

ORIGINAL

TSCA NON-CONFIDENTIAL BUSINESS INFORMATION

DOCUMENT DESCRIPTION	DOCUMENT CONTROL NUMBER	DATE RECEIVED
8EHQ-13-18967	88130000125	1/17/13

COMMENTS:

DOES NOT CONTAIN CBI

2013 JAN 17 AM 11:01



January 16, 2013

TSCA Confidential Business Information Center (7407M)
EPA East - Room 6428 Attn: Section 8(e)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460-0001



RE: 2-Bromo-3,3,3-Trifluoropropene [CAS: 1514-82-5], Reproductive Toxicity Screening Study

Dear Madam or Sir:

The following preliminary information on results from a one-generation reproductive screening study performed at Huntingdon Research Centre is being submitted on 2-bromo-3,3,3-trifluoropropene (CAS: 1514-82-5, 99% pure with stabilizers). A whole-body inhalation tests was performed in CRL:CD (SD) rats. Three groups of ten male and ten female adult rats received nominal concentrations of 200, 500, or 3000 ppm for 6 hours per day, 7 days per week. A control group receiving only air underwent the same study procedures. Exposures occurred for 15 days prior to pairing, through pairing, and then up until Day 10 after the birth of the offspring. The offspring did not receive direct exposure, only *in utero* and possibly through lactation. Clinical conditions, body weight, food consumption, macroscopic findings, microscopic pathology, and fertility parameters were examined in all groups.

Dose-related clinical signs during exposure were underactivity, unresponsiveness, piloerection and partially closed eyelids; these clinical signs were reversible. Treated animals had lower bodyweight gain and lower food intake compared to controls. There was a dose-related lengthening of the estrous cycles, pre-coital intervals, and gestation periods. At the highest dose, more females showed irregular cycles or being acyclic and there was reduced fertility, smaller size of the corpora lutea, lower post-implantation survival rate, live birth index, and live litter size, with only one female littering and the offspring subsequently dying. In the 500 ppm treated group, there was a lower post implantation survival, live birth index, and live litter size, with only half of the litters surviving to Day 10 of lactation. At the

CONTAINS NO CBI**Halotron Division**

3883 Howard Hughes Parkway, Suite 700 • Las Vegas, Nevada 89169

Tel: +1 (702) 735-2200 • Fax: +1 (702) 735-4876

www.halotron.com

lowest dose, there was a slightly lower implantation rate with two out of 10 litters experiencing lower litter size and viability. There were no treatment-related effects on the offspring that survived to Day 10 of lactation, nor were there any gross physical abnormalities in any of offspring.

Dose-dependent effects on sperm analysis included reduced sperm velocity (but not motility), reduced sperm count (highest dose only), and irregular sperm morphology (did not affect sperm vigor). Macroscopic examination of male reproductive organs indicated reduced prostate, epididymides, seminal vesicle and pituitary weights.

In the majority of males and some females, spleen capsular thickening and adhesions noted macroscopically and confirmed microscopically as capsular/subcapsular inflammation/capsular thickening and /or adhesions/inflammation/fibrosis. Adult animals experienced pale teeth at the upper two dose levels.

The draft version of reproductive toxicity screening study is attached, and the final report will be submitted to the EPA.

This chemical is being evaluated for potential use as a Halon alternative and toxicological testing is underway to characterize its possible health effects. The chemical has not yet been submitted for TSCA listing.

Sincerely,



Bradford Colton

Research Engineer

REPORT

**2-bromo-3,3,3-trifluoropropene: Reproductive/Developmental
Toxicity Screening Study in the CD Rat by Inhalation
Administration**

HLS study number:	WAG0015
Version ID:	Audited Draft 1 Report
Issue date:	18 December 2012

Details of Sponsor and Test Facilities

Sponsor American Pacific Corporation
3883 Howard Hughes Parkway
Suite 700
Las Vegas
Nevada 89169
USA

**Test facility
Primary location** Huntingdon Life Sciences
Huntingdon Research Centre
Woolley Road
Alconbury
Huntingdon
Cambridgeshire
PE28 4HS
UK

**Test facility
Oestrous cycles,
Sperm analysis
Histology,
Histopathology** Huntingdon Life Sciences
Eye Research Centre
Eye
Suffolk
IP23 7PX
UK

Table of Contents

Details of Sponsor and Test Facilities	2
Compliance with Good Laboratory Practice	8
Quality Assurance Statement.....	9
Contributing Scientists	10
Summary	11
1. Introduction	13
1.1 Objective.....	13
1.2 Regulatory compliance	13
1.3 Test system	13
1.4 Route of administration.....	13
1.5 Treatment groups and doses	13
2. Experimental Procedure.....	14
2.1 Study schedule and structure.....	14
2.1.1 Duration of treatment.....	14
2.1.2 Time schedule.....	14
2.1.3 Study design	14
2.1.4 Identity of treatment groups.....	15
2.2 Test substance and formulation	15
2.2.1 Test substance.....	15
2.2.2 Control	16
2.3 Animal management.....	16
2.3.1 Animal supply, acclimatisation and allocation.....	16
2.3.2 Animal housing, diet and water supply	16
2.3.3 Administration	18
2.4 Serial observations	18
2.4.1 Clinical observations	18
2.4.2 Mortality	19
2.4.3 Bodyweight	19
2.4.4 Food consumption.....	19
2.4.5 Water consumption	19
2.4.6 Oestrous cycles.....	19
2.4.7 Mating procedure	19
2.4.8 Parturition observations and gestation length.....	20
2.4.9 Records made during littering phase	20
2.5 Necropsy and histology.....	20
2.5.1 Time of necropsy.....	20
2.5.2 Method of kill	21
2.5.3 Macroscopic pathology.....	21
2.5.4 Sperm analysis.....	21
2.5.5 Organ weights	23
2.5.6 Fixation	24
2.5.7 Histology	24
2.6 Pathology.....	25
2.6.1 Light microscopy	25
2.7 Computer systems.....	25
2.8 Data treatment.....	26
2.8.1 Signs.....	27

2.8.2	Bodyweights.....	27
2.8.3	Food consumption.....	27
2.8.4	Water consumption.....	27
2.8.5	Oestrous cycles.....	28
2.8.6	Pre-coital interval.....	28
2.8.7	Mating performance and fertility.....	28
2.8.8	Gestation length.....	28
2.8.9	Litter size.....	28
2.8.10	Survival indices.....	29
2.8.11	Sex ratio.....	29
2.8.12	Sperm analysis.....	29
2.8.13	Organ weights.....	29
2.8.14	Pathology.....	30
2.8.15	Statistical analysis.....	30
2.9	Quality assurance and archiving procedures.....	32
2.9.1	Quality assurance.....	32
2.9.2	Archives.....	32
2.10	Deviations from protocol.....	33
3.	Results.....	34
3.1	Chamber atmosphere conditions.....	34
3.2	F0 maternal responses.....	34
3.2.1	Mortality and animal fates.....	34
3.2.2	Signs.....	34
3.2.3	Bodyweight.....	35
3.2.4	Food consumption.....	36
3.2.5	Water consumption.....	36
3.2.6	Oestrous cycle length.....	36
3.2.7	Pre-coital interval, mating performance and fertility.....	37
3.2.8	Gestation length and gestation index.....	38
3.2.9	Sperm analysis.....	38
3.2.10	Organ weights.....	39
3.2.11	Macropathology.....	39
3.2.12	Animals killed after scheduled treatment period.....	39
3.2.13	Histopathology.....	40
3.2.14	Animals killed after scheduled treatment period.....	40
3.2.15	Primordial ovarian follicle counts.....	42
3.3	F1 litter responses.....	42
3.3.1	Signs of offspring.....	42
3.3.2	Litter size, survival indices and sex ratio.....	42
3.3.3	Bodyweight.....	43
3.3.4	Offspring macropathology.....	43
4.	Discussion.....	44
5.	Conclusion.....	47
6.	References.....	48
6.1	Necropsy and histology.....	48
6.2	Statistics.....	48

List of Figures

Figure 1	Bodyweight - group mean values for males.....	50
Figure 2	Bodyweight - group mean values for females before pairing	51
Figure 3	Bodyweight - group mean values for females during gestation.....	52
Figure 4	Bodyweight - group mean values for females during lactation.....	53
Figure 5	Bodyweight - group mean values for offspring	54

List of Tables

Table 1	Summary of adult performance	56
Table 2	Clinical signs - group distribution of observations.....	57
Table 3	Signs associated with dosing - group distribution of observations	62
Table 4	Bodyweight and bodyweight change - group mean values for males	77
Table 5	Bodyweight and bodyweight change - group mean values for females before pairing.....	79
Table 6	Bodyweight and bodyweight change - group mean values for females during gestation.....	81
Table 7	Bodyweight and bodyweight change - group mean values for females during lactation	83
Table 8	Food consumption - group mean values before pairing.....	84
Table 9	Food consumption - group mean values for females during gestation.....	86
Table 10	Food consumption - group mean values for females during lactation.....	87
Table 11	Water consumption - group mean values for males and before pairing for females.....	88
Table 12	Water consumption - group mean values for females during gestation	90
Table 13	Water consumption - group mean values for females during lactation.....	92
Table 14	Oestrous cycles - group values	93
Table 15	Pre-coital interval - group values.....	95
Table 16	Number of copulation plugs at mating - group values.....	96
Table 17	Sperm count estimates from vaginal smears at mating - group values.....	97
Table 18	Mating performance and fertility - group values.....	98
Table 19	Gestation length and gestation index - group values.....	99
Table 20	Litter size - group mean values	100
Table 21	Offspring survival indices - group mean values	101
Table 22	Sex ratio - group mean values	102
Table 23	Bodyweight and bodyweight change - group mean values for male offspring	103

Table 24	Bodyweight and bodyweight change - group mean values for female offspring	104
Table 25	Sperm analysis - group mean values	105
Table 26	Sperm motion data - group mean values	106
Table 27	Sperm morphology - group mean values	107
Table 28	Organ weights - group mean unadjusted and adjusted values for males....	108
Table 29	Macropathology - group distribution of findings	109
Table 30	Histopathology - group distribution of findings.....	115
Table 31	Primordial ovarian follicle counts - group mean values.....	119

List of Appendices

Appendix 1	Clinical signs - individual observations for males.....	120
Appendix 2	Clinical signs - individual observations for females	123
Appendix 3	Signs associated with dosing - individual observations for males and females	134
Appendix 4	Signs associated with dosing - individual observations for females prior to mating, during gestation and lactation.....	194
Appendix 5	Bodyweight - Individual values for males	235
Appendix 6	Bodyweight - individual values for females before pairing	239
Appendix 7	Bodyweight - individual values for females after mating.....	242
Appendix 8	Bodyweight - individual values for females during lactation.....	244
Appendix 9	Food consumption - individual values for males and before pairing for females.....	246
Appendix 10	Food consumption - individual values for females after mating.....	248
Appendix 11	Food consumption - individual values for females during lactation	250
Appendix 12	Water consumption - individual values for males and before pairing for females	252
Appendix 13	Water consumption - individual values for females after mating	256
Appendix 14	Water consumption - individual values for females during lactation.....	260
Appendix 15	Oestrous cycle length, mating performance, fertility and gestation length - individual values	262
Appendix 16	Litter size - individual values	266
Appendix 17	Offspring survival indices - individual values	270
Appendix 18	Sex ratio - individual values	274
Appendix 19	Bodyweight - individual litter mean values for offspring	278
Appendix 20	Clinical signs - individual findings for offspring	285
Appendix 21	Macropathology - individual findings for offspring dying or killed before scheduled termination	289

Appendix 22	Macropathology - individual findings for offspring killed at scheduled termination	291
Appendix 23	Sperm analysis - individual values.....	292
Appendix 24	Sperm motion data - individual values	296
Appendix 25	Sperm morphology - individual values	300
Appendix 26	Organ weights - individual absolute values for males.....	304
Appendix 27	Macropathology and histopathology - individual findings.....	306
Appendix 28	Primordial ovarian follicle counts.....	386

List of Annexes

Annex 1	Certificate of analysis.....	394
Annex 2	Aerosol technology and inhalation analysis report.....	396
Annex 3	Pathology report.....	415
Annex 4	GLP compliance statements	425

Compliance with Good Laboratory Practice

2-bromo-3,3,3-trifluoropropene: Reproductive/Developmental Toxicity Screening Study in the CD Rat by Inhalation Administration

The study described in this report was conducted in compliance with the following Good Laboratory Practice standards and I consider the data generated to be valid.

The UK Good Laboratory Practice Regulations (Statutory Instrument 1999 No. 3106, as amended by Statutory Instrument 2004 No. 994).

OECD Principles of Good Laboratory Practice (as revised in 1997), ENV/MC/CHEM (98) 17.

EC Commission Directive 2004/10/EC of 11 February 2004 (Official Journal No L 50/44).

These principles of Good Laboratory Practice regulations are accepted by the regulatory authorities of the United States of America and Japan on the basis of intergovernmental agreements.

Amanda J Brooker BSc (Hons) MSc CBiol MSB
Study Director
Huntingdon Life Sciences

Date

Quality Assurance Statement

2-bromo-3,3,3-trifluoropropene: Reproductive/Developmental Toxicity Screening Study in the CD Rat by Inhalation Administration

The following inspections and audits have been carried out in relation to this study:

Study Phase	Date(s) of Inspection	Date of Reporting to Study Director and Management
Protocol Audit	03 Jul 2012	03 Jul 2012
Study set up	17 Jul 2012	17 Jul 2012
Protocol Amendment No.1	20 Jul 2012	20 Jul 2012
Protocol Amendment No.2	31 Jul 2012	02 Aug 2012
Study Management and Conduct	02 Aug 2012	03 Aug 2012
Pre-terminal	03 Sep 2012	04 Sep 2012
Protocol Amendment No.3 & 4	07 Sep 2012	07 Sep 2012
Protocol Amendment No.5	26 Oct 2012	26 Oct 2012
Protocol Amendment No.6	31 Oct 2012	31 Oct 2012
Report Audit	10 Oct 2012 - 12 Oct 12	12 Oct 2012
	05 Dec 2012-11 Dec 2012	11 Dec 2012

In addition, process based inspections were conducted of other routine and repetitive procedures employed on this type of study at or about the time this study was in progress. Similarly an inspection of the facility where this study was conducted was carried out on an annual basis. These inspections were reported to Company Management.

Dilys Smith MRQA
Lead Auditor
Department of Quality Assurance
Huntingdon Life Sciences

Date

Contributing Scientists

2-bromo-3,3,3-trifluoropropene: Reproductive/Developmental Toxicity Screening Study in the CD Rat by Inhalation Administration

Study management

Amanda J Brooker BSc (Hons) MSc CBiol MSB
Study Director

David P Myers BSc (Hons) PhD IDT
Senior Toxicologist

Steven J Crome BSc MSc
Head of Toxicologists (inhalation aspects)

Formulation analysis

Caroline Finucane PhD
Head of Formulation & Inhalation Analysis

Aerosol technology

Simon A Moore BSc (Hons) PhD MRSC
Head of Aerosol Technology

Oestrous cycles and mating performance

Martin J Collier BSc
Behavioural Scientist

Sperm analysis

Clare Bowden BSc (Hons) CBiol MSB
Operational Head, Sperm Analysis & Embryo Culture

Pathology

Miledi Azzalin DVM MRCVS
Pathologist
Department of Pathology

Statistics

Gareth D Thomas BSc (Hons)
Head of Statistics and Data Management

Summary

The objective of this study was an initial screening assessment of the influence of 2-bromo-3,3,3-trifluoropropene (a fire extinguisher agent), on reproductive performance and development in CrI:CD (SD) rats following inhalation administration. Three groups of ten male and ten female rats received 2-bromo-3,3,3-trifluoropropene by inhalation at target exposure levels of 200, 500 or 3000 ppm. The adults were treated daily for a minimum of 15 days before pairing until Day 10 after the birth of the F1 generation. Females were untreated from Day 20 after mating until Day 4 after birth inclusive. A similarly constituted Control group received air only for the same duration.

The F1 generation received no direct administration of the test substance; any exposure was in utero or via the milk.

During the study, clinical condition, bodyweight, food consumption, macroscopic and microscopic pathology investigations were undertaken in all adults. Oestrous cycles and gestation length were assessed and parturition observations were performed for F0 females. Organ weights were recorded for F0 males only. The clinical condition, litter size and survival, sex ratio and bodyweight of all offspring were assessed.

Results

The achieved chamber concentrations of 2 bromo-3,3,3-trifluoropropene were 198, 505 and 2900 ppm (99, 101 and 97% of the target concentration) for Groups 2, 3 and 4 respectively.

At 2900 ppm, treatment related findings included clinical signs during exposure of underactivity, unresponsiveness, piloerection and partially closed eyelids, occasionally in females these lasted after completion of exposure, and included hunched posture, but not at the end of the day; pale teeth in all males and the majority of females and slightly higher incidence of hairloss in males (confirmed at macroscopic examination); lower bodyweight gain of males throughout and females prior to pairing and during gestation; lower food intake; increased water intake for females; longer oestrous cycles (6 days or longer) with more females showing irregular cycles or being acyclic; reduced fertility (6/10 paired females were pregnant); longer pre-coital interval; at mating, fewer copulation plugs and lower estimates of sperm in the vaginal smear; extended duration of gestation with only 1 female littering on Day 25 of gestation and 2 females being sacrificed on Day 24 of gestation); lower implantation counts, with only one female littering and the offspring subsequently dying; effects on sperm analysis (reduced percentage progressively motile sperm, sperm velocity, increased BCF, reduced sperm count in the cauda epididymis, increase in abnormal sperm – breakages and abnormal head shape); reduced prostate, epididymides, seminal vesicle and pituitary weights; small prostate macroscopically in all males; in the majority of males and some females, spleen capsular thickening and adhesions noted macroscopically and confirmed microscopically as capsular/subcapsular inflammation/capsular thickening and /or adhesions/inflammation/fibrosis and reduced size of corpora lutea in the ovaries.

At 505 ppm, treatment related findings included clinical signs during exposure of underactivity and piloerection and occasionally unresponsiveness and partially closed eyelids, occasionally in females some of these lasted after completion of exposure but not at the end of the day; pale teeth in some males and females in the last week of treatment; lower

bodyweight gain of males throughout and slightly lower bodyweight gain of females during gestation; slight bodyweight loss for females in lactation; lower food intake; increased water intake for females prior to pairing and during gestation, with lower water intake during lactation; longer oestrous cycles (6 days or longer) in 5/10 females with more females showing irregular cycles or being acyclic; slightly longer pre-coital interval; at mating, fewer copulation plugs and lower estimates of sperm in the vaginal smear; extended duration of gestation (23-25 days); slightly lower implantation counts; lower post implantation survival, live birth index and live litter size on Day 1; clinical signs in offspring of cold to touch, unfed and reduced activity necessitating sacrifice along with an increased incidence of dead offspring resulting in only 4/9 litters surviving to Day 10 post partum; effects on sperm analysis (reduced sperm velocity, increase in abnormal sperm – breakages and abnormal head shape); reduced prostate, epididymides, seminal vesicle and pituitary weights; small prostate macroscopically in the majority of males; and spleen capsular thickening and adhesions noted macroscopically in the majority of males and occasional females and confirmed microscopically as capsular/subcapsular inflammation/capsular thickening and /or adhesions/inflammation/fibrosis.

At 198 ppm, slight effects on clinical signs during exposure, bodyweight, food and water intake were considered not adverse. Of uncertain significance was a slightly lower sperm count noted in the vaginal smear on the day of mating, but not statistically significantly affected at termination, and a shift to a 23 day duration of gestation, and an increase in abnormal sperm. The mean number of implantations was slightly lower than the Controls. Three out of 9 litters showed lower than expected post implantation survival of the conceptuses (63-74%) and two litters showed lower than expected pup viability indices (54 and 82%), and these differences contributed to lower total and live litter sizes than the Controls. Although only a few litters were involved, the reduction in total and live litter size on Day 1 of lactation formed part of a dose related trend and thus a relationship to treatment was considered likely.

Conclusion

Exposure of 2-bromo-3,3,3-trifluoropropene to rats in this screening study to assess the influence on reproductive performance and development following administration by inhalation at concentrations of 198, 505 or 2900 ppm was associated with adverse effects on male and female toxicity, and reproductive performance and development at 505 and 2900 ppm.

Exposure at 505 and 2900 ppm produced effects on oestrous cycles, fertility (2900 ppm only), extended duration of gestation, sperm counts and motility, implantation counts, reduced in utero and post partum survival, in the presence of signs of adult toxicity. In addition, at 2900 ppm, reduced size of corpora lutea in the ovaries was noted.

Exposure at 198 ppm was associated with slight effects on adult toxicity, but did have slight effects on reproductive performance (a possible shift to longer duration of gestation) and development (slightly lower implantation rate, higher post implantation survival and viability indices leading to lower litter size) as seen at 505 ppm and above.

Within this screening study, the no adverse effect level (NOAEL) for reproductive performance and development was considered to lie below 198 ppm.

1. Introduction

1.1 Objective

The objective of this study was an initial screening assessment of the influence of 2-bromo-3,3,3-trifluoropropene, a fire extinguisher agent, on reproductive performance and development following administration by inhalation for a minimum of 15 days before pairing until Day 10 after the birth of the F1 generation.

1.2 Regulatory compliance

The study was designed to meet the requirements of the following guidelines:

Organisation for Economic Co-operation and Development: Testing of Chemicals (Guideline 421; Reproduction/Developmental Toxicity Screening Test; 27 July 1994).

The study was conducted in accordance with the requirements of current, internationally recognised Good Laboratory Practice Standards, and the applicable sections of the United Kingdom Animals (Scientific Procedures) Act 1986.

1.3 Test system

The rat was chosen as the test species because of the requirement for a rodent species by regulatory agencies. The CrI:CD (SD) strain was used because of the historical control data available at this laboratory.

1.4 Route of administration

The inhalation route of administration was chosen to simulate the conditions of potential human exposure.

1.5 Treatment groups and doses

The exposure levels were based on results of 2 week dose range finding studies in rats performed in these laboratories (Huntingdon Life Sciences Report Numbers WAG0013 and WAG0024 respectively). In those studies, clinical signs were noted during exposure at target exposure levels of 500 ppm to 20000 ppm, with excessive body weight effects at 10000 ppm and above. Respiratory tract pathology was noted at target exposure levels of 1200 ppm and above.

It was considered suitable for the target exposure levels of this reproductive study to replicate that of the 90 day rat study (Huntingdon Life Sciences Report Number WAG0014). The high exposure concentration, 3000 ppm, was selected to allow assessment of reproductive effects at an exposure concentration anticipated to produce evidence of systemic toxicity. Lower exposure concentrations were chosen to allow assessment of any effects observed.

2. Experimental Procedure

2.1 Study schedule and structure

2.1.1 Duration of treatment

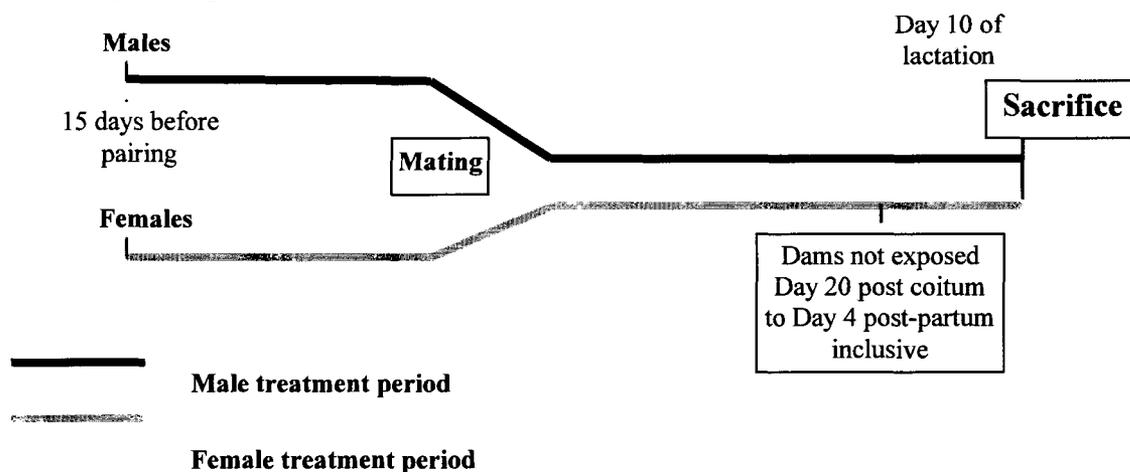
The test substance, 2-bromo-3,3,3-trifluoropropene, was administered to F0 adults for a minimum of 15 days before pairing until Day 9 after the birth of the F1 generation. The F0 female adults were killed on Day 10 after the birth of the F1 generation and the F1 males killed after the start of the F0 female kills. F0 females were untreated from Day 20 after mating to Day 4 after birth.

Animals of the F1 generation were not dosed, but may have been exposed to the test substance or metabolites in utero or through the milk.

2.1.2 Time schedule

Study initiation: (Protocol signed by Study Director)	09 July 2012
Experimental start date: (Animal arrival)	12 July 2012
Treatment commenced:	19 July 2012
Pairing commenced:	02 August 2012
Necropsy completed:	
F0 Males	07 September 2012
F0 Females and F1 animals	13 September 2012
Experimental completion date: (Pathology)	13 November 2012
Study completion:	When the Study Director signs the final report

2.1.3 Study design



2.1.4 Identity of treatment groups

The study consisted of one Control and three treated groups of rats, identified as follows:

Group	Treatment	Target exposure level (ppm)	Number of animals		Animal numbers	
			Male	Female	Male	Female
1	Control	0	10	10	201-210	241-250
2	2-bromo-3,3,3-trifluoropropene	200	10	10	211-220	251-260
3	2-bromo-3,3,3-trifluoropropene	500	10	10	221-230	261-270
4	2-bromo-3,3,3-trifluoropropene	3000	10	10	231-240	271-280

The F1 generation received no direct administration of the test substance, 2-bromo-3,3,3-trifluoropropene. Any exposure to the test substance or metabolites was through the mother to the offspring in utero and/or through the milk, or from transfer from the mother's fur following exposure from Day 5 after birth.

2.2 Test substance and formulation

2.2.1 Test substance

Information supplied by the Sponsor regarding the test substance is contained in the test substance data sheet, which is retained in study records, and the Certificate of Analysis, which is presented in Annex 1.

The following information is given in summary:

Identification:	2-bromo-3,3,3-trifluoropropene (stabilized)
Action:	Fire extinguisher agent
Description:	Clear liquid with a slight yellow hint
Storage conditions:	At ambient temperature
Supplier:	Sponsor
Batch number:	WNCC-BTP111128
Date of receipt:	02 March 2012
Expiry date:	12 January 2013
Purity:	99.9% excluding stabilisers

The Sponsor was responsible for the characterisation of the test substance and the documentation of the methods of synthesis, fabrication or derivation and stability.

2.2.2 Control

Group 1 (Control) animals were exposed to air only.

2.3 Animal management

2.3.1 Animal supply, acclimatisation and allocation

CrI:CD (SD) rats (a total of 45 males and 45 females) were received from Charles River (UK) Ltd. They were delivered at approximately 49 to 56 days of age and within a weight range of 250 to 300 g for males and 200 to 230 g for females.

On arrival, the animals were removed from the transit boxes and allocated to study cages. Using the sequence of cages in the battery, one animal at a time was placed in each cage with the procedure being repeated until each cage held the appropriate number of animals. Each sex was allocated separately.

The day after arrival a representative sample of animals were weighed and their clinical condition was satisfactory; based on this the animals were deemed acceptable for use on the study. On Day 1 (before dosing) variations in group bodyweights were confirmed to be within $\pm 20\%$ of the mean weight for each sex.

Each adult animal was assigned a number and identified uniquely within the study by a tail tattoo. Each cage label was colour-coded according to group and was numbered uniquely with cage and study number, as well as the identity of the occupant(s).

The adult animals were allowed to acclimatise to the conditions described below for 7 days before treatment commenced. For those animals selected for this study, their age at the start of treatment was 56 to 63 days and their bodyweights were in the range of 303 to 349 g for males and 204 to 247 g for females.

The offspring were numbered individually within each litter on Day 1 of age, using a toe tattoo.

The spare animals were removed from the study room after treatment commenced.

2.3.2 Animal housing, diet and water supply

Animals were housed inside a restricted access rodent facility (Building Y14, Room 010). The facility was designed and operated to minimise the entry of external biological and chemical agents and to minimise the transference of such agents between rooms. Before the study the room was cleaned and disinfected.

Each animal room was kept at positive pressure with respect to the outside by its own supply of filtered fresh air, which was passed to atmosphere and not re-circulated. The temperature and relative humidity controls were maintained within the range of 19 to 25°C and 40 to 70% respectively. Although conditions were occasionally outside the indicated ranges, these deviations were minor and/or of short duration and were not considered to have influenced

the health of the animals and/or the outcome of the study. Artificial lighting was controlled to give a cycle of 12 hours continuous light and 12 hours continuous dark per 24 hours, with the lights on at 6:00 GMT.

Alarms were activated if there was any failure of the ventilation system, or temperature limits were exceeded. A stand-by electricity supply was available to be automatically bought into operation should the public supply fail.

The animals were housed as shown below:

Study period	Number of animals/cage		Cage material	Cage flooring
	Male	Female		
Pre-pairing	5	5	Polycarbonate	Solid polycarbonate
Pairing	1	1	Polycarbonate	Stainless steel grid
Males after mating	Up to 5	-	Polycarbonate	Solid polycarbonate
Gestation	-	1	Polycarbonate	Solid polycarbonate
Lactation	-	1 (+ litter)	Polycarbonate	Solid polycarbonate

The cages were distributed on the racking to equalise, as far as possible, environmental influences amongst the groups. Wood based bedding was used in cages with solid floors and was sterilised by autoclaving and changed at appropriate intervals each week. The gridded cages were suspended over trays covered with absorbent paper which was changed daily during mating. IMS Nestlets were provided from Day 15 after mating and throughout parturition and lactation. Cages, cage-trays, food hoppers and water bottles were changed at appropriate intervals.

Each animal was provided with an Aspen chew block for environmental enrichment. Chew blocks were provided throughout the study (except during pairing and lactation), and were replaced when necessary. Each cage of animals was provided with a plastic shelter for environmental enrichment (except during pairing, gestation and lactation), which was replaced at the same time as the cages.

The animals were allowed free access to a standard rodent diet (SDS VRF1 Certified diet). This diet contained no added antibiotic or other chemotherapeutic or prophylactic agent.

Potable water taken from the public supply was freely available via polycarbonate or polypropylene bottles fitted with sipper tubes.

Each batch of diet was analysed routinely by the supplier for various nutritional components and chemical and microbiological contaminants. Supplier's analytical certificates were scrutinised and approved before any batch of diet was released for use. The quality of the water supply is governed by regulations published by the Department for Environment, Food and Rural Affairs. Certificates of analysis were received routinely from the water supplier, the bedding supplier and the suppliers of the Aspen chew blocks, IMS Nestlets and plastic shelters. Since the results of these various analyses did not provide evidence of contamination that might have prejudiced the study, they are not presented.

No other specific contaminants that were likely to have been present in the bedding, diet or water were analysed, as none that may have interfered with or prejudiced the outcome of the study was known.

2.3.3 Administration

Treatment was restricted to the F0 generation. Animals of the F1 generation were not treated directly but may have been exposed to the test substance or metabolites in utero or through the milk.

