	15	3.08	3.30	3.22	16	1	6.2
10626	7	3	10	3.73	3.19	3.57	11	1	9.1
10627	6	7	13	3.42	3.33	3.37	14	1	7.1
10628	8	7	15	3.47	3.38	3.43	15	0	0.0
10629	6	9	15	3.51	3.26	3.36	15	0	0.0
10630	8	5	13	3.42	3.14	3.32	13	0	0.0
10631	5	10	15	3.43	3.45	3.44	15	0	0.0
10632	5	9	14	3.27	2.92	3.05	16	2	12.5

a. TOTAL = SUM OF FETAL WEIGHTS/NUMBER OF LIVE FETUSES.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 14 (PAGE 3): LITTER OBSERVATIONS (CAESAREAN-DELIVERED FETUSES) - INDIVIDUAL DATA

	NUMBER OF LIVE FETUSES			AVERAGE FETAL BODY WEIGHT (G)			---- CONCEPTUSES ------ RESORBED		
RAT #	MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL a	N	N	%
DOSAGE GROUP V			20 MG/KG/DAY						
10633	9	5	14	3.54	3.24	3.43	14	0	0.0
10634	9	7	16	3.26	3.04	3.16	16	0	0.0
10635	5	6	11	3.25	3.11	3.18	12	1	8.3
10636	8	7	15	3.54	3.37	3.46	16	1	6.2
10637	8	7	15	3.17	2.92	3.05	15	0	0.0
10638	6	8	14	3.50	3.19	3.32	14	0	0.0
10639	9	7	16	3.33	3.16	3.25	17	1	5.9
10640	12	5	17	3.12	3.01	3.09	17	0	0.0
DOSAGE GROUP VI			25 MG/KG/DAY						
10641	4	9	13	3.46	3.31	3.35	13	0	0.0
10642	9	7	16	3.12	2.89	3.02	16	0	0.0
10643	8	7	15	3.45	3.35	3.40	15	0	0.0
10644	13	5	18	2.90	2.80	2.87	20	2	10.0
10645	7	7	14	3.16	3.02	3.09	14	0	0.0
10646	7	6	13	3.05	3.02	3.03	13	0	0.0
10647	3	7	10	3.43	3.02	3.14	11	1	9.1
10648	8	9	17	3.10	2.85	2.96	17	0	0.0

a. TOTAL = SUM OF FETAL WEIGHTS/NUMBER OF LIVE FETUSES.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N ELFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 14 (PAGE 4): LITTER OBSERVATIONS (CAESAREAN-DELIVERED FETUSES) - INDIVIDUAL DATA

	NUMBER OF LIVE FETUSES			AVERAGE FETAL BODY WEIGHT (G)			-- CONCEPTUSES ------ RESORBED		
RAT #	MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL a	N	N	%
DOSAGE GROUP VII			35 MG/KG/DAY						
10649	3	8	11	2.80	2.54	2.61	13	2	15.4
10650	5	8	13	1.98	1.85	1.90	16	3	18.8
10651	9	8	17	3.24	3.16	3.20	17	0	0.0
10652	8	6	14	3.23	2.94	3.11	14	0	0.0
10653	6	7	13	3.25	3.04	3.14	14	1	7.1
10654	7	10	17	3.21	2.95	3.06	18	1	5.6
10655	9	3	12	3.30	3.07	3.24	12	0	0.0
10656	11	6	17	3.25	3.07	3.19	17	0	0.0

a. TOTAL = SUM OF FETAL WEIGHTS/NUMBER OF LIVE FETUSES.

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE RANGE DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 15 (PAGE 1): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
DOSAGE GROUP I							0 (VEHICLE) MG/KG/DAY																
RAT # CLs																							
10601 6/ 7	FA	MA	FA	MA	FA	FA / FA		MA	FA	FA	MA	MA	MA										
	3.34	3.64	3.28	3.61	3.40	3.68	3.34	3.24	3.65	3.30	3.49	3.64	3.65										
10602 12/ 5	MA	FA	FA	MA	MA	FA	E	FA	FA	FA	FA	FA / FA		FA	MA	MA							
	3.37	3.38	3.55	3.31	3.69	3.19		3.57	3.58	3.29	3.59	3.71	3.52	3.63	4.00	4.18							
10603 11/ 8	FA	FA	MA	FA	MA	MA	MA	MA	MA / MA		FA	MA	MA	MA	MA	FA	MA						
	3.59	3.84	4.14	3.79	3.70	3.92	4.03	3.93	3.69	3.82	3.74	3.80	3.85	3.90	3.90	3.58	4.26						
10604 4/12	MA	FA	FA / FA		MA	FA	FA	MA	FA	FA	MA	MA	FA	FA	FA								
	3.81	3.54	3.86	2.62	3.74	3.35	3.38	3.73	3.39	3.13	3.53	3.60	3.72	3.58	3.81								
10605 8/ 6	FA	FA	FA	MA	MA	FA	FA	MA / MA		E	E	MA	MA										
	3.41	3.67	3.69	4.08	3.82	3.69	3.41	3.90	3.95			3.85	4.06										
10606 5/11	FA	FA	FA	FA	MA / MA		MA	FA	MA	FA	FA	FA	FA	MA	MA								
	3.80	3.56	3.48	3.61	3.68	3.71	3.68	3.47	3.57	3.07	3.40	3.07	3.31	3.42	3.64								
10607 5/ 8	MA / FA		FA	FA																			
	2.45	2.35	2.41	2.14																			
10608 10/10	MA	FA	FA	MA	FA	FA	FA	FA	FA	MA / MA		FA	MA	MA	MA	FA	MA	FA	FA				
	3.13	3.19	3.22	3.22	2.76	3.29	3.29	2.93	2.95	3.66	3.20	3.12	3.45	3.34	3.44	2.97	3.59	2.86	3.11				
DOSAGE GROUP II							1 MG/KG/DAY																
10609 7/11	MA	FA	MA	FA	MA	MA	MA / MA		FA	MA	MA	MA	FA	MA	FA	MA							
	3.39	3.15	3.29	3.64	3.45	3.73	3.07	3.27	3.17	3.28	3.43	3.29	3.29	3.23	3.18	3.68							
10610	NOT PREGNANT																						
10611 9/ 9	FA	FA	FA	FA	FA	MA	FA	FA / FA		FA	FA	E	FA	FA	FA	MA							
	3.84	3.60	3.39	3.82	3.56	4.06	3.59	3.93	3.47	3.50	3.46		3.82	3.68	3.70	3.96							
10612 9/ 9	MA	FA	FA	MA	MA	FA	FA / MA		FA	FA	FA	FA	MA	FA									
	3.23	3.50	3.44	3.55	3.86	3.72	3.23	3.27	3.45	3.48	3.45	3.43	3.74	3.62									
10613 10/ 7	FA	MA	FA	FA	MA	FA	MA	FA	MA / MA		MA	MA	MA	MA	FA	E							
	3.18	3.44	3.62	3.36	3.52	3.31	3.44	3.41	3.52	3.39	3.35	3.38	3.59	3.87	3.47								
10614 5/ 7	FA / FA		FA	FA	FA	MA	FA																
	2.95	2.94	2.77	3.06	3.22	3.31	2.84																
10615 5/ 9	MA	FA	FA	FA / MA		MA	FA	MA	MA	FA	FA	MA	MA										
	3.59	3.21	3.61	3.50	3.50	3.64	3.57	3.96	3.80	3.31	3.45	3.63	3.71										
10616 6/ 7	FA	MA	MA	FA	FA	MA / FA		MA	MA	MA	FA	MA	FA										
	3.33	3.56	3.66	3.41	3.06	3.39	3.39	3.70	3.36	3.33	3.49	3.54	3.30										

M = MALE F = FEMALE A = ALIVE E = EARLY RESORPTION L = LATE RESORPTION "/" DENOTES POSITION OF CERVIX
CLs = CORPORA LUTEA/OVARY FETAL BODY WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-ETFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 15 (PAGE 2): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

PETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
DOSAGE GROUP III							5 MG/KG/DAY																
RAT # CLs																							
10617 7/ 7	MA	MA	MA	FA	FA	MA	MA / FA		MA	MA	FA	FA	E	FA									
	3.39	3.35	3.99	3.36	3.39	3.87	3.74	3.01	3.40	3.69	3.07	3.54		3.56									
10618 7/10	MA	E	FA	FA	FA / FA		FA	FA	FA	MA	MA	FA	E	FA	FA								
	3.67		3.29	3.14	3.54	2.97	3.07	3.11	3.20	3.26	3.26	3.14		3.22	3.26								
10619 10/ 7	MA	FA	MA	FA	MA	MA	FA	FA	MA	FA / FA		MA	FA	MA	FA	FA							
	3.36	3.38	3.25	2.96	3.12	3.17	3.11	2.63	2.89	2.60	2.99	3.29	2.56	3.15	2.80	3.20							
10620 9/ 9	FA	MA	E	E	MA	FA	MA	E	FA / FA		MA	FA	MA	FA	MA	MA	MA	FA					
	3.28	4.00			3.52	3.51	3.28		3.40	3.38	3.26	3.43	3.31	3.07	2.72	3.49	3.43	3.46					
10621 10/ 6	FA	MA	MA	MA	MA	MA	FA	MA	FA / FA		FA	MA	MA	FA	MA								
	2.91	3.55	3.57	3.56	3.59	3.72	3.32	3.55	3.56	3.08	3.47	3.67	3.50	3.40	3.83								
10622 7/ 8	MA	FA	MA	MA	FA	FA	MA / FA		FA	MA	MA	MA	FA	FA	FA								
	3.25	3.20	3.10	3.18	3.07	2.85	2.54	2.95	3.10	3.04	3.32	2.72	3.38	3.16	2.86								
10623 4/ 9	FA	MA	MA	MA / FA		MA	MA	FA	FA	FA	MA	MA											
	2.96	3.28	3.40	3.34	3.24	3.81	3.41	3.02	3.13	3.04	3.40	3.46											
10624 6/12	FA	FA	MA	MA	FA	MA / MA		MA	FA	MA	MA	MA	FA	MA	MA	MA	FA						
	3.20	3.11	3.23	3.44	3.40	3.32	3.17	3.27	3.20	3.36	3.40	3.35	3.06	3.10	3.59	3.22	3.28						
DOSAGE GROUP IV							10 MG/KG/DAY																
10625 13/ 8	MA	MA	FA	FA	MA	E	FA	FA	FA	FA	FA	MA / FA		FA	MA	FA							
	2.64	3.09	2.76	3.49	3.34		3.33	3.52	3.44	3.16	3.45	3.13	3.26	3.59	3.20	2.98							
10626 3/ 9	FA	MA	MA / FL		MA	FA	MA	MA	MA	FA	MA												
	3.71	4.02	3.74	1.68	3.78	3.42	3.57	3.76	3.51	2.44	3.72												
10627 9/ 5	FA	FA	FA	MA	MA	MA	FA	FA	FA / FA		MA	E	MA	MA									
	3.25	3.30	3.17	3.77	3.49	3.50	3.56	3.40	3.17	3.47	3.74		3.40	2.64									
10628 6/10	FA	FA	MA	MA	FA / FA		MA	FA	MA	FA	FA	MA	MA	MA	MA								
	3.24	3.66	3.59	3.63	3.30	3.05	3.41	3.48	3.28	3.43	3.50	3.52	3.44	3.24	3.65								
10629 8/ 7	FA	MA	FA	FA	FA	FA	FA	FA / MA		MA	FA	MA	FA	MA	MA								
	3.13	3.60	3.39	3.65	3.31	2.94	3.50	2.85	3.51	3.22	3.34	3.50	3.22	3.46	3.75								
10630 10/ 5	MA	FA	FA	MA	MA	MA	MA	FA	FA	FA / MA		MA	MA										
	3.08	3.10	3.26	3.52	3.33	3.40	3.33	3.08	3.26	3.00	3.51	3.62	3.61										
10631 12/ 6	MA	FA	MA	FA	FA	FA	FA	FA	MA	MA	FA / FA		FA	MA	FA								
	3.32	3.61	3.30	3.52	3.23	3.20	3.39	3.30	3.44	3.63	3.52	3.54	3.48	3.47	3.71								
10632 8/ 9	FA	FA	MA	E	MA	FA	FA	E / FA		FA	FA	MA	MA	FA	FA	MA							
	3.08	3.02	3.47		3.38	3.15	1.49		3.01	3.12	3.10	2.63	3.40	3.26	3.07	3.48							

