Honeywell

Honeywell
P.O. Box 1039
Morristown, NJ 07962-1039

FYI-05-01492

June 29, 2005

TSCA Confidential Business Information Center (7407M)
EPA East - Room 6428 Attn: FYI
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460-0001

FYI-0705-01492

CONTAIN NO CBI

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OPPT CBIC
05 JUL -6 AM 6:06

Re.: Chlorotrifluoroethylene (CAS # 79-38-9)

Dear Sir or Madam:

On March 15, 2005, Honeywell reported preliminary findings from a developmental toxicity study conducted with chlorotrifluoroethylene (CTFE). A copy of the final report and a robust summary of the study are attached. Briefly, the design called for daily 6-hour exposures from day 6 through day 19 of gestation. The exposure levels selected were 0 (air control), 30, 90 and 180 ppm.

Exposure at 30 ppm was the no-observed-effect-level ((NOEL) for maternal toxicity and exposure at 90 ppm was the NOEL for developmental toxicity. Exposure at 180 ppm resulted in significant body weight loss in the dams. As a consequence, exposure to this group was terminated prior to the final scheduled exposure. However the rats were evaluated at the end of the gestation period along with the rats from the other groups.

There was no evidence for developmental abnormalities at any level. In summary, decreased body weight gain and food consumption was reported for the dams exposed to 90 and 180 ppm of CTFE. Decreased fetal weight and delayed ossification was seen in pups from dams exposed to 180 ppm. The body weight loss seen in the dams exposed to 180 ppm of CTFE was greater than expected based on our previous study. It was also noted that this sample contained a higher level of dimmer than was present in the sample used for the pilot study several years ago. To determine if the dimmer was responsible for the body weight loss seen in this study, we also conducted a probe study using samples of CTFE with both high and low levels of the dimmer. Similar body weight losses were seen with all samples. It was therefore concluded that the body weight loss was not a consequence of the exposure to the dimmer. These results have been included as an appendix to the final report. Based on my review of the SIDS dossier, these findings could have been anticipated. In a study by Potter et al. (1981), a 4-hour exposure to 100 ppm of CTFE resulted in diuresis, while a single 4-hour exposure at 220 ppm resulted in reversible renal toxicity.

8 5 0 5 0 0 0 0 0 0 2

2005 JUL 20 AM 8:53
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Sincerely,

Sheri L. Blystone, Ph.D.
Global Product Regulatory Leader

George M. Rusch, Ph.D., D.A.B.T., F.A.T.S.
Director Toxicology & Risk Assessment

Cc: Amy Benson – US EPA HPV Program

287468

Robust Summary
5.9 Developmental Toxicity/Teratogenicity

Species:	rat
Strain:	Sprague Dawley
Route of Admin,:	Inhalation
Exposure period:	days 6-19 of gestation
Freq. of Treatment:	6 hours/day
Doses:	exposure levels were 30, 90 and 180 ppm
Control group:	yes, concurrent air exposed
NOEL maternal:	30 ppm (31 ppm measured)
NOEL develop.:	90 ppm (89 ppm measured)
NOEL teratogen:	180 ppm (187 ppm measured)
Method:	OECD 414
Year:	2005 GLP: yes
Test Substance:	As prescribed by 1.1 – 1.4

Result: Groups of 25 time-mated female rats were exposed once daily for 6 hours/day, 7 days/week during gestation days 6-19 and euthanized and necropsied on gestation day 20. With the exception that the exposures to the high level exposure group were terminated during the 7th day of exposure. These animals received from 4 to 7 exposures. Exposure levels were monitored using an on-line IR sampling procedure. Exposure at 180 ppm resulted in significant body weight loss in the dams. As a consequence, exposure to this group was terminated prior to the final scheduled exposure. However the rats were evaluated at the end of the gestation period along with the rats from the other groups. There was no evidence for developmental abnormalities at any level. Decreased body weight gain and food consumption was reported for the dams exposed to 90 and 180 ppm of CTFE. Decreased fetal weight and delayed ossification was seen in pups from dams exposed to 180 ppm.

Reliability: (1) valid without restriction

Reference: Hoffman, Gary. Chlorotrifluoroethylene (CTFE) Embryo-Fetal Toxicity Study in Rats by Inhalation Exposure, Huntingdon Life Science Study No. 04-4261 23 June 2005

Additional reference Potter, C.L., Gandolfi, A.J., Nagle, R., and Clayton, J.W. Effects of inhaled Chlorotrifluoroethylene and Hexafluoropropylene on the rat kidney. Toxicol. And Applied Pharmacol. 59, 431-440, (1981). Ref. (33) in the SIDS dossier

Huntingdon

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Data Requirement

EPA OPPTS 870.3700
OECD 414

STUDY NO. 04-4261
HONEYWELL PROJECT NO. MA-198-81-4

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY IN RATS BY INHALATION EXPOSURE

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Final Report

Author: Gary M. Hoffman, B.A., D.A.B.T.

Performed by: Huntingdon Life Sciences
100 Mettlers Road
East Millstone, New Jersey 08875-2360

Submitted to: Honeywell
Engineered Materials Sector
101 Columbia Road, PO Box 2245R
Morristown, NJ 07962-1057

Attn: George M. Rusch, Ph.D., D.A.B.T.

Date: 23 June 2005

287468

STATEMENT OF COMPLIANCE

This study was conducted in compliance with the United States Environmental Protection Agency's Good Laboratory Practices as set forth in 40 CFR Part 792 (TSCA) and the Organization for Economic Cooperation and Development (OECD) Good Laboratory Practices as set forth in ENV/MC/CHEM/(98)17, with the following exceptions:

1. Gestation Day (GD) 0 body weights recorded by the animal supplier were non-GLP.

2. The Test Substance post-study analysis by the Sponsor was not performed under GLP conditions.

Gary M. Hoffman, B.A., D.A.B.T.
Study Director

23 Feb 05
Date

SIGNATURE PAGE

SCIENTIST

The following Scientist was responsible for the overall conduct of this study. Departmental supervisory personnel are listed on the personnel page of this report (Appendix S).

23 Jan 05

Gary M. Hoffman, B.A., D.A.B.T.
Study Director

Date

SCIENTIFIC REVIEW

The following Scientist has reviewed and approved this report:

23 Jan 05

Keith P. Hazelden, B.Sc., C. Biol., M.I.Biol.
Director, Reproductive and Developmental Toxicology

Date

QUALITY ASSURANCE STATEMENT

Listed below are the dates that this study was inspected by the Quality Assurance Unit of Huntingdon Life Sciences, East Millstone, New Jersey, and the dates that findings were reported to the Study Director and Management. This report reflects the raw data as far as can be reasonably established.

Type of Inspection	Date(s) of Inspection	Reported to Study Director and Management
GLP Protocol Review	29 Jun 04	29 Jun 04
Exposure, Monitoring and Equipment Records	24 Aug 04	24 Aug 04
Gestation Body Weight and Feeder Weight Data Collection and Protocol Amendment Number 1	1 Sep 04	1 Sep 04
Maternal Sacrifice, Fetal Evaluation and Training Records	7 Sep 04	7 Sep 04
Draft In-Life & Inhalation Report and Protocol Amendments 2 & 3	14 – 22 Dec 04	22 Dec 04
Exposure and Monitoring (Post-Study Range-Find Study)	8 Feb 05	10 Feb 05
Report Tables, Appendices and Data for Pathology Evaluations and Protocol Amendments 4 & 5	8 – 18 Feb 05	18 Feb 05
Draft In-Life & Inhalation Report for the Post-Study Range-Find Study and Study Data	1 – 6 Apr 05	6 Apr 05

JOAN MUHORO

Joan Muhoro, B.V.M, ALAT
Quality Assurance Auditor

21 JUN 05
Date

SUMMARY

This study was designed to assess the potential maternal and/or developmental toxicity of Chlorotrifluoroethylene (CTFE) in the pregnant rat when administered by whole-body inhalation exposure.

Time-mated female Sprague Dawley CD® rats (25/group) were exposed once daily for 6 hours/day for 7 consecutive days per week to 0 ppm (Air only), 30 ppm or 90 ppm of CTFE during Gestation Days (GD) 6 through 19 until euthanized and necropsied on Gestation Day 20. Group 4 (180 ppm) animals were exposed once daily for 6 hours/day, but the exposures were terminated during the 7th day of exposures because of the treatment effects discussed below. Since the start of the exposures was staggered over 4 days, 6 of these dams were exposed for 7 days, 7 of these dams were exposed for 6 days, 6 of these dams were exposed for 5 days and 6 of these dams were exposed for 4 days.

The following parameters were evaluated: viability, clinical observations, body weights and feed consumption. Exposure levels were determined using an IR sampling procedure 4 times per chamber per day. Particle size distribution measurements were also made once per chamber per week. At caesarean section, the animals were subjected to a macroscopic postmortem evaluation and corpora lutea/implantation data were recorded. The fetuses were examined for externally visible abnormalities, weighed and then examined for soft-tissue abnormalities using a microdissection procedure. Their skeletons were then stained with Alizarin Red S and examined for skeletal abnormalities and ossification state.

The mean (± standard deviation) analytical (IR) concentrations for the control and the respective exposure groups were as follows: 0±0, 31.1±2.3, 89.2±8.1 and 187±21 ppm.

There was no effect of treatment on survival. During the exposure periods, all animals were unremarkable except the 180 ppm exposed dams showed some eye closure, piloerection and lethargy during exposure day 7 prior to this exposure level's early termination. The 90 ppm exposed animals showed a marked increase in red nasal discharge after removal from the exposure chambers, especially during the period of gestation days 13-20. There were statistically significant effects on body weights during gestation days 6-10 (corresponding with the initial 1-4 exposures) for the 90 ppm group (15% less weight gain than control) and 180 ppm group (7% weight loss compared to control).

SUMMARY

significantly reduced (13%) fetal body weight in the 180 ppm exposed animals, compared to the Air Control animals. There was also slight reduction in the state of ossification of the fetal skeleton at the 180 ppm exposure level, but for the sporadic incidences of other fetal variants and abnormalities there was no indication of association with test substance exposure.

Since unexpected test substance related effects were seen during the study, the Sponsor requested that a post-study GC analysis of the test substance be conducted to evaluate for undesired dimer formation. Samples of the test substance from the Sponsor's cylinder and from chamber atmospheres (non-animal exposures) were collected into evacuated gas cylinders and shipped to the Sponsor's laboratory. Assays of these samples showed the presence of ~0.1% dimer formation (cis and trans 1,2-dichlororhexafluorocyclobutane). The potential toxicity of this concentration was not known and was evaluated in a follow-up in-vivo evaluation that indicated that CTFE, and not the presence of dimers, was the cause of the adverse responses.

In conclusion, exposure of time-mated female rats to target concentrations of 30, 90 or 180 ppm of CTFE by whole-body inhalation for gestation days 6-19 (days 6-12 for the 180 ppm group) resulted in no effects of exposure at 30 ppm, but decreased body weight gain and feed consumption at 90 and 180 ppm. Decreased fetal body weight, with slightly reduced state of skeletal ossification, was observed at 180 ppm. Therefore, a no observed effect level (NOAEL) for maternal toxicity of 30 ppm was determined while a NOAEL for developmental toxicity of 90 ppm was indicated.

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1. INTRODUCTION

This study was designed to assess the potential maternal and/or developmental toxicity of Chlorotrifluoroethylene in the pregnant rat when administered by whole-body inhalation exposure. Animals were treated during the period of major embryonic organogenesis, Gestation Days (GD) 6-19 inclusive, then sacrificed on GD 20 and subjected to caesarean section.

2. MATERIALS AND METHODS

2.1. STUDY MANAGEMENT

2.1.1. SPONSOR

Honeywell
Engineered Materials Sector
101 Columbia Road, PO Box 2245R
Morristown, New Jersey 07962-1057

2.1.2. SPONSOR STUDY MONITOR

George M. Rusch, Ph.D., DABT

2.1.3. TESTING FACILITY

Huntingdon Life Sciences
P.O. Box 2360
Mettlers Road
East Millstone, New Jersey 08875-2360

2.1.4. STUDY DIRECTOR

Gary M. Hoffman, B.A., DABT

2.2. STUDY DATES

2.2.1. STUDY INITIATION

5 August 2004 (Date Study Director signed the Protocol)

2.2.2. DATES OF ANIMAL RECEIPT (OECD EXPERIMENTAL START DATE)

20 & 23 August 2004

2.2.3. INITIATION OF EXPOSURES – FIRST GESTATION DAY 6 (EPA EXPERIMENTAL START DATE)

24 August 2004

2.2.4. DOSING TERMINATION – LAST GESTATION DAY 19

9 September 2004

2.2.5. NECROPSY – FIRST GESTATION DAY 20

7-10 September 2004

2.2.6. EXPERIMENTAL TERMINATION DATE – (DATE OF LAST DATA COLLECTION)

22 February 2005 (Date of completion of fetal examinations)

2.2.7. STUDY COMPLETION

23 June 2005 (Date Final Report is signed by the Study Director)

2.3. EXPERIMENTAL DESIGN[a]

Group	Group Designation	Exposure Levels[b] (ppm)	Treatment Gestation Days	Number of Animals				
				Time-Mated Females	Euthanized Gestation Day 20	Fetal Evaluations (Fetuses/Litter)		
						External	Soft Tissue	Skeletal
1	Air Control	0	6-19	25	All	All	~1/2	~1/2
2	Low	30	6-19	25	All	All	~1/2	~1/2
3	Mid	90	6-19	25	All	All	~1/2	~1/2
4[c]	High	180	6-12	25	All	All	~1/2	~1/2

[a]A post-study experiment (non-animal) was conducted on Monday 20 Sept 04 to allow for assessment of potential undesired dimer formation in the CTFE test sample. The Sponsor provided 3 evacuated 1 liter test cylinders: Cylinder#1 was used to collect sample from the CTFE cylinder (via a gas bag); Cylinder#2 was used to collect a sample from the CTFE 90 ppm chamber (via a sample port) and Cylinder#3 was used to collect a sample from the CTFE 180 ppm chamber (via a sample port). These samples were shipped to the Sponsor's chemist for evaluation.

[b]Exposures were 6 hours per day for 7 consecutive days per week. Exposure levels were expressed as ppm of test substance. The exposures were conducted via whole-body exposure.

[c]Group 4 exposures were terminated on 30 August 2004 during the 7th day of exposures.

Study Day 0 was defined as the first day of gestation.

2.4. JUSTIFICATIONS

2.4.1. ROUTE, DURATION AND FREQUENCY OF ADMINISTRATION

The inhalation route is one of the potential routes of human exposure to this test substance. The duration and frequency of the exposures are as recommended in the relevant Test Guideline, ensuring adequate exposure of post-implantation embryo-fetal development.

2.4.2. TEST ANIMAL SELECTION

The rat was used as a surrogate for humans in the detection of embryo-fetal toxicity and is a species in which known teratogens have been detected. This rodent species is commonly used in the conduct of embryo-fetal toxicity studies, and is that recommended by the relevant Test Guideline. Historical control data are also available with this strain of rat for comparative evaluation, if necessary.

2.4.3. NUMBER OF ANIMALS

The number of animals in this study was considered the minimum necessary to allow for meaningful interpretation of the data, as required by the referenced guidelines. Some of the endpoints of principal interest (*eg* embryo-fetal death, fetal malformations, abortion) are low-frequency events and a group size of 20 litters tends to provide the necessary degree of consistency between studies. In the expectation of pregnancy rates of 85-100%, the group size of 25 mated females was considered appropriate for this study, to provide a sufficient number of litters for evaluation in each group.

2.4.4. DOSE SELECTION

A pilot 2-week inhalation study was performed with male and female (including pregnant females exposed from GD 6-19) CD rats exposed to mean levels of 0, 33, 61, 119 and 241 ppm of CTFE. Effects were limited to depression in body weight gains, elevated kidney/body weight ratios and toxic nephrosis in animals exposed to 241 ppm. Depressed body weight gains were also seen

in males and pregnant females exposed to 119 ppm. No embryotoxic, fetotoxic or developmental effects were seen in any of the pregnant rats. In a subsequent 13-week inhalation study, male and female F-344 rats were exposed to mean levels of 0, 29, 62 and 121 ppm. Effects on the kidneys were indicated by increased organ weights, alterations in clinical chemistry parameters and clinical observations, and alterations in microscopic structure. Males also showed alterations in body weights and liver weights with slight effects even at 29 ppm. After a 2 week recovery period, effects were markedly reduced.

Based on the above information, a high exposure level of 180 ppm was selected for this study to provide slight maternal toxicity, while lower levels of 90 and 30 ppm were selected to provide a range of possible effects, including a NOEL or NOAEL.

2.5. TEST SUBSTANCE

Chlorotrifluoroethylene (CTFE)
MW = 116.47; CAS #79-38-9

2.5.1. TEST SUBSTANCE CATEGORY

Industrial chemical used as a monomer for the production of chlorofluorocarbon polymers

2.5.2. SUPPLIER

Honeywell
P.O. Box 2830
Baton Rouge, LA 70821

2.5.3. LOT NUMBER

BR4141

2.5.4. PURITY

99.95% (See Appendices O and P)

2.5.5. DATE RECEIVED

03 June 2004

2.5.6. EXPIRATION DATE

30 June 2005

2.5.7. DESCRIPTION

Colorless gas

2.5.8. IDENTIFICATION OF TEST ARTICLE

Information on the synthesis, methods, identity, strength, composition, stability and method of synthesis, fabrication and/or derivation of each batch of the test substance was documented by the Sponsor before its use in the study. This documentation will be maintained by the Sponsor.

2.5.9. STORAGE

Room temperature

2.5.10. ARCHIVAL SAMPLE

A small (< 1 Liter) gas cylinder was filled as an archival sample of this lot of test substance and stored in the Archives of the Testing Facility.

2.5.11. DISPOSITION

The unused portion of the test substance, as well as any empty test substance containers, was returned to the Sponsor following completion of the in-life phase of the final study with this test substance.

2.6. TEST ANIMALS

2.6.1. SPECIES

Albino Rats (Outbred), Sprague Dawley - derived
[Crl: CD® IGS BR, VAF/Plus®]

2.6.2. SUPPLIER

Charles River Laboratories
Kingston , NY 12484

2.6.3. NUMBER OF ANIMALS

Ordered: 104 time-mated rats.

Placed on study: 100 time-mated rats.

2.6.4. AGE AT RECEIPT

Time-mated female rats received on GD 0, 1 or 2 were between 75-90 days in age.

2.6.5. WEIGHT AT INITIATION OF EXPOSURES

Females weighed between 231-300 grams on Gestation Day 6.

2.6.6. ACCLIMATION PERIOD

Animals were acclimated for a minimum of 4 days from time of receipt until initiation of exposures on Gestation Day 6.

2.7. ANIMAL ASSIGNMENT

Animals were placed into study groups after receipt using a computerized randomization program. This ranked GD 4 body weights into blocks and randomly assigned each animal within each block into one of the study groups. Disposition records of all animals not utilized in the study are maintained in the study file.

2.8. ANIMAL IDENTIFICATION

Each animal was assigned a temporary identification number upon receipt. After selection for study, each animal was ear-tagged with a number assigned by the Testing Facility. This number plus the study number comprised a unique identification for each animal. Each study animal's cage was also allocated a cage card, which was color-coded for exposure level identification and contained the study number and animal number.

2.9. VETERINARY CARE

Animals were monitored by the technical staff for any conditions requiring possible veterinary care and treated as necessary. Miscellaneous, non-test article-related veterinarian evaluations and treatments (as necessary) for individual animals were reviewed by the Study Director and are

documented in the study file. Animals were treated as outlined in the Animal Welfare Act Compliance section of this protocol.

2.10. ANIMAL HUSBANDRY DURING NON-EXPOSURE PERIODS

2.10.1. FACILITIES MANAGEMENT/ANIMAL HUSBANDRY

Currently acceptable practices of good animal husbandry were followed e.g., *Guide for the Care and Use of Laboratory Animals*; National Academy Press, 1996. Huntingdon Life Sciences, East Millstone, New Jersey is fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC).

2.10.2. HOUSING

Animals were housed individually in suspended stainless steel wire mesh cages.

2.10.3. FEED

Certified Rodent Diet, No. 5002; (Meal) (PMI Feeds, Inc., St. Louis, MO) *ad libitum.*

2.10.4. FEED ANALYSIS

Analytical certifications of feed batches were performed by the manufacturer. The results are maintained on file by the manufacturer. There were no known contaminants in the feed which were expected to interfere with the objectives of this study.

2.10.5. WATER

Facility water was supplied by Elizabethtown Water Company, (Westfield, NJ) and provided *ad libitum* to individual animal cages through an automated watering system.

2.10.6. WATER ANALYSIS

Water analyses are conducted monthly by the Elizabethtown Water Company, Westfield, New Jersey (Raritan-Millstone Plant) to ensure that water meets standards specified under the EPA Federal Safe Drinking Water Act Regulations (40 CFR part 141). Water

analyses, provided by the supplier, will be maintained on file at the Testing Facility. In addition, water samples are collected biannually from representative rooms in the Testing Facility. Chemical and microbiological water analyses are conducted on these samples by a subcontract laboratory (Benchmark Analytics, Center Valley, PA). Results are maintained on file at the Testing Facility. There are no known contaminants in the water that were expected to interfere with this study.

2.10.7. ENVIRONMENTAL CONDITIONS

Light/Dark Cycle

A twelve-hour light/dark cycle controlled via an automatic timer was provided.

Temperature

Temperature was monitored in accordance with Testing Facility SOPs and maintained within the specified range to the maximum extent possible.

Desired Range:	18 to 26°C
Actual Range:	20.3 to 22.8°C
Daily Average Range:	21.2 to 21.9°C

Relative Humidity

Relative humidity was monitored in accordance with Testing Facility SOPs and maintained within the specified range to the maximum extent possible. Excursions outside the specified range were not considered to have affected the integrity of the study.

Desired Range:	30 to 70%
Actual Range:	48.80 to 89.31%
Daily Average Range:	49.36 to 58.05%

Air Changes

Animal quarters had 10-15 air changes per hour. The actual number of air changes per hour in each animal room is recorded at least twice each year and the Testing Facility retains these records.

2.11. TEST SUBSTANCE ADMINISTRATION AND CHAMBER OPERATION

See Appendix N, Inhalation Report.

2.12. EXPERIMENTAL EVALUATIONS

2.12.1. VIABILITY CHECKS

Animals were observed in their cages at least twice daily for mortality, morbidity and signs of severe toxicity.

2.12.2. DETAILED PHYSICAL EXAMINATIONS

In-Chamber: All animals were observed as a group at least once during each exposure.

Out-of-Chamber: Animals on study were examined daily from receipt through to terminal euthanasia on GD 20. Examinations included observations of general condition, skin and fur, eyes, nose, oral cavity, abdomen and external genitalia as well as evaluations of respiration. During the treatment period these evaluations were performed after exposures.

2.12.3. BODY WEIGHT

Body weights were recorded on GD 4, 6, 10, 13, 16, 19 and 20. Weight gain was also calculated for intervals as found appropriate, including GD 6-20.

2.12.4. FEED CONSUMPTION

Feed consumption was recorded and reported for intervals as found appropriate, *eg* GD 4-6, 6-10, 10-13, 13-16, 16-20 and 6-20.

2.13. TERMINAL OBSERVATIONS

2.13.1. METHOD OF EUTHANASIA

All dams were euthanized by carbon dioxide inhalation. All live fetuses were euthanized by an intraperitoneal overdose of sodium pentobarbital.

2.13.2. MACROSCOPIC EXAMINATIONS

A macroscopic postmortem examination was performed on all the dams. Macroscopic lesions or tissues with significant findings were saved in 10% Neutral Buffered Formalin (NBF).

2.13.2.1. Reproductive System

For all Gestation Day 20 animals, the intact uteri (ovaries attached) were removed from the abdominal cavity and weighed. Corpora lutea were counted and the number per ovary recorded. The number and location of the following were recorded for each uterine horn:

- live fetuses
- dead fetuses (no significant degeneration)
- late embryo-fetal deaths (recognizable dead fetus undergoing degeneration, regardless of size)
- early embryonic deaths (evidence of implantation but no recognizable fetus)

Females that did not deliver pups were sacrificed and their uteri examined for implantation sites and resorptions, including confirmation of any apparent non-pregnant status by means of staining with ammonium sulfide (method modified from Salewski, 1964) to detect non-visible implantation sites. The maternal carcass and uterus were then discarded.

2.14. FETAL EVALUATIONS

2.14.1. EXTERNAL EVALUATIONS

All live fetuses were weighed and individually identified. Each (live and dead) fetus was given a macroscopic external examination for defects, including observation of the palate. Any dead fetuses were also weighed.

2.14.2. FETAL SOFT TISSUE (VISCERAL) EVALUATIONS

Approximately one-half of the fetuses in each litter (nominally, alternating fetuses within the litter were randomly assigned using a

computerized randomization program - Toxicology Analysis System Customized, version 1.4) and were placed in suitable aldehyde (such as Modified Davidson's fixative) for preservation and decalcification. These fetuses were subjected to soft tissue examination by gross dissection of the torso and a razor blade sectioning technique (derived from that of Wilson and Warkany, 1965) for the head. All malformations and variations were recorded. During the dissection process, the sex of each fetus was confirmed by internal inspection of the gonads. Following complete dissection of the fetuses, all carcasses and sections were preserved in 10% neutral buffered formalin.

2.14.3. FETAL SKELETAL EVALUATIONS

Approximately one-half of the fetuses in each litter (nominally, alternating fetuses within the litter were randomly assigned using a computerized randomization program - Toxicology Analysis System Customized, version 1.4) had the sex internally evaluated and were then eviscerated and processed for staining of the skeleton using Alizarin Red S. Subsequently, these fetuses were evaluated for skeletal malformations and ossification variations. These specimens were then stored in 100% glycerin with a mold inhibitor.

2.15. STATISTICAL ANALYSIS

The following parameters were analyzed statistically, where it was considered necessary in support of interpretation. Statistical significance for differences from control was recognized at the 5% or 1%, two-sided levels.

2.15.1. CONTINUOUS DATA

Evaluation of equality of group means was made by the appropriate statistical method, followed by a multiple comparison procedure, if needed. The parametric method was the standard one-way analysis of variance (ANOVA) using the F ratio to assess significance (Dunlap and Duffy, 1975). If the ANOVA was significant, Dunnett's test (Dunlap, et.al., 1981) was used to determine which data, if any, differed from the control. The nonparametric method was the Kruskal-Wallis test (Siegel, S., 1956) and if differences were indicated, the pairwise comparison test (Siegel, S., 1956) was used to determine which means differed from control.

- Body weight and feed consumption data
- Corpora lutea
- Uterine implantation data (live fetuses, implantations)
- Pre- and post-implantation loss
- Fetal weight distinguished by sex and as a composite for both sexes (litter as experimental unit)
- Gravid uterine weights

2.15.2. INCIDENCE DATA

A Fisher's Exact Test with Bonferroni correction (Siegel, S., 1956) was performed to identify differences between the groups.

- Incidence of litters containing fetuses with malformations (external, soft tissue and skeletal - total affected and by finding)

2.16. DATA STORAGE

All data documenting experimental details and study procedures and observations were recorded and maintained as raw data. At the completion of the study, all reports, raw data, preserved specimens and retained samples will be maintained in the Archives of the Testing Facility for a period of 10 years after submission of the signed final report. The Sponsor will determine the final disposition of these materials.

2.17. REGULATORY REFERENCES

2.17.1. TEST GUIDELINES

This study complies with the Organization for Economic Cooperation and Development (22 January 2001). OECD Guidelines for Testing of Chemicals; OECD Guideline 414: Prenatal Developmental Toxicity Study and US EPA OPPTS Health Effects Test Guidelines 870.3700, Prenatal Developmental Toxicity Study EPA 712-C-98-207, August 1998.

2.17.2. GOOD LABORATORY PRACTICES

This study was conducted in compliance with Organization for Economic Cooperation and Development (OECD) Good Laboratory Practices as set forth in ENV/MC/CHEM(98)17 and EPA Good Laboratory Practices as set forth in 40 CFR Part 792 (TSCA).

2.17.3. ANIMAL WELFARE ACT COMPLIANCE

This study complied with all appropriate parts of the Animal Welfare Act Regulations: 9 CFR Parts 1 and 2 Final Rules, Federal Register, Volume 54, No. 168, August 31, 1989, pp. 36112-36163 effective October 30, 1989 and 9 CFR Part 3 Animal Welfare Standards; Final Rule, Federal Register, Volume 56, No. 32, February 15, 1991, pp. 6426-6505 effective March 18, 1991.

2.18. PROTOCOL DEVIATIONS

The following protocol deviations occurred during the study at the Testing Facility but did not affect the integrity of the study:

1. Due to technician oversight, fetus 4521-13 was eviscerated prior to recording the sex, which could not then be determined. Fetus 4507-4 was switched from visceral examination to skeletal examination due to external findings.

2. For 24 animals (out of 104) in Sets A, B and C utilized on study, the Supplier did not provide a Gestation Day 0 weight list.

3. RESULTS AND DISCUSSION

3.1. CHAMBER MONITORING

(Appendix N)

Chamber distribution analyses showed that the test substance was evenly distributed within each chamber.

The target and mean (± standard deviation) analytical (IR) and nominal concentrations (based on gas flows) are summarized as follows:

Group	Test Substance	Target Concentration (ppm)	Analytical Concentration (ppm)	Nominal Concentration (ppm)
1	Air Control	0	0.0 ± 0.0	0.0 ± 0.0
2	CTFE	30	31.1 ± 2.3	28.0 ± 0.0
3	CTFE	90	89.2 ± 8.1	77.0 ± 0.0
4*	CTFE	180	187 ± 21	169 ± 4.0

*This group's exposure was terminated during the 7th exposure because of treatment effects discussed below.

The analytically measured exposure levels of the airborne test substance were reasonably close to the targeted exposure levels and nominal concentrations. Chamber environmental conditions averaged 23°C temperature and 58% relative humidity.

Mean particle size distribution measurements for the exposures are summarized as follows:

Group	Test Substance	Mass Median Aerodynamic Diameter (µm)	Geometric Standard Deviation	Total Mass Concentration (mg/m³)
1	Air Control	1.089	2.003	4.27×10^{-3}
2	CTFE	1.061	1.803	4.04×10^{-3}
3	CTFE	1.129	2.253	4.84×10^{-3}
4	CTFE	1.095	3.587	8.54×10^{-3}

These results indicated that the atmospheres were gas only, as expected, since there was no substantial difference between the test substance chambers and the air control chamber.

3.2. MATERNAL DATA

3.2.1. MORTALITY AND PREGNANCY RATES

(Table 1, Appendix A)

There was no effect of treatment on survival, as all animals survived until the termination of the study. Pregnancy rates varied from 88-96% with no treatment effect seen.

3.2.2. CLINICAL OBSERVATIONS

(Tables 2 and 3, Appendices B, C and N)

During the exposure periods, all animals were unremarkable, except that the 180 ppm exposed dams showed some eye closure, piloerection and lethargy during exposure day 7, prior to this exposure level's early termination.

During the non-exposure periods, the 30 ppm exposed animals were unremarkable. The 90 ppm exposed animals showed a marked increase in red nasal discharge, especially during gestation days 13-20. The 180 ppm exposed dams showed some decreased feed consumption and consequent decreased fecal volume. The incidence of red nasal discharge in the 180 ppm animals was comparable to the 30 ppm exposed animals. This was most likely because the dams exposed to 90 ppm of CTFE were exposed for the entire gestation days 6-19 period, whereas the dams exposed to 180 ppm of CTFE were at most exposed during only gestation days 6-12, before their exposures were discontinued. Since the start of the exposures was staggered over 4 days, 6 of these dams were exposed for 7 days, 7 of these dams were exposed for 6 days, 6 of these dams were exposed for 5 days and 6 of these dams were exposed for 4 days

3.2.3. BODY WEIGHTS

(Tables 4 and 5, Appendices D and E)

There were no test substance related differences in absolute body weights or in body weight changes in the 30 ppm exposed animals, compared to the Air Control animals. However, there were statistically significantly reduced body weight gains during gestation days 6-10 (corresponding with the initial 1-4 exposures) for the 90 ppm exposed animals. The 90 ppm exposed animals did then show body weight gain comparable to the Air Control animals during gestation days 10-20, but overall showed 15% less weight gain during the exposure period (gestation days 6-20) than the Air Control animals. There was an average weight loss of 7% during gestation days 6-10 (corresponding with the initial 1-4 exposures) for the 180 ppm exposed animals. These 180 ppm exposed animals then showed recovery, with body weight gain greater than the Air Control animals during gestation days 10-20 (after being withdrawn from the daily exposures), such that overall they showed 12% less weight gain during the gestation days 6-20 period than the Air Control animals.

3.2.4. FEED CONSUMPTION

(Table 6, Appendix F)

There were no test substance related differences in feed consumption in the 30 ppm exposed animals, compared to the Air Control animals. However, corresponding to the exposure related body weight differences discussed above, there was statistically significantly reduced feed consumption during gestation days 6-10 (corresponding with the initial 1-4 exposures) for the 90 ppm (16% reduction) and 180 ppm (43% reduction) exposed animals. Similar to the body weights, there was recovery seen during the remainder of the gestation period for the 180 ppm group following cessation of treatment.

3.2.5. FEMALE NECROPSY DATA AND PREGNANCY OUTCOME

(Tables 7, 8 and 9; Appendices G, H and I)

There were no test substance related effects on pregnancy outcome, in terms of corpora lutea numbers, pre- or post-implantation loss, or litter size and gravid uterine weights. The slightly increased numbers of early embryonic deaths that occurred in the exposed groups, as compared with Air Control, were the result of a small minority of animals in those groups with more than the usual number of early deaths:

	Air Control	30 ppm	90 ppm	180 ppm
Animals with 1 early death	5	4	7	6
Animals with >1 early deaths	0	4	5	2

It is not uncommon for rats of this strain to have at least 1 early embryonic death in each pregnancy, often affecting over half of the litters in the group. In view of this, and the lack of an exposure concentration relationship, the incidences in this study were considered to have been fortuitous.

3.3. FETAL DATA

3.3.1. FETAL BODY WEIGHTS

(Table 8, Appendices I and J)

There were no test substance related differences in fetal body weights in the fetuses from the 30 and 90 ppm exposed animals, compared to the Air Control animals. However, there was statistically significantly reduced (13%) mean fetal body weight in the fetuses from the 180 ppm exposed animals, compared to the Air Control animals.

3.3.2. FETAL OBSERVATIONS

(Tables 10, 11 and 12, Appendices K, L and M)

There were low, sporadic incidences of fetal abnormalities and variants across all the groups. There was no indication of any association with exposure to the test substance.

The parameters of skeletal ossification gave consistent evidence of slightly reduced state of ossification at the 180 ppm exposure level. This change was commensurate with the observed reduction in fetal weight at this exposure level. There were no meaningful differences from Control at the lower exposure levels.

3.4. POST-STUDY TEST SUBSTANCE ANALYSIS AND RANGE-FINDING EVALUATION

(Appendices O and Q)

Since unexpected test substance related effects were seen during the study, the Sponsor requested that a post-study GC analysis of the test substance be conducted to evaluate for undesired dimer formation. Samples of the test substance from the Sponsor's cylinder and from chamber atmospheres (non-animal exposures) were collected into evacuated gas cylinders and shipped to the Sponsor's laboratory. Assays of these samples showed the presence of ~0.1% dimer formation (cis and trans 1,2-dichlororhexafluorocyclobutane). The potential toxicity of this concentration was not known and was evaluated in a follow-up in-vivo evaluation that indicated that CTFE, and not the presence of dimers, was the cause of the adverse responses.

4. CONCLUSION

Exposure of time-mated female rats to target concentrations of 30, 90 or 180 ppm of CTFE by whole-body inhalation for gestation days 6-19 (days 6-12 for the 180 ppm group) resulted in no effects of exposure at 30 ppm, but decreased body weight gain and feed consumption at 90 and 180 ppm. Decreased fetal body weight, with slightly reduced state of skeletal ossification, was observed at 180 ppm. Therefore, a no observed adverse effect level (NOAEL) for maternal toxicity of 30 ppm was determined while a NOAEL for developmental toxicity of 90 ppm was indicated.

CALCULATIONS

Feed Consumption:

Feed consumption (g/kg/day) =

[(total grams of feed presented - amount of feed remaining) ÷ (average kilogram body weight)] ÷ no. of days

Preimplantation Loss:

no. of corpora lutea – no. of implantation sites

Percent Preimplantation Loss:

[(no. of corpora lutea – no. of implantation sites)/no. of corpora lutea] X 100

Postimplantation Loss:

total no. of early and late resorptions and dead fetuses

Percent Postimplantation Loss:

(total no. of early and late resorptions and dead fetuses/no. of implantation sites) X 100

REFERENCES

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	General Preface	

General Notes

Individual animal data values presented in this report may be rounded. Unrounded individual animal data values are used to calculate the reported mean and standard deviation values. Therefore, use of the reported individual values to reproduce means, standard deviations and/or to perform any subsequent calculations may produce minor discrepancies between the calculated values and those presented in this report.

TABLE 1

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF SURVIVAL AND PREGNANCY

DOSE GROUP:		1	2	3	4
DOSE LEVEL (PPM):		0	30	90	180
No. of females mated	N	25	25	25	25
Pregnant	N	22	23	23	24
- Died/sacrificed moribund	N	0	0	0	0
- Elective sacrifice	N	0	0	0	0
Nonpregnant	N	3	2	2	1
- Died/sacrificed moribund	N	0	0	0	0
- Elective sacrifice	N	0	0	0	0
Total no. of females died/	N	0	0	0	0
sacrificed moribund	%	0.0	0.0	0.0	0.0
Examined at scheduled c-section	N	25	25	25	25
- Nonpregnant	N	3	2	2	1
- With total implant loss	N	0	0	0	0
	%	0.0	0.0	0.0	0.0
- With viable fetuses	N	22	23	23	24
	%	88.0	92.0	92.0	96.0

No statistically significant differences

	Summary of Daily Observations Preface	Table 2

Note:

Animals were observed for mortality, morbidity, and signs of severe toxicity at least twice daily. Only abnormal observations are listed.

Corresponding exposure levels for each group were as follows:

Group 1 - 0 ppm
Group 2 - 30 ppm
Group 3 - 90 ppm
Group 4 - 180 ppm

Summary of Daily Observations

Table 2

Observation	Group	Exposure Day 3	4	5	6	7	8	9	10
Decreased Feed Consumption	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	3	8	4	1	0
Decreased Fecal Volume	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	2	4	1	3	8	0	0	0
Red Nasal Discharge	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	1	0	0	0	0	0	0
General Alopecia	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	1	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0

TABLE 3

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF CLINICAL OBSERVATIONS DURING GESTATION - (frequency/animals)

DOSE GROUP:	1	2	3	4
DOSE LEVEL (PPM):	0	30	90	180
DAY 0 to 4				
Normal				
WITHIN NORMAL LIMITS	92/25	93/25	92/25	94/25
Dermal-General				
ALOPECIA - GENERAL	3/ 1	0/ 0	0/ 0	0/ 0
ALOPECIA - EXTREMITIES/SNOUT	0/ 0	0/ 0	1/ 1	0/ 0

TABLE 3

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF CLINICAL OBSERVATIONS DURING GESTATION - (frequency/animals)

DOSE GROUP:	1	2	3	4
DOSE LEVEL (PPM):	0	30	90	180
DAY 4 to 6				
Normal				
WITHIN NORMAL LIMITS	75/25	75/25	75/25	75/25

TABLE 3

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF CLINICAL OBSERVATIONS DURING GESTATION - (frequency/animals)

DOSE GROUP:	1	2	3	4
DOSE LEVEL (PPM):	0	30	90	180
DAY 6 to 10				
Normal				
WITHIN NORMAL LIMITS	125/25	123/25	122/25	116/25
Dermal-General				
ALOPECIA - GENERAL	0/ 0	0/ 0	3/ 1	1/ 1
Oral/Buccal				
NASAL DISCHARGE - RED	0/ 0	2/ 2	0/ 0	8/ 5

TABLE 3

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF CLINICAL OBSERVATIONS DURING GESTATION - (frequency/animals)

DOSE GROUP:	1	2	3	4
DOSE LEVEL (PPM):	0	30	90	180
DAY 10 to 13				
Normal				
WITHIN NORMAL LIMITS	98/25	99/25	89/24	85/24
Dermal-General				
ALOPECIA - GENERAL	0/ 0	0/ 0	4/ 1	7/ 3
ALOPECIA - EXTREMITIES/SNOUT	0/ 0	0/ 0	2/ 1	2/ 2
Oral/Buccal				
NASAL DISCHARGE - RED	2/ 2	1/ 1	5/ 5	7/ 6

TABLE 3

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF CLINICAL OBSERVATIONS DURING GESTATION - (frequency/animals)

DOSE GROUP:	1	2	3	4
DOSE LEVEL (PPM):	0	30	90	180
DAY 16 to 20				
Normal				
WITHIN NORMAL LIMITS	118/24	112/24	73/22	94/20
TERMINAL SACRIFICE	25/25	25/25	25/25	25/25
Gen. Appearance				
SOFT PROTRUSION - MID ABDOMEN	0/ 0	0/ 0	0/ 0	5/ 1
VAGINAL DISCHARGE	0/ 0	0/ 0	0/ 0	1/ 1
Dermal-General				
ALOPECIA - GENERAL	5/ 1	0/ 0	10/ 2	15/ 3
ALOPECIA - EXTREMITIES/SNOUT	0/ 0	0/ 0	5/ 1	10/ 2
SCABS	3/ 1	0/ 0	0/ 0	0/ 0
Oral/Buccal				
NASAL DISCHARGE - RED	2/ 2	13/ 5	39/15	5/ 3

TABLE 3

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF CLINICAL OBSERVATIONS DURING GESTATION - (frequency/animals)

DOSE GROUP:	1	2	3	4
DOSE LEVEL (PPM):	0	30	90	180
DAY 6 to 20				
Normal				
WITHIN NORMAL LIMITS	364/25	358/25	293/25	314/25
TERMINAL SACRIFICE	25/25	25/25	25/25	25/25
Gen. Appearance				
SOFT PROTRUSION - MID ABDOMEN	0/ 0	0/ 0	0/ 0	6/ 1
VAGINAL DISCHARGE	0/ 0	0/ 0	0/ 0	1/ 1
Dermal-General				
ALOPECIA - GENERAL	6/ 1	0/ 0	20/ 2	28/ 3
ALOPECIA - EXTREMITIES/SNOUT	0/ 0	0/ 0	9/ 1	16/ 2
SCABS	3/ 1	0/ 0	0/ 0	0/ 0
Oral/Buccal				
NASAL DISCHARGE - RED	5/ 3	17/ 5	55/15	18/ 9

TABLE 4

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF GESTATION BODY WEIGHTS (GRAMS)

DOSE GROUP:		1	2	3	4
DOSE LEVEL (PPM):		0	30	90	180
DAY 4	MEAN	256	254	254	253
	S.D.	13.0	14.8	14.0	13.7
	N	22	23	23	24
DAY 6	MEAN	274	272	271	269
	S.D.	12.5	16.5	13.5	15.7
	N	22	23	23	24
DAY 10	MEAN	295	291	280*	251**
	S.D.	13.1	20.3	15.2	26.7
	N	22	23	23	24
DAY 13	MEAN	315	311	297*	284**
	S.D.	14.0	21.6	16.4	27.4
	N	22	23	23	24
DAY 16	MEAN	340	334	322*	316**
	S.D.	16.4	24.2	20.1	27.1
	N	22	23	23	24
DAY 19	MEAN	381	377	362*	361*
	S.D.	23.0	28.3	24.6	30.3
	N	22	23	23	24
DAY 20	MEAN	398	393	377*	378*
	S.D.	25.1	30.4	26.0	31.1
	N	22	23	23	24

Statistical key: * = $p<0.05$ ** = $p<0.01$

TABLE 5

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF GESTATION BODY WEIGHT GAIN (GRAMS)

DOSE GROUP:		1	2	3	4
DOSE LEVEL (PPM):		0	30	90	180
DAYS 4 TO 6	MEAN	18	18	17	16
	S.D.	4.7	4.4	4.9	5.2
	N	22	23	23	24
DAYS 6 TO 10	MEAN	22	19	8**	-18**
	S.D.	6.5	5.8	6.7	19.3
	N	22	23	23	24
DAYS 10 TO 13	MEAN	20	20	17	33**
	S.D.	4.1	4.2	7.4	10.9
	N	22	23	23	24
DAYS 13 TO 16	MEAN	25	23	25	31*
	S.D.	5.1	5.5	6.8	8.8
	N	22	23	23	24
DAYS 16 TO 20	MEAN	58	59	55	62
	S.D.	12.0	11.6	10.0	8.2
	N	22	23	23	24
DAYS 6 TO 20	MEAN	124	121	106**	109*
	S.D.	19.9	18.9	20.6	18.4
	N	22	23	23	24

Statistical key: * = p<0.05 ** = p<0.01

TABLE 6

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF GESTATION FEED CONSUMPTION (GRAMS/KG/DAY)