The test substance was administered to rats using whole body exposure systems. Animals in the treated groups were exposed to aerosols generated from 2-bromo-3,3,3-trifluoropropene at target exposure levels of 200, 500 and 3000 ppm. Control animals were exposed to air only, using the same dosing procedure. The relevant treatment was administered once daily for a period of 6-hours, seven days per week. Exposure of pregnant females was not undertaken on and after Day 20 after mating and not reintroduced until Day 4 post partum.

The test atmosphere generation, administration, sampling and analysis and chamber environment, was shared with that of a concurrent 13 week study in rats (WAG0014) with the same test article and target concentrations, on weekdays (Monday to Friday).

Precise details of administration and analysis of the test atmospheres together with the results obtained are presented in Annex 2.

2.4 Serial observations

Dated and signed records of all activities relating to the day by day running and maintenance of the study within the animal unit as well as to the group observations and examinations outlined in this experimental procedure were recorded in the Study Daybook. In addition, observations relating to individual animals made throughout the day were recorded.

2.4.1 Clinical observations

Animals were inspected visually at least twice daily for evidence of ill-health or reaction to treatment. Cages and cage-trays were inspected daily for evidence of ill-health amongst the occupant(s). Any deviation from normal was recorded at the time in respect of nature and severity, date and time of onset, duration and progress of the observed condition, as appropriate.

In addition, a more detailed physical examination was performed once each week on each F0 animal (females only until mating) and for F0 females on Days 0, 7, 14 and 20 after mating and Days 1, 5, and 9 of lactation to monitor general health.

Daily during the first week of treatment, twice weekly during Weeks 2 to 4 and weekly thereafter for all adult animals (females only until mating) and, for females, on Days 0, 7, 14 and 19 after mating and Days 5 and 9 of lactation, detailed observations were recorded at the following times in relation to dose administration:

- Pre exposure observation
- Observations during exposure (limited to animals visible in the exposure chamber), recorded on a cage basis at approximately 2 and 4 hours after start of exposure
- Immediately after dosing on return of the animal to its cage
- As late as possible in the working day

For the observations during exposure, all animals in each group have been given any clinical signs observed as only a few animals could be observed).

2.4.2 Mortality

Debilitated animals were observed carefully and animals were killed for reasons of animal welfare where necessary. A complete necropsy was performed in all cases for animals killed or found dead, as described in the Necropsy section below.

2.4.3 Bodyweight

The weight of each adult was recorded during acclimatisation, on the day that treatment commenced (Week 0), twice weekly thereafter (females only until mating) and before necropsy.

The weight of each F0 female was also recorded on Days 0, 3, 7, 10, 14, 17 and 20 after mating and on Days 1, 5 and 10 of lactation.

2.4.4 Food consumption

The weight of food supplied to each cage, that remaining and an estimate of any spilled was recorded on a weekly basis (from the first day of treatment until pairing). From these records the mean weekly consumption per animal (g/rat/week) was calculated for each cage.

For each F0 female, the weight of food supplied, that remained and an estimate of any spilled was also recorded for the periods Days 0-2, 3-6, 7-9, 10-13, 14-16 and 17-19 after mating and Days 1-4 and 5-9 of lactation. From these records the mean daily consumption (g/rat/day) was calculated for each animal.

2.4.5 Water consumption

Water consumption was recorded by weight (over a 3 day period on each occasion) on a daily basis from Week 2 for each cage of male animals (excluding the pairing period), and in Week 2 for each cage of female animals, using water bottles fitted with sipper tubes.

For each F0 female, water consumption was also recorded daily from Day 0 after mating and from Day 1 of lactation, and has been tabulated for the periods Days 0-2, 3-5, 6-8, 9-11, 12-15, 16-17 and 18-19 after mating and Days 1-3 and 7-9 of lactation.

2.4.6 Oestrous cycles

For 15 days before pairing, daily vaginal smears were taken from all females, using cotton swabs moistened with saline. The smears were subsequently examined to establish the duration and regularity of the oestrus cycle. After pairing with the male, smearing was continued using pipette lavage, until evidence of mating was observed.

2.4.7 Mating procedure

Following a minimum of two weeks of treatment, males and females were paired on a one-to-one basis from within the same treatment group for a period of up to two weeks.

Each morning following pairing, the trays beneath the cages were checked for ejected copulation plugs and a vaginal smear was prepared from each female and examined for the presence of spermatozoa and the stage of the oestrus cycle. The day on which evidence of mating was found was designated Day 0 of gestation. Once mating occurred, the males and females were separated and smearing was discontinued.

The pre-coital interval was calculated for each female as the time elapsing between initial pairing and detection of mating.

2.4.8 Parturition observations and gestation length

From Day 20 after mating, females were inspected three times daily for evidence of parturition. The progress and completion of parturition was monitored, numbers of live and dead offspring were recorded and any difficulties observed were noted.

The duration of gestation was calculated as the time elapsing between the detection of mating and commencement of parturition. Half a day was subtracted in cases where parturition commenced overnight.

Females were sacrificed on Day 25 after mating if parturition was not complete or had not started.

2.4.9 Records made during littering phase

All litters were examined at approximately 24 hours after birth (Day 1 of age) and then daily thereafter. The records maintained were as follows:

Clinical signs: Daily records were maintained for evidence of ill health or reaction to treatment; these were on an individual offspring basis or for the litter as a whole, as appropriate.

Litter size: Daily records were maintained of mortality and consequent changes in litter size from Days 1-10 of age.

Sex ratio: The sex ratio of each litter was recorded on Days 1, 5 and 10 of age.

Bodyweight: Individual offspring bodyweights were recorded on Days 1, 5 and 10 of age.

2.5 Necropsy and histology

2.5.1 Time of necropsy

F0 males were killed after Day 10 of lactation of the majority of females.

F0 females surviving until the end of the scheduled study period were killed on Day 10 of lactation. Females that failed to produce a viable litter were killed on Day 25 after mating. Females whose litter died or was sacrificed before Day 10 of lactation were killed on the day the last offspring died.

Offspring were killed on Day 10 of age, unless they had shown evidence of ill health.

2.5.2 Method of kill

All adult animals were killed by carbon dioxide asphyxiation. Offspring were killed by intraperitoneal injection of sodium pentobarbitone.

The sequence in which the animals were killed after completion of the study was selected to allow satisfactory inter-group comparison.

2.5.3 Macroscopic pathology

All adult animals were subject to a detailed necropsy, which involved the following:

After a review of the history of each animal, a full macroscopic examination of the tissues was performed. All external features and orifices were examined visually. After ventral mid-line incision, the neck and associated tissues and the thoracic, abdominal and pelvic cavities and their viscera were exposed and examined in situ. Any abnormal position, morphology or interaction was recorded. External and cut surfaces of the organs and tissues were examined as appropriate. Any abnormality in the appearance or size of any organ and tissue was recorded and the required tissue samples preserved in appropriate fixative.

The requisite organs were weighed and external and cut surfaces of the organs and tissues were examined as appropriate. Any abnormality in the appearance or size of any organ and tissue was recorded and the required tissue samples preserved in appropriate fixative.

For F0 females, the numbers of implantation sites in each uterine horn was counted. For females failing to produce a viable litter, the number of uterine implantation sites was re-checked after staining with ammonium sulphide (modification of the Salewski staining technique (Salewski, E, 1964)).

Females whose litter died or was sacrificed before Day 10 of lactation were also examined for mammary tissue appearance.

For offspring surviving to scheduled termination, a careful external examination was performed for gross abnormalities and externally normal offspring were discarded without internal examination. Externally abnormal offspring were internally examined and any abnormal tissues were retained in an appropriate fixative.

Additionally the following procedures were applicable:

Premature deaths: Missing offspring and those grossly autolysed or grossly cannibalised could not be examined. All other offspring dying or sacrificed before Day 10 of age were examined as detailed above. The necropsy also included an assessment for the presence of milk in the stomach, where this was possible.

The retained tissues were checked before disposal of the carcass.

2.5.4 Sperm analysis

Immediately after scheduled sacrifice of each F0 generation male, the left vas deferens, epididymis and testis was removed and the epididymis and testis were weighed.

The following tests were performed:

Sperm motility: A sample of sperm was expressed from the vas deferens into pre-warmed (37°C) medium M199, which contained 0.5% w/v bovine serum albumin (BSA Fraction V). A sample for assessment was taken into a 100µm depth cannula by capillary action and where possible at least 200 sperm per animal analysed using the Hamilton Thorne IVOS Computer Assisted Sperm Analyser (CASA) version 12.3d. The percentages of motile and progressively motile sperm and sperm motion parameters were reported.

Sperm morphology: A 200µL aliquot of the sperm/medium mixture (described above) was diluted with 800µL of 10% neutral buffered formalin. After staining with nigrosine and eosin an air-dried smear was prepared and examined by light microscopy for the assessment of sperm morphology. Where possible at least 200 sperm were assessed for each male. The percentages of normal sperm and abnormal sperm and a summary of observations were reported.

Sperm count: The left cauda epididymis of each male was weighed and then frozen. After thawing, 10 mL of a mixture of 0.9% saline, 0.01% merthiolate and 0.05% Triton X-100 (SMT) was added and the cauda epididymis was homogenised for at least one minute. An aliquot of this mixture was added to a pre-prepared IDENT stain tube before being assessed for sperm count using CASA. The concentration (Million/g) and total number of sperm were reported.

Homogenisation-resistant spermatids count: The left testis of each male was frozen. After thawing, each testis was homogenised for at least two minutes in 25 mL of SMT. An aliquot of this mixture was added to a pre-prepared IDENT stain tube before being assessed for homogenisation-resistant spermatid count using CASA. The concentration (Million/g) and total number of spermatids were reported.

The codes in the tables and appendices have the following meaning:

% Motile - the percentage of cells which are moving at or above the minimum speed as defined in the set up parameters.

% Progressively motile - the percentage of cells moving with both VAP > progressive minimum VAP and STR > S0. (progressive minimum VAP is a delimiter used in determining whether a motile cell is labelled as rapid or medium. So is the threshold straightness.)

VAP - the average path velocity, this is the average velocity of the smoothed cell path.

VSL - the progressive or straight line velocity, this is the average velocity measured in a straight line from the beginning to the end of the track.

VCL - the curvilinear velocity or track speed, this is the average velocity measured over the actual point to point track followed by the cell.

ALH - amplitude of lateral head displacement, this is the mean over all cell tracks of twice the maximum displacement between each sperm track and its average path. This corresponds to the average of the sperm track width.

BCF - beat cross frequency, this is the frequency with which the sperm head crosses the sperm average path.

STR - straightness, the average value of the ratio VSL/VAP which measures the departure of the cell path from a straight line.

LIN -linearity, the average value of the ratio VSL/VCL which measures the departure of the cell track from a straight line.

Elongation - the average value of the ratio of minor to major axis of all sperm heads.

Area - the average size of all sperm heads.

Rapid - the fraction of cells moving with $VAP >$ progressive minimum VAP.

Medium - the fraction of cells moving with slow VAP cut-off $< VAP <$ progressive minimum VAP.

Slow - the fraction of cells moving with $VAP <$ slow VAP cut-off or $VSL <$ slow VSL cut-off.

Static - the fraction of all cells which are not moving at all.

2.5.5 Organ weights

The following organs, taken from each male, were dissected free of adjacent fat and other contiguous tissue and the weights recorded:

Epididymides (L&R)

Testes (L&R)

Pituitary

Prostrate

Seminal vesicles

L&R Bilateral organs weighed individually

Organ weights were also adjusted for terminal bodyweight, using the weight recorded before necropsy.

2.5.6 Fixation

Testes and epididymides were initially fixed in modified Davidson's fluid prior to transfer to 10% neutral buffered formalin. Samples (or the whole) of the other tissues listed below from all animals were preserved in 10% neutral buffered formalin:

For adult animals:

Abnormalities	Prostate
Epididymides+	Seminal vesicles#
Mammary area - caudal†#	Testes+
Ovaries	Uterus with cervix and oviducts#
Pituitary‡#	Vagina#

Not examined histologically

† Females with total litter loss only

‡ For males with suspect fertility only

+ Only right fixed and subject to histology and pathology; left organ used for sperm analysis

Samples of any abnormal tissues were also retained and processed for examination. In those cases where a lesion was not clearly delineated, contiguous tissue was fixed with the grossly affected region and sectioned as appropriate.

Samples of the mammary area (from females with total litter loss only), pituitary (from males of suspect fertility only), uterus with cervix and oviducts and vagina were not examined histologically, but are retained against any future requirement for microscopic examination.

2.5.7 Histology

For those animals specified in the Pathology section, the relevant tissues were subject to histological processing.

Tissue samples were dehydrated, embedded in paraffin wax, sectioned at approximately four to five micron thickness and stained with haematoxylin and eosin. The testes were stained using a standard periodic acid/Schiff (PAS) method.

Those tissues subject to histological processing included the following regions:

Epididymides	-	caput, corpus and cauda
Ovaries	-	qualitative evaluation of one section from each ovary

For bilateral organs, sections of both organs were prepared. A single section was prepared from each of the remaining tissues required for microscopic pathology.

2.6 Pathology

2.6.1 Light microscopy

Microscopic examination was performed as follows:

All tissues preserved for examination (as specified above) were examined for all animals of Groups 1 (Control) and 4 (2880 ppm) sacrificed on completion of the scheduled treatment period and for all animals killed or dying during the study.

Tissues reported at macroscopic examination as being grossly abnormal were examined for all animals in line with current practice (incisors or skin showing hair loss is not examined).

The following tissues, which were considered to exhibit a reaction to treatment at the high dose, were examined for all animals: Ovaries and Prostate.

Findings were either reported as "present" or assigned a severity grade. In the latter case one of the following five grades was used - minimal, slight, moderate, marked or severe. A reviewing pathologist undertook a peer review of the microscopic findings.

For the assessment of the ovaries, one mid-line section of each ovary was examined for the presence of primordial follicles, growing follicles and corpora lutea.

For the assessment of the right testis, a detailed qualitative examination was made, taking into account the tubular stages of the spermatogenic cycle. The examination was conducted in order to identify treatment related effects such as missing germ cell layers or types, retained spermatids, multinucleate or apoptotic germ cells and sloughing of spermatogenic cells into the lumen. Any cell- or stage-specificity of testicular findings was noted.

For the assessment of the epididymides, leukocyte infiltration, change in prevalence in cell types, aberrant cell types and phagocytosis of sperm was examined.

2.7 Computer systems

The computer systems with version numbers that were used on this study to acquire and quantify data include:

Hamilton Thorne IVOS Computer Assisted Sperm Analyser (CASA) (version 12.3d) used for Sperm analysis.

Liberate Release 2 in-house system used for reporting clinical signs, dosing signs, bodyweights, food consumption, water consumption, organ weights, macropathology and histopathology, statistics.

Quasar (version 1.3) and SAS (version 9.1.3) in-house statistical analysis packages used for bodyweight, food consumption and organ weight statistics.

Sample Registry System (version 1.0) used for Formulation and Inhalation Analysis data.

SAS (version 9.1.3) in house statistical analysis package used for sex ratio statistics.

StarTox (version 3.2) in-house statistical analysis package used for litter size and survival indices statistics.

StatXact 3 statistical analysis package used for mating performance and fertility and oestrous cycles and pre-coital interval statistics.

Waters Empower 2, Build 2154, Feature Release 4, Service Pack D and used for Formulation and Inhalation Analysis.

Xybion Path/Tox System (version 4.2.2) used for clinical signs, dosing signs, bodyweights, food consumption, water consumption, organ weights, macropathology and histopathology.

Xybion Pristima (version 6.3.2) used for Pharmacy test substance management.

2.8 Data treatment

This report contains serial observations pertaining to all weeks of treatment completed, together with signs data collected during the necropsy period.

Summary statistics (e.g. means and standard deviations) presented in this report were calculated from computer-stored individual raw data. The summary statistics and the individual data were stored in the computer to a certain number of decimal places, different for each parameter. For presentation purposes, however, they were usually rounded to fewer places. It is, therefore, not generally possible to reproduce the presented means and standard deviations exactly using the presented individual data.

The codes in the appendices have the following meaning:

T	Scheduled kill; fertility confirmed
W	Killed for reasons of animal welfare
F	Found dead
FTM	Failed to mate
NP	Not pregnant; no implantation sites visible
TR	Total resorption; implantation sites visible
TLL	Total litter loss
U	Unilateral pregnancy

Within the context of this study it was not 100% possible to confirm animals that were pregnant but where no pups were seen in the animal's cage, were total resorptions (litter loss in utero) or if any pups had been born but had been shortly afterwards eaten by the dam). These animals have been coded as TLL with the above proviso/caution.

Throughout the report the following abbreviations are used:

M	Male
F	Female
N/n	Number contributing to the mean (normally the number animals/litters)
SD	Standard deviation

2.8.1 Signs

Signs are considered in two parts: observations in association with treatment, classified as “dosing signs” and extended changes in condition, classified as “clinical signs”.

Signs considered to indicate a reaction to treatment are presented for each animal that shows signs, providing detail of type of sign, day of occurrence and information on the duration of the sign if applicable.

“Dosing signs have been presented in 2 ways, one to show the daily occurrence relative to the timing of exposure, and one to show progression/presence across the different phases of the study. Dosing signs recorded during the 6 hour exposure were recorded on a group basis; hence in this report all animals in a group will exhibit the same signs. Signs associated with dosing recorded prior or post exposure are recorded on an individual animal basis.

The overall group frequency of dosing signs and clinical signs were summarised in an incidence table.

2.8.2 Bodyweights

Individual values were reported for all days recorded. Group mean weight changes were calculated from the weight changes of individual animals surviving the specified period.

Bodyweight was plotted graphically with respect to the first day of the relevant period.

2.8.3 Food consumption

During the pre-pairing periods of the study where animals were housed 5 per cage, values are presented for the average amount of food consumed per rat in each cage in each experimental week (g/rat/week). Values presented allow for any animal that died or was killed during the week.

During the gestation and lactation phases, where females were individually housed, group mean values and SD were calculated from individual values for Days 0-2, 3-6, 7-9, 10-13, 14-16 and 17-19 after mating and Days 1-4 and 5-9 of lactation based on the numbers of females completing each phase.

Mean overall values for food consumption before pairing were calculated from the weekly group mean values presented.

2.8.4 Water consumption

Water consumption was calculated from measurements of initial and final weights (g) of the water bottle and contents for each cage (it was assumed that 1 mL of water weighed 1 g).

2.8.5 Oestrous cycles

The percentage females showing the following classifications of oestrous cycles before pairing are presented:

- Regular: All observed cycles of 4 or 5 days
- Irregular: At least one cycle of 2, 3 or 6 to 10 days
- Acyclic: At least 10 days without oestrus (beginning before pairing).

2.8.6 Pre-coital interval

Individual intervals were tabulated for the time elapsing between initial pairing and mating. Percentage of females with pre-coital intervals calculated for durations of 1-4, 5-8, 9-12 and 13-14 days of pairing.

2.8.7 Mating performance and fertility

Individual data was tabulated. Group values were calculated for males and females separately for the following:

$$\text{Percentage mating} = \frac{\text{Number animals mating}}{\text{Animals paired}} \times 100$$

$$\text{Conception rate (\%)} = \frac{\text{Number animals achieving pregnancy}}{\text{Animals mated}} \times 100$$

$$\text{Fertility index (\%)} = \frac{\text{Number animals achieving pregnancy}}{\text{Animals pairing}} \times 100$$

2.8.8 Gestation length

Gestation length was calculated as the number of gestation days up to and including the day on which offspring were first observed, with Day 1 = day of mating for calculation purposes. Where parturition had started overnight, this value was adjusted by subtracting half of one day. Gestation index was calculated for each group as:

$$\text{Gestation index (\%)} = \frac{\text{Number of live litters born}}{\text{Number pregnant}} \times 100$$

2.8.9 Litter size

Individual litter values were tabulated for the number of implantation sites, total at Day 1 (live and dead) and total live on Days 1, 5 and 10 of age. Group mean litter size and SD were calculated from the individual litter values.

2.8.10 Survival indices

The following were calculated for each litter:

$$\text{Post-implantation survival index (\%)} = \frac{\text{Total number of offspring born}}{\text{Total number of uterine implantation sites}} \times 100$$

Post-implantation survival index was expressed as 100% where the number of offspring exceeded the number of implantation sites recorded.

$$\text{Live birth index (\%)} = \frac{\text{Number of live offspring on Day 1 after littering}}{\text{Total number of offspring born}} \times 100$$

$$\text{Viability index (\%)} = \frac{\text{Number of live offspring on Day 10 after littering}}{\text{Number live offspring on Day 1 after littering}} \times 100$$

Group mean values were calculated from individual litter values.

2.8.11 Sex ratio

The percentage of male offspring in each litter was calculated at Day 1, and for live offspring on Days 1, 5 and 10 of age.

$$\text{Percentage males} = \frac{\text{Number of males in litter}}{\text{Total number of offspring in litter}} \times 100$$

Group mean values were calculated from individual litter values.

2.8.12 Sperm analysis

Individual values tabulated for the following:

Motility (vas deferens)	The percentage of motile and progressively motile sperm and a detailed assessment of motility were reported.
Morphology	The number and percentages of normal and abnormal sperm were reported. A summary of the types of abnormalities seen was made because there was evidence of an effect on the percentage normal sperm.
Count (Testis and Cauda epididymis)	The sperm concentration (Million/g) and total number were reported.

Group mean values were calculated from individual values.

2.8.13 Organ weights

The abbreviations used in the Appendix have the following meanings:

Lt	Left
Rt	Right

2.8.14 Pathology

The abbreviations used in the Appendix have the following meanings:

Fac. Con.	Factors contributing
Lt.	Left
Rt.	Right

Tissues which could not be examined are specified in the Appendix. The absence of a comment for a tissue scheduled for examination therefore indicates that the tissue was considered to be normal. In all tabular presentations of data the tissues specified in the protocol for histopathological examination precede other tissues.

For offspring, findings were presented on an individual basis.

2.8.15 Statistical analysis

All statistical analyses were carried out separately for males and females.

Data relating to food consumption during the pre-pairing period were analysed on a cage basis. For all other parameters, the analyses were carried out using the individual animal as the basic experimental unit.

The following data types were analysed at each timepoint separately:

- Bodyweight, using absolute weights and gains over appropriate study periods
- Food consumption, over appropriate study periods
- Organ weights, both absolute and adjusted for terminal bodyweight
- Litter data and survival indices
- Mating performance and fertility

The following sequence of statistical tests was used for bodyweight, food consumption, organ weights, litter size and survival indices data:

A parametric analysis was performed if Bartlett's test for variance homogeneity (Bartlett 1937) was not significant at the 1% level. For pre-treatment data, analysis of variance was used to test for any group differences. Where this was significant ($p < 0.05$) inter group comparisons using *t*-tests, with the error mean square from the one-way analysis of variance, were made. For all other analyses the F_1 approximate test was applied. This test is designed to detect significant departure from monotonicity of means when the main test for the comparison of the means is a parametric monotonic trend test, such as Williams' test (Williams 1971, 1972). The test statistic compares the mean square, NMS, for the deviations of the observed means from the maximum likelihood means, calculated under a constraint of monotonicity with the usual error mean square, EMS. The null hypothesis is that the true means are monotonically ordered. The test statistic is $F_1 = \text{NMS}/\text{EMS}$ which can be compared with standard tables of the *F*-distribution with 1 and EMS degrees of freedom. If the F_1 approximate test for monotonicity of dose-response was not significant at the 1% level, Williams' test for a monotonic trend was applied. If the

F_1 approximate test was significant, suggesting that the dose-response was not monotone, Dunnett's test (Dunnett 1955, 1964) was performed instead.

A non-parametric analysis was performed if Bartlett's test was still significant at the 1% level following both logarithmic and square-root transformations. For pre-treatment data, Kruskal-Wallis' test (Kruskal and Wallis 1952, 1953) was used to test for any group differences. Where this was significant ($p < 0.05$) inter group comparisons using Wilcoxon rank sum tests (Wilcoxon 1945) were made. For all other analyses the H_1 approximate test, the non-parametric equivalent of the F_1 test described above, was applied. This test is designed to be used when the main test for comparison of the means is a non-parametric monotonic trend test, such as Shirley's test (Shirley 1977). The test statistic compares the non-monotonicity sums of squares, NRSS, for the deviations of the observed mean ranks from the maximum likelihood mean ranks with the non-parametric equivalent of the error sums of squares, ERSS = $N(N+1)/12$. The test statistic is $H_1 = \text{NRSS}/\text{ERSS}$ which can be compared to standard tables of the χ^2 -distribution with 1 degree of freedom. If the H_1 approximate test for monotonicity of dose-response was not significant at the 1% level, Shirley's test for a monotonic trend was applied. If the H_1 approximate test was significant, suggesting that the dose-response was not monotone, Steel's test (Steel 1959) was performed instead.

For litter data, if 75% of the data (across all groups) were the same value, for example c, Fisher's Exact tests (Fisher 1973) were performed. Treatment groups were compared using pairwise comparisons of each dose group against the control both for i) values $< c$ versus values $\geq c$, and for ii) values $\leq c$ versus values $> c$, as applicable.

Sex ratio were analysed by generalised mixed linear model with binomial errors, a logit link function and litter as a random effect (Lipsitz et al 1991). Each treated group was compared to control using a Wald chi-square test. For sex ratio, the numerator was Number of males, the denominator was Number of live fetuses.

For gestation length, sperm counts and copulation plugs an exact two-tailed Linear-by-linear test (Cytel 1995), with equally spaced scores, was applied to all groups. If the test was statistically significant ($p < 0.05$), the highest dose group was excluded and the test re-applied. This 'step-down' process was repeated until the test was no longer statistically significant ($p \geq 0.05$).

For the number of females with one or more 'abnormal' oestrous cycle length of '3 or less' or '5 or more' days an exact one-tailed (upper-tail) Cochran-Armitage test (Cytel 1995) was applied to all groups. If the test was statistically significant ($p < 0.05$), the highest dose group was excluded and the test re-applied.

For the incidence of cycle lengths an exact one-tailed (upper-tail) Linear-by-linear test (Cytel 1995) was applied to all groups, using scores appropriate to the severity of the observation assuming 4 day cycles to be normal. The categories were scored as follows: a 4 day cycle was scored as 4 and a 5 day cycle was scored as 5 and abnormal (2, 3, 6 to 10 or 11 to 20 days) cycles were scored as 6. If the test was statistically significant ($p < 0.05$), the highest dose group was excluded and the test re-applied. This 'step-down' process was repeated until the test was no longer statistically significant ($p \geq 0.05$).

For pre-coital intervals an exact one-tailed (upper-tail) Linear-by-linear test (Cytel 1995) was applied to all groups, using the following scores: a 1-4 day interval was scored as 1, a 5-8 day intervals was scored as 2, a 9-12 day interval was scored as 3 and a 13-14 day interval was scored as 4. If the test was statistically significant ($p < 0.05$), the highest dose group was excluded and the test re-applied. This 'step-down' process was repeated until the test was no longer statistically significant ($p \geq 0.05$).

For number mating, number conceiving, number fertile and number of live litters born an exact one-tailed (lower-tail) Cochran-Armitage test (Cytel 1995) was applied to all groups. If the test was statistically significant ($p < 0.05$), the highest dose group was excluded and the test re-applied. This 'step down' process was repeated until the test was no longer statistically significant ($p \geq 0.05$).

If the exact version of the Linear-by-linear test could not be calculated (due to the size of the table containing the data), then the asymptotic version was used instead.

Key to Tables

Significant differences between Control and treated groups were expressed at the 5% ($p < 0.05$) or 1% ($p < 0.01$) level. The key to the annotation used on the tables that contain statistical results is given below.

- l Data were log transformed for the statistical analysis.
- Ca Treated groups compared to Control using Cochran-Armitage test
- Du Treated groups compared to Control using Dunnett's test.
- Lt Treated groups compared to Control using Linear-by-linear association test
- Sh Treated groups compared to Control using Shirley's test.
- Wa Treated groups compared to Control using Wald's test
- Wi Treated groups compared to Control using Williams' test.

Codes placed above adjusted means indicate that the comparisons were based on adjusted means.

- * $p < 0.05$
- ** $p < 0.01$

2.9 Quality assurance and archiving procedures

2.9.1 Quality assurance

Details of the Quality Assurance inspections and audits are presented on the Quality Assurance Statement.

2.9.2 Archives

Following completion of this study all raw data, specimens and samples, except those generated or used during any Sponsor's or supplier's analysis, were stored in the archives of Huntingdon Life Sciences. Types of sample and specimen which are unsuitable, by reason of

instability, for long term retention and archiving may be disposed of after the periods stated in Huntingdon Life Sciences Standard Operating Procedures.

A copy of the final report and all Quality Assurance inspection records will be retained indefinitely. All other appropriate specimens and records will be retained for a minimum period of one year from the date of issue of the final report. At the end of this retention period the Sponsor will be contacted and advice sought on future archiving requirements. Under no circumstances will any item be discarded without the Sponsor's knowledge.

2.10 Deviations from protocol

The following deviations from protocol occurred:

In Week 6 for females, the water consumption residues were not recorded in error and there was thus no data for Week/Day 6.4 to 6.7. As such this was repeated over Week/Day 7.1 to 7.3. There was therefore two sets of water consumption, each recorded over 3 days, in Week 7.

The animals were supplied at age 49-56 days and weight range 250-300g males and 200-230g females, not at 65 days and 310-350g males, 227-254g females as required by the protocol. As such the animals were approximately 8-9 weeks of age at the start of treatment, not 10 weeks.

The pituitary, prostates and seminal vesicles (with coagulating gland) from all males were weighed, not just those of suspect fertility.

The sex ratio of litters was also calculated and reported on Day 5 post partum, not just Day 1 and Day 10.

Water consumption was presented daily for individual values. Water consumption was tabulated on a weekly basis for males, and for females prior to pairing, and tabulated for females during gestation and lactation both on a daily basis and over the period specified in the protocol.

These deviations were considered to have not affected the integrity of the study.

3. Results

3.1 Chamber atmosphere conditions

Annex 2

The achieved chamber concentration data for 2-bromo-3,3,3-trifluoropropene after approximately 8 weeks of treatment are summarised as follows:

Group	Treatment	Chamber concentration (ppm)	
		Target	Achieved
1	Control	0	-
2	2-bromo-3,3,3-trifluoropropene	200	198
3	2-bromo-3,3,3-trifluoropropene	500	505
4	2-bromo-3,3,3-trifluoropropene	3000	2900

The achieved aerosol concentrations were 99, 101 and 97% of the target concentration for Groups 2, 3 and 4, respectively. Adjustments were made to the exposure systems as appropriate to ensure that the achieved aerosol concentrations were close to target.

3.2 F0 maternal responses

3.2.1 Mortality and animal fates

Table 1

At 505 ppm, 5 females and litters were sacrificed during lactation. In these cases the litter had a high number of dead pups, and the offspring tended to show signs of poor condition, being cold with reduced activity and were killed with the dams. In one case, all pups that were born were found dead at the completion of parturition check (total litter loss pre-Day 1).

At 2900 ppm, 2 females were sacrificed on Day 24 after mating. Female 276 had partially closed eyes, hunched posture and piloerection, and female 279 had piloerection and perigenital staining and was noted to be attempting parturition. Both females were pregnant. The single dam (female 273) with a live litter born at 2900 ppm was killed for reasons of animal welfare following total litter loss.