M = MALE F = FEMALE A = ALIVE E = EARLY RESORPTION L = LATE RESORPTION "/" DENOTES POSITION OF CERVIX
CLs = CORPORA LUTEA/OVARY FETAL BODY WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 15 (PAGE 3): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

FETUS #		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
DOSAGE GROUP V								20 MG/KG/DAY																
RAT #	CLs																							
10633	4/11	MA	FA	MA	MA / FA	MA	FA	FA	MA	MA	FA	MA	MA	MA										
		3.79	3.65	3.70	3.65	2.88	3.58	3.03	3.34	3.56	3.34	3.29	3.53	3.42	3.25									
10634	8/ 8	FA	MA	FA	MA	MA	MA	MA	MA / FA	FA	FA	FA	FA	MA	MA	MA	FA							
		2.80	3.11	3.18	3.43	3.07	3.22	3.43	3.16	2.63	3.26	3.24	3.24	3.43	3.32	3.18	2.95							
10635	7/ 5	FA	MA	FA	FA	FA	MA	FA / FA		MA	MA	MA	E											
		3.29	3.48	3.19	3.31	3.14	3.15	2.81	2.93	3.19	3.15	3.29												
10636	8/ 8	MA	FA	MA	E	FA	FA	FA	FA / FA		FA	MA	MA	MA	MA	MA	MA							
		3.35	3.26	3.64		3.50	3.45	3.35	3.57	3.00	3.46	3.53	3.59	3.61	3.71	3.48	3.44							
10637	9/ 6	FA	FA	MA	MA	MA	MA	FA	FA	FA / FA		MA	FA	MA	MA	MA								
		2.58	2.89	3.02	3.12	3.15	3.12	2.94	3.21	2.87	2.94	3.19	2.99	3.36	3.14	3.23								
10638	6/ 8	MA	FA	FA	MA	FA	FA / FA		MA	FA	MA	FA	MA	FA	MA									
		3.50	3.09	3.53	3.49	3.06	3.31	3.09	3.16	3.22	3.33	2.84	3.69	3.41	3.82									
10639	8/ 9	MA	MA	MA	FA	FA	MA	FA	MA / MA		E	MA	FA	FA	FA	MA	FA	MA						
		3.34	3.52	3.75	3.34	3.40	3.24	2.71	3.58	3.09		3.25	3.19	3.37	3.25	3.34	2.83	2.83						
10640	8/11	MA	MA	MA	MA	FA	MA	MA / MA		FA	MA	FA	FA	MA	MA	FA	MA	MA						
		3.21	3.21	3.43	3.19	3.05	3.04	2.99	3.16	3.00	3.28	2.99	3.14	3.13	3.06	2.87	2.77	3.04						
DOSAGE GROUP VI								25 MG/KG/DAY																
10641	7/ 6	FA	FA	MA	FA	FA	FA	MA / MA		FA	FA	FA	FA	MA										
		3.49	3.42	3.69	3.47	3.14	3.22	3.21	3.53	3.11	3.30	3.24	3.38	3.40										
10642	7/10	FA	FA	MA	MA	MA	FA	MA / FA		MA	FA	MA	MA	FA	MA	FA	MA							
		3.05	2.68	3.17	3.07	3.07	3.02	3.26	2.90	3.15	2.88	3.06	3.24	2.92	3.20	2.76	2.89							
10643	9/ 8	MA	FA	FA	FA	MA	MA	MA	FA	FA / MA		FA	FA	MA	MA	MA								
		3.44	3.33	3.41	3.44	3.68	3.52	3.47	3.33	3.25	3.51	3.17	3.51	3.22	3.25	3.51								
10644	9/11	MA	MA	FA	FA	FA	E	MA	MA	MA / MA		MA	E	FA	MA	MA	MA	MA	FA	MA	MA			
		2.92	2.64	2.79	2.81	2.83		3.10	2.97	3.00	3.01	2.74		2.66	2.89	3.02	2.81	2.95	2.90	2.89	2.73			
10645	8/ 8	FA	FA	MA	MA	MA	FA / MA		FA	FA	MA	FA	MA	MA	FA									
		3.05	3.16	3.26	3.26	3.05	3.06	3.02	3.01	3.16	3.34	2.97	3.13	3.09	2.76									
10646	7/ 8	MA	FA	FA	MA	MA / MA		FA	MA	FA	FA	MA	MA	FA										
		3.07	3.04	3.16	3.02	2.97	2.95	3.02	3.13	2.77	3.15	3.12	3.07	2.98										
10647	3/ 8	FA	E	FA / MA		FA	FA	MA	FA	FA	FA	MA												
		3.25		3.18	3.37	3.18	2.66	3.61	2.84	2.92	3.12	3.32												
10648	11/ 7	MA	FA	MA	MA	FA	FA	MA	FA	FA	MA / MA		MA	MA	MA	FA	FA	FA	FA					
		2.99	2.90	3.12	2.77	3.12	2.73	3.15	2.95	2.75	3.26	3.12	3.19	3.17	3.03	2.76	2.81	2.59						

M = MALE F = FEMALE A = ALIVE E = EARLY RESORPTION L = LATE RESORPTION "/" DENOTES POSITION OF CERVIX
CLs = CORPORA LUTEA/OVARY FETAL BODY WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-011P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS (SPONSOR'S STUDY NUMBER: T-6316.7)

TABLE 15 (PAGE 4): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
DOSAGE GROUP VII							35 MG/KG/DAY																
RAT # CLs																							
10649 7/ 6	FA	E	FA	MA	FA	MA	MA / FA		E	FA	FA	FA	FA										
	2.36		2.61	2.85	2.44	2.80	2.75	2.35		2.61	2.30	2.57	3.08										
10650a 8/ 9	FA	FA	FA	E	E	FA	MA /	E	MA	MA	FA	FA	MA	FA	FA	MA							
	2.01	1.75	2.08			2.20	2.15		2.04	2.12	1.66	1.14	1.64	2.02	1.95	1.95							
10651 10/ 8	FA	MA	FA	FA	FA	FA	MA	MA	MA	FA / MA		MA	MA	MA	FA	MA	FA						
	3.04	3.34	3.03	3.13	2.96	3.35	3.25	3.03	3.14	3.22	2.98	3.19	3.35	3.20	3.10	3.66	3.46						
10652 7/ 8	MA	MA	MA	FA	MA	MA	FA / FA		MA	FA	MA	FA	MA	FA									
	3.07	3.29	3.51	3.07	3.27	3.00	2.88	3.19	3.21	3.20	3.45	2.72	3.04	2.59									
10653 9/ 5	FA	MA	MA	FA	FA	MA	MA	FA	E / FA		FA	MA	MA	FA									
	3.04	3.20	3.09	2.71	2.90	3.46	2.93	3.22		3.27	2.94	3.29	3.55	3.17									
10654 9/13	FA	MA	FA	FA	MA	MA	FA	FA	FA / MA		FA	E	FA	MA	MA	MA	FA	FA					
	2.76	3.03	3.06	3.20	2.97	3.22	2.86	2.80	3.12	3.21	2.98		2.81	3.46	3.37	3.24	3.01	2.87					
10655 5/ 7	MA	MA	MA	FA	FA / FA		MA	MA	MA	MA	MA	MA											
	3.23	3.36	3.40	3.17	3.23	2.82	3.53	3.32	3.03	3.21	3.10	3.52											
10656 9/10	MA	FA	MA	FA	FA	MA	MA	MA	MA / MA		FA	FA	MA	FA	MA	MA	MA						
	3.37	3.30	3.12	2.85	3.22	3.35	3.33	3.52	3.13	3.22	3.11	3.36	3.45	2.56	3.21	2.84	3.25						

M = MALE F = FEMALE A = ALIVE E = EARLY RESORPTION L = LATE RESORPTION */* DENOTES POSITION OF CERVIX
CLs = CORPORA LUTEA/OVARY FETAL BODY WEIGHTS WERE RECORDED IN GRAMS (G).

a. Fetuses 10650-1 and 10650-10 had cleft palate and an edematous body, and fetuses 10650-2, 10650-3, 10650-6, 10650-7, 10650-9, 10650-11, 10650-12, 10650-13, 10650-14, 10650-15 and 10650-16 had cleft palate.

ATTACHMENT 1

PROTOCOL AND AMENDMENT

10 171400

RESEARCH Argus LABORATORIES

Argus Research Laboratories, Inc.
905 Sheehy Drive, Building A
Horsham, Pennsylvania 19044
T: (215) 443-8710 F: (215) 443-8587

PROTOCOL 418-011P

SPONSOR'S STUDY NUMBER: T-6316.7

STUDY TITLE: Oral (Gavage) Dosage-Range Developmental Toxicity Study of N-EtFOSE in Rats

PURPOSE: The purpose of this study is to provide information for the selection of dosages to be used in the developmental toxicity (embryo-fetal toxicity and teratogenic potential) study of N-EtFOSE administered orally via gavage to Crl:CD®BR VAF/Plus® presumed pregnant female rats.