DOSE GROUP:		1	2	3	4
DOSE LEVEL (PPM):		0	30	90	180
DAYS 4 TO 6	MEAN	83	85	86	83
	S.D.	6.5	5.9	5.2	6.2
	N	22	23	23	24
DAYS 6 TO 10	MEAN	81	80	68**	46**
	S.D.	6.2	5.2	8.5	15.2
	N	22	23	23	24
DAYS 10 TO 13	MEAN	82	82	76	80
	S.D.	5.1	5.1	6.3	17.4
	N	22	23	23	24
DAYS 13 TO 16	MEAN	76	78	77	89**
	S.D.	5.6	5.3	6.6	8.8
	N	22	23	23	24
DAYS 16 TO 20	MEAN	73	76	74	81**
	S.D.	5.6	3.2	5.5	6.2
	N	22	23	23	24
DAYS 6 TO 20	MEAN	78	79	74**	74*
	S.D.	4.8	3.7	5.1	5.7
	N	22	23	23	24

Statistical key: * = $p<0.05$ ** = $p<0.01$

TABLE 7

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF MATERNAL NECROPSY OBSERVATIONS

DOSE GROUP:		1	2	3	4
DOSE LEVEL (PPM):		0	30	90	180
FEMALES	N	25	25	25	25
KIDNEY	N	0	1	1	0
DILATED RENAL PELVIS	N	0	0	1	0
	%	0.0	0.0	4.0	0.0
CYSTIC KIDNEY	N	0	1	0	0
	%	0.0	4.0	0.0	0.0
UTERUS	N	2	0	0	0
ABNORMAL CONTENTS	N	1	0	0	0
	%	4.0	0.0	0.0	0.0
FUSED PLACENTAS	N	1	0	0	0
	%	4.0	0.0	0.0	0.0

TABLE 8

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF CESAREAN SECTION DATA

DOSE GROUP:		1	2	3	4
DOSE LEVEL (PPM):		0	30	90	180
Pregnant (at scheduled sacrifice)	N	22	23	23	24
Dams with no Viable Fetuses	N	0	0	0	0
Dams with Viable Fetuses	N	22	23	23	24
Corpora Lutea	TOTAL	329	342	352	357
No. per animal	MEAN	15.0	14.9	15.3	14.9
	S.D.	1.62	2.12	1.49	1.96
Implantation Sites	TOTAL	301	322	332	343
No. per animal	MEAN	13.7	14.0	14.4	14.3
	S.D.	3.12	1.78	1.90	1.92
Preimplantation Loss	TOTAL	28	20	20	14
No. per animal	MEAN	1.3	0.9	0.9	0.6
	S.D.	2.12	0.81	1.52	0.65
% per animal	MEAN%	9.4	5.5	5.5	3.9
	S.D.	18.98	4.88	9.50	4.36
Live Fetuses	TOTAL	296	297	309	330
No. per animal	MEAN	13.5	12.9	13.4	13.8
	S.D.	3.10	2.83	2.68	1.75
Males	TOTAL	144	142	151	154
	MEAN%	51.1	47.7	48.8	46.9
	S.D.	16.05	12.24	8.92	15.45
Females	TOTAL	152	155	158	175
	MEAN%	48.9	52.3	51.2	53.1
	S.D.	16.05	12.24	8.92	15.45

No statistically significant differences

TABLE 8

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF CESAREAN SECTION DATA

DOSE GROUP:		1	2	3	4
DOSE LEVEL (PPM):		0	30	90	180
Postimplantation Loss No. per animal	TOTAL	5	25	23	13
	MEAN	0.2	1.1	1.0	0.5
	S.D.	0.43	2.31	1.38	0.93
% implants per animal	MEAN%	1.6	7.8	7.6	3.6
	S.D.	2.99	16.10	11.62	5.68
Dead Fetuses No. per animal	TOTAL	0	0	0	0
	MEAN	0.0	0.0	0.0	0.0
	S.D.	0.00	0.00	0.00	0.00
% of implants per animal	MEAN%	0.0	0.0	0.0	0.0
	S.D.	0.00	0.00	0.00	0.00
Resorptions: Early No. per animal	TOTAL	5	25	23	12
	MEAN	0.2	1.1	1.0	0.5
	S.D.	0.43	2.31	1.38	0.93
% of implants per animal	MEAN%	1.6	7.8	7.6	3.3
	S.D.	2.99	16.10	11.62	5.68
Resorptions: Late No. per animal	TOTAL	0	0	0	1
	MEAN	0.0	0.0	0.0	0.0
	S.D.	0.00	0.00	0.00	0.20
% of implants per animal	MEAN%	0.0	0.0	0.0	0.3
	S.D.	0.00	0.00	0.00	1.36

No statistically significant differences

TABLE 8

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF CESAREAN SECTION DATA

DOSE GROUP:		1	2	3	4
DOSE LEVEL (PPM):		0	30	90	180
Fetal Body Weight (g)	MEAN	3.9	3.8	3.8	3.4**
	S.D.	0.46	0.50	0.50	0.50
	N	22	23	23	24
Male Fetuses	MEAN	4.0	3.9	3.8	3.5**
	S.D.	0.49	0.52	0.55	0.52
Female Fetuses	MEAN	3.8	3.7	3.7	3.3**
	S.D.	0.39	0.48	0.47	0.47

Statistical key: ** = $p<0.01$

TABLE 9

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF GRAVID UTERINE WEIGHT AND NET BODY WEIGHT CHANGE (GRAMS)

DOSE GROUP:		1	2	3	4
DOSE LEVEL (PPM):		0	30	90	180
NET BODY WT. CHANGE[a]	MEAN	124	121	106**	109*
	S.D.	19.9	18.9	20.6	18.4
	N	22	23	23	24
GRAVID UTERINE WT.	MEAN	83	80	81	79
	S.D.	18.9	17.5	15.8	12.7
	N	22	23	23	24
NET WEIGHT CHANGE[b]	MEAN	42	41	25**	30**
	S.D.	11.6	9.1	13.6	12.6
	N	22	23	23	24

Statistical key: * = $p<0.05$ ** = $p<0.01$

[a]NET BODY WT. CHANGE = TERMINAL BODY WT. MINUS DAY 6 BODY WEIGHT
[b]NET WEIGHT CHANGE = NET BODY WT. CHANGE MINUS UTERINE WEIGHT

TABLE 10

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF FETAL OBSERVATIONS - MALFORMATIONS

DOSE GROUP:	1	2	3	4
DOSE LEVEL (PPM):	0	30	90	180
Litters Examined Externally	22	23	23	24
Fetuses Examined	296	297	309	330
ANASARCA				
Fetal Incidence	0	0	0	1
Litter Incidence	0	0	0	1
Litters Examined Viscerally	21	23	23	24
Fetuses Examined	146	147	155	165
RETINAS FOLDED				
Fetal Incidence	1	1	1	0
Litter Incidence	1	1	1	0
Litters Examined Skeletally	22	23	23	24
Fetuses Examined	150	150	154	165
Number with findings	0	0	0	0
TOTAL MALFORMATIONS				
NUMBER WITH EXTERNAL MALFORMATIONS				
Fetal Incidence	0	0	0	1
Litter Incidence	0	0	0	1
NUMBER WITH VISCERAL MALFORMATIONS				
Fetal Incidence	1	1	1	0
Litter Incidence	1	1	1	0
NUMBER WITH SKELETAL MALFORMATIONS				
Fetal Incidence	0	0	0	0
Litter Incidence	0	0	0	0
TOTAL NUMBER WITH MALFORMATIONS				
Fetal Incidence	1	1	1	1
Litter Incidence	1	1	1	1

No statistically significant differences

TABLE 11

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF FETAL OBSERVATIONS - VARIATIONS

DOSE GROUP:	1	2	3	4
DOSE LEVEL (PPM):	0	30	90	180
Litters Examined Externally	22	23	23	24
Fetuses Examined	296	297	309	330
Number with findings	0	0	0	0
Litters Examined Viscerally	21	23	23	24
Fetuses Examined	146	147	155	165
ADDITIONAL SUBCLAVIAN ARTERY				
Fetal Incidence	1	1	0	0
Litter Incidence	1	1	0	0
PULMONARY TRUNK DILATED				
Fetal Incidence	0	0	0	1
Litter Incidence	0	0	0	1
DISPLACED TESTIS				
Fetal Incidence	4	1	1	3
Litter Incidence	4	1	1	3
RENAL PAPILLA (E) NOT DEVELOPED (GRADE 0)				
Fetal Incidence	0	0	4	2
Litter Incidence	0	0	3	1
UNDESCENDED THYMUS				
Fetal Incidence	13	3	3	11
Litter Incidence	7	3	1	9
LEFT-SIDED UMBILICAL ARTERY				
Fetal Incidence	0	0	0	2
Litter Incidence	0	0	0	2

No statistically significant differences

TABLE 3

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF CLINICAL OBSERVATIONS DURING GESTATION - (frequency/animals)

DOSE GROUP:	1	2	3	4
DOSE LEVEL (PPM):	0	30	90	180
DAY 13 to 16				
Normal				
WITHIN NORMAL LIMITS	97/25	95/25	68/22	80/21
Gen. Appearance				
SOFT PROTRUSION - MID ABDOMEN	0/ 0	0/ 0	0/ 0	2/ 1
VAGINAL DISCHARGE	0/ 0	0/ 0	0/ 0	1/ 1
Dermal-General				
ALOPECIA - GENERAL	2/ 1	0/ 0	7/ 2	12/ 3
ALOPECIA - EXTREMITIES/SNOUT	0/ 0	0/ 0	4/ 1	8/ 2
Oral/Buccal				
NASAL DISCHARGE - RED	1/ 1	5/ 3	21/10	1/ 1

TABLE 11

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF FETAL OBSERVATIONS - VARIATIONS

DOSE GROUP:	1	2	3	4
DOSE LEVEL (PPM):	0	30	90	180
Litters Examined Skeletally	22	23	23	24
Fetuses Examined	150	150	154	165
FISSURE - PARIETAL				
Fetal Incidence	0	2	2	1
Litter Incidence	0	1	2	1
SUTURAL BONE (PARIETAL/INTERPARIETAL)				
Fetal Incidence	1	0	0	0
Litter Incidence	1	0	0	0
27 PRESACRAL VERTEBRA(E)				
Fetal Incidence	0	0	0	1
Litter Incidence	0	0	0	1
STERNEBRA(E) MISALIGNED				
Fetal Incidence	0	1	0	0
Litter Incidence	0	1	0	0
RIB(S) 14TH RUDIMENTARY				
Fetal Incidence	22	10	9	8
Litter Incidence	9	6	4	5
COSTAL CARTILAGE MISALIGNED				
Fetal Incidence	0	1	0	0
Litter Incidence	0	1	0	0

No statistically significant differences

Summary of Ossification Parameters — Table 12

Group	1	2	3	4
Dose Level (ppm)	0	30	90	180
Number of Fetuses Examined (Litters)	150 (22)	150 (23)	154 (23)	165 (24)
Fetuses (Litters) Affected				
Incomplete Ossification / Unossified Skull Bones				
Less Than 3 Affected	40 (18)	48 (20)	58 (20)	82 (24)
3 to 5 Affected	22 (13)	22 (13)	17 (11)	21 (11)
More Than 5 Affected	12 (6)	12 (7)	9 (8)	16 (8)
Cervical Centrum(a) Ossified				
1 Affected	44 (17)	38 (18)	46 (18)	18 (9)
2+ Affected	15 (8)	9 (5)	19 (12)	5 (3)
Unossified / Incomplete Ossification of Sternebra(e)				
1 Sternebra Affected	38 (16)	36 (16)	51 (20)	39 (17)
2 Sternebrae Affected	30 (13)	27 (12)	23 (12)	58 (20)
3 or more Sternebrae Affected	5 (2)	10 (3)	8 (2)	23 (6)
Number of Caudal Vertebrae Ossified (*Litter Mean*)	3.9	3.9	3.8	3.3
Incomplete Ossification of Vertebral Centrum(a)				
1 Affected	10 (7)	13 (10)	13 (9)	15 (8)
2+ Affected	1 (1)	5 (4)	6 (3)	12 (5)
Ossification of 1st Cervical Arch (Ventral/Odontoid Process)	48 (15)	42 (16)	41 (15)	32 (14)
Unossified / Incompletely Ossified Vertebral Arches				
1 Pair	5 (4)	7 (5)	9 (6)	21 (12)
2+ Pairs	9 (4)	19 (7)	12 (5)	40 (12)
Incompletely Ossified / Unossified Pelvic Bones				
1-2 Affected	6 (3)	6 (4)	9 (3)	19 (8)
3-4 Affected	0 (0)	5 (1)	1 (1)	7 (1)
5-6 Affected	0 (0)	0 (0)	0 (0)	0 (0)
Vertebral Arches / Centra Fused				
1 Vert.	16 (13)	19 (11)	17 (12)	3 (2)
2+ Vert.	22 (10)	34 (12)	38 (16)	6 (4)
5th Metacarpals Ossified	120 (21)	113 (21)	128 (21)	84 (20)
Incompletely Ossified / Unossified Metacarpals	2 (2)	2 (2)	3 (2)	7 (2)
Incompletely Ossified / Unossified Metatarsals	6 (1)	12 (2)	9 (2)	21 (4)

Summary of Ossification Parameters — Table 12

Group	1	2	3	4
Dose Level (ppm)	0	30	90	180
Number of Fetuses Examined (Litters)	150 (22)	150 (23)	154 (23)	165 (24)
Mean Incidence per Litter				
Incomplete Ossification / Unossified Skull Bones				
Less Than 3 Affected	1.8	2.1	2.5	3.4
3 to 5 Affected	1.0	1.0	0.7	0.9
More Than 5 Affected	0.5	0.5	0.4	0.7
Cervical Centrum(a) Ossified				
1 Affected	2.0	1.7	2.0	0.8
2+ Affected	0.7	0.4	0.8	0.2
Unossified / Incomplete Ossification of Sternebra(e)				
1 Sternebra Affected	1.7	1.6	2.2	1.6
2 Sternebrae Affected	1.4	1.2	1.0	2.4
3 or more Sternebrae Affected	0.2	0.4	0.3	1.0
Incomplete Ossification of Vertebral Centrum(a)				
1 Affected	0.5	0.6	0.6	0.6
2+ Affected	0.0	0.2	0.3	0.5
Ossification of 1st Cervical Arch (Ventral/Odontoid Process)	2.2	1.8	1.8	1.3
Unossified / Incompletely Ossified Vertebral Arches				
1 Pair	0.2	0.3	0.4	0.9
2+ Pairs	0.4	0.8	0.5	1.7
Incompletely Ossified / Unossified Pelvic Bones				
1-2 Affected	0.3	0.3	0.4	0.8
3-4 Affected	0.0	0.2	0.0	0.3
5-6 Affected	0.0	0.0	0.0	0.0
Vertebral Arches / Centra Fused				
1 Vert.	0.7	0.8	0.7	0.1
2+ Vert.	1.0	1.5	1.7	0.3
5th Metacarpals Ossified	5.5	4.9	5.6	3.5
Incompletely Ossified / Unossified Metacarpals	0.1	0.1	0.1	0.3
Incompletely Ossified / Unossified Metatarsals	0.3	0.5	0.4	0.9

APPENDIX A

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 1 0 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY	PREGNANCY STATUS
1501	TERMINAL SACRIFICE	7-SEP-04	20	P
1502	TERMINAL SACRIFICE	7-SEP-04	20	P
1503	TERMINAL SACRIFICE	7-SEP-04	20	P
1504	TERMINAL SACRIFICE	7-SEP-04	20	NP
1505	TERMINAL SACRIFICE	7-SEP-04	20	P
1506	TERMINAL SACRIFICE	7-SEP-04	20	P
1507	TERMINAL SACRIFICE	8-SEP-04	20	P
1508	TERMINAL SACRIFICE	8-SEP-04	20	P
1509	TERMINAL SACRIFICE	8-SEP-04	20	P
1510	TERMINAL SACRIFICE	8-SEP-04	20	P
1511	TERMINAL SACRIFICE	8-SEP-04	20	P
1512	TERMINAL SACRIFICE	8-SEP-04	20	P
1513	TERMINAL SACRIFICE	9-SEP-04	20	NP
1514	TERMINAL SACRIFICE	9-SEP-04	20	P
1515	TERMINAL SACRIFICE	9-SEP-04	20	P
1516	TERMINAL SACRIFICE	9-SEP-04	20	P
1517	TERMINAL SACRIFICE	9-SEP-04	20	P
1518	TERMINAL SACRIFICE	9-SEP-04	20	P
1519	TERMINAL SACRIFICE	9-SEP-04	20	P
1520	TERMINAL SACRIFICE	10-SEP-04	20	NP
1521	TERMINAL SACRIFICE	10-SEP-04	20	P
1522	TERMINAL SACRIFICE	10-SEP-04	20	P
1523	TERMINAL SACRIFICE	10-SEP-04	20	P
1524	TERMINAL SACRIFICE	10-SEP-04	20	P
1525	TERMINAL SACRIFICE	10-SEP-04	20	P

NP-NOT PREGNANT, P-PREGNANT

APPENDIX A

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 2 30 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY	PREGNANCY STATUS
2501	TERMINAL SACRIFICE	7-SEP-04	20	P
2502	TERMINAL SACRIFICE	7-SEP-04	20	P
2503	TERMINAL SACRIFICE	7-SEP-04	20	P
2504	TERMINAL SACRIFICE	7-SEP-04	20	NP
2505	TERMINAL SACRIFICE	7-SEP-04	20	P
2506	TERMINAL SACRIFICE	7-SEP-04	20	P
2507	TERMINAL SACRIFICE	7-SEP-04	20	P
2508	TERMINAL SACRIFICE	8-SEP-04	20	P
2509	TERMINAL SACRIFICE	8-SEP-04	20	P
2510	TERMINAL SACRIFICE	8-SEP-04	20	P
2511	TERMINAL SACRIFICE	8-SEP-04	20	P
2512	TERMINAL SACRIFICE	8-SEP-04	20	P
2513	TERMINAL SACRIFICE	8-SEP-04	20	P
2514	TERMINAL SACRIFICE	9-SEP-04	20	NP
2515	TERMINAL SACRIFICE	9-SEP-04	20	P
2516	TERMINAL SACRIFICE	9-SEP-04	20	P
2517	TERMINAL SACRIFICE	9-SEP-04	20	P
2518	TERMINAL SACRIFICE	9-SEP-04	20	P
2519	TERMINAL SACRIFICE	9-SEP-04	20	P
2520	TERMINAL SACRIFICE	10-SEP-04	20	P
2521	TERMINAL SACRIFICE	10-SEP-04	20	P
2522	TERMINAL SACRIFICE	10-SEP-04	20	P
2523	TERMINAL SACRIFICE	10-SEP-04	20	P
2524	TERMINAL SACRIFICE	10-SEP-04	20	P
2525	TERMINAL SACRIFICE	10-SEP-04	20	P

NP-NOT PREGNANT, P-PREGNANT

APPENDIX A

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 3 90 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY	PREGNANCY STATUS
3501	TERMINAL SACRIFICE	7-SEP-04	20	P
3502	TERMINAL SACRIFICE	7-SEP-04	20	P
3503	TERMINAL SACRIFICE	7-SEP-04	20	P
3504	TERMINAL SACRIFICE	7-SEP-04	20	P
3505	TERMINAL SACRIFICE	7-SEP-04	20	P
3506	TERMINAL SACRIFICE	7-SEP-04	20	P
3507	TERMINAL SACRIFICE	8-SEP-04	20	P
3508	TERMINAL SACRIFICE	8-SEP-04	20	P
3509	TERMINAL SACRIFICE	8-SEP-04	20	P
3510	TERMINAL SACRIFICE	8-SEP-04	20	P
3511	TERMINAL SACRIFICE	8-SEP-04	20	P
3512	TERMINAL SACRIFICE	8-SEP-04	20	P
3513	TERMINAL SACRIFICE	9-SEP-04	20	P
3514	TERMINAL SACRIFICE	9-SEP-04	20	P
3515	TERMINAL SACRIFICE	9-SEP-04	20	NP
3516	TERMINAL SACRIFICE	9-SEP-04	20	P
3517	TERMINAL SACRIFICE	9-SEP-04	20	P
3518	TERMINAL SACRIFICE	9-SEP-04	20	P
3519	TERMINAL SACRIFICE	10-SEP-04	20	P
3520	TERMINAL SACRIFICE	10-SEP-04	20	NP
3521	TERMINAL SACRIFICE	10-SEP-04	20	P
3522	TERMINAL SACRIFICE	10-SEP-04	20	P
3523	TERMINAL SACRIFICE	10-SEP-04	20	P
3524	TERMINAL SACRIFICE	10-SEP-04	20	P
3525	TERMINAL SACRIFICE	10-SEP-04	20	P

NP-NOT PREGNANT, P-PREGNANT

APPENDIX A

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 4 180 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY	PREGNANCY STATUS
4501	TERMINAL SACRIFICE	7-SEP-04	20	P
4502	TERMINAL SACRIFICE	7-SEP-04	20	P
4503	TERMINAL SACRIFICE	7-SEP-04	20	P
4504	TERMINAL SACRIFICE	7-SEP-04	20	P
4505	TERMINAL SACRIFICE	7-SEP-04	20	P
4506	TERMINAL SACRIFICE	7-SEP-04	20	NP
4507	TERMINAL SACRIFICE	8-SEP-04	20	P
4508	TERMINAL SACRIFICE	8-SEP-04	20	P
4509	TERMINAL SACRIFICE	8-SEP-04	20	P
4510	TERMINAL SACRIFICE	8-SEP-04	20	P
4511	TERMINAL SACRIFICE	8-SEP-04	20	P
4512	TERMINAL SACRIFICE	8-SEP-04	20	P
4513	TERMINAL SACRIFICE	8-SEP-04	20	P
4514	TERMINAL SACRIFICE	9-SEP-04	20	P
4515	TERMINAL SACRIFICE	9-SEP-04	20	P
4516	TERMINAL SACRIFICE	9-SEP-04	20	P
4517	TERMINAL SACRIFICE	9-SEP-04	20	P
4518	TERMINAL SACRIFICE	9-SEP-04	20	P
4519	TERMINAL SACRIFICE	9-SEP-04	20	P
4520	TERMINAL SACRIFICE	10-SEP-04	20	P
4521	TERMINAL SACRIFICE	10-SEP-04	20	P
4522	TERMINAL SACRIFICE	10-SEP-04	20	P
4523	TERMINAL SACRIFICE	10-SEP-04	20	P
4524	TERMINAL SACRIFICE	10-SEP-04	20	P
4525	TERMINAL SACRIFICE	10-SEP-04	20	P

NP-NOT PREGNANT, P-PREGNANT

	Individual Daily Observations Preface	Appendix B

Note:

Animals were observed for mortality, morbidity and signs of severe toxicity at least twice daily. Only animals with abnormal observations are listed.

Individual Daily Observations

Appendix B

Animal Number	Group	Observations	Exposure Day 3	4	5	6	7	8	9	10
Group 3 – 90 ppm										
3512	3	General Alopecia	-	M	-	-	-	-	-	-
Group 4 – 180 ppm										
4501	4	Decreased Fecal Volume	-	A	A	A	A/V	-	-	-
		Decreased Feed Consumption	-	-	-	-	A[1]	✓	-	-
4503	4	Decreased Fecal Volume	-	A	-	A	A	-	-	-
		Decreased Feed Consumption	-	-	-	✓	A[1]	✓	-	-
4507	4	Decreased Feed Consumption	-	-	-	✓	✓	-	-	-
		Decreased Fecal Volume	-	-	-	A	A	-	-	-
4513	4	Decreased Fecal Volume	A	A	-	-	-	-	-	-
		Red Nasal Discharge	-	P	-	-	-	-	-	-
4514	4	Decreased Fecal Volume	A	A	-	-	-	-	-	-
4515	4	Decreased Feed Consumption	-	-	-	-	✓	-	-	-
		Decreased Fecal Volume	-	-	-	-	A	-	-	-
4516	4	Decreased Feed Consumption	-	-	-	✓	-	-	-	-

A=AM Finding; ✓ =AM and PM Finding; P=Present; M=Moderate; /V=Vet Request.
[1]PM observations could not be confirmed due to new feeders being presented.

Individual Daily Observations

Appendix B

Animal Number	Group	Observations	Exposure Day 3	4	5	6	7	8	9	10
Group 4 – 180 ppm										
4520	4	Decreased Feed Consumption	-	-	-	-	✓	-	-	-
		Decreased Fecal Volume	-	-	-	-	A	-	-	-
4521	4	Decreased Feed Consumption	-	-	-	-	✓	✓	✓/V	-
		Decreased Fecal Volume	-	-	-	-	A	-	-	-
4522	4	Decreased Feed Consumption	-	-	-	-	✓	-	-	-
		Decreased Fecal Volume	-	-	-	-	A	-	-	-
4523	4	Decreased Feed Consumption	-	-	-	-	✓	A	-	-
		Decreased Fecal Volume	-	-	-	-	A	-	-	-

A=AM Finding; ✓=AM and PM Finding; P=Present; M=Moderate; /V=Vet Request.
[1]PM observations could not be confirmed due to new feeders being presented.

APPENDIX C

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 1 0 PPM

FEMALE#	OBSERVATIONS	DAY OF GESTATION 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1501	TERMINAL SACRIFICE																					P
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
1502	TERMINAL SACRIFICE																					P
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
1503	TERMINAL SACRIFICE																					P
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
1504	TERMINAL SACRIFICE																					P
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
1505	TERMINAL SACRIFICE																					P
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
1506	TERMINAL SACRIFICE																					P
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
1507	TERMINAL SACRIFICE																					P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
1508	TERMINAL SACRIFICE																					P
	NASAL DISCHARGE - RED												P							P		
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P		P	P	P	P	P	P	P		P
1509	TERMINAL SACRIFICE																					P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
1510	TERMINAL SACRIFICE																					P
	NASAL DISCHARGE - RED												P			P						
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P		P	P		P	P	P	P	P	P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX C

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 1 0 PPM

FEMALE#	OBSERVATIONS	DAY OF GESTATION	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1511	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
1512	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
1513	TERMINAL SACRIFICE																						P
	ALOPECIA - GENERAL																	2	2	2	2	2	2
	SCABS																				P	P	P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P							
1514	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
1515	TERMINAL SACRIFICE																						P
	ALOPECIA - GENERAL		2	2	2																		
	WITHIN NORMAL LIMITS					P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
1516	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
1517	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
1518	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
1519	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
1520	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS				P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX C

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 1 0 PPM

FEMALE#	OBSERVATIONS	DAY OF GESTATION	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1521	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
1522	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
1523	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
1524	TERMINAL SACRIFICE																						P
	NASAL DISCHARGE - RED																			P			
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P		P	P	P
1525	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX C

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 2 30 PPM

FEMALE#	OBSERVATIONS	DAY OF GESTATION 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
2501	TERMINAL SACRIFICE																					P
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
2502	TERMINAL SACRIFICE																					P
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
2503	TERMINAL SACRIFICE																					P
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
2504	TERMINAL SACRIFICE																					P
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
2505	TERMINAL SACRIFICE																					P
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
2506	TERMINAL SACRIFICE																					P
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
2507	TERMINAL SACRIFICE																					P
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
2508	TERMINAL SACRIFICE																					P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
2509	TERMINAL SACRIFICE																					P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
2510	TERMINAL SACRIFICE																					P
	NASAL DISCHARGE - RED																				P	
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P		P
2511	TERMINAL SACRIFICE																					P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX C

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 2 30 PPM

FEMALE#	OBSERVATIONS	DAY OF GESTATION	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
2512	TERMINAL SACRIFICE																						P
	NASAL DISCHARGE - RED																		P	P		P	
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P	P	P	P	P	P			P		P
2513	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
2514	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
2515	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
2516	TERMINAL SACRIFICE																						P
	NASAL DISCHARGE - RED												P						P	P	P		
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P		P	P	P	P	P				P	P
2517	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
2518	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
2519	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
2520	TERMINAL SACRIFICE																						P
	NASAL DISCHARGE - RED											P					P	P	P	P	P	P	P
	WITHIN NORMAL LIMITS				P	P	P	P	P	P	P		P	P	P	P							
2521	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS				P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX C

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 2 30 PPM

FEMALE#	OBSERVATIONS	DAY OF GESTATION	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
2522	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS				P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
2523	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS				P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
2524	TERMINAL SACRIFICE																						P
	NASAL DISCHARGE - RED																					P	
	WITHIN NORMAL LIMITS				P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P		P
2525	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS				P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX C

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 3 90 PPM

FEMALE#	OBSERVATIONS	DAY OF GESTATION 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
3501	TERMINAL SACRIFICE																					P
	NASAL DISCHARGE - RED																	P	P	P	P	
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P	P	P	P	P					P
3502	TERMINAL SACRIFICE																					P
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
3503	TERMINAL SACRIFICE																					P
	NASAL DISCHARGE - RED													P		P		P	P	P	P	
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P			P		P					P
3504	TERMINAL SACRIFICE																					P
	NASAL DISCHARGE - RED													P						P	P	
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P		P	P	P	P	P			P
3505	TERMINAL SACRIFICE																					P
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
3506	TERMINAL SACRIFICE																					P
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
3507	TERMINAL SACRIFICE																					P
	ALOPECIA - GENERAL															2	2	2	2	2	2	2
	WITHIN NORMAL LIMITS	P	P	P	P	P	P	P	P	P	P	P	P	P	P							
3508	TERMINAL SACRIFICE																					P
	WITHIN NORMAL LIMITS	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
3509	TERMINAL SACRIFICE																					P
	NASAL DISCHARGE - RED																		P	P	P	
	WITHIN NORMAL LIMITS	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P				P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX C

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 3 90 PPM

FEMALE#	OBSERVATIONS	DAY OF GESTATION	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
3510	TERMINAL SACRIFICE																						P
	NASAL DISCHARGE - RED													P					P			P	
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P		P	P	P	P		P	P		P
3511	TERMINAL SACRIFICE																						P
	ALOPECIA - EXTREMITIES/SNOUT														2	2	2	2	2	2	2	2	2
	NASAL DISCHARGE - RED																					P	P
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P	P									
3512	TERMINAL SACRIFICE																						P
	ALOPECIA - GENERAL										2	2	2	2	2	2	2	2	2	3	3	3	3
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P													
3513	TERMINAL SACRIFICE																						P
	NASAL DISCHARGE - RED																				P	P	
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P			P
3514	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
3515	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
3516	TERMINAL SACRIFICE																						P
	NASAL DISCHARGE - RED																P	P	P	P	P		
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P						P	P
3517	TERMINAL SACRIFICE																						P
	NASAL DISCHARGE - RED																	P	P				
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P			P	P	P	P
3518	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX C

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 3 90 PPM

FEMALE#	OBSERVATIONS	DAY OF GESTATION	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
3519	TERMINAL SACRIFICE																						P
	NASAL DISCHARGE - RED																P	P	P	P	P	P	
	WITHIN NORMAL LIMITS				P	P	P	P	P	P	P	P	P	P	P	P							P
3520	TERMINAL SACRIFICE																						P
	NASAL DISCHARGE - RED																					P	
	WITHIN NORMAL LIMITS				P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P		P
3521	TERMINAL SACRIFICE																						P
	NASAL DISCHARGE - RED															P	P		P	P	P	P	
	WITHIN NORMAL LIMITS				P	P	P	P	P	P	P	P	P	P	P			P					P
3522	TERMINAL SACRIFICE																						P
	NASAL DISCHARGE - RED																P				P	P	
	WITHIN NORMAL LIMITS				P	P	P	P	P	P	P	P	P	P	P	P		P	P	P			P
3523	TERMINAL SACRIFICE																						P
	ALOPECIA - EXTREMITIES/SNOUT					2																	
	WITHIN NORMAL LIMITS				P		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
3524	TERMINAL SACRIFICE																						P
	NASAL DISCHARGE - RED																	P				P	
	WITHIN NORMAL LIMITS				P	P	P	P	P	P	P	P	P	P	P	P	P		P	P	P		P
3525	TERMINAL SACRIFICE																						P
	NASAL DISCHARGE - RED															P	P	P	P	P	P	P	
	WITHIN NORMAL LIMITS				P	P	P	P	P	P	P	P	P	P	P								P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX C

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 4 180 PPM

FEMALE#	OBSERVATIONS	DAY OF GESTATION	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
4501	TERMINAL SACRIFICE																						P
	ALOPECIA - GENERAL															2	2	3	3	3	3	3	3
	ALOPECIA - EXTREMITIES/SNOUT															3	3	3	3	3	2	2	2
	NASAL DISCHARGE - RED													?									
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P			P								
4502	TERMINAL SACRIFICE																						P
	SOFT PROTRUSION - MID ABDOMEN																	P	P	P	P	P	P
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P		P	P	P						
4503	TERMINAL SACRIFICE																						P
	VAGINAL DISCHARGE																		P				
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P	P	P	P	P	P		P	P	P	P
4504	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
4505	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
4506	TERMINAL SACRIFICE																						P
	ALOPECIA - EXTREMITIES/SNOUT															2	2	2	2	2	2	2	2
	NASAL DISCHARGE - RED													P	P								
	WITHIN NORMAL LIMITS			P	P	P	P	P	P	P	P	P											
4507	TERMINAL SACRIFICE																						P
	NASAL DISCHARGE - RED													P						P			
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P			P	P	P	P	P		P	P	P
4508	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX C

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 4 180 PPM

FEMALE#	OBSERVATIONS	DAY OF GESTATION	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
4509	TERMINAL SACRIFICE																						P
	NASAL DISCHARGE - RED																			P			
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P			P	P	P
4510	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
4511	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
4512	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
4513	TERMINAL SACRIFICE																						P
	ALOPECIA - GENERAL														2	2	2	2	2	2	2	2	2
	NASAL DISCHARGE - RED										P	P		P									
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P				P										
4514	TERMINAL SACRIFICE																						P
	NASAL DISCHARGE - RED											P	P										
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P			P	P	P	P	P	P	P	P	P	P
4515	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
4516	TERMINAL SACRIFICE																						P
	NASAL DISCHARGE - RED											P	P										
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P			P	P	P	P	P	P	P	P	P	P
4517	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX C

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 4 180 PPM

FEMALE#	OBSERVATIONS	DAY OF GESTATION	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
4518	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
4519	TERMINAL SACRIFICE																						P
	ALOPECIA - GENERAL												2	2	2	2	2	2	2	2	2	2	2
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P											
4520	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS				P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
4521	TERMINAL SACRIFICE																						P
	NASAL DISCHARGE - RED											P											
	WITHIN NORMAL LIMITS				P	P	P	P	P	P	P		P	P	P	P	P	P	P	P	P	P	P
4522	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS				P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
4523	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS				P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
4524	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS				P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
4525	TERMINAL SACRIFICE																						P
	NASAL DISCHARGE - RED											P									P	P	P
	WITHIN NORMAL LIMITS				P	P	P	P	P	P	P		P	P	P	P	P	P	P	P			

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

APPENDIX D

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GESTATION BODY WEIGHTS (GRAMS)

GROUP 1 0 PPM

ANIMAL#		DAY OF GESTATION 4	6	10	13	16	19	20
1501		231	255	283	309	338	377	400
1502		241	265	291	310	338	373	398
1503		245	265	288	313	343	387	400
1504x	NP	249	278	307	311	317	322	325
1505		255	275	298	317	343	378	397
1506		258	271	295	312	340	376	389
1507		235	251	269	284	306	347	362
1508		252	275	293	302	323	360	373
1509		255	281	301	322	350	390	405
1510		259	280	301	321	336	389	404
1511		263	284	297	314	338	388	409
1512		266	283	315	332	355	412	427
1513x	NP	238	251	260	259	263	271	277
1514		250	262	289	311	341	382	402
1515		259	277	294	318	347	390	404
1516		263	282	284	305	333	375	392
1517		264	277	306	322	348	383	402
1518		280	300	326	350	375	424	442
1519		284	297	312	333	363	408	427
1520x	NP	229	242	250	254	258	268	260
1521		243	261	286	308	338	383	401
1522		246	259	279	299	319	353	374
1523		257	264	283	296	307	318	319
1524		258	273	298	322	353	405	420
1525		269	282	308	324	353	393	408
MEAN		256	274	295	315	340	381	398
S.D.		13.0	12.5	13.1	14.0	16.4	23.0	25.1
N		22	22	22	22	22	22	22

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX D

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GESTATION BODY WEIGHTS (GRAMS)

GROUP 2 30 PPM

ANIMAL#	DAY OF GESTATION 4	6	10	13	16	19	20
2501	217	231	247	260	279	323	341
2502	238	256	264	287	305	350	367
2503	246	267	289	313	332	381	397
2504x NP	252	263	277	290	286	284	283
2505	252	275	295	318	342	386	403
2506	261	281	306	324	344	374	390
2507	274	299	322	341	367	422	440
2508	242	259	270	283	299	329	340
2509	248	272	303	323	339	371	387
2510	255	272	293	312	346	393	404
2511	259	277	292	316	348	403	426
2512	265	287	310	325	348	378	392
2513	266	291	316	346	369	420	439
2514x NP	238	251	262	264	269	276	274
2515	244	257	274	294	316	362	376
2516	260	274	291	315	340	385	406
2517	263	277	303	320	350	400	419
2518	267	277	294	313	332	355	363
2519	284	298	318	337	363	409	429
2520	236	251	262	281	300	339	356
2521	240	254	264	281	303	344	355
2522	246	264	289	314	328	364	377
2523	250	262	275	298	323	379	391
2524	265	288	306	331	364	419	437
2525	268	287	308	324	348	385	403
MEAN	254	272	291	311	334	377	393
S.D.	14.8	16.5	20.3	21.6	24.2	28.3	30.4
N	23	23	23	23	23	23	23

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX D

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GESTATION BODY WEIGHTS (GRAMS)

GROUP 3 90 PPM

ANIMAL#	DAY OF GESTATION 4	6	10	13	16	19	20
3501	232	251	247	276	298	343	362
3502	236	261	260	281	306	343	360
3503	242	260	271	292	310	352	369
3504	247	268	278	287	309	340	354
3505	252	273	282	298	332	388	402
3506	256	280	297	314	334	382	396
3507	238	257	264	275	297	336	352
3508	250	265	271	291	309	347	362
3509	255	273	276	285	309	348	352
3510	260	282	290	291	313	345	359
3511	262	287	292	309	335	383	399
3512	272	290	292	328	354	384	397
3513	242	254	265	283	308	342	357
3514	256	266	266	274	287	310	319
3515x NP	258	276	284	284	285	274	280
3516	260	272	276	293	326	366	386
3517	270	277	292	307	328	354	367
3518	281	292	308	324	362	413	433
3519	229	248	267	281	306	342	366
3520x NP	243	263	268	262	266	276	278
3521	247	263	282	298	321	363	379
3522	247	263	278	305	341	387	399
3523	257	272	275	298	320	370	383
3524	269	287	302	321	359	399	422
3525	276	297	301	319	336	381	395
MEAN	254	271	280	297	322	362	377
S.D.	14.0	13.5	15.2	16.4	20.1	24.6	26.0
N	23	23	23	23	23	23	23

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX D

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GESTATION BODY WEIGHTS (GRAMS)

GROUP 4 180 PPM

ANIMAL#	DAY OF GESTATION 4	6	10	13	16	19	20
4501	235	254	198	217	266	317	329
4502	240	256	234	263	295	337	357
4503	241	258	226	241	284	341	362
4504	251	274	279	298	334	376	402
4505	254	271	268	301	330	376	391
4506x NP	257	265	250	271	273	283	284
4507	227	244	190	232	261	296	313
4508	252	267	258	287	309	353	367
4509	253	273	254	282	310	360	374
4510	261	284	249	285	314	356	372
4511	262	286	245	293	345	406	414
4512	270	293	269	313	355	409	424
4513	276	298	260	302	345	396	419
4514	243	249	237	264	285	331	346
4515	256	269	261	288	318	356	371
4516	259	276	255	311	343	386	402
4517	261	269	274	295	316	351	362
4518	265	275	285	311	342	393	419
4519	270	285	271	310	344	395	415
4520	228	241	235	265	285	325	340
4521	243	254	209	263	294	337	353
4522	246	258	243	286	310	343	362
4523	248	256	254	282	309	348	367
4524	263	285	290	320	346	393	406
4525	274	286	287	319	339	390	404
MEAN	253	269	251	284	316	361	378
S.D.	13.7	15.7	26.7	27.4	27.1	30.3	31.1
N	24	24	24	24	24	24	24

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX E

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GESTATION BODY WEIGHT GAIN (GRAMS)

GROUP 1 0 PPM

ANIMAL#	DAY OF GESTATION 4 - 6	6 - 10	10 - 13	13 - 16	16 - 20	6 - 20
1501	24	28	26	29	63	145
1502	24	26	19	27	60	133
1503	20	23	25	30	57	135
1504x NP	29	29	5	6	8	47
1505	21	22	20	26	54	121
1506	14	24	17	28	49	117
1507	16	18	15	21	57	112
1508	23	18	9	21	50	98
1509	26	21	21	28	55	124
1510	21	22	19	15	69	125
1511	21	13	18	24	71	125
1512	17	32	17	23	73	144
1513x NP	13	9	-1	4	14	26
1514	12	27	22	30	61	140
1515	18	17	24	29	57	127
1516	19	3	20	29	59	110
1517	13	29	17	26	54	125
1518	20	27	23	26	66	142
1519	14	14	21	30	64	129
1520x NP	14	8	4	4	2	18
1521	18	25	22	30	64	140
1522	14	19	20	20	55	115
1523	7	20	12	12	12	56
1524	14	25	24	31	67	148
1525	13	26	17	29	55	126
MEAN	18	22	20	25	58	124
S.D.	4.7	6.5	4.1	5.1	12.0	19.9
N	22	22	22	22	22	22

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX E

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GESTATION BODY WEIGHT GAIN (GRAMS)

GROUP 2 30 PPM

ANIMAL#	DAY OF GESTATION 4 - 6	6 - 10	10 - 13	13 - 16	16 - 20	6 - 20
2501	14	16	13	19	62	110
2502	18	8	22	18	63	111
2503	21	22	24	19	65	130
2504x NP	11	15	12	-3	-4	20
2505	23	20	23	24	61	128
2506	20	25	18	20	47	109
2507	25	23	19	26	73	140
2508	16	11	13	16	41	81
2509	24	31	20	16	48	114
2510	16	21	20	33	58	132
2511	19	15	24	32	78	149
2512	23	23	15	23	44	105
2513	25	25	30	22	71	148
2514x NP	14	11	2	5	5	23
2515	13	16	21	22	60	118
2516	15	17	24	25	67	132
2517	14	26	17	30	70	143
2518	10	17	18	19	32	86
2519	15	20	18	26	65	130
2520	15	11	19	19	56	105
2521	14	10	17	23	51	101
2522	19	25	25	14	49	113
2523	12	13	23	25	68	129
2524	23	18	25	34	72	149
2525	18	21	16	24	55	116
MEAN	18	19	20	23	59	121
S.D.	4.4	5.8	4.2	5.5	11.6	18.9
N	23	23	23	23	23	23

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX E

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GESTATION BODY WEIGHT GAIN (GRAMS)

GROUP 3 90 PPM

ANIMAL#	DAY OF GESTATION 4 - 6	6 - 10	10 - 13	13 - 16	16 - 20	6 - 20
3501	19	-5	29	23	63	110
3502	26	-1	21	25	54	99
3503	18	12	20	18	59	109
3504	21	10	9	22	46	87
3505	21	10	16	35	69	129
3506	24	18	17	20	62	116
3507	20	7	11	22	56	95
3508	14	7	20	18	53	98
3509	18	3	9	24	44	80
3510	22	8	2	21	46	77
3511	24	6	16	26	64	112
3512	18	2	36	26	43	107
3513	13	10	18	25	48	102
3514	10	1	7	13	32	53
3515x NP	18	8	1	1	-5	4
3516	12	4	17	33	60	114
3517	7	15	16	21	39	90
3518	11	16	17	37	72	142
3519	19	19	14	25	61	118
3520x NP	20	5	-6	3	12	15
3521	16	19	16	24	58	116
3522	16	15	27	36	58	136
3523	15	3	23	21	63	110
3524	19	15	18	39	62	134
3525	22	4	18	17	59	98
MEAN	17	8	17	25	55	106
S.D.	4.9	6.7	7.4	6.8	10.0	20.6
N	23	23	23	23	23	23

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX E

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GESTATION BODY WEIGHT GAIN (GRAMS)

GROUP 4 18(PPM

ANIMAL#		DAY OF GESTATION 4 - 6	6 - 10	10 - 13	13 - 16	16 - 20	6 - 20
4501		20	-57	20	48	63	75
4502		16	-22	29	32	62	101
4503		17	-32	15	43	78	104
4504		23	5	19	36	68	127
4505		17	-3	33	29	61	120
4506x	NP	8	-15	21	2	11	19
4507		17	-54	42	29	53	69
4508		14	-8	29	22	57	100
4509		20	-19	28	28	65	101
4510		23	-35	36	29	58	88
4511		24	-41	48	52	70	128
4512		23	-24	45	42	69	131
4513		22	-38	41	43	75	121
4514		6	-12	26	22	60	96
4515		14	-8	27	30	54	102
4516		17	-21	57	31	59	125
4517		8	5	21	21	46	93
4518		11	10	27	30	78	144
4519		15	-14	38	35	70	130
4520		13	-6	29	20	55	99
4521		11	-46	54	31	59	99
4522		13	-15	43	24	51	103
4523		8	-2	29	27	59	112
4524		22	5	30	26	59	121
4525		12	1	32	21	65	118
MEAN		16	-18	33	31	62	109
S.D.		5.2	19.3	10.9	8.8	8.2	18.4
N		24	24	24	24	24	24

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX F

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GESTATION FEED CONSUMPTION -- (GRAMS/KG/DAY)