3.2.2 Signs

Table 2-3 and Appendices 1-4

Appendices 1 and 2 show signs noted at the physical examination. Appendix 3 shows signs during and after exposure by phase of the study; the signs noted during exposure apply to all animals in the group being exposed. Appendix 4 shows, for females, the incidence of individual signs associated with dosing as the study progressed prior to mating and through gestation and lactation.

Pale teeth were noted in all males and 9/10 females at 2900 ppm (first noted from Week 5 in some and present from Week 7 in all animals) and in 3/10 males and 3/10 females at 505 ppm (only noted in Week 8, the final week of the study).

Hairloss was noted at a higher incidence than controls in males at 2900 ppm.

Occasionally, in some females at 2900 ppm, piloerection, hunched posture, and underactivity were noted at the physical examination, generally performed weekly.

During the 6 hour exposures, the following signs were noted:

At 2900 ppm underactivity, unresponsiveness, piloerection and eyelids partially closed were noted throughout. In males these signs were not apparent after completion of exposures. In females some of the above signs and also hunched posture were noted following exposure, occasionally in Week 2 (hunched posture only) and generally throughout gestation, but these were not present at the check for signs at the end of the working day (up to 2 hours later).

At 505 ppm, underactivity and piloerection were noted throughout, and unresponsiveness and eyelids partially closed were noted on fewer occasions. In males the signs were not noted following exposure, but in females during gestation and lactation, underactivity and piloerection, and in females during gestation only, eyelids partially closed were noted after exposure but not at the end of the working day.

At 198 ppm underactivity, unresponsiveness, piloerection and partially closed eyelids were noted at a much reduced incidence than that seen at higher levels; only underactivity and piloerection were noted immediately after exposure during gestation only.

3.2.3 Bodyweight

Figures 1-5, Tables 4-7 and Appendices 5-8

Mean bodyweight gain of males over the treatment period was lower than the controls in all groups given the test article (gain Day 1-50: 77, 63 and 47% of control at 198, 505 and 2900 ppm respectively). The effect was apparent from Week 1.

Mean bodyweight gain of females over the 2 week period prior to pairing was lower than the controls at 2900 ppm (gain Day 1-15: 19% of control). There were no effects of treatment on bodyweight gain of females over the 2 week period prior to pairing at 198 or 505 ppm.

Group mean bodyweight on Day 0 of gestation for females at 2900 ppm was lower than the controls, reflecting the difference established prior to pairing. Mean bodyweight gain during gestation was lower than the controls in females at 505 and 2900 ppm (gain Day 0-20: 83 and 43% of control respectively). At 198 ppm, mean bodyweight gain was marginally lower than the controls during Days 0-20 (92% of control).

During lactation, at 505 ppm slight mean bodyweight loss occurred once treatment was reintroduced on Day 5 of lactation (2g loss compared to 20g gain in the control group), and as such overall bodyweight gain during lactation was lower than the controls (13% of control). At 198 ppm bodyweight gain during Days 1-10 of lactation was 59% that of the control. No litters survived at 2900 ppm and hence no adult female bodyweights were recorded.

3.2.4 Food consumption

Tables 8-10 and Appendices 9-11

Mean food consumption of males and females was lower than the controls in all treated groups over the 2 weeks prior to pairing, with the effect most marked in Week 1. Overall food consumption for the 2 week period prior to pairing was 88, 76 and 76% of controls for males and 92, 82 and 70% of controls for females at 198, 505 and 2900 ppm respectively.

During the gestation phase, food consumption of treated pregnant females remained low and at a similar magnitude to that noted prior to pairing for treated females compared with controls (Day 0-19: 90, 89 and 78% of control at 198, 505 and 2900 ppm).

During the lactation phase, food consumption was lower than controls for females at 198 and 505 ppm (73 and 60% of control respectively). No litters survived at 2900 ppm and hence no food consumption data was generated for lactating females.

3.2.5 Water consumption

Tables 11-13 and Appendices 12-14

Water consumption was recorded for males and females from Week 2 of the treatment phase onwards following a visual increase in consumption noted for females in Week 1.

Measured water consumption of females in Week 2 was 17, 59 and 72% higher than the controls at 198, 505 and 2900 ppm respectively.

During the gestation phase, water consumption was slightly higher than the controls for all groups of treated females from Day 3 (up to 23% higher than the controls in females at 505 ppm), although the magnitude of the difference was less marked than that recorded prior to pairing.

During the lactation phase, water consumption, once treatment was reintroduced on Day 5, was slightly lower for females at 198 and 505 ppm compared with control.

There were no effects on water consumption of males in Weeks 2, 5, 6 or 7 (water consumption was not recorded during the 2 week pairing period).

3.2.6 Oestrous cycle length

Table 14 and Appendix 15

There was an effect on oestrous cycles in females. It is expected that control and unaffected animals have a preponderance of 4 or 5 day oestrous cycles, considered regular. All control females and females at 198 ppm had only 4 or 5 day cycles.

At 2900 ppm, only 1 female only had regular cycle lengths, although the cycle lengths recorded for this female were all 5 days in duration. Three females also had irregular cycles (at least one cycle of 2 or 3 days, or 6-10 days), one female had a period of extended oestrus, and the remaining 5 females were considered to also have, or only be, acyclic (at least 10 days without oestrus). Assessment of cycle lengths showed, in females at 2900 ppm, a

statistically significant incidence of females with longer cycle lengths, and a statistically significant incidence of longer specific cycle lengths, with 46% of the total recorded cycle lengths being 6 to 10 days, and 18% of the recorded cycle lengths being 11-20 days, compared with no similarly longer cycle lengths being observed in the control group. Only 33% of the total recorded cycle lengths at 2900 ppm were regular (4 or 5 days) compared to all of those in the control group.

At 505 ppm, only 5/10 females had regular cycle lengths, although in 4 of these 5 animals the cycle lengths were all 5 days. Four females had one or more irregular cycles and one female was acyclic (with a period of 12 days without oestrous). Assessment of the cycle lengths showed a statistically significant incidence of females with longer cycle lengths, and a statistically significant incidence of longer specific cycle lengths, with 21% of recorded cycle lengths being 6 or more days long. Although 79% of the recorded cycle lengths were considered regular (compared to 100% in the control group), 61% were of 5 days duration compared to only 18% of those in the control group.

At 198 ppm, all females had regular cycle lengths (4 or 5 days), and there was thus considered to be no adverse effect. There was, however, a statistically significant shift towards the longer cycle length with 70% of all cycles being 5 days duration compared with only 18% of the control cycles.

3.2.7 Pre-coital interval, mating performance and fertility

Tables 15-18 and Appendix 15

At 2900 ppm, only 7 of the pairings had evidence of mating and of these only 4 occurred in the first 4 days after pairing (the time considered to generally reflect a mating at the first oestrous possibility). However, review of the time of successful mating showed that 6 of the 7 females mated at the first oestrus recorded after pairing with only one mating at the second oestrous cycle. There was a statistically significant trend towards lower numbers of copulation plugs at mating. Copulation plugs give an indication of the number of times that mating occurred. Only 29% of the matings had 4-6 recorded copulation plugs compared to 80% of the controls; the remaining 71% of matings had 2 or 3 copulation plugs. Sperm count estimated at mating showed a slightly lower estimate of the presence of sperm in the vaginal smear taken on the day of mating, with the majority of smears having continuous few sperm or many scattered sperm compared to the solid masses of sperm seen more frequently in the control group. Of the 7 pairs of males and females showing evidence of mating, 6 pairings produced a pregnancy.

At 505 ppm all 10 pairings showed evidence of mating but 3 of these were in days 5-8 after pairing, not as would be usually expected in the first 4 days after pairing. A review of the time of successful mating showed that all but one females mated successfully at the first oestrous possibility. There was a statistically significant trend towards lower numbers of copulation plugs at mating. Only 20% of the matings had 4-6 recorded copulation plugs compared to 80% of the controls; the remaining 80% of matings had 1, 2 or 3 copulation plugs. Sperm count estimated at mating showed a trend towards slightly lower estimates of the presence of sperm in the vaginal smear taken on the day of mating, with the majority of smears having continuous few sperm or many scattered sperm compared to solid masses of sperm as seen more frequently in the control group. Four of the matings had no sperm present

in the vaginal smear; in the absence of this occurrence at 2900 ppm, this specific finding is of uncertain significance. All 10 pairings were successful in producing a pregnancy.

At 198 ppm and in the control group, the majority of animals showed evidence of mating (pre-coital interval) in the first 4 days after pairing (i.e. at the first mating opportunity). With the exception of a trend towards a lower sperm count category in the vaginal smear on the day of successful mating, there were no effects on the number of copulation plugs, or mating performance.

3.2.8 Gestation length and gestation index

Table 19 and Appendix 15

The duration of gestation in females from all treated groups was longer than the controls.

In the control group, the females showed the typical pattern of a majority of gestation lengths of 22 days. Females at 198 ppm had gestation lengths of 23 days, and those at 505 ppm had gestation lengths of 23, 24 or 25 days. After 25 days of gestation only one female at 2880 ppm had completed parturition.

The gestation index was reduced at 2900 ppm (only 17%) reflecting the single litter born from those mating in this group.

3.2.9 Sperm analysis

Tables 25-27 and Appendices 23-25

No adverse effects on percent motile sperm or testicular spermatid numbers were seen after treatment with 2-bromo-3,3,3-trifluoropropene at exposure levels up to 2900 ppm.

Slight but statistically significant reductions in percent progressively motile sperm, velocities and percent medium sperm were observed after treatment at 2900 ppm. In addition a statistically significant increase in Beat Cross Frequency was seen at this level. Significant reductions in velocities were also apparent at the lower exposure levels of 198 and 505 ppm.

A slight but statistically significant reduction in number of sperm in the cauda epididymis was apparent after treatment at 2900 ppm. This correlated with a lower cauda epididymal weight; the sperm/g was however unaffected.

Slight reductions in percent normal sperm were observed in all treated groups, these changes were statistically significant at 505 and 2900 ppm. The corresponding increase in percent total abnormal sperm was significant at all exposure levels. Observed abnormalities were primarily breakages (including decapitate sperm) and abnormal head shape.

The increased Beat Cross Frequency suggests there was no reduction in vigour of the sperm but that their forward movement was affected, whilst the breakages suggest sperm fragility was increased.

3.2.10 Organ weights

Table 28 and Appendix 26

At 2900 ppm, several organ weights were lower than the controls, notably prostate (52% of control), seminal vesicles (71% of control), epididymides (87% of control) and pituitary (77% of control).

At 505 ppm, prostate (74% of control), seminal vesicles (70% of control) and pituitary (85% of control) weights were reduced.

At 198 ppm, prostate (77% of control), seminal vesicles (83% of control) and pituitary (85% of control) weights were reduced.

3.2.11 Macropathology

Table 29, Appendix 27 and Annex 3

3.2.12 Animals killed after scheduled treatment period

The macroscopic examinations performed in the F0 animals revealed intergroup differences in the prostate, spleen, incisor teeth and skin.

Prostate

A reduction in size of the prostate was seen in all males exposed to 2900 ppm, in the majority of males exposed to 505 ppm and in one male exposed to 198 ppm.

Summary of findings in the prostate of F0 animals after scheduled treatment period

Group/sex	1M	2M	3M	4M
Exposure Level (ppm)	0	198	505	2900
Small	0	1	7	10
Number of animals examined	10	10	10	10

Spleen

Capsular thickening was seen in the spleen of the majority of males exposed to 2900, 505 or 198 ppm and in occasional females exposed to 2900 or 505 ppm. Capsular adhesions were seen in occasional treated males across all groups, in a few females exposed to 2900 ppm and one female exposed to 505 ppm.

Summary of findings in the spleen of F0 animals after scheduled treatment period

Group/sex	1M	2M	3M	4M	1F	2F	3F	4F
Exposure Level (ppm)	0	198	505	2900	0	198	505	2900
Capsule thickened	0	8	6	9	0	0	2	3
Adhesions	0	2	3	4	0	0	1	4
Number of animals examined	10	10	10	10	10	10	9	8

Teeth

Pale incisor teeth were seen in all male and female animals exposed to 2900 ppm, in the majority of males and three females exposed to 505 ppm and in one control male.

Summary of findings in the teeth of F0 animals after scheduled treatment period

Group/sex Exposure Level (ppm)	1M 0	2M 198	3M 505	4M 2900	1F 0	2F 198	3F 505	4F 2900
Incisor(s) pale	1	0	6	10	0	0	3	8
Number of animals examined	10	10	10	10	10	10	9	8

Skin

An increased incidence of hair loss was noted in occasional males exposed to 2900ppm.

Summary of findings in the skin of F0 animals after scheduled treatment period

Group/sex Exposure Level (ppm)	1M 0	2M 198	3M 505	4M 2900	1F 0	2F 198	3F 505	4F 2900
Hair loss	0	1	2	4	2	2	0	0
Number of animals examined	10	10	10	10	10	10	9	8

The nature and incidence of all other findings were consistent with the common background of macroscopic changes seen at these laboratories.

3.2.13 Histopathology

Table 30, Appendix 27 and Annex 3

3.2.14 Animals killed after scheduled treatment period

Treatment related findings

Changes related to treatment with 2-bromo-3,3,3-trifluoropropene were seen in the F0 ovaries.

Ovary

A slight reduction in the size of corpora lutea was seen in the ovaries of 4 females exposed to 2900 ppm and in a single female exposed to 198 ppm.

Summary of findings in the ovary of F0 animals after scheduled treatment period

Group/sex	1F	2F	3F	4F
Exposure Level (ppm)	0	198	505	2900
Reduced Size of Corpora Lutea				
Slight	0	1	0	4
Total	0	1	0	4
Number of tissues examined	10	10	9	8

Findings of an uncertain relationship to treatment

Findings of an uncertain relationship to treatment were identified in the spleen. This tissue was examined microscopically only when macroscopic abnormalities had been observed at necropsy. No spleen from control animals was examined.

Spleen

Minimal to moderate capsular/subcapsular inflammation and/or capsular thickening and/or adhesions/inflammation/fibrosis were observed in the majority of treated males exposed to 198, 505 or 2900 ppm and in occasional females exposed to 505 or 2900 ppm.

Summary of findings of an uncertain relationship to treatment in the spleen of F0 animals after scheduled treatment period

Group/sex	1M	2M	3M	4M	1F	2F	3F	4F
Exposure Level (ppm)	0	198	505	2900	0	198	505	2900
Capsular/Subcapsular Inflammation								
Minimal	0	5	3	3	0	0	1	3
Slight	0	3	2	2	0	0	0	1
Moderate	0	0	1	2	0	0	0	0
Total	0	8	6	7	0	0	1	4
Capsular Thickening								
Minimal	0	4	4	2	0	0	0	4
Slight	0	0	2	4	0	0	2	1
Moderate	0	0	0	1	0	0	0	1
Total	0	4	6	7	0	0	2	6
Adhesions/Inflammation/Fibrosis								
Minimal	0	3	2	2	0	0	2	1
Slight	0	2	1	3	0	0	0	3
Moderate	0	0	1	1	0	0	0	0
Total	0	5	4	6	0	0	2	4
Number of tissues examined	0	8	7	9	0	0	2	6

The incidence and distribution of all other findings were consistent with the common background seen at these laboratories.

The histopathological examination of testes and epididymides from the F0 generation animals performed after scheduled treatment period revealed no findings attributable to treatment with the test article 2-bromo-3,3,3-trifluoropropene.

The seminiferous tubules were evaluated with respect to their stage in the spermatogenic cycle and the integrity of the various cell types present within the different stages. No significant cell or stage-specific abnormalities were seen in the sections of testes either stained with haematoxylin & eosin (H&E) or periodic acid Schiff (PAS).

Evaluation of the epididymides did not reveal any changes in leukocyte infiltration, cell populations, or sperm numbers. There were no findings to correlate with the organ weight variation reported at necropsy.

3.2.15 Primordial ovarian follicle counts

Table 31 and Appendix 28

There were no treatment related effects on the primordial ovarian follicle counts.

3.3 F1 litter responses

3.3.1 Signs of offspring

Appendix 20

At 505 ppm the majority of offspring born were noted as being cold on Day 1, with those from dams where the litter was sacrificed early or died frequently being noted as dark in colour or inactive. In surviving offspring, no later signs were generally noted.

3.3.2 Litter size, survival indices and sex ratio

Table 20-22 and Appendices 16-18

At 2900 ppm the mean number of implantations in the pregnant females was reduced (9.5 compared with 15.9 in the control group). Only one female produced a litter, in this female there was low post implantation survival (25%) and a low live birth index (33%) such that only one pup was alive on Day 1 post partum. This pup was sacrificed due to poor condition on Day 1 post partum.

At 505 ppm the mean number of implantations was slightly lower than the controls. Post implantation survival, the live birth index and the viability index were all lower than the controls, resulting in a lower total and live litter size on Day 1 post partum, and lower litter size by Day 10 post partum (mean of 8.3 compared to 14.7 in the control group). In addition, a number of offspring were sacrificed due to poor condition including reduced activity and reduced body temperature.

At 198 ppm there was a slightly lower mean number of implantations. Post implantation survival was slightly reduced which resulted in a lower total and live litter size on Day 1 post partum. Group mean survival from birth to Day 10 post partum was lower than the controls; primarily due to lower survival in 2/9 litters.

There were considered to be no effects of treatment on the mean sex ratio. Although mean values showed an apparent reduction in the percentage of males per litter between birth and Day 10 post partum, review of the individual data and offspring dying did not show any selective demise of the males.

3.3.3 Bodyweight

Figure 5, Tables 23-24 and Appendix 19

There were no effects on mean male or female pup weight on Day 1 at 198 or 505 ppm. With the longer duration of gestation at 198 and 505 ppm, it might be expected that pup weight would be higher, and this was the case at 198 ppm. Bodyweight gain from Day 1 to Day 10 was slightly lower than the controls at 198 and 505 ppm.

There was only a single female pup weighed at 2900 ppm, the weight was slightly lower than the control (5.5g compared to 6.4g).

3.3.4 Offspring macropathology

Appendices 21-22

In offspring that died or were sacrificed prior to Day 10, no milk in the stomach was frequently recorded, especially in those dying in the very early days of lactation. This was most apparent at 505 ppm where there were a higher number of deaths.

There were no treatment related effects on the offspring sacrificed on Day 10 of lactation.

4. Discussion

Exposure of 2-bromo-3,3,3-trifluoropropene to rats was undertaken as an initial screening assessment of the influence on reproductive performance and development following administration by inhalation for a minimum of 15 days before pairing until Day 10 after the birth of the F1 generation. Females were not exposed between Day 20 after mating and Day 4 of lactation inclusive.

All females exposed to 2900 ppm and half of those exposed to 505 ppm were killed before Day 10 of lactation as they failed to mate (sacrificed on Day 25 after the last pairing), failed to litter (sacrificed on Day 25 after mating), lost the litter post-partum (sacrificed on the Day of litter loss) or were sacrificed due to poor health. As such, these females did not continue on to Day 10 of lactation.

There was an effect on oestrous cycles of females at 505 and 2900 ppm, as indicated by an increased incidence of "abnormal". Only 1/10 females at 2900 ppm and 5/10 females at 505 ppm had "normal" cycles.

Mating performance was affected at 505 and 2900 ppm with a reduction in the number of pairings with evidence of mating, and on the day of mating, a reduced presence of copulation plugs or sperm within the vaginal smear. The fertility index was reduced at 2900 ppm, probably linked with the marked effect on oestrous cycles. There was also a reduced number of implantations evident at sacrifice.

Of females that showed evidence of mating, the delayed pre-coital interval is considered in part to reflect the reduction in regular oestrous cycles in these groups, as successful matings tended to occur at the first oestrous opportunity after pairing, regardless of whether this was in the "expected" 4 days post pairing (the time of a "normal" oestrous cycle).

The duration of gestation was extended at 505 and 2900 ppm. Routinely pregnant females complete parturition on Day 22 after mating. At 2900 ppm only one of the six pregnant females littered, on Day 25 after mating. Two other females were sacrificed on Day 24 after mating, the signs indicated this was possibly associated with stress involved in commencement of parturition. The remaining 3 females were sacrificed on Day 25 after mating as parturition had not commenced and there was no indication of this occurring – these females were found to have been pregnant but had no viable conceptuses at necropsy, it is unclear if these females had shown total litter loss in utero or had commenced parturition and the pups born were eaten prior to being observed at the animal room checks. At 505 ppm 9 of the 10 pregnant females produced a litter, although in one case all pups were found to be dead at the Day 1 check. The duration of gestation, in females at 505 ppm, was extended to between 23 and 25 days.

At 2900 and 505 ppm, a lower number of implantations, coupled with reduced in utero survival and reduced post partum viability resulted in reduced number of offspring surviving to Day 10 post partum; this being a combination of all offspring in the litter dying, or offspring and the dam being sacrificed due to the clinical signs seen. There was a higher incidence of offspring in treated groups being noted as cold, inactive or unfed.

A reduction in the number of sperm in the cauda epididymis at 2900 ppm correlated with the lower caudal epididymal weight, although the number of sperm/g epididymis was unaffected

and there were no changes noted histologically. This also correlated with the lower estimates of sperm present in the vaginal smear of females on the day of copulation. At 2900 ppm and generally at 505 ppm, a reduced percentage progressively motile sperm and sperm velocity and an increased Beat Cross Frequency suggested that whilst there was no reduction in vigour of the sperm, their forward movement was affected, and an increase in abnormal sperm (mainly breakages) suggested that sperm fragility was increased.

The reduced bodyweight gain and food intake of males at 505 and 2900 ppm and of females at 2900 ppm only was considered an adverse effect of treatment but was not considered sufficient to have been linked to the effect on oestrous cycles or mating performance or the lower numbers of implantations. At 505 ppm 4 females and their offspring did not survive to Day 10 post partum.

The clinical signs noted during exposure, notably reduced activity and unresponsiveness, were not unexpected following findings on the preliminary range finding study. Clinically the signs had resolved immediately after exposure or before the end of the working day. However, in a concurrent 13 week study in these laboratories [WAG0014] these clinical signs have also been seen and motor activity monitoring in Week 13 showed reduced low and high level activity at similar exposure levels on the morning after exposure. It is uncertain what effect, if any, the reduced activity had on the mating performance.

Water intake was generally higher in females at 505 or 2900 ppm prior to pairing and throughout gestation. During lactation however, water consumption was lower. The significance of this is unclear but it may reflect a lower demand on the lactating dams in treated groups due to the lower number of offspring present.

No histopathological findings were seen to account for the irregular oestrus cycles or the prolonged gestation lengths.

The examination of the ovaries from the F0 generation females revealed the presence of histopathological changes attributable to treatment. A reduction in size of corpora lutea was observed in the ovaries of four females exposed to 2900 ppm and one female exposed to 198 ppm. The corpora lutea were quite small and appeared to be not newly formed. As this change was not consistent with the increasing exposure level across the treated groups, the presence in a single female exposed to 198 ppm was considered to be incidental. In all cases in the 2900 ppm group, the females with small corpora lutea were found to be non pregnant; since this finding was not apparent amongst the pregnant females in this group it may relate to their pregnant status rather than being a specific effect of treatment.

An increased incidence of small prostates was observed at the macroscopic examination. This was consistent with a reduction in prostate weight seen with increasing exposure level. No microscopic correlate for the small prostates could be identified. A low incidence of inflammatory changes was observed in all groups including controls and was considered to be incidental as these types of changes are occasionally seen in rats of this age.

Capsular thickening and adhesions were observed in the spleen of the majority of treated males and occasional treated females at the macroscopic examination. Most of these macroscopic observations correlated with findings of capsular/subcapsular inflammation and/or capsular thickening and/or adhesions/inflammation/fibrosis seen at the microscopic examination and are likely to be related to treatment. However, as no controls and only

tissues with macroscopic changes were sampled and microscopically examined, conclusions as to the significance of these changes could not be made.

The significance of the increased incidence of pale incisors and hair loss of the skin observed clinically and at the macroscopic examination was not further clarified as these tissues are not routinely examined microscopically.

Full evaluation of the spleen capsular thickening and adhesions, pale incisors and hairloss are considered to be within the remit of the concurrent 13 week toxicity study in the rat at the same target exposure concentrations [WAG0014].

It was considered that the effects seen at 505 and 2900 ppm were considered adverse.

At 198 ppm some similar effects were apparent but the magnitude of the responses tended to be much lower and most likely not to be adverse. These not adverse effects included the effects on bodyweight, food intake, water intake, and probably the shift to a 5 day oestrous cycle length (which is still considered normal). There was a slightly lower sperm count noted in the vaginal smear on the day of copulation, although at termination the epididymal sperm count was not statistically significantly reduced, there was no effect on the epididymal weight and as such any adversity of this sperm count is unclear. The significance of the slight shift to a longer duration of gestation (23 days instead of 22 days) is unclear.

At 198 ppm, the mean number of implantations was slightly lower than in Controls. Three out of 9 litters showed lower than expected post implantation survival of the conceptuses (63-74%) and two litters showed lower than expected pup viability indices (54 and 82%), and these differences contributed to lower total and live litter sizes than in Controls. Although only a few litters were involved, the reduction in total and live litter size on Day 1 of lactation formed part of a dose related trend and thus a relationship to treatment was considered likely.

In general, treatment affected both the male reproductive system (effects on sperm) and the female reproductive system (oestrous cycles). However, which sex(es) contributed to the reductions in implantation counts and the pre and post natal survival of the offspring cannot be determined within the context of this screening study. By pairing males treated for 2 weeks at 505 ppm with undosed females and females treated at 505 ppm for 2 weeks with undosed males the contribution of each sex to the reduced implantation counts and offspring survival could be determined.

5. Conclusion

Exposure of 2-bromo-3,3,3-trifluoropropene to rats in this screening study to assess of the influence on reproductive performance and development following administration by inhalation at concentrations of 198, 505 or 2900 ppm was associated with adverse effects on male and female toxicity, and reproductive performance and development at 505 and 2900 ppm.

Exposure at 505 and 2900 ppm produced effects on oestrous cycles, fertility (2900 ppm only), extended duration of gestation, sperm counts and motility, implantation counts, reduced in utero and post partum survival, in the presence of signs of adult toxicity. In addition, at 2900 ppm, reduced size of corpora lutea in the ovaries was noted.

Exposure at 198 ppm was associated with slight effects on adult toxicity, but did have slight effects on reproductive performance (a possible shift to longer duration of gestation) and development (slightly lower implantation rate, higher post implantation survival and viability indices leading to lower litter size) as seen at 505 ppm and above.

Within this screening study, the no adverse effect level (NOAEL) for reproductive performance and development was considered to lie below 198 ppm.

6. References

6.1 Necropsy and histology

Salewski E (1964). Farbemethode zum makroskopischen nachweis von implantationsstellen am uterus der Ratte. *Naunyn - Schmiedebergs Arch. exp. Pathol. Pharmacol.*, 247, 367.

6.2 Statistics

Angervall L and Carlström E (1963). Theoretical criteria for the use of relative organ weights and similar ratios in biology. *J Theoret Biol* 4, 254-9

Bartlett MS (1937) .Properties of sufficiency and statistical tests. *Proceedings of the Royal Society. Series A* 160, 268-282.

Cytel (1995). StatXact 3 for Windows: Statistical Software for Exact Nonparametric Inference. *Cytel Software Corporation, NC, USA.*

Dunnett CW (1955). A multiple comparison procedure for comparing several treatments with a control. *Journal of the American Statistical Association* 50, 1096-1121.

Dunnett CW (1964). New tables for multiple comparisons with a control. *Biometrics* 20, 482-491.

Fisher RA (1973). *Statistical Methods for Research Workers*, 14th edn., p.96. Hafner Publishing Company, New York, USA.

Huntingdon Life Sciences Study number: WAG0013
2-bromo-3,3,3-trifluoropropene: Dose Range Finding Study by Inhalation Administration to Rats for 2 Weeks.

Huntingdon Life Sciences Study number: WAG0014
2-bromo-3,3,3-trifluoropropene: Toxicity Study by Inhalation Administration to Rats for 13 Weeks.

Huntingdon Life Sciences Study number: WAG0024
2-bromo-3,3,3-trifluoropropene: Dose Range Finding Study by Inhalation Administration to Rats for 2 Weeks.

Lipsitz SH, Laird NM, and Harrington DP (1991). Generalized Estimating Equations for Correlated Binary Data: Using the Odds Ratio as a Measure of Association, *Biometrika*, 78, 153-160.

SAS Institute (2002) SAS OnlineDoc® *Version Nine*. SAS Institute Inc., Cary, NC, USA.

Shirley EAC (1977). A non-parametric equivalent of Williams' test for contrasting increasing dose levels of a treatment. *Biometrics* 33, 386-389.

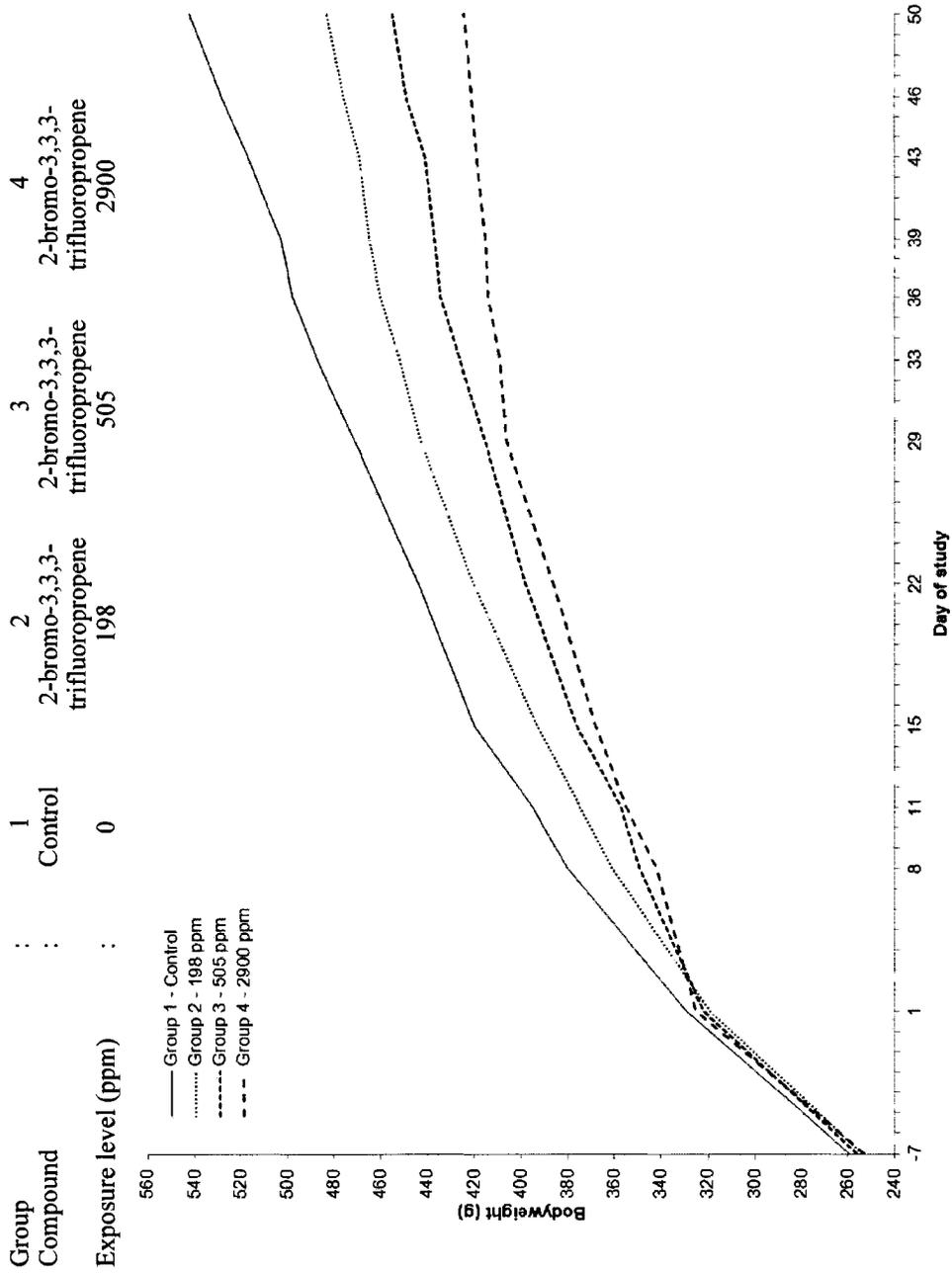
Steel RGD (1959). A multiple comparison rank sum test: treatments versus control. *Biometrics* 15, 560-572.