TESTING FACILITY: Argus Research Laboratories, Inc.
905 Sheehy Drive, Building A
Horsham, Pennsylvania 19044-1297
Telephone: (215) 443-8710
Telefax: (215) 443-8587

STUDY DIRECTOR: Raymond G. York, Ph.D., DABT
Associate Director of Research

SPONSOR: 3M Toxicology Services
3M Center, Building 220-2E-02
St. Paul, Minnesota 55144-1000

STUDY MONITOR: Marvin T. Case, D.V.M., Ph.D.
Telephone: (612) 733-5180
Telefax: (612) 733-1773

ALTERNATE STUDY MONITOR: Andrew M. Seacat, Ph.D.
Telephone: (612) 575-3161
Telefax: (612) 733-1773

10 171401

REGULATORY CITATIONS:

U.S. Food and Drug Administration (1994). International Conference on Harmonisation; Guideline on detection of toxicity to reproduction for medicinal products. *Federal Register*, September 22, 1994, Vol. 59, No. 183.

U.S. Food and Drug Administration. Good Laboratory Practice Regulations; Final Rule. 21 CFR Part 58.

Japanese Ministry of Health and Welfare (1997). *Good Laboratory Practice Standard for Safety Studies on Drugs*, MHW Ordinance Number 21, March 26, 1997.

European Economic Community (1989). *Council decision on 28 July 1989 on the acceptance by the European Economic Community of an OECD decision/recommendation on compliance with principles of good laboratory practice*. Official Journal of the European Communities: Legislation. 32 (No. L 315; 28 October): 1-17.

REGULATORY COMPLIANCE:

This study will be conducted in the spirit of the Good Laboratory Practice (GLP) regulations cited above in that the Testing Facility personnel will adhere to the Standard Operating Procedures for laboratory operations and data collection. The Testing Facility Quality Assurance Unit (QAU) will not audit the protocol, the raw data, the reports or the critical phases of the study.

All changes or revisions of this protocol shall be documented, signed by the Study Director and the Sponsor, dated and maintained with the protocol.

STUDY SCHEDULE:

See ATTACHMENT 1 to the protocol.

10 171402

TEST ARTICLE AND VEHICLE:

Identification:

Test Article:

Name:	N–EtFOSE.
Physical Description:	Waxy solid.
Lot/Batch Number:	FM-3929 (30035, 30037, 30039).
Specific Gravity:	~1.7.
Purity:	99.1%.
Expiration Date:	May, 2000.

Information on the identity, composition, strength and purity of the test article is on file with the Sponsor.

Vehicle:

2% Tween® 80 in Reverse Osmosis Membrane Processed Deionized Water (R.O. Deionized Water). Supplier and lot identification of Tween® 80 to be documented in the raw data.

Neither the Sponsor nor the Study Director is aware of any potential contaminants likely to be present in the vehicle that would interfere with the results of this study. Therefore, no analyses other than those mentioned in this protocol will be conducted.

Safety Precautions:

Gloves, mask, appropriate eye protection and a uniform/lab coat are to be worn during formulation preparation and administration. The Material Safety Data Sheet (MSDS) is attached to the protocol (ATTACHMENT 2).

Storage:

Bulk Test Article:	Room temperature.
Vehicle Components:	Room temperature.
Prepared Vehicle:	Room temperature.
Prepared Formulations:	Frozen (-20°C).

All test article shipments to the Testing Facility should be addressed to the attention of Julian Gulbinski, Manager of Formulations, at the previously cited address and telephone number.

Shipments should include information concerning storage conditions and shipping cartons should be labeled appropriately. The recipient should be notified in advance of shipment.

10 171403

FORMULATION:

Frequency of Preparation:

Formulations (suspensions) will be prepared daily at the Testing Facility. Vehicle will be prepared weekly at the Testing Facility.

Detailed preparation procedures are attached to this protocol (ATTACHMENT 3).

Adjustment for Purity:

The test article will be considered 100% pure for the purpose of dosage calculations.

Testing Facility Reserve Samples:

The Sponsor will reserve a sample (1 g) of each lot of the bulk test article used during the course of this study. The Testing Facility will reserve a sample (5 mL) of each lot of the vehicle components used during the course of this study. Samples will be stored under the previously cited conditions.

ANALYSES:

Samples additional to those described below may be taken if deemed necessary during the course of the study.

Bulk Test Article Sampling:

No analyses of the bulk test article will be conducted during the course of this study. Information on the stability of the bulk test article is on file with the Sponsor.

Analyses of Prepared Formulations:

At the request of the Sponsor, no analyses of prepared test article formulations will be conducted during the course of the study. However, records will be maintained to document how the test article formulations were prepared.

DISPOSITION:

Prepared formulations will be discarded at the Testing Facility. All remaining bulk test article will be returned to the Study Monitor at the previously cited address.

TEST SYSTEM:

Species/Strain and Reason for Selection:

The Crl:CD®BR VAF/Plus® (Sprague-Dawley) rat was selected as the Test System because: 1) it is one mammalian species accepted and widely used throughout industry for nonclinical studies of developmental toxicity (embryo-fetal toxicity/teratogenicity); 2) this strain has been demonstrated to be sensitive to developmental toxins; 3) historical data and experience exist at the Testing Facility[1-3]; and 4) the test article is pharmacologically active in the species and strain.

Number:

Initial population acclimated: 75 virgin female rats.
Population selected for study: 56 mated female rats (8 per dosage group).

Body Weight and Age:

Female rats will be ordered to have body weights of 200 g to 225 g each at receipt, at which time they will be expected to be at least 60 days of age. Actual body weights will be recorded the day after receipt and will be documented in the raw data.

Sex:

Female rats will be given the test article. Male rats of the same source and strain will be used only as breeders and are not considered part of the Test System.

Source:

Charles River Laboratories, Inc.

The rats will be shipped in filtered cartons by air freight and/or truck from Charles River Laboratories, Inc., to the Testing Facility.

Identification:

Rats are permanently identified using Monel® self-piercing ear tags (Gey Band and Tag Co., Inc., No. MSPT 20101). Male rats are given unique permanent identification numbers upon assignment to the Testing Facility's breeder male rat population. Female rats are assigned temporary numbers at receipt and given unique permanent identification numbers when assigned to the study on the basis of day 0 of presumed gestation body weights.

10 171405

ANIMAL HUSBANDRY:

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

Housing:

The rats will be individually housed in stainless steel, wire-bottomed cages except during the cohabitation period. During cohabitation, each pair of rats will be housed in the male rat's cage. No nesting materials will be supplied because the female rats will be sacrificed before parturition is expected.

Room Air, Temperature and Humidity:

The animal room is independently supplied with at least ten changes per hour of 100% fresh air that has been passed through 99.97% HEPA filters (Airo Clean® room). Room temperature will be maintained at 64°F (18°C) to 79°F (26°C) and monitored constantly. Room humidity will also be monitored constantly and maintained at 30% to 70%.

Light:

An automatically controlled 12-hour light:12-hour dark fluorescent light cycle will be maintained. Each dark period will begin at 1900 hours EST.

Diet:

Rats will be given Certified Rodent Diet® #5002 (PMI Nutrition International) available *ad libitum* from individual feeders.

Water:

Water will be available *ad libitum* from individual bottles attached to the cages or from an automatic watering access system. All water will be from a local source and passed through a reverse osmosis membrane before use. Chlorine will be added to the processed water as a bacteriostat; processed water is expected to contain no more than 1.2 ppm chlorine at the time of analysis. Water is analyzed monthly for possible bacterial contamination and twice annually for possible chemical contamination.

Contaminants:

Neither the Sponsor nor the Study Director is aware of any potential contaminants likely to be present in the certified diet or in the drinking water at levels that would interfere with the results of this study. Therefore, no analyses other than those routinely performed by the feed supplier or those mentioned in this protocol will be conducted.

RANDOMIZATION AND COHABITATION:

Upon arrival, male and female rats will be assigned to individual housing on the basis of computer-generated random units. After acclimation, virgin female rats will be cohabited with breeder male rats, one male rat per female rat. The cohabitation period will consist of a maximum of five days. Female rats with spermatozoa observed in a smear of the vaginal contents and/or a copulatory plug observed *in situ* will be considered to be at day 0 of presumed gestation and assigned to individual housing.

Healthy mated female rats will be assigned to dosage groups based on computer-generated (weight-ordered) randomization procedures.

ADMINISTRATION:

Route and Reason for Choice:

The oral (gavage) route was selected for use because: 1) in comparison with the dietary route, the exact dosage can be accurately administered; and 2) it is one of the possible routes of human exposure.

Method and Frequency:

Female rats will be given the test article once daily on days 6 through 17 of presumed gestation, the period of organogenesis. Dosages will be adjusted for the most recently recorded body weight and given at approximately the same time each day.

Rationale for Dosage Selection:

Dosages will be selected by the Sponsor on the basis of previous studies conducted with the test article.

Dosage Levels, Concentrations and Volumes:

Dosage Group	Number of Rats	Dosage (mg/kg/day)	Concentration (mg/mL)	Dosage Volume (mL/kg)	Argus Batch Number
I	8	0 (Vehicle)	0	5	B-418-011P-A(Day.Month.Year)
II	8	1	0.2	5	B-418-011P-B(Day.Month.Year)
III	8	5	1	5	B-418-011P-C(Day.Month.Year)
IV	8	10	2	5	B-418-011P-D(Day.Month.Year)
V	8	20	4	5	B-418-011P-E(Day.Month.Year)
VI	8	25	5	5	B-418-011-P-F(Day.Month.Year)
VII	8	35	7	5	B-418-011-P-G(Day.Month.Year)

The test article will be considered 100% pure for the purpose of dosage calculations.

TESTS, ANALYSES AND MEASUREMENTS:

Viability:

All Periods: At least twice daily.

Clinical Observations and/or General Appearance:

Acclimation Period: Weekly.

Predosage Period: Day 0 of presumed gestation.

Dosage Period: Twice daily. Once approximately one hour postdosage and then four to six hours later.

Postdosage Period: Once daily.

Clinical observations may be recorded more frequently than cited above, if deemed appropriate by the Study Director and/or Study Monitor.

Body Weights:

Acclimation Period: Weekly.

Predosage Period: Days 0 and 4 of presumed gestation.

Dosage Period: Daily.

Postdosage Period: Daily.

10 171408

Feed Consumption Values (recorded and tabulated):

Predosage Period:	Days 0 and 4 of presumed gestation.
Dosage Period:	Days 6, 8, 10, 12, 14 and 16 of presumed gestation.
Postdosage Period:	Days 18 and 20 of presumed gestation.

Feed consumption values may be recorded more frequently if it is necessary to replenish the feed. These intervals will not be tabulated.

Mating Performance:

Mating will be evaluated daily during the cohabitation period and confirmed by observation of spermatozoa in a smear of the vaginal contents and/or a copulatory plug observed *in situ*.

Caesarean-Sectioning Observations:

Rats will be Caesarean-sectioned on day 20 of presumed gestation. The fetuses will be removed from the uterus and placed in individual containers. The rats will be examined for number and distribution of:

Corpora Lutea.

Implantation Sites.
[Placentae that appear abnormal (size, color or shape) will be noted in the raw data.]

Live and Dead Fetuses.
(A live fetus is defined as one that responds to stimuli; a dead fetus is defined as a term fetus that does not respond to stimuli and that is not markedly autolyzed; dead fetuses demonstrating marked to extreme autolysis are considered to be late resorptions.)