GROUP 1 0 PPM

ANIMAL#	DAY OF GESTATION 4 - 6	6 - 10	10 - 13	13 - 16	16 - 20	6 - 20
1501	84	80	93	79	72	81
1502	92	88	83	79	79	82
1503	90	91	89	82	75	84
1504x NP	102	94	88	68	66	79
1505	84	81	82	71	66	75
1506	72	76	75	75	69	74
1507	74	78	82	74	73	77
1508	79	76	74	67	64	70
1509	78	81	82	76	75	79
1510	80	78	78	71	72	75
1511	79	76	75	69	69	72
1512	80	88	84	77	76	81
1513x NP	82	73	71	70	82	74
1514	89	89	85	82	81	84
1515	84	76	79	72	66	73
1516	84	66	74	73	70	71
1517	95	93	86	77	69	81
1518	91	85	85	74	78	81
1519	83	76	76	68	65	71
1520x NP	82	70	72	75	72	72
1521	94	83	84	81	71	80
1522	83	84	81	86	81	83
1523	73	79	79	81	76	79
1524	83	85	88	88	85	87
1525	82	82	82	80	73	79
MEAN	83	81	82	76	73	78
S.D.	6.5	6.2	5.1	5.6	5.6	4.8
N	22	22	22	22	22	22

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX F

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GESTATION FEED CONSUMPTION -- (GRAMS/KG/DAY)

GROUP 2 30 PPM

ANIMAL#		DAY OF GESTATION 4 - 6	6 - 10	10 - 13	13 - 16	16 - 20	6 - 20
2501		79	79	77	74	74	76
2502		75	72	73	61	67	68
2503		86	79	83	70	71	76
2504x	NP	88	81	79	72	63	74
2505		84	80	85	80	78	81
2506		91	86	83	77	74	80
2507		93	86	83	75	79	81
2508		75	70	75	75	71	73
2509		89	86	86	76	77	81
2510		73	74	77	80	79	78
2511		80	78	81	77	79	79
2512		86	80	78	79	75	78
2513		92	89	93	79	77	85
2514x	NP	90	83	79	79	78	80
2515		88	82	84	76	77	80
2516		88	79	84	77	74	79
2517		87	87	86	82	80	84
2518		82	77	82	78	73	77
2519		94	86	89	77	76	82
2520		82	75	72	75	74	74
2521		80	73	77	82	76	77
2522		83	80	85	83	78	81
2523		82	77	82	86	79	81
2524		90	84	82	88	78	83
2525		84	81	82	78	72	78
MEAN		85	80	82	78	76	79
S.D.		5.9	5.2	5.1	5.3	3.2	3.7
N		23	23	23	23	23	23

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX F

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GESTATION FEED CONSUMPTION -- (GRAMS/KG/DAY)

GROUP 3 90 PPM

ANIMAL#	DAY OF GESTATION 4 - 6	6 - 10	10 - 13	13 - 16	16 - 20	6 - 20
3501	95	49	88	86	84	77
3502	81	54	75	72	66	67
3503	85	71	83	76	76	76
3504	85	67	75	73	77	73
3505	85	72	78	76	72	74
3506	82	71	76	77	75	75
3507	92	74	78	79	74	76
3508	80	67	75	67	69	70
3509	76	59	64	69	67	65
3510	96	72	73	77	74	74
3511	84	66	72	76	76	73
3512	88	55	82	68	72	69
3513	91	68	74	70	67	70
3514	79	58	64	68	73	66
3515x NP	97	76	74	64	60	69
3516	81	64	75	83	76	75
3517	87	74	78	76	68	74
3518	80	68	76	78	73	74
3519	85	73	70	82	81	76
3520x NP	110	74	69	81	75	75
3521	86	76	76	74	68	74
3522	87	88	91	95	86	90
3523	92	65	81	85	84	79
3524	85	75	76	80	75	76
3525	90	66	75	77	76	73
MEAN	86	68	76	77	74	74
S.D.	5.2	8.5	6.3	6.6	5.5	5.1
N	23	23	23	23	23	23

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX F

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GESTATION FEED CONSUMPTION -- (GRAMS/KG/DAY)

GROUP 4 180 PPM

ANIMAL#	DAY OF GESTATION 4 - 6	6 - 10	10 - 13	13 - 16	16 - 20	6 - 20
4501	92	20	32	106	98	64
4502	90	51	63	102	82	74
4503	75	32	35	93	91	63
4504	92	80	83	86	79	82
4505	84	51	85	88	84	77
4506x NP	75	34	72	81	84	68
4507	80	17	78	93	81	67
4508	77	51	81	80	70	71
4509	86	48	88	85	79	75
4510	74	32	59	89	78	65
4511	91	39	86	110	89	81
4512	84	50	85	89	77	75
4513	77	34	67	96	84	71
4514	86	47	94	86	81	77
4515	80	54	83	80	77	73
4516	95	52	102	98	84	84
4517	70	63	77	71	68	70
4518	83	67	92	85	81	81
4519	80	50	98	83	74	76
4520	84	44	87	83	81	74
4521	80	19	85	94	81	70
4522	84	47	87	87	80	75
4523	79	47	90	84	74	74
4524	86	58	96	85	79	79
4525	86	61	82	83	83	77
MEAN	83	46	80	89	81	74
S.D.	6.2	15.2	17.4	8.8	6.2	5.7
N	24	24	24	24	24	24

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX G

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL MATERNAL NECROPSY OBSERVATIONS

GROUP 1 0 PPM

ANIMAL#		ORGAN	OBSERVATION
1501			NO REMARKABLE OBSERVATIONS
1502			NO REMARKABLE OBSERVATIONS
1503			NO REMARKABLE OBSERVATIONS
1504	NP	SALEWSKI'S TEST	NO FOCI PRESENT
1505			NO REMARKABLE OBSERVATIONS
1506			NO REMARKABLE OBSERVATIONS
1507			NO REMARKABLE OBSERVATIONS
1508			NO REMARKABLE OBSERVATIONS
1509			NO REMARKABLE OBSERVATIONS
1510		UTERUS	FUSED PLACENTAS 2ND AND 3RD
1511			NO REMARKABLE OBSERVATIONS
1512		UTERUS	ABNORMAL CONTENTS RED GELATINOUS MATERIAL SURROUNDING PLACENTA #4 TISSUE SAVED
1513	NP	EXTERNAL EXAM	ALOPECIA GENERAL EXTERNAL FINDING CONFIRMED
		EXTERNAL EXAM	SCABS-TOP OF HEAD EXTERNAL FINDING CONFIRMED RED, 0.2-0.5CM. IN DIAMETER TISSUE SAVED
		SALEWSKI'S TEST	NO FOCI PRESENT

NP=NOT PREGNANT

APPENDIX G

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL MATERNAL NECROPSY OBSERVATIONS

GROUP 1 0 PPM

ANIMAL#		ORGAN	OBSERVATION
1514			NO REMARKABLE OBSERVATIONS
1515			NO REMARKABLE OBSERVATIONS
1516			NO REMARKABLE OBSERVATIONS
1517			NO REMARKABLE OBSERVATIONS
1518			NO REMARKABLE OBSERVATIONS
1519			NO REMARKABLE OBSERVATIONS
1520	NP	SALEWSKI'S TEST	NO FOCI PRESENT
1521			NO REMARKABLE OBSERVATIONS
1522			NO REMARKABLE OBSERVATIONS
1523			NO REMARKABLE OBSERVATIONS
1524			NO REMARKABLE OBSERVATIONS
1525			NO REMARKABLE OBSERVATIONS

NP=NOT PREGNANT

APPENDIX G

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL MATERNAL NECROPSY OBSERVATIONS

GROUP 2 30 PPM

ANIMAL#		ORGAN	OBSERVATION
2501			NO REMARKABLE OBSERVATIONS
2502			NO REMARKABLE OBSERVATIONS
2503			NO REMARKABLE OBSERVATIONS
2504	NP	SALEWSKI'S TEST	NO FOCI PRESENT
2505			NO REMARKABLE OBSERVATIONS
2506			NO REMARKABLE OBSERVATIONS
2507		KIDNEY	CYSTIC KIDNEY; SLIGHT; LEFT TISSUE SAVED
2508			NO REMARKABLE OBSERVATIONS
2509			NO REMARKABLE OBSERVATIONS
2510			NO REMARKABLE OBSERVATIONS
2511			NO REMARKABLE OBSERVATIONS
2512			NO REMARKABLE OBSERVATIONS
2513			NO REMARKABLE OBSERVATIONS
2514	NP	SALEWSKI'S TEST	NO FOCI PRESENT
2515			NO REMARKABLE OBSERVATIONS
2516			NO REMARKABLE OBSERVATIONS

NP=NOT PREGNANT

APPENDIX G

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL MATERNAL NECROPSY OBSERVATIONS

GROUP 2 30 PPM

ANIMAL#	ORGAN	OBSERVATION
2517		NO REMARKABLE OBSERVATIONS
2518		NO REMARKABLE OBSERVATIONS
2519		NO REMARKABLE OBSERVATIONS
2520		NO REMARKABLE OBSERVATIONS
2521		NO REMARKABLE OBSERVATIONS
2522		NO REMARKABLE OBSERVATIONS
2523		NO REMARKABLE OBSERVATIONS
2524		NO REMARKABLE OBSERVATIONS
2525		NO REMARKABLE OBSERVATIONS

APPENDIX G

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL MATERNAL NECROPSY OBSERVATIONS

GROUP 3 90 PPM

ANIMAL#	ORGAN	OBSERVATION
3501	KIDNEY	DILATED RENAL PELVIS; MODERATE; BILATERAL TISSUE SAVED
3502		NO REMARKABLE OBSERVATIONS
3503		NO REMARKABLE OBSERVATIONS
3504		NO REMARKABLE OBSERVATIONS
3505		NO REMARKABLE OBSERVATIONS
3506		NO REMARKABLE OBSERVATIONS
3507	EXTERNAL EXAM	ALOPECIA GENERAL EXTERNAL FINDING CONFIRMED
3508		NO REMARKABLE OBSERVATIONS
3509		NO REMARKABLE OBSERVATIONS
3510		NO REMARKABLE OBSERVATIONS
3511	EXTERNAL EXAM	ALOPECIA EXTREMITIES/SNOUT EXTERNAL FINDING CONFIRMED
3512	EXTERNAL EXAM	ALOPECIA GENERAL EXTENAL FINDINGS CONFIRMED
3513		NO REMARKABLE OBSERVATIONS
3514		NO REMARKABLE OBSERVATIONS

APPENDIX G

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL MATERNAL NECROPSY OBSERVATIONS

GROUP 3 90 PPM

ANIMAL#		ORGAN	OBSERVATION
3515	NP	SALEWSKI'S TEST	NO FOCI PRESENT
3516			NO REMARKABLE OBSERVATIONS
3517			NO REMARKABLE OBSERVATIONS
3518			NO REMARKABLE OBSERVATIONS
3519			NO REMARKABLE OBSERVATIONS
3520	NP	SALEWSKI'S TEST	NO FOCI PRESENT
3521			NO REMARKABLE OBSERVATIONS
3522			NO REMARKABLE OBSERVATIONS
3523			NO REMARKABLE OBSERVATIONS
3524			NO REMARKABLE OBSERVATIONS
3525			NO REMARKABLE OBSERVATIONS

NP=NOT PREGNANT

APPENDIX G

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL MATERNAL NECROPSY OBSERVATIONS

GROUP 4 180 PPM

ANIMAL#		ORGAN	OBSERVATION
4501		EXTERNAL EXAM	ALOPECIA EXTREMITIES/SNOUT EXTERNAL FINDING CONFIRMED.
4502		EXTERNAL EXAM	SOFT PROTRUSION-MID ABDOMINAL EXTERNAL FINDING NOT CONFIRMED
4503			NO REMARKABLE OBSERVATIONS
4504			NO REMARKABLE OBSERVATIONS
4505			NO REMARKABLE OBSERVATIONS
4506	NP	EXTERNAL EXAM	ALOPECIA EXTREMITIES/SNOUT EXTERNAL FINDING CONFIRMED
		SALEWSKI'S TEST	NO FOCI PRESENT
4507		EXTERNAL EXAM	HOOKED TAIL
4508			NO REMARKABLE OBSERVATIONS
4509			NO REMARKABLE OBSERVATIONS
4510			NO REMARKABLE OBSERVATIONS
4511			NO REMARKABLE OBSERVATIONS
4512			NO REMARKABLE OBSERVATIONS
4513		EXTERNAL EXAM	ALOPECIA GENERAL EXTERNAL FINDING CONFIRMED
4514			NO REMARKABLE OBSERVATIONS

NP=NOT PREGNANT

APPENDIX G

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL MATERNAL NECROPSY OBSERVATIONS

GROUP 4 180 PPM

ANIMAL#	ORGAN	OBSERVATION
4515		NO REMARKABLE OBSERVATIONS
4516		NO REMARKABLE OBSERVATIONS
4517		NO REMARKABLE OBSERVATIONS
4518		NO REMARKABLE OBSERVATIONS
4519	EXTERNAL EXAM	ALOPECIA GENERAL EXTERNAL FINDING CONFIRMED
4520		NO REMARKABLE OBSERVATIONS
4521		NO REMARKABLE OBSERVATIONS
4522		NO REMARKABLE OBSERVATIONS
4523		NO REMARKABLE OBSERVATIONS
4524		NO REMARKABLE OBSERVATIONS
4525		NO REMARKABLE OBSERVATIONS

APPENDIX H

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GRAVID UTERINE WEIGHT AND NET BODY WEIGHT CHANGE (GRAMS)

GROUP 1 0 PPM

ANIMAL#	UTERUS WEIGHT	ADJUSTED WEIGHT[a]	NET WEIGHT CHANGE FROM DAY 6[b]	WEIGHT CHANGE FROM DAY 6[c]
1501	91	310	54	145
1502	84	314	49	133
1503	82	319	53	135
1504x NP	2	323	45	47
1505	90	307	32	121
1506	88	300	29	117
1507	80	283	32	112
1508	75	298	23	98
1509	85	320	39	124
1510	85	319	40	125
1511	100	309	25	125
1512	101	327	44	144
1513x NP	1	276	25	26
1514	81	322	60	140
1515	86	318	40	127
1516	85	307	25	110
1517	83	319	42	125
1518	96	346	46	142
1519	99	327	30	129
1520x NP	0	260	18	18
1521	99	302	41	140
1522	59	316	56	115
1523	10	309	45	56
1524	85	336	63	148
1525	77	331	49	126
MEAN	83.	315.	42.	124.
S.D.	18.9	13.8	11.6	19.9
N	22	22	22	22

[a]ADJUSTED WEIGHT = TERMINAL BODY WEIGHT MINUS GRAVID UTERINE WEIGHT
[b]NET WEIGHT CHANGE FROM DAY 6 = WEIGHT CHANGE FROM DAY 6 MINUS UTERINE WEIGHT
[c]WEIGHT CHANGE FROM DAY 6 = TERMINAL BODY WEIGHT MINUS DAY 6 BODY WEIGHT

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

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APPENDIX H

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GRAVID UTERINE WEIGHT AND NET BODY WEIGHT CHANGE (GRAMS)

GROUP 2 30 PPM

ANIMAL#	UTERUS WEIGHT	ADJUSTED WEIGHT[a]	NET WEIGHT CHANGE FROM DAY 6[b]	WEIGHT CHANGE FROM DAY 6[c]
2501	84	257	26	110
2502	83	284	28	111
2503	92	305	38	130
2504x NP	2	281	18	20
2505	89	314	39	128
2506	69	322	41	109
2507	94	346	46	140
2508	59	281	23	81
2509	63	324	52	114
2510	82	322	50	132
2511	103	322	45	149
2512	61	331	44	105
2513	98	341	50	148
2514x NP	1	273	22	23
2515	85	290	33	118
2516	96	310	36	132
2517	93	326	50	143
2518	38	325	48	86
2519	95	334	36	130
2520	63	293	42	105
2521	71	283	30	101
2522	54	323	59	113
2523	87	304	42	129
2524	105	332	44	149
2525	83	319	33	116
MEAN	80.	313.	41.	121.
S.D.	17.5	22.0	9.1	18.9
N	23	23	23	23

[a] ADJUSTED WEIGHT = TERMINAL BODY WEIGHT MINUS GRAVID UTERINE WEIGHT
[b] NET WEIGHT CHANGE FROM DAY 6 = WEIGHT CHANGE FROM DAY 6 MINUS UTERINE WEIGHT
[c] WEIGHT CHANGE FROM DAY 6 = WEIGHT CHANGE FROM DAY 6 MINUS UTERINE WEIGHT

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX H

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GRAVID UTERINE WEIGHT AND NET BODY WEIGHT CHANGE (GRAMS)

GROUP 3 90 PPM

ANIMAL#		UTERUS WEIGHT	ADJUSTED WEIGHT [a]	NET WEIGHT CHANGE FROM DAY 6 [b]	WEIGHT CHANGE FROM DAY 6 [c]
3501		86	276	25	110
3502		91	269	7	99
3503		82	287	27	109
3504		67	288	20	87
3505		110	292	19	129
3506		87	309	29	116
3507		76	276	19	95
3508		78	285	20	98
3509		86	267	-6	80
3510		66	293	11	77
3511		88	310	24	112
3512		86	311	21	107
3513		82	275	20	102
3514		30	289	23	53
3515x	NP	1	278	2	4
3516		85	301	29	114
3517		70	297	21	90
3518		103	331	39	142
3519		62	304	56	118
3520x	NP	1	277	14	15
3521		81	298	35	116
3522		82	317	54	136
3523		89	294	21	110
3524		97	324	37	134
3525		85	310	13	98
MEAN		81.	296.	25.	106.
S.D.		15.8	17.3	13.6	20.6
N		23	23	23	23

[a]ADJUSTED WEIGHT = TERMINAL BODY WEIGHT MINUS GRAVID UTERINE WEIGHT
[b]NET WEIGHT CHANGE FROM DAY 6 = WEIGHT CHANGE FROM DAY 6 MINUS UTERINE WEIGHT
[c]WEIGHT CHANGE FROM DAY 6 = WEIGHT CHANGE FROM DAY 6 MINUS UTERINE WEIGHT

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX H

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GRAVID UTERINE WEIGHT AND NET BODY WEIGHT CHANGE (GRAMS)

GROUP 4 180 PPM

ANIMAL#	UTERUS WEIGHT	ADJUSTED WEIGHT[a]	NET WEIGHT CHANGE FROM DAY 6[b]	WEIGHT CHANGE FROM DAY 6[c]
4501	59	269	15	75
4502	88	269	13	101
4503	85	277	19	104
4504	90	312	38	127
4505	73	318	47	120
4506x NP	2	282	17	19
4507	56	257	13	69
4508	80	287	20	100
4509	86	288	15	101
4510	74	298	14	88
4511	100	314	28	128
4512	101	323	30	131
4513	95	324	26	121
4514	78	267	18	96
4515	75	296	27	102
4516	73	328	52	125
4517	67	296	27	93
4518	92	327	52	144
4519	95	320	35	130
4520	64	276	34	99
4521	72	281	26	99
4522	62	299	41	103
4523	79	289	33	112
4524	82	324	39	121
4525	67	337	51	118
MEAN	79.	299.	30.	109.
S.D.	12.7	23.2	12.6	18.4
N	24	24	24	24

[a]ADJUSTED WEIGHT = TERMINAL BODY WEIGHT MINUS GRAVID UTERINE WEIGHT
[b]NET WEIGHT CHANGE FROM DAY 6 = WEIGHT CHANGE FROM DAY 6 MINUS UTERINE WEIGHT
[c]WEIGHT CHANGE FROM DAY 6 = WEIGHT CHANGE FROM DAY 6 MINUS UTERINE WEIGHT

NP=NOT PREGNANT x=EXCLUDED FROM MEAN

APPENDIX I

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FEMALE REPRODUCTION DATA AND MEAN FETAL WEIGHTS (GRAMS)

GROUP 1 0 PPM

ANIMAL#	CORPORA LUTEA	%PREIMPL. LOSS	IMPLANT SITES	FETUSES LIVE	FETUSES DEAD (n)	FETUSES DEAD %	RESORPTIONS EARLY	RESORPTIONS LATE	RESORPTIONS TOTAL (n)	RESORPTIONS TOTAL %	SEX MALE	SEX FEMALE	AVERAGE FETAL BODY WEIGHT MALES	AVERAGE FETAL BODY WEIGHT FEMALES	AVERAGE FETAL BODY WEIGHT LITTER
1501	16	6.3	15	15	0	0.0	0	0	0	0.0	5	10	4.0	3.7	3.8
1502	14	0.0	14	14	0	0.0	0	0	0	0.0	6	8	3.9	3.6	3.7
1503	14	14.3	12	12	0	0.0	0	0	0	0.0	7	5	4.3	4.1	4.2
1504	NP														
1505	15	6.7	14	14	0	0.0	0	0	0	0.0	6	8	4.2	4.2	4.2
1506	15	6.7	14	14	0	0.0	0	0	0	0.0	8	6	4.0	3.8	3.9
1507	16	18.8	13	13	0	0.0	0	0	0	0.0	8	5	4.1	3.6	3.9
1508	13	0.0	13	12	0	0.0	1	0	1	7.7	4	8	3.7	3.7	3.7
1509	16	6.3	15	14	0	0.0	1	0	1	6.7	5	9	3.8	3.7	3.7
1510	16	12.5	14	14	0	0.0	0	0	0	0.0	6	8	3.7	3.8	3.7
1511	16	0.0	16	16	0	0.0	0	0	0	0.0	7	9	4.3	3.9	4.1
1512	15	0.0	15	14	0	0.0	1	0	1	6.7	5	9	4.7	4.4	4.5
1513	NP														
1514	16	12.5	14	14	0	0.0	0	0	0	0.0	5	9	3.7	3.6	3.6
1515	16	6.3	15	14	0	0.0	1	0	1	6.7	7	7	3.8	3.8	3.8
1516	14	0.0	14	14	0	0.0	0	0	0	0.0	5	5	3.9	3.6	3.8
1517	14	0.0	14	13	0	0.0	1	0	1	7.1	10	3	3.9	4.0	4.0
1518	15	0.0	15	15	0	0.0	0	0	0	0.0	9	6	4.2	3.9	4.1
1519	18	5.6	17	17	0	0.0	0	0	0	0.0	9	8	3.8	3.6	3.7
1520	NP														
1521	18	5.6	17	17	0	0.0	0	0	0	0.0	6	11	4.0	3.8	3.8
1522	14	7.1	13	13	0	0.0	0	0	0	0.0	7	6	2.3	2.4	2.3
1523	11	90.9	1	1	0	0.0	0	0	0	0.0	1	0	4.9	-	4.9
1524	14	0.0	14	14	0	0.0	0	0	0	0.0	8	6	3.9	4.0	3.9
1525	13	7.7	12	12	0	0.0	0	0	0	0.0	6	6	4.2	4.0	4.1
MEAN	15.0	9.4	13.7	13.5	0.0	0.0	0.2	0.0	0.2	1.6	6.5	6.9	4.0	3.8	3.9
S.D.	1.62	18.98	3.12	3.10	0.00	0.00	0.43	0.00	0.43	2.99	2.02	2.47	0.49	0.39	0.46
N	22	22	22	22	22	22	22	22	22	22	22	22	22	21	22

NP=NOT PREGNANT

APPENDIX I

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FEMALE REPRODUCTION DATA AND MEAN FETAL WEIGHTS (GRAMS)

GROUP 2 30 PPM

ANIMAL#	CORPORA LUTEA	%PREIMPL. LOSS	IMPLANT SITES	FETUSES LIVE	FETUSES DEAD (n)	FETUSES DEAD %	RESORPTIONS EARLY	RESORPTIONS LATE	RESORPTIONS TOTAL (n)	RESORPTIONS TOTAL %	SEX MALE	SEX FEMALE	AVERAGE FETAL BODY WEIGHT MALES	AVERAGE FETAL BODY WEIGHT FEMALES	AVERAGE FETAL BODY WEIGHT LITTER
2501	13	0.0	13	13	0	0.0	0	0	0	0.0	6	7	4.1	3.8	3.9
2502	14	0.0	14	14	0	0.0	0	0	0	0.0	4	10	3.8	3.5	3.6
2503	17	11.8	15	15	0	0.0	0	0	0	0.0	7	8	4.2	4.0	4.1
2504	NP														
2505	16	12.5	14	14	0	0.0	0	0	0	0.0	7	7	3.9	3.7	3.8
2506	12	8.3	11	11	0	0.0	0	0	0	0.0	6	5	4.0	3.9	4.0
2507	17	5.9	16	16	0	0.0	0	0	0	0.0	5	9	3.7	3.6	3.6
2508	12	8.3	11	10	0	0.0	1	0	1	9.1	5	5	3.6	3.2	3.4
2509	12	0.0	12	9	0	0.0	3	0	3	25.0	[illegible]	6	3.7	3.9	3.9
2510	14	7.1	13	13	0	0.0	0	0	0	0.0	10	3	3.9	3.5	3.8
2511	17	5.9	16	16	0	0.0	0	0	0	0.0	11	5	4.1	3.9	4.0
2512	18	5.6	17	9	0	0.0	8	0	8	47.1	6	3	4.1	4.0	4.1
2513	17	11.8	15	15	0	0.0	0	0	0	0.0	5	10	4.2	4.1	4.1
2514	NP														
2515	13	0.0	13	13	0	0.0	0	0	0	0.0	3	5	4.1	3.9	4.0
2516	14	0.0	14	14	0	0.0	0	0	0	0.0	7	7	4.4	4.2	4.3
2517	18	16.7	15	15	0	0.0	0	0	0	0.0	5	10	4.1	3.9	4.0
2518	13	0.0	13	5	0	0.0	8	0	8	61.5	2	3	4.4	4.0	4.2
2519	17	0.0	17	16	0	0.0	1	0	1	5.9	8	8	3.9	3.6	3.7
2520	15	6.7	14	14	0	0.0	0	0	0	0.0	5	9	2.3	2.3	2.3
2521	13	0.0	13	11	0	0.0	2	0	2	15.4	5	6	4.2	3.8	4.0
2522	13	7.7	12	11	0	0.0	1	0	1	8.3	4	7	2.6	2.4	2.5
2523	14	7.1	13	13	0	0.0	0	0	0	0.0	7	6	4.4	4.3	4.3
2524	18	5.6	17	17	0	0.0	0	0	0	0.0	8	9	4.0	3.8	3.9
2525	15	6.7	14	13	0	0.0	1	0	1	7.1	6	7	4.0	4.0	4.0
MEAN	14.9	5.5	14.0	12.9	0.0	0.0	1.1	0.0	1.1	7.8	6.2	6.7	3.9	3.7	3.8
S.D.	2.12	4.88	1.78	2.83	0.00	0.00	2.31	0.00	2.31	16.10	2.08	2.20	0.52	0.48	0.50
N	23	23	23	23	23	23	23	23	23	23	23	23	23	23	23

NP=NOT PREGNANT

APPENDIX I

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FEMALE REPRODUCTION DATA AND MEAN FETAL WEIGHTS (GRAMS)

GROUP 3 90 PPM

ANIMAL#	CORPORA LUTEA	%PREIMPL. LOSS	IMPLANT SITES	FETUSES LIVE	FETUSES DEAD (n)	FETUSES DEAD %	RESORPTIONS EARLY	RESORPTIONS LATE	RESORPTIONS TOTAL (n)	RESORPTIONS TOTAL %	SEX MALE	SEX FEMALE	AVERAGE FETAL BODY WEIGHT MALES	AVERAGE FETAL BODY WEIGHT FEMALES	AVERAGE FETAL BODY WEIGHT LITTER
3501	17	11.8	15	15	0	0.0	0	0	0	0.0	6	9	3.8	3.7	3.7
3502	17	0.0	17	17	0	0.0	0	0	0	0.0	9	8	3.5	3.3	3.4
3503	15	0.0	15	14	0	0.0	1	0	1	6.7	8	6	3.7	3.6	3.7
3504	15	13.3	13	10	0	0.0	3	0	3	23.1	5	5	4.2	4.2	4.2
3505	17	0.0	17	17	0	0.0	0	0	0	0.0	6	11	4.0	3.9	3.9
3506	14	0.0	14	14	0	0.0	0	0	0	0.0	5	9	4.2	3.8	4.0
3507	13	0.0	13	12	0	0.0	1	0	1	7.7	7	5	4.2	3.9	4.1
3508	13	0.0	13	13	0	0.0	0	0	0	0.0	4	9	3.7	3.6	3.6
3509	16	6.3	15	15	0	0.0	0	0	0	0.0	6	9	4.0	3.6	3.8
3510	13	0.0	13	11	0	0.0	2	0	2	15.4	5	6	3.6	3.5	3.5
3511	15	0.0	15	14	0	0.0	1	0	1	6.7	7	7	4.2	4.0	4.1
3512	17	5.9	16	15	0	0.0	1	0	1	6.3	9	6	3.7	3.2	3.5
3513	14	7.1	13	13	0	0.0	0	0	0	0.0	6	7	4.2	3.9	4.0
3514	16	43.8	9	5	0	0.0	4	0	4	44.4	2	3	2.3	2.6	2.5
3515	NP														
3516	15	6.7	14	14	0	0.0	0	0	0	0.0	6	8	3.9	3.8	3.9
3517	16	6.3	15	10	0	0.0	5	0	5	33.3	5	5	4.6	4.3	4.5
3518	17	0.0	17	17	0	0.0	0	0	0	0.0	8	9	4.0	3.8	3.9
3519	15	6.7	14	14	0	0.0	0	0	0	0.0	7	7	2.3	2.3	2.3
3520	NP														
3521	15	6.7	14	13	0	0.0	1	0	1	7.1	8	5	3.8	4.0	3.9
3522	16	12.5	14	13	0	0.0	1	0	1	7.1	7	6	4.2	3.9	4.0
3523	15	0.0	15	14	0	0.0	1	0	1	6.7	8	6	4.0	3.9	4.0
3524	18	0.0	18	16	0	0.0	2	0	2	11.1	9	7	4.0	3.8	3.9
3525	13	0.0	13	13	0	0.0	0	0	0	0.0	8	5	4.2	3.8	4.0
MEAN	15.3	5.5	14.4	13.4	0.0	0.0	1.0	0.0	1.0	7.6	6.6	6.9	3.8	3.7	3.8
S.D.	1.49	9.50	1.90	2.68	0.00	0.00	1.38	0.00	1.38	11.62	1.75	1.89	0.55	0.47	0.50
N	23	23	23	23	23	23	23	23	23	23	23	23	23	23	23

NP=NOT PREGNANT

APPENDIX I

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FEMALE REPRODUCTION DATA AND MEAN FETAL WEIGHTS (GRAMS)

GROUP 4 180 PPM

ANIMAL#	CORPORA LUTEA	%PREIMPL. LOSS	IMPLANT SITES	FETUSES LIVE	FETUSES DEAD (n)	FETUSES DEAD %	RESORPTIONS EARLY	RESORPTIONS LATE	RESORPTIONS TOTAL (n)	RESORPTIONS TOTAL %	SEX MALE	SEX FEMALE	AVERAGE FETAL BODY WEIGHT MALES	AVERAGE FETAL BODY WEIGHT FEMALES	AVERAGE FETAL BODY WEIGHT LITTER
4501	13	7.7	12	12	0	0.0	0	0	0	0.0	5	7	2.8	2.8	2.8
4502	16	6.3	15	15	0	0.0	0	0	0	0.0	5	10	3.5	3.6	3.6
4503	15	0.0	15	14	0	0.0	0	1	1	6.7	8	6	3.8	3.4	3.6
4504	16	6.3	15	15	0	0.0	0	0	0	0.0	11	4	3.8	3.5	3.7
4505	12	0.0	12	12	0	0.0	0	0	0	0.0	5	7	3.5	3.4	3.5
4506	NP														
4507	13	15.4	11	10	0	0.0	1	0	1	9.1	6	4	3.6	3.4	3.5
4508	13	0.0	13	13	0	0.0	0	0	0	0.0	7	6	3.7	3.6	3.7
4509	17	5.9	16	15	0	0.0	1	0	1	6.3	4	11	3.2	3.0	3.0
4510	15	6.7	14	13	0	0.0	1	0	1	7.1	1	12	3.8	3.6	3.6
4511	19	0.0	19	17	0	0.0	2	0	2	10.5	6	11	3.2	3.1	3.2
4512	17	0.0	17	17	0	0.0	0	0	0	0.0	10	7	3.8	3.5	3.7
4513	15	0.0	15	15	0	0.0	0	0	0	0.0	8	7	4.0	3.9	3.9
4514	13	0.0	13	13	0	0.0	0	0	0	0.0	7	6	3.8	3.7	3.8
4515	14	7.1	13	12	0	0.0	1	0	1	7.7	8	4	3.9	3.7	3.9
4516	14	7.1	13	12	0	0.0	1	0	1	7.7	6	6	3.6	3.5	3.6
4517	11	0.0	11	11	0	0.0	0	0	0	0.0	6	5	3.9	3.6	3.7
4518	16	6.3	15	14	0	0.0	1	0	1	6.7	5	9	4.3	3.9	4.1
4519	16	0.0	16	16	0	0.0	0	0	0	0.0	11	5	3.6	3.4	3.6
4520	14	0.0	14	14	0	0.0	0	0	0	0.0	5	9	2.6	2.4	2.5
4521	15	6.7	14	14	0	0.0	0	0	0	0.0	4	9	3.3	3.1	3.2
4522	15	0.0	15	15	0	0.0	0	0	0	0.0	5	10	2.2	2.1	2.1
4523	19	10.5	17	13	0	0.0	4	0	4	23.5	5	8	3.8	3.5	3.6
4524	15	6.7	14	14	0	0.0	0	0	0	0.0	8	6	3.6	3.5	3.5
4525	14	0.0	14	14	0	0.0	0	0	0	0.0	8	6	2.4	2.4	2.4
MEAN	14.9	3.9	14.3	13.8	0.0	0.0	0.5	0.0	0.5	3.6	6.4	7.3	3.5	3.3	3.4
S.D.	1.96	4.36	1.92	1.75	0.00	0.00	0.93	0.20	0.93	5.68	2.32	2.35	0.52	0.47	0.50
N	24	24	24	24	24	24	24	24	24	24	24	24	24	24	24

NP=NOT PREGNANT

APPENDIX J

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL BODY WEIGHTS (GRAMS)

GROUP 1 0 PPM

FEMALE#	MEAN	FETUS# 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
1501	3.8	4.1	4.0	3.8	3.7	3.6	3.8/	3.7	3.8	3.9	3.8	4.2	4.0	3.7	3.9	3.4				
1502	3.7	3.5	3.7	4.0	4.1/	4.1	3.5	3.7	3.2	3.3	3.7	3.6	3.7	3.9	3.9					
1503	4.2	4.2	4.4	4.5	4.0/	4.0	4.2	4.3	4.0	4.3	4.0	4.5	4.4							
1504	NP																			
1505	4.2	4.2	4.1	4.4	4.1	4.1/	4.3	4.5	4.1	4.3	4.5	4.2	4.0	4.0	4.1					
1506	3.9	3.5	4.0	4.0	3.8	3.9	4.2/	3.8	3.6	4.0	4.1	3.7	4.2	4.2	3.6					
1507	3.9	4.1	4.0	4.2	3.7	4.0	3.8	3.9/	4.2	3.9	4.3	3.4	3.7	3.4						
1508	3.7	3.7	3.1	4.0	3.6	3.5	3.4	3.7/	3.9	3.7	E	4.0	3.8	3.5						
1509	3.7	3.2	3.6	3.7	3.9	E	3.7	4.1/	3.6	3.9	3.6	3.6	3.7	3.9	4.1	3.6				
1510	3.7	3.1	3.6	3.1	3.8	3.9	3.9	4.2	3.9	3.4	3.6	4.2/	4.1	4.1	3.5					
1511	4.1	3.9	4.0	4.4	4.0	4.3	3.9	4.0	3.8/	3.8	3.8	4.0	4.4	4.4	4.0	3.9	4.5			
1512	4.5	4.8	4.3	5.1	4.7	4.5	4.4/	4.4	E	4.6	4.2	4.5	4.5	4.4	4.2	4.5				
1513	NP																			
1514	3.6	3.3	3.8	3.5	3.7	3.6	3.5	3.6/	3.6	4.0	3.9	3.7	3.6	3.5	3.6					
1515	3.8	E	3.9	3.7	3.1	3.8	4.2	4.0	3.8	4.3/	3.9	3.9	3.8	3.0	4.0	3.7				
1516	3.8	3.6	3.8	3.7	3.6	3.8	4.2	3.4/	4.1	4.1	3.6	4.0	4.3	4.2	3.3					
1517	4.0	E	4.3	4.2	4.0	4.0/	4.2	4.1	4.2	3.8	3.9	4.3	3.9	3.7	2.8					
1518	4.1	4.4	3.8	4.2	3.8	4.3	4.1	4.4/	4.2	4.1	4.1	3.9	4.2	3.8	3.8	4.0				
1519	3.7	3.8	3.6	4.2	3.5	3.5	3.7	3.7	3.6	3.9	3.9/	3.5	3.4	4.0	3.7	3.8	3.9	3.6		
1520	NP																			
1521	3.8	3.9	3.5	3.7	3.8	3.5	3.7	3.8	3.9	3.5	4.2/	4.1	3.9	3.7	4.2	3.8	3.8	4.2		
1522	2.5	2.1/	2.5	2.5	2.4	2.5	2.4	2.1	2.3	2.4	2.5	2.1	2.0	2.2						
1523	4.0	4.9/																		
1524	3.9	3.8	3.7	3.9	3.9	3.9	4.0	4.0/	4.0	4.3	4.1	3.9	4.0	4.0	3.7					
1525	4.1	3.7	3.9	4.3	4.1	4.4	4.5	4.1	4.0/	4.1	4.3	4.0	4.0							
MEAN	3.9																			
S.D.	0.45																			
N	22																			

E-Early resorption
/-Denotes position of cervix

NP=NOT PREGNANT

Huntingdon Life Sciences 04-4261

APPENDIX J

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL BODY WEIGHTS (GRAMS)

GROUP 2 30 PPM

FEMALE#	MEAN	FETUS# 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
2501	3.[illegible]	4.2	3.6	3.9	4.1	3.6	4.0/	3.9	4.3	3.9	3.8	4.0	4.2	3.6						
2502	3.[illegible]	3.5	3.8	3.8	3.4	3.6/	3.6	3.8	3.8	3.8	3.1	3.3	3.7	3.5	3.4					
2503	4.1	4.0	3.9	4.0	4.1	4.2	4.0	3.9/	4.1	4.4	3.9	3.9	4.3	4.2	4.3	3.8				
2504	NP																			
2505	3.8	4.0	3.8	3.9	4.0	3.7	3.7	4.0/	3.5	3.6	4.1	3.9	3.7	3.9	3.5					
2506	4.[illegible]	3.6	4.0	4.1	3.9	3.7	4.1/	3.7	4.0	4.3	4.2	3.9								
2507	3.6	3.5	3.6	3.7	3.9	3.7	3.7/	3.3	3.7	3.4	3.6	3.8	3.8	3.6	3.6	3.7	3.5			
2508	3.[illegible]	3.4	3.0	3.2	3.0	3.6	3.5	E	3.5/	3.6	3.6	3.7								
2509	3.[illegible]	3.8	3.5	E	3.8	E	E /	3.7	4.1	4.0	3.9	3.9	4.0							
2510	3.8	3.6	4.1	3.8	3.7	3.8	3.2	3.9/	3.7	4.2	4.1	4.1	4.0	3.7						
2511	3.[illegible]	3.6	3.5	4.1	4.2	3.8	4.1	3.8	4.5/	0.1	4.1	3.9	4.5	4.3	4.2	4.0	3.9			
2512	4.1	4.3	E	E	3.9	E	3.9/	3.6	4.0	4.4	4.0	E	E	4.3	E	4.2	E	E		
2513	4.[illegible]	4.1	3.6	4.3	4.4	4.1	4.3/	4.1	4.4	4.4	4.3	3.9	4.1	4.1	4.0	4.0				
2514	NP																			
2515	4.[illegible]	4.2	3.7	4.2	3.7	4.3	4.3	4.0	3.9	3.9	4.0/	4.3	3.9	4.1						
2516	4.3	4.7	3.8	4.3	4.4	4.1	4.4	4.4/	4.2	4.3	4.4	4.5	4.3	4.3	4.3					
2517	4.0	4.0	3.9	4.0	3.9	3.8	3.7	3.8	3.8	3.9	3.8	4.2/	4.5	3.8	4.1	4.3				
2518	4.[illegible]	4.3	E	E /	E	E	4.7	3.9	E	E	E	E	3.8	4.2						
2519	3.[illegible]	E	3.8	3.7	3.9	3.5	4.0	3.6	3.4	3.9	4.1/	3.7	3.8	4.0	3.5	3.7	3.5	3.6		
2520	2.[illegible]	2.3	2.3	2.2	2.1	2.3	2.5	2.3	2.3	2.5/	2.3	2.3	2.2	2.3	2.2					
2521	4.0	3.7	3.9	4.4	3.7	4.2	E /	3.9	4.0	4.2	4.2	4.2	E	3.1						
2522	2.[illegible]	2.5	2.3	2.4	2.4	2.5	2.6/	E	2.6	2.7	2.4	2.3	2.6							
2523	4.3	4.5	4.4	4.1	4.2	4.2/	4.4	4.2	4.3	4.4	4.3	4.6	4.2	4.6						
2524	3.9	3.8	3.6	3.8	4.2	4.1	3.7	3.9	3.6	4.0/	4.4	3.9	3.9	3.9	3.9	3.8	4.0	3.6		
2525	4.0	3.9	3.9	3.8	4.1	3.3	E /	4.4	4.0	3.9	4.1	4.2	3.9	4.1	3.7					

MEAN	3.8
S.D.	0.50
N	23

E-Early resorption
/-Denotes position of cervix

NP=NOT PREGNANT

Huntingdon Life Sciences 04-4261

APPENDIX J

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL BODY WEIGHTS (GRAMS)

GROUP 3 90 PPM

FEMALE#	MEAN	FETUS# 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
3501	3.7	3.5	3.6	3.8	3.8	3.7	3.7/	3.8	4.0	3.8	3.6	3.7	3.9	3.7	3.8	3.8				
3502	3.4	2.8	3.6	3.4	3.4	3.5	3.5	2.8/	3.6	3.5	3.4	3.5	3.5	3.4	3.2	3.6	3.6	3.4		
3503	3.7	3.5	3.7	E	3.5	3.5	3.7	3.8	3.3/	3.9	3.7	3.8	3.8	4.0	3.5	3.6				
3504	4.2	E	4.1	4.3	4.6	4.0	4.0	E	E /	4.1	4.1	4.3	4.5	4.1						
3505	3.9	3.8	3.9	3.8	3.8	3.8	4.0	3.9	4.0/	4.0	4.1	4.1	3.9	3.9	4.0	4.0	3.9	4.2		
3506	4.0	3.7	4.0	4.0	3.9	3.9	3.7	4.3	3.8/	4.2	3.4	4.3	4.0	4.2	3.9					
3507	4.1	4.2	4.4	4.3	E	4.0	4.0/	3.9	3.8	3.7	4.0	4.2	4.1	4.1						
3508	3.6	3.4	3.8	3.7	3.9	3.7	4.0	3.3/	3.7	3.7	3.3	3.4	4.0	3.2						
3509	3.8	3.9	4.0	3.5	4.2	3.9	3.8	3.8	3.9/	3.8	3.2	3.6	3.8	3.8	4.1	3.4				
3510	3.5	3.6	3.5	3.6	3.4	E /	3.5	3.6	3.7	E	4.0	3.6	3.3	3.2						
3511	4.1	3.7	4.0	4.2	4.3	E	4.1	4.2	4.5/	4.1	4.1	4.1	3.9	4.4	4.1	4.1				
3512	3.5	3.0	3.2	3.5	3.2	3.0	3.7/	3.5	3.7	3.3	3.3	E	3.6	3.8	4.0	4.1	3.5			
3513	4.0	4.1	4.1	4.1	3.8	3.8	4.2/	4.1	4.2	3.9	4.2	3.9	4.2	3.9						
3514	2.5	E	E	2.6/	2.6	E	2.6	1.6	2.9	E										
3515	NP																			
3516	3.9	3.6	4.0	4.0	3.8	3.7	4.1	4.1	4.1/	3.9	3.8	4.0	3.6	3.7	3.6					
3517	4.5 /	3.9	4.6	4.3	4.5	E	4.5	4.7	5.1	4.3	E	4.4	E	E	4.6	E				
3518	3.9	3.9	4.0	3.4	4.1	3.8	3.8	3.7	4.0/	4.2	4.0	4.2	3.7	3.9	4.1	3.8	3.7	3.7		
3519	2.3	2.2	2.4	2.3	2.3/	2.2	2.1	2.2	2.3	2.3	2.2	2.4	2.4	2.1	2.3					
3520	NP																			
3521	3.9	3.2	3.7	3.9	3.9	4.0	4.0	3.8	4.3/	4.1	E	4.3	4.3	3.8	2.9					
3522	4.0	3.9	4.0	3.9	4.0	4.2	4.2	3.9	4.1	3.6	4.4/	3.6	4.2	4.4	E					
3523	4.0	4.0	4.1	4.1	E	3.6	3.9	4.0	4.0	4.0	3.8	4.3/	3.8	3.8	3.8	4.2				
3524	3.9	4.2	3.5	3.8	4.0	3.6	4.1	4.0	4.0	4.3/	3.6	3.7	3.6	4.1	3.9	E	E	4.0	4.0	
3525	4.0	4.3	4.4	4.1	4.1	3.9/	3.1	3.5	4.2	4.3	3.7	4.4	4.3	4.0						