Williams DA (1971). A test for differences between treatment means when several dose levels are compared with a zero dose control. *Biometrics* **27**, 103-117.

Williams DA (1972). The comparison of several dose levels with a zero dose control. *Biometrics*, **28**, 519-531.

FIGURE I

Bodyweight - group mean values for males - F0 generation



Pairing commenced Day 15

FIGURE 2

Bodyweight - group mean values for females before pairing - F0 generation

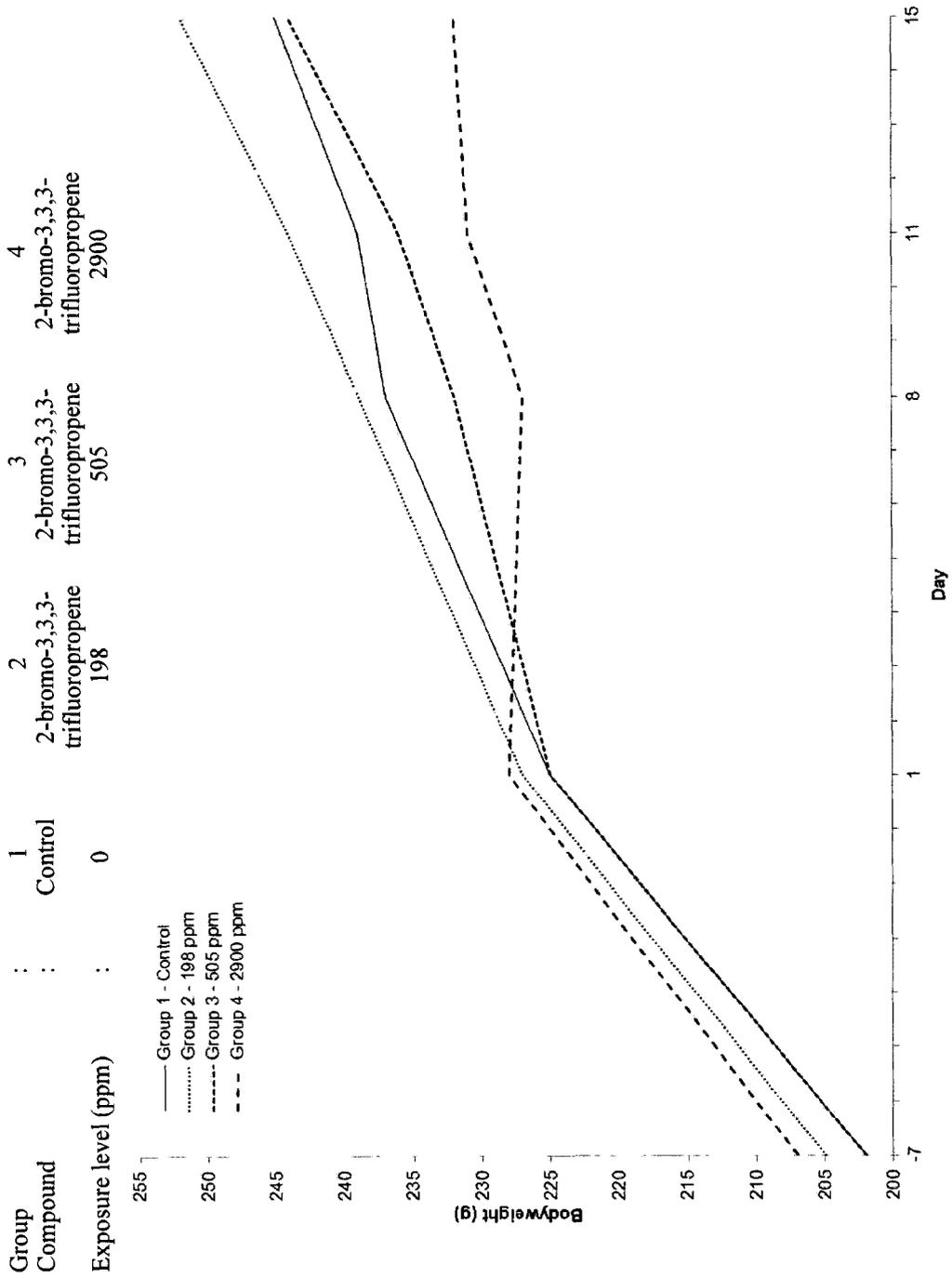
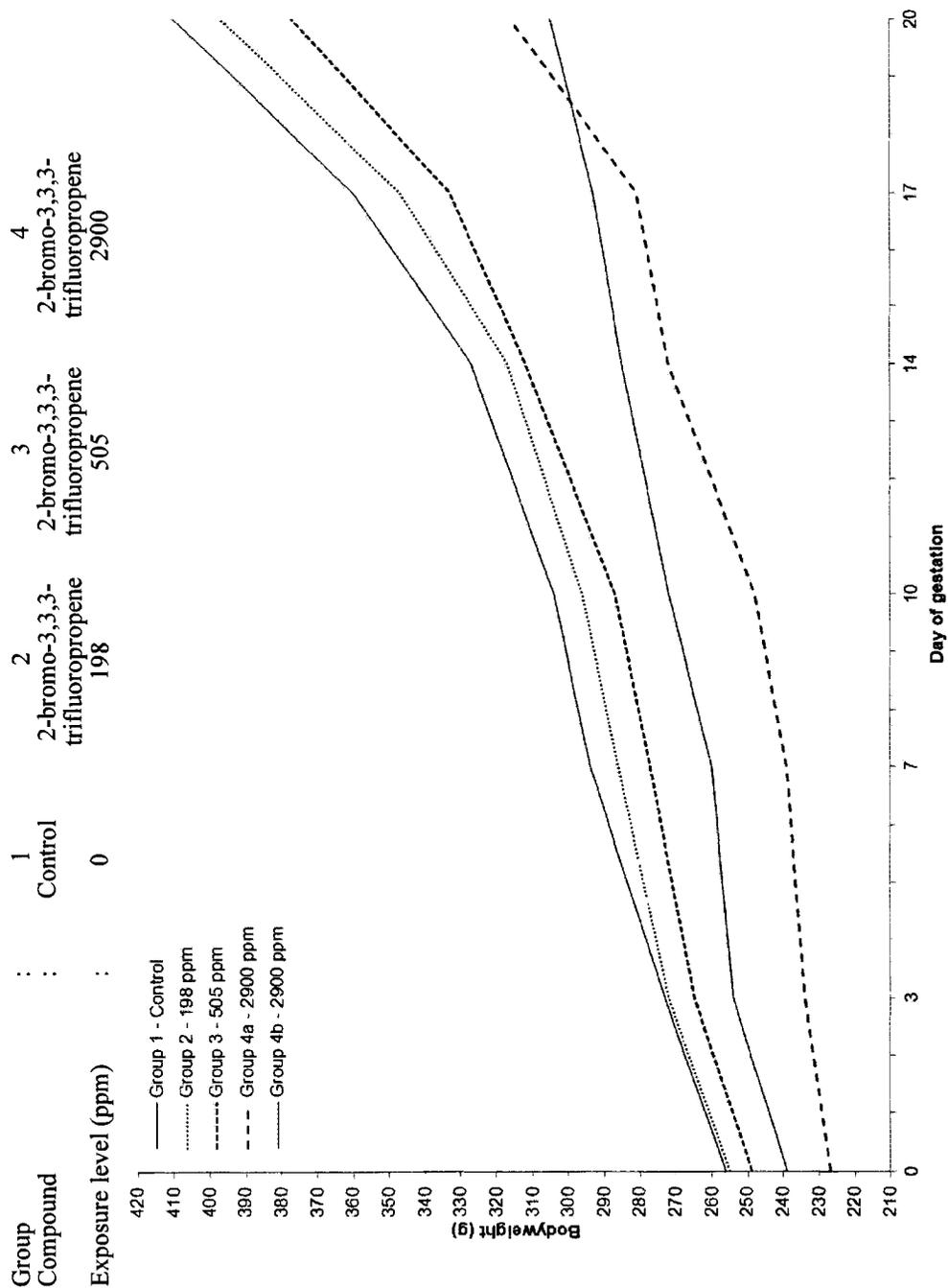


FIGURE 3

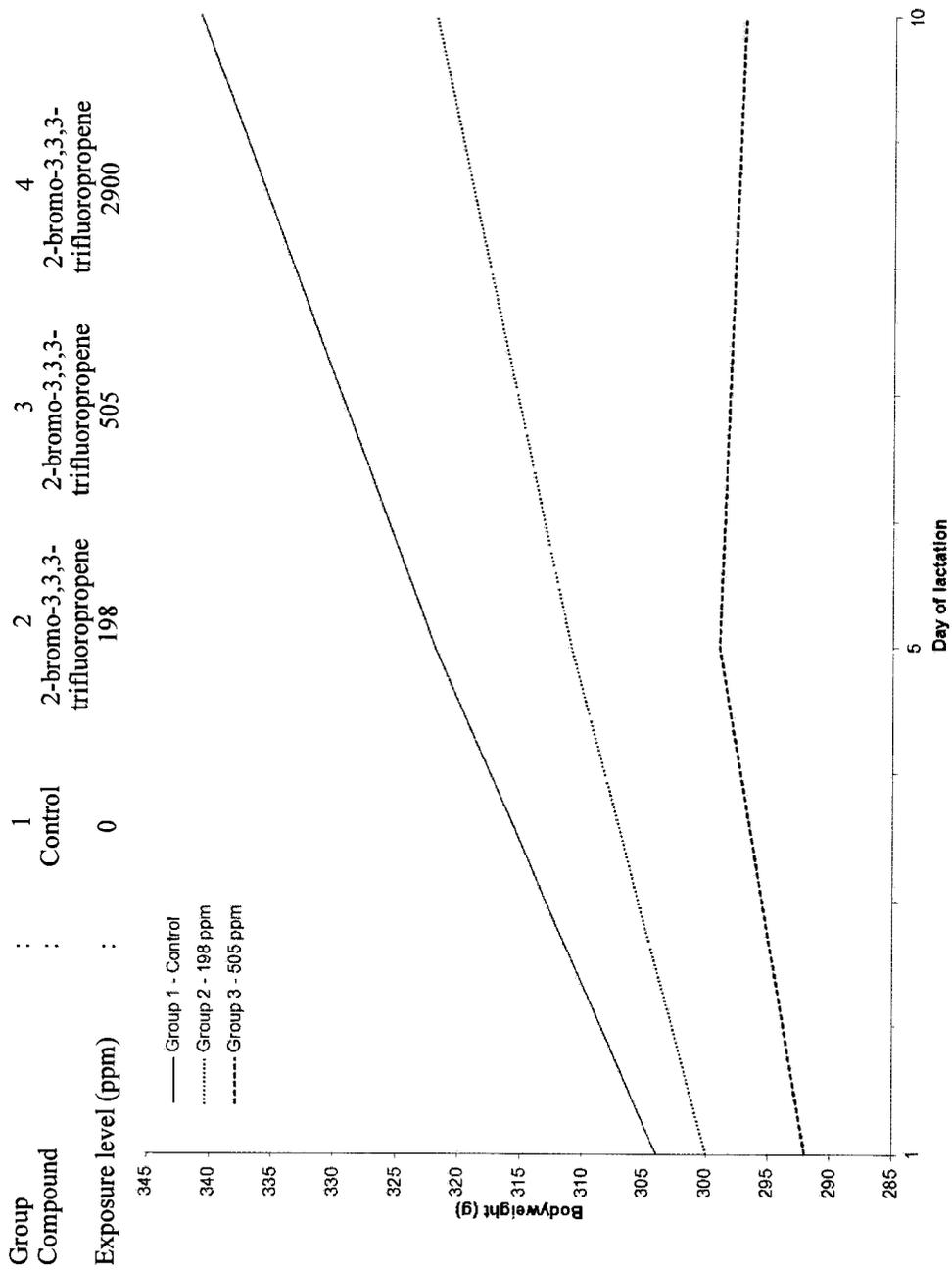
Bodyweight - group mean values for females during gestation - F0 generation



a Mean of females which littered
b Mean of all pregnant females

FIGURE 4

Bodyweight - group mean values for females during lactation - F0 generation



Treatment reintroduced Day 5 of lactation

FIGURE 5

Bodyweight - group mean values for offspring - male animals - F1 generation

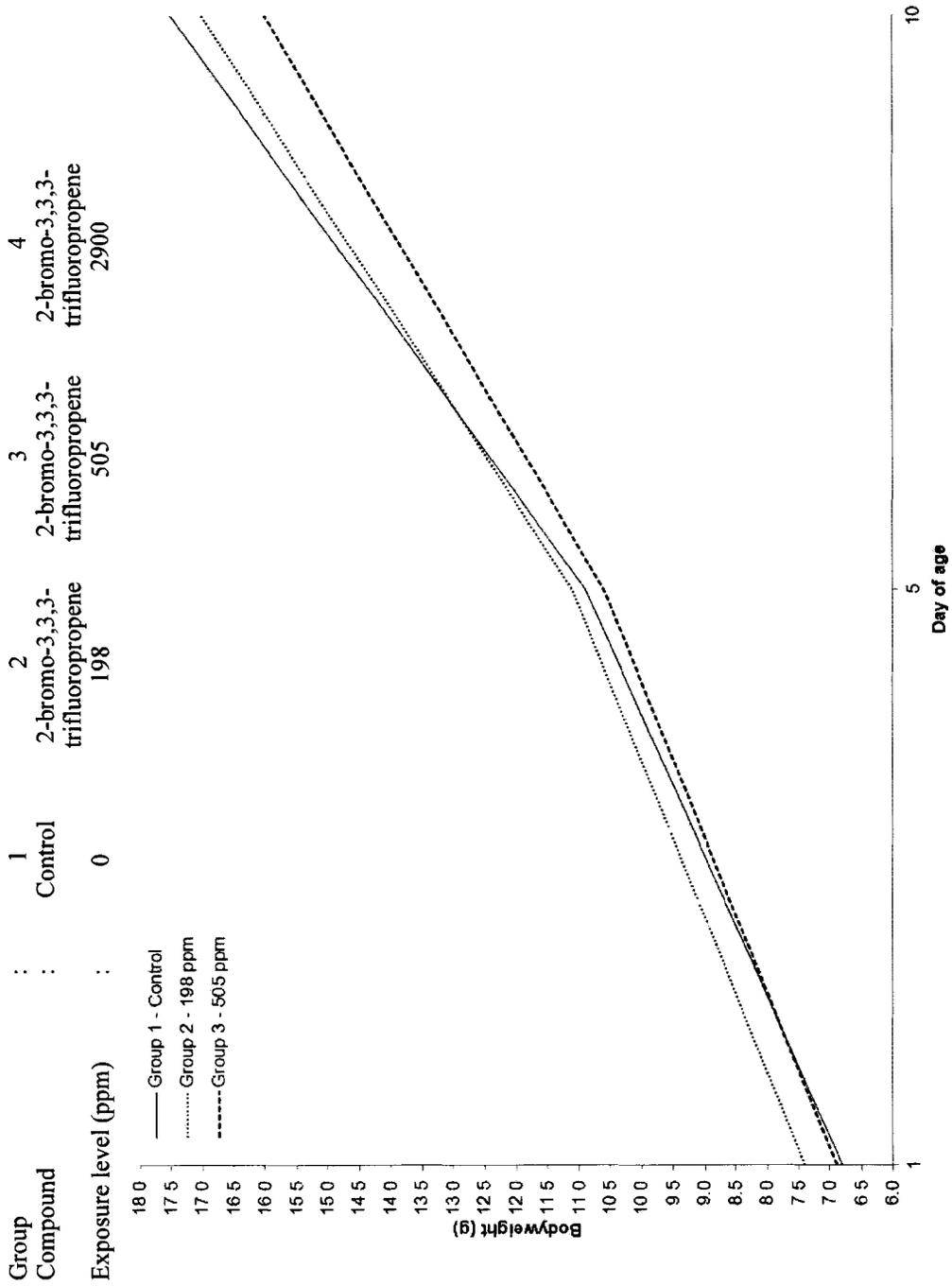


FIGURE 5 - continued

Bodyweight - group mean values for offspring - female animals - F1 generation

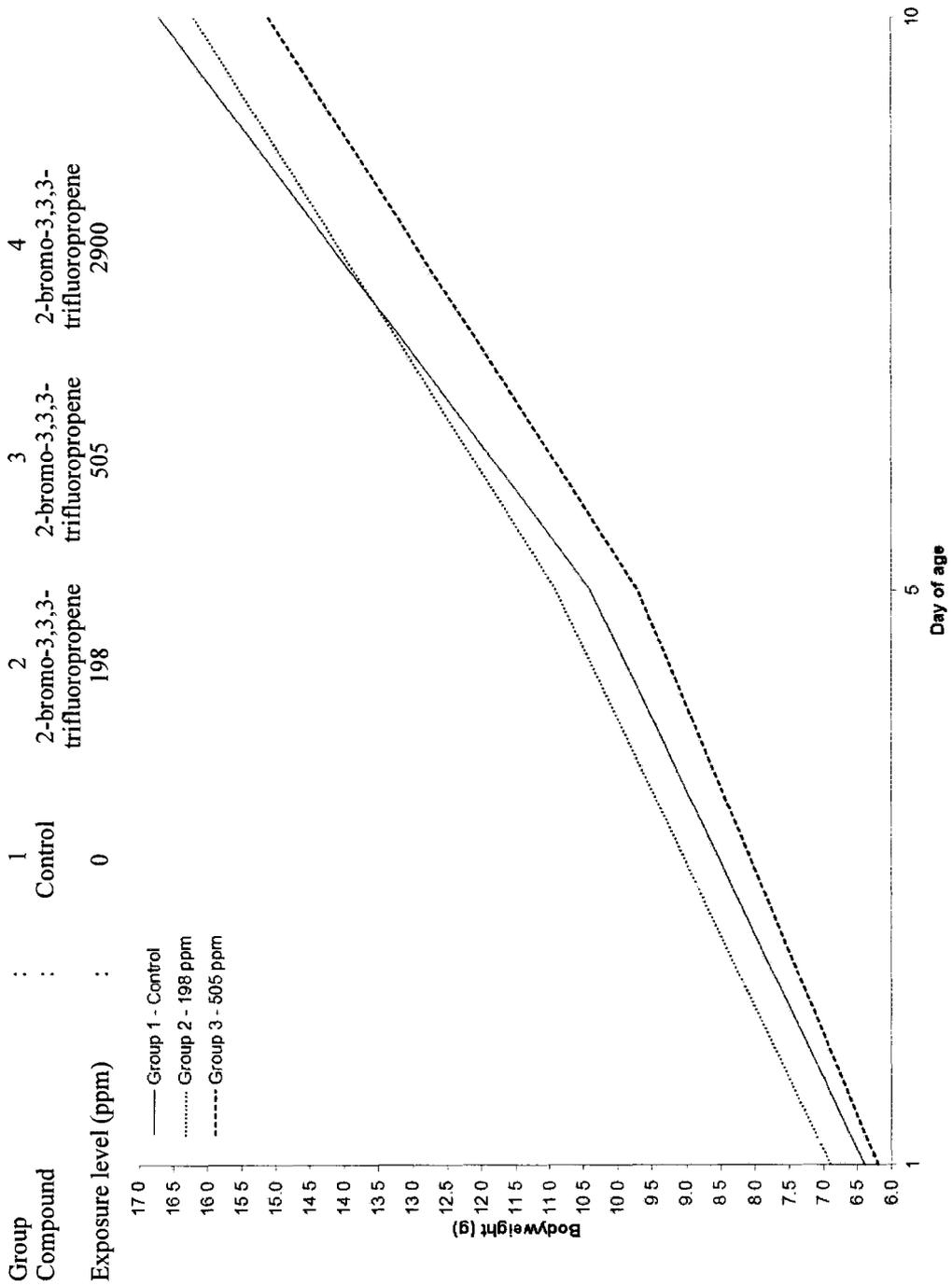


TABLE 1

Summary of adult performance

Group	1	2	3	4				
Compound	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900				
Exposure level (ppm)	0							
					Achieved concentration (ppm):			
					Group:			
					1	2	3	4
					0	197	505	2880
Males								
Animals paired:	10	10	10	10	10	10	10	10
Animals which failed to mate	0	0	0	0	0	0	0	3 (232, 235, 237)
Females								
Animals paired:	10	10	10	10	10	10	10	10
Animals which failed to mate	0	0	0	0	0	0	0	3 (272, 275, 277)
Failed to produce a litter (non-pregnant)	0	0	0	1 (257)	0	0	0	1 (280)
Number of animals pregnant	10	9	10	6	10	10	6	6
Failed to produce a litter (total resorption)	0	0	0	0	0	1 (263)	0	3 (271, 274, 278)
Animals sacrificed Day 24 gestation (pregnant)	0	0	0	0	0	0	0	2 (276, 279)
Total litter loss pre Day 1 of lactation	0	0	0	0	0	1 (266)	0	0
Live litter born	10	9	10	8	10	8	1	1
Total litter loss post-partum	0	0	0	0	0	4 (262 ^a , 265, 267, 270)	1	1 (273)
Litter surviving to Day 10 post partum	10	9	10	9	10	4	0	0

() Animal number
^a Includes dam/pups killed for welfare reasons

Request ID: 284416

TABLE 2

Clinical signs - group distribution of observations for males - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Weeks -1 - 8

Category	Observation	Group/sex:				Number of animals affected			
		Number in group:		Number in group:		1M	2M	3M	4M
		10	10	10	10	0	0	0	0
Coat	Hair loss, Cervical	0	0	0	0	0	0	0	2
	Hair loss, Cervical (Left)	0	0	0	0	0	0	0	1
	Hair loss, Head	0	0	0	0	0	0	1	5
Teeth	Abnormal Colour, Pale	0	0	0	0	0	0	3	10

Request ID: 284417

TABLE 2 - continued

Clinical signs - group distribution of observations for females before pairing - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Category	Observation	Group/sex: Number in group:								Number of animals affected								
		IF		2F		3F		4F		IF		2F		3F		4F		
		10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	
Behaviour	Aggressive	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	Irritable	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Vocalisation	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2
Build Conformation	Thin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	Hair loss, Head Piloerection	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Muscle Reaction	Reduced Body Tone	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2
	Hunched	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	4
Staining	Abnormal Colour, Brown, Head	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	5
	Abnormal Colour, Brown, Muzzle	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	Abnormal Colour, Eye (Left)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	Abnormal Colour, Eye (Right)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	Abnormal Colour, Red, Muzzle	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Teeth	Abnormal Colour, Pale	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3

Request ID: 284418

TABLE 2 - continued

Clinical signs - group distribution of observations for females after mating - F0 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900

Exposure level (ppm) : 0

Days 0 - 25

Category	Observation	Group/sex: Number in group:				Number of animals affected			
		1F 10	2F 10	3F 10	4F 7				
Behaviour	Irritable	0	0	1	0				
	Underactive	0	0	0	2				
Body temperature	Reduced	0	0	0	1				
Build Conformation	Thin	0	0	0	1				
Coat	Hair loss, Forelimb (Right)	0	1	0	0				
	Hair loss, Forelimbs	1	0	1	0				
	Hair loss, Head	1	0	1	0				
	Hair loss, Ventral Body Surface	0	0	1	0				
	Piloerection	0	0	0	3				
Eyelids	Partially Closed	0	0	0	1				
Muscle Reaction	Reduced Body Tone	0	0	0	1				
	Reduced Body Tone, Whole Body	0	0	0	1				
Posture	Hunched	0	0	0	1				
Staining	Abnormal Colour, Brown, Head	0	1	2	5				
	Abnormal Colour, Brown, Muzzle	0	0	0	2				

Request ID: 284418

TABLE 2 - continued

Clinical signs - group distribution of observations for females after mating - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Days 0 - 25	Observation	Group/sex:				Number of animals affected			
		Number in group:				1F	2F	3F	4F
Staining	Abnormal Colour, Red, Perigenital	10	10	10	10	0	0	0	1
Teeth	Abnormal Colour, Pale	10	10	10	10	0	0	3	6

Request ID: 284419

TABLE 2 - continued

Clinical signs - group distribution of observations for females during lactation - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Days 1 - 10

Category	Observation	Group/sex: Number in group:				Number of animals affected			
		1F	2F	3F	4F	1F	2F	3F	4F
Coat	Hair loss, Forelimb (Left)	0	1	0	0	0	1	0	0
	Hair loss, Forelimb (Right)	0	1	0	0	0	1	0	0
	Hair loss, Forelimbs	4	3	0	0	4	3	0	0
	Hair loss, Head	1	0	0	0	1	0	0	0
	Hair loss, Hindlimb (Right)	1	1	0	0	1	1	0	0
	Hair loss, Ventral Body Surface	0	3	0	0	0	3	0	0
Staining	Abnormal Colour, Brown, Head	1	2	2	0	1	2	2	0
	Abnormal Colour, Head	0	0	1	0	0	0	1	0
Teeth	Abnormal Colour, Pale	0	0	2	1	0	0	2	1

Request ID: 284420

TABLE 3

Signs associated with dosing - group distribution of observations for males - F0 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900

Exposure level (ppm) : 0

Sign	Day Number	Group/sex and number of animals showing sign			
		1M	2M	3M	4M
Behaviour Underactive	1	0	10	10	10
	2	0	10	10	10
	3	0	10	10	10
	4	0	10	10	10
	5	0	10	10	10
	6	0	10	10	10
	7	0	10	10	10
	11	0	0	0	10
	14	0	0	0	10
	18	0	0	0	10
	21	0	0	0	10
	25	0	10	10	10
	28	0	10	10	10
	32	0	0	0	10
	35	0	0	0	10
	40	0	0	0	10
	47	0	0	0	10

Signs recorded during exposure on a group basis, all animals in the group assumed to have the same sign

Request ID: 284420

TABLE 3 - continued

Signs associated with dosing - group distribution of observations for males - F0 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900

Exposure level (ppm) : 0

Sign	Day Number	Group/sex and number of animals showing sign			
		1M	2M	3M	4M
Behaviour (continued...) Unresponsive	1	0	10	10	10
	2	0	0	10	10
	3	0	10	10	0
	4	0	0	0	10
	5	0	0	0	10
	6	0	0	10	10
	7	0	0	10	10
	11	0	0	0	10
	14	0	0	0	10
	18	0	0	10	10
	21	0	0	10	10
	25	0	0	10	10
	32	0	0	0	10
	40	0	0	0	10
47	0	0	0	10	

Signs recorded during exposure on a group basis, all animals in the group assumed to have the same sign

Request ID: 284420

TABLE 3 - continued

Signs associated with dosing - group distribution of observations for males - F0 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900

Exposure level (ppm) : 0

Sign	Day Number	Group/sex and number of animals showing sign			
		1M	2M	3M	4M
Breathing Shallow	1	0	0	0	10
	2	0	0	0	10
	3	0	0	0	10
	4	0	0	0	10
	5	0	0	0	10
	6	0	0	0	10
	7	0	0	0	10
Slow	14	0	0	10	10
	25	0	0	10	10
	28	0	0	0	10
	35	0	0	10	10
	40	0	0	0	10

Signs recorded during exposure on a group basis, all animals in the group assumed to have the same sign

TABLE 3 - continued

Request ID: 284420

Signs associated with dosing - group distribution of observations for males - F0 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900
 Compound :
 Exposure level (ppm) : 0

Sign	Day Number	Group/sex and number of animals showing sign			
		1M	2M	3M	4M
Coat Piloerection	1	0	0	10	10
	2	0	10	10	10
	3	0	10	10	10
	4	0	10	10	10
	5	0	10	10	10
	6	0	10	10	10
	7	0	10	10	10
	14	0	10	10	10
	18	0	0	10	10
	21	0	0	10	10
	25	0	10	0	0
	28	0	10	10	10
	32	0	0	10	10
	35	0	1	10	0
40	0	0	10	10	
47	0	0	10	10	
Eye (Left) Lachrymation	1	0	0	10	0
	1	0	0	10	0
Eye (Right) Lachrymation	1	0	0	10	0
	1	0	0	10	0

Signs recorded during exposure on a group basis, all animals in the group assumed to have the same sign

Request ID: 284420

TABLE 3 - continued

Signs associated with dosing - group distribution of observations for males - F0 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900

Exposure level (ppm) : 0

Sign	Day Number	Group/sex and number of animals showing sign			
		1M	2M	3M	4M
Eyelids (Left) Partially Closed	1	0	0	10	10
	3	0	0	10	10
	4	0	0	10	10
	5	0	0	10	10
	6	0	0	0	10
	7	0	0	0	10
	11	0	0	10	10
	14	0	10	10	10
	18	0	0	0	10
	21	0	0	0	10
	25	0	0	0	10
	28	0	0	0	10
	35	0	0	10	10
	40	0	0	0	10
	47	0	0	0	10

Signs recorded during exposure on a group basis, all animals in the group assumed to have the same sign

Request ID: 284420

TABLE 3 - continued

Signs associated with dosing - group distribution of observations for males - F0 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900

Exposure level (ppm) : 0

Sign	Day Number	Group/sex and number of animals showing sign			
		1M	2M	3M	4M
Eyelids (Right) Partially Closed	1	0	0	10	10
	3	0	0	10	10
	4	0	0	10	10
	5	0	0	10	10
	6	0	0	0	10
	7	0	0	0	10
	11	0	0	10	10
	14	0	10	10	10
	18	0	0	0	10
	21	0	0	0	10
	25	0	0	0	10
	28	0	0	0	10
	35	0	0	10	10
	40	0	0	0	10
47	0	0	0	10	

Signs recorded during exposure on a group basis, all animals in the group assumed to have the same sign

Request ID: 284421

TABLE 3 - continued

Signs associated with dosing - group distribution of observations for females before pairing - F0 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900

Exposure level (ppm) : 0

Sign	Day Number	Group/sex and number of animals showing sign			
		1F	2F	3F	4F
Behaviour Underactive	1	0	10	10	10
	2	0	10	10	10
	3	0	10	10	10
	4	0	10	10	10
	5	0	10	10	10
	6	0	10	10	10
	7	0	10	10	10
	8	0	0	0	0
	11	0	0	0	0
	14	0	0	0	0
	18	0	0	0	0
	21	0	0	0	0
	25	0	0	0	0
	28	0	0	0	0
	32	0	0	0	0
	35	0	0	0	0
	40	0	0	0	0
47	0	0	0	0	

Signs recorded during exposure on a group basis, all animals in the group assumed to have the same sign

TABLE 3 - continued

Request ID: 284421

Signs associated with dosing - group distribution of observations for females before pairing - F0 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900