Early and Late Resorptions.
(A conceptus is defined as a late resorption if it is grossly evident that organogenesis has occurred; if this is not the case, the conceptus is defined as an early resorption.)

Fetal Observations:

Fetuses will be examined for sex and for gross external alterations. Late resorptions and dead fetuses will be examined for gross external alterations to the extent possible. The body weight of each fetus will be recorded. Only body weights of live fetuses will be used to determine litter fetal body weight averages. Fetuses with gross external alterations will be fixed in Bouin's solution; all other fetuses will be discarded. Representative photographs of fetal gross external alterations will be taken.

METHOD OF SACRIFICE:

Rats will be sacrificed by carbon dioxide asphyxiation. Live fetuses will be sacrificed by an intraperitoneal injection of euthanasia solution (Beuthanasia®-D Special, manufactured by Schering-Plough Animal Health).

NECROPSY:

Gross lesions will be retained in neutral buffered 10% formalin for possible future evaluation (a table of random units will be used to select one control group rat from which all tissues examined at necropsy will be retained, in order to provide control tissues for any possible histopathological evaluations of gross lesions). Unless specifically cited below, all other tissues will be discarded.

Scheduled Sacrifice:

On day 20 of presumed gestation, female rats will be Caesarean-sectioned, and a gross necropsy of the thoracic, abdominal and pelvic viscera will be performed. Uteri of apparently nonpregnant rats will be stained with 10% ammonium sulfide to confirm the absence of implantation sites[5].

Rats Found Dead or Moribund:

Rats that die or are sacrificed because of moribund condition, abortion or premature delivery will be examined for the cause of death or moribund condition on the day the observation is made. The rats will be examined for gross lesions. Pregnancy status and uterine contents of female rats will be recorded. Aborted fetuses and/or delivered pups will be examined to the extent possible, using the same methods described for fetuses. Uteri of apparently nonpregnant rats will be stained with 10% ammonium sulfide to confirm the absence of implantation sites[5].

STATISTICAL EVALUATION:

Averages and percentages will be calculated. Litter values will be used where appropriate. Additional procedures and/or analyses may be performed if deemed appropriate.

DATA ACQUISITION, VERIFICATION AND STORAGE:

Data will be hand- and/or computer-recorded. Records will be reviewed by the Study Director and/or appropriate management personnel within 21 days after generation. All original records will be stored in the archives of the Testing Facility. All original data will be bound and indexed. A copy of all raw data will be supplied to the Sponsor upon request. Preserved tissues will be stored at the Testing Facility at no charge for one year after mailing of the draft final report, after which time the Sponsor will be contacted to determine the disposition of these materials.

RECORDS TO BE MAINTAINED:

Protocol and Amendments.
Test Article, Vehicle and/or Reagent Receipt, Preparation and Use.
Animal Acquisition.
Randomization Schedules.
Mating History.
Treatment (if prescribed by Staff Veterinarian).
General Comments.
Clinical Observations and/or General Appearance.
Body Weights.
Feed Consumption Values.
Caesarean-Sectioning and Fetal Observations.
Gross Necropsy Observations.
Organ Weights (if required).
Photographs (if required).
Study Maintenance (room and environmental records).
Feed and Water Analyses.
Packing and/or Shipment Lists.

KEY PERSONNEL:

Executive Director of Research: Mildred S. Christian, Ph.D., ATS
Director of Research: Alan M. Hoberman, Ph.D., DABT
Associate Director of Research and Study Director: Raymond G. York, Ph.D., DABT
Director of Laboratory Operations: John F. Barnett, B.S.
Manager of Study Coordination: Valerie A. Sharper, M.S.
Manager of Animal Operations and Member, Institutional Animal Care and Use Committee: Dena C. Lebo, V.M.D.
Manager of Regulatory Compliance: Kathleen A. Moran, M.S.
Consultant, Veterinary Pathology: W. Ray Brown, D.V.M., Ph.D., ACVP

REPORT:

A letter report for the purpose of dosage selection for the full study will be prepared immediately following completion of the in-life phase.

A summary report will be prepared including: abstract, summaries of the methods, results and conclusion; table of contents; copy of the protocol; amendments; summary and individual tables; and reports of supporting data (if appropriate). The report will be included as an appendix to the full study report. The Sponsor will receive one copy of the draft report and two copies of the final report.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE STATEMENT:

The procedures described in this protocol have been reviewed by the Testing Facility's Institutional Animal Care and Use Committee. All procedures described in this protocol that involve study animals will be conducted in a manner to avoid or minimize discomfort, distress or pain to the animals.

The Sponsor's signature below documents the fact that information concerning the necessity for conducting this study and the fact that this is not an unnecessarily duplicative study may be obtained from the Sponsor. No alternative (*in vitro*) procedures were available for meeting the stated purposes of the study.

10 171412

REFERENCES:

1. Christian, M.S. and Voytek, P.E. (1982). *In Vivo Reproductive and Mutagenicity Tests*. Environmental Protection Agency, Washington, D.C. National Technical Information Service, U.S. Department of Commerce, Springfield, VA 22161.

2. Christian, M.S. (1984). Reproductive toxicity and teratology evaluations of naltrexone (Proceedings of Naltrexone Symposium, New York Academy of Sciences, November 7, 1983), J. Clin. Psychiat. 45(9):7-10.

3. Lang, P.L. (1988). *Embryo and Fetal Developmental Toxicity (Teratology) Control Data in the Charles River Crl:CD®BR Rat*. Charles River Laboratories, Inc., Wilmington, MA 01887-0630. (Data base provided by Argus Research Laboratories, Inc.)

4. Institute of Laboratory Animal Resources (1996). *Guide for the Care and Use of Laboratory Animals*. National Academy Press, Washington, D.C.

5. Salewski, E. (1964). Färbemethode zum makroskopischen Nachweis von Implantationsstellen am Uterus der Ratte. Arch. Pathol. Exp. Pharmakol. 247:367.

10 171413

PROTOCOL APPROVAL:

FOR THE TESTING FACILITY

George E. Dearlove, Ph.D., DABT
Associate Director of Research

10-JUN-98
Date

Raymond G. York, Ph.D., DABT
Associate Director of Research
Study Director

10-JUN-98
Date

Dena C. Lebo, V.M.D.
Member, Institutional Animal Care and
Use Committee

10 June 98
Date

FOR THE SPONSOR

Marvin T. Case, D.V.M., Ph.D.
Study Monitor

11 June 1998
Date

10 171414

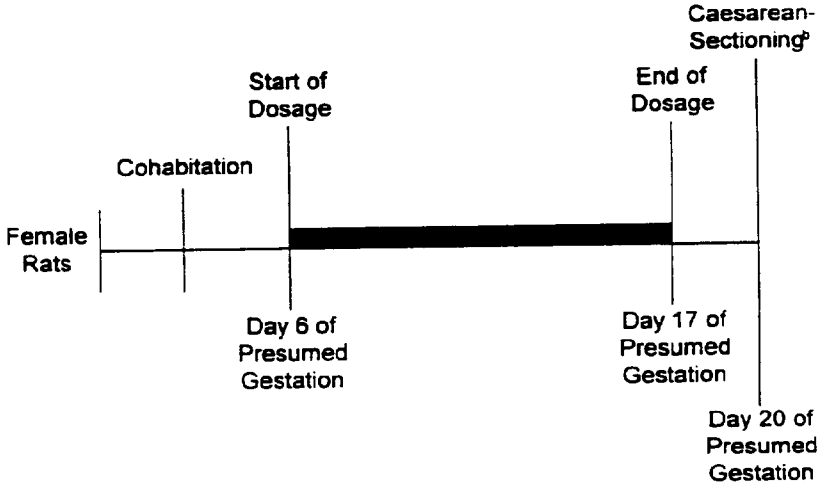
ATTACHMENT 1

SCHEMATIC OF STUDY DESIGN AND STUDY SCHEDULE

ATTACHMENT 1

STUDY SCHEMATIC

DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY[a]



■ Dosage Period.

a. For additional details see "Tests, Analyses and Measurements" section of the protocol.

b. Fetal evaluations (all fetuses - external examinations).

10 171416

ATTACHMENT 1

SCHEDULE[a]

16 JUN 98	Arrival Date - Acclimation Begins.
22 JUN 98 PM - 27 JUN 98 AM	Cohabitation Period.
23 JUN 98 - 27 JUN 98	Day 0 of Presumed Gestation.
29 JUN 98 - 14 JUL 98	Dosage Period (Days 6 through 17 of presumed gestation).
13 JUL 98 - 17 JUL 98	Caesarean-Sectioning Period (Day 20 of presumed gestation).
24 JUL 98	Letter Report.
29 SEP 98	Summary Report.

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a. The study initiation date is the date the Study Director signs the protocol.

10 171417

ATTACHMENT 2

MATERIAL SAFETY DATA SHEET

10 171418

N-ETFOSE 418-011P:PAGE 77

MATERIAL SAFETY DATA SHEET

3M
3M Center
St. Paul, Minnesota
55144-1000
1-800-364-3577 or (612) 737-6501 (24 hours)

DIVISION: 3M CHEMICALS
TRADE NAME:
FC-10 FLUORAD Brand Fluorochemical Alcohol
ID NUMBER/U.P.C.:
98-0211-1113-7 00-51135-09495-2 98-0211-1183-0 00-51135-09542-3
98-0211-1575-7 00-51135-02145-3 98-0211-6620-6 00-51135-10439-2
ZF-0002-0572-2
ISSUED: January 29, 1998
SUPERSEDES: November 05, 1997
DOCUMENT: 10-3778-7

1. INGREDIENT	C.A.S. NO.	PERCENT
PERFLUOROOCTANESULFONAMIDO ALCOHOL.....	1691-99-2	80.0 - 90.0
PERFLUOROHEXANESULFONAMIDO ALCOHOL.....	34455-03-3	3.0 - 7.0
PERFLUOROHEPTANESULFONAMIDO ALCOHOL.....	68555-73-7	2.0 - 6.0
PERFLUOROBUTANESULFONAMIDO ALCOHOL.....	34449-89-3	2.0 - 6.0
PERFLUOROPENTANESULFONAMIDO ALCOHOL.....	68555-72-6	1.0 - 3.0

2. PHYSICAL DATA

BOILING POINT:.....	ca. 118 C @ 1 mm Hg
VAPOR PRESSURE:.....	< 10 mmHg Calc @ 20 C
VAPOR DENSITY:.....	> 1.0 Air=1 Calc @ 20 C.
EVAPORATION RATE:.....	< 1.0 BuOAc=1
SOLUBILITY IN WATER:.....	neglig.
SPECIFIC GRAVITY:.....	ca. 1.7 Water=1 (of melt)
PERCENT VOLATILE:.....	0 %
pH:.....	N/A
VISCOSITY:.....	N/D
MELTING POINT:.....	N/D

10 171419

Abbreviations: N/D - Not Determined N/A - Not Applicable CA - Approximately

MSDS: FC-10 FLUORAD Brand Fluorochemical Alcohol
January 29, 1998

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2. PHYSICAL DATA (continued)

APPEARANCE AND ODOR:
Amber waxy solid

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3. FIRE AND EXPLOSION HAZARD DATA

FLASH POINT:..... > 148 C Setaflash
FLAMMABLE LIMITS - LEL:..... N/A
FLAMMABLE LIMITS - UEL:..... N/A
AUTOIGNITION TEMPERATURE:..... N/A

EXTINGUISHING MEDIA:
Water, Carbon dioxide, Dry chemical, Foam

SPECIAL FIRE FIGHTING PROCEDURES:
Wear full protective clothing, including helmet, self-contained, positive pressure or pressure demand breathing apparatus, bunker coat and pants, bands around arms, waist and legs, face mask, and protective covering for exposed areas of the head.