MEAN 3.8
S.D. 0.50
N 23

E-Early resorption
/-Denotes position of cervix

NP=NOT PREGNANT

Huntingdon Life Sciences 04-4261

APPENDIX J

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL BODY WEIGHTS (GRAMS)

GROUP 4 180 PPM

FEMALE#	MEAN	FETUS# 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
4501	2.8	2.6	2.8	2.9	2.8	2.7/	2.9	2.8	2.9	2.7	3.0	2.9	2.5							
4502	3.6	3.0	3.4	3.3	3.6	3.6	3.4	3.5	3.5	3.6	3.6/	3.7	3.7	3.9	3.8	3.7				
4503	3.6	2.8	3.9	2.7	4.0	3.9	3.3	3.8	3.7	L /	3.8	3.6	3.8	3.6	4.0	3.6				
4504	3.7	3.4	3.4	3.2	3.8	3.7	3.6	4.0	3.9	3.5	3.6/	4.2	3.9	3.6	3.8	3.9				
4505	3.5	3.2	3.5	3.7	3.4	3.4	2.9/	3.4	3.6	4.0	3.5	3.7	3.4							
4506	NP																			
4507	3.5	3.4	3.3	3.5	4.2	E /	3.4	3.7	3.5	3.5	3.5	3.2								
4508	3.7	3.8	3.9	3.7	3.4	3.5	3.7	3.4	3.6/	3.6	3.6	3.8	3.6	3.9						
4509	3.0	3.0	3.3	3.0	2.9	3.0	3.1	3.1	2.9/	2.9	2.7	3.1	3.0	3.5	E	3.3	2.8			
4510	3.6	3.4	E	3.6	3.8	3.6	3.5	3.7	3.3/	3.6	3.6	3.6	3.4	3.7	3.6					
4511	3.2	E	E	3.4	3.3	3.1	3.1	3.2	3.0	2.6/	3.4	3.5	3.3	3.2	2.8	3.4	2.6	3.3	3.3	3.3
4512	3.7	3.5	3.5	3.6	3.9	3.8	3.9	4.0/	3.8	3.9	3.4	4.0	3.7	3.0	3.4	3.8	3.9	3.7		
4513	3.9	3.8	3.6	4.0	3.8	3.9	3.9/	3.9	4.1	3.7	3.8	4.3	3.9	3.9	4.0	4.3				
4514	3.8	3.8	3.9	3.8	3.9	3.8	3.8	3.8/	3.8	3.6	4.0	3.7	3.6	3.5						
4515	3.9	4.0	3.5	3.8	3.8	3.5	4.1	3.9/	4.0	E	3.8	3.9	4.2	3.8						
4516	3.6	3.4	3.6	3.5	3.5	E	3.5	3.5/	3.3	3.3	3.6	3.8	4.1	3.6						
4517	3.[illegible]	4.0	3.7	3.8	3.7	3.7	3.9	2.9/	3.9	3.7	3.9	3.8								
4518	4.[illegible]	4.1	3.8	4.2	4.3	4.0	4.3	3.7	4.1/	4.3	4.6	4.4	3.6	E	4.0	3.7				
4519	3.[illegible]	3.3	3.3	3.9	3.6	3.8	3.2	3.4	3.6	3.5/	3.8	3.7	3.7	3.5	3.7	3.5	3.6			
4520	2.5	2.4	2.4	2.5	2.6	2.7	2.5	2.3	2.5	2.4/	2.5	2.3	2.6	2.4	2.7					
4521	3.[illegible]	3.2	3.2	3.1	3.3	3.2	3.4/	3.2	3.1	3.0	3.4	3.1	3.2	3.2	3.0					
4522	2.[illegible]	2.1	2.0	2.2	2.1	2.3	2.0/	2.1	2.0	2.1	2.1	1.9	2.2	1.9	2.2	2.2				
4523	3.6	E	E	3.4	3.3	3.8	3.4	3.2	3.4	4.0	3.4	4.0/	3.9	3.9	3.8	3.5	E	E		
4524	3.5	3.5	3.7	3.8	3.9/	3.4	3.4	3.9	3.6	3.5	3.3	3.4	3.0	3.6	3.6					
4525	2.[illegible]	2.6	2.4	2.2	2.6	2.6	2.5	2.5	2.2	2.3	2.3	2.1/	2.3	2.5	2.6					

MEAN 3.[illegible]
S.D. 0.50
N 2[illegible]

E-Early resorption
/-Denotes position of cervix

NP=NOT PREGNANT

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
1501	1 M			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS
1502	1 F			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
1503	1 M			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
1503	(CONTINUED)			
	4 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
1505	1 F			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
1506	1 F			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
1506	(CONTINUED)			
	10 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
1507	1 M			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
1508	1 M			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS OBSERVATION
1509	1 M		WITHIN NORMAL LIMITS
	2 F		WITHIN NORMAL LIMITS
	3 F		WITHIN NORMAL LIMITS
	4 F		WITHIN NORMAL LIMITS
	6 M		WITHIN NORMAL LIMITS
	7 M		WITHIN NORMAL LIMITS
	8 F		WITHIN NORMAL LIMITS
	9 M		WITHIN NORMAL LIMITS
	10 F		WITHIN NORMAL LIMITS
	11 F		WITHIN NORMAL LIMITS
	12 F		WITHIN NORMAL LIMITS
	13 F		WITHIN NORMAL LIMITS
	14 M		WITHIN NORMAL LIMITS
	15 F		WITHIN NORMAL LIMITS
1510	1 M		WITHIN NORMAL LIMITS
	2 F		WITHIN NORMAL LIMITS
	3 M		WITHIN NORMAL LIMITS
	4 F		WITHIN NORMAL LIMITS
	5 M		WITHIN NORMAL LIMITS
	6 F		WITHIN NORMAL LIMITS
	7 M		WITHIN NORMAL LIMITS
	8 M		WITHIN NORMAL LIMITS
	9 F		WITHIN NORMAL LIMITS
	10 F		WITHIN NORMAL LIMITS
	11 M		WITHIN NORMAL LIMITS
	12 F		WITHIN NORMAL LIMITS
	13 F		WITHIN NORMAL LIMITS
	14 F		WITHIN NORMAL LIMITS
1511	1 F		WITHIN NORMAL LIMITS
	2 F		WITHIN NORMAL LIMITS
	3 M		WITHIN NORMAL LIMITS
	4 F		WITHIN NORMAL LIMITS

SEX CODES: M=Male, F=Female
CLASS CODES: M=Malformation

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
1511 (CONTINUED)				
	5 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
	16 M			WITHIN NORMAL LIMITS
1512	1 M			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS
1514	1 F			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

Huntingdon Life Sciences 04-4261

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
1514	(CONTINUED)			
	7 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
1515	2 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS
1516	1 M			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

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APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
1516	(CONTINUED)			
	11 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
1517	2 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
1518	1 M			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
1519	1 M			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
	16 M			WITHIN NORMAL LIMITS
	17 M			WITHIN NORMAL LIMITS
1521	1 M			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS
	16 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

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APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
1521	(CONTINUED)			
	17 M			WITHIN NORMAL LIMITS
1522	1 M			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
1523	1 M			WITHIN NORMAL LIMITS
1524	1 M			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
1525	1 F			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 2 30 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
2501	1 M			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
2502	1 F			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
2503	1 F			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 2 30 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
2503	(CONTINUED)			
	6 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS
2505	1 F			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
2506	1 F			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 2 30 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
2506	(CONTINUED)			
	9 M			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
2507	1 F			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
	16 F			WITHIN NORMAL LIMITS
2508	1 F			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS

SEX CODES: M=Male, F=Female
CLASS CODES: M=Malformation

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 2 30 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
2509	1 F			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
2510	1 M			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
2511	1 M			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 2 30 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
2511	(CONTINUED)			
	11 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS
	16 M			WITHIN NORMAL LIMITS
2512	1 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
2513	1 F			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

Huntingdon Life Sciences 04-4261

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 2 30 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
2515	1 M			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
2516	1 M			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
2517	1 M			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

Huntingdon Life Sciences 04-4261

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 2 30 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
2517	(CONTINUED)			
	6 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
2518	1 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
2519	2 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS
	16 F			WITHIN NORMAL LIMITS
	17 M			WITHIN NORMAL LIMITS

SEX CODES: M=Male, F=Female
CLASS CODES: M=Malformation

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 2 30 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
2520	1 M			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
2521	1 F			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
2522	1 F			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 2 30 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
2522	(CONTINUED)			
	9 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
2523	1 M			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
2524	1 M			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS

SEX CODES: M=Male, F=Female.
CLASS CODES: M=Malformation

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 2 30 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
2524	(CONTINUED)			
	16 M			WITHIN NORMAL LIMITS
	17 M			WITHIN NORMAL LIMITS
2525	1 F			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

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APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 3 90 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
3501	1 F			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS
3502	1 F			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
	16 M			WITHIN NORMAL LIMITS
	17 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

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APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 3 90 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
3503	1 M			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
3504	2 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
3505	1 M			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

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APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 3 90 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
3505	(CONTINUED)			
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
	16 F			WITHIN NORMAL LIMITS
	17 M			WITHIN NORMAL LIMITS
3506	1 F			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
3507	1 M			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 3 90 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
3507	(CONTINUED)			
	11 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
3508	1 F			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
3509	1 M			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

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APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 3 90 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
3510	1 M			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
3511	1 F			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
3512	1 F			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 3 90 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
3512 (CONTINUED)				
	8 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
	16 F			WITHIN NORMAL LIMITS
3513	1 F			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
3514	3 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
3516	1 F			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 3 90 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
3516	(CONTINUED)			
	6 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
3517	1 F			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
3518	1 M			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 3 90 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
3518	(CONTINUED)			
	14 M			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS
	16 M			WITHIN NORMAL LIMITS
	17 F			WITHIN NORMAL LIMITS
3519	1 M			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
3521	1 M			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 3 90 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
3522	1 M			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
3523	1 F			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
3524	1 M			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS

SEX CODES: M=Male, F=Female
CLASS CODES: M=Malformation

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 3 90 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
3524	(CONTINUED)			
	6 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
	17 M			WITHIN NORMAL LIMITS
	18 M			WITHIN NORMAL LIMITS
3525	1 M			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

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APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 4 18(PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
4501	1 F			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
4502	1 M			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS
4503	1 F			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 4 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
4503	(CONTINUED)			
	6 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 L	CROWN-RUMP		DISTANCE
				2.3CM
	10 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
4504	1 M			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS
4505	1 M			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS

SEX CODES: M=Male, F=Female,
CLASS CODES: M=Malformation
FETAL STATUS CODES: L-late resorption

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 4 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
4505 (CONTINUED)				
	7 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
4507	1 M			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M	GROSS EXAM	M	ANASARCA
	6 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
4508	1 M			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS

SEX CODES: M=Male, F=Female
CLASS CODES: M=Malformation

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APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 4 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
4509	1 M			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS
	16 F			WITHIN NORMAL LIMITS
4510	1 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
4511	3 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 4 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
4511 (CONTINUED)				
	7 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
	16 M			WITHIN NORMAL LIMITS
	17 F			WITHIN NORMAL LIMITS
	18 M			WITHIN NORMAL LIMITS
	19 M			WITHIN NORMAL LIMITS
4512	1 M			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
	16 M			WITHIN NORMAL LIMITS
	17 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 4 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
4513	1 M			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
4514	1 M			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
4515	1 M			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

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APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 4 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
4515	(CONTINUED)			
	5 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
4516	1 M			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
4517	1 M			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 4 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
4518	1 F			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS
4519	1 F			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS
	16 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: 4=Malformation

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APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 4 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
4520	1 M			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
4521	1 F			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 [1]			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
4522	1 M			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS

SEX CODES: M=Male, F=Female
CLASS CODES: M=Malformation

[1]Due to oversight, data not recorded.

APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 4 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
4522	(CONTINUED)			
	5 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
4523	3 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS
4524	1 F			WITHIN NORMAL LIMITS
	2 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

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APPENDIX K

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 4 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
4524	(CONTINUED)			
	9 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
4525	1 M			WITHIN NORMAL LIMITS
	2 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation

APPENDIX L

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL VISCERAL OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
1501	2 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
1502	1 F	TORSO	V	UNDESCENDED THYMUS LEFT HORN
	3 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
1503	2 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
1505	2 F	TORSO	V	UNDESCENDED THYMUS LEFT HORN
	4 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female,
CLASS CODES: M=Malformation V=Variation

APPENDIX L

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL VISCERAL OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
1506	1 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 M	TORSO	V	DISPLACED TESTIS LEFT - MEDIALLY
	13 M			WITHIN NORMAL LIMITS
1507	2 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 M	HEAD	M	RETINAS FOLDED; RIGHT
	10 M			WITHIN NORMAL LIMITS
	12 M	HEART	V	ADDITIONAL SUBCLAVIAN ARTERY LEFT
1508	1 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
1509	2 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation V=Variation

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APPENDIX L

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL VISCERAL OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
1510	1 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 M	TORSO	V	UNDESCENDED THYMUS LEFT HORN
	13 F	TORSO	V	UNDESCENDED THYMUS LEFT HORN
1511	2 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
	16 M			WITHIN NORMAL LIMITS
1512	1 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
1514	1 F	TORSO	V	UNDESCENDED THYMUS LEFT HORN
	3 F	TORSO	V	UNDESCENDED THYMUS LEFT HORN
	5 F			WITHIN NORMAL LIMITS
	7 M	TORSO	V	UNDESCENDED THYMUS LEFT HORN

SEX CODES: M=Male, F=Female
CLASS CODES: M=Malformation V=Variation

APPENDIX L

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL VISCERAL OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
1514	(CONTINUED)			
	9 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
1515	3 F	TORSO	V	UNDESCENDED THYMUS RIGHT HORN
	5 M	TORSO	V	UNDESCENDED THYMUS LEFT HORN
	7 M	TORSO	V	UNDESCENDED THYMUS RIGHT HORN
	9 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 M	TORSO	V	DISPLACED TESTIS BILATERAL - CRANIALLY
		TORSO	V	UNDESCENDED THYMUS LEFT HORN
	15 F			WITHIN NORMAL LIMITS
1516	1 M			WITHIN NORMAL LIMITS
	3 M	TORSO	V	UNDESCENDED THYMUS LEFT HORN
	5 F	TORSO		RENAL PAPILLA (E) NOT FULLY DEVELOPED (GRADE 1) RIGHT
	7 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	11 M	TORSO		RENAL PAPILLA (E) NOT FULLY DEVELOPED (GRADE 1) RIGHT
	13 M			WITHIN NORMAL LIMITS
1517	3 M	TORSO	V	DISPLACED TESTIS RIGHT - CRANIALLY
	5 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS

SEX CODES: M=Male, F=Female
CLASS CODES: M=Malformation V=Variation

APPENDIX L

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL VISCERAL OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
1517	(CONTINUED)			
	11 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
1518	1 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
1519	2 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
	16 M			WITHIN NORMAL LIMITS
1521	2 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
	16 F			WITHIN NORMAL LIMITS
1522	1 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation V=Variation

APPENDIX L

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL VISCERAL OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
1522 (CONTINUED)				
	9 M	TORSO	V	DISPLACED TESTIS RIGHT - MEDIALLY
	11 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
1524	1 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 M	TORSO	V	UNDESCENDED THYMUS LEFT HORN
	13 M			WITHIN NORMAL LIMITS
1525	2 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation V=Variation

APPENDIX L

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL VISCERAL OBSERVATIONS

GROUP 2 30 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
2501	2 F			WITHIN NORMAL LIMITS
	4 M	TORSO		RENAL PAPILLA (E) NOT FULLY DEVELOPED (GRADE 1) LEFT
	6 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
2502	1 F			WITHIN NORMAL LIMITS
	3 M	TORSO	V	DISPLACED TESTIS LEFT - MEDIALLY
	5 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
2503	2 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
2505	2 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS

SEX CODES: M=Male, F=Female
CLASS CODES: M=Malformation V=Variation

APPENDIX L

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL VISCERAL OBSERVATIONS

GROUP 2 30 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
2506	1 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
2507	2 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
	16 F			WITHIN NORMAL LIMITS
2508	1 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
2509	2 M	TORSO	V	UNDESCENDED THYMUS
				LEFT HORN
	7 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
2510	1 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS

SEX CODES: M=Male, F=Female
CLASS CODES: M=Malformation V=Variation

APPENDIX L

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL VISCERAL OBSERVATIONS

GROUP 2 30 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
2510	(CONTINUED)			
	13 M			WITHIN NORMAL LIMITS
2511	2 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
	16 M			WITHIN NORMAL LIMITS
2512	1 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
2513	2 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 M	TORSO	V	UNDESCENDED THYMUS RIGHT HORN
	10 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
2515	2 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 F	HEART	V	ADDITIONAL SUBCLAVIAN ARTERY LEFT
	10 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation V=Variation

APPENDIX L

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL VISCERAL OBSERVATIONS

GROUP 2 30 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
2516	1 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
2517	2 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 F	HEAD	M	RETINAS FOLDED; LEFT
	10 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
2518	1 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
2519	3 F			WITHIN NORMAL LIMITS
	5 F	TORSO	V	UNDESCENDED THYMUS RIGHT HORN
	7 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS
	17 M			WITHIN NORMAL LIMITS
2520	1 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female.
CLASS CODES: M=Malformation V=Variation

APPENDIX L

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL VISCERAL OBSERVATIONS

GROUP 2 30 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
2520	(CONTINUED)			
	9 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
2521	2 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
2522	1 F	TORSO		RENAL PAPILLA (E) NOT FULLY DEVELOPED (GRADE 1) RIGHT
	3 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
2523	2 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
2524	1 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS
	17 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation V=Variation

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APPENDIX L

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL VISCERAL OBSERVATIONS

GROUP 2 30 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
2525	2 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation V=Variation

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APPENDIX L

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL VISCERAL OBSERVATIONS

GROUP 3 90 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
3501	2 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
3502	1 F	TORSO	V	UNDESCENDED THYMUS RIGHT HORN
	3 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	7 M	TORSO	V	UNDESCENDED THYMUS LEFT HORN
	9 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	15 M	TORSO	V	UNDESCENDED THYMUS LEFT HORN
	17 F			WITHIN NORMAL LIMITS
3503	2 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
3504	2 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation V=Variation

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APPENDIX L

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL VISCERAL OBSERVATIONS

GROUP 3 90 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
3505	2 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
	16 F			WITHIN NORMAL LIMITS
3506	1 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 F	TORSO	V	RENAL PAPILLA (E) NOT DEVELOPED (GRADE 0) RIGHT
	7 M			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
3507	2 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
3508	1 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female.
CLASS CODES: M=Malformation V=Variation

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CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL VISCERAL OBSERVATIONS

GROUP 3 90 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
3509	2 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
3510	1 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
3511	2 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
3512	1 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
	16 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation V=Variation

APPENDIX L

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL VISCERAL OBSERVATIONS

GROUP 3 90 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
3513	2 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
3514	3 F			WITHIN NORMAL LIMITS
	6 F	TORSO		RENAL PAPILLA (E) NOT FULLY DEVELOPED (GRADE 1) LEFT
	8 M			WITHIN NORMAL LIMITS
3516	1 F			WITHIN NORMAL LIMITS
	3 F	HEAD	M	RETINAS FOLDED; RIGHT
	5 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
3517	2 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
3518	1 M	TORSO	V	RENAL PAPILLA (E) NOT DEVELOPED (GRADE 0) LEFT
	3 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS

SEX CODES: M=Male, F=Female.
CLASS CODES: M=Malformation V=Variation

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APPENDIX L

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL VISCERAL OBSERVATIONS

GROUP 3 90 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
3518	(CONTINUED)			
	15 F			WITHIN NORMAL LIMITS
	17 F			WITHIN NORMAL LIMITS
3519	2 F	TORSO		RENAL PAPILLA (E) NOT FULLY DEVELOPED (GRADE 1) RIGHT
	4 M	TORSO	V	RENAL PAPILLA (E) NOT DEVELOPED (GRADE 0) RIGHT
	6 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	14 M	TORSO	V	RENAL PAPILLA (E) NOT DEVELOPED (GRADE 0) LEFT
3521	2 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
3522	1 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
3523	2 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation V=Variation

APPENDIX L

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL VISCERAL OBSERVATIONS

GROUP 3 90 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
3523	(CONTINUED)			
	13 F			WITHIN NORMAL LIMITS
	15 M	TORSO	V	DISPLACED TESTIS RIGHT - CRANIALLY
3524	1 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	17 M			WITHIN NORMAL LIMITS
3525	2 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS

SEX CODES: M=Male, F=Female
CLASS CODES: M=Malformation V=Variation

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APPENDIX L

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL VISCERAL OBSERVATIONS

GROUP 4 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
4501	2 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
4502	1 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	13 M	TORSO	V	LEFT-SIDED UMBILICAL ARTERY
	15 F			WITHIN NORMAL LIMITS
4503	2 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
4504	1 M	TORSO	V	UNDESCENDED THYMUS
				RIGHT HORN
	3 F			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	11 M	TORSO	V	UNDESCENDED THYMUS
				BILATERAL HORN
	13 M			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation V=Variation

APPENDIX L

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL VISCERAL OBSERVATIONS

GROUP 4 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
4505	2 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 F	TORSO	V	UNDESCENDED THYMUS RIGHT HORN
4507	2 F			WITHIN NORMAL LIMITS
	7 M	TORSO		RENAL PAPILLA (E) NOT FULLY DEVELOPED (GRADE 1) RIGHT
	9 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
4508	1 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
4509	2 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 F	TORSO	V	UNDESCENDED THYMUS LEFT HORN
	15 F			WITHIN NORMAL LIMITS
4510	1 F			WITHIN NORMAL LIMITS
	4 M	HEART	V	PULMONARY TRUNK DILATED; SLIGHT
	6 F	TORSO	V	LEFT-SIDED UMBILICAL ARTERY

SEX CODES: M-Male, F=Female.
CLASS CODES: M=Malformation V=Variation

APPENDIX L

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL VISCERAL OBSERVATIONS

GROUP 4 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
4510 (CONTINUED)				
	8 F	TORSO		RENAL PAPILLA (E) NOT FULLY DEVELOPED (GRADE 1) RIGHT
	10 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 F	TORSO	V	UNDESCENDED THYMUS RIGHT HORN
4511	4 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
	16 M			WITHIN NORMAL LIMITS
	18 M			WITHIN NORMAL LIMITS
4512	1 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
	17 F			WITHIN NORMAL LIMITS
4513	2 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation V=Variation

APPENDIX L

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL VISCERAL OBSERVATIONS

GROUP 4 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
4514	1 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 F	TORSO	V	UNDESCENDED THYMUS RIGHT HORN
	9 F			WITHIN NORMAL LIMITS
	11 M	TORSO	V	UNDESCENDED THYMUS RIGHT HORN
	13 F			WITHIN NORMAL LIMITS
4515	2 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 M	TORSO	V	UNDESCENDED THYMUS LEFT HORN
	11 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
4516	1 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
4517	2 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
4518	1 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation V=Variation

APPENDIX L

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL VISCERAL OBSERVATIONS

GROUP 4 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
4518	(CONTINUED)			
	7 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
4519	2 M	TORSO	V	DISPLACED TESTIS RIGHT - MEDIALLY
	4 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
	16 M			WITHIN NORMAL LIMITS
4520	1 M	TORSO	V	DISPLACED TESTIS RIGHT - MEDIALLY
	3 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
4521	2 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 M	TORSO	V	UNDESCENDED THYMUS LEFT HORN
	8 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: M=Malformation V=Variation

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APPENDIX L

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL VISCERAL OBSERVATIONS

GROUP 4 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
4522	1 M	TORSO	V	DISPLACED TESTIS LEFT - MEDIALLY
	3 F	TORSO	V	UNDESCENDED THYMUS RIGHT HORN
	5 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
4523	4 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
4524	1 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
4525	2 F			WITHIN NORMAL LIMITS
	4 M	TORSO	V	RENAL PAPILLA (E) NOT DEVELOPED (GRADE 0) RIGHT
	6 M	TORSO	V	RENAL PAPILLA (E) NOT DEVELOPED (GRADE 0) LEFT
		TORSO	V	UNDESCENDED THYMUS LEFT HORN
	8 M	TORSO		RENAL PAPILLA (E) NOT FULLY DEVELOPED (GRADE 1) BILATERAL

SEX CODES: M-Male, F=Female,
CLASS CODES: M=Malformation V=Variation

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APPENDIX L

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL VISCERAL OBSERVATIONS

GROUP 4 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
4525	(CONTINUED)			
	10 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	14 F	TORSO		RENAL PAPILLA (E) NOT FULLY DEVELOPED (GRADE 1) RIGHT

SEX CODES: M=Male, F=Female
CLASS CODES: M=Malformation V=Variation

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APPENDIX M

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL SKELETAL OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
1501	1 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS
1502	2 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
1503	1 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
1505	1 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	5 F	RIBS	V	RIB(S) 14TH RUDIMENTARY; LEFT
	7 F	RIBS	V	RIB(S) 14TH RUDIMENTARY; BILATERAL
	9 F	RIBS	V	RIB(S) 14TH RUDIMENTARY; RIGHT
	11 F			WITHIN NORMAL LIMITS
	13 M	RIBS	V	RIB(S) 14TH RUDIMENTARY; RIGHT

SEX CODES: M-Male, F=Female
CLASS CODES: V=Variation

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APPENDIX M

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL SKELETAL OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
1506	2 M			WITHIN NORMAL LIMITS
	4 M	RIBS	V	RIB(S) 14TH RUDIMENTARY; LEFT
	6 M			WITHIN NORMAL LIMITS
	8 F	RIBS	V	RIB(S) 14TH RUDIMENTARY; LEFT
	10 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	14 F	RIBS	V	RIB(S) 14TH RUDIMENTARY; RIGHT
1507	1 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	7 M	RIBS	V	RIB(S) 14TH RUDIMENTARY; RIGHT
	9 F			WITHIN NORMAL LIMITS
	11 F	RIBS	V	RIB(S) 14TH RUDIMENTARY; LEFT
	13 F	RIBS	V	RIB(S) 14TH RUDIMENTARY; BILATERAL
1508	2 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	11 F	SKULL	V	SUTURAL BONE (PARIETAL/INTERPARIETAL); LEFT BETWEEN PARIETAL AND INTERPARIETAL
	13 F			WITHIN NORMAL LIMITS
1509	1 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 F	RIBS	V	RIB(S) 14TH RUDIMENTARY; BILATERAL
	10 F	RIBS	V	RIB(S) 14TH RUDIMENTARY; BILATERAL
	12 F			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: V=Variation

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APPENDIX M

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL SKELETAL OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
1510	2 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
1511	1 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	7 F	RIBS	V	RIB(S) 14TH RUDIMENTARY; RIGHT
	9 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
1512	2 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS
1514	2 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 F	RIBS	V	RIB(S) 14TH RUDIMENTARY; BILATERAL
	10 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: V=Variation

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APPENDIX M

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL SKELETAL OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
1515	2 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
1516	2 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
1517	2 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
1518	2 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 M	RIBS	V	RIB(S) 14TH RUDIMENTARY; BILATERAL
	12 M	RIBS	V	RIB(S) 14TH RUDIMENTARY; LEFT
	14 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: V=Variation

APPENDIX M

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL SKELETAL OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
1519	1 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
	17 M			WITHIN NORMAL LIMITS
1521	1 M			WITHIN NORMAL LIMITS
	3 F	RIBS	V	RIB(S) 14TH RUDIMENTARY; RIGHT
	5 F	RIBS	V	RIB(S) 14TH RUDIMENTARY; LEFT
	7 M	RIBS	V	RIB(S) 14TH RUDIMENTARY; BILATERAL
	9 F	RIBS	V	RIB(S) 14TH RUDIMENTARY; BILATERAL
	11 M			WITHIN NORMAL LIMITS
	13 M	RIBS	V	RIB(S) 14TH RUDIMENTARY; BILATERAL
	15 F			WITHIN NORMAL LIMITS
	17 M			WITHIN NORMAL LIMITS
1522	2 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 M	RIBS	V	RIB(S) 14TH RUDIMENTARY; BILATERAL
	10 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
1523	1 M			WITHIN NORMAL LIMITS
1524	2 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female,
CLASS CODES: V=Variation

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APPENDIX M

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL SKELETAL OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
1524	(CONTINUED)			
	12 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
1525	1 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: V=Variation

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APPENDIX M

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL SKELETAL OBSERVATIONS

GROUP 2 30 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
2501	1 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
2502	2 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
2503	1 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS
2505	1 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 M	RIBS	V	RIB(S) 14TH RUDIMENTARY; RIGHT
	13 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: V=Variation

APPENDIX M

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL SKELETAL OBSERVATIONS

GROUP 2 30 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS OBSERVATION
2506	2 M	RIBS	V RIB(S) 14TH RUDIMENTARY; BILATERAL
	4 F		WITHIN NORMAL LIMITS
	6 F		WITHIN NORMAL LIMITS
	8 F	RIBS	V RIB(S) 14TH RUDIMENTARY; RIGHT
	10 M	RIBS	V RIB(S) 14TH RUDIMENTARY; BILATERAL
2507	1 F		WITHIN NORMAL LIMITS
	3 F		WITHIN NORMAL LIMITS
	5 F		WITHIN NORMAL LIMITS
	7 F		WITHIN NORMAL LIMITS
	9 M	RIBS	V RIB(S) 14TH RUDIMENTARY; RIGHT
	11 M		WITHIN NORMAL LIMITS
	13 F		WITHIN NORMAL LIMITS
	15 M		WITHIN NORMAL LIMITS
2508	2 F		WITHIN NORMAL LIMITS
	4 F		WITHIN NORMAL LIMITS
	6 F		WITHIN NORMAL LIMITS
	9 M		WITHIN NORMAL LIMITS
	11 M	STERNEBRAE	V STERNEBRA(E) MISALIGNED 3RD AND 4TH
		RIBS	V COSTAL CARTILAGE MISALIGNED
2509	1 F		WITHIN NORMAL LIMITS
	4 F		WITHIN NORMAL LIMITS
	8 F		WITHIN NORMAL LIMITS
	10 F		WITHIN NORMAL LIMITS
	12 M		WITHIN NORMAL LIMITS
2510	2 M		WITHIN NORMAL LIMITS
	4 F	RIBS	V RIB(S) 14TH RUDIMENTARY; BILATERAL
	6 F		WITHIN NORMAL LIMITS
	8 F		WITHIN NORMAL LIMITS
	10 M	RIBS	V RIB(S) 14TH RUDIMENTARY; BILATERAL

SEX CODES: M-Male, F=Female
CLASS CODES: V=Variation

Huntingdon Life Sciences 04-4261

APPENDIX M

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL SKELETAL OBSERVATIONS

GROUP 2 30 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
2510	(CONTINUED)			
	12 M			WITHIN NORMAL LIMITS
2511	1 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS
2512	4 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
2513	1 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS
2515	1 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: V=Variation I=Incidental

Huntingdon Life Sciences 04-4261

APPENDIX M

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL SKELETAL OBSERVATIONS

GROUP 2 30 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
2516	2 F			WITHIN NORMAL LIMITS
	4 M	RIBS	V	RIB(S) 14TH RUDIMENTARY; RIGHT
	6 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
2517	1 M			WITHIN NORMAL LIMITS
	3 F	SKULL	V	FISSURE - PARIETAL; LEFT PARIETAL
	5 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 F	SKULL	V	FISSURE - PARIETAL; RIGHT PARIETAL
	13 F			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
2518	6 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
2519	2 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
	16 F			WITHIN NORMAL LIMITS
2520	2 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: V=Variation I=Incidental

APPENDIX M

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL SKELETAL OBSERVATIONS

GROUP 2 30 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
2520	(CONTINUED)			
	8 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
2521	1 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
2522	2 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
2523	1 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
2524	2 F			WITHIN NORMAL LIMITS
	4 M	RIBS	V	RIB(S) 14TH RUDIMENTARY; LEFT
	6 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
	16 M	RIBS	V	RIB(S) 14TH RUDIMENTARY; LEFT

SEX CODES: M=Male, F=Female
CLASS CODES: V=Variation I=Incidental

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APPENDIX M

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL SKELETAL OBSERVATIONS

GROUP 2 30 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
2525	1 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: V=Variation

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APPENDIX M

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL SKELETAL OBSERVATIONS

GROUP 3 90 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
3501	1 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS
3502	2 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
	16 M	RIBS	V	RIB(S) 14TH RUDIMENTARY; LEFT
3503	1 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
3504	3 F			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: V=Variation

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APPENDIX M

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL SKELETAL OBSERVATIONS

GROUP 3 90 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
3505	1 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
	17 M			WITHIN NORMAL LIMITS
3506	2 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
3507	1 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
3508	2 F			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: V=Variation

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APPENDIX M

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL SKELETAL OBSERVATIONS

GROUP 3 90 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
3509	1 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS
3510	2 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
3511	1 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 F	RIBS	V	RIB(S) 14TH RUDIMENTARY; LEFT
	14 M	RIBS	V	RIB(S) 14TH RUDIMENTARY; BILATERAL
3512	2 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
3513	1 F	SKULL	V	FISSURE - PARIETAL; LEFT PARIETAL
	3 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: V=Variation

Huntingdon Life Sciences 04-4261

APPENDIX M

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL SKELETAL OBSERVATIONS

GROUP 3 90 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
3513	(CONTINUED)			
	5 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
3514	4 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
3516	2 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
3517	1 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
3518	2 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
	16 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: V=Variation

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APPENDIX M

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL SKELETAL OBSERVATIONS

GROUP 3 90 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
3519	1 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
3521	1 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	7 M	SKULL	V	FISSURE - PARIETAL; RIGHT PARIETAL
	9 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
3522	2 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
3523	1 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: V=Variation

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APPENDIX M

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL SKELETAL OBSERVATIONS

GROUP 3 90 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
3524	2 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 F	RIBS	V	RIB(S) 14TH RUDIMENTARY; BILATERAL
	10 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
	18 M			WITHIN NORMAL LIMITS
3525	1 M	RIBS	V	RIB(S) 14TH RUDIMENTARY; LEFT
	3 M	RIBS	V	RIB(S) 14TH RUDIMENTARY; BILATERAL
	5 F			WITHIN NORMAL LIMITS
	7 F	RIBS	V	RIB(S) 14TH RUDIMENTARY; BILATERAL
	9 M			WITHIN NORMAL LIMITS
	11 F	RIBS	V	RIB(S) 14TH RUDIMENTARY; LEFT
	13 M	RIBS	V	RIB(S) 14TH RUDIMENTARY; BILATERAL

SEX CODES: M-Male, F=Female
CLASS CODES: V=Variation

Huntingdon Life Sciences 04-4261

APPENDIX M

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL SKELETAL OBSERVATIONS

GROUP 4 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
4501	1 F			WITHIN NORMAL LIMITS
	3 F	RIBS	V	RIB(S) 14TH RUDIMENTARY; LEFT
	5 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 F	RIBS	V	RIB(S) 14TH RUDIMENTARY; LEFT
	11 M			WITHIN NORMAL LIMITS
4502	2 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
4503	1 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
4504	2 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
4505	1 M			WITHIN NORMAL LIMITS
	3 M	RIBS	V	RIB(S) 14TH RUDIMENTARY; LEFT
	5 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: V=Variation

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APPENDIX M

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL SKELETAL OBSERVATIONS

GROUP 4 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
4505	(CONTINUED)			
	7 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
4507	1 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	4 M	SACRAL VERT.	V	27 PRESACRAL VERTEBRA(E)
		RIBS	V	RIB(S) 14TH RUDIMENTARY; BILATERAL
	6 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
4508	2 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
4509	1 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	16 F			WITHIN NORMAL LIMITS
4510	3 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: V=Variation

Huntingdon Life Sciences 04-4261

APPENDIX M

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL SKELETAL OBSERVATIONS

GROUP 4 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
4511	3 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
	17 F			WITHIN NORMAL LIMITS
	19 M			WITHIN NORMAL LIMITS
4512	2 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 M	RIBS	V	RIB(S) 14TH RUDIMENTARY; LEFT
	8 M	RIBS	V	RIB(S) 14TH RUDIMENTARY; BILATERAL
	10 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 F			WITHIN NORMAL LIMITS
	16 M			WITHIN NORMAL LIMITS
4513	1 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	15 M			WITHIN NORMAL LIMITS
4514	2 M			WITHIN NORMAL LIMITS
	4 M	SKULL	V	FISSURE - PARIETAL; LEFT PARIETAL
	6 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: V=Variation

APPENDIX M

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL SKELETAL OBSERVATIONS

GROUP 4 - 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
4514	(CONTINUED)			
	12 M			WITHIN NORMAL LIMITS
4515	1 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 M			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
4516	2 M			WITHIN NORMAL LIMITS
	4 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
4517	1 M			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 M	RIBS	V	RIB(S) 14TH RUDIMENTARY; LEFT
	7 F	RIBS	V	RIB(S) 14TH RUDIMENTARY; BILATERAL
	9 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
4518	2 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 M			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS
4519	1 F			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: V=Variation

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APPENDIX M

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL SKELETAL OBSERVATIONS

GROUP 4 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
4519	(CONTINUED)			
	7 M			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS
4520	2 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 M			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
4521	1 F			WITHIN NORMAL LIMITS
	3 F			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 F			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	13 [1]			WITHIN NORMAL LIMITS
4522	2 F			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 F			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 F			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
4523	3 F			WITHIN NORMAL LIMITS
	5 F			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: V=Variation

[1]Due to oversight, data not recorded.

APPENDIX M

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL SKELETAL OBSERVATIONS

GROUP 4 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
4523	(CONTINUED)			
	11 M			WITHIN NORMAL LIMITS
	13 M			WITHIN NORMAL LIMITS
	15 F			WITHIN NORMAL LIMITS
4524	2 M			WITHIN NORMAL LIMITS
	4 M			WITHIN NORMAL LIMITS
	6 F			WITHIN NORMAL LIMITS
	8 M			WITHIN NORMAL LIMITS
	10 F			WITHIN NORMAL LIMITS
	12 M			WITHIN NORMAL LIMITS
	14 M			WITHIN NORMAL LIMITS
4525	1 M			WITHIN NORMAL LIMITS
	3 M			WITHIN NORMAL LIMITS
	5 M			WITHIN NORMAL LIMITS
	7 F			WITHIN NORMAL LIMITS
	9 M			WITHIN NORMAL LIMITS
	11 F			WITHIN NORMAL LIMITS
	13 F			WITHIN NORMAL LIMITS

SEX CODES: M-Male, F=Female
CLASS CODES: V=Variation

Group 1	Individual Ossification Parameters	Appendix M

		Number of Fetuses Affected																					
Animal Number	Number of Fetuses	Unossified / Incomplete Ossification of Skull Bones			Cervical Centrum(a) Ossified		Unossified / Incomplete Ossification of Sternebra(e)			Number of Caudal Vertebrae Ossified (*Litter Mean*) [a]	Incomplete Ossification of Vertebral Centrum(a)		Ossification of 1st Cervical Arch (Ventral / Odontoid Process)	Incomplete Ossification / Unossification of Vertebral Arches		Unossified / Incomplete Ossification of Pelvic Bones			Vertebral Arches / Centra Fused		5th Metacarpals Ossified	Incompletely Ossified / Unossified Metacarpals	Incompletely Ossified / Unossified Metatarsals
		<3	3-5	>5	1	2+	1	2	3+		1	2+		1 pair	2+ pairs	1-2	3-4	5-6	1 vert.	2+ vert.			
1501	8	1	1	0	6	1	2	6	0	3.9	0	0	0	1	0	1	0	0	1	1	4	0	0
1502	7	4	1	2	3	0	1	6	0	3.3	0	0	0	2	0	0	0	0	0	0	4	0	0
1503	6	0	0	0	0	0	1	1	0	4.0	0	0	3	0	0	0	0	0	3	1	6	0	0
1505	7	2	0	0	5	1	2	0	0	4.3	2	0	0	0	0	0	0	0	0	5	7	0	0
1506	7	3	0	0	2	0	6	0	0	4.1	1	0	4	0	0	0	0	0	1	1	6	0	0
1507	7	2	3	1	2	0	2	2	0	4.0	0	0	1	0	0	0	0	0	0	0	6	0	0
1508	6	0	2	1	0	0	0	1	0	3.5	1	0	1	0	1	1	0	0	0	0	1	1	0
1509	7	2	1	0	0	0	4	1	0	4.1	0	0	1	1	0	0	0	0	1	0	6	0	0
1510	7	0	0	0	2	0	4	1	0	4.0	2	0	3	0	0	0	0	0	1	1	7	0	0
1511	8	3	0	0	3	0	1	0	0	4.1	0	0	7	0	0	0	0	0	1	2	8	0	0
1512	7	1	0	1	2	3	0	0	0	5.6	0	0	1	0	0	0	0	0	0	7	7	0	0
1514	7	1	2	4	1	0	4	1	0	4.0	0	0	0	0	1	0	0	0	1	0	5	0	0
1515	7	4	0	0	3	2	0	0	1	4.0	1	0	4	0	0	0	0	0	1	0	7	0	0
1516	7	2	2	0	2	0	1	1	0	4.0	2	0	7	1	0	0	0	0	1	2	6	0	0
1517	7	1	0	0	2	1	1	1	0	4.1	0	0	3	0	0	0	0	0	0	0	6	0	0
1518	7	1	1	0	1	5	0	0	0	4.3	0	0	6	0	0	0	0	0	0	0	6	0	0
1519	9	6	1	0	2	0	2	6	0	3.6	0	0	3	1	1	0	0	0	1	0	8	0	0
1521	9	1	2	0	3	1	2	0	0	4.0	0	0	3	0	0	0	0	0	1	0	7	0	0
1522	6	2	1	0	0	0	0	2	4	0.7	0	1	0	0	6	4	0	0	0	0	0	1	6
1523	1	0	0	0	1	0	0	0	0	5.0	0	0	1	0	0	0	0	0	0	1	1	0	0
1524	7	3	3	0	4	0	1	0	0	4.6	0	0	0	0	0	0	0	0	2	0	7	0	0
1525	6	1	2	3	0	1	4	1	0	4.2	0	0	0	0	0	0	0	0	1	1	5	0	0
Number of Fetuses (Litters)	150 (22)	40 (18)	22 (13)	12 (6)	44 (17)	15 (8)	38 (16)	30 (13)	5 (2)	3.9	9 (7)	1 (1)	48 (15)	6 (4)	9 (4)	6 (3)	0 (0)	0 (0)	16 (13)	22 (10)	120 (21)	2 (2)	6 (1)

[a]Fetuses with damaged tails not included in mean.

Group 2	Individual Ossification Parameters	Appendix M

Animal Number	Number of Fetuses	Number of Fetuses Affected: Unossified / Incomplete Ossification of Skull Bones			Cervical Centrum(a) Ossified		Unossified / Incomplete Ossification of Sternebra(e)			Number of Caudal Vertebrae Ossified (*Litter Mean*)[a]	Incomplete Ossification of Vertebral Centrum(a)		Ossification of 1st Cervical Arch (Ventral / Odontoid Process)	Incomplete Ossification / Unossification of Vertebral Arches		Unossified / Incomplete Ossification of Pelvic Bones			Vertebral Arches / Centra Fused		5th Metacarpals Ossified	Incompletely Ossified / Unossified Metacarpals	Incompletely Ossified / Unossified Metatarsals
		<3	3-5	>5	1	2+	1	2	3+		1	2+		1 pair	2+ pairs	1-2	3-4	5-6	1 vert.	2+ vert.			
2501	7	2	3	1	3	4	2	1	0	4.7	0	0	6	0	1	0	0	0	1	3	6	0	0
2502	7	2	1	0	1	0	3	3	0	2.9	1	0	0	0	0	0	0	0	0	0	1	1	0
2503	8	5	2	0	1	0	3	0	0	4.0	0	0	1	0	0	0	0	0	0	2	8	0	0
2505	7	3	0	0	3	0	2	0	0	4.3	1	1	5	1	0	0	0	0	0	0	7	0	0
2506	5	1	0	0	2	1	0	1	0	4.6	0	0	1	0	0	0	0	0	0	3	4	0	0
2507	8	1	1	2	1	0	2	6	0	3.0	1	0	0	3	1	0	0	0	2	0	4	0	0
2508	5	1	1	0	1	0	2	2	1	4.0	1	0	0	0	0	0	0	0	0	0	3	0	0
2509	5	2	1	0	2	0	1	1	0	3.8	0	0	1	1	0	0	0	0	2	0	5	0	0
2510	6	0	2	1	3	1	2	2	0	4.3	0	0	0	1	1	0	0	0	1	0	5	0	0
2511	8	3	0	1	0	0	3	0	0	4.4	0	0	2	0	0	0	0	0	2	2	5	0	0
2512	4	1	0	0	3	0	1	0	0	5.0	0	0	3	0	0	0	0	0	2	0	4	0	0
2513	8	1	0	0	1	0	2	0	0	4.1	1	0	1	0	0	0	0	0	2	1	8	0	0
2515	7	2	1	0	3	0	0	0	0	4.6	0	0	4	0	0	0	0	0	3	1	7	0	0
2516	7	4	0	0	3	1	0	0	0	4.9	1	0	4	0	0	0	0	0	1	6	7	0	0
2517	8	4	1	0	6	0	7	0	0	4.0	0	0	4	0	0	0	0	0	1	7	6	0	0
2518	2	1	0	0	0	0	0	0	0	5.0	0	0	0	0	0	0	0	0	0	0	2	0	0
2519	8	4	1	0	1	2	1	1	0	4.0	0	0	3	0	0	0	0	0	0	4	8	0	0
2520	7	2	4	1	0	0	0	1	6	0.3	4	2	0	0	7	2	5	0	0	0	0	0	7
2521	6	0	2	3	1	0	1	3	0	4.2	1	0	3	1	2	2	0	0	0	2	3	0	0
2522	5	1	2	3	0	0	0	2	3	1.2	1	1	0	0	5	1	0	0	0	0	0	1	5
2523	7	1	0	0	2	0	0	0	0	4.6	0	0	1	0	0	0	0	0	2	1	7	0	0
2524	8	5	0	0	1	0	1	0	0	4.0	1	1	2	0	0	0	0	0	0	0	8	0	0
2525	7	3	0	0	0	0	3	4	0	4.0	0	0	1	0	2	1	0	0	0	2	5	0	0
Number of Fetuses (Litters)	150 (23)	49 (20)	22 (13)	12 (7)	38 (18)	9 (5)	36 (16)	27 (12)	10 (3)	3.9	13 (10)	5 (4)	42 (16)	7 (5)	19 (7)	6 (4)	5 (1)	0 (0)	19 (11)	34 (12)	113 (21)	2 (2)	12 (2)

[a]Fetuses with damaged tails not included in mean.