Exposure level (ppm) : 0

Sign	Day Number	Group/sex and number of animals showing sign			
		1F	2F	3F	4F
Behaviour (continued...) Unresponsive	1	0	10	10	10
	2	0	0	10	10
	3	0	10	10	0
	4	0	0	0	10
	5	0	0	0	10
	6	0	0	10	10
	7	0	0	10	10
	8	0	0	0	3
	11	0	0	0	10
	14	0	0	0	10
	18	0	0	9	8
	21	0	0	1	6
	25	0	0	0	4
	32	0	0	0	3
40	0	0	0	3	
47	0	0	0	3	

Signs recorded during exposure on a group basis, all animals in the group assumed to have the same sign

Request ID: 284421

TABLE 3 - continued

Signs associated with dosing - group distribution of observations for females before pairing - F0 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900
 Compound :
 Exposure level (ppm) : 0

Sign	Day Number	Group/sex and number of animals showing sign			
		1F	2F	3F	4F
Breathing Shallow	1	0	0	0	10
	2	0	0	0	10
	3	0	0	0	10
	4	0	0	0	10
	5	0	0	0	10
	6	0	0	0	10
	7	0	0	0	10
Slow	14	0	0	10	10
	25	0	0	0	4
	28	0	0	0	3
	35	0	0	0	3
	40	0	0	0	3

Signs recorded during exposure on a group basis, all animals in the group assumed to have the same sign

Request ID: 284421

TABLE 3 - continued

Signs associated with dosing - group distribution of observations for females before pairing - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Sign	Day Number	Group/sex and number of animals showing sign			
		1F	2F	3F	4F
Coat Piloerection	1	0	0	10	10
	2	0	10	10	10
	3	0	10	10	10
	4	0	10	10	10
	5	0	10	10	10
	6	0	10	10	10
	7	0	10	10	10
	8	0	0	0	3
	11	0	10	0	0
	14	0	10	10	10
	18	0	0	9	8
	21	0	0	1	6
	25	0	1	0	0
	28	0	0	0	3
	32	0	0	0	3
40	0	0	0	3	
47	0	0	0	3	
Eye (Left) Lachrymation	1	0	0	10	0

Signs recorded during exposure on a group basis, all animals in the group assumed to have the same sign

Request ID: 284421

TABLE 3 - continued

Signs associated with dosing - group distribution of observations for females before pairing - F0 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900
 Exposure level (ppm) : 0

Sign	Day Number	Group/sex and number of animals showing sign			
		1F	2F	3F	4F
Eye (Right) Lachrymation	1	0	0	10	0
Eyelids (Left) Partially Closed	1	0	0	10	10
	3	0	0	10	10
	4	0	0	10	10
	5	0	0	10	10
	6	0	0	0	10
	7	0	0	0	10
	8	0	0	0	3
	11	0	0	10	10
	14	0	10	10	10
	18	0	0	0	8
	21	0	0	0	6
	25	0	0	0	4
	28	0	0	0	3
	35	0	0	0	3
40	0	0	0	3	
47	0	0	0	3	

Signs recorded during exposure on a group basis, all animals in the group assumed to have the same sign

Request ID: 284421

TABLE 3 - continued

Signs associated with dosing - group distribution of observations for females before pairing - F0 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900

Exposure level (ppm) : 0

Sign	Day Number	Group/sex and number of animals showing sign			
		IF	2F	3F	4F
Eyelids (Right) Partially Closed	1	0	0	10	10
	3	0	0	10	10
	4	0	0	10	10
	5	0	0	10	10
	6	0	0	0	10
	7	0	0	0	10
	8	0	0	0	3
	11	0	0	10	10
	14	0	10	10	10
	18	0	0	0	8
	21	0	0	0	6
	25	0	0	0	4
	28	0	0	0	3
	35	0	0	0	3
40	0	0	0	3	
47	0	0	0	3	
Posture Hunched	8	0	0	0	3
	8	0	0	0	3
Staining Other Colour (see comment)	8	0	0	0	3
	8	0	0	0	3

Signs recorded during exposure on a group basis, all animals in the group assumed to have the same sign

Request ID: 284422

TABLE 3 - continued

Signs associated with dosing - group distribution of observations for females after mating - F0 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900

Exposure level (ppm) : 0

Sign	Group/sex and number of animals showing sign			
	IF	2F	3F	4F
Behaviour Underactive	0	3	6	5
	7	5	10	7
	14	3	10	7
	19	0	10	7
Unresponsive	0	0	2	5
	7	0	6	2
	14	0	0	5
	19	0	1	2
Breathing Shallow	0	0	1	0
	0	0	5	2
	7	0	7	6
Slow	14	0	5	2
	19	0	10	6

Signs recorded during exposure on a group basis, all animals in the group assumed to have the same sign

Request ID: 284422

TABLE 3 - continued

Signs associated with dosing - group distribution of observations for females after mating - F0 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900

Exposure level (ppm) : 0

Sign	Day Number	Group/sex and number of animals showing sign			
		IF	2F	3F	4F
Coat					
Piloerection	0	0	3	1	4
	7	0	9	3	3
	14	0	1	7	6
	19	0	5	5	3
Eyelids (Left)					
Partially Closed	0	0	0	5	5
	7	0	0	5	7
	14	0	0	5	3
	19	0	0	8	6
Eyelids (Right)					
Partially Closed	0	0	0	5	5
	7	0	0	5	7
	14	0	0	5	3
	19	0	0	8	6
Muscle Reaction					
Reduced Body Tone	14	0	0	0	1
Posture					
Hunched	14	0	0	0	1

Signs recorded during exposure on a group basis, all animals in the group assumed to have the same sign

Request ID: 284423

TABLE 3 - continued

Signs associated with dosing - group distribution of observations for females during lactation - F0 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900

Exposure level (ppm) : 0

Sign	Day Number	Group/sex and number of animals showing sign			
		1F	2F	3F	4F
Behaviour Underactive	5	0	0	2	-
	9	0	0	4	-
Coat Piloerection	5	0	0	2	-

Signs recorded during exposure on a group basis, all animals in the group assumed to have the same sign

Request ID: 284760

TABLE 4

Bodyweight and bodyweight change - group mean values for males - F0 generation (g)

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900

Exposure level (ppm) : 0

Group /Sex	Day -7	Day 1	Day 8	Day 11	Day 15	Day 22	Day 29	Day 33	Day 36	Day 39	Day 43	Day 46
Statistical test:	Wi	Wi	Wi	Wi	Wi	Wi	Wi	Wi	Wi	Wi	Wi	Wi
1M	Mean 259	329	380	395	420	444	471	487	498	503	517	528
	SD 7.7	9.4	13.4	17.8	21.0	26.8	26.4	29.5	30.6	30.3	29.9	29.5
	N 10	10	10	10	10	10	10	10	10	10	10	10
2M	Mean 254	319	361*	375*	393*	420	443*	452*	460*	465*	469**	476**
	SD 9.4	12.8	27.2	33.6	39.5	44.1	47.6	48.8	52.1	51.7	49.9	52.1
	N 10	10	10	10	10	10	10	10	10	10	10	10
3M	Mean 256	322	349**	357**	376**	398**	415**	426**	434**	437**	441**	449**
	SD 6.6	8.0	12.3	14.7	16.8	19.5	20.3	22.2	22.3	22.8	26.9	27.3
	N 10	10	10	10	10	10	10	10	10	10	10	10
4M	Mean 253	325	342**	355**	368**	386**	406**	409**	414**	415**	419**	421**
	SD 9.4	12.1	16.0	17.2	20.4	19.0	21.7	24.0	22.5	26.1	26.5	30.9
	N 10	10	10	10	10	10	10	10	10	10	10	10

Pairing commenced Day 15

Request ID: 284760

TABLE 4 - continued

Bodyweight and bodyweight change - group mean values for males - F0 generation (g)

Group Compound	Exposure level (ppm)	1		2		3		4	
		Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900				
Group /Sex	Day	Change 1-15		Change 15-50		Change 1-50		As % of Control	
Statistical test:	50	Wi	Wi	Wi	Wi	Wi	Wi	Wi	Wi
1M	Mean	542	91	-	121	-	212	-	-
	SD	33.0	15.4	-	19.9	-	27.9	-	-
	N	10	10	-	10	-	10	-	-
2M	Mean	483**	74	81	90**	74	164**	77	77
	SD	52.0	30.6	-	17.4	-	44.0	-	-
	N	10	10	-	10	-	10	-	-
3M	Mean	455**	54**	60	79**	65	133**	63	63
	SD	27.4	13.7	-	15.4	-	22.1	-	-
	N	10	10	-	10	-	10	-	-
4M	Mean	424**	43**	47	56**	46	99**	47	47
	SD	31.9	14.3	-	19.1	-	29.3	-	-
	N	10	10	-	10	-	10	-	-

Pairing commenced Day 15

Request ID: 284761

TABLE 5 - continued

Bodyweight and bodyweight change - group mean values for females before pairing - F0 generation (g)

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Day	Day	Change		As % of Control
			1-15	Wi	
IF	Mean	50	53	20	-
	SD			7.1	
	N			10	
2F	Mean			24	121
	SD			10.3	
	N			10	
3F	Mean			19	95
	SD			6.5	
	N			10	
4F	Mean	250	253	4**	19
	SD	7.9	9.8	14.7	
	N	3	3	10	

Pairing commenced Day 15

Request ID: 284780

TABLE 6

Bodyweight and bodyweight change - group mean values for females during gestation - F0 generation (g)

Group Compound	Exposure level (ppm)	1 Control		2 2-bromo-3,3,3-trifluoropropene 198		3 2-bromo-3,3,3-trifluoropropene 505		4 2-bromo-3,3,3-trifluoropropene 2900		Change 0-10	As % of Control	Change 10-20	As % of Control
		Day	Wi	Day	Wi	Day	Wi	Day	Wi				
1F	Mean	256	273	294	327	360	410	49	106	-	-	-	-
	SD	12.4	14.2	18.4	19.8	21.9	26.2	8.3	14.4				
	N	10	10	10	10	10	10	10	10				
2F	Mean	255	272	286	317	347	397	41	100	85	85	100	95
	SD	13.0	13.4	17.4	23.1	28.8	38.5	15.5	26.4				
	N	9	9	9	9	9	9	9	9				
3F	Mean	249	265	277*	312	333*	377*	38	90	78	78	90	85
	SD	9.9	8.7	9.8	11.9	15.4	22.7	8.6	18.7				
	N	9	9	9	9	9	9	9	9				
4Fa	Mean	227	234	239	272	281	316	21	68	43	43	68	64
	N	1	1	1	1	1	1	1	1			1	
4Fb	Mean	239	254	260	285	293	305	33	33	67	67	33	31
	SD	15.3	10.1	14.5	14.3	13.3	17.0	12.4	26.2				
	N	6	6	6	6	6	6	6	6			6	6

a Mean of females which littered, not included in statistical evaluation
 b Mean of all pregnant females, not included in statistical evaluation
 Treatment withdrawn after Day 19 of gestation

Request ID: 284780

TABLE 6 - continued

Bodyweight and bodyweight change - group mean values for females during gestation - F0 generation (g)

Group	1	2	3	4
Compound	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	0	v	500	3000
Group /Sex	Change 0-20	As % of Control		
Statistical test:	Wi			
1F	Mean 154	-		
	SD 18.4			
	N 10			
2F	Mean 142	92		
	SD 27.7			
	N 9			
3F	Mean 128*	83		
	SD 16.3			
	N 9			
4Fa	Mean 89	58		
	N 1			
4Fb	Mean 66	43		
	SD 30.1			
	N 6			

a Mean of females which littered, not included in statistical evaluation

b Mean of all pregnant females, not included in statistical evaluation

Treatment withdrawn after Day 19 of gestation

Request ID: 284763

TABLE 7

Bodyweight and bodyweight change - group mean values for females during lactation - F0 generation (g)

Group /Sex	Day 1		Day 5		Day 10		Change 1-5		Change 5-10		Change 1-10		As % of Control
	Wi	N	Wi	N	Wi	N	Wi	N	Wi	N	Wi	N	
1F	Mean	304	322	341	18	20	-	-	-	-	37	-	-
	SD	19.4	26.2	23.2	12.9	12.5	-	-	-	14.7	-	-	-
	N	10	10	10	10	10	10	10	10	10	10	10	10
2F	Mean	300	311	322	11	11	61	57	22*	59	9.6	59	59
	SD	20.0	23.2	27.1	9.2	10.5	9	9	9	9	9	9	9
	N	9	9	9	9	9	9	9	9	9	9	9	9
3F	Mean	292	299	297**	7	7	42	-	-2**	13	5**	13	13
	SD	12.3	6.8	15.2	6.7	13.7	4	4	4	4	15.8	4	4
	N	4	4	4	4	4	4	4	4	4	4	4	4

Treatment reintroduced Day 5 of lactation

Request ID: 284799

TABLE 8

Food consumption - group mean values for males and females before pairing - F0 generation (g/animal/week)

Group /Sex	Mean	SD	N	Week -1		Week 1		Week 2		Week 3		Week 4	
				As % of Control									
1M	207	8.3	2	-	220	10.9	2	212	10.3	2	216	10.6	2
2M	198	3.1	2	87	191	9.5	2	190	19.3	2	191	14.4	2
3M	200	3.8	2	74	162	7.9	2	165	1.9	2	164	4.9	2
4M	204	8.9	2	88	149	5.4	2	179	8.6	2	164	7.0	2

Request ID: 284799

TABLE 8 - continued

Food consumption - group mean values for males and females before pairing - F0 generation (g/animal/week)

Group Compound	Exposure level (ppm)	1		2		3		4	
		Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	
		0	v	v	v	v	v	v	v
		3000	500	500	500	500	500	500	3000
Group /Sex		Week -1	Week 1	Week 2	Week 2	Week 2	Week 2	Week 1-2	As % of Control
1F	Mean	137	133	-	130	-	132	-	-
	SD	2.6	2.1		1.6		1.9		
	N	2	2		2		2		
2F	Mean	137	117	88	124	95	121	92	92
	SD	0.1	0.4		2.7		1.6		
	N	2	2		2		2		
3F	Mean	136	101	76	114	88	108	82	82
	SD	1.1	0.5		1.5		0.5		
	N	2	2		2		2		
4F	Mean	138	86	65	98	75	92	70	70
	SD	8.9	5.7		4.1		4.9		
	N	2	2		2		2		

Request ID: 284781

TABLE 9

Food consumption - group mean values for females during gestation - F0 generation (g/animal/day)

Group Compound	1		2		3		4	
	Control		2-bromo-3,3,3-trifluoropropene 198		2-bromo-3,3,3-trifluoropropene 505		2-bromo-3,3,3-trifluoropropene 2900	
Exposure level (ppm)	0		0		0		0	
Group /Sex	Day 0-2	Day 3-6	Day 7-9	Day 10-13	Day 14-16	Day 17-19	Day 0-19	As % of Control
Statistical test:	Wi	Wi	Wi	Wi	Wi	Wi	Wi	
1F	Mean 24	26	26	27	28	29	27	-
	SD 3.5	3.3	2.9	2.9	3.1	3.5	2.6	
	N 10	10	10	10	10	10	10	
2F	Mean 22	21**	21**	25*	25	30	24*	90
	SD 2.4	2.9	3.3	2.3	3.6	3.2	2.1	
	N 9	9	9	9	9	9	9	
3F	Mean 21	22**	22**	24**	24**	29	24**	89
	SD 1.7	1.9	2.6	1.9	2.2	1.1	1.5	
	N 9	9	9	9	9	9	9	
4Fa	Mean 15	16	17	20	21	29	20	74
	N 1	1	1	1	1	1	1	
4Fb	Mean 19	19	20	21	21	24	21	78
	SD 2.0	2.8	1.6	2.2	3.3	3.3	1.4	
	N 6	6	6	6	6	6	6	

a Mean of females which littered, not included in statistical evaluation
b Mean of all pregnant females, not included in statistical evaluation

Request ID: 285999

TABLE 10

Food consumption - group mean values for females during lactation - F0 generation (g/animal/day)

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Day 1-4	Day 5-9	Day 1-9		As % of Control
			Wi	Wi	
Statistical test:					
1F	Mean	40	56	49	-
	SD	4.4	5.1	4.6	
	N	10	10	10	
2F	Mean	31**	39***	35**	73
	SD	5.6	6.2	5.7	
	N	9	9	9	
3F	Mean	28**	30**	29**	60
	SD	5.0	4.9	4.9	
	N	4	4	4	

Treatment reintroduced Day 5 of lactation

TABLE 11

Water consumption - group mean values for males and before pairing for females - F0 generation (mL/animal/day)

Group Compound : : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm) : 0

Group /Sex	Animal Number	Week 2	Week 5	Week 6§	Week 7
1M	Mean	45	41	42	42
	SD	3.5	1.4	4.2	2.1
	N	2	2	2	2
2M	Mean	43	38	40	37
	SD	8.5	6.4	7.8	5.7
	N	2	2	2	2
3M	Mean	44	40	42	40
	SD	2.8	0.0	0.0	0.7
	N	2	2	2	2
4M	Mean	47	39	39	39
	SD	0.0	2.1	4.9	4.2
	N	2	2	2	2

Calculated for 3 days/week

§ Calculated over a one day period Week 6 in error, Week 7 consumption recorded over a 6 day period to provide additional data

TABLE 11 - continued

Water consumption - group mean values for males and before pairing for females - F0 generation (mL/animal/day)

Group	1	2	3	4
Compound	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	0			
Group /Sex	Animal Number	Week 2	As % of Control	
1F	Mean	29	-	
	SD	0.0		
	N	2		
2F	Mean	34	117	
	SD	0.0		
	N	2		
3F	Mean	46	159	
	SD	2.1		
	N	2		
4F	Mean	50	172	
	SD	9.9		
	N	2		

Calculated for 3 days/week

TABLE 12

Water consumption - group mean values for females during gestation - F0 generation (mL/animal/day)

Group Compound	Exposure level (ppm)	1		2		3		4					
		Day											
1F	0	1	2	3	4	5	6	7	8	9	10	11	12
Mean	51	67	62	52	53	58	56	58	58	61	68	63	64
SD	18.3	10.7	10.9	13.2	9.2	11.2	9.0	9.2	8.9	10.3	10.5	9.9	10.5
N	10	10	10	10	10	10	10	10	10	10	10	10	9
2F	43	56	66	67	61	63	64	69	67	68	74	72	74
Mean	13.4	17.0	22.3	13.9	15.7	15.7	14.2	10.6	13.3	12.5	10.3	13.1	14.1
SD	9	9	9	9	9	9	9	9	9	9	9	9	9
N	9	9	9	9	9	9	9	9	9	9	9	9	9
3F	54	63	67	62	59	65	62	63	64	69	80	78	73
Mean	13.7	15.5	15.5	17.6	15.7	16.5	13.2	11.2	12.1	13.5	8.4	9.4	16.7
SD	9	9	9	9	9	9	9	9	9	9	9	9	9
N	9	9	9	9	9	9	9	9	9	9	9	9	9
4Fa	34	42	75	80	68	51	70	73	68	74	57	79	43
Mean	1	1	1	1	1	1	1	1	1	1	1	1	1
N	1	1	1	1	1	1	1	1	1	1	1	1	1
4Fb	60	63	74	70	62	63	65	67	63	68	73	84	69
Mean	14.5	19.9	11.9	13.3	8.9	12.8	10.7	14.5	12.4	16.3	12.8	11.8	16.8
SD	6	6	6	6	6	6	6	6	6	6	6	6	5
N	6	6	6	6	6	6	6	6	6	6	6	6	5

a Mean of females which littered, not included in statistical evaluation

b Mean of all pregnant females, not included in statistical evaluation

TABLE 12 - continued

Water consumption - group mean values for females during gestation - F0 generation (mL/animal/day)

Group	/Sex	1		2		3		4	
		Day	Day	Day	Day	Day	Day	Day	Day
Compound		Control	2-bromo-3,3,3-trifluoropropene						
Exposure level (ppm)		0	198	505	505	505	505	2900	2900
		13	14	15	16	17	18	0-2	3-5
		69	65	68	68	72	74	60	54
1F	Mean	8.6	7.6	10.4	9.8	9.6	9.0	10.5	8.4
	SD	10	10	10	10	10	10	10	10
	N	77	78	77	82	75	67	55	64
2F	Mean	11.0	11.3	13.7	16.2	12.9	10.1	15.7	12.6
	SD	9	9	9	9	9	9	9	9
	N	87	82	86	91	91	89	61	62
3F	Mean	14.2	16.6	20.4	5.7	11.2	11.1	13.4	14.5
	SD	9	9	9	9	9	9	9	9
	N	44	47	74	53	49	47	50	66
4Fa	Mean	1	1	1	1	1	1	1	1
	N	74	72	90	85	70	74	66	65
4Fb	Mean	19.9	16.4	14.0	18.2	21.4	22.5	10.1	9.6
	SD	6	6	6	6	6	6	6	6
	N	69	64	68	65	65	67	63	62
		10	10	10	10	10	10	10	10
		77	71	76	75	75	77	70	70
		79	82	82	82	82	82	82	82
		12.0	9	9	9	9	9	9	9
		9	9	9	9	9	9	9	9
		91	76	82	76	76	82	63	62
		8.2	6.9	15.5	6.9	6.9	15.5	11.8	14.5
		9	9	9	9	9	9	9	9
		51	52	52	52	52	52	50	66
		1	1	1	1	1	1	1	1
		77	77	77	75	75	77	66	65
		18.2	14.2	14.2	6.3	6.3	14.2	10.1	9.6
		6	6	6	6	6	6	6	6

a Mean of females which littered, not included in statistical evaluation

b Mean of all pregnant females, not included in statistical evaluation

TABLE 13

Water consumption - group mean values for females during lactation - F0 generation (mL/animal/day)

Group /Sex	Animal Number	1		2		3		4		5		6		7		8		9		Days		
		Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	Day 15	Day 16	Day 17	Day 18	Day 19	Day 20	
1F	Mean	71	75	63	80	88	89	90	105	100	92											
	SD	29.2	30.8	11.8	21.4	13.8	12.2	13.0	10.1	17.9	10.6											
	N	10	10	10	10	10	10	10	10	10	10											
2F	Mean	63	76	57	52	67	82	76	84	93	65											
	SD	39.8	37.1	23.1	12.9	11.6	66.8	12.5	20.2	18.4	11.8											
	N	9	9	9	9	9	9	9	9	9	9											
3F	Mean	33	44	54	64	53	70	79	86	74	44											
	SD	6.3	8.5	13.1	12.3	13.6	27.6	12.1	8.4	19.5	8.4											
	N	4	4	4	4	4	4	4	4	4	4											

TABLE 14 - continued

Oestrous cycles - incidence of specific cycle lengths - group values - F0 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900

Exposure level (ppm) : 0

Group	Number of animals	Number of cycles				Cycle length (days)			
		1	2	3	4	5	6-10	11-20	
1	10	39	0	0	32	7	0	0	
		n (%)			(82)	(18)			
2**	10	33	0	0	10	23	0	0	
		n (%)			(30)	(70)			
3**	10	33	0	0	6	20	6	1	
		n (%)			(18)	(61)	(18)	(3)	
4**	10	28	1	0	1	8	13	5	
		n (%)	(4)		(4)	(29)	(46)	(18)	

Statistical test: Lt

n Number of cycles in category

TABLE 15

Pre-coital interval - group values - F0 generation

Group Compound	: 1 Control	: 2 2-bromo-3,3,3-trifluoropropene 198	: 3 2-bromo-3,3,3-trifluoropropene 505	: 4 2-bromo-3,3,3-trifluoropropene 2900	Exposure level (ppm)	Number of animals			
						1-4	5-8	9-12	13-14
Group									
1	n (%)	9 (90)	1 (10)	0					
2	n (%)	9 (90)	0	1 (10)					
3	n (%)	7 (70)	3 (30)	0					
4	n (%)	4 (57)	2 (29)	1 (14)					

Statistical test: Lt

TABLE 16

Number of copulation plugs at mating - group values - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group	Number of animals	Number of copulation plugs			
		1	2	3	4 - 6
1	10	0	0	2	8
		n (%)		(20)	(80)
2	10	1	1	1	7
		n (%)	(10)	(10)	(70)
3*	10	1	1	6	2
		n (%)	(10)	(60)	(20)
4*	7	0	2	3	2
		n (%)	(29)	(43)	(29)

Historical control data ^a

288	%	0.4	7.6	15.6	72.7
-----	---	-----	-----	------	------

^a From 29 studies of similar type and age at pairing

TABLE 17

Sperm count estimates from vaginal smears at mating - group values - F0 generation

Group Compound	1 Control	2 2-bromo-3,3,3- trifluoropropene 198	3 2-bromo-3,3,3- trifluoropropene 505	4 2-bromo-3,3,3- trifluoropropene 2900
Exposure level (ppm)	0			
	Number of animals			
Group	0	1	2	3
Statistical test: Lt				
1	1 (10)	0	1 (10)	2 (20)
2	0	3 (30)	2 (20)	4 (40)
3	4 (40)	1 (10)	1 (10)	2 (20)
4	0	0	2 (29)	4 (57)
	n (%)	n (%)	n (%)	n (%)

- ⊖
- 0 No sperm
 - 1 Occasional sperm
 - 2 Continuous few sperm
 - 3 Many scattered sperm
 - 4 Solid masses of sperm

TABLE 18

Mating performance and fertility - group values - F0 generation

Group and sex	Group 1		Group 2		Group 3		Group 4	
	Number paired	Number mating	Number achieving pregnancy	Percentage mating	Conception rate (%)	Fertility index (%)	Number paired	Number mating
Compound		Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene		
Exposure level (ppm)		0	198	505	2900			
Group and sex								
1M	10	10	10	100	100	100		
2M	10	10	9	100	90	90		
3M	10	10	10	100	100	100		
4M	10	7	6	70*	86	60*		
1F	10	10	10	100	100	100		
2F	10	10	9	100	90	90		
3F	10	10	10	100	100	100		
4F	10	7	6	70*	86	60*		

TABLE 19

Gestation length and gestation index - group values - F0 generation

Group Compound	: 1 : Control	: 2 2-bromo-3,3,3- trifluoropropene 198	: 3 2-bromo-3,3,3- trifluoropropene 505	: 4 2-bromo-3,3,3- trifluoropropene 2900	Gestation length (days)						Number of live litters born	Gestation index (%)	
					22	22.5	23	23.5	24	24.5			25
Exposure level (ppm)	0												
Group	n	n	n	n	n	n	n	n	n	n	n	n	n
Statistical test:	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
1	10	6 (60)	3 (10)	0	0	0	0	0	0	0	0	10	100
2**	9	0	4 (44)	5 (56)	0	0	0	0	0	0	0	9	100
3**	10	0	1 (11)	3 (33)	0	2 (22)	1 (11)	2 (22)	2 (22)	2 (22)	2 (22)	9	90
4**	6	0	0	0	0	0	0	0	0	1 (100)	1	17**	

TABLE 20

Litter size - group mean values for litters that survived to Day 10 of lactation - F1 generation

Group	Compound	Exposure level (ppm)	Implantations	Total litter size		Live litter size on Day						
				Day 1	Sh	1	5	10	Wi	Wi	Wi	
1	Control	0	10	15.0	10	14.9	14.8	11.8**	10.6**	10.6**	14.7	14.7
				1.2	10	1.2	1.4	3.1	3.3	3.3	1.3	1.3
				10	10	10	10	9	9	9	10	10
2	2-bromo-3,3,3-trifluoropropene	198	9	12.2*	9	11.8**	10.6**	10.8**	8.5**	8.3**	10.6**	10.6**
				3.3	9	3.1	3.3	1.9	2.1	2.1	3.3	3.3
				9	9	9	9	4	4	4	9	9
3	2-bromo-3,3,3-trifluoropropene	505	4	11.8**	4	10.8**	8.5**	10.8**	8.5**	8.3**	8.3**	8.3**
				1.0	4	1.9	2.1	1.9	2.1	2.1	2.1	2.1
				4	4	4	4	4	4	4	4	4
4	2-bromo-3,3,3-trifluoropropene	2900	6	8.9**	6	11.4*	8.5**	11.4*	8.5**	8.3**	8.3**	8.3**
				4.3	6	2.2	2.1	2.2	2.1	2.1	2.1	2.1
				9	9	5	4	5	4	4	4	4
				9.5	6							
				6	6							
				12.0	1	1.0	1.0	1.0	1.0	1.0	1.0	1.0
				1#	1	1	1	1	1	1	1	1

Implantations only recorded for one female, not included in statistical evaluation. Group 4 not included in statistical analysis.

a Females surviving to Day 10 post partum

b All pregnant females/females that littered where applicable

TABLE 21

Offspring survival indices - group mean values for litters that survived to Day 10 of lactation - F1 generation

Group Compound	1 Control	2 2-bromo-3,3,3- trifluoropropene 198	3 2-bromo-3,3,3- trifluoropropene 505	4 2-bromo-3,3,3- trifluoropropene 2900
Exposure level (ppm)	0			

Group	Post implantation survival index (%)		Live birth index (%)		Viability index (%)	
	Wi	Sh	Sh	Sh	Sh	Sh
1	Mean 94.5	10	Mean 99.4	10	Mean 98.6	10
2	Mean 86.0	9	Mean 96.8	9	Mean 90.3	9
3	Mean ^a 76.8*	4	Mean 91.3	4	Mean 78.2*	4
4	Mean ^b 56.5**	10	Mean 51.7**	9	Mean 62.6**	5
	Mean ^a 25.0	1#	Mean 33.3	1#		
	Mean ^b 4.2**	6				

Implantations only recorded for one female, not included in statistical evaluation

a Females surviving to Day 10 post partum

b All pregnant females/females that littered where applicable

TABLE 22

Sex ratio - group mean values for litters that survived to Day 10 of lactation - F1 generation

Group Compound	1 Control			2 2-bromo-3,3,3-trifluoropropene 198			3 2-bromo-3,3,3-trifluoropropene 505			4 2-bromo-3,3,3-trifluoropropene 2900			
	Exposure level (ppm)	0	0	0	0	0	0	0	0	0	0		
Group	Total on Day						Live on Day						
	M	F	%M	Wa	M	F	%M	Wa	M	F	%M	Wa	
1	Mean	7.3	7.7	48.2	7.2	7.7	48.0	7.2	7.2	7.6	48.2	7.2	7.5
	SD	2.5	2.1	15.5	2.3	2.1	15.2	2.3	2.3	2.0	14.8	2.3	2.0
	n	10	10	10	10	10	10	10	10	10	10	10	10
2	Mean	6.3	5.8	51.2	6.1	5.7	50.8	5.3	5.3	5.2	49.2	5.3	5.2
	SD	2.6	1.9	12.2	2.5	1.9	13.4	2.4	2.4	1.9	12.3	2.4	1.9
	n	9	9	9	9	9	9	9	9	9	9	9	9
3	Mean	5.8	5.0	53.4	5.8	5.0	53.4	4.0	4.0	4.5	45.1	4.0	4.3
	SD	2.1	2.0	15.2	2.1	2.0	15.2	2.2	2.2	1.0	14.7	2.2	0.5
	n	4	4	4	4	4	4	4	4	4	4	4	4

TABLE 23

Bodyweight and bodyweight change - group mean values (g) for male offspring from litters surviving to Day 10 of lactation - F1 generation