UNUSUAL FIRE AND EXPLOSION HAZARDS:
See Hazardous Decomposition section for products of combustion.

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4. REACTIVITY DATA

STABILITY: Stable

INCOMPATIBILITY - MATERIALS/CONDITIONS TO AVOID:
Not applicable.

HAZARDOUS POLYMERIZATION: Hazardous polymerization will not occur.

HAZARDOUS DECOMPOSITION PRODUCTS:
Carbon Monoxide and Carbon Dioxide, Oxides of Nitrogen, Oxides of Sulfur, Hydrogen Fluoride, Toxic Vapors, Gases or Particulates.

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5. ENVIRONMENTAL INFORMATION

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10 171420

SPILL RESPONSE:
Refer to other sections of this MSDS for information regarding physical and health hazards, respiratory protection, ventilation, and personal protective equipment. Collect spilled material. Clean up residue. Place in a U.S. DOT-approved container.

N/A - Not Applicable CA - Approximately

MSDS: FC-10 FLUORAD Brand Fluorochemical Alcohol PAGE 3
January 29, 1998

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5. ENVIRONMENTAL INFORMATION (continued)

RECOMMENDED DISPOSAL:
Incinerate in a permitted hazardous waste incinerator in the presence of a combustible material. Combustion products will include HF. Dispose of waste product in a facility permitted to accept chemical waste.

ENVIRONMENTAL DATA:
Laboratory tests showed no biodegradation. 96-Hr. LD50 Fathead Minnow (Pimephales promelas) - No mortality at water saturation. No statistically significant effect on % hatch, % survival, weight, and length in 30 day Fathead Minnow egg fry study. Lab tests showed 200 fold bioconcentration of FC-10 into muscle fillets of channel catfish.

REGULATORY INFORMATION:
Volatile Organic Compounds: N/A.
VOC Less H2O & Exempt Solvents: N/A.

This product complies with the chemical registration requirements of TSCA, EINECS, CDSL, AICS and Korea.

EPCRA HAZARD CLASS:
FIRE HAZARD: No PRESSURE: No REACTIVITY: No ACUTE: Yes CHRONIC: Yes

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6. SUGGESTED FIRST AID

EYE CONTACT:
Immediately flush eyes with large amounts of water. Get immediate medical attention.

SKIN CONTACT:
Immediately wash skin with soap and large amounts of water. Remove contaminated clothing. If signs/symptoms occur, call a physician. Wash contaminated clothing before reuse and dispose of contaminated shoes.

INHALATION:
If signs/symptoms occur, remove person to fresh air. If signs/symptoms continue, call a physician.

IF SWALLOWED:
Call a physician IMMEDIATELY. If swallowed, induce vomiting immediately as directed by medical personnel. Never give anything by mouth to an unconscious person.

10 171421

N/A - Not Applicable CA - Approximately

MSDS: FC-10 FLUORAD Brand Fluorochemical Alcohol
January 29, 1998

7. PRECAUTIONARY INFORMATION

EYE PROTECTION:
Avoid eye contact. Wear safety glasses with side shields.

SKIN PROTECTION:
Avoid skin contact. Wear appropriate gloves when handling this material. A pair of gloves made from the following material(s) are recommended: butyl rubber. Use one or more of the following personal protection items as necessary to prevent skin contact: coveralls.

RECOMMENDED VENTILATION:
Use with appropriate local exhaust ventilation. Provide sufficient ventilation to maintain emissions below recommended exposure limits. If exhaust ventilation is not adequate, use appropriate respiratory protection.

RESPIRATORY PROTECTION:
Avoid breathing of airborne material. Select one of the following NIOSH approved respirators based on airborne concentration of contaminants and in accordance with OSHA regulations: half-mask dust respirator, full-face supplied air respirator.

PREVENTION OF ACCIDENTAL INGESTION:
Do not eat, drink or smoke when using this product. Wash exposed areas thoroughly with soap and water. Wash hands after handling and before eating.

RECOMMENDED STORAGE:
Store away from heat. Keep container closed when not in use.

FIRE AND EXPLOSION AVOIDANCE:
Nonflammable.

OTHER PRECAUTIONARY INFORMATION:
No smoking: Smoking while using this product can result in contamination of the tobacco and/or smoke and lead to the formation of the hazardous decomposition products mentioned in section 4 of this MSDS.

10 171422

HMIS HAZARD RATINGS: HEALTH: 1 FLAMMABILITY: 1 REACTIVITY: 0
PERSONAL PROTECTION: X (See precautions, section 7.)

EXPOSURE LIMITS

INGREDIENT	VALUE	UNIT	TYPE	AUTH	SKIN*
PERFLUOROOCTANESULFONAMIDO ALCOHOL...	0.1	MG/M3	TWA	3M	Y
PERFLUOROHEXANESULFONAMIDO ALCOHOL...	0.1	MG/M3	TWA	3M	Y
PERFLUOROHEPTANESULFONAMIDO ALCOHOL.....	0.1	MG/M3	TWA	3M	Y

N/A - Not Applicable CA - Approximately

MSDS: FC-10 FLUORAD Brand Fluorochemical Alcohol
January 29, 1998

EXPOSURE LIMITS (continued)

INGREDIENT	VALUE	UNIT	TYPE	AUTH	SKIN*
PERFLUOROBUTANESULFONAMIDO ALCOHOL...	0.1	MG/M3	TWA	3M	Y
PERFLUOROPENTANESULFONAMIDO ALCOHOL.....	0.1	MG/M3	TWA	3M	Y

* SKIN NOTATION: Listed substances indicated with 'Y' under SKIN refer to the potential contribution to the overall exposure by the cutaneous route including mucous membrane and eye, either by airborne or, more particularly, by direct contact with the substance. Vehicles can alter skin absorption.

SOURCE OF EXPOSURE LIMIT DATA:
- 3M: 3M Recommended Exposure Guidelines

8. HEALTH HAZARD DATA

EYE CONTACT:
No adverse health effects are expected from eye contact.

SKIN CONTACT:
Product is not expected to be irritating to the skin.

May be absorbed through the skin and persist in the body for an extended time.

INHALATION:
May be absorbed by inhalation and persist in the body for an extended time.

IF SWALLOWED:
Ingestion is not a likely route of exposure to this product.

Illness may occur after a single swallowing of relatively large quantities of this material.

MUTAGENICITY:
Not mutagenic in in-vitro assays.

REPRODUCTIVE/DEVELOPMENTAL TOXINS:
Substance was not teratogenic in the rat at doses as high as 30 milligrams per kilogram per day via oral route.

OTHER HEALTH HAZARD INFORMATION:
This product is not known to contain any substances regulated under California Proposition 65.

A Product Toxicity Summary Sheet is available.

10 171423

N/A - Not Applicable CA - Approximately

MSDS: FC-10 FLUORAD Brand Fluorochemical Alcohol
January 29, 1998

SECTION CHANGE DATES

HEADING	SECTION CHANGED SINCE November 05, 1997 ISSUE

Abbreviations: N/D - Not Determined N/A - Not Applicable CA - Approximately

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10 171424

ATTACHMENT 3

TEST ARTICLE AND CONTROL ARTICLE PREPARATION PROCEDURE

10 171425

ATTACHMENT 3

TEST ARTICLE AND CONTROL ARTICLE PREPARATION PROCEDURE

Test Article: N-EtFOSE

Vehicle: 2% Tween® 80, in R.O. Water

A. Purpose: The purpose of this procedure is to provide a method for the preparation of dosage suspensions of N-EtFOSE and the control article for oral administration to rats on Argus Study 418-011P.

B. General Information:

1. All suspension containers will be labeled and color coded. Each label will specify the protocol number, test article identification, Argus batch number, concentration, dosage level, preparation date, expiration date and storage conditions.

2a. Suspensions will be prepared:
_X_ Daily ___ Weekly ___ For___ days of use

2b. Vehicle will be prepared:
___ Daily _X_ Weekly ___ For___ days of use

3. Suspensions will be prepared at a final dosage volume of 5 mL/kg.

4. Safety:
_X_ Gloves, lab coat, goggles or safety glasses and faceshield
_X_ Dust-Mist Respirator
___ Half-Face Respirator
___ Full-Face Respirator/Positive Pressure Hood
___ Tyvek Suit/Apron

5. Dosage solutions adjusted for Free base and % Purity.
___ Yes _X_ No (Calculations based on 100%)
___ Free Base ___ Purity

6. Sampling requirements: Cited in protocol.

7. Storage: Cited in protocol.

10 171426

ATTACHMENT 3

TEST ARTICLE AND CONTROL ARTICLE PREPARATION PROCEDURE

NOTE: Test article will be prepared as a serial dilution from the high dosage to the low dosage. Once the final volumes are achieved, stir bars are to be added to the containers; mixing should occur during sampling and/or administration.

C. Preparation of Vehicle

1. Add the required amount of R.O. deionized water to an appropriately labeled container. Heat the water to 50°C, ±5°C, add the required amount of Tween® 80 and mix until uniform (See TEST ARTICLE CALCULATIONS).

D. Test Article Suspension Preparation:

1. To prepare the 7-mg/mL, Group VII suspension, add the required amount of test article (See TEST ARTICLE CALCULATIONS) into an appropriately sized, labeled container. Add the required amount of vehicle and heat the mixture to 80°C, ±5°C for approximately 30 minutes.

2. Once the test article has dissolved; spin over night while the solution cools. (Be sure there is a visible vortex, this will achieve the desired emulsion.)

3. To prepare the 5-mg/mL, Group VI suspension, remove the required amount of stock suspension (Group VII) (See TEST ARTICLE CALCULATIONS), add the required amount of vehicle and mix.

4. To prepare the 4-mg/mL, Group V suspension, remove the required amount of stock suspension (Group VI) (See TEST ARTICLE CALCULATIONS), add the required amount of vehicle and mix.

5. To prepare the 2-mg/mL, Group IV suspension, remove the required amount of stock suspension (Group V) (See TEST ARTICLE CALCULATIONS), add the required amount of vehicle and mix.