Group 3	Individual Ossification Parameters	Appendix M

Animal Number	Number of Fetuses	Number of Fetuses Affected																					
		Unossified / Incomplete Ossification of Skull Bones			Cervical Centrum(a) Ossified		Unossified / Incomplete Ossification of Sternebra(e)			Number of Caudal Vertebrae Ossified (*Litter Mean*)[a]	Incomplete Ossification of Vertebral Centrum(a)		Ossification of 1st Cervical Arch (Ventral / Odontoid Process)	Incomplete Ossification / Unossification of Vertebral Arches		Unossified / Incomplete Ossification of Pelvic Bones			Vertebral Arches / Centra Fused		5th Metacarpals Ossified	Incompletely Ossified / Unossified Metacarpals	Incompletely Ossified / Unossified Metatarsals
		<3	3-5	>5	1	•2+	1	2	3+		1	2+		1 pair	2+ pairs	1-2	3-4	5-6	1 vert.	2+ vert.			
3501	8	2	0	0	0	0	3	4	0	4.0	0	1	3	0	0	0	0	0	1	1	8	0	0
3502	8	6	0	1	2	1	3	1	0	3.6	0	0	1	2	1	0	1	0	0	0	6	0	0
3503	7	3	1	1	1	0	4	2	0	3.3	1	0	1	1	1	0	0	0	1	0	6	0	0
3504	5	2	0	0	4	1	1	0	0	4.8	0	0	2	0	0	0	0	0	0	5	4	0	0
3505	9	5	0	0	5	1	6	1	0	4.3	0	0	4	0	0	0	0	0	0	1	9	0	0
3506	7	2	2	0	3	1	3	3	0	4.1	0	0	2	0	0	0	0	0	2	5	6	0	0
3507	6	4	1	0	1	1	1	3	0	3.7	0	0	2	0	0	0	0	0	2	2	6	0	0
3508	6	2	1	0	2	0	1	0	0	3.5	1	0	1	0	0	0	0	0	0	0	6	0	0
3509	8	0	0	0	1	0	3	1	0	4.5	2	0	0	0	0	0	0	0	1	1	7	0	0
3510	5	2	0	2	0	0	3	1	0	4.4	2	0	0	2	0	0	0	0	0	1	5	0	0
3511	7	0	0	0	3	1	1	0	0	5.0	1	0	3	0	0	0	0	0	0	3	7	0	0
3512	7	1	1	0	5	1	2	0	0	4.1	0	0	5	1	1	1	0	0	0	0	3	0	0
3513	7	1	0	0	3	3	3	0	0	4.4	0	0	0	0	0	0	0	0	2	1	7	0	0
3514	2	0	1	1	0	0	0	0	2	0.5	0	2	0	0	2	1	0	0	0	0	0	1	2
3516	7	3	0	0	3	2	2	0	0	4.0	0	0	5	0	0	0	0	0	2	1	7	0	0
3517	5	1	0	1	2	1	0	0	0	4.8	0	0	0	0	0	0	0	0	1	4	5	0	0
3518	8	3	2	0	3	0	2	1	0	3.8	0	0	2	1	0	0	0	0	0	1	8	0	0
3519	7	4	2	1	0	0	0	1	6	0.0	2	3	0	0	7	7	0	0	0	0	0	2	7
3521	7	2	3	1	0	0	3	4	0	3.4	1	0	0	2	0	0	0	0	2	0	2	0	0
3522	6	2	1	0	3	3	3	0	0	5.0	0	0	3	0	0	0	0	0	1	5	6	0	0
3523	7	3	0	0	1	0	2	0	0	3.9	2	0	2	0	0	0	0	0	1	1	7	0	0
3524	8	7	0	1	2	0	4	1	0	3.6	0	0	0	0	0	0	0	0	1	1	7	0	0
3525	7	3	2	0	2	3	1	0	0	4.6	1	0	5	0	0	0	0	0	0	5	6	0	0
Number of Fetuses (Litters)	154 (23)	58 (20)	17 (11)	9 (8)	46 (18)	19 (12)	51 (20)	23 (12)	8 (2)	3.8	13 (9)	6 (3)	41 (15)	9 (6)	12 (5)	9 (3)	1 (1)	0 (0)	17 (12)	38 (16)	128 (21)	3 (2)	9 (2)

[a]Fetuses with damaged tails not included in mean.

Group 4	Individual Ossification Parameters	Appendix M

Animal Number	Number of Fetuses	Number of Fetuses Affected																					
		Unossified / Incomplete Ossification of Skull Bones			Cervical Centrum(a) Ossified		Unossified / Incomplete Ossification of Sternebra(e)			Number of Caudal Vertebrae Ossified (*Litter Mean*) [a]	Incomplete Ossification of Vertebral Centrum(a)		Ossification of 1st Cervical Arch (Ventral / Odontoid Process)	Incomplete Ossification / Unossification of Vertebral Arches		Unossified / Incomplete Ossification of Pelvic Bones			Vertebral Arches / Centra Fused		5th Metacarpals Ossified	Incompletely Ossified / Unossified Metacarpals	Incompletely Ossified / Unossified Metatarsals
		<3	3-5	>5	1	2+	1	2	3+		1	2+		1 pair	2+ pairs	1-2	3-4	5-6	1 vert.	2+ vert.			
4501	6	3	2	0	0	0	0	2	4	2.7	4	0	0	0	6	1	0	0	0	0	0	0	0
4502	7	3	0	0	0	0	1	2	0	3.0	1	0	3	1	0	0	0	0	0	0	3	0	0
4503	7	2	0	0	1	1	1	3	0	3.7	0	0	0	0	0	0	0	0	0	1	4	0	0
4504	7	4	0	0	3	0	5	0	0	4.1	0	0	5	0	0	0	0	0	0	0	7	0	0
4505	6	4	0	2	2	0	1	4	0	3.7	0	0	0	2	2	2	0	0	0	0	3	0	0
4507	6	1	2	1	0	0	1	2	1	3.3	0	1	2	0	0	0	0	0	1	0	4	0	1
4508	6	4	1	0	0	0	1	4	0	2.8	0	0	2	2	2	0	0	0	0	0	2	0	0
4509	8	4	3	0	0	0	3	3	2	3.1	0	1	0	1	3	0	0	0	0	0	2	0	0
4510	6	1	0	0	2	0	2	1	0	3.8	1	0	0	3	0	0	0	0	0	1	6	0	0
4511	9	3	2	4	0	0	1	7	0	2.6	0	0	0	2	2	1	0	0	0	0	1	0	0
4512	8	6	0	0	3	2	2	0	0	4.1	0	0	5	0	0	0	0	0	0	0	8	0	0
4513	8	6	1	0	0	0	3	1	0	4.1	0	0	3	1	1	0	0	0	0	0	7	0	0
4514	6	4	0	0	0	0	2	1	0	3.8	0	0	1	0	0	0	0	0	0	0	5	0	0
4515	6	3	1	2	0	0	2	4	0	3.7	1	0	2	0	0	0	0	0	2	3	6	0	0
4516	6	1	2	1	0	0	4	2	0	3.5	1	0	2	1	1	0	0	0	0	0	5	0	0
4517	6	4	0	0	2	0	0	1	0	4.5	0	0	1	0	0	0	0	0	0	1	4	0	0
4518	7	1	0	0	2	2	0	0	0	4.9	0	0	0	0	0	0	0	0	0	0	7	0	0
4519	8	4	1	2	0	0	4	3	0	3.8	0	0	1	1	1	1	0	0	0	0	4	0	0
4520	7	2	3	2	0	0	0	3	4	1.4	1	3	0	0	7	7	0	0	0	0	0	0	6
4521	7	6	0	0	2	0	0	6	0	3.3	0	0	3	1	0	0	0	0	0	0	2	0	0
4522	7	6	0	0	0	0	0	0	7	0.1	2	5	0	0	7	0	7	0	0	0	0	5	7
4523	7	2	0	2	1	0	2	5	0	2.9	0	0	1	3	0	1	0	0	0	0	2	0	0
4524	7	4	3	0	0	0	4	2	0	3.3	0	0	1	3	1	1	0	0	0	0	2	0	0
4525	7	4	0	0	0	0	0	2	5	0.0	4	2	0	0	7	5	0	0	0	0	0	2	7
Number of Fetuses (Litters)	165 (24)	82 (24)	21 (11)	16 (8)	18 (9)	5 (3)	39 (17)	58 (20)	23 (6)	3.3	15 (8)	12 (5)	32 (14)	21 (12)	40 (12)	19 (8)	7 (1)	0 (0)	3 (2)	6 (4)	84 (20)	7 (2)	21 (4)

[a]Fetuses with damaged tails not included in mean.

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	Inhalation Report	Appendix N

1. INTRODUCTION

This appendix presents the methodology for exposure, atmosphere generation, monitoring and results of a 6-hour per day exposure regimen of inhaled Chlorotrifluoroethylene (CTFE) gas during early organogenesis (Gestation Days 6 through 19) in pregnant females rats.

2. MATERIALS AND METHODS

2.1. HUSBANDRY DURING EXPOSURE PERIODS

2.1.1. HOUSING

Animals were individually housed in a 1000 Liter glass and stainless steel whole-body exposure chamber. The placement of the animals in the whole-body exposure chamber was rotated daily to ensure uniform exposure of the animals. A description of the animal rotation is included in the raw data.

2.1.2. FEED

None was provided during exposure.

2.1.3. WATER

None was provided during exposure.

2.1.4. ENVIRONMENTAL CONDITIONS

Chamber temperature and relative humidity were monitored continuously and recorded every half-hour during exposure and maintained, to the maximum extent possible, within the ranges presented below. Excursions outside the specified range did not affect the integrity of the study.

Temperature

Desired: 20 to 24°C
Actual: 21 to 25°C

Relative Humidity

Desired: 40 to 60%
Actual: 49 to 77%

2.2. TEST SUBSTANCE ADMINISTRATION AND CHAMBER OPERATIONS

2.2.1. ROUTE OF ADMINISTRATION

Inhalation as a gas, via whole-body exposures

2.2.2. TEST SUBSTANCE ADMINISTRATION

The test substance was administered as a gas in the breathing air of the animals. The test atmosphere was generated by an appropriate procedure determined during pre-study trials. The trials were performed to evaluate the optimal set of conditions and equipment to generate a stable atmosphere at the target exposure levels and maintain uniform conditions throughout the exposure chambers.

2.2.3. TARGET EXPOSURE LEVELS

Group 1 - 0 ppm
Group 2 - 30 ppm
Group 3 - 90 ppm
Group 4 - 180 ppm

2.2.4. CHAMBER OPERATIONS

The whole-body exposure chambers each had a volume of approximately 1000 Liters. Each chamber was operated at a minimum flow rate of 200 Liters per minute. The final airflow was set to provide at least one air change (calculated by dividing the chamber volume by the airflow rate) in 5.0 minutes (12 air changes/hour) and a T99 equilibrium time (calculated by multiplying the air change by the exponential factor 4.6) of at most 23 minutes.

Initial settings for each group were as follows:

Group	Airflow Rate (Lpm)	Air Change (min)	T_{99} (min)
1	207	4.8	22
2	211	4.7	22
3	207	4.8	22
4	212	4.7	22

This chamber size and airflow rates were considered adequate to maintain the animal loading factor below 5% and the oxygen level at 19% or higher. At the end of the exposure, all animals remained in chamber for a minimum of 23 minutes. During this time, the chamber was operated at the same flow rate as used during the exposure using clean air only. Recordings of airflow rate and static pressure were made at the initiation of the exposures and every half-hour during the exposure.

The chamber atmospheres were exhausted through the in-house filtering system, which consisted of a coarse filter, a HEPA filter, and an activated charcoal bed.

See Figures 1 and 2 and Table III (Inhalation Report) for equipment list.

2.2.5. EXPOSURE PROCEDURE

Group 1

Room air was directed into the inlet of 1000 Liter glass and stainless steel exposure chamber.

Groups 2 - 4

The test substance was delivered from the Sponsor's cylinder, through a regulator and two backpressure gauges, and branched, via ¼" tubing, to the three exposure systems. For each system, ¼" tubing directed the test substance to a mass flowmeter,

regulated by a metering valve, and then into the inlet of a 1000 Liter stainless steel and glass whole-body exposure chamber, where it mixed with room air.

See Figures 1 and 2, and Table III for equipment list.

2.3. EXPOSURE CONCENTRATION DETERMINATION

2.3.1. NOMINAL CONCENTRATION

A nominal exposure concentration was calculated. The flow of air through the chamber was monitored using appropriate calibrated equipment. The test substance (TS) consumed during the exposure was divided by the total volume of air passing through the chamber (volumetric flow rate times total exposure time) to give the nominal concentration.

Calculation

$$\text{Nominal Concentration (ppm)} = \frac{\text{Average Actual TS Flow (ccm)}}{\text{Chamber Flow (Lpm)}} \times 1000$$

See Table III for equipment list.

2.3.2. CHAMBER SAMPLING

Determination of the exposure levels were made using a MIRAN® Ambient Air analyzer equipped with a strip chart recorder. The test atmosphere was drawn from the normal sampling portal through the MIRAN® and measurements were recorded at least 4 times during each exposure. The exposure levels were determined by comparison of the measured absorbance to a calibrated response curve constructed using the same instrument settings.

See Table III for equipment list.

2.3.3. PARTICLE SIZE DISTRIBUTION

Particle size samples were drawn once during each week of exposure for the chambers and room air using a TSI Aerodynamic Particle Sizer to confirm the absence of particulate test substance condensate in the exposure atmosphere. The samples were drawn for 20 seconds at a rate of 5.0 Lpm. The mass median aerodynamic diameter, geometric standard deviation and total mass concentration were calculated. A computer was used to program the system to the appropriate settings prior to sampling. The particle size distributions were calculated by the computer and printed out.

See Table III for equipment list.

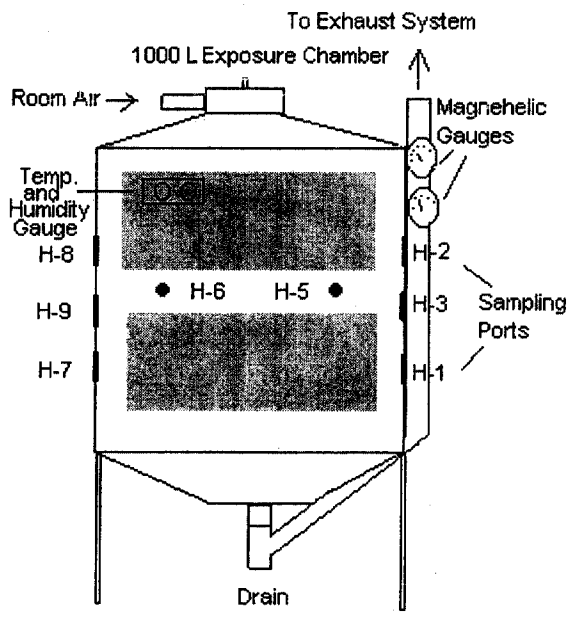
2.4. POST-STUDY TEST SUBSTANCE ANALYSIS

Based on the toxic effects of CTFE (body weight loss and/or decreased weight gain) seen at 90 and 180 ppm, a post-study experiment (non-animal) was conducted to evaluate CTFE for toxic dimer formation. The Sponsor provided 3 evacuated 1 Liter test cylinders: Cylinder#1 was used to collect a sample from the CTFE cylinder (via a gas bag), Cylinder#2 was used to collect a sample from the CTFE 90 ppm chamber (via a sample port) and Cylinder#3 was used to collect sample from the CTFE 180 ppm chamber (via a sample port). The samples were shipped to the Sponsor (S. Ferguson at Honeywell, Buffalo Research Laboratory) for analysis.

Results of these sample analyses are presented in Appendix O.

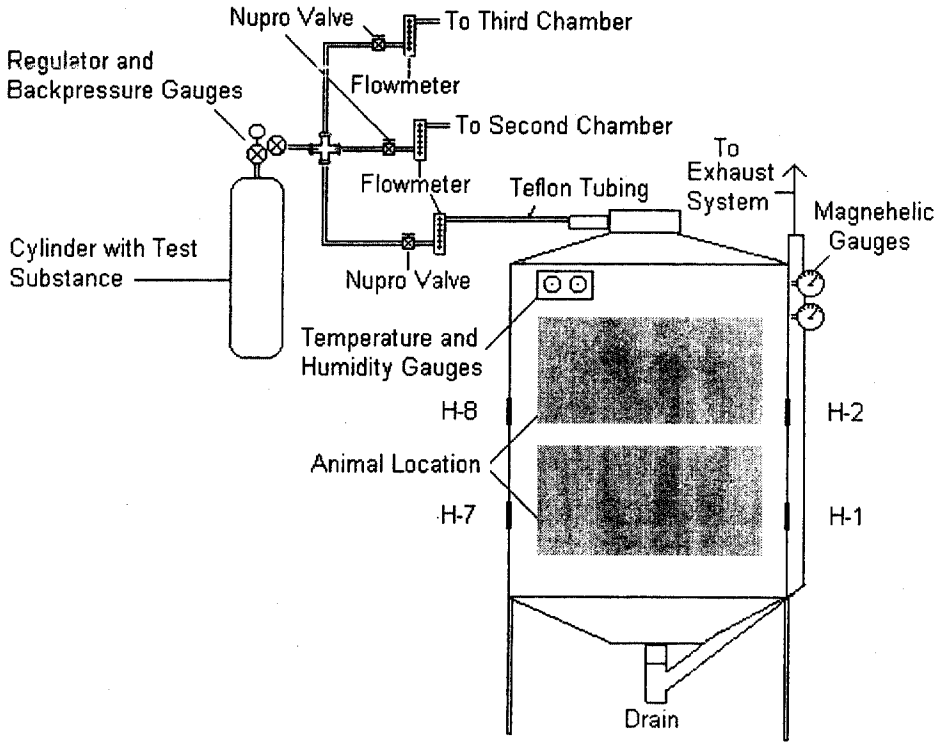
Group 1	Inhalation Report	Appendix N

Figure 1
Chamber Generation System
and Whole-Body Exposure Chamber



Note: Animals were individually housed on three levels within the exposure chamber.

Figure 2
Chamber Generation System
and Whole-Body Exposure Chamber



Note: Sampling Ports H-11 (left-bottom), H-12 (left-top), H-13 (right-bottom) and H-14 (right-top) used for pretest distribution sampling, were located on the back wall of the chambers.

	Inhalation Report	Appendix N

Table I
Summary of In-Chamber Observations

Exposure Number	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Group 1 – 0 ppm												
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All
Group 2 – 30 ppm												
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All
Group 3 – 90 ppm												
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All
Group 4 – 180 ppm[a]												
Within Normal Limits	All	All	All	All	All	All	-					
Eyes closed							Some[b]					
Pilorection							Some[b]					
Lethargic							Some[b]					

All = 100% of the animals exhibiting a given observation; Some = 21-50% of the animals exhibiting a given observation.
Note: In-chamber observations are based on all animals present in the exposure chamber at the time.
[a]Exposures were stopped during Exposure 7 due to observed effects.
[b]Group 4 animals were observed hourly during Exposure 7. These represent observations noted during the 4th hour prior to exposure cessation. Observations during the first 3 hours were considered to be within normal limits.

	Inhalation Report	Appendix N

Table I
Summary of In-Chamber Observations

Exposure Number	**13**	**14**	**15**	**16**	**17**
Group 1 – 0 ppm					
Within Normal Limits	All	All	All	All	All
Group 2 – 30 ppm					
Within Normal Limits	All	All	All	All	All
Group 3 – 90 ppm					
Within Normal Limits	All	All	All	All	All

All = 100% of the animals exhibiting a given observation; Some = 21-50% of the animals exhibiting a given observation.
Note: In-chamber observations are based on all animals present in the exposure chamber at the time.

	Inhalation Report	Appendix N

Table II
Chamber Monitoring Results
Preface

Key to Abbreviations

MMAD	=	Mass Median Aerodynamic Diameter
GSD	=	Geometric Standard Deviation
TMC	=	Total Mass Concentration

Table II
Chlorotrifluoroethylene: Embryo-Fetal Toxicity Study in Rats by Inhalation Exposure

Chamber Monitoring Results
Cumulative Exposure Record
Group 1 - 0 ppm (Air Control)

Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration Mean (ppm)	Individual (ppm)				Particle Size Determinations MMAD (µm)	GSD	TMC (mg/m³)	Chamber Environment Mean Temperature (°C)	Humidity (%)
24-Aug-04	1	0	0.00	0.00	0.00	0.00	0.00				22	57
25-Aug-04	2	0	0.00	0.00	0.00	0.00	0.00				22	56
26-Aug-04	3	0	0.0004	0.24	0.00	0.00	0.00				23	57
27-Aug-04	4	0	0.00	0.00	0.00	0.00	0.00				23	62
28-Aug-04	5	0	0.00	0.00	0.00	0.00	0.00	0.8292	2.001	6.23E-03	24	62
29-Aug-04	6	0	0.00	0.00	0.00	0.00	0.00				24	56
30-Aug-04	7	0	0.00	0.00	0.00	0.00	0.00				24	56
31-Aug-04	8	0	0.00	0.00	0.00	0.00	0.00				24	60
1-Sep-04	9	0	0.00	0.00	0.00	0.00	0.00				24	59
2-Sep-04	10	0	0.00	0.00	0.00	0.00	0.00				24	56
3-Sep-04	11	0	0.00	0.00	0.00	0.00	0.00	1.348	2.004	2.31E-03	23	59
4-Sep-04	12	0	0.00	0.00	0.00	0.00	0.00				23	62
5-Sep-04	13	0	0.00	0.00	0.00	0.00	0.00				23	59
6-Sep-04	14	0	0.00	0.00	0.00	0.00	0.00				24	57
7-Sep-04	15	0	0.00	0.00	0.00	0.00	0.00				23	56
8-Sep-04	16	0	0.00	0.00	0.00	0.00	0.00				22	57
9-Sep-04	17	0	0.00	0.00	0.00	0.00	0.00				21	58
	Mean	**0.0**		**0.0011**				**1.089**	**2.003**	**0.004**	**23.1**	**58.2**
	S.D.	**0.0**		**0.0162**				**0.4**	**0.0**	**0.0**	**0.9**	**2.2**

Table II
Chlorotrifluoroethylene: Embryo-Fetal Toxicity Study in Rats by Inhalation Exposure

Chamber Monitoring Results
Cumulative Exposure Record
Group 2 - 30 ppm

Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration Mean (ppm)	Individual (ppm)				Particle Size Determinations MMAD (µm)	GSD	TMC (mg/m³)	Chamber Environment Mean Temperature (°C)	Humidity (%)
24-Aug-04	1	28	34.3	34	33	36	34				21	58
25-Aug-04	2	28	32.3	29	29	34	37				22	57
26-Aug-04	3	28	31.8	32	29	34	32				22	57
27-Aug-04	4	28	31.3	32	32	30	31				22	64
28-Aug-04	5	28	33.8	37	36	30	32	0.8057	1.716	5.65E-03	23	63
29-Aug-04	6	28	30.5	28	31	33	30				23	58
30-Aug-04	7	28	28.0	26	28	29	29				22	58
31-Aug-04	8	28	31.0	31	30	31	32				22	62
1-Sep-04	9	28	31.5	33	28	35	30				23	59
2-Sep-04	10	28	30.3	30	29	30	32				23	58
3-Sep-04	11	28	30.8	32	31	30	30	1.317	1.890	2.42E-03	22	62
4-Sep-04	12	28	30.0	30	29	29	32				22	64
5-Sep-04	13	28	30.0	30	30	30	30				22	61
6-Sep-04	14	28	31.5	31	31	32	32				23	60
7-Sep-04	15	28	29.5	29	30	31	28				22	58
8-Sep-04	16	28	30.8	29	34	30	30				21	58
9-Sep-04	17	28	31.5	31	30	36	29				21	60
	Mean	**28.0**		**31.1**				**1.061**	**1.803**	**4.04E-03**	**22.1**	**59.8**
	S.D.	**0.0**		**2.3**				**0.4**	**0.1**	**0.0**	**0.7**	**2.4**

Table II
Chlorotrifluoroethylene: Embryo-Fetal Toxicity Study in Rats by Inhalation Exposure

Chamber Monitoring Results
Cumulative Exposure Record
Group 3 - 90 ppm

Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration Mean (ppm)	Individual (ppm)				Particle Size Determinations MMAD (µm)	GSD	TMC (mg/m^3)	Chamber Environment Mean Temperature (°C)	Humidity (%)
24-Aug-04	1	77	98.3	93	92	110	98				22	56
25-Aug-04	2	77	82.8	79	80	81	91				23	55
26-Aug-04	3	77	85.5	110	71	96	65				23	57
27-Aug-04	4	77	91.0	88	91	92	93				24	62
28-Aug-04	5	77	92.0	100	94	81	93	0.8458	2.633	6.92E-03	24	62
29-Aug-04	6	77	84.8	82	83	78	96				24	56
30-Aug-04	7	77	78.5	73	77	82	82				23	57
31-Aug-04	8	77	84.5	84	82	85	87				24	61
1-Sep-04	9	77	86.3	88	78	94	85				24	57
2-Sep-04	10	77	84.8	87	81	86	85				24	55
3-Sep-04	11	77	92.8	95	93	92	91	1.412	1.872	2.76E-03	23	60
4-Sep-04	12	77	94.0	93	90	95	98				23	64
5-Sep-04	13	77	90.5	91	91	90	90				23	60
6-Sep-04	14	77	92.3	96	92	91	90				23	59
7-Sep-04	15	77	89.5	91	88	95	84				23	57
8-Sep-04	16	77	91.3	100	89	88	88				22	57
9-Sep-04	17	77	98.0	98	100	100	94				22	58
	Mean	**77.0**		**89.2**				**1.129**	**2.253**	**4.84E-03**	**23.2**	**58.4**
	S.D.	**0.0**		**8.1**				**0.4**	**0.5**	**0.0**	**0.7**	**2.7**

Table II
Chlorotrifluoroethylene: Embryo-Fetal Toxicity Study in Rats by Inhalation Exposure

Chamber Monitoring Results Cumulative Exposure Record Group 4 - 180 ppm												
Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration					Particle Size Determinations			Chamber Environment Mean	
			Mean (ppm)	Individual (ppm)				MMAD (µm)	GSD	TMC (mg/m^3)	Temperature (°C)	Humidity (%)
24-Aug-04	1	170	210	210	210	210	210				22	54
25-Aug-04	2	160	183	170	180	170	210				23	53
26-Aug-04	3	170	153	150	170	130	160				23	54
27-Aug-04	4	170	203	190	210	210	200				23	60
28-Aug-04	5	170	188	200	180	170	200	1.095	3.587	8.54E-03	23	60
29-Aug-04	6	170	195	180	200	190	210				23	55
30-Aug-04	7	170	180	170	190	180	a				23	54
	Mean	**169**		**187**				**1.095**	**3.587**	**8.54E-03**	**22.9**	**55.7**
	S.D.	**4**		**21**				**-**	**-**	**-**	**0.4**	**3.0**

[a]Group 4 exposures terminated during Exposure 7 (after 3.5 hours) due to physical condition of the animals.

	Inhalation Report	Appendix N

Table III
Equipment List

Exposure Chamber
1000 Liter glass and stainless steel chamber (Wahmann).

Compound Reservoir
Gas Cylinder (Sponsor provided)

Flowmeter
Dwyer®, size 0-20 Lpm (Dwyer® Instruments).
Top Trak™ Mass Flow Meter, size 0 – 1 Lpm and 0 – 100 ccm, Model 821-04-1 (Sierra Instruments) calibrated prestudy with a 1 – 250 sccm and 20ccm-6 Lpm Gilibrator®Bubble Generator, P/N D800286 and D800287 646-L.
Glass flowmeter, size 1-100 mL (Hewlet Packard) used to confirm results of Gilibrator® Bubble Generator.

Chamber Air Flow
Dwyer® Magnehelic® gauge (Dwyer® Instruments Inc.), calibrated prestudy with a Dry Gas Meter , Model 2M (Singer) or Side Trak™ III mass flowmeter, equipped with a Digital Meter (Group 1 only), Model 831-N2 (Sierra Instruments, Inc.).

Chamber Static Pressure
Dwyer® Magnehelic® gauge (Dwyer® Instruments Inc.), calibrated prestudy with Dwyer® Mark II Manometer, Model 25 (Dwyer® Instruments, Inc.).

Regulators
MG Industries Series 300.

Pressure/Vacuum Gauges
GAST® vacuum gauge, Model 169-01.
MG Industries backpressure gauges, P/N ID201/ID206.

Metering Valve
Metering Valve, Model SS-31RS4 (Whitey®).

Vacuum Pumps
Thomas Industries Inc., Model 707CM50.

Tubing
Clear plastic, sizes ¼", ½" (Norton, Baxter).
Stainless steel cross.
Teflon®, size ¼ ".
Stainless Steel, size ½".

	Inhalation Report	Appendix N

Table III
Equipment List

Plastic tubing ⅛" (Tygon)

Air Analyzer

MIRAN® 1A-CVF Ambient Air Analyzer (Wilks) with a Cole Parmer Strip Chart Recorder, Model 201, and a Micronta® LCD Benchtop Digital Multimeter, Model No. 22-195 Balston® Microfibre™ Disposable Filter Unit (Grade DQ) was attached in-line.

Syringe, size 0 – 0.5 and 0 – 1.0 mL (Precision).

Syringe, size 0 - 25 and 0 – 250 µL, 1 – 1000 µL Gas-tight Nos. 1001 and 1725 (Hamilton).

Particle Sizer

TSI Aerodynamic Particle Sizer, Model 331001, and a DELL computer, Model 486P/25, equipped with an Epson LQ-5707 printer, Model P630B.

Environmental Monitoring

VWR Temperature and Humidity Gauge, tested prestudy with a Big Digit Traceable Hygrometer/Thermometer.

Balance

Pelouze, No. 4040

	Inhalation Report	Appendix N

Table IV
Chamber Distribution Records (Pre-study)

Group (target)	Date	Port	IR Conc (ppm)	Ratio to H-1
2 (30 ppm)	06 August 2004	H-1	34	1.00
		H-2	33	0.97
		H-8	34	1.00
		H-7	33	0.97
	18 August 2004	H-1	32	1.00
		H-14	32	1.00
		H-13	31	0.97
		H-1	34	1.00
		H-12	33	0.97
		H-11	33	0.97
	20 August 2004	H-1	26	1.00
		H-2	26	1.00
		H-7	27	1.04
		H-8	28	1.08
		H-1	27	1.00
		H-14	27	1.00
		H-13	28	1.04
		H-12	28	1.04
		H-11	28	1.04
3 (90 ppm)	13 August 2004	H-1	97	1.00
		H-2	100	1.03
		H-7	79	0.81
		H-1	72	1.00
		H-8	97	1.35
		H-1	90	1.00
		H-11	100	1.11
		H-12	110	1.22
		H-1	80	1.00
		H-13	100	1.25
		H-14	100	1.25
		H-1	93	1.00
		H-7	97	1.04
		H-8	99	1.06

	Inhalation Report	Appendix N

Table IV
Chamber Distribution Records (Pre-study)

Group (target)	Date	Port	IR Conc (ppm)	Ratio to H-1
	18 August 2004	H-1	93	1.00
		H-14	86	0.92
		H-13	86	0.92
		H-1	91	1.00
		H-2	88	0.97
		H-7	86	0.95
	20 August 2004	H-1	90	1.00
		H-2	91	1.01
		H-7	90	1.00
		H-8	91	1.01
		H-1	94	1.00
		H-14	95	1.01
		H-13	92	0.98
		H-1	87	1.00
		H-12	96	1.10
		H-11	96	1.10
4 (180 ppm)	18 August 2004	H-1	170	1.00
		H-2	170	1.00
		H-7	170	1.00
		H-8	170	1.00
		H-1	170	1.00
		H-14	170	1.00
		H-13	160	0.94
		H-1	170	1.00
		H-12	170	1.00
		H-11	160	0.94
	20 August 2004	H-1	170	1.00
		H-2	170	1.00
		H-7	170	1.00
		H-8	170	1.00
		H-1	170	1.00
		H-14	170	1.00
		H-13	170	1.00
		H-1	180	1.00
		H-12	170	0.94
		H-11	170	0.94

Table V
Miran Calibration

Methodology for CTFE

Settings: The instrument settings for the Miran 04 Unit are summarized below:

wavelength, microns	8.4
pathlength, dial setting	14.00
slit width, mm	1
range, absorbance	1A
response, seconds	40
gain	High
chart speed, cm/min	1
chart volts	1

Calibrations: The Miran® was turned on and allowed to warm up for approximately 10 minutes. The cell was flushed with room air for approximately one minute. The loop was closed, the unit was zeroed and the calibration series was performed as shown below. The resultant data were plotted to obtain a calibration curve. Each observer used a separate syringe for calibration.

Injection Volume (μL)	Calculated Concentration[1] (ppm)	Absorbance Operator 1 (volts)	Absorbance Operator 2 (volts)	Absorbance Average (volts)
135	24.0	0.1348	0.1321	0.1335
170	30.1	0.1764	0.1714	0.1739
510	90.4	0.415	0.3861	0.4006
1000	177	0.596	0.593	0.595
1240	220	0.665	0.674	0.670

[1]Calculated Conc. (ppm) = $\frac{\text{Injection volume } (\mu L)}{5.64 \text{ L (Volume of Miran closed-loop)}}$

	Inhalation Report	Appendix N

Table V
Miran Calibration

Calibration Check: A three-point calibration check of the Miran® was performed for each exposure prior to sampling the chambers. The parameters are shown below:

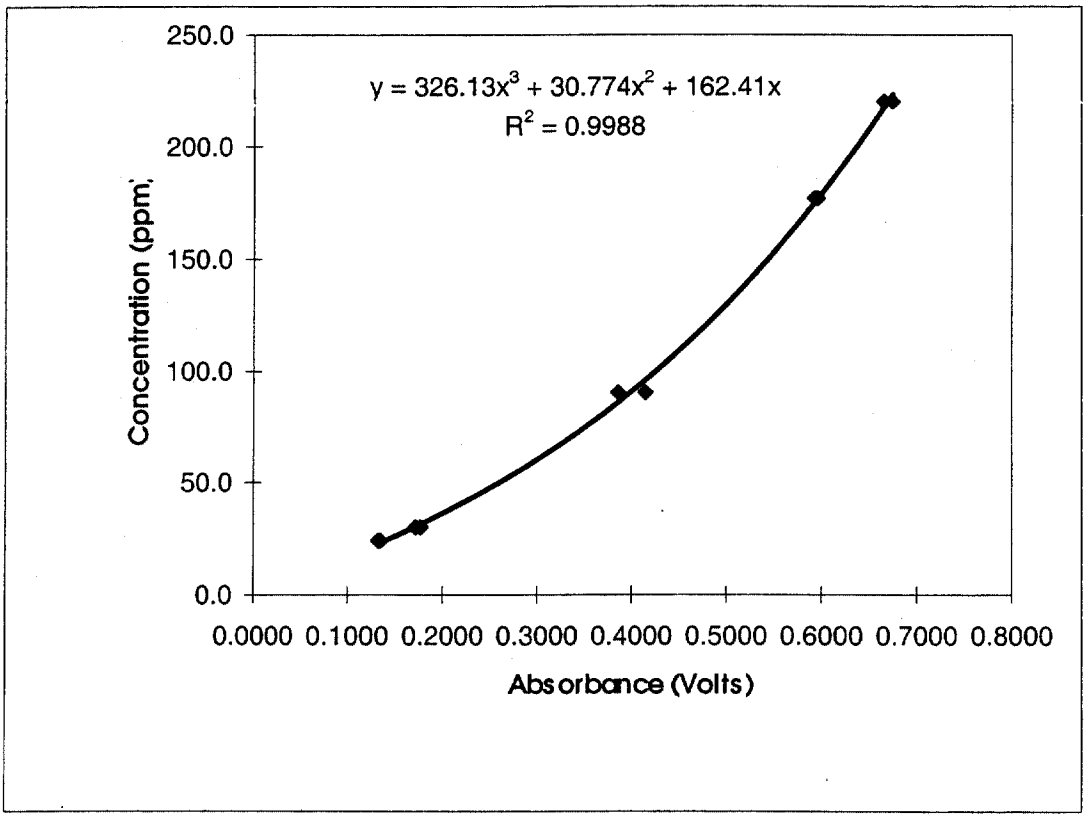
Injection Volume (µL)	Calculated Concentration (ppm)	Expected Absorbance Reading (volts)	Acceptable Absorbance Range (volts)
170	30.1	0.1739	0.1478 – 0.2000
510	90.4	0.401	0.3409 – 0.461
1000	177	0.595	0.506 – 0.684

The absorbance was recorded after each injection. The absorbance was considered satisfactory if it was within 15% of the original calibration series. If any of the absorbance values fell outside the 15% range, the injection was rechecked as follows. The volume for the value that was out of range was reinjected twice. The closer pair of the three injections was averaged and the results were compared to the original curve. If the average of the pair was within the 15% range, the original was accepted. If the value of the average was outside the 15% range, the Study Director decided if a new graph was to be prepared.

	Inhalation Report	Appendix N

Table V
Miran Calibration

Calibration Curve for CTFE
(Groups 1 - 4)



	Sponsor's Post-Study Analytical Report	Appendix O

HONEYWELL
Buffalo Research Laboratory
Analysis Request

Analytical Results
Report Form

Project # 955019
Report by: S.Ferguson
DATE: 10/08/04

CFTE GC Results - Weight %
Huntingdon Samples

COMPONENT		AR#34903 Collected on dry ice 9/21/2004 Run #1	AR#34903 Collected on dry ice 9/21/2004 Run #2	AR#34903 Collected on dry ice 9/21/2004 Average 2 runs
FC-133a		0.0051	0.0054	0.0053
FC-1122		0.0320	0.0314	0.0317
FC-20		ND	ND	ND
DME		ND	ND	ND
FC-40		ND	ND	ND
FC-123		ND	ND	ND
FC-123a		ND	ND	ND
FC-1132a		ND	ND	ND
Methanol		ND	ND	ND
FC-113		ND	ND	ND
FC-1123		0.0002	0.0003	0.0003
Triethylamine		ND	ND	ND
1113 Dimer #1		0.0478	0.0463	0.0471
1113 Dimer #2		0.0656	0.0645	0.0651
Unknowns		0.0009	0.0007	0.0008
FC-1113		99.8484	99.8514	99.8499

Honeywell
Buffalo Research Laboratory
Analysis Request

ANALYTICAL RESULTS
Report Form

PROJECT NO:955019
Report by: S. Ferguson
DATE: 10/08/04

Ref. Notebook No./Page
40245 Pg. 13,14

Other Reference & Notes
DB-1301 Fast column

CFTE-Huntingdon
Results Reported in Volume %

(Curve:R-Squared = 0.952837)

Component	Standard #1 0.0073%	Standard #2 0.0147%	Standard #3 0.0293%	AR#34904 91ppm (2 runs)	AR#34905 250ppm (2 runs)	
FC-1113	0.0065%	0.0154%	0.0280%	0.0041%	0.0179%	
		0.0133%		0.0044%	0.0189%	
		0.0154%				

	Sponsor's Test Substance Certificate of Analysis	Appendix P

Honeywell

Lot: BR4141
Vessel: G1113X140
Lab ID: BB18701
Date: 5/20/04

P.O. Box 2830
Baton Rouge, La. 70821
Phone# (225) 383-5222
Fax# (225) 346-3689

Genetron® 1113 Standard Grade

Certificate of Analysis

Test	Specification	Result	Units	Method
G1113	99.7 min.	99.95	%	AP-QCL-002
G1123 / 1122	0.10 max.	0.0235	%	AP-QCL-002
G1122	0.05 max.	0.0232	%	AP-QCL-002
Methanol	0.01 max.	Not detected	%	AP-QCL-002
Other organic impurities	0.05 max.	0.0251	%	AP-QCL-002
Peroxide	NOT DETECTED	Not detected	%	AP-QCL-070
Acid as HCl	0.0005 max.	Not detected	%	AP-QCL-070
Moisture	0.0020 max.	0.0002	%	AP-QCL-090
Oxygen	0.0050 max.	0.0012	%	AP-QCL-011
Non-Condensables	report only		%	AP-QCL-010

Approved By: Daniel Niwa
Quality Control Leader

Appendix Q

STUDY NO. 04-4261
HONEYWELL PROJECT NO. MA-198-81-4

CHLOROTRIFLUOROETHYLENE (CTFE):
EMBRYO-FETAL TOXICITY STUDY IN RATS BY
INHALATION EXPOSURE

POST-STUDY RANGE-FINDING EVALUATION
FINAL REPORT

Author: Gary M. Hoffman, B.A., D.A.B.T.

Performed by: Huntingdon Life Sciences
100 Mettlers Road
East Millstone, New Jersey 08875-2360

Submitted to: Honeywell
Engineered Materials Sector
101 Columbia Road, PO Box 2245R
Morristown, New Jersey 07962-1057

Attn: George M. Rusch, Ph.D., D.A.B.T.

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY IN RATS BY INHALATION EXPOSURE

SUMMARY

This study was designed to assess further the comparable effects of Chlorotrifluoroethylene (CTFE) with no dimers, or as originally tested (0.1% dimers) during the Main Study, or increasing percentages of dimers for their potential maternal and/or developmental toxicity in the pregnant rat when administered by whole-body inhalation exposure. Time-mated female Sprague Dawley CD® rats (5/group) were exposed once daily for 6 hours/day for 5 consecutive days (Gestation Days 6-10) to 0 ppm (Air only – Group 1), 180 ppm (CTFE no dimers - Group 2), 180 ppm (CTFE 0.1% dimers – Group 3), 180 ppm (CTFE 0.5% dimers – Group 4) or 180 ppm (2.0% dimers – Group 5). From Gestation Days 6-20, the following parameters were evaluated for all animals: viability, clinical observations, body weights and feed consumption. Exposure levels were determined using an IR sampling procedure 4 times per chamber per day. At caesarean section on Gestation Day 20, all animals were euthanized and subjected to a macroscopic postmortem evaluation. The fetuses were examined for externally visible abnormalities.

The mean (± standard deviation) analytical (IR) concentrations for the control and the respective exposure groups were as follows: 0±0, 180±15, 181±12, 191±12 and 183±11 ppm. There was no effect of treatment on survival or pregnancy rates. During the exposure periods, all animals were unremarkable except that some of the exposed dams showed some decreased activity and/or labored breathing during their 5th exposure. During the non-exposure periods, the CTFE exposed animals showed ano-genital staining, red/brown stains on the fur, red nasal discharge, decreased activity and labored breathing. There was little evidence of a dose relationship for these findings, except that there was a slightly higher prevalence in Groups 4 and 5, most evident during the exposure period, GD 6-10. There were statistically significantly reduced body weights and feed consumption during gestation days 6-10 (corresponding with the CTFE exposures) for the test substance exposed animals. These animals then showed rapid recovery in body weights and feed consumption following cessation of the exposures. There were no test substance related effects on maternal or fetal necropsy findings or litter sizes at GD 20.

In conclusion, exposure of time-mated female rats to target concentrations of 180 ppm of CTFE, with and without dimers (0.1 to 2.0%), by whole-body inhalation for gestation days 6-10 resulted in some adverse clinical signs, decreased body weight and feed consumption in all exposed groups. However, the observations were generally similar for all CTFE exposed groups indicating that CTFE, and not the presence of dimers, was the cause of the adverse responses.

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1. INTRODUCTION

This study was designed to assess the comparable effects of Chlorotrifluoroethylene (CTFE) with and without dimers, for their potential maternal and/or developmental toxicity in the pregnant rat when administered by whole-body inhalation exposure. Animals were treated during the period of early organogenesis, Gestation Days (GD) 6-10 inclusive, then sacrificed on GD 20 and subjected to cesarean section.