Group	Compound	Exposure level (ppm)	Day of age			Change		
			1	5	10	1 to 5	1 to 10	
	Control	0						
	2-bromo-3,3,3-trifluoropropene	198						
	2-bromo-3,3,3-trifluoropropene	505						
	2-bromo-3,3,3-trifluoropropene	2900						
Group	Compound	Exposure level (ppm)	1	5	10	1 to 5	1 to 10	
1	Mean		6.8	10.9	17.5	4.1	10.7	
	SD		0.3	0.6	1.0	0.4	0.9	
	n		10	10	10	10	10	
2	Mean		7.4	11.1	17.0	3.8	9.6	
	SD		0.6	1.0	1.2	0.6	0.8	
	n		9	9	9	9	9	
3	Mean		6.9	10.6	16.0	3.7	9.1*	
	SD		0.7	1.8	2.7	1.3	2.2	
	n		4	4	4	4	4	

TABLE 24

Bodyweight and bodyweight change - group mean values (g) for female offspring from litters surviving to Day 10 of lactation - F1 generation

Group Compound	Exposure level (ppm)	Day of age				Change	
		1	5	10	1 to 5	1 to 10	
1	0	Du 6.4	Wi 10.4	Wi 16.7	Sh 4.0	Wi 10.3	
2	0	Du 0.4	Wi 0.6	Wi 1.1	Sh 0.3	Wi 0.9	
3	0	Du 10	Wi 10	Wi 10	Sh 10	Wi 10	
4	0	Du 6.9**	Wi 10.9	Wi 16.2	Sh 3.9	Wi 9.3	
5	0	Du 0.4	Wi 1.0	Wi 1.6	Sh 0.7	Wi 1.4	
6	0	Du 9	Wi 9	Wi 9	Sh 9	Wi 9	
7	0	Du 6.2	Wi 9.7	Wi 15.1	Sh 3.4	Wi 8.8	
8	0	Du 0.2	Wi 1.5	Wi 2.5	Sh 1.4	Wi 2.4	
9	0	Du 4	Wi 4	Wi 4	Sh 4	Wi 4	
10	0	Du 5.5	Wi 1	Wi 1	Sh 1	Wi 1	

@ Not mean value, presented for information only, weight of single pup on Day 1. Not included in statistical evaluation

TABLE 26

Sperm motion data - group mean values

Group	Compound	Exposure level (ppm)	1		2		3		4		Rapid (%)	Medium (%)	Slow (%)	Static (%)
			Control	0	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900	Area (um sq)	Elongation (%)	LN (%)				
				Wi	Wi	Wi	Wi	Wi	Wi	Wi	Wi	Wi	Wi	Sh
1	Mean	138	102	299	22	25	74	35	24	487	67	3	24	6
	SD	8	9	24	2	2	4	2	5	95	15	2	15	3
	n	10	10	10	10	10	10	10	10	10	10	10	10	10
2	Mean	126*	92	265**	22	27	73	36	25	506	54	5*	36	5
	SD	13	10	22	1	2	4	2	4	124	19	2	19	4
	n	10	10	10	10	10	10	10	10	10	10	10	10	10
3	Mean	119**	85*	240**	21	26	71	37	25	445	52	5*	36	8
	SD	14	13	29	2	3	3	2	2	87	25	2	22	11
	n	9	9	9	9	9	9	9	9	9	9	9	9	9
4	Mean	125**	90**	260**	22	28**	72	37	26	525	51	7**	35	8
	SD	13	13	31	1	1	4	2	4	155	13	2	10	4
	n	10	10	10	10	10	10	10	10	10	10	10	10	10

TABLE 27

Sperm morphology - group mean values

Group Compound	Exposure level (ppm)	: 1 Control	: 2 2-bromo-3,3,3-trifluoropropene 198	: 3 2-bromo-3,3,3-trifluoropropene 505	: 4 2-bromo-3,3,3-trifluoropropene 2900	Normal		Total abnormal		Decapitate		Head abnormal		Detached/broken neck/midpiece/tail		Other abnormality		
						number	%	number	%	number	%	number	%	number	%	number	%	number
1	10	2000	197	98.6	3	1.5	1.4	0.7	1.0	0.5	0.2	0.1	0.4	0.2				
			Mean															
			SD															
2	10	2013	194	96.6	7	3.4**	3.0	1.5	3.0	1.5	0.6	0.3	0.4	0.2				
			Mean															
			SD															
3	8	1600	192	95.8*	8	4.2**	4.8	2.4	2.6	1.3	1.3	0.6*	0.1	0.1				
			Mean															
			SD															
4	10	2000	181	90.3**	20	9.8**	10.3	5.2**	6.8	3.4**	2.7	1.4**	1.2	0.6**				
			Mean															
			SD															

Statistical test:

Sh

Sh

Sh

Sh

IWi

Sh

Sh

Sh

Wi

Request ID: 284533

TABLE 28

Organ weights - group mean unadjusted and adjusted values (g) for males - F0 generation

Group Compound	1		2		3		4	
	Control	2-bromo-3,3,3-trifluoropropene						
Exposure level (ppm)	:	0	198	505	2900			
Group /Sex	Terminal Bodyweight	Epididymides	Pituitary	Prostate	Seminal Vesicles	Testes		
Unadjusted Means								
Statistical test:								
1M	Mean	Sh	Wi	0.015	1.364	1.667	3.59	
	SD	1.337	543	0.002	0.165	0.406	0.26	
	N	0.120	32	10	10	10	10	
2M	Mean	1.269	483**	0.011	1.008	1.357	3.68	
	SD	0.048	54	0.002	0.078	0.320	0.20	
	N	10	10	10	10	10	10	
3M	Mean	1.214	453**	0.011	0.937	1.128	3.50	
	SD	0.147	28	0.002	0.249	0.173	0.48	
	N	10	10	10	10	10	10	
4M	Mean	1.164**	423**	0.009	0.625	1.125	3.46	
	SD	0.056	30	0.002	0.169	0.277	0.23	
	N	10	10	10	10	10	10	
Adjusted Means								
Statistical test:								
1M	Mean	Wi	Wi	Wi	Wi	Wi	Wi	
	Mean	0.013	1.297	1.627	1.627	1.627	3.55	
	Mean	0.011*	1.000**	1.352	1.352	1.352	3.67	
	Mean	0.011*	0.960**	1.142*	1.142*	1.142*	3.52	
	Mean	0.010*	0.677**	1.156*	1.156*	1.156*	3.49	

Request ID: 289375

TABLE 29

Macropathology - group distribution of findings for males - F0 generation

Group Compound	: 1 Control	: 2 2-bromo-3,3,3-trifluoropropene 198	: 3 2-bromo-3,3,3-trifluoropropene 505	: 4 2-bromo-3,3,3-trifluoropropene 2900	Group/Sex:			
					1M	2M	3M	4M
Exposure level (ppm)	: 0				Number Examined:			
					10	10	10	10
Prostate								
Small					0	1	7	10
Lt. epididymis								
Small					0	0	1	0
Lt. testis								
Prominent tubules					0	0	1	0
Small					0	0	1	0
Teeth								
Incisor(s) pale					1	0	6	10
Spleen								
Adhesions					0	2	3	4
Capsule thickened					0	8	6	9
Skin								
Hair loss					0	1	2	4
Scab(s)					0	0	1	0

Request ID: 289377

TABLE 29 - continued

Macropathology - group distribution of findings for decedent females - F0 generation

Group	1	2	3	4	
Compound	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	
Exposure level (ppm)	0	198	505	2900	
Tissue and Finding	Group/Sex: IF 2F 3F 4F				
	Number Examined:				
Teeth					
Incisor(s) pale					2
Spleen					
Adhesions					1
Kidneys					
Pale area(s)					1
Pelvic dilatation					1

Request ID: 289386

TABLE 29 - continued

Macropathology - group distribution of findings for females killed after scheduled treatment period - F0 generation

Group	1	2	3	4	Group/Sex:			
					1F	2F	3F	4F
Compound	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	10	10	9	8
Exposure level (ppm)	0	198	505	2900	Number Examined:			
Tissue and Finding								
Ovaries								
Cyst(s)					0	0	1	0
Vagina								
Abnormal contents					0	0	0	1
Teeth								
Incisor(s) pale					0	0	3	8
Spleen								
Adhesions					0	0	1	4
Capsule thickened					0	0	2	3
Enlarged					0	0	0	1
Skin								
Hair loss					2	2	0	0
Kidneys								
Irregular surface					0	0	0	1
Pale area(s)					0	0	0	1
Pelvic dilatation					0	1	0	1

Request ID: 289386

TABLE 29 - continued

Macropathology - group distribution of findings for females killed after scheduled treatment period - F0 generation

Group	1	2	3	4
Compound	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	0	198	505	2900
Tissue and Finding	Group/Sex: IF 2F 3F 4F			
	Number Examined: 10 10 9 8			
Stomach				
Cyst(s)		0	1	0
Liver				
Pale		0	0	1

Request ID: 289378

TABLE 29 - continued

Macropathology - group distribution of findings for all females - F0 generation

Group	1	2	3	4	Group/Sex:											
Compound	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	Number Examined:											
Exposure level (ppm)	0	198	505	2900	1F	2F	3F	4F	1F	2F	3F	4F	1F	2F	3F	4F
Ovaries					10	10	10	10	0	0	0	0	0	0	1	0
Cyst(s)																
Vagina									0	0	0	0	0	0	0	1
Abnormal contents																
Teeth									0	0	3	10				
Incisor(s) pale																
Spleen									0	0	1	5				
Adhesions									0	0	2	3				
Capsule thickened									0	0	0	1				
Enlarged																
Skin									2	2	0	0				
Hair loss																
Kidneys									0	0	0	1				
Irregular surface									0	0	0	2				
Pale area(s)									0	1	0	2				
Pelvic dilatation									0	1	0	2				

Request ID: 289378

TABLE 29- continued

Macropathology - group distribution of findings for all females - F0 generation

Group	1	2	3	4
Compound	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	0	198	505	2900
Tissue and Finding	Group/Sex: 1F 2F 3F 4F			
	Number Examined: 10 10 10 10			
Stomach				
Cyst(s)				
Liver				
Pale				

Request ID: 289389

TABLE 30

Histopathology - group distribution of findings for males - F0 generation

Group Compound	1 Control	2 2-bromo-3,3,3-trifluoropropene 198	3 2-bromo-3,3,3-trifluoropropene 505	4 2-bromo-3,3,3-trifluoropropene 2900	Group/Sex:			
					1M	2M	3M	4M
Exposure level (ppm)	0				10	10	10	10
Tissue and Finding					10	10	10	10
Rt. Epididymis					Number Examined: 10	0	0	10
Rt. Testis					Number Examined: 10	0	0	10
Spermatocytes Degeneration					0	0	0	1
Spleen					Number Examined: 0	8	7	9
Adhesions/Inflammation/Fibrosis					0	5	4	6
Capsular Thickening					0	4	6	7
Capsular/Subcapsular Inflammation					0	8	6	7
Prostate					Number Examined: 10	10	10	10
Abscessation					0	0	1	1
Acinar Cell Atrophy					1	0	2	0
Interstitial Inflammation					2	2	3	3
Lt. Epididymis					Number Examined: 0	0	1	0
Lt. Testis					Number Examined: 0	0	1	0
Skin					Number Examined: 0	0	1	0
Epidermal Hyperplasia					0	0	1	0
Scab(s)					0	0	1	0

Request ID: 289391

TABLE 30 - continued

Histopathology - group distribution of findings for decedent females - F0 generation

Group Compound	1 Control	2 2-bromo-3,3,3- trifluoropropene 198	3 2-bromo-3,3,3- trifluoropropene 505	4 2-bromo-3,3,3- trifluoropropene 2900
Exposure level (ppm)	0			
Tissue and Finding	Group/Sex: Number:			
	1F	2F	3F	4F
Ovaries	0	0	1	2
Spleen				
Adhesions/Inflammation/Fibrosis	0	0	0	1
Capsular Thickening	0	0	0	1
Extramedullary Haemopoiesis	0	0	0	1
Kidneys				
Cortical Tubular Basophilia	0	0	0	1
Cortical Tubular Dilatation	0	0	0	1
Cortical Tubular Necrosis	0	0	0	1
Pelvic Dilatation	0	0	0	1

Request ID: 289390

TABLE 30 - continued

Histopathology - group distribution of findings for females killed after scheduled treatment period - F0 generation

Group Compound	1 Control	2 2-bromo-3,3,3-trifluoropropene 198	3 2-bromo-3,3,3-trifluoropropene 505	4 2-bromo-3,3,3-trifluoropropene 2900	Group/Sex:				
					IF	2F	3F	4F	
Exposure level (ppm)	0				10	10	10	10	8
Tissue and Finding									
Ovaries					10	10	9	8	
Cyst(s)					0	0	1	0	
Reduced Size of Corpora Lutea					0	1	0	4	
Spleen					0	0	2	6	
Adhesions/Inflammation/Fibrosis					0	0	2	4	
Capsular Thickening					0	0	2	6	
Capsular/Subcapsular Inflammation					0	0	1	4	
Extramedullary Haemopoiesis					0	0	1	2	
Kidneys					0	1	0	2	
Cortical Tubular Basophilia					0	1	0	1	
Cortical Tubular Dilatation					0	1	0	2	
Pelvic Dilatation					0	1	0	1	
Liver					0	0	0	1	
Stomach					0	1	0	0	
Squamous Cyst - Limiting Ridge					0	1	0	0	

Request ID: 289392

TABLE 30 - continued

Histopathology - group distribution of findings for all females - F0 generation

Group Compound	1 Control	2 2-bromo-3,3,3-trifluoropropene 198	3 2-bromo-3,3,3-trifluoropropene 505	4 2-bromo-3,3,3-trifluoropropene 2900	Group/Sex:								
					1F		2F		3F		4F		
Exposure level (ppm)	0				10	10	10	10	10	10	10	10	10
Tissue and Finding													
Ovaries					Number Examined:								
Cyst(s)					10	10	10	10	10	10	10	10	10
Reduced Size of Corpora Lutea					0	0	1	0	0	1	0	0	4
Spleen					Number Examined:								
Adhesions/Inflammation/Fibrosis					0	0	0	2	7				
Capsular Thickening					0	0	0	2	5				
Capsular/Subcapsular Inflammation					0	0	0	2	7				
Extramedullary Haemopoiesis					0	0	0	1	4				
Kidneys					Number Examined:								
Cortical Tubular Basophilia					0	1	0	0	3				
Cortical Tubular Dilatation					0	1	0	0	2				
Cortical Tubular Necrosis					0	1	0	0	3				
Pelvic Dilatation					0	0	0	0	1				
Liver					Number Examined:								
					0	0	0	0	1				
Stomach					Number Examined:								
Squamous Cyst - Limiting Ridge					0	1	0	0	0				
					0	1	0	0	0				

TABLE 31

Primordial ovarian follicle counts - group mean values (F0 generation)

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex		Follicle count
1F	Mean	16.8
	SD	8.94
	N	10
2F	Mean	17.9
	N	10
3F	Mean	12.3
	SD	5.78
	N	10
4F	Mean	15.4
	SD	7.13
	N	10

Request ID: 284403

APPENDIX 1

Clinical signs - individual observations for males - F0 generation

Group : 1 2 3 4
 Compound : Control 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene
 Exposure level (ppm) : 0 198 505 2900

Group /Sex	Animal Number	Death Code	Phase	Category	Observation	Week(s)
3M	222	T	Pre-treatment Treatment	Teeth	No abnormalities detected Abnormal Colour, Pale	8
	223	T	Pre-treatment Treatment	Coat	No abnormalities detected Hair loss, Head	6-8
	225	T	Pre-treatment Treatment	Teeth	No abnormalities detected Abnormal Colour, Pale	8
	229	T	Pre-treatment Treatment	Teeth	No abnormalities detected Abnormal Colour, Pale	8

T Terminal sacrifice
 Only animals with observations are presented

Request ID: 284403

APPENDIX 1 - continued

Clinical signs - individual observations for males - F0 generation

Group : 1 2 3 4
 Compound : Control 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene
 Exposure level (ppm) : 0 198 505 2900

Group /Sex	Animal Number	Death Code	Phase	Category	Observation	Week(s)
4M	231	T	Pre-treatment Treatment	Coat	No abnormalities detected Hair loss, Cervical	8
				Teeth	Hair loss, Head Abnormal Colour, Pale	6-8 7-8
	232	T	Pre-treatment Treatment	Coat	No abnormalities detected Hair loss, Head	7-8
				Teeth	Abnormal Colour, Pale	7-8
	233	T	Pre-treatment Treatment	Coat	No abnormalities detected Hair loss, Cervical	8
				Teeth	Hair loss, Head Abnormal Colour, Pale	7-8 7-8
	234	T	Pre-treatment Treatment	Coat	No abnormalities detected Hair loss, Cervical (Left)	8
				Teeth	Hair loss, Head Abnormal Colour, Pale	5-8 7-8
	235	T	Pre-treatment Treatment	Teeth	No abnormalities detected Abnormal Colour, Pale	5-8
	236	T	Pre-treatment Treatment	Teeth	No abnormalities detected Abnormal Colour, Pale	6-7

T Terminal sacrifice
 Only animals with observations are presented

Request ID: 284403

APPENDIX 1 - continued

Clinical signs - individual observations for males - F0 generation

Group Compound : 1 Control : 2 2-bromo-3,3,3-trifluoropropene 198 : 3 2-bromo-3,3,3-trifluoropropene 505 : 4 2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm) : 0

Group /Sex	Animal Number	Death Code	Phase	Category	Observation	Week(s)
4M	237	T	Pre-treatment Treatment	Teeth	No abnormalities detected Abnormal Colour, Pale	6-7
	238	T	Pre-treatment Treatment	Teeth	No abnormalities detected Abnormal Colour, Pale	5-7
	239	T	Pre-treatment Treatment	Coat Teeth	No abnormalities detected Hair loss, Head Abnormal Colour, Pale	7 5-7
	240	T	Pre-treatment Treatment	Teeth	No abnormalities detected Abnormal Colour, Pale	5-7

T Terminal sacrifice
Only animals with observations are presented

Request ID: 284404

APPENDIX 2

Clinical signs - individual observations for females - F0 generation

Group : 1 2 3 4
 Compound : Control 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene
 Exposure level (ppm) : 0 198 505 2900

Group /Sex	Animal Number	Death Code	Phase	Category	Observation	Day(s)
1F	241	T	Pre-treatment		No abnormalities detected	
			Treatment		No abnormalities detected	
			Gestation Lactation	Coat	No abnormalities detected Hair loss, Forelimbs	9-10
245	T	Pre-treatment		No abnormalities detected		
		Treatment	Behaviour	Irritable Vocalisation	12 12	
		Gestation Lactation	Coat	No abnormalities detected Hair loss, Forelimbs	5, 9-10	
247	T	Pre-treatment		No abnormalities detected		
		Treatment		No abnormalities detected		
		Gestation Lactation	Staining	No abnormalities detected Abnormal Colour, Brown, Head	10	
248	T	Pre-treatment		No abnormalities detected		
		Treatment		No abnormalities detected		
		Gestation Lactation	Coat	No abnormalities detected Hair loss, Forelimbs Hair loss, Hindlimb (Right)	10 5, 9	

T Terminal sacrifice
 Only animals with observations are presented

Request ID: 284404

APPENDIX 2 - continued

Clinical signs - individual observations for females - F0 generation

Group : 1 2 3 4
 Compound : Control 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene
 Exposure level (ppm) : 0 198 505 2900

Group /Sex	Animal Number	Death Code	Phase	Category	Observation	Day(s)
1F	250	T	Pre-treatment		No abnormalities detected	12, 19
			Treatment	Coat	Hair loss, Head	14, 20
			Gestation	Coat	Hair loss, Forelimbs	0, 7, 14, 20
			Lactation	Coat	Hair loss, Head	1, 5, 9-10
					Hair loss, Forelimbs	1, 5, 9

T Terminal sacrifice
 Only animals with observations are presented

Request ID: 284404

APPENDIX 2 - continued

Clinical signs - individual observations for females - F0 generation

Group : 1 2 3 4
 Compound : Control 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene
 Exposure level (ppm) : 0 198 505 2900

Group /Sex	Animal Number	Death Code	Phase	Category	Observation	Day(s)
2F	251	T	Pre-treatment Treatment Gestation Lactation		No abnormalities detected No abnormalities detected No abnormalities detected Abnormal Colour, Brown, Head	9-10
	252	T	Pre-treatment Treatment Gestation Lactation	Staining Coat	No abnormalities detected No abnormalities detected No abnormalities detected Hair loss, Forelimbs	10
	253	T	Pre-treatment Treatment Gestation Lactation	Coat	No abnormalities detected No abnormalities detected No abnormalities detected Hair loss, Forelimbs Hair loss, Ventral Body Surface	9-10 9-10
	255	T	Pre-treatment Treatment Gestation Lactation	Coat Coat	No abnormalities detected No abnormalities detected Hair loss, Forelimb (Right) Hair loss, Forelimb (Left) Hair loss, Forelimb (Right) Hair loss, Hindlimb (Right) Hair loss, Ventral Body Surface	20 9-10 5, 9-10 10 5, 9-10

T Terminal sacrifice
 Only animals with observations are presented

APPENDIX 2 - continued

Request ID: 284404

Clinical signs - individual observations for females - F0 generation

Group : 1 2 3 4
 Compound : Control 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene
 Exposure level (ppm) : 0 198 505 2900

Group /Sex	Animal Number	Death Code	Phase	Category	Observation	Day(s)
2F	257 NP	T	Pre-treatment Treatment Gestation	Reason for Dispatch <i>Comments:</i>	No abnormalities detected No abnormalities detected Failed to litter (non-pregnant) <i>failed to litter</i>	25 25
	258	T	Pre-treatment Treatment Gestation Lactation	Staining	No abnormalities detected No abnormalities detected No abnormalities detected Abnormal Colour, Brown, Head	9-10
	259	T	Pre-treatment Treatment Gestation Lactation	Coat	No abnormalities detected No abnormalities detected No abnormalities detected Hair loss, Forelimbs Hair loss, Ventral Body Surface	5, 9-10 10
	260	T	Pre-treatment Treatment Gestation Lactation	Staining	No abnormalities detected No abnormalities detected Abnormal Colour, Brown, Head No abnormalities detected	14, 20

T Terminal sacrifice
 NP Not pregnant
 Only animals with observations are presented

Request ID: 284404

APPENDIX 2 - continued

Clinical signs - individual observations for females - F0 generation

Group : 1 2 3 4
 Compound : Control 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene
 Exposure level (ppm) : 0 198 505 2900

Group /Sex	Animal Number	Death Code	Phase	Category	Observation	Day(s)
3F	261	T	Pre-treatment Treatment Gestation Lactation	Teeth Teeth	No abnormalities detected No abnormalities detected Abnormal Colour, Pale Abnormal Colour, Pale	14, 20 1, 5, 9-10
	262	W	Pre-treatment Treatment Gestation Lactation	Staining Other Reason for Dispatch	No abnormalities detected No abnormalities detected No abnormalities detected Abnormal Colour, Head No evidence of lactating Total litter loss post partum/general poor condition of dam	1 1 1
	264	T	Pre-treatment Treatment Gestation Lactation	Behaviour Behaviour Behaviour	Aggressive Vocalisation Aggressive Vocalisation Irritable No abnormalities detected	5 5 5, 12, 19 5, 12, 19 7
	265	TLL	Pre-treatment Treatment Gestation Lactation	Reason for Dispatch <i>Comments:</i>	No abnormalities detected No abnormalities detected No abnormalities detected Total litter loss post partum <i>Total Litter Loss</i>	1 1

T Terminal sacrifice
 W Killed for welfare reasons
 TLL Total litter loss
 Only animals with observations are presented

Request ID: 284404

APPENDIX 2 - continued

Clinical signs - individual observations for females - F0 generation

Group : 1 2 3 4
 Compound : Control 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene
 Exposure level (ppm) : 0 198 505 2900

Group /Sex	Animal Number	Death Code	Phase	Category	Observation	Day(s)
3F	266	TLL	Pre-treatment Treatment Gestation	Coat	No abnormalities detected No abnormalities detected Hair loss, Forelimbs Hair loss, Head Hair loss, Ventral Body Surface Abnormal Colour, Pale Showing no interest in offspring Total litter loss (prior to Day 1 lactation) A	25 0, 7, 14, 20 20, 25 14, 20, 25 Pre Day 1 lactation
	267	TLL	Pre-treatment Treatment Gestation Lactation	Teeth Reason for Dispatch Teeth Teeth Other Reason for despatch	No abnormalities detected No abnormalities detected Abnormal Colour, Pale General poor clinical condition Abnormal Colour, Pale No evidence of lactating Total litter Loss	14, 20 1 1 1 1
	268	T	Pre-treatment Treatment Gestation Lactation	Staining Staining	No abnormalities detected No abnormalities detected Abnormal Colour, Brown, Head Abnormal Colour, Brown, Head	14, 20 10

TLL Total litter loss
 T Terminal sacrifice
 Only animals with observations are presented

Request ID: 284404

APPENDIX 2 - continued

Clinical signs - individual observations for females - F0 generation

Group : 1 2 3 4
 Compound : Control 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene
 Exposure level (ppm) : 0 198 505 2900

Group /Sex	Animal Number	Death Code	Phase	Category	Observation	Day(s)
3F	269	T	Pre-treatment Treatment Gestation Lactation	Staining Staining	No abnormalities detected No abnormalities detected Abnormal Colour, Brown, Head Abnormal Colour, Brown, Head	14, 20 5, 9-10
	270	TLL	Pre-treatment Treatment Gestation Lactation	Reason for despatch	No abnormalities detected No abnormalities detected No abnormalities detected No abnormalities detected Total litter loss	2

TLL Total litter loss
 T Terminal sacrifice
 Only animals with observations are presented

Request ID: 284404

APPENDIX 2 - continued

Clinical signs - individual observations for females - F0 generation

Group Compound : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm) : 0

Group /Sex	Animal Number	Death Code	Phase	Category	Observation	Day(s)
4F	273	TLL	Pre-treatment	Behaviour	Aggressive Vocalisation	5
			Treatment	Behaviour	Aggressive Vocalisation	5
			Gestation	Coat	Piloerection	5, 8-10
			Lactation	Posture	Hunched	5, 8-10
				Teeth	Abnormal Colour, Pale	8-10
				Reason for Dispatch	General poor clinical condition	20
				Teeth	Abnormal Colour, Pale	2
				Reason for despatch	Total litter loss	1
						2
274	TR	T	Pre-treatment	Muscle Reaction	No abnormalities detected	16-17
			Treatment	Staining	Reduced Body Tone	16-17
			Gestation	Muscle Reaction	Abnormal Colour, Brown, Head	0
				Reason for Dispatch	Reduced Body Tone	25
				Staining	General poor clinical condition	0, 7, 14, 20, 25
				Teeth	Abnormal Colour, Brown, Head	14, 20, 25
				Reason for despatch	Abnormal Colour, Pale	25
					Failed to litter	
275	FTM	T	Pre-treatment	Staining	No abnormalities detected	54
			Treatment	Teeth	Abnormal Colour, Brown, Head	33, 40, 47, 54
				Reason for despatch	Abnormal Colour, Pale	54
					Failed to mate	

TLL Total litter loss
T Terminal sacrifice
FTM Failed to mate
Only animals with observations are presented

Request ID: 284404

APPENDIX 2 - continued

Clinical signs - individual observations for females - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Group /Sex	Animal Number	Death Code	Phase	Category	Observation	Day(s)
4F	276	W	Pre-treatment Treatment Gestation	Behaviour Body temperature Coat Posture Staining Teeth Reason for Dispatch	No abnormalities detected No abnormalities detected Underactive Reduced Piloerection Hunched Abnormal Colour, Brown, Head Abnormal Colour, Pale General poor clinical condition	24 24 24 24 7, 14, 20, 24 14, 20, 24 24
	277 FTM	T	Pre-treatment Treatment	Coat Posture Staining Teeth Reason for Dispatch	No abnormalities detected Piloerection Hunched Abnormal Colour, Brown, Head Abnormal Colour, Pale Failed to mate	13, 16-17, 19, 26 13, 16-17, 19, 26 12-13, 16-17, 19, 26, 33, 40, 47, 54 33, 40, 47, 54 54
	278 TR	T	Pre-treatment Treatment Gestation	Staining Teeth Reason for Dispatch	No abnormalities detected No abnormalities detected Abnormal Colour, Brown, Muzzle Abnormal Colour, Pale Failed to litter	0, 7, 14, 20, 25 14, 20, 25 25

W Killed for welfare reasons
T Terminal sacrifice
FTM Failed to mate TR Total resorption
Only animals with observations are presented

APPENDIX 2 - continued

Request ID: 284404

Clinical signs - individual observations for females - F0 generation

Group : 1 2 3 4
 Compound : Control 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene
 Exposure level (ppm) : 0 198 505 2900

Group /Sex	Animal Number	Death Code	Phase	Category	Observation	Day(s)
4F	279	W	Pre-treatment	Behaviour	Vocalisation	5
			Treatment	Behaviour	Vocalisation	5, 12, 19, 26
			Gestation	Staining	Abnormal Colour, Brown, Head	12, 19, 26
				Coat	Piloerection	24
				Staining	Abnormal Colour, Brown, Head	0, 7, 14, 20
				Teeth	Abnormal Colour, Red, Perigenital	24
				Other	Abnormal Colour, Pale	7, 14, 20, 24
				Reason for Dispatch	Appeared distressed and attempting parturition	24
					General poor clinical condition	24
280	NP	T	Pre-treatment		No abnormalities detected	
			Treatment	Staining	Abnormal Colour, Brown, Head	12
			Gestation	Staining	Abnormal Colour, Brown, Head	0, 7, 14, 20, 25
				Teeth	Abnormal Colour, Pale	25
				Reason for Dispatch	Failed To Litter	25

W Killed for welfare reasons
 T Terminal sacrifice
 NP Not pregnant
 Only animals with observations are presented

Request ID: 284715

APPENDIX 3

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Pre exposure	Weeks			At the end of the working day
				During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage	
2M	211	Behaviour Underactive Unresponsive Coat		1 1	1,4 1		
		Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed	1, 5	1-2, 4-5	2 2		
	212	Behaviour Underactive Unresponsive Coat		1 1	1,4 1		
		Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed	1	1-2, 4	2 2		

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Pre exposure	During dosing (~2 hours)	During dosing (~4 hours)	Weeks	
						On return to the home cage	At the end of the working day
2M	213	Behaviour					
		Underactive		1	1, 4		
		Unresponsive		1	1		
		Coat					
		Piloerection		1	1-2, 4		
		Eyelids (Left)				2	
	214	Behaviour					
		Underactive		1	1, 4		
		Unresponsive		1	1		
		Coat					
		Piloerection		1	1-2, 4		
		Eyelids (Left)				2	
		Eyelids (Right)			2		
		Partially Closed					

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Group /Sex Number	Animal Sign	Pre exposure	Weeks		
			During dosing (~2 hours)	During dosing (~4 hours)	At the end of the working day
2M 215	Behaviour				
	Underactive		1	1, 4	
	Unresponsive		1	1	
	Coat				
	Piloerection		1	1-2, 4	
	Eyelids (Left)				2
2M 216	Partially Closed				
	Eyelids (Right)				2
2M 216	Behaviour				
	Underactive		1	1, 4	
	Unresponsive		1	1	
	Coat				
	Piloerection		1	1-2, 4	
	Eyelids (Left)				2
2M 216	Partially Closed				
	Eyelids (Right)				2