ATTACHMENT 3

TEST ARTICLE AND CONTROL ARTICLE PREPARATION PROCEDURE

6. To prepare the 1-mg/mL, Group III suspension, remove the required amount of stock suspension (Group IV) (See TEST ARTICLE CALCULATIONS), add the required amount of vehicle and mix.

7. To prepare the 0.2-mg/mL, Group II suspension, remove the required amount of stock suspension (Group III) (See TEST ARTICLE CALCULATIONS), add the required amount of vehicle and mix.

Written by: _____

Approved by: George E Date: 10-Jun-98

Clarification: ✓ No ___ Yes (See attached clarification form.)

Initials/Date : Christopher K. Kappel 7/22/95

10 171428

RESEARCH Argus LABORATORIES

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PROTOCOL 418-011P

ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS

SPONSOR'S STUDY NUMBER: T-6316.7

Amendment 1 - June 18, 1998

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1. Clinical Observations and/or General Appearance (page 8 of the protocol):

Clinical observations during the dosage period will be taken twice daily, prior to dosage administration and once approximately one hour postdosage, rather than once approximately one hour postdosage and then four to six hours later.

Reason for Change:

This change was made at the request of the Sponsor to match the time frames of the other reproductive/developmental toxicity studies using the same test article.

George E. Dearlove 18-Jun-98 — Raymond G. York 18-JUN-98

George E. Dearlove, Ph.D., DABT Date
Associate Director of Research

Raymond G. York, Ph.D., DABT Date
Associate Director of Research
and Study Director

Dena C. Lebo 18 June 98 — Marvin T Case 22 Jun 98

Dena C. Lebo, V.M.D. Date
Member, Institutional Animal Care and Use Committee

Marvin T. Case, D.V.M., Ph.D. Date
Study Monitor

10 171429

APPENDIX G

HISTORICAL CONTROL DATA

10 171430

SUMMARY OF REPRODUCTIVE INDICES
CD RAT

PERIOD	JUNE 1995 - JUNE 1997
NUMBER OF STUDIES	97
NUMBER OF RATS:	
TESTED	2132
PREGNANT	1967
FOUND DEAD	3
ABORTED	0
DELIVERED	0
NUMBER OF RATS PREGNANT AT CAESAREAN-SECTIONING	1957
NUMBER OF RATS WITH SINGLE CONCEPTUS LITTER:	
LIVE	5
RESORBED	0
ABORTED	0

	MEAN or %	RANGE/STUDY MEAN or %
% PREGNANT	92.8	(64.0-100)
AVERAGE # CORPORA LUTEA	17.3	(15.2-21.0)
AVERAGE # IMPLANTATIONS	15.6	(12.9-18.0)
AVERAGE LITTER SIZE		
AVERAGE # LIVE FETUSES	14.8	(11.8-17.0)
AVERAGE # DEAD FETUSES	0.1	(0-1.1)
AVERAGE # RESORPTIONS	0.8	(0-1.6)
AVERAGE # EARLY RESORPTIONS	0.7	(0-1.6)
AVERAGE # LATE RESORPTIONS	0.0	(0-0.2)

10 171431

SUMMARY OF REPRODUCTIVE INDICES
CD RAT

	MEAN or %	RANGE/STUDY MEAN or %
AVERAGE % DAMS WITH ANY RESORPTIONS	48.4	(0-75.0)
AVERAGE % DAMS WITH ALL CONCEPTUSES RESORBED	0.1	(0-4.5)
AVERAGE % DAMS WITH ONE OR MORE LIVE FETUSES	99.9	(95.4-100)
AVERAGE SEX RATIO, (% MALES/LITTER)	50.2	(42.1-57.0)
AVERAGE FETAL BODY WEIGHT (G)	3.47	(3.10-3.78)
AVERAGE FOR MALES (G)	3.56	(3.17-3.90)
AVERAGE FOR FEMALES (G)	3.37	(2.98-3.66)
AVERAGE % DEAD OR RESORBED CONCEPTUSES/LITTER	5.0	(0-10.9)

SUMMARY OF MATERNAL NECROPSY OBSERVATIONS
CD RAT

PERIOD	JUNE 1995 - JUNE 1997
# STUDIES	120
# RATS TESTED	2579
# RATS PREGNANT	2387
# RATS DIED	4
# RATS ABORTED	0
# RATS DELIVERED	439
# RATS WITH 100% RESORPTION	1

EXTERNAL OBSERVATIONS	N	MEAN %	RANGE N	/STUDY %
Red substance around nose and/or mouth	1	0.04	0-1	(0-3.3)
Incisors misaligned broken and/or missing	2	0.08	0-2	(0-6.7)
Chromodacryorrhea	2	0.08	0-2	(0-6.7)
Alopecia	3	0.12	0-3	(0-10.0)
White substance present in anterior chamber of eyes	1	0.04	0-1	(0-4.2)
GROSS LESIONS				
SUBMANDIBULAR LYMPH NODES				
Dark red	1	0.04	0-1	(0-3.3)
JUGULAR VEIN				
Distended with blood	1	0.04	0-1	(0-3.3)
CHEST				
Subcutaneous fat, dark red on ventral side	1	0.04	0-1	(0-3.3)
THORACIC CAVITY				
Filled with light red fluid	1	0.04	0-1	(0-4.0)
THYMUS				
Discolored areas	2	0.08	0-2	(0-6.7)
Large	1	0.04	0-1	(0-4.0)
AXILLA				
Mass present	1	0.04	0-1	(0-4.0)

10 171433

SUMMARY OF MATERNAL NECROPSY OBSERVATIONS
CD RAT

GROSS LESIONS	N	MEAN %	RANGE N	/STUDY %
LIVER				
Adhesion between left lateral lobe and left lateral abdominal wall	1	0.04	0-1	(0-4.0)
STOMACH/INTESTINE				
Stomach, fluid-filled	1	0.04	0-1	(0-4.0)
Stomach and intestines distended with gas	1	0.04	0-1	(0-4.0)
Intestines, empty	1	0.04	0-1	(0-4.0)
Cecum contained a black substance	1	0.04	0-1	(0-4.0)
BACK				
Spine, protrusion of bone on dorsal thoracic portion	1	0.04	0-1	(0-4.0)
KIDNEY(S)				
Pelvis, slight/moderate dilation with or without fluid	17	0.66	0-2	(0-12.5)
Pelvis, marked/extreme dilation	5	0.19	0-1	(0-4.0)
Mottled	2	0.08	0-1	(0-4.0)
Large	2	0.08	0-1	(0-4.0)
Small	1	0.04	0-1	(0-4.0)
Cortex pitted	1	0.04	0-1	(0-3.4)
Left; pelvis contained yellow fluid	1	0.04	0-1	(0-4.0)
ABDOMINAL CAVITY				
Filled with light red fluid	1	0.04	0-1	(0-4.0)
SPLEEN				
Two white areas on serosal surface	1	0.04	0-1	(0-4.0)
BLADDER				
Fluid-filled	1	0.04	0-1	(0-4.0)
Wall thick, contained one calculi	1	0.04	0-1	(0-12.5)

10 171434

SUMMARY OF MATERNAL NECROPSY OBSERVATIONS
CD RAT

GROSS LESIONS	N	MEAN %	RANGE N	/STUDY %
URETERS				
Distended with clear fluid	1	0.04	0-1	(0-4.0)
VAGINA/CERVIX				
Cervix distended with fluid	1	0.04	0-1	(0-4.0)
Cervix contained a thick, brown substance	1	0.04	0-1	(0-4.0)
Cervix contained a dark red, gelatinous substance	1	0.04	0-1	(0-4.0)
Cervix contained green, viscous fluid	1	0.04	0-1	(0-4.0)
Vagina contained brown, viscous fluid	1	0.04	0-1	(0-2.1)
UTERUS				
Contained red-brown fluid and one dead, brown fetus	1	0.04	0-1	(0-4.0)
Right horn, absent	2	0.08	0-1	(0-16.7)
Right horn, threadlike	1	0.04	0-1	(0-2.1)
Left horn, lumen absent on cervical end; ovarian end, distended with clear fluid	1	0.04	0-1	(0-4.0)
Right horn, clear masses, contained gelatinous substance	1	0.04	0-1	(0-4.0)
FORELIMB				
Lesion present	1	0.04	0-1	(0-3.3)

10 171435

SUMMARY OF FETAL EXTERNAL ALTERATIONS
CD RAT

PERIOD JUNE 1995 - JUNE 1997

# STUDIES INCLUDED	86
# LITTERS EXAMINED	1745
# LIVE FETUSES EXAMINED	25613

ALTERATION			N	%	RANGE /STUDY N	%
HEAD						
	Exencephaly	L	5	0.29	0-1	(0-4.5)
		F	5	0.02	0-1	(0-0.4)
	Hematoma	L	1	0.06	0-1	(0-2.2)
		F	1	0.00	0-1	(0-0.2)
	Microcephaly	L	1	0.06	0-1	(0-4.0)
		F	1	0.00	0-1	(0-0.3)
EYES						
	Eye bulges	L	14	0.80	0-2	(0-12.5)
	depressed	F	15	0.06	0-2	(0-0.9)
	Lids open	L	1	0.06	0-1	(0-4.2)
		F	1	0.00	0-1	(0-0.3)
	Microphthalmia	L	1	0.06	0-1	(0-4.0)
		F	1	0.00	0-1	(0-0.3)
EARS						
	Low set	L	3	0.17	0-1	(0-12.5)
		F	3	0.01	0-1	(0-0.9)
SNOUT						
	Short	L	2	0.11	0-1	(0-4.2)
		F	2	0.01	0-1	(0-0.3)
TONGUE						
	Absent	L	1	0.06	0-1	(0-4.0)
		F	1	0.00	0-1	(0-0.3)
PALATE						
	Cleft	L	4	0.23	0-1	(0-4.5)
		F	4	0.02	0-1	(0-0.4)

L: LITTER INCIDENCE
F: FETAL INCIDENCE

10 171436

SUMMARY OF FETAL EXTERNAL ALTERATIONS
CD RAT

ALTERATION			N	%	RANGE /STUDY N	%
JAWS						
	Micrognathia	L	5	0.29	0-1	(0-4.5)
		F	5	0.02	0-1	(0-0.3)
	Agnathia	L	1	0.06	0-1	(0-12.5)
		F	1	0.00	0-1	(0-0.9)
BODY						
	Edema	L	2	0.11	0-1	(0-4.5)
		F	2	0.01	0-1	(0-0.4)
	Umbilical hernia	L	7	0.40	0-1	(0-16.7)
		F	7	0.03	0-1	(0-1.1)
	Gastroschisis	L	1	0.06	0-1	(0-4.0)
		F	1	0.00	0-1	(0-0.2)
	Trunk short	L	3	0.17	0-2	(0-9.1)
		F	3	0.01	0-2	(0-0.7)
	Spina bifida	L	1	0.06	0-1	(0-4.0)
		F	1	0.00	0-1	(0-0.2)
	Extra limb pro-	L	1	0.06	0-1	(0-4.5)
	truding from back	F	1	0.00	0-1	(0-0.4)
	Hematoma	L	1	0.06	0-1	(0-2.4)
		F	1	0.00	0-1	(0-0.2)
PLACENTA						
	Enlarged	L	1	0.06	0-1	(0-16.7)
		F	1	0.00	0-1	(0-1.1)
FORELIMBS						
	Two digits present	L	1	0.06	0-1	(0-4.3)
	on forepaw	F	1	0.00	0-1	(0-0.3)
HINDLIMBS						
	Rotated	L	1	0.06	0-1	(0-4.0)
		F	1	0.00	0-1	(0-0.2)
ANUS						
	No opening present	L	2	0.11	0-1	(0-4.5)
		F	2	0.01	0-1	(0-0.4)