2. MATERIALS AND METHODS

2.1. STUDY MANAGEMENT

2.1.1. SPONSOR

Honeywell
Engineered Materials Sector
101 Columbia Road, PO Box 2245R
Morristown, New Jersey 07962-1057

2.1.2. SPONSOR STUDY MONITOR

George M. Rusch, Ph.D., DABT

2.1.3. TESTING FACILITY

Huntingdon Life Sciences
100 Mettlers Road
East Millstone, New Jersey 08875-2360

2.1.4. STUDY DIRECTOR

Gary M. Hoffman, B.A., DABT

2.2. STUDY DATES

2.2.1. STUDY INITIATION

5 August 2004 (Date Study Director signed the Protocol)

2.2.2. DATES OF ANIMAL RECEIPT

03 February 2005

2.2.3. INITIATION OF EXPOSURES – GESTATION DAY 6

08 February 2005

2.2.4. TERMINATION OF EXPOSURES – GESTATION DAY 10

12 February 2005

2.2.5. NECROPSY – GESTATION DAY 20

22 February 2005

2.3. EXPERIMENTAL DESIGN

Group	Group Designation	Exposure Levels[b] (ppm)	Treatment Gestation Days	Number of Animals		
				Time-Mated Females	Euthanized Gestation Day 20	Gross Fetal Evaluations (Fetuses/Litter)
1	Air Control	0	6-10	5	All	All
2	CTFE (no dimers)	180	6-10	5	All	All
3	CTFE (0.1% dimers)[a]	180	6-10	5	All	All
4	CTFE (0.5% dimers)	180	6-10	5	All	All
5	CTFE (2.0% dimers)	180	6-10	5	All	All

[a]Original Main Study sample received 03 June 2004.

[b]Exposures were 6 hours per day for 5 consecutive days. Exposure levels were expressed as ppm of test substance. The exposures were conducted via whole-body exposure.

Study Day 0 was defined as the first day of gestation. Study Day 6 was the first day of exposures.

2.4. JUSTIFICATIONS

2.4.1. ROUTE, DURATION AND FREQUENCY OF ADMINISTRATION

The inhalation route is one of the potential routes of human exposure to this test substance.

2.4.2. TEST ANIMAL SELECTION

The rat was used as a surrogate for humans in the detection of embryo-fetal toxicity and is a species in which known teratogens have been detected. This rodent species is commonly used in the conduct of embryo-fetal toxicity studies and was the species used in the original developmental toxicity study. Historical control data are also available with this strain of rat for comparative evaluation, if necessary.

2.4.3. NUMBER OF ANIMALS

The group size of 5 mated females was considered the minimum to evaluate the anticipated treatment effects of body weight loss and/or decreased weight gain. The number of test groups is considered the minimum to adequately evaluate the effect of the absence and/or presence (at 3 levels of concentration) of the suspect dimers.

2.4.4. EXPOSURE LEVEL SELECTION

Due to toxic effects (body weight loss and/or decreased weight gain) seen at 90 and 180 ppm during the Main Study during the initial 5 days of exposures (GD 6-10), a post-study (non-animal) experiment was conducted to evaluate undesired dimer formation in the Test Substance (see Protocol Amendment 3). Although these dimers are not normally present in the CTFE as produced and sold, Sponsor GC analysis did indicate these were present. Toxicity of this magnitude would not have been predicted based upon a pilot developmental toxicity study conducted with CTFE because it did not contain appreciable levels of dimers. Therefore, further evaluation (with time-mated animals) of the comparable effects of the Test Substance with no dimers (Group 2), as

dimers (Group 4) and with more (2.0%) dimers (Group 5) was necessary.

2.5. TEST SUBSTANCE

Chlorotrifluoroethylene (CTFE: no dimer, 0.1%, 0.5% and 2.0%)
MW = 116.47; CAS #79-38-9

2.5.1. TEST SUBSTANCE CATEGORY

Industrial chemical used as a monomer for the production of chlorofluorocarbon polymers

2.5.2. SUPPLIER

Honeywell
20 Peabody Street
Buffalo, NY 14210

2.5.3. LOT NUMBER

Day Tank 12/17/04 (Group 2)
BR4141 (original Main Study sample for Group 3)
Day Tank 12/17/04 – Standard A (Group 4)
Day Tank 12/17/04 – Standard B (Group 5)

2.5.4. PURITY

99.94% (Day Tank 12/17/04)
99.95% (BR4141)
99.46% (Day Tank 12/17/04 – Standard A)
98.04% (Day Tank 12/17/04 – Standard B)

2.5.5. DATE RECEIVED

03 June 2004 (original Main Study sample for Group 3)
18 January 2005 (Groups 2, 4 and 5 Post-Study Range-Finding Evaluation samples)

2.5.6. EXPIRATION DATE

30 June 2005 (original Main Study sample for Group 3)

2.2.2. DATES OF ANIMAL RECEIPT (OECD EXPERIMENTAL START DATE)

20 & 23 August 2004

2.2.3. INITIATION OF EXPOSURES – FIRST GESTATION DAY 6 (EPA EXPERIMENTAL START DATE)

24 August 2004

2.2.4. DOSING TERMINATION – LAST GESTATION DAY 19

9 September 2004

2.2.5. NECROPSY – FIRST GESTATION DAY 20

7-10 September 2004

2.2.6. EXPERIMENTAL TERMINATION DATE – (DATE OF LAST DATA COLLECTION)

22 February 2005 (Date of completion of fetal examinations)

2.2.7. STUDY COMPLETION

22 June 2005 (Date Final Report is signed by the Study Director)

2.6.2. SUPPLIER

Charles River Laboratories
Raleigh, NC 27610

2.6.3. NUMBER OF ANIMALS

Ordered: 27 time-mated female rats.

Placed on study: 25 time-mated female rats.

2.6.4. AGE AT RECEIPT

Time-mated female rats, received on GD 1, were between 75-95 days in age.

2.6.5. WEIGHT AT INITIATION OF EXPOSURES

Females weighed between 243-302 grams on Gestation Day 6.

2.6.6. ACCLIMATION PERIOD

Animals were acclimated for 5 days from time of receipt until initiation of exposures on Gestation Day 6.

2.7. ANIMAL ASSIGNMENT

Animals were placed into study groups after receipt using a computerized randomization program. This ranked GD 4 body weights into blocks and randomly assigned each animal within each block into one of the study groups. Disposition of all animals not utilized in the study is maintained in the study file.

2.8. ANIMAL IDENTIFICATION

Each animal was assigned a temporary identification number upon receipt. After selection for study, each animal was ear-tagged with a number assigned by the Testing Facility. This number plus the study number comprised a unique identification for each animal. Each study animal's cage was also allocated a cage card, which was color-coded for exposure level identification and contained the study number and animal number.

2.9. VETERINARY CARE

Animals were monitored by the technical staff for any conditions requiring possible veterinary care.

2.10. ANIMAL HUSBANDRY DURING NON-EXPOSURE PERIODS

2.10.1. FACILITIES MANAGEMENT/ANIMAL HUSBANDRY

Currently acceptable practices of good animal husbandry were followed e.g., *Guide for the Care and Use of Laboratory Animals*; National Academy Press, 1996. Huntingdon Life Sciences, East Millstone, New Jersey is fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC).

2.10.2. HOUSING

Animals were housed individually in suspended stainless steel wire mesh cages.

2.10.3. FEED

Certified Rodent Diet, No. 5002; (Meal) (PMI Feeds, Inc., St. Louis, MO) *ad libitum.*

2.10.4. FEED ANALYSIS

Analytical certifications of feed batches were performed by the manufacturer. The results are maintained on file by the manufacturer. There were no known contaminants in the feed which were expected to interfere with the objectives of this study.

2.10.5. WATER

Facility water was supplied by Elizabethtown Water Company, (Westfield, NJ) and provided *ad libitum* to individual animal cages through an automated watering system.

2.10.6. WATER ANALYSIS

Water analyses are conducted monthly by the Elizabethtown Water Company, Westfield, New Jersey (Raritan-Millstone Plant) to

ensure that water meets standards specified under the EPA Federal Safe Drinking Water Act Regulations (40 CFR part 141). Water analyses, provided by the supplier, will be maintained on file at the Testing Facility. In addition, water samples are collected biannually from representative rooms in the Testing Facility. Chemical and microbiological water analyses are conducted on these samples by a subcontract laboratory (Benchmark Analytics, Center Valley, PA). Results are maintained on file at the Testing Facility. There are no known contaminants in the water that were expected to interfere with this study.

2.10.7. ENVIRONMENTAL CONDITIONS

Light/Dark Cycle

A twelve-hour light/dark cycle controlled via an automatic timer was provided.

Temperature

Temperature was monitored in accordance with Testing Facility SOPs and maintained within the specified range to the maximum extent possible. Excursions outside the specified range were not considered to have affected the integrity of the study.

Desired Range:	18 to 26 °C
Actual Range:	14 to 25 °C
Daily Average Range:	20 to 24 °C

Relative Humidity

Relative humidity was monitored in accordance with Testing Facility SOPs and maintained within the specified range to the maximum extent possible. Excursions outside the specified range were not considered to have affected the integrity of the study.

Desired Range:	30 to 70%
Actual Range:	10 to 98%
Daily Average Range:	22 to 52%

Air Changes

Animal quarters had 10-15 air changes per hour. The actual number of air changes per hour in each animal room is recorded at least twice each year and the Testing Facility retains these records.

2.11. TEST SUBSTANCE ADMINISTRATION AND CHAMBER OPERATION

Refer to Inhalation Report (Appendix J).

2.12. EXPERIMENTAL EVALUATIONS

2.12.1. VIABILITY CHECKS

Animals were observed in their cages at least twice daily for mortality, morbidity and signs of severe toxicity.

2.12.2. DETAILED PHYSICAL EXAMINATIONS

In-Chamber: All animals were observed as a group once during each exposure.

Out-of-Chamber: Animals on study were examined daily (except on Day 11) from receipt through to terminal euthanasia on GD 20. Examinations included observations of general condition, skin and fur, eyes, nose, oral cavity, abdomen and external genitalia as well as evaluations of respiration. During the treatment period these evaluations were performed after exposures.

2.12.3. BODY WEIGHT

Body weights were recorded on GD 4, 6, 10, 13, 16, 19 and 20. Weight gain was calculated for the following intervals: GD 4-6, 6-10, 10-13, 13-16, 16-20 and 6-20.

2.12.4. FEED CONSUMPTION

Feed consumption was recorded and calculated for the following intervals: GD 4-6, 6-10, 10-13, 13-16, 16-20 and 6-20.

2.13. TERMINAL OBSERVATIONS

2.13.1. METHOD OF EUTHANASIA

All dams were euthanized by carbon dioxide inhalation. All live fetuses were euthanized by an intraperitoneal overdose of sodium pentobarbital.

2.13.2. MACROSCOPIC EXAMINATIONS

A macroscopic postmortem examination was performed on all the dams and fetuses.

2.14. FETAL EVALUATIONS

Each (live and dead) fetus was given a macroscopic external examination for defects, including observation of the palate.

2.15. STATISTICAL ANALYSIS

The following parameters were analyzed statistically, where it was considered necessary in support of interpretation:

Body weights and feed consumption

Cesarean section data

2.15.1. CONTINUOUS DATA

Statistical significance for differences from control was recognized at the 5% or 1%, two-sided levels. Evaluation of equality of group means was made by the appropriate statistical method, followed by a multiple comparison procedure, if needed. The parametric method was the standard one-way analysis of variance (ANOVA) using the f ratio to assess significance (Dunlap and Duffy, 1975). If the ANOVA was significant, Dunnett's test (Dunlap, et.al., 1981) was used to determine which data, if any, differed from the control. the nonparametric method was the Kruskal-Wallis test (Siegel, S., 1956) and if differences were indicated, the pairwise comparison test (Siegel, S., 1956) was used to determine which means differed from control.

2.15.2. INCIDENCE DATA

A Fisher's Exact Test with Bonferroni correction (Siegel, S., 1956) was performed to identify differences between the groups.

2.16. DATA STORAGE

All data documenting experimental details and study procedures and observations were recorded and maintained as raw data. At the completion of the study, all reports, raw data, preserved specimens and retained samples will be maintained in the Archives of the Testing Facility for a period of 10 years after submission of the signed final report. The Sponsor will determine the final disposition of these materials.

2.17. REGULATORY REFERENCES

2.17.1. TEST GUIDELINES

The design of follow-up studies of this kind is not defined by Regulatory Guidelines.

2.17.2. GOOD LABORATORY PRACTICES

This study was conducted in compliance with Organization for Economic Cooperation and Development (OECD) Good Laboratory Practices as set forth in ENV/MC/CHEM(98)17 and EPA Good Laboratory Practices as set forth in 40 CFR Part 792 (TSCA).

2.17.3. ANIMAL WELFARE ACT COMPLIANCE

This study complied with all appropriate parts of the Animal Welfare Act Regulations: 9 CFR Parts 1 and 2 Final Rules, Federal Register, Volume 54, No. 168, August 31, 1989, pp. 36112-36163 effective October 30, 1989 and 9 CFR Part 3 Animal Welfare Standards; Final Rule, Federal Register, Volume 56, No. 32, February 15, 1991, pp. 6426-6505 effective March 18, 1991.

2.18. PROTOCOL DEVIATIONS

The following protocol deviations occurred during the study at the Testing Facility but did not affect the integrity of the study:

1. Due to technician oversight, Animal Nos. 1572, 2572, 3572, 4572, and 5572 were not rotated on 10 February 2005 (Exposure Day 3).

2. Due to technician oversight, the detailed physical observations were not performed on Study Day 11.

3. Due to technician oversight, data collection of macroscopic examination was not completed on Dam No. 5571.

4. An archival sample of test substances received on 18 January 2005 was not taken as per protocol. However, these samples were for post-study range-find study only.

3. RESULTS AND DISCUSSION

3.1. CHAMBER MONITORING

(Appendix I)

The target and mean (± standard deviation) analytical (IR) and nominal concentrations (based on gas flows) are summarized as follows:

Group	Test Substance	Target Concentration (ppm)	Analytical Concentration (ppm)	Nominal Concentration (ppm)
1	Air Control	0	0.0 ± 0.0	0.0 ± 0.0
2	CTFE (no dimers)	180	180 ± 15	210 ± 0.0
3	CTFE (0.1% dimers)	180	181 ± 12	210 ± 0.0
4	CTFE (0.5% dimers)	180	191 ± 12	240 ± 0.0
5	CTFE (2.0% dimers)	180	183 ± 11	180 ± 0.0

The analytically measured exposure levels of the airborne test substance were reasonably close to the targeted exposure levels and nominal concentrations. Chamber environmental conditions averaged 25°C temperature and 19% relative humidity.

Mean particle size distribution measurements for the exposures are summarized as follows:

Group	Test Substance	Mass Median Aerodynamic Diameter (μm)	Geometric Standard Deviation	Total Mass Concentration (mg/m^3)
1	Air Control	13.58	1.689	4.84×10^{-3}
2	CTFE (no dimers)	1.035	1.232	8.02×10^{-6}
3	CTFE (0.1% dimers)	2.599	1.607	1.58×10^{-4}
4	CTFE (0.5% dimers)	2.847	1.634	1.50×10^{-4}
5	CTFE (2.0% dimers)	2.593	1.706	2.24×10^{-4}

These results indicated that the atmospheres were gas only, as expected, since there was no substantial difference between the test substance chambers and the air control chamber.

3.2. MATERNAL DATA

3.2.1. MORTALITY AND PREGNANCY RATES

(Table 1, Appendix A)

There was no effect of treatment on survival, as all animals survived until the termination of the study. Pregnancy rates were 100% for all groups.

3.2.2. CLINICAL OBSERVATIONS

(Tables 2 and 3, Appendices B, C and I)

During the exposure periods, all animals were unremarkable except that the Groups 4 and 5 exposed dams showed some decreased activity and/or labored breathing during their 5th exposure.

During the non-exposure periods, the CTFE exposed animals showed ano-genital staining, red/brown stains on the fur, red nasal discharge, decreased activity and labored breathing. There was little evidence of a dose relationship for these findings, except that there was a slightly higher prevalence in Groups 4 and 5, most evident during the exposure period, GD 6-10.

3.2.3. BODY WEIGHTS

(Tables 4 and 5, Appendices D and E)

There were statistically significantly reduced body weights (8-12%) during gestation days 6-10 (corresponding with the CTFE exposures) for the test substance exposed animals. These animals then showed rapid recovery following cessation of the exposures, with weight gain during GD 10-13 substantially greater than in the Air Control animals.

3.2.4. FEED CONSUMPTION

(Table 6, Appendix F)

There was statistically significantly reduced feed consumption, corresponding to the exposure related body weight differences discussed above, during gestation days 6-10 (corresponding with the CTFE exposures) for the test substance exposed animals. Following cessation of the exposures, feed consumption among the CTFE exposed animals rapidly returned to normal levels.

3.2.5. FEMALE NECROPSY DATA

(Table 7, Appendix G)

There were no necropsy findings among the dams at GD 20.

3.3. FETAL OBSERVATIONS

(Tables 8 and 9, Appendix H and I)

There were no test substance related effects on fetal necropsy findings and litter size.

4. CONCLUSION

Exposure of time-mated female rats to target concentrations of 180 ppm of CTFE, with and without dimers (0.1 to 2.0%), by whole-body inhalation for gestation days 6-10 resulted in some adverse clinical signs, decreased body weight and feed consumption in all exposed groups. However, the observations were generally similar for all CTFE exposed groups indicating that CTFE, and not the presence of dimers, was the cause of the adverse responses.

	General Preface	

General Notes

1. Individual animal data values presented in this report may be rounded. Unrounded individual animal data values are used to calculate the reported mean and standard deviation values. Therefore, use of the reported individual values to reproduce means, standard deviations and/or to perform any subsequent calculations may produce minor discrepancies between the calculated values and those presented in this report.

2. Due to computer limitations, only exposure levels appear on the printouts for tables and appendices instead of detailed CTFE dimer group designations.

Corresponding exposure levels for each group were as follows:

Group 1 - 0 ppm
Group 2 - 180 ppm CTFE (no dimers)
Group 3 - 180 ppm CTFE (0.1% dimers)
Group 4 - 180 ppm CTFE (0.5% dimers)
Group 5 - 180 ppm CTFE (2.0% dimers)

Huntingdon Life Sciences 04-4261A

TABLE 1

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF SURVIVAL AND PREGNANCY

DOSE GROUP:		1	2	3	4	5
DOSE LEVEL (PPM):		0	180	180	180	180
No. of females mated	N	5	5	5	5	5
Pregnant	N	5	5	5	5	5
- Died/sacrificed moribund	N	0	0	0	0	0
- Elective sacrifice	N	0	0	0	0	0
Nonpregnant	N	0	0	0	0	0
- Died/sacrificed moribund	N	0	0	0	0	0
- Elective sacrifice	N	0	0	0	0	0
Total no. of females died/	N	0	0	0	0	0
sacrificed moribund	%	0.0	0.0	0.0	0.0	0.0
Examined at scheduled c-section	N	5	5	5	5	5
- Nonpregnant	N	0	0	0	0	0
- With total implant loss	N	0	0	0	0	0
	%	0.0	0.0	0.0	0.0	0.0
- With viable fetuses	N	5	5	5	5	5
	%	100.0	100.0	100.0	100.0	100.0

No statistically significant differences

	Summary of Daily Observations Preface	Table 2

Note:

Animals were observed for mortality, morbidity, and signs of severe toxicity at least twice daily (from Study Day 1). However, only abnormal observations are listed.

Corresponding exposure levels for each group were as follows:

Group 1 - 0 ppm
Group 2 - 180 ppm CTFE (no dimers)
Group 3 - 180 ppm CTFE (0.1% dimers)
Group 4 - 180 ppm CTFE (0.5% dimers)
Group 5 - 180 ppm CTFE (2.0% dimers)

	Summary of Daily Observations	Table 2

Observation	Group	Study Day 8	9	10	11	12
Decreased Fecal Volume	1	0	0	0	0	0
	2	1	2	2	1	1
	3	2	2	3	1	0
	4	0	5	5	1	0
	5	1	3	3	1	0
Decreased Feed Consumption	1	0	0	0	0	0
	2	0	3	3	3	2
	3	0	3	3	4	1
	4	0	2	2	2	0
	5	1	3	3	3	1
Pale	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
	4	0	0	0	0	0
	5	0	0	0	1	0

Huntingdon Life Sciences 04-4261A

TABLE 3

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF CLINICAL OBSERVATIONS DURING GESTATION - (frequency/animals)

DOSE GROUP:	1	2	3	4	5
DOSE LEVEL (PPM):	0	180	180	180	180
DAY 6 to 10					
Normal					
WITHIN NORMAL LIMITS	25/ 5	15/ 5	19/ 5	15/ 5	14/ 5
Dermal-General					
YELLOW ANO-GENITAL STAINING	0/ 0	5/ 2	1/ 1	7/ 3	9/ 4
ALOPECIA - GENERAL	0/ 0	4/ 1	4/ 1	3/ 1	0/ 0
RED/BROWN STAINS - EXTREMITIES/SNOUT	0/ 0	1/ 1	0/ 0	5/ 2	4/ 2
Oral/Buccal					
NASAL DISCHARGE - RED	0/ 0	0/ 0	1/ 1	1/ 1	2/ 2
Behavior/Activity					
DECREASED ACTIVITY	0/ 0	0/ 0	0/ 0	1/ 1	1/ 1
Respiration					
LABORED BREATHING	0/ 0	0/ 0	0/ 0	2/ 1	6/ 3

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TABLE 3

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF CLINICAL OBSERVATIONS DURING GESTATION - (frequency/animals)

DOSE GROUP:	1	2	3	4	5
DOSE LEVEL (PPM):	0	180	180	180	180
DAY 10 to 20					
Normal					
WITHIN NORMAL LIMITS	50/ 5	38/ 4	31/ 4	35/ 4	39/ 5
TERMINAL SACRIFICE	5/ 5	5/ 5	5/ 5	5/ 5	5/ 5
Dermal-General					
YELLOW ANO-GENITAL STAINING	0/ 0	1/ 1	0/ 0	5/ 2	10/ 2
ALOPECIA - GENERAL	0/ 0	10/ 1	18/ 2	10/ 1	0/ 0
RED/BROWN STAINS - EXTREMITIES/SNOUT	0/ 0	0/ 0	0/ 0	2/ 2	0/ 0
ALOPECIA - EXTREMITIES/SNOUT	0/ 0	0/ 0	6/ 2	3/ 1	0/ 0
Oral/Buccal					
NASAL DISCHARGE - RED	0/ 0	0/ 0	1/ 1	1/ 1	2/ 2
Respiration					
LABORED BREATHING	0/ 0	0/ 0	0/ 0	1/ 1	3/ 3
Miscellaneous					
DECREASED FECAL VOLUME	0/ 0	1/ 1	0/ 0	0/ 0	0/ 0

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TABLE 3

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF CLINICAL OBSERVATIONS DURING GESTATION - (frequency/animals)

DOSE GROUP:	1	2	3	4	5
DOSE LEVEL (PPM):	0	180	180	180	180
DAY 6 to 20					
Normal					
WITHIN NORMAL LIMITS	70/ 5	50/ 5	47/ 5	48/ 5	51/ 5
TERMINAL SACRIFICE	5/ 5	5/ 5	5/ 5	5/ 5	5/ 5
Dermal-General					
YELLOW ANO-GENITAL STAINING	0/ 0	5/ 2	1/ 1	10/ 3	17/ 4
ALOPECIA - GENERAL	0/ 0	13/ 1	21/ 2	12/ 1	0/ 0
RED/BROWN STAINS - EXTREMITIES/SNOUT	0/ 0	1/ 1	0/ 0	5/ 2	4/ 2
ALOPECIA - EXTREMITIES/SNOUT	0/ 0	0/ 0	6/ 2	3/ 1	0/ 0
Oral/Buccal					
NASAL DISCHARGE - RED	0/ 0	0/ 0	1/ 1	1/ 1	2/ 2
Behavior/Activity					
DECREASED ACTIVITY	0/ 0	0/ 0	0/ 0	1/ 1	1/ 1
Respiration					
LABORED BREATHING	0/ 0	0/ 0	0/ 0	2/ 1	6/ 3
Miscellaneous					
DECREASED FECAL VOLUME	0/ 0	1/ 1	0/ 0	0/ 0	0/ 0

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TABLE 4

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF GESTATION BODY WEIGHTS (GRAMS)

DOSE GROUP:		1	2	3	4	5
DOSE LEVEL (PPM):		0	180	180	180	180
DAY 4	MEAN	259	256	257	257	262
	S.D.	18.1	16.5	12.0	18.0	18.8
	N	5	5	5	5	5
DAY 6	MEAN	267	266	270	267	272
	S.D.	18.5	14.2	9.6	18.8	19.2
	N	5	5	5	5	5
DAY 10	MEAN	288	235**	248*	240**	246*
	S.D.	21.2	16.6	21.8	22.4	25.1
	N	5	5	5	5	5
DAY 13	MEAN	301	271	286	280	282
	S.D.	21.3	12.0	13.4	20.1	17.5
	N	5	5	5	5	5
DAY 16	MEAN	329	296	316	304	314
	S.D.	26.9	13.6	9.3	23.0	22.0
	N	5	5	5	5	5
DAY 19	MEAN	373	335	353	342	360
	S.D.	31.7	17.1	9.8	27.6	26.1
	N	5	5	5	5	5
DAY 20	MEAN	392	350	374	362	379
	S.D.	34.7	19.9	10.1	33.3	29.2
	N	5	5	5	5	5

Statistical key: * = $p<0.05$ ** = $p<0.01$

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TABLE 5

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF GESTATION BODY WEIGHT GAIN (GRAMS)

DOSE GROUP:		1	2	3	4	5
DOSE LEVEL (PPM):		0	180	180	180	180
DAYS 4 TO 6	MEAN	9	10	14	10	9
	S.D.	4.7	3.2	4.3	3.0	2.2
	N	5	5	5	5	5
DAYS 6 TO 10	MEAN	20	-31**	-23**	-27**	-25**
	S.D.	4.6	21.0	22.1	19.7	17.7
	N	5	5	5	5	5
DAYS 10 TO 13	MEAN	13	36**	38**	40**	36**
	S.D.	2.6	8.3	9.1	14.5	8.4
	N	5	5	5	5	5
DAYS 13 TO 16	MEAN	28	25	30	25	32
	S.D.	9.6	8.3	6.7	5.7	8.9
	N	5	5	5	5	5
DAYS 16 TO 20	MEAN	64	54	59	57	65
	S.D.	8.2	9.6	4.4	11.9	10.6
	N	5	5	5	5	5
DAYS 6 TO 20	MEAN	125	84**	104	94*	107
	S.D.	18.3	15.0	10.9	19.2	23.5
	N	5	5	5	5	5

Statistical key: * = $p<0.05$ ** = $p<0.01$

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TABLE 6

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF GESTATION FEED CONSUMPTION (GRAMS/KG/DAY)

DOSE GROUP:		1	2	3	4	5
DOSE LEVEL (PPM):		0	180	180	180	180
DAYS 4 TO 6	MEAN	83	86	86	81	82
	S.D.	12.0	3.0	5.8	4.2	9.9
	N	5	5	5	5	5
DAYS 6 TO 10	MEAN	80	36**	43*	38**	39**
	S.D.	8.2	18.6	19.2	16.7	21.3
	N	5	5	5	5	5
DAYS 10 TO 13	MEAN	83	76	88	84	82
	S.D.	7.4	12.5	4.3	7.6	15.0
	N	5	5	5	5	5
DAYS 13 TO 16	MEAN	82	88	91	88	91
	S.D.	4.5	13.0	4.4	10.5	6.2
	N	5	5	5	5	5
DAYS 16 TO 20	MEAN	76	79	81	79	82
	S.D.	6.5	6.2	5.3	4.8	6.4
	N	5	5	5	5	5
DAYS 6 TO 20	MEAN	80	70*	76	72	73
	S.D.	6.2	4.6	5.4	3.0	6.0
	N	5	5	5	5	5

Statistical key: * = $p<0.05$ ** = $p<0.01$

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TABLE 7

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF MATERNAL NECROPSY OBSERVATIONS

DOSE GROUP:		1	2	3	4	5
DOSE LEVEL (PPM):		0	180	180	180	180
FEMALES	N	5	5	5	5	4
TOTAL MATERNAL NECROPSY OBSERVATIONS	N	0	0	0	0	0

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TABLE 8

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF CESAREAN SECTION DATA

DOSE GROUP:		1	2	3	4	5
DOSE LEVEL (PPM):		0	180	180	180	180
Pregnant (at scheduled sacrifice)	N	5	5	5	5	5
Dams with no Viable Fetuses	N	0	0	0	0	0
Dams with Viable Fetuses	N	5	5	5	5	5
Implantation Sites	TOTAL	73	62	69	68	77
No. per animal	MEAN	14.6	12.4	13.8	13.6	15.4
	S.D.	2.61	3.05	0.84	1.52	1.52
Live Fetuses	TOTAL	72	62	64	61	74
No. per animal	MEAN	14.4	12.4	12.8	12.2	14.8
	S.D.	2.51	3.05	0.45	2.95	2.17

No statistically significant differences

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TABLE 8

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF CESAREAN SECTION DATA

DOSE GROUP:		1	2	3	4	5
DOSE LEVEL (PPM):		0	180	180	180	180
Postimplantation Loss	TOTAL	1	0	5	7	3
No. per animal	MEAN	0.2	0.0	1.0	1.4	0.6
	S.D.	0.45	0.00	0.71	2.61	1.34
% implants per animal	MEAN%	1.3	0.0	7.1	10.2	4.0
	S.D.	2.80	0.00	4.73	18.59	8.94
Dead Fetuses	TOTAL	0	0	0	0	0
No. per animal	MEAN	0.0	0.0	0.0	0.0	0.0
	S.D.	0.00	0.00	0.00	0.00	0.00
% of implants per animal	MEAN%	0.0	0.0	0.0	0.0	0.0
	S.D.	0.00	0.00	0.00	0.00	0.00
Resorptions: Early	TOTAL	1	0	5	6	3
No. per animal	MEAN	0.2	0.0	1.0	1.2	0.6
	S.D.	0.45	0.00	0.71	2.68	1.34
% of implants per animal	MEAN%	1.3	0.0	7.1	8.6	4.0
	S.D.	2.80	0.00	4.73	19.17	8.94
Resorptions: Late	TOTAL	0	0	0	1	0
No. per animal	MEAN	0.0	0.0	0.0	0.2	0.0
	S.D.	0.00	0.00	0.00	0.45	0.00
% of implants per animal	MEAN%	0.0	0.0	0.0	1.7	0.0
	S.D.	0.00	0.00	0.00	3.73	0.00

No statistically significant differences

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TABLE 9

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

SUMMARY OF FETAL EXTERNAL OBSERVATIONS

DOSE GROUP:		1	2	3	4	5
DOSE LEVEL (PPM):		0	180	180	180	180
Litters Evaluated	N	5	5	5	5	5
Fetuses Evaluated	N	72	62	64	61	74
Live	N	72	62	64	61	74
Dead	N	0	0	0	0	0
TOTAL FETAL EXTERNAL OBSERVATIONS	N	0	0	0	0	0

OBSERVATION CODE: M-MALFORMATION V-VARIATION

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APPENDIX A

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 1 0 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY	PREGNANCY STATUS
1570	TERMINAL SACRIFICE	22-FEB-05	20	P
1571	TERMINAL SACRIFICE	22-FEB-05	20	P
1572	TERMINAL SACRIFICE	22-FEB-05	20	P
1573	TERMINAL SACRIFICE	22-FEB-05	20	P
1574	TERMINAL SACRIFICE	22-FEB-05	20	P

NP-NOT PREGNANT, P-PREGNANT

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APPENDIX A

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 2 180 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY	PREGNANCY STATUS
2570	TERMINAL SACRIFICE	22-FEB-05	20	P
2571	TERMINAL SACRIFICE	22-FEB-05	20	P
2572	TERMINAL SACRIFICE	22-FEB-05	20	P
2573	TERMINAL SACRIFICE	22-FEB-05	20	P
2574	TERMINAL SACRIFICE	22-FEB-05	20	P

NP-NOT PREGNANT, P-PREGNANT

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APPENDIX A

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 3 180 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY	PREGNANCY STATUS
3570	TERMINAL SACRIFICE	22-FEB-05	20	P
3571	TERMINAL SACRIFICE	22-FEB-05	20	P
3572	TERMINAL SACRIFICE	22-FEB-05	20	P
3573	TERMINAL SACRIFICE	22-FEB-05	20	P
3574	TERMINAL SACRIFICE	22-FEB-05	20	P

NP-NOT PREGNANT, P-PREGNANT

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APPENDIX A

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 4 180 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY	PREGNANCY STATUS
4570	TERMINAL SACRIFICE	22-FEB-05	20	P
4571	TERMINAL SACRIFICE	22-FEB-05	20	P
4572	TERMINAL SACRIFICE	22-FEB-05	20	P
4573	TERMINAL SACRIFICE	22-FEB-05	20	P
4574	TERMINAL SACRIFICE	22-FEB-05	20	P

NP-NOT PREGNANT, P-PREGNANT

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APPENDIX A

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 5 180 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY	PREGNANCY STATUS
5570	TERMINAL SACRIFICE	22-FEB-05	20	P
5571	TERMINAL SACRIFICE	22-FEB-05	20	P
5572	TERMINAL SACRIFICE	22-FEB-05	20	P
5573	TERMINAL SACRIFICE	22-FEB-05	20	P
5574	TERMINAL SACRIFICE	22-FEB-05	20	P

NP-NOT PREGNANT, P-PREGNANT

	Individual Daily Observations Preface	Appendix B

Note:

Animals were observed for mortality, morbidity and signs of severe toxicity at least twice daily. Only animals with abnormal observations are listed.

	Individual Daily Observations	Appendix B

Animal Number	Group	Observations	Study Day 8	9	10	11	12
Group 2 – 180 ppm CTFE (no dimers)							
2571	2	Decreased Fecal Volume	-	A	A	-	-
		Decreased Feed Consumption	-	✓	✓	✓	✓
2572	2	Decreased Fecal Volume	-	-	-	-	-
		Decreased Feed Consumption	-	✓	✓	A	-
2574	2	Decreased Fecal Volume	A	A	A	A	A
		Decreased Feed Consumption	-	✓	✓	✓	✓
Group 3 – 180 ppm CTFE (0.1% dimers)							
3571	3	Decreased Feed Consumption	-	-	-	P	-
3572	3	Decreased Fecal Volume	-	A	A	A	-
		Decreased Feed Consumption	-	✓	✓	✓	✓
3573	3	Decreased Fecal Volume	A	A	A	-	-
		Decreased Feed Consumption	-	✓	✓	A	-
3574	3	Decreased Fecal Volume	A	-	A	-	-
		Decreased Feed Consumption	-	✓	✓	A	-
Group 4 – 180 ppm CTFE (0.5% dimers)							
4570	4	Decreased Fecal Volume	-	A	A	-	-
		Decreased Feed Consumption	-	✓	✓	✓	-

A=AM Finding; ✓ =AM and PM Finding; P=PM Finding.

Individual Daily Observations

Appendix B

Animal Number	Group	Observations	Study Day 8	9	10	11	12
Group 4 – 180 ppm CTFE (0.5% dimers)							
4571	4	Decreased Fecal Volume	-	A	A	A	-
		Decreased Feed Consumption	-	-	-	P	-
4572	4	Decreased Fecal Volume	-	A	A	-	-
		Decreased Feed Consumption	-	✓	✓	-	-
4573	4	Decreased Fecal Volume	-	A	A	-	-
		Decreased Feed Consumption	-	-	-	-	-
4574	4	Decreased Fecal Volume	-	A	A	-	-
		Decreased Feed Consumption	-	-	-	-	-
Group 5 – 180 ppm CTFE (0.5% dimers)							
5570	5	Decreased Fecal Volume	-	A	A	-	-
		Decreased Feed Consumption	-	✓	✓	A	-
5572	5	Decreased Fecal Volume	-	A	A	-	-
		Decreased Feed Consumption	-	P	✓	✓	-
5573	5	Decreased Fecal Volume	A*	A	A	A	-
		Decreased Feed Consumption	A*	✓	✓	✓	✓
		Pale	-	-	-	P	-

A=AM Finding; ✓ =AM and PM Finding; P=PM Finding. *Observations were not followed up in the PM for this animal due to technician oversight.

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APPENDIX C

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 1 0 PPM

FEMALE#	OBSERVATIONS	DAY OF GESTATION 0	1	2	3	4	5	6	7	8	9	10	11[a]	12	13	14	15	16	17	18	19	20
1570	TERMINAL SACRIFICE																					P
	WITHIN NORMAL LIMITS	P	P	P	P	P	P	P	P	P	P	P		P	P	P	P	P	P	P	P	P
1571	TERMINAL SACRIFICE																					P
	WITHIN NORMAL LIMITS	P	P	P	P	P	P	P	P	P	P	P		P	P	P	P	P	P	P	P	P
1572	TERMINAL SACRIFICE																					P
	WITHIN NORMAL LIMITS	P	P	P	P	P	P	P	P	P	P	P		P	P	P	P	P	P	P	P	P
1573	TERMINAL SACRIFICE																					P
	WITHIN NORMAL LIMITS	P	P	P	P	P	P	P	P	P	P	P		P	P	P	P	P	P	P	P	P
1574	TERMINAL SACRIFICE																					P
	WITHIN NORMAL LIMITS	P	P	P	P	P	P	P	P	P	P	P		P	P	P	P	P	P	P	P	P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

[a]Due to technician oversight, clinical observations were not performed on Day 11.

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APPENDIX C

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 2 180 PPM

FEMALE#	OBSERVATIONS	DAY OF GESTATION	0	1	2	3	4	5	6	7	8	9	10	11[a]	12	13	14	15	16	17	18	19	20
2570	TERMINAL SACRIFICE																						P
	YELLOW ANO-GENITAL STAINING									1	1	1	1										
	WITHIN NORMAL LIMITS		P	P	P	P	P	P							P	P	P	P	P	P	P	P	P
2571	TERMINAL SACRIFICE																						P
	ALOPECIA - GENERAL									3	3	3	3		3	3	3	3	3	3	3	3	3
	WITHIN NORMAL LIMITS		P	P	P	P	P	P															
2572	TERMINAL SACRIFICE																						P
	YELLOW ANO-GENITAL STAINING												1										
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P		P		P	P	P	P	P	P	P	P	P
2573	TERMINAL SACRIFICE																						P
	RED/BROWN STAINS - EXTREMITIES/SNOUT										1												
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P			P	P		P	P	P	P	P	P	P	P	P
2574	TERMINAL SACRIFICE																						P
	DECREASED FECAL VOLUME														P								
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P			P	P	P	P	P	P	P	P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

[a]Due to technician oversight, clinical observations were not performed on Day 11.

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APPENDIX C

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 3 180 PPM

FEMALE#	OBSERVATIONS	DAY OF GESTATION	0	1	2	3	4	5	6	7	8	9	10	11[a]	12	13	14	15	16	17	18	19	20
3570	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P		P	P	P	P	P	P	P	P	P
3571	TERMINAL SACRIFICE																						P
	ALOPECIA - GENERAL									2	2	3	3		3	3	3	3	3	3	3	3	3
	ALOPECIA - EXTREMITIES/SNOUT																				3	3	3
	WITHIN NORMAL LIMITS		P	P	P	P	P	P															
3572	TERMINAL SACRIFICE																						P
	NASAL DISCHARGE - RED												P										
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P			P	P	P	P	P	P	P	P	P
3573	TERMINAL SACRIFICE																						P
	YELLOW ANO-GENITAL STAINING									1													
	ALOPECIA - GENERAL														3	3	3	3		3	3	3	3
	ALOPECIA - EXTREMITIES/SNOUT																				3	3	3
	WITHIN NORMAL LIMITS		P	P	P	P	P	P			P	P	P						P				
3574	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P		P	P	P	P	P	P	P	P	P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

[a]Due to technician oversight, clinical observations were not performed on Day 11.

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APPENDIX C

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 4 180 PPM

FEMALE#	OBSERVATIONS	DAY OF GESTATION	0	1	2	3	4	5	6	7	8	9	10	11[a]	12	13	14	15	16	17	18	19	20
4570	TERMINAL SACRIFICE																						P
	YELLOW ANO-GENITAL STAINING									2													
	WITHIN NORMAL LIMITS		P	P	P	P	P	P			P	P	P		P	P	P	P	P	P	P	P	P
4571	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P		P	P	P	P	P	P	P	P	P
4572	TERMINAL SACRIFICE																						P
	YELLOW ANO-GENITAL STAINING											1	1										
	ALOPECIA - GENERAL										2	2	2		2	2	2	2	2	2	2	2	2
	RED/BROWN STAINS - EXTREMITIES/SNOUT											1	1										
	ALOPECIA - EXTREMITIES/SNOUT																				2	2	2
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P														
4573	TERMINAL SACRIFICE																						P
	YELLOW ANO-GENITAL STAINING									1	2	1	1		1	1	1						
	RED/BROWN STAINS - EXTREMITIES/SNOUT									1	1		1										
	LABORED BREATHING											P	P										
	WITHIN NORMAL LIMITS		P	P	P	P	P	P										P	P	P	P	P	P
4574	TERMINAL SACRIFICE																						P
	NASAL DISCHARGE - RED												P										
	DECREASED ACTIVITY											P											
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P				P	P	P	P	P	P	P	P	P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

[a]Due to technician oversight, clinical observations were not performed on Day 11.

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APPENDIX C

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 5 180 PPM

FEMALE#	OBSERVATIONS	DAY OF GESTATION	0	1	2	3	4	5	6	7	8	9	10	11[a]	12	13	14	15	16	17	18	19	20
5570	TERMINAL SACRIFICE																						P
	YELLOW ANO-GENITAL STAINING									2													
	RED/BROWN STAINS - EXTREMITIES/SNOUT									1		1											
	NASAL DISCHARGE - RED												P										
	LABORED BREATHING											P	P										
	WITHIN NORMAL LIMITS		P	P	P	P	P	P			P				P	P	P	P	P	P	P	P	P
5571	TERMINAL SACRIFICE																						P
	YELLOW ANO-GENITAL STAINING									3													
	WITHIN NORMAL LIMITS		P	P	P	P	P	P			P	P	P		P	P	P	P	P	P	P	P	P
5572	TERMINAL SACRIFICE																						P
	YELLOW ANO-GENITAL STAINING										1	1	1										
	DECREASED ACTIVITY											P											
	LABORED BREATHING											P	P										
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P						P	P	P	P	P	P	P	P	P
5573	TERMINAL SACRIFICE																						P
	YELLOW ANO-GENITAL STAINING									3	2	2	2		2	2	2	2	2	2	1	1	
	RED/BROWN STAINS - EXTREMITIES/SNOUT									1	1												
	NASAL DISCHARGE - RED												P										
	LABORED BREATHING											P	P										
	WITHIN NORMAL LIMITS		P	P	P	P	P	P															P
5574	TERMINAL SACRIFICE																						P
	WITHIN NORMAL LIMITS		P	P	P	P	P	P	P	P	P	P	P		P	P	P	P	P	P	P	P	P

CODE: 1-SLIGHT 2-MODERATE 3-MARKED P-PRESENT

[a]Due to technician oversight, clinical observations were not performed on Day 11.