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Weeks			
			Pre exposure	During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage
2M	217	Behaviour				
		Underactive		1	1, 4	
		Unresponsive		1	1	
		Coat				
		Piloerection		1	1-2, 4	
		Eyelids (Left)				
		Partially Closed			2	
		Eyelids (Right)				
		Partially Closed			2	
	218	Behaviour				
		Underactive		1	1, 4	
		Unresponsive		1	1	
		Coat				
		Piloerection		1	1-2, 4	
		Eyelids (Left)				
		Partially Closed			2	
		Eyelids (Right)				
		Partially Closed			2	

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex Number	Animal Sign	Pre exposure	During dosing (~2 hours)	Weeks	
				During dosing (~4 hours)	At the end of the working day
2M 219	Behaviour				
	Underactive		1	1, 4	
	Unresponsive		1	1	
	Coat				
	Piloerection		1	1-2, 4	
	Eyelids (Left)				2
2M 220	Partially Closed Eyelids (Right)				2
	Partially Closed				
2M 220	Behaviour				
	Underactive		1	1, 4	
	Unresponsive		1	1	
	Coat				
	Piloerection		1	1-2, 4	
	Eyelids (Left)				2
2M 220	Partially Closed Eyelids (Right)				2
	Partially Closed				

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Weeks				At the end of the working day
			Pre exposure	During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage	
3M	221	Behaviour					
		Underactive		1-7	1-7		
		Unresponsive		1, 3-4	1, 3-4		
		Breathing					
		Shallow			2		
		Slow		5	4-5		
		Coat					
		Piloerection		1-7	1-7		
		Eyelids (Left)					
		Partially Closed		1-2, 5	1-2, 5		
		Eyelids (Right)					
		Partially Closed		1-2, 5	1-2, 5		
		Eye (Left)					
		Lachrymation		1			
		Eye (Right)					
		Lachrymation		1			

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Pre exposure	Weeks			At the end of the working day
				During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage	
3M	222	Behaviour					
		Underactive		1-7	1-7		
		Unresponsive		1, 3-4	1, 3-4		
		Breathing					
		Shallow			2		
		Slow			4-5		
		Coat					
		Piloerection		1-7	1-7		
		Eyelids (Left)					
		Partially Closed		1-2, 5	1-2, 5		
		Eyelids (Right)					
		Partially Closed		1-2, 5	1-2, 5		
		Eye (Left)					
		Lachrymation		1			
		Eye (Right)					
		Lachrymation		1			

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Pre exposure	Weeks		
				During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage
3M	223	Behaviour				
		Underactive		1-7	1-7	
		Unresponsive		1, 3-4	1, 3-4	
		Breathing				
		Shallow			2	
		Slow		5	4-5	
		Coat				
		Piloerection		1-7	1-7	
		Eyelids (Left)				
		Partially Closed		1-2, 5	1-2, 5	
		Eyelids (Right)				
		Partially Closed		1-2, 5	1-2, 5	
		Eye (Left)				
		Lachrymation		1		
		Eye (Right)				
		Lachrymation		1		

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Group /Sex	Animal Number	Sign	Pre exposure	Weeks			At the end of the working day
				During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage	
3M	224	Behaviour					
		Underactive		1-7	1-7		
		Unresponsive		1, 3-4	1, 3-4		
		Breathing			2		
		Shallow		5	4-5		
		Slow					
		Coat					
		Piloerection		1-7	1-7	1	
		Eyelids (Left)					
		Partially Closed		1-2, 5	1-2, 5		
		Eyelids (Right)					
		Partially Closed		1-2, 5	1-2, 5		
		Eye (Left)					
		Lachrymation		1			
		Eye (Right)					
		Lachrymation		1			

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Pre exposure	Weeks		
				During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage
3M	225	Behaviour				
		Underactive		1-7	1-7	
		Unresponsive		1, 3-4	1, 3-4	
		Breathing				
		Shallow			2	
		Slow		5	4-5	
		Coat				
		Piloerection		1-7	1-7	
		Eyelids (Left)				
		Partially Closed		1-2, 5	1-2, 5	
		Eyelids (Right)				
		Partially Closed		1-2, 5	1-2, 5	
		Eye (Left)				
		Lachrymation		1		
		Eye (Right)				
		Lachrymation		1		

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Group /Sex	Animal Number	Sign	Pre exposure	Weeks			At the end of the working day
				During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage	
3M	226	Behaviour					
		Underactive		1-7	1-7		
		Unresponsive		1, 3-4	1, 3-4		
		Breathing					
		Shallow			2		
		Slow		5	4-5		
		Coat					
		Piloerection		1-7	1-7		
		Eyelids (Left)					
		Partially Closed		1-2, 5	1-2, 5		
		Eyelids (Right)					
		Partially Closed		1-2, 5	1-2, 5		
		Eye (Left)					
		Lachrymation		1			
		Eye (Right)					
		Lachrymation		1			

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Pre exposure	Weeks		
				During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage
3M	227	Behaviour				
		Underactive		1-7	1-7	
		Unresponsive		1, 3-4	1, 3-4	
		Breathing				
		Shallow			2	
		Slow		5	4-5	
		Coat				
		Piloerection		1-7	1-7	
		Eyelids (Left)				
		Partially Closed		1-2, 5	1-2, 5	
		Eyelids (Right)				
		Partially Closed		1-2, 5	1-2, 5	
		Eye (Left)				
		Lachrymation		1		
		Eye (Right)				
		Lachrymation		1		

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Pre exposure	Weeks			At the end of the working day
				During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage	
3M	228	Behaviour					
		Underactive		1-7	1-7		
		Unresponsive		1, 3-4	1, 3-4		
		Breathing					
		Shallow			2		
		Slow		5	4-5		
		Coat					
		Piloerection		1-7	1-7		
		Eyelids (Left)					
		Partially Closed		1-2, 5	1-2, 5		
		Eyelids (Right)					
		Partially Closed		1-2, 5	1-2, 5		
		Eye (Left)					
		Lachrymation		1			
		Eye (Right)					
		Lachrymation		1			

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Pre exposure	Weeks		
				During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage
3M	229	Behaviour				
		Underactive		1-7	1-7	
		Unresponsive		1, 3-4	1, 3-4	
		Breathing				
		Shallow			2	
		Slow		5	4-5	
		Coat				
		Piloerection		1-7	1-7	
		Eyelids (Left)				
		Partially Closed		1-2, 5	1-2, 5	
		Eyelids (Right)				
		Partially Closed		1-2, 5	1-2, 5	
		Eye (Left)				
		Lachrymation		1		
		Eye (Right)				
		Lachrymation		1		

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Group /Sex	Animal Number	Sign	Pre exposure	Weeks		
				During dosing (~2 hours)	During dosing (~4 hours)	At the end of the working day
3M	230	Behaviour				
		Underactive		1-7	1-7	
		Unresponsive		1, 3-4	1, 3-4	
		Breathing				
		Shallow		5	2	
		Slow			4-5	
		Coat				
		Piloerection		1-7	1-7	
		Eyelids (Left)				
		Partially Closed		1-2, 5	1-2, 5	
		Eyelids (Right)				
		Partially Closed		1-2, 5	1-2, 5	
		Eye (Left)				
		Lachrymation		1		
		Eye (Right)				
		Lachrymation		1		

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Pre exposure	Weeks			At the end of the working day
				During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage	
4M	231	Behaviour					
		Underactive		1-7	1-7		
		Unresponsive		1-7	1-7		
		Breathing					
		Shallow		1	1-2		
		Slow		4-6	4-6		
		Coat					
		Piloerection		1-7	1-7		1
		Eyelids (Left)					
		Partially Closed		1-7	1-7		
		Eyelids (Right)					
		Partially Closed		1-7	1-7		

APPENDIX 3 - continued

Request ID: 284715

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Group /Sex	Animal Number	Sign	Pre exposure	Weeks		
				During dosing (~2 hours)	During dosing (~4 hours)	At the end of the working day
4M	232	Behaviour				
		Underactive		1-7	1-7	
		Unresponsive		1-7	1-7	
		Breathing				
		Shallow		1	1-2	
		Slow		4-6	4-6	
		Coat				
		Piloerection		1-7	1-7	
		Eyelids (Left)				
		Partially Closed		1-7	1-7	
		Eyelids (Right)				
		Partially Closed		1-7	1-7	

APPENDIX 3 - continued

Request ID: 284715

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Pre exposure	Weeks		
				During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage
4M	233	Behaviour Underactive Unresponsive Breathing Shallow Slow Coat Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed		1-7 1-7 1 4-6 1-7 1-7 1-7	1-7 1-7 1-2 4-6 1-7 1-7 1-7	At the end of the working day

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Weeks				At the end of the working day
			Pre exposure	During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage	
4M	234	Behaviour					
		Underactive		1-7	1-7		
		Unresponsive		1-7	1-7		
		Breathing					
		Shallow		1	1-2		
		Slow		4-6	4-6		
		Coat					
		Piloerection		1-7	1-7		
		Eyelids (Left)					
		Partially Closed		1-7	1-7		
		Eyelids (Right)					
		Partially Closed		1-7	1-7		

APPENDIX 3 - continued

Request ID: 284715

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Weeks			
			Pre exposure	During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage
4M	235	Behaviour				
		Underactive		1-7	1-7	1
		Unresponsive		1-7	1-7	
		Breathing		1	1-2	
		Shallow		4-6	4-6	
		Slow				
		Coat				
		Piloerection		1-7	1-7	1
		Eyelids (Left)				
		Partially Closed		1-7	1-7	
		Eyelids (Right)				
		Partially Closed		1-7	1-7	

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Pre exposure	Weeks			At the end of the working day
				During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage	
4M	236	Behaviour					
		Underactive		1-7	1-7		
		Unresponsive		1-7	1-7		
		Breathing					
		Shallow		1	1-2		
		Slow		4-6	4-6		
		Coat					
		Piloerection		1-7	1-7		
		Eyelids (Left)					
		Partially Closed		1-7	1-7		
		Eyelids (Right)					
		Partially Closed		1-7	1-7		

APPENDIX 3 - continued

Request ID: 284715

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Pre exposure	Weeks		
				During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage
4M	237	Behaviour				
		Underactive		1-7	1-7	
		Unresponsive		1-7	1-7	
		Breathing				
		Shallow		1	1-2	
		Slow		4-6	4-6	
		Coat				
		Piloerection		1-7	1-7	
		Eyelids (Left)				
		Partially Closed		1-7	1-7	
		Eyelids (Right)				
		Partially Closed		1-7	1-7	

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Pre exposure	Weeks			At the end of the working day
				During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage	
4M	238	Behaviour					
		Underactive		1-7	1-7		
		Unresponsive		1-7	1-7		
		Breathing					
		Shallow		1	1-2		
		Slow		4-6	4-6		
		Coat					
		Piloerection		1-7	1-7		
		Eyelids (Left)					
		Partially Closed		1-7	1-7		
		Eyelids (Right)					
		Partially Closed		1-7	1-7		

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group /Sex	Animal Number	Sign	Weeks				At the end of the working day
			Pre exposure	During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage	
			1	2	3	4	
Compound	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900		
Exposure level (ppm)	:	0					
4M	239	Behaviour Underactive Unresponsive Breathing Shallow Slow Coat Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed		1-7 1-7 1 4-6 1-7	1-7 1-7 1-2 4-6 1-7	1-7 1-7	

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Pre exposure	Weeks			At the end of the working day
				During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage	
4M	240	Behaviour					
		Underactive		1-7	1-7		
		Unresponsive		1-7	1-7		
		Breathing					
		Shallow		1	1-2		
		Slow		4-6	4-6		
		Coat					
		Piloerection		1-7	1-7		1
		Eyelids (Left)					
		Partially Closed		1-7	1-7		
		Eyelids (Right)					
		Partially Closed		1-7	1-7		

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Group /Sex	Animal Number	Sign	Weeks				
			Pre exposure	During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage	At the end of the working day
2F	251	Behaviour					
		Underactive		1	1		
		Unresponsive		1	1		
		Coat					
		Piloerection		1	1-2		
		Eyelids (Left)				2	
		Partially Closed					
		Eyelids (Right)			2		
		Partially Closed					
252		Behaviour					
		Underactive		1	1		
		Unresponsive		1	1		
		Coat					
		Piloerection		1	1-2		
		Eyelids (Left)				2	
		Partially Closed					
		Eyelids (Right)			2		
		Partially Closed					

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Pre exposure	Weeks			At the end of the working day
				During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage	
2F	253	Behaviour					
		Underactive	1	1	1		
		Unresponsive	1	1	1		
		Coat					
		Piloerection	1	1-2			
		Eyelids (Left)					
		Partially Closed					
		Eyelids (Right)					
		Partially Closed					
254		Behaviour					
		Underactive	1	1	1		
		Unresponsive	1	1	1		
		Coat					
		Piloerection	1	1-2			
		Eyelids (Left)					
		Partially Closed					
		Eyelids (Right)					
		Partially Closed					

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex Number	Animal Sign	Pre exposure	Weeks			At the end of the working day
			During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage	
2F 255	Behaviour					
	Underactive		1	1, 4		
	Unresponsive		1	1		
	Coat					
	Piloerection		1	1-2, 4		
	Eyelids (Left)				2	
256	Partially Closed					
	Eyelids (Right)			2		
	Partially Closed					
	Behaviour					
	Underactive		1	1		
	Unresponsive		1	1		
256	Coat					
	Piloerection		1	1-2		
	Eyelids (Left)					
	Partially Closed				2	
	Eyelids (Right)					2
Partially Closed						

APPENDIX 3 - continued

Request ID: 284715

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Pre exposure	Weeks		
				During dosing (~2 hours)	During dosing (~4 hours)	At the end of the working day
2F	257	Behaviour				
		Underactive	1	1	1	
		Unresponsive	1	1	1	
		Coat				
		Piloerection	1	1-2		
		Eyelids (Left)			2	
		Partially Closed				
		Eyelids (Right)			2	
		Partially Closed				
	258	Behaviour				
		Underactive	1	1	1	
		Unresponsive	1	1	1	
		Coat				
		Piloerection	1	1-2		
		Eyelids (Left)			2	
		Partially Closed				
		Eyelids (Right)			2	
		Partially Closed				

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Pre exposure	Weeks		
				During dosing (~2 hours)	During dosing (~4 hours)	At the end of the working day
2F	259	Behaviour				
		Underactive		1	1	
		Unresponsive		1	1	
		Coat				
		Piloerection		1	1-2	
		Eyelids (Left)				2
260		Partially Closed				
		Eyelids (Right)			2	
		Partially Closed				
		Behaviour				
		Underactive		1	1	
		Unresponsive		1	1	
		Coat				
		Piloerection		1	1-2	
		Eyelids (Left)				
		Partially Closed			2	
		Eyelids (Right)				
		Partially Closed			2	

APPENDIX 3 - continued

Request ID: 284715

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Pre exposure	Weeks		
				During dosing (~2 hours)	During dosing (~4 hours)	At the end of the working day
3F	261	Behaviour				
		Underactive	1-3	1-3	1-3	
		Unresponsive	1	1, 3	1, 3	
		Breathing				
		Shallow		2		
		Coat				
		Piloerection	1-3	1-3	1-3	
		Eyelids (Left)				
		Partially Closed	1-2	1-2	1-2	
		Eyelids (Right)				
		Partially Closed	1-2	1-2	1-2	
		Eye (Left)				
		Lachrymation	1	1	1	
		Eye (Right)				
		Lachrymation	1	1	1	

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Group /Sex	Animal Number	Sign	Pre exposure	Weeks			At the end of the working day
				During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage	
3F	262	Behaviour					
		Underactive		1-3	1-3		
		Unresponsive		1	1,3		
		Breathing					
		Shallow			2		
		Coat					
		Piloerection		1-3	1-3		
		Eyelids (Left)					
		Partially Closed		1-2	1-2		
		Eyelids (Right)					
		Partially Closed		1-2	1-2		
		Eye (Left)					
		Lachrymation		1			
		Eye (Right)					
		Lachrymation		1			

APPENDIX 3 - continued

Request ID: 284715

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Pre exposure	Weeks		
				During dosing (~2 hours)	During dosing (~4 hours)	At the end of the working day
3F	263	Behaviour				
		Underactive		1-3	1-3	
		Unresponsive		1	1, 3	
		Breathing				
		Shallow			2	
		Coat				
		Piloerection		1-3	1-3	
		Eyelids (Left)				
		Partially Closed		1-2	1-2	
		Eyelids (Right)				
		Partially Closed		1-2	1-2	
		Eye (Left)				
		Lachrymation		1		
		Eye (Right)				
		Lachrymation		1		

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Pre exposure	Weeks		On return to the home cage	At the end of the working day
				During dosing (~2 hours)	During dosing (~4 hours)		
3F	264	Behaviour					
		Underactive		1-3	1-3		
		Unresponsive		1	1, 3		
		Breathing					
		Shallow			2		
		Coat					
		Piloerection		1-3	1-3		
		Eyelids (Left)					
		Partially Closed		1-2	1-2		
		Eyelids (Right)					
		Partially Closed		1-2	1-2		
		Eye (Left)					
		Lachrymation		1			
		Eye (Right)					
		Lachrymation		1			

APPENDIX 3 - continued

Request ID: 284715

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex Number	Animal Sign	Pre exposure	Weeks		
			During dosing (~2 hours)	During dosing (~4 hours)	At the end of the working day
3F	265	Behaviour			
		Underactive	1-2	1-2	
		Unresponsive	1	1	
		Breathing Shallow		2	
		Coat			
		Piloerection	1-2	1-2	
		Eyelids (Left)			
		Partially Closed	1-2	1-2	
		Eyelids (Right)			
		Partially Closed	1-2	1-2	
		Eye (Left)			
		Lachrymation	1		
		Eye (Right)			
		Lachrymation	1		

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group /Sex	Animal Number	Sign	Pre exposure	Weeks		
				During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage
3F	266	Behaviour				
		Underactive		1-3	1-3	
		Unresponsive		1, 3	1, 3	
		Breathing				
		Shallow			2	
		Coat				
		Piloerection		1-3	1-3	
		Eyelids (Left)				
		Partially Closed		1-2	1-2	
		Eyelids (Right)				
		Partially Closed		1-2	1-2	
		Eye (Left)				
		Lachrymation		1		
		Eye (Right)				
		Lachrymation		1		

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group Animal /Sex Number Sign	Weeks			
	Pre exposure	During dosing (~2 hours)	During dosing (~4 hours)	At the end of the working day
3F 267 Behaviour				
Underactive		1-3	1-3	
Unresponsive		1	1, 3	
Breathing Shallow			2	
Coat				
Piloerection		1-3	1-3	
Eyelids (Left)				
Partially Closed		1-2	1-2	
Eyelids (Right)				
Partially Closed		1-2	1-2	
Eye (Left)				
Lachrymation		1		
Eye (Right)				
Lachrymation		1		

APPENDIX 3 - continued

Request ID: 284715

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group : 1
 Compound : Control
 Exposure level (ppm) : 0

Group /Sex	Animal Number	Sign	Pre exposure	Weeks			On return to the home cage	At the end of the working day
				During dosing (~2 hours)	During dosing (~4 hours)	During dosing		
3F	268	Behaviour						
		Underactive		1-3		1-3		
		Unresponsive		1		1, 3		
		Breathing						
		Shallow				2		
		Coat						
		Piloerection		1-3		1-3		
		Eyelids (Left)						
		Partially Closed		1-2		1-2		
		Eyelids (Right)						
		Partially Closed		1-2		1-2		
		Eye (Left)						
		Lachrymation		1				
		Eye (Right)						
		Lachrymation		1				

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Group /Sex	Animal Number	Sign	Pre exposure	Weeks		
				During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage
3F	269	Behaviour				
		Underactive		1-3	1-3	
		Unresponsive		1	1,3	
		Breathing Shallow			2	
		Coat				
		Piloerection		1-3	1-3	1
		Eyelids (Left)				
		Partially Closed		1-2	1-2	
		Eyelids (Right)				
		Partially Closed		1-2	1-2	
		Eye (Left)				
		Lachrymation		1		
		Eye (Right)				
		Lachrymation		1		

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Pre exposure	Weeks		
				During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage
3F	270	Behaviour				
		Underactive	1-3	1-3	1-3	At the end of the working day
		Unresponsive	1	1,3	1,3	
		Breathing				
		Shallow		2		
		Coat				
		Piloerection	1-3	1-3		
		Eyelids (Left)				
		Partially Closed	1-2	1-2		
		Eyelids (Right)				
		Partially Closed	1-2	1-2		
		Eye (Left)				
		Lachrymation	1			
		Eye (Right)				
		Lachrymation	1			

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Group /Sex	Animal Number	Sign	Pre exposure	Weeks		At the end of the working day
				During dosing (~2 hours)	During dosing (~4 hours)	
4F	271	Behaviour				
		Underactive		1-3	1-3	
		Unresponsive		1-3	1-3	
		Breathing Shallow		1	1-2	
		Coat				
		Piloerection		1-3	1-3	
		Eyelids (Left)				
		Partially Closed		1-3	1-3	
		Eyelids (Right)				
		Partially Closed		1-3	1-3	
		Posture				
		Hunched	2	2	2	
		Staining				
		Other Colour (see comment)				
		Comments:				
		<i>brown staining head</i>				2

APPENDIX 3 - continued

Request ID: 284715

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Group /Sex Number	Animal Sign	Pre exposure	Weeks			At the end of the working day
			During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage	
4F 272	FTM Behaviour Underactive Unresponsive Breathing Shallow Slow Coat Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed		1-7 1-7 1 4-6 1-7 1-7 1-7 1-7 1-7 1-7	1-7 1-7 1-2 4-6 1-7 1-7 1-7 1-7 1-7 1-7	1 1 1 1 1 1 1 1 1 1	

FTM Failed to mate

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Group /Sex	Animal Number	Sign	Pre exposure	Weeks			At the end of the working day
				During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage	
4F	273	Behaviour					
		Underactive		1-2	1-2		
		Unresponsive		1-2	1-2		
		Breathing					
		Shallow		1	1-2		
		Coat					
		Piloerection		1-2	1-2		
		Eyelids (Left)					
		Partially Closed		1-2	1-2		
		Eyelids (Right)					
		Partially Closed		1-2	1-2		
		Posture					
		Hunched	2	2	2	2	2
		Staining					
		Other Colour (see comment)				2	2
		Comments:					
		<i>brown staining head</i>				2	2

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Pre exposure	Weeks		
				During dosing (~2 hours)	During dosing (~4 hours)	At the end of the working day
4F	274	Behaviour Underactive Unresponsive Breathing Shallow Coat Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed		1-2 1-2 1 1-2 1-2 1-2 1-2 1-2	1-2 1-2 1-2 1-2 1-2 1-2	

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group : 1 2 3 4
 Compound : Control 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene
 Exposure level (ppm) : 0 198 505 2900

Group /Sex	Animal Number	Sign	Weeks			
			Pre exposure	During dosing (~2 hours)	During dosing (~4 hours)	At the end of the working day
4F	275	FTM Behaviour				
		Underactive		1-7	1-7	
		Unresponsive		1-7	1-7	
		Breathing		1	1-2	
		Shallow		4-6	4-6	
		Slow				
		Coat				
		Piloerection		1-7	1-7	
		Eyelids (Left)				
		Partially Closed		1-7	1-7	
		Eyelids (Right)				
		Partially Closed		1-7	1-7	
		Posture				
		Hunched				2
		Staining				
		Other Colour (see comment)	2	2	2	2
		Comments:				
		Brown staining head	2	2	2	2

FTM Failed to mate

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Pre exposure	Weeks			At the end of the working day
				During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage	
4F	276	Behaviour					
		Underactive		1-3	1-3		
		Unresponsive		1-3	1-3		
		Breathing					
		Shallow		1	1-2		
		Coat					
		Piloerection		1-3	1-3		
		Eyelids (Left)					
		Partially Closed		1-3	1-3		
		Eyelids (Right)					
		Partially Closed		1-3	1-3		
277 FTM		Behaviour					
		Underactive		1-7	1-7		
		Unresponsive		1-7	1-7		
		Breathing					
		Shallow		1	1-2		
		Slow		4-6	4-6		
		Coat					
		Piloerection		1-7	1-7		
		Eyelids (Left)					
		Partially Closed		1-7	1-7		
		Eyelids (Right)					
		Partially Closed		1-7	1-7		

FTM Failed to mate

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group : 1 2 3 4
 Compound : Control 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene
 Exposure level (ppm) : 0 198 505 2900

Group /Sex	Animal Number	Sign	Pre exposure	Weeks			At the end of the working day
				During dosing (~2 hours)	During dosing (~4 hours)	On return to the home cage	
4F	278	Behaviour					
		Underactive		1-3	1-3		
		Unresponsive		1-3	1-3		
		Breathing					
		Shallow		1	1-2		
		Coat					
		Piloerection		1-3	1-3		
		Eyelids (Left)					
		Partially Closed		1-2	1-3		
		Eyelids (Right)					
Partially Closed		1-2	1-3				
279		Behaviour					
		Underactive		1-4	1-4		
		Unresponsive		1-4	1-4		
		Breathing					
		Shallow		1	1-2		
		Slow		4	4		
		Coat					
		Piloerection		1-3	1-3		
		Eyelids (Left)					
		Partially Closed		1-4	1-4		
Eyelids (Right)							
Partially Closed		1-4	1-4				

Request ID: 284715

APPENDIX 3 - continued

Signs associated with dosing - individual observations for males and females during treatment - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Pre exposure	Weeks			On return to the home cage	At the end of the working day
				During dosing (~2 hours)	During dosing (~4 hours)	During dosing (~4 hours)		
4F	280	Behaviour Underactive Unresponsive Breathing Shallow Coat Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed		1-3 1-3 1 1-3 1-2 1-3	1-3 1-3 1-2 1-3 1-3 1-3			

Request ID: 284712

APPENDIX 3 - continued

Signs associated with dosing - individual observations for females after mating - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex Number	Animal Sign	Pre exposure	During dosing (~2 hours)	Days	
				Additional observation	During dosing (~4 hours)
2F 251	Behaviour				7
	Underactive Coat Piloerection				7, 19
252	Behaviour		7, 14		0, 7, 14
	Underactive Coat Piloerection		7, 19		0, 7, 19
253	Coat		7		7
	Piloerection				
254	Coat		7		7
	Piloerection				
255	Behaviour		14		0, 14
	Underactive Coat Piloerection		14		0, 14
256	Coat		7		7
	Piloerection				

Request ID: 284712

APPENDIX 3 - continued

Signs associated with dosing - individual observations for females after mating - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Group /Sex	Animal Number	Sign	Pre exposure	During dosing (~2 hours)	Days	
					Additional observation	During dosing (~4 hours)
2F	257 NP	Coat Piloerection		7		7
	258	Behaviour Underactive Coat Piloerection		7, 14		0, 7, 14
	259	Behaviour Underactive Coat Piloerection		7, 19		0, 7, 19
	260	Behaviour Underactive Coat Piloerection				7
						7, 19
NP		Not pregnant				

Request ID: 284712

APPENDIX 3 - continued

Signs associated with dosing - individual observations for females after mating - F0 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900

Exposure level (ppm) : 0

Group /Sex Number	Animal Sign	Pre exposure	During dosing (~2 hours)	Days	
				Additional observation	During dosing (~4 hours)
3F 261	Behaviour				
	Underactive		7, 14, 19		7, 14, 19
	Unresponsive		7		7
	Breathing				
	Slow				7, 19
	Coat				
	Piloerection		14		14
Eyelids (Left)	Partially Closed				19
	Eyelids (Right)				19
	Partially Closed				19
262	Behaviour				
	Underactive		0, 7, 14, 19		0, 7, 14, 19
	Unresponsive				7
	Breathing				
	Slow		0, 14, 19		0, 14, 19
	Coat				
	Piloerection		7, 14		7, 14, 19
Eyelids (Left)	Partially Closed		0, 7, 19		0, 7, 14, 19
	Eyelids (Right)				
	Partially Closed		0, 7, 19		0, 7, 14, 19

APPENDIX 3 - continued

Request ID: 284712

Signs associated with dosing - individual observations for females after mating - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Pre exposure	During dosing (~2 hours)	Days Additional observation	During dosing (~4 hours)
3F	263 U TR	Behaviour Underactive Unresponsive Breathing Slow Coat		0, 7, 19 0		0, 7, 14, 19
		Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed		19 19		0, 7, 14, 19 19
	264	Behaviour Underactive Unresponsive Breathing Slow Coat		0, 7, 14, 19		0, 7, 14, 19 7
		Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed		7, 14 0, 7, 19		7, 14, 19 0, 7, 14, 19
				0, 7, 19		0, 7, 14, 19

U Unilateral implantation
TR Total resorption

APPENDIX 3 - continued

Request ID: 284712

Signs associated with dosing - individual observations for females after mating - F0 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900
 Compound :
 Exposure level (ppm) : 0

Group /Sex	Animal Number	Sign	Pre exposure	During dosing (~2 hours)	Days	
					Additional observation	During dosing (~4 hours)
3F	265	Behaviour		0, 7, 14, 19		0, 7, 14, 19
		Underactive				
		Breathing				
		Shallow		7, 19		0
		Slow				7, 19
		Coat				
	266	Piloerection		0, 14, 19		0, 14, 19
		Eyelids (Left)				
		Partially Closed		7, 19		7, 19
		Eyelids (Right)		7, 19		7, 19
	266	Behaviour		0, 7, 14, 19		0, 7, 14, 19
		Underactive		19		
		Unresponsive				
		Breathing				
		Slow		0		0, 14, 19
		Coat				
	266	Piloerection		7		7
		Eyelids (Left)				
		Partially Closed		0		0, 14, 19
		Eyelids (Right)		0		0, 14, 19
		Partially Closed				0

APPENDIX 3 - continued

Request ID: 284712

Signs associated with dosing - individual observations for females after mating - F0 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900
 Compound :
 Exposure level (ppm) :

Group /Sex	Animal Number	Sign	Pre exposure	During dosing (~2 hours)	Days	
					Additional observation	During dosing (~4 hours)
3F	267	Behaviour				
		Underactive		7, 14, 19		7, 14, 19
		Unresponsive		7		7
		Breathing				
		Slow				7, 19
		Coat				
		Piloerection		14		14
		Eyelids (Left)				
		Partially Closed				19
		Eyelids (Right)				19
		Partially Closed				
268		Behaviour				
		Underactive		7, 14, 19		7, 14, 19
		Unresponsive		7		7
		Breathing				
		Slow				7, 19
		Coat				
		Piloerection		14		14
		Eyelids (Left)				
		Partially Closed				19
		Eyelids (Right)				19
Partially Closed						

Request ID: 284712

APPENDIX 3 - continued

Signs associated with dosing - individual observations for females after mating - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Pre exposure	During dosing (~2 hours)	Days		
					Additional observation	During dosing (~4 hours)	
3F	269	Behaviour					
		Underactive		0, 7, 19			0, 7, 14, 19
		Unresponsive		0			
		Breathing			19		0, 7, 14, 19
		Slow					
		Coat					
		Piloerection		19		19	
		Eyelids (Left)				0, 7, 14	
		Partially Closed					
		Eyelids (Right)				0, 7, 14	
270		Behaviour					
		Underactive		7, 14, 19		7, 14, 19	
		Unresponsive		7		7	
		Breathing				7, 19	
		Slow					
		Coat					
		Piloerection		14		14	
		Eyelids (Left)				19	
		Partially Closed					
		Eyelids (Right)				19	
		Partially Closed				19	