L: LITTER INCIDENCE
F: FETAL INCIDENCE

10 171437

SUMMARY OF FETAL EXTERNAL ALTERATIONS
CD RAT

ALTERATION			N	%	RANGE /STUDY N	%
TAIL						
	Threadlike	L	5	0.29	0-1	(0-5.3)
		F	5	0.02	0-1	(0-0.4)
	Agenesis	L	3	0.17	0-1	(0-4.5)
		F	3	0.01	0-1	(0-0.3)
	Split	L	1	0.06	0-1	(0-4.5)
		F	1	0.00	0-1	(0-0.4)
	Short	L	2	0.11	0-1	(0-4.3)
		F	2	0.01	0-1	(0-0.3)
	Constricted	L	1	0.06	0-1	(0-2.4)
		F	1	0.00	0-1	(0-0.2)

L: LITTER INCIDENCE
F: FETAL INCIDENCE

10 171438

SUMMARY OF FETAL SOFT TISSUE ALTERATIONS
CD RAT

PERIOD	JUNE 1995 - JUNE 1997
# STUDIES INCLUDED	36
# LITTERS EXAMINED	845
# FETUSES EXAMINED	6091

	ALTERATION		N	%	RANGE/STUDY N	RANGE/STUDY %
BRAIN						
	Lateral ventricles, moderate dilation	L	1	0.12	0-1	(0-3.4)
		F	1	0.02	0-1	(0-0.6)
	Lateral ventricles, marked dilation	L	1	0.12	0-1	(0-4.2)
		F	1	0.02	0-1	(0-0.6)
	Third ventricle, marked dilation	L	1	0.12	0-1	(0-4.2)
		F	1	0.02	0-1	(0-0.6)
	Lateral and third ventricles, irregularly shaped	L	1	0.12	0-1	(0-4.2)
		F	1	0.02	0-1	(0-0.6)
EYES						
	Microphthalmia	L	3	0.36	0-1	(0-4.0)
		F	3	0.05	0-1	(0-0.6)
PALATE						
	Cleft	L	2	0.24	0-1	(0-4.0)
		F	2	0.03	0-1	(0-0.6)
TONGUE						
	Small	L	1	0.12	0-1	(0-4.3)
		F	1	0.02	0-1	(0-0.6)
	Absent	L	1	0.12	0-1	(0-4.0)
		F	1	0.02	0-1	(0-0.6)
JAW						
	Micrognathia	L	1	0.12	0-1	(0-4.0)
		F	1	0.02	0-1	(0-0.6)
HEART						
	Septal defect	L	1	0.12	0-1	(0-4.0)
		F	1	0.02	0-1	(0-0.6)

L: LITTER INCIDENCE
F: FETAL INCIDENCE

10 171439

SUMMARY OF FETAL SOFT TISSUE ALTERATIONS
CD RAT

ALTERATION		N	%	RANGE/STUDY N	%
VESSELS					
Innominate, absent	L	8	0.95	0-2	(0-8.0)
	F	8	0.13	0-2	(0-1.2)
Innominate, arises on left	L	1	0.12	0-1	(0-4.0)
	F	1	0.02	0-1	(0-0.6)
Subclavian artery, absent	L	1	0.12	0-1	(0-3.4)
	F	1	0.02	0-1	(0-0.6)
Ductus arteriosus, absent	L	1	0.12	0-1	(0-3.4)
	F	1	0.02	0-1	(0-0.6)
Umbilical artery, displaced	L	10	1.18	0-2	(0-8.3)
	F	11	0.18	0-2	(0-1.2)
Situs inversus	L	1	0.12	0-1	(0-4.2)
	F	1	0.02	0-1	(0-0.6)
Aorta, descends to right	L	1	0.12	0-1	(0-4.0)
	F	1	0.02	0-1	(0-0.6)
Pulmonary artery, descends to right behind aorta	L	1	0.12	0-1	(0-4.0)
	F	1	0.02	0-1	(0-0.6)
LUNGS					
Right apical, cardiac and diaphragmatic lobes appear as one	L	1	0.12	0-1	(0-4.0)
	F	1	0.02	0-1	(0-0.6)
Intermediate lobe, absent	L	1	0.12	0-1	(0-4.0)
	F	1	0.02	0-1	(0-0.6)
BODY					
Edema	L	1	0.12	0-1	(0-4.0)
	F	1	0.02	0-1	(0-0.6)
ABDOMINAL CAVITY					
Situs inversus of liver, intestines, stomach, spleen, pancreas and kidneys	L	1	0.12	0-1	(0-4.0)
	F	1	0.02	0-1	(0-0.6)
KIDNEYS					
Pelvis, slight dilation	L	1	0.12	0-1	(0-3.7)
	F	1	0.02	0-1	(0-0.6)

L: LITTER INCIDENCE
F: FETAL INCIDENCE

10 171440

SUMMARY OF FETAL SOFT TISSUE ALTERATIONS
CD RAT

ALTERATION		N	%	RANGE/STUDY N	%
SPLEEN					
Absent	L	1	0.12	0-1	(0-4.0)
	F	1	0.02	0-1	(0-0.5)
URETERS					
Distended	L	2	0.24	0-2	(0-8.7)
	F	3	0.05	0-3	(0-1.7)

L: LITTER INCIDENCE
F: FETAL INCIDENCE

10 171441

SUMMARY OF FETAL SKELETAL ALTERATIONS
CD RAT

PERIOD	JUNE 1995 - JUNE 1997
# STUDIES INCLUDED	35
# LITTERS EXAMINED	820
# FETUSES EXAMINED	6318

ALTERATION		N	%	RANGE/STUDY N	RANGE/STUDY %
SKULL					
Frontal(s): incompletely or not ossified	L	2	0.24	0-1	(0-4.2)
	F	2	0.03	0-1	(0-0.6)
Parietal(s): not ossified	L	2	0.24	0-1	(0-4.2)
	F	2	0.03	0-1	(0-0.6)
Nasal(s): short	L	3	0.36	0-1	(0-4.2)
	F	3	0.05	0-1	(0-0.6)
Basisphenoid: incompletely ossified	L	1	0.12	0-1	(0-4.0)
	F	1	0.02	0-1	(0-0.5)
Sphenoid: irregularly shaped	L	1	0.12	0-1	(0-4.0)
	F	1	0.02	0-1	(0-0.5)
~~Orbit: small~~	~~L~~	~~2~~	~~0.24~~	~~0-1~~	~~(0-4.0)~~
	F	2	0.03	0-1	(0-0.6)
Maxillae and Premaxillae: short	L	3	0.36	0-1	(0-4.2)
	F	3	0.05	0-1	(0-0.6)
Skull: incompletely or not ossified	L	2	0.24	0-1	(0-4.2)
	F	3	0.05	0-2	(0-1.2)
Skull: fused	L	1	0.12	0-1	(0-4.0)
	F	1	0.02	0-1	(0-0.5)
VERTEBRAE					
Cervical: Arch, open	L	1	0.12	0-1	(0-4.0)
	F	1	0.02	0-1	(0-0.5)
: Fused	L	1	0.12	0-1	(0-4.0)
	F	1	0.02	0-1	(0-0.5)
Thoracic: Centrum, bifid	L	71	8.66	0-8	(0-29.6)
	F	77	1.22	0-9	(0-4.7)
: Centra, unilateral ossification	L	8	0.98	0-2	(0-8.0)
	F	8	0.13	0-2	(0-1.0)
: Centrum, incompletely or not ossified	L	3	0.36	0-2	(0-8.3)
	F	4	0.06	0-3	(0-1.8)

L: LITTER INCIDENCE
F: FETAL INCIDENCE

10 171442

SUMMARY OF FETAL SKELETAL ALTERATIONS
CD RAT

ALTERATION		N	%	RANGE/STUDY N	RANGE/STUDY %
VERTEBRAE (CONT.)					
Thoracic (cont.)					
: Centra, fused	L	1	0.12	0-1	(0-4.2)
	F	1	0.02	0-1	(0-0.5)
: Arch, open	L	1	0.12	0-1	(0-4.0)
	F	1	0.02	0-1	(0-0.5)
: Arch, small	L	1	0.12	0-1	(0-3.4)
	F	1	0.02	0-1	(0-0.5)
Lumbar: Centrum, bifid	L	2	0.24	0-1	(0-3.8)
	F	2	0.03	0-1	(0-0.5)
: Centra, fused	L	1	0.12	0-1	(0-4.3)
	F	1	0.02	0-1	(0-0.6)
: Centrum, incompletely or not ossified	L	2	0.24	0-2	(0-8.3)
	F	3	0.05	0-3	(0-1.8)
: Arches, incompletely or not ossified	L	15	1.83	0-3	(0-12.0)
	F	21	0.33	0-4	(0-2.1)
: 1, present	L	1	0.12	0-1	(0-4.3)
	F	1	0.02	0-1	(0-0.6)
: Arch, open	L	1	0.12	0-1	(0-4.0)
	F	1	0.02	0-1	(0-0.5)
: Centra, unilateral ossification	L	2	0.24	0-1	(0-4.2)
	F	2	0.03	0-1	(0-0.6)
Sacral: None, present	L	1	0.12	0-1	(0-4.3)
	F	1	0.02	0-1	(0-0.6)
: Arch, open	L	1	0.12	0-1	(0-4.0)
	F	1	0.02	0-1	(0-0.5)
Caudal: None present	L	1	0.12	0-1	(0-4.3)
	F	1	0.02	0-1	(0-0.6)
: 1, present	L	1	0.12	0-1	(0-4.3)
	F	1	0.02	0-1	(0-0.6)
RIBS					
Cervical Rib(s) present	L	31	3.78	0-5	(0-20.0)
	F	32	0.51	0-5	(0-2.7)
One or more, wavy	L	44	5.36	0-7	(0-31.8)
	F	73	1.16	0-15	(0-8.3)
One or more, incompletely ossified (hypoplastic), or not ossified	L	33	4.02	0-5	(0-22.7)
	F	53	0.84	0-9	(0-5.0)