Huntingdon Life Sciences 04-4261A

APPENDIX D

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GESTATION BODY WEIGHTS (GRAMS)

GROUP 1 0 PPM

	DAY OF GESTATION						
ANIMAL#	4	6	10	13	16	19	20
1570	239	243	256	271	296	336	351
1571	244	257	282	296	316	356	376
1572	257	264	285	295	320	361	379
1573	269	283	306	317	362	412	438
1574	283	288	308	325	350	398	417
MEAN	259	267	288	301	329	373	392
S.D.	18.1	18.5	21.2	21.3	26.9	31.7	34.7
N	5	5	5	5	5	5	5

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APPENDIX D

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GESTATION BODY WEIGHTS (GRAMS)

GROUP 2 180 PPM

	DAY OF GESTATION						
ANIMAL#	4	6	10	13	16	19	20
2570	236	248	233	265	291	323	343
2571	249	264	216	264	283	323	344
2572	249	259	243	270	288	321	327
2573	268	277	258	292	317	359	380
2574	277	284	224	264	303	347	357
MEAN	256	266	235	271	296	335	350
S.D.	16.5	14.2	16.6	12.0	13.6	17.1	19.9
N	5	5	5	5	5	5	5

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APPENDIX D

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GESTATION BODY WEIGHTS (GRAMS)

GROUP 3 180 PPM

	DAY OF GESTATION						
ANIMAL#	4	6	10	13	16	19	20
3570	244	260	259	290	313	358	380
3571	249	269	266	298	320	351	376
3572	252	263	214	264	301	340	358
3573	267	279	262	293	326	367	385
3574	271	281	239	285	317	351	373
MEAN	257	270	248	286	316	353	374
S.D.	12.0	9.6	21.8	13.4	9.3	9.8	10.1
N	5	5	5	5	5	5	5

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APPENDIX D

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GESTATION BODY WEIGHTS (GRAMS)

GROUP 4 180 PPM

ANIMAL#	DAY OF GESTATION 4	6	10	13	16	19	20
4570	243	253	244	274	298	340	361
4571	244	250	201	252	277	305	313
4572	251	264	250	280	304	339	363
4573	262	274	258	285	302	341	364
4574	286	296	248	307	341	383	408
MEAN	257	267	240	280	304	342	362
S.D.	18.0	18.8	22.4	20.1	23.0	27.6	33.3
N	5	5	5	5	5	5	5

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APPENDIX D

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GESTATION BODY WEIGHTS (GRAMS)

GROUP 5 180 PPM

ANIMAL#	DAY OF GESTATION 4	6	10	13	16	19	20
5570	243	252	232	276	303	355	377
5571	249	260	255	287	322	366	388
5572	261	268	233	275	294	331	341
5573	268	275	225	263	303	348	368
5574	291	302	286	310	349	401	421
MEAN	262	272	246	282	314	360	379
S.D.	18.8	19.2	25.1	17.5	22.0	26.1	29.2
N	5	5	5	5	5	5	5

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APPENDIX E

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GESTATION BODY WEIGHT GAIN (GRAMS)

GROUP 1 0 PPM

ANIMAL#	DAY OF GESTATION 4 - 6	6 - 10	10 - 13	13 - 16	16 - 20	6 - 20
1570	4	13	14	25	55	108
1571	13	25	14	19	60	119
1572	7	21	10	25	59	115
1573	14	23	11	45	76	155
1574	5	20	16	26	66	129
MEAN	9	20	13	28	64	125
S.D.	4.7	4.6	2.6	9.6	8.2	18.3
N	5	5	5	5	5	5

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APPENDIX E

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GESTATION BODY WEIGHT GAIN (GRAMS)

GROUP 2 180 PPM

ANIMAL#	DAY OF GESTATION 4 - 6	6 - 10	10 - 13	13 - 16	16 - 20	6 - 20
2570	12	-15	32	26	52	95
2571	15	-48	48	19	61	80
2572	10	-16	26	18	39	68
2573	8	-19	34	25	64	104
2574	7	-60	40	39	54	73
MEAN	10	-31	36	25	54	84
S.D.	3.2	21.0	8.3	8.3	9.6	15.0
N	5	5	5	5	5	5

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APPENDIX E

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GESTATION BODY WEIGHT GAIN (GRAMS)

GROUP 3 180 PPM

ANIMAL#	DAY OF GESTATION 4 - 6	6 - 10	10 - 13	13 - 16	16 - 20	6 - 20
3570	16	-1	31	23	66	120
3571	20	-4	32	23	56	107
3572	11	-49	50	38	57	96
3573	12	-17	31	33	59	106
3574	10	-42	46	32	56	92
MEAN	14	-23	38	30	59	104
S.D.	4.3	22.1	9.1	6.7	4.4	10.9
N	5	5	5	5	5	5

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APPENDIX E

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GESTATION BODY WEIGHT GAIN (GRAMS)

GROUP 4 180 PPM

ANIMAL#	DAY OF GESTATION 4 - 6	6 - 10	10 - 13	13 - 16	16 - 20	6 - 20
4570	10	-9	31	24	63	109
4571	5	-49	51	25	37	64
4572	13	-13	30	24	58	99
4573	12	-16	28	17	61	90
4574	10	-49	60	33	67	111
MEAN	10	-27	40	25	57	94
S.D.	3.0	19.7	14.5	5.7	11.9	19.2
N	5	5	5	5	5	5

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APPENDIX E

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GESTATION BODY WEIGHT GAIN (GRAMS)

GROUP 5 180 PPM

ANIMAL#	DAY OF GESTATION 4 - 6	6 - 10	10 - 13	13 - 16	16 - 20	6 - 20
5570	10	-20	44	27	74	125
5571	11	-5	32	35	66	128
5572	7	-35	42	19	47	73
5573	7	-50	38	39	65	93
5574	12	-16	24	39	72	119
MEAN	9	-25	36	32	65	107
S.D.	2.2	17.7	8.4	8.9	10.6	23.5
N	5	5	5	5	5	5

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APPENDIX F

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GESTATION FEED CONSUMPTION -- (GRAMS/KG/DAY)

GROUP 1 0 PPM

ANIMAL#	DAY OF GESTATION 4 - 6	6 - 10	10 - 13	13 - 16	16 - 20	6 - 20
1570	73	73	81	83	80	79
1571	97	92	95	86	84	89
1572	75	73	76	75	68	73
1573	95	85	85	85	78	83
1574	75	78	80	79	72	77
MEAN	83	80	83	82	76	80
S.D.	12.0	8.2	7.4	4.5	6.5	6.2
N	5	5	5	5	5	5

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APPENDIX F

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GESTATION FEED CONSUMPTION -- (GRAMS/KG/DAY)

GROUP 2 180 PPM

ANIMAL#	DAY OF GESTATION 4 - 6	6 - 10	10 - 13	13 - 16	16 - 20	6 - 20
2570	88	53	87	83	76	75
2571	86	27	79	96	87	72
2572	88	39	76	77	72	66
2573	84	54	82	78	77	73
2574	81	9	55	107	85	64
MEAN	86	36	76	88	79	70
S.D.	3.0	18.6	12.5	13.0	6.2	4.6
N	5	5	5	5	5	5

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APPENDIX F

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GESTATION FEED CONSUMPTION -- (GRAMS/KG/DAY)

GROUP 3 180 PPM

ANIMAL#	DAY OF GESTATION 4 - 6	6 - 10	10 - 13	13 - 16	16 - 20	6 - 20
3570	91	65	95	90	83	83
3571	92	60	88	92	79	80
3572	84	25	86	96	74	70
3573	83	43	84	85	79	73
3574	79	23	86	93	88	73
MEAN	86	43	88	91	81	76
S.D.	5.8	19.2	4.3	4.4	5.3	5.4
N	5	5	5	5	5	5

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APPENDIX F

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GESTATION FEED CONSUMPTION -- (GRAMS/KG/DAY)

GROUP 4 180 PPM

ANIMAL#	DAY OF GESTATION 4 - 6	6 - 10	10 - 13	13 - 16	16 - 20	6 - 20
4570	84	53	87	82	75	74
4571	77	20	91	97	80	72
4572	82	51	82	84	81	75
4573	76	48	71	76	74	67
4574	86	20	88	100	86	73
MEAN	81	38	84	88	79	72
S.D.	4.2	16.7	7.6	10.5	4.8	3.0
N	5	5	5	5	5	5

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APPENDIX F

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL GESTATION FEED CONSUMPTION -- (GRAMS/KG/DAY)

GROUP 5 180 PPM

ANIMAL#	DAY OF GESTATION 4 - 6	6 - 10	10 - 13	13 - 16	16 - 20	6 - 20
5570	85	37	95	89	79	75
5571	89	56	93	93	81	81
5572	71	35	89	86	74	71
5573	71	6	61	101	91	65
5574	91	59	70	86	85	75
MEAN	82	39	82	91	82	73
S.D.	9.9	21.3	15.0	6.2	6.4	6.0
N	5	5	5	5	5	5

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APPENDIX G

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL MATERNAL NECROPSY OBSERVATIONS

GROUP 1 0 PPM

ANIMAL#	ORGAN	OBSERVATION
1570		NO REMARKABLE OBSERVATIONS
1571		NO REMARKABLE OBSERVATIONS
1572		NO REMARKABLE OBSERVATIONS
1573		NO REMARKABLE OBSERVATIONS
1574		NO REMARKABLE OBSERVATIONS

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APPENDIX G

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL MATERNAL NECROPSY OBSERVATIONS

GROUP 2 180 PPM

ANIMAL#	ORGAN	OBSERVATION
2570		NO REMARKABLE OBSERVATIONS
2571	EXTERNAL EXAM	ALOPECIA-GENERAL EXTERNAL FINDING CONFIRMED
2572		NO REMARKABLE OBSERVATIONS
2573		NO REMARKABLE OBSERVATIONS
2574		NO REMARKABLE OBSERVATIONS

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APPENDIX G

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL MATERNAL NECROPSY OBSERVATIONS

GROUP 3 180 PPM

ANIMAL#	ORGAN	OBSERVATION
3570		NO REMARKABLE OBSERVATIONS
3571		NO REMARKABLE OBSERVATIONS
3572		NO REMARKABLE OBSERVATIONS
3573	EXTERNAL EXAM	ALOPECIA-GENERAL EXTERNAL FINDINGS CONFIRMED
	EXTERNAL EXAM	ALOPECIA-EXTREMITIES/SNOUT EXTERNAL FINDINGS CONFIRMED
3574		NO REMARKABLE OBSERVATIONS

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APPENDIX G

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL MATERNAL NECROPSY OBSERVATIONS

GROUP 4 180 PPM

ANIMAL#	ORGAN	OBSERVATION
4570		NO REMARKABLE OBSERVATIONS
4571		NO REMARKABLE OBSERVATIONS
4572	EXTERNAL EXAM	ALOPECIA-GENERAL EXTERNAL FINDING NOT CONFIRMED
	EXTERNAL EXAM	ALOPECIA-EXTREMITIES/SNOUT EXTERNAL FINDING NOT CONFIRMED
4573		NO REMARKABLE OBSERVATIONS
4574		NO REMARKABLE OBSERVATIONS

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APPENDIX G

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL MATERNAL NECROPSY OBSERVATIONS

GROUP 5 180 PPM

ANIMAL#	ORGAN	OBSERVATION
5570		NO REMARKABLE OBSERVATIONS
5571		NO REMARKABLE OBSERVATIONS EXAMINATION NOT COMPLETED
5572		NO REMARKABLE OBSERVATIONS
5573		NO REMARKABLE OBSERVATIONS
5574		NO REMARKABLE OBSERVATIONS

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APPENDIX H

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FEMALE REPRODUCTION DATA

GROUP 1 0 PPM

ANIMAL#	IMPLANT SITES	FETUSES LIVE	DEAD (n)	DEAD %	RESORPTIONS EARLY	LATE	TOTAL (n)	TOTAL %
1570	12	12	0	0.0	0	0	0	0.0
1571	12	12	0	0.0	0	0	0	0.0
1572	15	15	0	0.0	0	0	0	0.0
1573	18	18	0	0.0	0	0	0	0.0
1574	16	15	0	0.0	1	0	1	6.3
MEAN	14.6	14.4	0.0	0.0	0.2	0.0	0.2	1.3
S.D.	2.61	2.51	0.00	0.00	0.45	0.00	0.45	2.80
N	5	5	5	5	5	5	5	5

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APPENDIX H

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FEMALE REPRODUCTION DATA

GROUP 2 180 PPM

ANIMAL#	IMPLANT SITES	FETUSES LIVE	DEAD (n)	DEAD %	RESORPTIONS EARLY	LATE	TOTAL (n)	TOTAL %
2570	10	10	0	0.0	0	0	0	0.0
2571	12	12	0	0.0	0	0	0	0.0
2572	9	9	0	0.0	0	0	0	0.0
2573	15	15	0	0.0	0	0	0	0.0
2574	16	16	0	0.0	0	0	0	0.0
MEAN	12.4	12.4	0.0	0.0	0.0	0.0	0.0	0.0
S.D.	3.05	3.05	0.00	0.00	0.00	0.00	0.00	0.00
N	5	5	5	5	5	5	5	5

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APPENDIX H

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FEMALE REPRODUCTION DATA

GROUP 3 180 PPM

ANIMAL#	IMPLANT SITES	FETUSES LIVE	DEAD (n)	DEAD %	RESORPTIONS EARLY	LATE	TOTAL (n)	TOTAL %
3570	13	13	0	0.0	0	0	0	0.0
3571	15	13	0	0.0	2	0	2	13.3
3572	14	13	0	0.0	1	0	1	7.1
3573	14	13	0	0.0	1	0	1	7.1
3574	13	12	0	0.0	1	0	1	7.7
MEAN	13.8	12.8	0.0	0.0	1.0	0.0	1.0	7.1
S.D.	0.84	0.45	0.00	0.00	0.71	0.00	0.71	4.73
N	5	5	5	5	5	5	5	5

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APPENDIX H

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FEMALE REPRODUCTION DATA

GROUP 4 180 PPM

ANIMAL#			IMPLANT SITES	FETUSES LIVE	DEAD (n)	DEAD %	RESORPTIONS EARLY	LATE	TOTAL (n)	TOTAL %
4570	0	0.0	15	15	0	0.0	0	0	0	0.0
4571	0	0.0	14	8	0	0.0	6	0	6	42.9
4572	0	0.0	12	12	0	0.0	0	0	0	0.0
4573	0	0.0	12	11	0	0.0	0	1	1	8.3
4574	0	0.0	15	15	0	0.0	0	0	0	0.0
MEAN	0.0	0.0	13.6	12.2	0.0	0.0	1.2	0.2	1.4	10.2
S.D.	0.00	0.00	1.52	2.95	0.00	0.00	2.68	0.45	2.61	18.59
N	0	0	5	5	5	5	5	5	5	5

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APPENDIX H

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FEMALE REPRODUCTION DATA

GROUP 5 180 PPM

ANIMAL#	IMPLANT SITES	FETUSES LIVE	DEAD (n)	DEAD %	RESORPTIONS EARLY	LATE	TOTAL (n)	TOTAL %
5570	18	18	0	0.0	0	0	0	0.0
5571	15	15	0	0.0	0	0	0	0.0
5572	15	12	0	0.0	3	0	3	20.0
5573	14	14	0	0.0	0	0	0	0.0
5574	15	15	0	0.0	0	0	0	0.0
MEAN	15.4	14.8	0.0	0.0	0.6	0.0	0.6	4.0
S.D.	1.52	2.17	0.00	0.00	1.34	0.00	1.34	8.94
N	5	5	5	5	5	5	5	5

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APPENDIX I

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS OBSERVATION
1570	1		WITHIN NORMAL LIMITS
	2		WITHIN NORMAL LIMITS
	3		WITHIN NORMAL LIMITS
	4		WITHIN NORMAL LIMITS
	5		WITHIN NORMAL LIMITS
	6		WITHIN NORMAL LIMITS
	7		WITHIN NORMAL LIMITS
	8		WITHIN NORMAL LIMITS
	9		WITHIN NORMAL LIMITS
	10		WITHIN NORMAL LIMITS
	11		WITHIN NORMAL LIMITS
	12		WITHIN NORMAL LIMITS
1571	1		WITHIN NORMAL LIMITS
	2		WITHIN NORMAL LIMITS
	3		WITHIN NORMAL LIMITS
	4		WITHIN NORMAL LIMITS
	5		WITHIN NORMAL LIMITS
	6		WITHIN NORMAL LIMITS
	7		WITHIN NORMAL LIMITS
	8		WITHIN NORMAL LIMITS
	9		WITHIN NORMAL LIMITS
	10		WITHIN NORMAL LIMITS
	11		WITHIN NORMAL LIMITS
	12		WITHIN NORMAL LIMITS
1572	1		WITHIN NORMAL LIMITS
	2		WITHIN NORMAL LIMITS
	3		WITHIN NORMAL LIMITS
	4		WITHIN NORMAL LIMITS
	5		WITHIN NORMAL LIMITS
	6		WITHIN NORMAL LIMITS
	7		WITHIN NORMAL LIMITS
	8		WITHIN NORMAL LIMITS

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APPENDIX I

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
1572	(CONTINUED)			
	9			WITHIN NORMAL LIMITS
	10			WITHIN NORMAL LIMITS
	11			WITHIN NORMAL LIMITS
	12			WITHIN NORMAL LIMITS
	13			WITHIN NORMAL LIMITS
	14			WITHIN NORMAL LIMITS
	15			WITHIN NORMAL LIMITS
1573	1			WITHIN NORMAL LIMITS
	2			WITHIN NORMAL LIMITS
	3			WITHIN NORMAL LIMITS
	4			WITHIN NORMAL LIMITS
	5			WITHIN NORMAL LIMITS
	6			WITHIN NORMAL LIMITS
	7			WITHIN NORMAL LIMITS
	8			WITHIN NORMAL LIMITS
	9			WITHIN NORMAL LIMITS
	10			WITHIN NORMAL LIMITS
	11			WITHIN NORMAL LIMITS
	12			WITHIN NORMAL LIMITS
	13			WITHIN NORMAL LIMITS
	14			WITHIN NORMAL LIMITS
	15			WITHIN NORMAL LIMITS
	16			WITHIN NORMAL LIMITS
	17			WITHIN NORMAL LIMITS
	18			WITHIN NORMAL LIMITS
1574	1			WITHIN NORMAL LIMITS
	2			WITHIN NORMAL LIMITS
	3			WITHIN NORMAL LIMITS
	4			WITHIN NORMAL LIMITS
	5			WITHIN NORMAL LIMITS
	6			WITHIN NORMAL LIMITS
	7			WITHIN NORMAL LIMITS

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APPENDIX I

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
1574	(CONTINUED)			
	8			WITHIN NORMAL LIMITS
	9			WITHIN NORMAL LIMITS
	10			WITHIN NORMAL LIMITS
	12			WITHIN NORMAL LIMITS
	13			WITHIN NORMAL LIMITS
	14			WITHIN NORMAL LIMITS
	15			WITHIN NORMAL LIMITS
	16			WITHIN NORMAL LIMITS

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APPENDIX I

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 2 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS OBSERVATION
2570	1		WITHIN NORMAL LIMITS
	2		WITHIN NORMAL LIMITS
	3		WITHIN NORMAL LIMITS
	4		WITHIN NORMAL LIMITS
	5		WITHIN NORMAL LIMITS
	6		WITHIN NORMAL LIMITS
	7		WITHIN NORMAL LIMITS
	8		WITHIN NORMAL LIMITS
	9		WITHIN NORMAL LIMITS
	10		WITHIN NORMAL LIMITS
2571	1		WITHIN NORMAL LIMITS
	2		WITHIN NORMAL LIMITS
	3		WITHIN NORMAL LIMITS
	4		WITHIN NORMAL LIMITS
	5		WITHIN NORMAL LIMITS
	6		WITHIN NORMAL LIMITS
	7		WITHIN NORMAL LIMITS
	8		WITHIN NORMAL LIMITS
	9		WITHIN NORMAL LIMITS
	10		WITHIN NORMAL LIMITS
	11		WITHIN NORMAL LIMITS
	12		WITHIN NORMAL LIMITS
2572	1		WITHIN NORMAL LIMITS
	2		WITHIN NORMAL LIMITS
	3		WITHIN NORMAL LIMITS
	4		WITHIN NORMAL LIMITS
	5		WITHIN NORMAL LIMITS
	6		WITHIN NORMAL LIMITS
	7		WITHIN NORMAL LIMITS
	8		WITHIN NORMAL LIMITS
	9		WITHIN NORMAL LIMITS

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APPENDIX I

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 2 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
2573	1			WITHIN NORMAL LIMITS
	2			WITHIN NORMAL LIMITS
	3			WITHIN NORMAL LIMITS
	4			WITHIN NORMAL LIMITS
	5			WITHIN NORMAL LIMITS
	6			WITHIN NORMAL LIMITS
	7			WITHIN NORMAL LIMITS
	8			WITHIN NORMAL LIMITS
	9			WITHIN NORMAL LIMITS
	10			WITHIN NORMAL LIMITS
	11			WITHIN NORMAL LIMITS
	12			WITHIN NORMAL LIMITS
	13			WITHIN NORMAL LIMITS
	14			WITHIN NORMAL LIMITS
	15			WITHIN NORMAL LIMITS
2574	1			WITHIN NORMAL LIMITS
	2			WITHIN NORMAL LIMITS
	3			WITHIN NORMAL LIMITS
	4			WITHIN NORMAL LIMITS
	5			WITHIN NORMAL LIMITS
	6			WITHIN NORMAL LIMITS
	7			WITHIN NORMAL LIMITS
	8			WITHIN NORMAL LIMITS
	9			WITHIN NORMAL LIMITS
	10			WITHIN NORMAL LIMITS
	11			WITHIN NORMAL LIMITS
	12			WITHIN NORMAL LIMITS
	13			WITHIN NORMAL LIMITS
	14			WITHIN NORMAL LIMITS
	15			WITHIN NORMAL LIMITS
	16			WITHIN NORMAL LIMITS

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APPENDIX I

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 3 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
3570	1			WITHIN NORMAL LIMITS
	2			WITHIN NORMAL LIMITS
	3			WITHIN NORMAL LIMITS
	4			WITHIN NORMAL LIMITS
	5			WITHIN NORMAL LIMITS
	6			WITHIN NORMAL LIMITS
	7			WITHIN NORMAL LIMITS
	8			WITHIN NORMAL LIMITS
	9			WITHIN NORMAL LIMITS
	10			WITHIN NORMAL LIMITS
	11			WITHIN NORMAL LIMITS
	12			WITHIN NORMAL LIMITS
	13			WITHIN NORMAL LIMITS
3571	1			WITHIN NORMAL LIMITS
	2			WITHIN NORMAL LIMITS
	3			WITHIN NORMAL LIMITS
	4			WITHIN NORMAL LIMITS
	5			WITHIN NORMAL LIMITS
	6			WITHIN NORMAL LIMITS
	7			WITHIN NORMAL LIMITS
	9			WITHIN NORMAL LIMITS
	10			WITHIN NORMAL LIMITS
	12			WITHIN NORMAL LIMITS
	13			WITHIN NORMAL LIMITS
	14			WITHIN NORMAL LIMITS
	15			WITHIN NORMAL LIMITS
3572	1			WITHIN NORMAL LIMITS
	2			WITHIN NORMAL LIMITS
	3			WITHIN NORMAL LIMITS
	4			WITHIN NORMAL LIMITS
	5			WITHIN NORMAL LIMITS
	6			WITHIN NORMAL LIMITS

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APPENDIX I

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 3 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS OBSERVATION
3572	(CONTINUED)		
	7		WITHIN NORMAL LIMITS
	8		WITHIN NORMAL LIMITS
	9		WITHIN NORMAL LIMITS
	11		WITHIN NORMAL LIMITS
	12		WITHIN NORMAL LIMITS
	13		WITHIN NORMAL LIMITS
	14		WITHIN NORMAL LIMITS
3573	1		WITHIN NORMAL LIMITS
	2		WITHIN NORMAL LIMITS
	4		WITHIN NORMAL LIMITS
	5		WITHIN NORMAL LIMITS
	6		WITHIN NORMAL LIMITS
	7		WITHIN NORMAL LIMITS
	8		WITHIN NORMAL LIMITS
	9		WITHIN NORMAL LIMITS
	10		WITHIN NORMAL LIMITS
	11		WITHIN NORMAL LIMITS
	12		WITHIN NORMAL LIMITS
	13		WITHIN NORMAL LIMITS
	14		WITHIN NORMAL LIMITS
3574	1		WITHIN NORMAL LIMITS
	2		WITHIN NORMAL LIMITS
	3		WITHIN NORMAL LIMITS
	4		WITHIN NORMAL LIMITS
	5		WITHIN NORMAL LIMITS
	7		WITHIN NORMAL LIMITS
	8		WITHIN NORMAL LIMITS
	9		WITHIN NORMAL LIMITS
	10		WITHIN NORMAL LIMITS
	11		WITHIN NORMAL LIMITS
	12		WITHIN NORMAL LIMITS
	13		WITHIN NORMAL LIMITS

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APPENDIX I

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 4 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
4570	1			WITHIN NORMAL LIMITS
	2			WITHIN NORMAL LIMITS
	3			WITHIN NORMAL LIMITS
	4			WITHIN NORMAL LIMITS
	5			WITHIN NORMAL LIMITS
	6			WITHIN NORMAL LIMITS
	7			WITHIN NORMAL LIMITS
	8			WITHIN NORMAL LIMITS
	9			WITHIN NORMAL LIMITS
	10			WITHIN NORMAL LIMITS
	11			WITHIN NORMAL LIMITS
	12			WITHIN NORMAL LIMITS
	13			WITHIN NORMAL LIMITS
	14			WITHIN NORMAL LIMITS
	15			WITHIN NORMAL LIMITS
4571	4			WITHIN NORMAL LIMITS
	5			WITHIN NORMAL LIMITS
	6			WITHIN NORMAL LIMITS
	7			WITHIN NORMAL LIMITS
	8			WITHIN NORMAL LIMITS
	9			WITHIN NORMAL LIMITS
	12			WITHIN NORMAL LIMITS
	14			WITHIN NORMAL LIMITS
4572	1			WITHIN NORMAL LIMITS
	2			WITHIN NORMAL LIMITS
	3			WITHIN NORMAL LIMITS
	4			WITHIN NORMAL LIMITS
	5			WITHIN NORMAL LIMITS
	6			WITHIN NORMAL LIMITS
	7			WITHIN NORMAL LIMITS
	8			WITHIN NORMAL LIMITS
	9			WITHIN NORMAL LIMITS

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APPENDIX I

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 4 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS OBSERVATION
4572	(CONTINUED)		
	10		WITHIN NORMAL LIMITS
	11		WITHIN NORMAL LIMITS
	12		WITHIN NORMAL LIMITS
4573	1		WITHIN NORMAL LIMITS
	2		WITHIN NORMAL LIMITS
	3		WITHIN NORMAL LIMITS
	4		WITHIN NORMAL LIMITS
	5		WITHIN NORMAL LIMITS
	6		WITHIN NORMAL LIMITS
	7		WITHIN NORMAL LIMITS
	8		WITHIN NORMAL LIMITS
	9		WITHIN NORMAL LIMITS
	10 L		WITHIN NORMAL LIMITS
	11		WITHIN NORMAL LIMITS
	12		WITHIN NORMAL LIMITS
4574	1		WITHIN NORMAL LIMITS
	2		WITHIN NORMAL LIMITS
	3		WITHIN NORMAL LIMITS
	4		WITHIN NORMAL LIMITS
	5		WITHIN NORMAL LIMITS
	6		WITHIN NORMAL LIMITS
	7		WITHIN NORMAL LIMITS
	8		WITHIN NORMAL LIMITS
	9		WITHIN NORMAL LIMITS
	10		WITHIN NORMAL LIMITS
	11		WITHIN NORMAL LIMITS
	12		WITHIN NORMAL LIMITS
	13		WITHIN NORMAL LIMITS
	14		WITHIN NORMAL LIMITS
	15		WITHIN NORMAL LIMITS

FETAL STATUS CODES: L-late resorption

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APPENDIX I

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 5 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
5570	1			WITHIN NORMAL LIMITS
	2			WITHIN NORMAL LIMITS
	3			WITHIN NORMAL LIMITS
	4			WITHIN NORMAL LIMITS
	5			WITHIN NORMAL LIMITS
	6			WITHIN NORMAL LIMITS
	7			WITHIN NORMAL LIMITS
	8			WITHIN NORMAL LIMITS
	9			WITHIN NORMAL LIMITS
	10			WITHIN NORMAL LIMITS
	11			WITHIN NORMAL LIMITS
	12			WITHIN NORMAL LIMITS
	13			WITHIN NORMAL LIMITS
	14			WITHIN NORMAL LIMITS
	15			WITHIN NORMAL LIMITS
	16			WITHIN NORMAL LIMITS
	17			WITHIN NORMAL LIMITS
	18			WITHIN NORMAL LIMITS
5571	1			WITHIN NORMAL LIMITS
	2			WITHIN NORMAL LIMITS
	3			WITHIN NORMAL LIMITS
	4			WITHIN NORMAL LIMITS
	5			WITHIN NORMAL LIMITS
	6			WITHIN NORMAL LIMITS
	7			WITHIN NORMAL LIMITS
	8			WITHIN NORMAL LIMITS
	9			WITHIN NORMAL LIMITS
	10			WITHIN NORMAL LIMITS
	11			WITHIN NORMAL LIMITS
	12			WITHIN NORMAL LIMITS
	13			WITHIN NORMAL LIMITS
	14			WITHIN NORMAL LIMITS
	15			WITHIN NORMAL LIMITS

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APPENDIX I

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 5 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS OBSERVATION
5572	1		WITHIN NORMAL LIMITS
	2		WITHIN NORMAL LIMITS
	5		WITHIN NORMAL LIMITS
	6		WITHIN NORMAL LIMITS
	7		WITHIN NORMAL LIMITS
	8		WITHIN NORMAL LIMITS
	9		WITHIN NORMAL LIMITS
	10		WITHIN NORMAL LIMITS
	11		WITHIN NORMAL LIMITS
	12		WITHIN NORMAL LIMITS
	14		WITHIN NORMAL LIMITS
	15		WITHIN NORMAL LIMITS
5573	1		WITHIN NORMAL LIMITS
	2		WITHIN NORMAL LIMITS
	3		WITHIN NORMAL LIMITS
	4		WITHIN NORMAL LIMITS
	5		WITHIN NORMAL LIMITS
	6		WITHIN NORMAL LIMITS
	7		WITHIN NORMAL LIMITS
	8		WITHIN NORMAL LIMITS
	9		WITHIN NORMAL LIMITS
	10		WITHIN NORMAL LIMITS
	11		WITHIN NORMAL LIMITS
	12		WITHIN NORMAL LIMITS
	13		WITHIN NORMAL LIMITS
	14		WITHIN NORMAL LIMITS
5574	1		WITHIN NORMAL LIMITS
	2		WITHIN NORMAL LIMITS
	3		WITHIN NORMAL LIMITS
	4		WITHIN NORMAL LIMITS
	5		WITHIN NORMAL LIMITS
	6		WITHIN NORMAL LIMITS

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APPENDIX I

CHLOROTRIFLUOROETHYLENE (CTFE): EMBRYO-FETAL TOXICITY STUDY
IN RATS BY INHALATION EXPOSURE

INDIVIDUAL FETAL EXTERNAL OBSERVATIONS

GROUP 5 180 PPM

FEMALE#	FETUS#/SEX	ORGAN	CLASS	OBSERVATION
5574	(CONTINUED)			
	7			WITHIN NORMAL LIMITS
	8			WITHIN NORMAL LIMITS
	9			WITHIN NORMAL LIMITS
	10			WITHIN NORMAL LIMITS
	11			WITHIN NORMAL LIMITS
	12			WITHIN NORMAL LIMITS
	13			WITHIN NORMAL LIMITS
	14			WITHIN NORMAL LIMITS
	15			WITHIN NORMAL LIMITS

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Miran Calibration and Chamber Distribution were the same as Main Study.

1. INTRODUCTION

This appendix presents the methodology for exposure atmosphere generation and monitoring, and results of a 6-hour per day exposure regimen of inhaled Chlorotrifluoroethylene (CTFE) gas with and without dimers, during early organogenesis (Gestation Days 6 through 10) in pregnant females rats.

2. MATERIALS AND METHODS

2.1. HUSBANDRY DURING EXPOSURE PERIODS

2.1.1. HOUSING

Animals were individually housed in a 100 Liter glass and Plexiglass whole-body exposure chamber. The placement of the animals in the whole-body exposure chamber was rotated daily to ensure uniform exposure of the animals. A description of the animal rotation is included in the raw data.

2.1.2. FEED

None was provided during exposure.

2.1.3. WATER

None was provided during exposure.

2.1.4. ENVIRONMENTAL CONDITIONS

Chamber temperature and relative humidity were monitored continuously and recorded every half-hour during exposure and maintained, to the maximum extent possible, within the ranges presented below. Excursions outside the specified range did not affect the integrity of the study.

Temperature

Desired: 20 to 24°C
Actual: 23 to 27°C

Relative Humidity

Desired: 40 to 60%
Actual: 12 to 24%

2.2. TEST SUBSTANCE ADMINISTRATION AND CHAMBER OPERATIONS

2.2.1. ROUTE OF ADMINISTRATION

Inhalation as a gas, via whole-body exposures

2.2.2. TEST SUBSTANCE ADMINISTRATION

The test substance was administered as a gas in the breathing air of the animals. The test atmosphere was generated by an appropriate procedure determined during pre-study trials. The trials were performed to evaluate the optimal set of conditions and equipment to generate a stable atmosphere at the target exposure levels and maintain uniform conditions throughout the exposure chambers.

2.2.3. TARGET EXPOSURE LEVELS

Group 1 - 0 ppm
Group 2 - 180 ppm CTFE (no dimers)
Group 3 - 180 ppm CTFE (0.1% dimers)
Group 4 - 180 ppm CTFE (0.5% dimers)
Group 5 - 180 ppm CTFE (2.0% dimers)

2.2.4. CHAMBER OPERATIONS

The whole-body exposure chambers each had a volume of approximately 100 Liters. Each chamber was operated at a minimum flow rate of 20 Liters per minute. The final airflow was set to provide at least one air change (calculated by dividing the chamber volume by the airflow rate) in 5.0 minutes (12 air changes/hour) and a T99 equilibrium time (calculated by

multiplying the air change by the exponential factor 4.6) of at most 23 minutes.

This chamber size and airflow rates were considered adequate to maintain the animal loading factor below 5% and the oxygen level at 19% or higher. At the end of the exposure, all animals remained in chamber for a minimum of 23 minutes. During this time, the chamber was operated at the same flow rate as used during the exposure using clean air only. Recordings of airflow rate and static pressure were made at the initiation of the exposures and every half-hour during the exposure.

The chamber atmospheres were exhausted through the in-house filtering system, which consisted of a coarse filter, a HEPA filter, and an activated charcoal bed.

See Figures 1 and 2 and Table III (Inhalation Report) for equipment list.

2.2.5. EXPOSURE PROCEDURE

Group 1

Houseline air was delivered from a regulator with a backpressure gauge via ¼" tubing to a flowmeter regulated by a metering valve. A backpressure gauge was attached to the outlet of a flowmeter and air was delivered into the inlet of a 100 Liter glass and Plexiglass whole-body exposure chamber via ¼" tubing. The exposure chamber and generation system were enclosed in a 10 meter cubed Harford glass and stainless steel chamber.

Groups 2 - 5

The test substance was delivered from the Sponsor's cylinder, through a backpressure gauge and metering valve via ¼" Teflon tubing to a mass flowmeter. The flowmeter was regulated by a metering valve which regulated the flow of test substance via ¼" Teflon tubing to one side of the stainless steel "T". Houseline air

was delivered from a regulator with a backpressure gauge via ¼" tubing to a flowmeter regulated by a metering valve to one side of a stainless steel "T", and then into the inlet of a 100 Liter glass and Plexiglass whole-body exposure chamber. The exposure chamber and generation system were enclosed in a 10 meter cubed Harford glass and stainless steel chamber.

See Figures 1 and 2, and Table III for equipment list.

2.3. EXPOSURE CONCENTRATION DETERMINATION

2.3.1. NOMINAL CONCENTRATION

A nominal exposure concentration was calculated. The flow of air through the chamber was monitored using appropriate calibrated equipment. The test substance (TS) consumed during the exposure was divided by the total volume of air passing through the chamber (volumetric flow rate times total exposure time) to give the nominal concentration.

Calculation

$$\text{Nominal Concentration (ppm)} = \frac{\text{Average Actual TS Flow (ccm)}}{\text{Chamber Flow (Lpm)}} \times 1000$$

See Table III for equipment list.

2.3.2. CHAMBER SAMPLING

Determination of the exposure levels were made using a MIRAN® Ambient Air analyzer equipped with a strip chart recorder. The test atmosphere was drawn from the normal sampling portal through the MIRAN® and measurements were recorded at least 4 times during each exposure. The exposure levels were determined by comparison of the measured absorbance to a calibrated response curve constructed using the same instrument settings.

See Table III for equipment list.

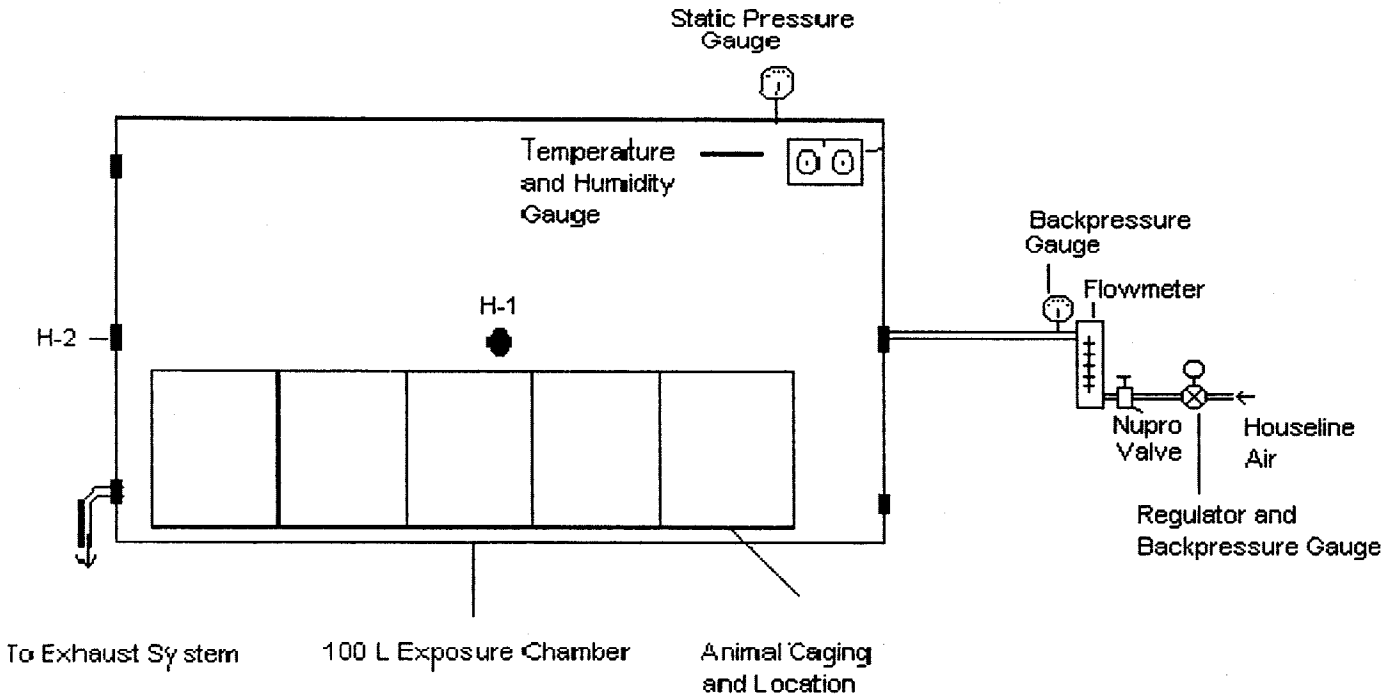
2.3.3. PARTICLE SIZE DISTRIBUTION

Particle size samples were drawn once during the exposure period for the chambers and room air using a TSI Aerodynamic Particle Sizer to confirm the absence of particulate test substance condensate in the exposure atmosphere. The samples were drawn for 20 seconds at a rate of 5.0 Lpm. The mass median aerodynamic diameter, geometric standard deviation and total mass concentration were calculated. A computer was used to program the system to the appropriate settings prior to sampling. The particle size distributions were calculated by the computer and printed out.

See Table III for equipment list.

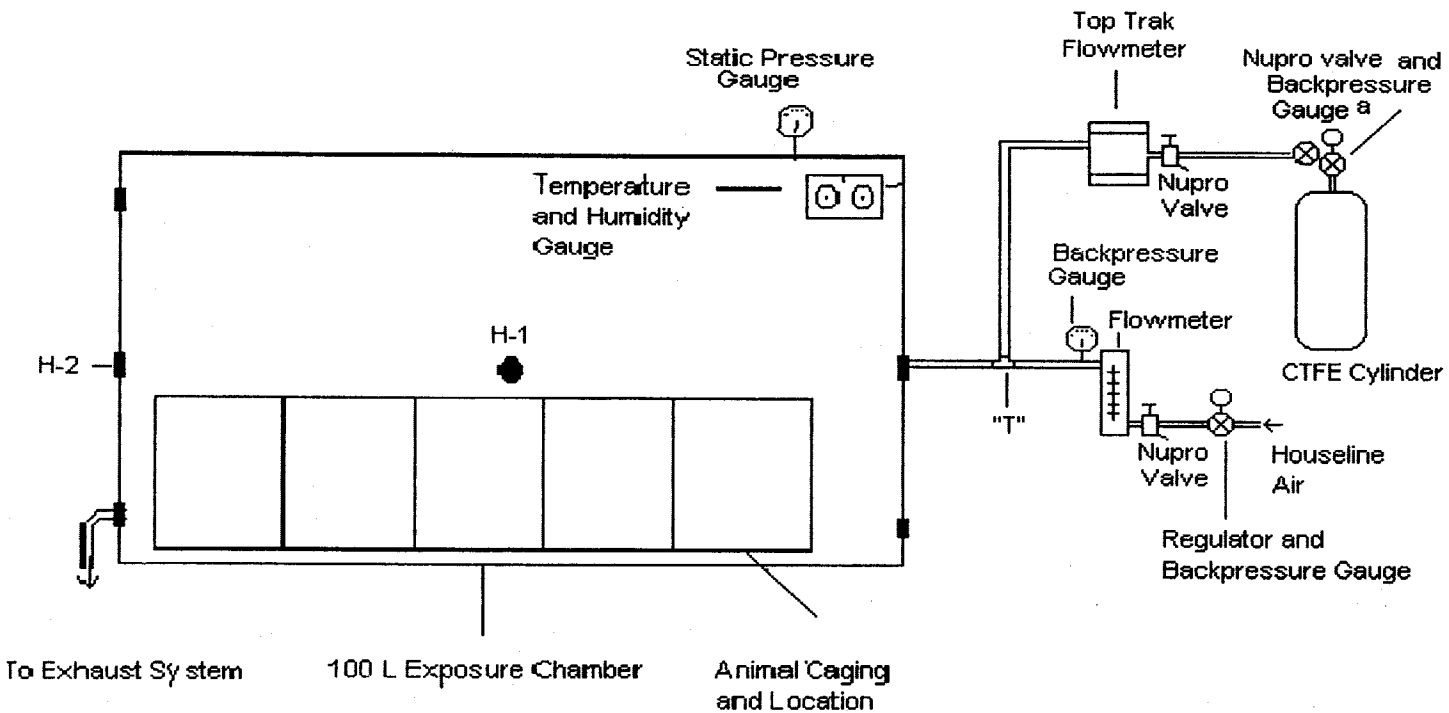
Group 1	Inhalation Report	Appendix J

Figure 1
Chamber Generation System
and Whole-Body Exposure Chamber



Groups 2-5	Inhalation Report	Appendix J

Figure 2
Chamber Generation System
and Whole-Body Exposure Chamber



[a]One backpressure gauge was used for all Groups except Group 3, which used two backpressure gauges.

	Inhalation Report	Appendix J

Table I
Summary of In-Chamber Observations

Exposure Number	1	2	3	4	5
Group 1 – 0 ppm					
Within Normal Limits	All	All	All	All	All
Group 2 – 180 ppm CTFE (no dimers)					
Within Normal Limits	All	All	All	All	All
Group 3 – 180 ppm CTFE (0.1% dimers)					
Within Normal Limits	All	All	All	All	All
Group 4 – 180 ppm CTFE (0.5% dimers)					
Within Normal Limits	All	All	All	All	Some
Decreased Activity	-	-	-	-	Most
Group 5 – 180 ppm CTFE (2.0% dimers)					
Within Normal Limits	All	All	All	All	Some
Labored Breathing	-	-	-	-	Few
Decreased Activity	-	-	-	-	Few

All = 100% of the animals exhibiting a given observation; Some = 21-50% of the animals exhibiting a given observation; Most = 51-99% of the animals exhibiting a given observation; Few = < 20% of the animals exhibiting a given observation.
Note: In-chamber observations are based on all animals present in the exposure chamber at the time.

Table II
Chamber Monitoring Results
Preface

Key to Abbreviations

MMAD	=	Mass Median Aerodynamic Diameter
GSD	=	Geometric Standard Deviation
TMC	=	Total Mass Concentration

Table II
Chlorotrifluoroethylene: Embryo-Fetal Toxicity Study in Rats by Inhalation Exposure

Chamber Monitoring Results
Cumulative Exposure Record
Group 1 - 0 ppm (Air Control)

Study Day	Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration Mean (ppm)	Individual (ppm)				Particle Size Determinations MMAD (µm)	GSD	TMC (mg/m^3)	Chamber Environment Mean Temperature (°C)	Humidity (%)
6	8-Feb-05	1	0	0.00	0.00	0.00	0.00	0.00				26	18
7	9-Feb-05	2	0	0.00	0.00	0.00	0.00	0.00	13.58	1.689	4.84E-03	27	18
8	10-Feb-05	3	0	0.00	0.00	0.00	0.00	0.00				26	19
9	11-Feb-05	4	0	0.00	0.00	0.00	0.00	0.00				24	19
10	12-Feb-05	5	0	0.00	0.00	0.00	0.00	0.00				24	18
		Mean	**0.0**		**0.00**				**13.58**	**1.689**	**4.84E-03**	**25.4**	**18.4**
		S.D.	**0.0**		**0.00**				**-**	**-**	**-**	**1.3**	**0.5**

Table II
Chlorotrifluoroethylene: Embryo-Fetal Toxicity Study in Rats by Inhalation Exposure

Chamber Monitoring Results
Cumulative Exposure Record
Group 2 - 180 ppm CTFE (no dimers)

Study Day	Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration: Mean (ppm)	Individual (ppm)				Particle Size Determinations: MMAD (µm)	GSD	TMC (mg/m^3)	Chamber Environment: Mean Temperature (°C)	Humidity (%)
6	8-Feb-05	1	210	180	210	150	180	180				26	16
7	9-Feb-05	2	210	175	170	180	160	190	1.035	1.232	8.02E-06	27	17
8	10-Feb-05	3	210	178	190	180	170	170				26	16
9	11-Feb-05	4	210	188	180	180	200	190				24	16
10	12-Feb-05	5	210	180	200	160	180	180				24	14
		Mean	**210**		**180**				**1.035**	**1.232**	**8.02E-06**	**25.4**	**15.8**
		S.D.	**0.0**		**15**				**-**	**-**	**-**	**1.3**	**1.1**

Table II
Chlorotrifluoroethylene: Embryo-Fetal Toxicity Study in Rats by Inhalation Exposure

Chamber Monitoring Results
Cumulative Exposure Record
Group 3 - 180 ppm CTFE (0.1% dimers)

Study Day	Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration: Mean (ppm)	Individual (ppm)				Particle Size Determinations: MMAD (µm)	GSD	TMC (mg/m³)	Chamber Environment: Mean Temperature (°C)	Mean Humidity (%)
6	8-Feb-05	1	210	188	200	180	190	180				26	21
7	9-Feb-05	2	210	178	200	170	150	190	2.599	1.607	1.58E-04	26	21
8	10-Feb-05	3	210	180	170	180	190	180				26	21
9	11-Feb-05	4	210	180	160	190	180	190				24	21
10	12-Feb-05	5	210	180	180	180	180	180				24	21
		Mean	**210**		**181**				**2.599**	**1.607**	**1.58E-04**	**25.2**	**21.0**
		S.D.	**0.0**		**12**				**-**	**-**	**-**	**1.1**	**0.0**

Table II
Chlorotrifluoroethylene: Embryo-Fetal Toxicity Study in Rats by Inhalation Exposure

Chamber Monitoring Results
Cumulative Exposure Record
Group 4 - 180 ppm CTFE (0.5% dimers)

Study Day	Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration: Mean (ppm)	Individual (ppm)				Particle Size Determinations: MMAD (µm)	GSD	TMC (mg/m^3)	Chamber Environment Mean: Temperature (°C)	Humidity (%)
6	8-Feb-05	1	240	195	220	190	180	190				25	20
7	9-Feb-05	2	240	190	210	180	170	200	2.847	1.634	1.50E-04	26	21
8	10-Feb-05	3	240	190	200	190	190	180				25	21
9	11-Feb-05	4	240	185	190	190	180	180				23	20
10	12-Feb-05	5	240	193	210	190	190	180				23	19
		Mean	**240**		**191**				**2.847**	**1.634**	**1.50E-04**	**24.4**	**20.2**
		S.D.	**0.0**		**12**				**-**	**-**	**-**	**1.3**	**0.8**

Table II
Chlorotrifluoroethylene: Embryo-Fetal Toxicity Study in Rats by Inhalation Exposure

Chamber Monitoring Results
Cumulative Exposure Record
Group 5 - 180 ppm CTFE (2.0% dimers)

Study Day	Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration: Mean (ppm)	Individual (ppm)				Particle Size Determinations: MMAD (µm)	GSD	TMC (mg/m^3)	Chamber Environment: Mean Temperature (°C)	Mean Humidity (%)
6	8-Feb-05	1	180	183	180	190	180	180				26	20
7	9-Feb-05	2	180	183	180	170	190	190	2.593	1.706	2.24E-04	26	20
8	10-Feb-05	3	180	180	190	180	180	170				26	20
9	11-Feb-05	4	180	188	180	180	190	200				24	21
10	12-Feb-05	5	180	180	170	210	180	160				24	17
		Mean	**180**		**183**				**2.593**	**1.706**	**2.24E-04**	**25.2**	**19.6**
		S.D.	**0.0**		**11**				**-**	**-**	**-**	**1.1**	**1.5**

Table III
Equipment List

Exposure Chamber
100 Liter glass and Plexiglas™ chamber with a glass front.

Compound Reservoir
Gas Cylinders (Sponsor provided)

Flowmeter
Dwyer®, size 0-20, 0-30 and 0-40 Lpm (Dwyer® Instruments)
Top Trak™ Mass Flow Meter, 0 – 30 lpm and 0 – 100 sccm, Model 821 – 04 – 1 (Sierra Instruments) calibrated prestudy with a 1 – 250 sccm Gilibrator®Bubble Generator, P/N D800286 and D800287 646-L.

Chamber Air Flow
Dwyer® size 0-30 and 0-40 Lpm flowmeter (Dwyer® Instruments) calibrated pre-study with a Top Trak™ Mass Flow Meter, 0 – 30 Lpm and 0 – 100 sccm, Model 822 – 13 – OV1 – PV1 – V1 (Sierra Instruments).

Chamber Static Pressure
Dwyer® Magnehelic® gauge (Dwyer® Instruments Inc.), calibrated prestudy with Dwyer® Mark II Manometer, Model 25 (Dwyer® Instruments, Inc.).

Regulators
MG Industries P/N 300.
Union Carbide, Model N SG 3800 30.
Norgreen, P/N 9892K23 or R07-219RGKA.

Pressure/Vacuum Gauges
Union Carbide backpressure gauge, P/N SG 8363.
Norgreen backpressure gauge, P/N 9892K23.
MG Industries backpressure gauges, P/N ID201/ID206.
U.S. Gauge backpressure gauge, P/N 12672.1.
Matheson® backpressure gauge, P/N 63-3161.
Ashcroft backpressure gauge, P/N 737-47.
GAST® backpressure gauge, Model P/N 183-01.
GAST® vacuum gauge.

Metering Valve
Metering Valve, Model SS-4L Series, (Nupro® Co.).
Metering Valve, Model SS-31RS4, (Whitey®).

Table III
Equipment List

Vacuum Pumps
Thomas Industries Inc., Model 707CM50.

Tubing
Clear plastic, sizes ¼", ½", 1" (Norton, Baxter).
Stainless steel "T".
Teflon®, size ¼".

Air Analyzer
MIRAN® 1A-CVF Ambient Air Analyzer (Wilks) with a Cole Parmer Strip Chart Recorder, Model 201, and a Micronta® LCD Benchtop Digital Multimeter, Model No. 22-195 Balston® Microfibre™ Disposable Filter Unit (Grade DQ) was attached in-line.

Particle Sizer
TSI Aerodynamic Particle Sizer, Model 331001, and a DELL computer, Model 486P/25, equipped with an Epson LQ-5707 printer, Model P630B.

Environmental Monitoring
VWR Temperature and Humidity Gauge, tested prestudy with a Big Digit Traceable Hygrometer/Thermometer.

Balance
Sartorius LC4200 (Sartorius Corporation).

	Certificate of Analysis (Sponsor's Test Substance)	Appendix K

HONEYWELL
lo Research Laboratory
ertificate of Analysis

roject # 955019
eport by: S.Ferguson
ATE: 01/20/05

lotebook#40245-27
lotebook#40427-06

CFTE (G-1113) Standard - Weight %

COMPONENT		G-1113 Standard A #35452	G-1113 Standard B #35453	G-1113 Solvent G1113 Day Tank 121704 #35389
C-133a		0.0113	0.0102	0.0102
C 1122		0.0254	0.0244	0.0244
C 20		ND	ND	ND
ME		ND	ND	ND
C-40		ND	ND	ND
C-123		ND	ND	ND
C-123a		0.0004	0.0005	0.0005
C-1132a		ND	ND	ND
lethanol		ND	ND	ND
C-113		0.0005	0.0008	0.0008
C-1123		0.0002	0.0002	0.0002
riethylamine		ND	ND	ND
otal-1,2 dichlorohexafluorocyclobutane		0.50	1.92	0.02
nknowns		0.0050	0.0051	0.0051
C-1113		99.46	98.04	99.94

Certified by:

S.L. Ferguson

search Chemist
1/19/2005

Appendix R

PROTOCOL

CHLOROTRIFLUOROETHYLENE (CTFE)

EMBYRO-FETAL TOXICITY STUDY IN RATS BY INHALATION EXPOSURE

CONFIDENTIAL

HLS Study No.:	**04-4261**
Protocol Version:	**Final**
Date:	**23 July 2004**

Huntingdon Life Sciences
Study No. 04-4261

Final Protocol

PROTOCOL SIGNATURES/PREFACE

(Confidential Information - to be distributed on a need-to-know basis)

Study Title: Chlorotrifluoroethylene: Embyro-Fetal Toxicity Study in Rats by Inhalation Exposure

HLS Study No.: 04-4261

This is the Final Protocol. It has been reviewed and approved by:

5 Aug 04
Date

Gary M. Hoffman, B.A., DABT
Study Director
Huntingdon Life Sciences
Address: 100 Mettlers Road
East Millstone, NJ 08875-2360
Phone No.: 732-873-2550 x2920
Fax No.: 732-873-3992
Email: hoffmang@princeton.huntingdon.com

2 August 2004
Date

George M. Rusch, Ph.D., DABT
Director of Toxicology and Risk Assessment
Honeywell
Engineered Materials Sector
101 Columbia Road, PO Box 2245R
Morristown, NJ 07962-1057
Phone No.: 1-973-455-3672
Fax No.: 1-973-455-3345
Email: george.rusch@honeywell.com

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1. INTRODUCTION

HLS Study No.:	04-4261
Study Title:	Chlorotrifluoroethylene: Embyro-Fetal Toxicity Study in Rats by Inhalation Exposure
Test Substance:	Chlorotrifluoroethylene (CTFE)
Testing Facility:	Huntingdon Life Sciences 100 Mettlers Road East Millstone, NJ 08875-2360

Purpose:

This study is designed to assess the potential maternal and/or developmental toxicity of Chlorotrifluoroethylene in the pregnant rat when administered by whole-body inhalation exposure. Animals will be treated during the period of major embryonic organogenesis, Gestation Days (GD) 6-19 inclusive, then sacrificed on GD 20 and subjected to caesarean section.

2. STUDY PERSONNEL

Study Director	Gary M. Hoffman, B.A., DABT
Alternate Contact	Elizabeth Horsley, Ph.D. Reproductive Toxicologist Tel.: 732-873-2550 x3512
Senior Reproductive Toxicologist	Keith P. Hazelden, BSc, CBiol, MIBiol Director of Reproductive & Developmental Toxicology Tel.: 732-873-2550 x2590

Additional key personnel will be documented in the project file and presented in the final report.

3. PROPOSED STUDY DATES

Study Initiation Date	Date Study Director Signs Protocol
Receipt of test animals:	20 August 2004 (Experimental Start Date)* & 23 August 2004 (GD 0, 1, or 2)
Initiation of exposures:	24 August 2004 (Experimental Start Date)** (First GD 6)
Termination of exposures:	9 September 2004 (Last GD 19)
Necropsy:	7-10 September 2004 (GD 20)
Experimental Termination:	10 September 2004 (Date of last data collection)
Submission of Draft Final Report:	29 December 2004 (without fetal evaluations) 28 February 2005 (with fetal evaluations)
Study Completion Date:	Date Final Report signed by Study Director

*as per OECD GLPs; ** as per EPA GLPs

4. EXPERIMENTAL DESIGN

Group	Group Designation	Exposure Levels[a] (ppm)	Treatment Gestation Days	Number of Animals				
				Time-Mated Females	Euthanized Gestation Day 20[b]	Fetal Evaluations (Fetuses/Litter)		
						External	Soft Tissue	Skeletal
1	Air Control	0	6-19	25	All	All	~1/2	~1/2
2	Low	30	6-19	25	All	All	~1/2	~1/2
3	Mid	90	6-19	25	All	All	~1/2	~1/2
4	High	180	6-19	25	All	All	~1/2	~1/2

[a]Exposures will be 6 hours per day for 7 consecutive days per week. Exposure levels are expressed as ppm of test substance. The exposures will be conducted via whole-body exposure.
[b]Complete postmortem evaluations will also be performed on animals which are found dead or euthanized in a moribund condition during the course of the study.

The first day of exposures will be defined as Day 0 of the study.

4.1. JUSTIFICATION FOR ROUTE, DURATION AND FREQUENCY OF ADMINISTRATION

The inhalation route is one of the potential routes of human exposure to this test substance. The duration and frequency of the exposures are as recommended in the relevant Test Guideline, ensuring adequate exposure of post-implantation embryo-fetal development.

4.2. JUSTIFICATION FOR TEST ANIMAL SELECTION

The rat is used as a surrogate for humans in the detection of embryo-fetal toxicity and is a species in which known teratogens have been detected. This rodent species is commonly used in the conduct of embryo-fetal toxicity studies, and is that recommended by the relevant Test Guideline. Historical control data are also available with this strain of rat for comparative evaluation, if necessary.

4.3. JUSTIFICATION FOR NUMBER OF ANIMALS

The number of animals in this study is considered the minimum necessary to allow for meaningful interpretation of the data. Some of the endpoints of principal interest (*eg* embryo-fetal death, fetal malformations, abortion) are low-frequency events and a group size of ~20 litters tends to provide the necessary degree of consistency between studies. In the expectation of pregnancy rates of 80-100%, the group size of 25 mated female rats is considered appropriate for this study and will provide a sufficient number of litters for evaluation in each group.

4.4. EXPOSURE LEVEL SELECTION AND JUSTIFICATION

A pilot 2-week inhalation study was performed with male and female (including pregnant females exposed from GD6-19) CD rats exposed to mean levels of 0, 33, 61, 119 and 241 ppm of CTFE. Effects were limited to depression in body weight gains, elevated kidney/body weight ratios and toxic nephrosis in animals exposed to 241 ppm. Depressed body weight gains were also seen in males and pregnant females exposed to 119 ppm. No embryotoxic, fetotoxic or developmental effects were seen in any of the pregnant rats. In a subsequent 13-week inhalation study, male and female F-344 rats were exposed to mean levels of 0, 29, 62 and 121 ppm. Effects on the kidneys were indicated by increased organ weights, alterations in clinical chemistry parameters and clinical observations, and alterations in microscopic structure. Males also showed alterations in body weights and liver weights with slight effects even at 29 ppm. After a 2 week recovery period, effects were markedly reduced.

Based on the above information, a high exposure level of 180 ppm was selected for this study to provide slight maternal toxicity while lower levels of 90 and 30 ppm were selected to provide a range of possible effects including a NOEL or NOAEL.

5. TEST SUBSTANCE

5.1. TEST SUBSTANCE

Chlorotrifluoroethylene (CTFE)
MW = 116.47; CAS #79-38-9

Test Substance Category: Industrial chemical used as a monomer for the production of chlorofluorocarbon polymers

Description, lot number, storage, expiration date (if available) and handling procedures, as well as other pertinent information will be documented in the study data.

5.2. IDENTIFICATION OF TEST SUBSTANCE

Unless otherwise noted, the identity, strength, composition, stability and method of synthesis, fabrication and/or derivation of each batch of the test substance will be documented by the Sponsor before its use in the study. This documentation will be maintained by the Sponsor at the address indicated on the signature page of this protocol.

5.3. ARCHIVAL SAMPLES

An archival sample from each lot of test substance will be taken and stored in the Archives of the Testing Facility. If multiple studies are conducted with the same substance, a common archival sample may be taken and appropriately labeled.

5.4. UNUSED TEST SUBSTANCE

The unused portion of the test substance, as well as any empty test substance containers, will be returned to the Sponsor following completion of the in-life phase of the final study with this test substance.

6. TEST ANIMALS

6.1. SPECIES AND STRAIN

Albino Rats (Outbred), Sprague Dawley - derived
[Crl: CD® IGS BR, VAF/Plus®]

6.2. SUPPLIER

Charles River Laboratories
Documentation of the specific breeding facility will be maintained in the study file.

6.3. ANIMAL REQUIREMENTS/SPECIFICATIONS

6.3.1. NUMBER

Ordered: 104 time-mated rats.

Placed on study: 100 time-mated rats.

6.3.2. AGE AND WEIGHT

Time-mated female rats 75-95 days in age and weighing 210-270 grams on Gestation Day 0 (GD 0 weight range will be provided by the Supplier, non-GLP) will be used. Animals will be received on GD 0, 1 or 2.

6.4. ACCLIMATION PERIOD

Animals will be acclimated for a minimum of 3 days from time of receipt until initiation of exposures (GD 6).

6.5. ANIMAL CARE AND HUSBANDRY

6.5.1. FACILITIES MANAGEMENT/ANIMAL HUSBANDRY

Currently acceptable practices of good animal husbandry will be followed, e.g., *Guide for the Care and Use of Laboratory Animals*; National Academy Press, 1996. Huntingdon Life Sciences Inc. is fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC).

6.5.2. VETERINARY CARE

Animals are monitored by the technical staff for any conditions requiring possible veterinary care. If any such conditions are identified, a staff veterinarian will be notified for an examination and evaluation. Animals will be treated as outlined in the Animal Welfare Act Compliance section of this protocol.

6.5.3. ENVIRONMENTAL CONDITIONS

Light/Dark Cycle

Twelve-hour light/dark cycle provided by an automatic timer.

Temperature

Temperature will be monitored in accordance with HLS SOPs to ensure that the desired range of 18-26°C is maintained. Temperature will be maintained within this range to the maximum extent possible. The actual temperature range will be included in the final report.

Humidity

Humidity will be monitored in accordance with HLS SOPs to ensure that the desired range of 30 to 70% is maintained. Humidity will be maintained within this range to the maximum extent possible. The actual humidity range will be included in the final report.

Air Changes

Animal quarters will have 10-15 air changes per hour. The actual number of air changes per hour in each animal room is recorded at least twice each year and the Testing Facility retains these records.

6.5.4. HOUSING

Animals will be housed individually in suspended stainless steel wire mesh cages.

6.5.5. FEED

Certified Rodent Diet, No. 5002; (Meal) (PMI Feeds, Inc., St. Louis, MO) *ad libitum.*

6.5.6. FEED ANALYSIS

Analytical certification of batches of feed provided by the manufacturer will be maintained on file. There are no known contaminants in the feed that are expected to interfere with the objectives of this study.

6.5.7. WATER

Facility water is supplied by Elizabethtown Water Company, (Westfield, NJ) and will be provided *ad libitum* to individual animal cages through an automated watering system.

6.5.8. WATER ANALYSIS

Water analyses are conducted monthly by the Elizabethtown Water Company to ensure that water meets standards specified under the EPA Federal Safe Drinking Water Act Regulations (40 CFR part 141). Water analyses, provided by the supplier, will be maintained on file at the Testing Facility. In addition, water samples are collected biannually from representative rooms in the Testing Facility. Chemical and microbiological water analyses are conducted on these samples by a subcontract laboratory. Results are maintained on file at the Testing Facility. There are no known contaminants in the water that are expected to interfere with this study.

6.6. ANIMAL HUSBANDRY DURING EXPOSURE

Housing: Individual in suspended, stainless steel wire mesh cages.

Feed: None.

Water: None.

6.7. ANIMAL IDENTIFICATION

Each animal will be assigned a temporary identification number upon receipt. After selection for study, each animal will be ear-tagged with a number assigned by the Testing Facility. This number plus the study number will comprise a unique identification for each animal. If the tag is lost, it will be replaced. Each study animal's cage will also be allocated a cage card, which will be color-coded for exposure level identification and will contain the study number and animal number.

6.8. ASSIGNMENT OF ANIMALS INTO GROUPS

Animals will be placed into study groups after receipt using a computerized randomization program. This ranks GD 4 body weights into blocks and randomly assigns each animal within each block into one of the study groups. Animals may be replaced based on physical examinations and/or body weight changes up to GD 6, prior to exposures. Disposition of all animals not utilized in the study will be maintained in the study file.

7. TEST SUBSTANCE ADMINISTRATION

7.1. ROUTE OF ADMINISTRATION

Inhalation by whole-body exposure.

7.2. FREQUENCY OF ADMINISTRATION

Once daily.

7.3. DURATION OF ADMINISTRATION

The test substance will be administered for 6 hours/day, 7 days per week for Gestation Days (GD) 6-19.

7.4. ADMINISTRATION OF TEST SUBSTANCE

The test substance will be administered as a gas in the breathing air of the animals. The test atmosphere will be generated by an appropriate procedure determined during pre-study trials. The trials will be performed to evaluate the optimal set of conditions and equipment to generate a stable atmosphere at the target exposure levels and maintain uniform conditions throughout the exposure chambers. The method will be described in the raw data of the study and in the report.

The whole-body exposure chambers will each have a volume of approximately 1000 liters. Each chamber will be operated at a minimum flow rate of 200 liters per minute. The final airflow will be set to provide at least one air change in 5.0 minutes (12 air changes/hour) and a T99 equilibrium time of at most 23 minutes. This chamber size and airflow rate is considered adequate to maintain the oxygen level at least 19% and the animal loading factor below 5%. At the end of each exposure, all animals will remain in the chamber for a minimum of the T99 equilibrium time. During this time, the chamber will be operated at approximately the same flow rate using clean air only.

7.5. EXPOSURE CONCENTRATION DETERMINATION

A nominal exposure concentration will be calculated. The flow of air through the chamber will be monitored using appropriate calibrated equipment. The test substance consumed during the exposure will be divided by the total volume of air passing through the chamber (volumetric flow rate times total exposure time) to give the nominal concentration.

During each exposure, measurements of airborne concentrations will be performed in the animals' breathing zone at least 4 times using an appropriate sampling procedure and infrared spectrophotometric analytical procedure. If more than the normal amount of trials is required because of test substance generation or monitoring problems (80 technician hours), the Sponsor will be consulted prior to additional trials (additional cost).

7.6. PARTICLE SIZE DISTRIBUTION ANALYSIS

During each week of exposure, particle size determinations will be performed using a TSI Aerodynamic Particle Sizer to demonstrate the absence of any condensation aerosol.

7.7. CHAMBER AND EXPOSURE ROOM ENVIRONMENT

Chamber temperature, humidity, airflow rate and static pressure will be monitored continuously and recorded every 30 minutes during exposure. Chamber temperature and relative humidity will be maintained, to the maximum extent possible, between 20 to 24°C and 40 to 60%, respectively.

7.8. SUMMARY OF CHAMBER ACTIVITY

The minimum frequency of chamber activity is summarized below:

Activity	Frequency/chamber
Measured Test Substance Concentration	4X/day
Particle Size	1X/week
Temperature	13X/day
Relative Humidity	13X/day
Airflow Rate	13X/day
Static Pressure	13X/day
Nominal Test Substance Concentration (excluding the air control chamber)	1X/day
Rotation Pattern of Exposure Cages	1X/day
Loading/Unloading Verification	1X/day

8. IN-LIFE EXPERIMENTAL OBSERVATIONS

8.1. CLINICAL OBSERVATIONS

8.1.1. VIABILITY OBSERVATIONS (Cage-Side)

Observations for mortality, morbidity, and signs of severe toxicity will be made at least twice daily. Animals in extremely poor health or in a possibly moribund condition will be identified for further monitoring and possible euthanasia.

8.1.2. DETAILED PHYSICAL EXAMINATIONS

In-Chamber: All animals will be observed as a group at least once during each exposure.

Out-of-Chamber: Animals on study will be examined daily from receipt through to terminal euthanasia on GD 20. Examinations will include observations of general condition, skin and fur, eyes, nose, oral cavity, abdomen and external genitalia as well as evaluations of respiration. During the treatment period these evaluations will be performed after exposures.

8.2. BODY WEIGHTS

Body weights will be recorded on GD 4, 6, 10, 13, 16, 19 and 20. Weight gain will also be calculated for intervals as found appropriate, including (but not limited to) GD 6-20.

8.3. FEED CONSUMPTION

Feed consumption will be recorded and reported for intervals as found appropriate, *eg* GD 4-6, 6-10, 10-13, 13-16, 16-20 and 6-20.

9. TERMINAL OBSERVATIONS

9.1. METHOD OF EUTHANASIA

All dams will be euthanized by an overdose of carbon dioxide inhalation. All live fetuses will be euthanized by an intraperitoneal overdose of sodium pentobarbital.

9.2. MACROSCOPIC POSTMORTEM EXAMINATIONS

A macroscopic postmortem examination will be performed on all the dams, including those dying spontaneously or euthanized in either a moribund condition or after prematurely delivering a litter. Macroscopic lesions or tissues with significant findings may be saved (10% Neutral Buffered Formalin) at the discretion of the Supervising Fetal Pathologist or Study Director, if considered necessary for elucidating any pathological condition.

Females that are found dead or sacrificed prior to schedule termination will have implantation data (*ie* number of fetuses and early/late embryo-fetal deaths) determined at necropsy. Corpora lutea will not be counted for these animals.

Dams showing signs of premature delivery will be euthanized on the day such evidence is observed. Reproductive tracts will be examined for implantation data (implantation sites, live/dead fetuses and early/late embryo-fetal deaths). Fetuses obtained earlier than Gestation Day (GD) 20 will be evaluated for external malformations, euthanized and discarded.

Any dams initiating delivery on GD 20 will be immediately euthanized and the fetuses processed with the other GD 20 fetuses.

Dams surviving on GD 20 will have the following examinations of their pregnancies:

The intact uteri (ovaries attached) will be removed from the abdominal cavity. Corpora lutea will be counted and the number per ovary recorded. The number and location of the following will be recorded for each uterine horn:

- live fetuses
- dead fetuses (no significant degeneration)
- late embryo-fetal deaths (recognizable dead fetus undergoing degeneration, regardless of size)
- early embryonic deaths (evidence of implantation but no recognizable fetus)

Each placenta will be examined macroscopically, but will only be retained if further elucidation of a finding is considered necessary by the examiner. The maternal carcass and uterus will then be discarded.

9.3. FETAL EVALUATIONS

9.3.1. External Evaluations

All live fetuses will be weighed and individually identified using a tag affixed around the neck. Each (live and dead) fetus will be given a macroscopic external examination for defects including observation of the palate. Dead fetuses will also be weighed.

9.3.2. Fetal Soft Tissue (Visceral) Evaluation

Approximately one-half of the fetuses in each litter (alternating fetuses within the litter, nominally) will be placed in Bouin's fixative for preservation and decalcification. These fetuses will be subjected to soft tissue examination by gross dissection of the torso and a razor blade sectioning technique (derived from that of Wilson, J.S., Warkany, J. (1965), Teratology: Principles and Techniques. The University of Chicago Press. Chicago and London. P 271) for the head. All malformations and variations will be recorded. During the dissection process, the sex of each fetus will be confirmed after internal inspection of the gonads. Following complete dissection of the fetuses, all carcasses and sections will be preserved in 10% neutral buffered formalin.

9.3.3. Fetal Skeletal Evaluations

Approximately one-half of the fetuses in each litter (alternating fetuses within the litter, nominally) will be eviscerated and

processed for staining of the skeleton using Alizarin Red S. Subsequently, these fetuses will be evaluated for skeletal malformations and ossification variations. These skeletons will then be stored in 100% glycerin with a mold inhibitor.

9.3.4. Dead Fetuses

These will be removed from the uterus, examined for external malformations and weighed. Only those with obvious external malformations will be preserved (10% neutral buffered formalin) for possible future examination. All other dead fetuses, and early embryonic deaths, will be discarded.

10. ARCHIVING OF RECORDS AND SPECIMENS

All data documenting experimental details and study procedures and observations will be recorded and maintained as raw data.

At the completion of the study, all reports, raw data, preserved specimens and retained samples will be maintained in the Testing Facility's Archives for a period of **10 years** after submission of the signed final report.

The Sponsor will be contacted in order to determine the final disposition of these materials. The Sponsor is responsible for all costs associated with the storage of these materials beyond 10 years from the issuance of the final report and for any costs associated with the shipment of these materials to the Sponsor or to any other facility designated by the Sponsor.

11. STATISTICAL EVALUATIONS

Parameters will be analyzed statistically where it is considered necessary in support of interpretation. Statistical significance of differences from control will be recognized at the 5% or 1%, two-sided levels.

11.1. CONTINUOUS DATA

For example (not limited to):

- Body weight and feed consumption data
- Corpora lutea
- Uterine implantation data (live fetuses, implantations)
- Pre- or post-implantation loss
- Fetal weight (by sex and as a composite for both sexes), litter as the experimental unit

Evaluation of equality of group means will be made by the appropriate statistical method, followed by a multiple comparison test if needed: Bartlett's test (Bartlett, 1937; Sokal and Rohlf, 1995) will be performed to determine if groups have equal variances. All data will be analyzed only by parametric methods. The parametric method will be the standard one-way analysis of variance (ANOVA) using the F ratio to assess significance (Armitage, 1971; Dunlap and Duffy, 1975). If significant differences among the means are indicated, additional tests will be used to determine which means are significantly different from the control: Dunnett's (Dunlap et al., 1981; Dunnett, 1955, 1964), Williams (Williams, 1971, 1972), or Cochran and Cox's modified t-test (Cochran and Cox, 1959). The nonparametric method will be the Kruskal-Wallis test (Kruskal and Wallis, 1952, 1953) and if differences are indicated, Shirley's test (Shirley, 1977) or Steel's test (Steel, 1959) will be used to determine which means differ from control. Bartlett's test for equality of variance will be conducted at the 1% significance level; all other statistical tests will be conducted at the 5% and 1% significance levels.

References for these procedures are: Armitage, P. 1971. Statistical Methods in Medical Research. Oxford, UK: Blackwell Scientific Publications; Bartlett, M.S. 1937. Properties of sufficiency and statistical tests. Proceedings of the Royal Society, Series A, 160: 268-282; Cochran, W.G. and Cox, G.M. 1959. Experimental Designs, New York: John Wiley, pp. 100-102; Dunlap, W.P. and Duffy, J.A. 1975. Fortran IV Functions for Calculating Exact Probabilities Associated with Z, Chi-Square, T and F Values. Behav. Res. Methods and Instrumentations 7:59-60; Dunlap, W.P., Marx, M.S. and Agamy, G.G. 1981. Fortran IV functions for calculating probabilities associated with Dunnett's test. Behav. Res. Methods and Instrumentation 13: 363-366; Dunnett, C.W. 1955. A multiple comparison procedure for comparing several treatments with a control. Journal of the American Statistical Association 50: 1096-1121; Dunnett, C.W. 1964. New tables for multiple comparisons with a control. Biometrics 20-3: 482-491; Kruskal, W.H. and Wallis, W.A. 1952. Use of Ranks in one-criterion variance analysis. Journal of the American Statistical Association 47: 583-621; Kruskal, W.H. and Wallis, W.A. 1953. Errata for Kruskal-Wallis (1952) Journal of the American Statistical Association 48: 907-911; Shirley, E.A.C. 1977. A non-parametric equivalent of Williams' test for contrasting increasing dose levels of a treatment. Biometrics 33: 386-389; Sokal, R.R. and Rohlf, F.J. 1995. Biometry. 3rd Edition. San Francisco: W.H. Freeman pp. 369-371; Steel, R.G.D. 1959. A multiple comparison rank sum test: treatment versus control. Biometrics 15: 560-572.; Williams, D.A. 1971. A test for differences between treatment means when several dose levels are compared with a zero dose control. Biometrics 27: 103-117; Williams,

D.A. 1972. The comparison of several dose levels with a zero dose control. Biometrics 28: 519-531.

11.2. INCIDENCE DATA

For example (not limited to):

- Incidence of females showing premature delivery or otherwise showing total pregnancy loss (no live fetuses)
- Incidence of litters containing fetuses with observations (individual findings or groups of findings; external, soft tissue and/or skeletal)

A Fisher Exact Test with Bonferonni correction (Seigel, S. 1956. Nonparametric Statistics for the Behavioral Sciences. New York: McGraw-Hill.) will be performed to identify differences between the control and treatment groups. All statistical tests will be conducted at the 5% and 1%, two-sided risk levels.

12. REPORTING

12.1. STATUS REPORTS

Periodic verbal and written updates on study progress will be provided by the Study Director. In general, a written status report will be submitted weekly and following the GD 20 terminations.

12.2. FINAL REPORT

Two hard copies (1 unbound and 1 bound) of an audited draft report will be submitted following termination of the study. After receipt and review of the Sponsor's comments, appropriate changes will be made and two hard copies (1 unbound and 1 bound) and one electronic copy of a signed, final report will be issued. (Additional copies will be provided at additional cost). Six months after issuance of the draft report, if no requested revisions or instructions to finalize have been communicated by the Sponsor, the draft report will be issued as the final report, signed by the Study Director, and submitted to the Sponsor. Any modifications or changes to the draft report requested 6 months after issuance will be performed at additional cost to the Sponsor. The report will minimally include:

12.2.1. Body of Report

- Compliance Statement
- Quality Assurance Statement
- Abstract

- Introduction
- Experimental Design
- Materials and Methods
- Results and Discussion
- Conclusion and No-Observed-Effect-Level (NOEL) or No-Observed-Adverse-Effect-Level (NOAEL) Statement
- Statistical Procedures
- Protocol Deviations and Study Impact Statements

12.2.2. Summary Tables

- Mortality data
- Pregnancy data
- Summary of maternal clinical observation
- Maternal body weight and weight change data during gestation
- Maternal feed consumption data
- Mean number of corpora lutea, implantation sites, resorptions and fetuses
- Summary of maternal macroscopic postmortem examination data
- Pre-implantation loss
- Post-implantation loss
- Mean fetal weight
- Total number of male and female fetuses per group and mean percent male/percent female per group
- Incidence of litters and fetuses with observations (external, visceral and skeletal)

12.2.3. Appendix Tables (Individual data)

- Individual animal termination history
- Individual clinical observations
- Individual maternal body weight data and weight change data
- Individual maternal feed consumption data
- Individual uterine implantation data and corpora lutea data
- Maternal macroscopic postmortem observations
- Individual fetal observations (external, visceral and skeletal)

12.2.4. Appendices

- Personnel involved in the study
- Protocol and Amendment(s)

13. REGULATORY REFERENCES

13.1. TEST GUIDELINES

This study complies with the Organization for Economic Cooperation and Development (22 January 2001). OECD Guidelines for Testing of Chemicals; OECD Guideline 414: Prenatal Developmental Toxicity Study and US EPA OPPTS Health Effects Test Guidelines 870.3700, Prenatal Developmental Toxicity Study EPA 712-C-98-207, August 1998.

13.2. GOOD LABORATORY PRACTICES

This study will be conducted in compliance with Organization for Economic Cooperation and Development (OECD) Good Laboratory Practices as set forth in ENV/MC/CHEM(98)17 and EPA Good Laboratory Practices as set forth in 40 CFR Part 792 (TSCA).

13.3. ANIMAL WELFARE ACT COMPLIANCE

This study will comply with all appropriate parts of the Animal Welfare Act regulations: 9 CFR Parts 1 and 2 Final Rules, Federal Register, Volume 54, No. 168, August 31, 1989, pp. 36112-36163 effective October 30, 1989 and 9 CFR Part 3 Animal Welfare Standards; Final Rule, Federal Register, Volume 56, No. 32, February 15, 1991, pp. 6426-6505 effective March 18, 1991. The Sponsor should make particular note of the following:

1. The Sponsor's signature on this protocol documents for the study described, there are no generally accepted non-animal alternatives and the study does not unnecessarily duplicate previous experiments.

2. All procedures used in this study have been designed to avoid discomfort, distress and pain to the animals. All methods are described in this study protocol or in written laboratory standard operating procedures.

3. Any procedures outlined in this study protocol which are expected to cause more than momentary or slight pain or distress to the animals will be performed with appropriate sedatives, analgesics or anaesthetics unless the withholding of these agents is justified for scientific reasons, in writing, by the Sponsor and the Study Director and approved by the IACUC; in which case the procedure will continue for the minimum time necessary. Documentation of the justification for withholding treatment for pain or distress and IACUC

approval of the procedures will be made prior to study initiation on the IACUC Protocol Review form.

4. Animals experiencing more than momentary or slight pain or distress due to the test substance, injury or illness may be treated by the Testing Facility's veterinary staff with approved analgesics or agents to relieve pain after consultation with the Study Director/Sponsor. However, in emergency situations, the veterinary staff is authorized to administer emergency treatment as necessary. Any subsequent treatment or euthanasia will be administered after consultation with the Study Director. The Sponsor will be advised by the Study Director of all emergency situations in as timely a manner as possible.

5. Methods of euthanasia used during this study are in conformance with the above referenced regulations.

13.4. INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC)

The IACUC Protocol Review subcommittee has reviewed this protocol and found it to be in compliance with all appropriate animal welfare regulations.

14. QUALITY ASSURANCE MONITORING

The Quality Assurance Unit of Huntingdon Life Sciences (East Millstone, NJ) will monitor the facilities, equipment, personnel, methods, practices, records, protocols, study conduct, raw data, draft and final reports and controls used/produced at the Testing Facility in this study, to assure that they are in conformance with this protocol, company Standard Operating Procedures, and the appropriate Good Laboratory Practice regulations.

15. ALTERATION OF PROTOCOL

Alterations to this protocol may be made as the study progresses. All protocol amendments will be signed by the Study Director and a Sponsor representative. Any amendments potentially affecting animal welfare will also be signed by two members of the Institutional Animal Care and Use Committee prior to implementation of the amendment.

Protocol Amendment No. 1

Study Title: Chlorotrifluoroethylene: Embyro-Fetal Toxicity Study in Rats by Inhalation Exposure

Changes

1. Macroscopic Postmortem Examination, page 12:
Add: **Females that do not deliver pups will be sacrificed and their uterus' examined for implantation sites and resorptions, including confirmation of apparent non-pregnant status by means of staining with ammonium sulphide (modified Salewski test).**

2. Fetal Soft Tissue Evaluations, page 13:
Revise: Approximately one-half of the fetuses in each litter (alternating fetuses within the litter, nominally) will be placed in **suitable aldehyde (such as Modified Davidson's)** ~~Bouin's~~ fixative for preservation and decalcification.....

3. Fetal Skeletal Evaluations, page 13:
Revise: Approximately one-half of the fetuses in each litter (alternating fetuses within the litter, nominally) **will have the sex internally evaluated and then** will be eviscerated and processed for staining of the skeleton using Alizarin Red S....

Reasons for Changes

1. Clarification of procedure for any non-pregnant test animals.
2. Clarification of procedure for fetal processing.
3. Clarification of procedure for fetal processing.

Additional Cost Required: No

Amendment approved by:

Gary M. Hoffman, B.A., DABT
Study Director

30 Aug 04
Date

George M. Rusch, Ph.D., DABT
Sponsor Representative

27 Aug. 2004
Date

Post-it® Fax Note 7671	Date 8/27/04	# of pages ▶ 1
To Gary Hoffman	From George M Rusch	
Co./Dept. HLS	Co. Honeywell	
Phone # 732-873-2550	Phone # 973-455-3672	
Fax # 732-873 3992	Fax #	

Protocol Amendment No. 2

Study Title: Chlorotrifluoroethylene: Embyro-Fetal Toxicity Study in Rats by Inhalation Exposure

Changes

1. Macroscopic Postmortem Examination, page 12:
Add: **The gravid uterine weights will be recorded and statistically analyzed (as per section 11.1) and reported for dams surviving to GD20.**

2. Fetal External Evaluations, page 13:
Revise: All live fetuses will be weighed and individually identified ~~using a tag affixed around the neck~~.....

Reasons for Changes

1. Clarification of procedure for pregnant test animals.
2. Clarification of procedure for fetal processing. Instead of the tags, they will be stored in individually marked cassettes.

Additional Cost Required: No

Amendment approved by:

Gary M. Hoffman, B.A., DABT
Study Director

13 Sept 04
Date

George M. Rusch, Ph.D., DABT
Sponsor Representative

10 Sept 2004
Date

Protocol Amendment No. 3

Study Title: Chlorotrifluoroethylene: Embyro-Fetal Toxicity Study in Rats by Inhalation Exposure

Changes

1. Experimental Design, page 3:
Add: **The Group 4 exposures were terminated on 30 August 2004 during the 7th day of exposures.**

2. Experimental Design, page 3:
Add: **We will conduct a post-study experiment on Monday 20Sept04:**
The Sponsor will provide 3 evacuated 1 liter test cylinders:
Cylinder#1 will be used to collect sample from CTFE cylinder (via a gas bag)
Cylinder#2 will be used to collect sample from CTFE 90 ppm chamber (via a sample port)
Cylinder#3 will be used to collect sample from CTFE 180 ppm chamber (via a sample port)
We will then ship the samples to the Sponsor's chemist.

Reasons for Changes

1. See effects discussed in #2 below.

2.The Sponsor is concerned about the toxic effects (body weight loss and/or decreased weight gain) seen at 90 and 180 ppm during the study. Therefore, he contacted his chemist and was told that ~20 years ago (when range-find work conducted at Sponsor's lab) that CTFE was stabilized to prevent dimer formation. However, they don't routinely stabilize anymore and there may be toxic dimers in the current CTFE test sample. This experiment will allow evaluation if there was undesired dimer formation.

Additional Cost Required: Yes

Amendment approved by:

GaryM. Hoffman, B.A., DABT
Study Director

20 Sept 04
Date

George M. Rusch, Ph.D., DABT
Sponsor Representative

Sept. 20, 2004
Date

Protocol Amendment No. 4

Study Title: Chlorotrifluoroethylene: Embyro-Fetal Toxicity Study in Rats by Inhalation Exposure

Changes

1. Proposed Study Dates, page 2:
Revise: Experimental Termination: **February 2005** ~~10 September 2004~~ (Date of last data collection = **date fetal pathology evaluations completed**)

2. Experimental Design, page 3:
Revise: The first day of **gestation** ~~exposures~~ will be defined as Day 0 of the study.

Reasons for Changes

1. Clarification of study dates per GLPs.
2. Clarification of study scheduling.

Additional Cost Required: No

Amendment approved by:

Gary M. Hoffman, B.A., DABT
Study Director

15 March 05
Date

George M. Rusch, Ph.D., DABT
Sponsor Representative

March 14, 2005
Date

Protocol Amendment No. 5

Study Title: Chlorotrifluoroethylene: Embyro-Fetal Toxicity Study in Rats by Inhalation Exposure

Changes

1. Experimental Design, page 3:
Add: **A post-study range-find study will be conducted as follows:**

Group	Exposure Levels (ppm)	Sample Description	Treatment Gestation Days	Time-Mated Females	Euthanized Gestation Day 20	Gross Fetal Evaluations (Fetuses/Litter)
1	0	Air Control	6-10	5	All	All
2	180	CTFE (no dimers)	6-10	5	All	All
3	180	CTFE (0.1% dimers)*	6-10	5	All	All
4	180	CTFE (0.5% dimers)	6-10	5	All	All
5	180	CTFE (2.0% dimers)	6-10	5	All	All

***original Main Study sample received 3June04.**

All procedures will be as per original protocol for the Main Study except exposures will be conducted only for Gestation Days 6-10, exposures will be conducted in 100 liter chambers (at approximately 20 LPM) and only gross examinations of dams and pups will be conducted.

Proposed Study Schedule:
Day 0: 2 February 2005 (25 rats + extras)
Receive time-mated rats: 3 or 4 February 2005
Sort: 7 February 2005
Exposures: 8-12 February 2005
C-sections: 22 February 2005 (25 rats)
Draft report: 8 April 2005

All samples will be returned to the Sponsor's analytical lab (attn: John Welch, Honeywell, Buffalo, NY, 1-716-827-6245) upon study completion for post-study assay that will be amended to our report.

Reasons for Changes

The Sponsor was concerned about the toxic effects (body weight loss and/or decreased weight gain) seen at 90 and 180 ppm during the Main Study during the initial 5 days of exposures (GD 6-10). Therefore, a post-study (non-animal) experiment (see Amendment #3) was conducted to evaluate if there was undesired dimer formation in the Test Substance and the GC analysis did indicate these were present. These dimers are not normally present in the CTFE as produced and sold and toxicity of this magnitude would not have been predicted based upon a pilot developmental toxicity study conducted with CTFE that did not contain appreciable levels of dimers. The Sponsor therefore wants to evaluate

Protocol Amendment No. 5

further (with time-mated animals) the comparable effects of the Test Substance with no dimers (Group 2), as originally tested (Group 3), with more (0.5%) dimers (Group 4) and with more (2.0%) dimers (Group 5).

This comparative study should allow a conclusion if the presence of the dimers adversely affected the results of the Main Study and if the Main Study should be further tested with a dimer-free Test Substance. The number of test animals per group is considered the minimum to statistically evaluate the anticipated treatment effects of body weight loss and/or decreased weight gain. The number of test groups is considered the minimum to adequately evaluate the effect of the absence and/or presence (at 3 levels of concentration) of the suspect dimers.

Additional Cost Required: Yes

Amendment approved by:

HLS IACUC	12 Jan 05 Date
HLS IACUC	12 JAN 05 Date
Gary M. Hoffman, B.A., DABT Study Director	12 Jan 05 Date
George M. Rusch, Ph.D., DABT Sponsor Representative	JAN 6, 2005 Date

	Testing Facility Personnel	Appendix S

TITLE/DEPARTMENT	NAME/DEGREE
SENIOR VICE PRESIDENT, SAFETY ASSESSMENT	Sylvie J. Gosselin, D.V.M., Ph.D., Diplomate A.C.V.P.
DIRECTOR, REPRODUCTIVE AND DEVELOPMENTAL TOXICOLOGY	Keith P. Hazelden, B.Sc., M.I.Biol.
DIRECTOR, ANALYTICAL SERVICES	Barbara A. Litzenberger, B.S., M.T. (ASCP)
DIRECTOR, TOXICOLOGY OPERATIONS	Ian Vanterpool, F.I.A.T.
DIRECTOR, QUALITY ASSURANCE	Nicki S. Iacono, B.S.
STUDY DIRECTOR	Gary M. Hoffman, B.A., D.A.B.T.
STUDY MONITOR	Janet E. Scimone, B.A.
VETERINARIAN	Teresa S. Kusznir, V.M.D.
MANAGER/SUPERVISOR	
Rodent and Reproductive Toxicology	Sally Wilcox, B.Sc.
Inhalation Toxicology	Stuart Cracknell, CBiol, MIBiol.
Pharmacy	Michael S. McCarthy
Necropsy and Fetal Pathology	G. Elizabeth Baxter, B.S.

	Report Amendments	Appendix T

There are no amendments for this report at this time.