L: LITTER INCIDENCE
F: FETAL INCIDENCE

10 171443

SUMMARY OF FETAL SKELETAL ALTERATIONS
CD RAT

ALTERATION		N	%	RANGE/STUDY N	RANGE/STUDY %
RIBS (CONT.)					
Fused	L	3	0.36	0-1	(0-4.3)
	F	3	0.05	0-1	(0-0.6)
Split	L	2	0.24	0-1	(0-4.0)
	F	2	0.03	0-1	(0-0.5)
Two segments	L	1	0.12	0-1	(0-3.7)
	F	1	0.02	0-1	(0-0.5)
MANUBRIUM					
Duplicated	L	1	0.12	0-1	(0-3.8)
	F	1	0.02	0-1	(0-0.4)
STERNEBRAE					
One or more incompletely ossified or not ossified	L	114	13.90	0-7	(0-33.3)
	F	164	2.60	0-11	(0-6.2)
Duplicated	L	1	0.12	0-1	(0-3.8)
	F	1	0.02	0-1	(0-0.4)
Fused	L	1	0.12	0-1	(0-3.7)
	F	1	0.02	0-1	(0-0.5)
Asymmetric	L	1	0.12	0-1	(0-4.2)
	F	1	0.02	0-1	(0-0.5)
PELVIS					
Pubis(es) and/or Ischium(a): incompletely or not ossified	L	139	16.95	0-9	(0-39.1)
	F	224	3.54	0-16	(0-9.0)
Pubis(es): incompletely ossified	L	114	13.90	0-9	(0-39.1)
	F	185	2.93	0-16	(0-8.9)
Pubis(es): not ossified	L	8	0.98	0-3	(0-13.6)
	F	8	0.13	0-3	(0-1.6)
Ischium(a): incompletely or not ossified	L	50	6.10	0-4	(0-16.7)
	F	70	1.11	0-9	(0-4.7)
FORELIMBS					
Metacarpals: 1, present	L	1	0.12	0-1	(0-4.3)
	F	1	0.02	0-1	(0-0.6)
: 2, present	L	1	0.12	0-1	(0-4.3)
	F	1	0.02	0-1	(0-0.6)
Foredigits: 2, present	L	1	0.12	0-1	(0-4.3)
	F	1	0.02	0-1	(0-0.6)
Forephalanges: 1, present	L	1	0.12	0-1	(0-4.3)
	F	1	0.02	0-1	(0-0.6)

L: LITTER INCIDENCE
F: FETAL INCIDENCE

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SUMMARY OF FETAL OSSIFICATION SITES
SKELETAL AVERAGES
CD RAT
(CAESAREAN-SECTIONED DAY 20 GESTATION)

PERIOD:	JUNE 1995 - JUNE 1997
# STUDIES INCLUDED	33
# LITTERS EXAMINED	772
# FETUSES EXAMINED	5944

	FETUS/LITTER	
SKELETAL AVERAGES	MEAN	RANGE/STUDY
HYOID	0.84	(0.69-0.95)
VERTEBRAE		
CERVICAL	7.00	--
THORACIC	13.03	(12.99-13.15)
LUMBAR	5.97	(5.85-6.00)
SACRAL	3.00	(2.96-3.00)
CAUDAL	4.83	(4.35-5.21)
RIBS (pairs)	13.02	(12.99-13.08)
STERNUM		
MANUBRIUM	1.00	(0.98-1.00)
STERNAL CENTERS	3.57	(3.26-3.85)
XIPHOID	0.99	(0.94-1.00)
FOREPAWS (Calculated as average per limb)		
CARPALS	0.00	--
METACARPALS	3.49	(3.33-3.62)
DIGITS	5.00	--
PHALANGES	5.05	(4.90-5.27)
HINDPAWS (Calculated as average per limb)		
TARSALS	0.00	--
METATARSALS	3.99	(3.93-4.04)
DIGITS	5.00	--
PHALANGES	4.96	(4.77-5.13)

10 171445

SUMMARY OF FETAL OSSIFICATION SITES
SKELETAL AVERAGES
CD RAT
(CAESAREAN-SECTIONED DAY 21 GESTATION)

PERIOD:	JUNE 1995 - JUNE 1997
# STUDIES INCLUDED	2
# LITTERS EXAMINED	48
# FETUSES EXAMINED	374

SKELETAL AVERAGES	FETUS/LITTER MEAN	RANGE/STUDY
HYOID	0.97	(0.96-0.97)
VERTEBRAE		
CERVICAL	7.00	--
THORACIC	13.04	(13.02-13.06)
LUMBAR	5.96	(5.94-5.98)
SACRAL	3.00	--
CAUDAL	7.46	(7.23-7.67)
RIBS (pairs)	13.03	(13.01-13.05)
STERNUM		
MANUBRIUM	1.00	--
STERNAL CENTERS	3.98	(3.97-3.98)
XIPHOID	1.00	--
FOREPAWS (Calculated as average per limb)		
CARPALS	0.00	--
METACARPALS	3.98	(3.98-3.99)
DIGITS	5.00	--
PHALANGES	7.64	(7.53-7.75)
HINDPAWS (Calculated as average per limb)		
TARSALS	0.02	--
METATARSALS	4.61	(4.60-4.62)
DIGITS	5.00	--
PHALANGES	5.84	(5.78-5.89)

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APPENDIX H

STATEMENT OF THE STUDY DIRECTOR

PRIMEDICA

Argus Research Laboratories, Inc.
905 Sheehy Drive, Building A
Horsham, PA 19044
Telephone: (215) 443-8710
Telefax: (215) 443-8587

PROTOCOL 418-011: ORAL (GAVAGE) DEVELOPMENTAL TOXICITY STUDY OF N-EtFOSE IN RATS
SPONSOR'S STUDY NUMBER: T-6316.7

STATEMENT OF THE STUDY DIRECTOR

This final report accurately reflects the raw data obtained during the performance of the study. No significant deviations from the U.S. Food and Drug Administration (FDA) Good Laboratory Practice Regulations; Final Rule[a], the Japanese Ministry of Health and Welfare (MHW) *Good Laboratory Practice Standard for Safety Studies on Drugs*[b] and the European Economic Community (EEC) *Council decision on 28 July 1989 on the acceptance by the European Economic Community of an OECD decision/recommendation on compliance with principles of good laboratory practice*[c] occurred that affected the quality or integrity of the study.

17-Dec-98

Raymond G. York, Ph.D., DABT Date
Associate Director of Research
and Study Director

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a. U.S. Food and Drug Administration. Good Laboratory Practice Regulations; Final Rule. 21 CFR Part 58.

b. Japanese Ministry of Health and Welfare (1988). *Good Laboratory Practice Standard for Safety Studies on Drugs*, MHW Ordinance Number 21, March 26, 1997.

c. European Economic Community (1989). *Council decision on 28 July 1989 on the acceptance by the European Economic Community of an OECD decision/recommendation on compliance with principles of good laboratory practice*. Official Journal of the European Communities: Legislation. 32(No. L 315; 28 October): 1-17.

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APPENDIX I

QUALITY ASSURANCE UNIT FINAL REPORT STATEMENT

10 171449

PRIMEDICA

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905 Sheehy Drive, Building A
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QUALITY ASSURANCE UNIT FINAL REPORT STATEMENT

Study Director: Raymond G. York, Ph.D., DABT

Executive Director of Research: Mildred S. Christian, Ph.D., Fellow, ATS

Protocol 418-011: Oral (Gavage) Developmental Toxicity Study of N-EtFOSE in Rats
Sponsor's Study Number: T-6316.7

The draft protocol for this study was audited for adherence to U.S. Food and Drug Administration (FDA) Good Laboratory Practice Regulations, Japanese Ministry of Health and Welfare (MHW); Good Laboratory Practice Standard for Safety Studies on Drugs, and European Economic Community (1989) council decision on 28 July 1989 on the acceptance by the European Economic Community of an OECD decision/recommendation on compliance with principles of good laboratory practice on 13 JUL 98.

Critical phases of this study were inspected five times; study information and raw data were audited twice (see tables 1 and 2 for dates and phases/data).

The draft final report and the raw data for this study [except for Appendix F, the Pilot Report, which was conducted in the spirit of Good Laboratory Practice (GLP)] were compared and audited for accuracy, for adherence to protocol requirements, and for adherence to U.S. Food and Drug Administration (FDA) Good Laboratory Practice Regulations, Japanese Ministry of Health and Welfare (MHW); Good Laboratory Practice Standard for Safety Studies on Drugs, and European Economic Community (1989) council decision on 28 July 1989 on the acceptance by the European Economic Community of an OECD decision/recommendation on compliance with principles of good laboratory practice between 12 NOV 98 and 02 DEC 98, and for revisions requested by the Sponsor on 10 DEC 98 and 17 DEC 98.

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This study was conducted according to U.S. Food and Drug Administration (FDA) Good Laboratory Practice Regulations, Japanese Ministry of Health and Welfare (MHW); Good Laboratory Practice Standard for Safety Studies on Drugs, and European Economic Community (1989) council decision on 28 July 1989 on the acceptance by the European Economic Community of an OECD decision/recommendation on compliance with principles of good laboratory practice.

Barbara J. Patterson 17Dec98 Heather L. Rabuttino 17Dec98

Barbara J. Patterson, B.A. Date
Director of Operations
and Compliance

Heather L. Rabuttino, M.S. Date
Quality Assurance Supervisor
and Principal Auditor

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TABLE 1

CRITICAL PHASES INSPECTED

Cohabitation

Date of inspection: 21 AUG 98

Date results reported to the Study Director and Management: 21 AUG 98

Test Article Preparation

Date of inspection: 02 SEP 98

Date results reported to the Study Director and Management: 28 SEP 98

Test Article Administration - Gavage

Date of inspection: 03 SEP 98

Date results reported to the Study Director and Management: 28 SEP 98

Blood Collection

Date of inspection: 10 SEP 98

Date results reported to the Study Director and Management: 10 SEP 98

Caesarean-Sectioning

Date of inspection: 10 SEP 98

Date results reported to the Study Director and Management: 28 SEP 98

TABLE 2

RAW DATA AUDIT(S)

The following study information and raw data were audited on 08 OCT 98, and 15 OCT 98 to 17 OCT 98:

Protocol.
Protocol amendments.
List of personnel and computer operator codes.
Error codes and codes for clinical sign observations.
Animal receipt, randomization, physical examination and acclimation.
In-life transaction record.
Feed consumption.
Cohabitation.
Caesarean-sectioning.
Maternal gross observations.
Fetal gross observations.
Fetal fixative assignment.
Fetal visceral examination.
Fetal skeletal examination.
Necropsy.
Tissue packing lists.
Male breeder colony records.
General comments.
Study maintenance records.
Temperature and relative humidity reports.
Feed and water analyses.
Edit requests.
Dosage volumes.
Deviations.
Data review page.
Key for test facility computer back-up record abbreviations.
Blood collection data and packing lists.

The results of this audit were reported to the Study Director and Management on 21 OCT 98.

The following study information and raw data were audited on 08 OCT 98 and 10 OCT 98:

Vehicle receipt, preparation and use.
Test article receipt, preparation and use.
Test article packing lists.

The results of this audit were reported to the Study Director and Management on 21 OCT 98.