Request ID: 284712

APPENDIX 3 - continued

Signs associated with dosing - individual observations for females after mating - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Group /Sex	Animal Number	Sign	Pre exposure	Days		
				During dosing (~2 hours)	Additional observation	During dosing (~4 hours)
4F	271	TR Behaviour	14	0, 7, 14, 19		0, 7, 14, 19
		Underactive		0, 19		0, 19
		Unresponsive				
		Breathing		14, 19		7, 14, 19
		Slow				
		Coat				
		Piloerection	14	0, 7, 19		0, 7, 19
		Eyelids (Left)				
		Partially Closed	14	0, 14, 19		0, 7, 14, 19
		Eyelids (Right)				
		Partially Closed	14	0, 14, 19		0, 7, 14, 19
		Muscle Reaction				
		Reduced Body Tone	14			

TR Total resorption

APPENDIX 3 - continued

Request ID: 284712

Signs associated with dosing - individual observations for females after mating - F0 generation

Group	1	2	3	4		
Compound	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene		
Exposure level (ppm)	0	198	505	2900		
Group /Sex	Animal Number	Sign	Pre exposure	During dosing (~2 hours)	Additional observation	During dosing (~4 hours)
4F	273	Behaviour				
		Underactive		0, 7, 14, 19		0, 7, 14, 19
		Unresponsive		0, 14		0, 14
		Breathing				
		Slow		7, 19		0, 7, 19
		Coat				
		Piloerection		0, 7, 14		0, 7, 14
		Eyelids (Left)				
		Partially Closed		0, 7, 14, 19		0, 7, 14, 19
		Eyelids (Right)				
		Partially Closed		0, 7, 14, 19		0, 7, 14, 19
274 TR		Behaviour				
		Underactive		0, 7, 19	0	7, 14, 19
		Unresponsive		0, 14	0	14
		Coat				
		Piloerection		0, 7, 19	0	7, 19
		Eyelids (Left)				
		Partially Closed		0, 7	0	7
		Eyelids (Right)				
		Partially Closed		0, 7	0	7
		Posture				
		Hunched		14		14
TR		Total resorption				

Request ID: 284712

APPENDIX 3 - continued

Signs associated with dosing - individual observations for females after mating - F0 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900
 Compound :
 Exposure level (ppm) : 0

Group /Sex	Animal Number	Sign	Pre exposure	During dosing (~2 hours)	Days Additional observation	During dosing (~4 hours)
4F	276 W	Behaviour		0, 7, 14, 19		0, 7, 14, 19
		Underactive		0		0
		Unresponsive				
		Breathing		7, 19		7, 19
		Slow				
		Coat				
		Piloerection		0, 14		0, 14
		Eyelids (Left)				
		Partially Closed		0, 7, 19		0, 7, 19
		Eyelids (Right)				
		Partially Closed		0, 7, 19		0, 7, 19
278 TR		Behaviour		7, 14, 19		7, 14, 19
		Underactive		7, 14		7, 14
		Unresponsive				
		Breathing		7, 19		7, 19
		Slow				
		Coat				
		Piloerection		14		14
		Eyelids (Left)				
		Partially Closed		7, 19		7, 19
		Eyelids (Right)				
		Partially Closed		7, 19		7, 19

W Killed for welfare reasons
 TR Total resorption

Request ID: 284712

APPENDIX 3 - continued

Signs associated with dosing - individual observations for females after mating - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Pre exposure	During dosing (~2 hours)	Additional observation	Days	During dosing (~4 hours)
4F	279 W	Behaviour					
		Underactive		0, 7, 14, 19			0, 7, 14, 19
		Unresponsive		0, 14, 19			0, 14, 19
		Breathing					
		Slow		0, 7, 14, 19			0, 7, 14, 19
		Coat					
		Piloerection		14, 19			14, 19
		Eyelids (Left)					
		Partially Closed		0, 7, 14, 19			0, 7, 14, 19
		Eyelids (Right)					
		Partially Closed		0, 7, 14, 19			0, 7, 14, 19
280 NP		Behaviour					
		Underactive		7, 14, 19			7, 14, 19
		Unresponsive		7, 14			7, 14
		Breathing					
		Slow		7, 19			7, 19
		Coat					
		Piloerection		14			14
		Eyelids (Left)					
		Partially Closed		7, 19			7, 19
		Eyelids (Right)					
		Partially Closed		7, 19			7, 19

W Killed for welfare reasons
NP Not pregnant

Request ID: 284713

APPENDIX 3 - continued

Signs associated with dosing - individual observations for females during lactation - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Sign	Days			
			During dosing (~2 hours)	During dosing (~4 hours)	During dosing (~4 hours)	During dosing (~4 hours)
3F	261	Behaviour Underactive	9	9	9	
	264	Behaviour Underactive	9	9	9	
	268	Behaviour Underactive Coat Piloerection	5, 9	5, 9	5, 9	
	269	Behaviour Underactive Coat Piloerection	5	5	5	

APPENDIX 4

Request ID: 284710

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	Treatment Phase	Sign	Day(s)
2F	251	T	Treatment	Behaviour Underactive Unresponsive Coat	1-7 1, 3
				Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed	2-7, 11, 14 14
			Gestation	Behaviour Underactive Coat	7
			Lactation	Piloerection No abnormalities detected	7, 19

T Terminal sacrifice

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Group /Sex	Animal Number	Death Code	Phase	Treatment	Sign	Day(s)
2F	252	T		Treatment	Behaviour Underactive Unresponsive Coat Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed Behaviour Underactive Coat	1-7 1, 3 2-7, 11, 14 14 14 0, 7, 14 0, 7, 19
T				Gestation	No abnormalities detected	
T				Lactation	No abnormalities detected	

T Terminal sacrifice

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	Treatment Phase	Sign	Day(s)
2F	253	T	Treatment	Behaviour Underactive Unresponsive Coat	1-7 1, 3
				Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed	2-7, 11, 14 14 14
			Gestation	Coat	14
			Lactation	Piloerection No abnormalities detected	7

T Terminal sacrifice

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	Phase	Sign	Day(s)
2F	254	T	Treatment	Behaviour Underactive Unresponsive Coat	1-7 1, 3
				Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed Coat	2-7, 11, 14 14 14 7
			Gestation	Piloerection	
			Lactation	No abnormalities detected	

T Terminal sacrifice

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	Treatment Phase	Sign	Day(s)
2F	255	T	Treatment	Behaviour Underactive Unresponsive Coat	1-7, 25 1, 3
				Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed	2-7, 11, 14, 25 14 14
			Gestation	Behaviour Underactive Coat	0, 14 0, 14
			Lactation	Piloerection No abnormalities detected	

T Terminal sacrifice

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	Treatment Phase	Sign	Day(s)
2F	256	T	Treatment	Behaviour Underactive Unresponsive Coat Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed Coat	1-7 1, 3 2-7, 11, 14 14 14
			Gestation	Coat	
			Lactation	Piloerection No abnormalities detected	7

T Terminal sacrifice

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	Treatment Phase	Sign	Day(s)
2F	257	NP	Treatment	Behaviour	1-7
				Underactive	1, 3
				Unresponsive	
				Coat	2-7, 11, 14
				Piloerection	
				Eyelids (Left)	14
				Partially Closed	
				Eyelids (Right)	14
				Partially Closed	
			Gestation	Coat	7
				Piloerection	

T Terminal sacrifice
NP Not pregnant

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group Compound	1	2	3	4
	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	0	198	505	2900

Group /Sex	Animal Number	Death Code	Phase	Sign	Day(s)
2F	258	T	Treatment	Behaviour Underactive Unresponsive Coat	1-7 1, 3
				Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed	2-7, 11, 14 14 14
			Gestation	Behaviour Underactive Coat	0, 7, 14
			Lactation	Piloerection No abnormalities detected	0, 7, 19

T Terminal sacrifice

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	Treatment Phase	Sign	Day(s)
2F	259	T	Treatment	Behaviour Underactive Unresponsive Coat	1-7 1, 3
				Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed	2-7, 11, 14 14 14
			Gestation	Behaviour Underactive Coat	7
			Lactation	Piloerection No abnormalities detected	7, 19

T Terminal sacrifice

APPENDIX 4 - continued

Request ID: 284710

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Group /Sex	Animal Number	Death Code	Phase	Sign	Day(s)
2F	260	T	Treatment	Behaviour Underactive Unresponsive Coat	1-7 1, 3
				Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed	2-7, 11, 14 14
			Gestation	Behaviour Underactive Coat	7
			Lactation	Piloerection No abnormalities detected	7, 19

T Terminal sacrifice

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	Phase	Treatment	Sign	Day(s)
3F	261	T			Behaviour Underactive Unresponsive Breathing Shallow Coat	1-7, 11, 14, 18 1-3, 6-7, 18 14
					Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed Eye (Left) Lachrymation Eye (Right) Lachrymation	1-7, 14, 18 1, 3-5, 11, 14 1, 3-5, 11, 14
				Gestation	Behaviour Underactive Unresponsive Breathing Slow Coat Piloerection Eyelids (Left) Partially Closed	1 1 7, 14, 19 7 7, 19 14 19

T Terminal sacrifice

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group Compound	1	2	3	4
	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	0	198	505	2900

Group /Sex	Animal Number	Death Code	Phase	Sign	Day(s)
3F	261	T	Gestation	Eyelids (Right)	19
			Lactation	Partially Closed Behaviour Underactive	9

T Terminal sacrifice

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	Phase	Treatment	Sign	Day(s)
3F	262	W			Behaviour Underactive Unresponsive Breathing Shallow Coat Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed Eye (Left) Lachrymation Eye (Right) Lachrymation Behaviour Underactive Unresponsive Breathing Slow Coat Piloerection Eyelids (Left) Partially Closed	1-7, 11, 14, 18 1-3, 6-7, 18 14 1-7, 14, 18 1, 3-5, 11, 14 1, 3-5, 11, 14 1 1 0, 7, 14, 19 7 0, 14, 19 7, 14, 19 0, 7, 14, 19
W				Gestation		
W					Killed for welfare reasons	

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	Phase	Sign	Day(s)
3F	262	W	Gestation	Eyelids (Right) Partially Closed	0, 7, 14, 19

W Killed for welfare reasons

APPENDIX 4 - continued

Request ID: 284710

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900

Exposure level (ppm) : 0

Group /Sex	Animal Number	Death Code	Phase	Treatment	Sign	Day(s)
3F	263 U	TR	T	Treatment	Behaviour Underactive Unresponsive Breathing Shallow Coat Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed Eye (Left) Lachrymation Eye (Right) Lachrymation Behaviour Underactive Unresponsive Breathing Slow Coat Piloerection Eyelids (Left) Partially Closed	1-7, 11, 14, 18 1-3, 6-7, 18 14 1-7, 14, 18 1, 3-5, 11, 14 1, 3-5, 11, 14 1 1 0, 7, 14, 19 0 0, 7, 14, 19 19 0, 7, 14
				Gestation		

U Unilateral implantation
T Terminal sacrifice
TR Total resorption

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	Phase	Sign	Day(s)
3F	263 U TR	T	Gestation	Eyelids (Right) Partially Closed	0, 7, 14

U Unilateral implantation
T Terminal sacrifice
TR Total resorption

APPENDIX 4 - continued

Request ID: 284710

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	Phase	Treatment	Sign	Day(s)
3F	264	T			Behaviour Underactive Unresponsive Breathing Shallow Coat Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed Eye (Left) Lachrymation Eye (Right) Lachrymation	1-7, 11, 14, 18 1-3, 6-7, 18 14 1-7, 14, 18 1, 3-5, 11, 14 1, 3-5, 11, 14
				Gestation	Behaviour Underactive Unresponsive Breathing Slow Coat Piloerection Eyelids (Left) Partially Closed	1 1 0, 7, 14, 19 7 0, 14, 19 7, 14, 19 0, 7, 14, 19

T Terminal sacrifice

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	Phase	Sign	Day(s)
3F	264	T	Gestation	Eyelids (Right) Partially Closed	0, 7, 14, 19
			Lactation	Behaviour Underactive	9

T Terminal sacrifice

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	Phase	Sign	Day(s)
3F	265	TLL	Treatment	Behaviour Unresponsive Breathing Shallow Coat Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed Eye (Left) Lachrymation Eye (Right) Lachrymation	1-7, 11, 14 1-3, 6-7 14 1-7, 14 1, 3-5, 11, 14 1, 3-5, 11, 14
			Gestation	Behaviour Underactive Breathing Shallow Slow Coat Piloerection Eyelids (Left) Partially Closed	1 1 0, 7, 14, 19 0 7, 19 0, 14, 19 7, 19

TLL Total litter loss

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	Phase	Sign	Day(s)
3F	265	TLL	Gestation	Eyelids (Right) Partially Closed	7, 19

TLL Total litter loss

APPENDIX 4 - continued

Request ID: 284710

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	Phase	Sign	Day(s)
3F	266	TLL	Treatment	Behaviour Underactive Unresponsive Breathing Shallow Coat	1-7, 11, 14, 18, 21 1-3, 6-7, 18, 21 14
				Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed Eye (Left) Lachrymation Eye (Right) Lachrymation	1-7, 14, 18, 21 1, 3-5, 11, 14 1, 3-5, 11, 14
			Gestation	Behaviour Underactive Unresponsive Breathing Slow Coat Piloerection Eyelids (Left) Partially Closed	1 1 0, 7, 14, 19 19 0, 14, 19 7 0, 14, 19

TLL Total litter loss

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	Phase	Sign	Day(s)
3F	266	TLL	Gestation	Eyelids (Right) Partially Closed	0, 14, 19

TLL Total litter loss

APPENDIX 4 - continued

Request ID: 284710

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group	1	2	3	4	
Compound	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	
Exposure level (ppm)	0	198	505	2900	
Group /Sex	Animal Number	Death Code	Phase	Sign	Day(s)
3F	267	TLL	Treatment	Behaviour Underactive Unresponsive Breathing Shallow Coat Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed Eye (Left) Lachrymation Eye (Right) Lachrymation Behaviour Underactive Unresponsive Breathing Slow Coat Piloerection Eyelids (Left) Partially Closed	1-7, 11, 14, 18 1-3, 6-7, 18 14 1-7, 14, 18 1, 3-5, 11, 14 1, 3-5, 11, 14 1 1 7, 14, 19 7 7, 19 14 19
			Gestation		
TLL	Total litter loss				

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	Phase	Sign	Day(s)
3F	267	TLL	Gestation	Eyelids (Right) Partially Closed	19

TLL Total litter loss

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	Phase	Treatment	Sign	Day(s)
3F	268	T			Behaviour Underactive Unresponsive Breathing Shallow Coat	1-7, 11, 14, 18 1-3, 6-7, 18 14
					Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed Eye (Left) Lachrymation Eye (Right) Lachrymation	1-7, 14, 18 1, 3-5, 11, 14 1, 3-5, 11, 14
				Gestation	Behaviour Underactive Unresponsive Breathing Slow Coat Piloerection Eyelids (Left) Partially Closed	1 1 7, 14, 19 7 7, 19 14 19

T Terminal sacrifice

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	Phase	Sign	Day(s)
3F	268	T	Gestation	Eyelids (Right) Partially Closed	19
			Lactation	Behaviour Underactive Coat Piloerection	5, 9 5

T Terminal sacrifice

APPENDIX 4 - continued

Request ID: 284710

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	Phase	Treatment	Sign	Day(s)
3F	269	T			Behaviour Underactive Unresponsive Breathing Shallow Coat	1-7, 11, 14, 18 1-3, 6-7, 18 14
					Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed Eye (Left) Lachrymation Eye (Right) Lachrymation	1-7, 14, 18 1, 3-5, 11, 14 1, 3-5, 11, 14
				Gestation	Behaviour Underactive Unresponsive Breathing Slow Coat Piloerection Eyelids (Left) Partially Closed	1 1 0, 7, 14, 19 0 0, 7, 14, 19 19 0, 7, 14

T Terminal sacrifice

APPENDIX 4 - continued

Request ID: 284710

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	Phase	Sign	Day(s)
3F	269	T	Gestation	Eyelids (Right)	0, 7, 14
			Lactation	Partially Closed Behaviour	
				Underactive Coat	5, 9
				Piloerection	5

T Terminal sacrifice

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group : 1 2 3 4
 Compound : Control 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene
 Exposure level (ppm) : 0 198 505 2900

Group /Sex	Animal Number	Death Code	Phase	Sign	Day(s)
3F	270	TLL	Treatment	Behaviour Unresponsive Breathing Shallow Coat Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed Eye (Left) Lachrymation Eye (Right) Lachrymation Behaviour Underactive Unresponsive Breathing Slow Coat Piloerection Eyelids (Left) Partially Closed	1-7, 11, 14, 18 1-3, 6-7, 18 14 1-7, 14, 18 1, 3-5, 11, 14 1, 3-5, 11, 14 1 1 7, 14, 19 7 7, 19 14 19
			Gestation		

TLL Total litter loss

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	Phase	Sign	Day(s)
3F	270	TLL	Gestation	Eyelids (Right) Partially Closed	19

TLL Total litter loss

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	T Phase	Treatment	Sign	Day(s)
4F	271	TR	T	Treatment	Behaviour Underactive Unresponsive Breathing Shallow Coat Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed Posture Hunched Staining Other Colour (see comment) <i>Comments:</i> <i>brown staining head</i>	1-8, 11, 14, 18, 21 1-2, 4-8, 11, 14, 18, 21 1-7, 14 1-8, 14, 18, 21 1, 3-8, 11, 14, 18, 21 1, 3-8, 11, 14, 18, 21 8 8 8
				Gestation	Behaviour Underactive Unresponsive Breathing Slow Coat Piloerection	0, 7, 14, 19 0, 19 7, 14, 19 0, 7, 14, 19

T Terminal sacrifice
TR Total resorption

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group : 1 2 3 4
 Compound : Control 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene
 Exposure level (ppm) : 0 198 505 2900

Group /Sex	Animal Number	Death Code	Phase	Sign	Day(s)
4F	271 TR	T	Gestation	Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed Muscle Reaction Reduced Body Tone	0, 7, 14, 19 0, 7, 14, 19 14
	272 FTM	T	Treatment	Behaviour Underactive Unresponsive Breathing Shallow Slow Coat Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed	1-7, 11, 14, 18, 21, 25, 28, 32, 35, 40, 47 1-2, 4-7, 11, 14, 18, 21, 25, 32, 40, 47 1-7, 14 25, 28, 35, 40 1-7, 14, 18, 21, 28, 32, 40, 47 1, 3-7, 11, 14, 18, 21, 25, 28, 35, 40, 47 1, 3-7, 11, 14, 18, 21, 25, 28, 35, 40, 47

T Terminal sacrifice
 TR Total resorption
 FTM Failed to mate

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group : 1 2 3 4
 Compound : Control 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene
 Exposure level (ppm) : 0 198 505 2900

Group /Sex	Animal Number	Death Code	Phase	Sign	Day(s)
4F	273	TLL	Treatment	Behaviour Underactive Unresponsive Breathing Shallow Coat Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed Posture Hunched Staining Other Colour (see comment)	1-8, 11, 14 1-2, 4-8, 11, 14 1-7, 14 1-8, 14 1, 3-8, 11, 14 1, 3-8, 11, 14 8 8
			Gestation	Comments: <i>brown staining head</i> Behaviour Underactive Unresponsive Breathing Slow Coat Piloerection	8 8 0, 7, 14, 19 0, 14 0, 7, 19 0, 7, 14

TLL Total litter loss

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Group /Sex	Animal Number	Death Code	Phase	Sign	Day(s)
4F	273	TLL	Gestation	Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed	0, 7, 14, 19 0, 7, 14, 19

TLL Total litter loss

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	Phase	Sign	Day(s)
4F	274	TR	Treatment	Behaviour Underactive Unresponsive Breathing Shallow Coat	1-7, 11, 14 1-2, 4-7, 11, 14 1-7, 14
				Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed	1-7, 14 1, 3-7, 11, 14 1, 3-7, 11, 14
			Gestation	Behaviour Underactive Unresponsive Coat	0, 7, 14, 19 0, 14
				Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed Posture Hunched	0, 7, 19 0, 7 0, 7 14

T Terminal sacrifice
TR Total resorption

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	Treatment Phase	Sign	Day(s)
4F	275	FTM	T	Behaviour	
				Underactive	1-8, 11, 14, 18, 21, 25, 28, 32, 35, 40, 47
				Unresponsive	1-2, 4-8, 11, 14, 18, 21, 25, 32, 40, 47
				Breathing	
				Shallow	1-7, 14
				Slow	25, 28, 35, 40
				Coat	
				Piloerection	1-8, 14, 18, 21, 28, 32, 40, 47
				Eyelids (Left)	
				Partially Closed	1, 3-8, 11, 14, 18, 21, 25, 28, 35, 40, 47
				Eyelids (Right)	
				Partially Closed	1, 3-8, 11, 14, 18, 21, 25, 28, 35, 40, 47
				Posture	
				Hunched	8
				Staining	
				Other Colour (see comment)	8
				Comments:	
				<i>Brown staining head</i>	8

T Terminal sacrifice
FTM Failed to mate

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group Compound : 1 Control : 2 2-bromo-3,3,3-trifluoropropene 198 : 3 2-bromo-3,3,3-trifluoropropene 505 : 4 2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm) : 0

Group /Sex	Animal Number	Death Code	Phase	Sign	Day(s)
4F	276	W	Treatment	Behaviour Unreactive Unresponsive Breathing Shallow Coat Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed	1-7, 11, 14, 18, 21 1-2, 4-7, 11, 14, 18, 21 1-7, 14 1-7, 14, 18, 21 1, 3-7, 11, 14, 18, 21 1, 3-7, 11, 14, 18, 21
			Gestation	Behaviour Unreactive Unresponsive Breathing Slow Coat Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed	0, 7, 14, 19 0 7, 19 0, 14 0, 7, 19 0, 7, 19

W Killed for welfare reasons

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group : 1
Compound : Control
Exposure level (ppm) : 0

2-bromo-3,3,3-trifluoropropene 198

2-bromo-3,3,3-trifluoropropene 505

2-bromo-3,3,3-trifluoropropene 2900

Group /Sex	Animal Number	Death Code	Phase	Sign	Day(s)
4F	277	FTM	T	Treatment	
				Behaviour	
				Underactive	1-7, 11, 14, 18, 21, 25, 28, 32, 35, 40, 47
				Unresponsive	1-2, 4-7, 11, 14, 18, 21, 25, 32, 40, 47
				Breathing	
				Shallow	1-7, 14
				Slow	25, 28, 35, 40
				Coat	
				Piloerection	1-7, 14, 18, 21, 28, 32, 40, 47
				Eyelids (Left)	
				Partially Closed	1, 3-7, 11, 14, 18, 21, 25, 28, 35, 40, 47
				Eyelids (Right)	
				Partially Closed	1, 3-7, 11, 14, 18, 21, 25, 28, 35, 40, 47

T Terminal sacrifice
FTM Failed to mate

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	Phase	Sign	Day(s)
4F	278	TR	Treatment	Behaviour Underactive Unresponsive Breathing Shallow Coat	1-7, 11, 14, 18 1-2, 4-7, 11, 14, 18 1-7, 14
				Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed	1-7, 14, 18 1, 3-7, 11, 14, 18
			Gestation	Behaviour Underactive Unresponsive Breathing Slow Coat	1, 3-7, 11, 14, 18 7, 14, 19 7, 14 7, 19
				Piloerection Eyelids (Left) Partially Closed Eyelids (Right) Partially Closed	14 7, 19 7, 19

T Terminal sacrifice
TR Total resorption

APPENDIX 4 - continued

Request ID: 284710

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	Phase	Treatment	Sign	Day(s)
4F	279	W			Behaviour	1-7, 11, 14, 18, 21, 25
					Underactive	1-7, 14, 18, 21
					Unresponsive	1, 3-7, 11, 14, 18, 21, 25
					Breathing	1, 3-7, 11, 14, 18, 21, 25
					Shallow	1, 3-7, 11, 14, 18, 21, 25
					Slow	0, 7, 14, 19
					Coat	0, 14, 19
					Piloerection	0, 7, 14, 19
					Eyelids (Left)	14, 19
					Partially Closed	0, 7, 14, 19
					Eyelids (Right)	0, 7, 14, 19
					Partially Closed	0, 7, 14, 19
					Behaviour	
					Underactive	
					Unresponsive	
					Breathing	
					Slow	
					Coat	
					Piloerection	
					Eyelids (Left)	
					Partially Closed	
					Eyelids (Right)	
					Partially Closed	

W Killed for welfare reasons

Request ID: 284710

APPENDIX 4 - continued

Signs associated with dosing - individual observations prior to mating, during gestation and lactation for females - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Death Code	T Phase	Treatment	Sign	Day(s)
4F	280	NP	T		Behaviour	
					Underactive	1-7, 11, 14, 18
					Unresponsive	1-2, 4-7, 11, 14, 18
					Breathing	
					Shallow	
					Coat	1-7, 14
					Piloerection	
					Eyelids (Left)	1-7, 14, 18
					Partially Closed	
					Eyelids (Right)	1, 3-7, 11, 14, 18
					Partially Closed	
				Gestation	Behaviour	
					Underactive	7, 14, 19
					Unresponsive	7, 14
					Breathing	
					Slow	7, 19
					Coat	
					Piloerection	14
					Eyelids (Left)	
					Partially Closed	7, 19
					Eyelids (Right)	
					Partially Closed	7, 19

T Terminal sacrifice
NP Not pregnant

Request ID: 284396

APPENDIX 5

Bodyweight - individual values for males - F0 generation (g)

Group	Animal Number	Day	Day	Day	Day	Day	Day	Day	Day	Day	Day	Day	Day	Day	Day	Day	Day	
/Sex		-7	1	8	11	15	22	29	33	36	39	43	46					
			Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900												
1M	201	257	327	377	394	410	414	460	477	490	495	510	522					
	202	248	318	363	380	405	411	438	442	456	453	463	476					
	203	268	332	373	372	409	431	446	458	457	468	487	499					
	204	255	328	375	389	416	447	478	499	514	516	533	541					
	205	270	349	401	424	450	478	506	521	532	530	538	553					
	206	249	332	402	422	462	487	515	539	545	545	551	563	574				
	207	257	322	373	386	404	433	453	471	484	484	495	502	512				
	208	259	328	371	398	414	450	488	477	488	504	512	521	536				
	209	259	339	391	409	433	467	493	493	507	520	528	547	555				
	210	269	319	374	381	401	421	421	450	472	475	479	501	510				
2M	211	256	327	384	400	424	457	477	485	499	503	490	496					
	212	251	304	326	335	345	372	382	388	392	391	399	401					
	213	253	320	360	369	396	422	448	466	475	483	490	504					
	214	274	338	408	432	458	495	522	533	547	547	551	561					
	215	239	303	362	388	410	434	457	474	487	487	500	510					
	216	262	339	389	412	438	468	505	510	518	518	526	533					
	217	258	321	365	377	388	406	425	432	436	441	453	461					
	218	247	313	338	347	362	379	402	413	413	415	426	427	432				
	219	248	308	325	332	341	360	397	400	400	411	415	423	431				
	220	255	322	351	354	370	405	417	411	417	423	429	429	434				

Request ID: 284396

APPENDIX 5 - continued

Bodyweight - individual values for males - F0 generation (g)

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Day
1M	201	534
	202	479
	203	512
	204	563
	205	570
	206	591
	207	529
	208	545
	209	570
	210	524
2M	211	503
	212	413
	213	505
	214	567
	215	516
	216	545
	217	468
	218	438
	219	436
	220	438

Request ID: 284396

APPENDIX 5 - continued

Bodyweight - individual values for males - F0 generation (g)

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900
 Compound :
 Exposure level (ppm) : 0

Group /Sex	Animal Number	Day																										
3M	221	255	323	340	345	368	385	413	421	430	437	445	459	221	255	323	340	345	368	385	413	421	430	437	445	459		
	222	251	307	332	344	354	374	380	389	397	396	399	405	222	251	307	332	344	354	374	380	389	397	399	405	405		
	223	254	318	343	355	371	393	405	416	419	424	418	425	223	254	318	343	355	371	393	405	416	419	424	418	425		
	224	249	319	358	370	384	416	421	425	434	431	426	434	224	249	319	358	370	384	416	421	425	434	431	426	434		
	225	248	322	356	366	398	421	446	435	456	459	463	472	225	248	322	356	366	398	421	446	435	456	459	463	472		
	226	258	317	338	338	359	378	416	407	416	419	426	433	438	226	258	317	338	338	359	378	416	407	416	419	426	433	438
	227	257	330	375	385	407	431	475	455	479	479	483	497	504	227	257	330	375	385	407	431	475	455	479	479	483	497	504
	228	268	332	349	353	372	391	426	406	436	430	436	442	442	228	268	332	349	353	372	391	426	406	436	430	436	442	442
	229	254	322	344	347	367	383	417	407	417	428	432	436	450	229	254	322	344	347	367	383	417	407	417	428	432	436	450
	230	266	333	354	367	385	406	427	422	444	443	444	456	462	230	266	333	354	367	385	406	427	422	444	443	456	462	
4M	231	242	314	341	355	375	405	425	444	452	451	457	467	231	242	314	341	355	375	405	425	444	452	451	457	467		
	232	254	337	350	358	372	387	408	401	411	406	415	407	232	254	337	350	358	372	387	408	401	411	406	415	407		
	233	253	316	315	326	331	352	369	362	380	370	385	375	233	253	316	315	326	331	352	369	362	380	370	385	375		
	234	246	312	321	339	344	369	387	383	392	395	401	409	234	246	312	321	339	344	369	387	383	392	395	401	409		
	235	246	333	355	366	387	406	430	425	437	437	444	450	235	246	333	355	366	387	406	430	425	437	437	444	450		
	236	276	343	356	373	389	382	431	429	426	426	450	447	236	276	343	356	373	389	382	431	429	426	426	450	447		
	237	252	310	337	343	361	384	393	393	397	397	397	396	396	237	252	310	337	343	361	384	393	393	397	397	397	396	
	238	259	325	333	351	356	376	396	403	396	399	397	389	387	238	259	325	333	351	356	376	396	403	396	399	397	389	387
	239	252	339	367	385	396	416	431	425	442	435	442	440	449	239	252	339	367	385	396	416	431	425	442	435	442	440	449
	240	252	322	341	353	368	385	408	406	418	416	418	416	418	240	252	322	341	353	368	385	408	406	418	416	418	416	418

Request ID: 284396

APPENDIX 5 - continued

Bodyweight - individual values for males - F0 generation (g)

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Day
		50
3M	221	462
	222	412
	223	431
	224	443
	225	478
	226	444
	227	510
	228	451
	229	449
	230	475
4M	231	468
	232	406
	233	380
	234	410
	235	457
	236	459
	237	403
	238	385
	239	447
	240	423

Request ID: 284397

APPENDIX 6

Bodyweight - individual values for females before pairing - F0 generation (g)

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900
 Compound :
 Exposure level (ppm) : 0

Group /Sex	Animal Number	Day -7	Day 1	Day 8	Day 11	Day 15	Day 22
1F	241	206	237	247	250	257	
	242	193	213	231	233	240	
	243	196	224	232	233	240	
	244	194	219	239	238	248	
	245	209	224	227	243	248	
	246	207	237	255	254	257	
	247	189	215	219	219	223	
	248	219	247	255	254	258	
	249	196	214	230	235	242	
	250	210	224	235	234	242	
2F	251	215	234	241	247	258	
	252	206	224	234	238	242	
	253	203	231	231	233	242	
	254	198	231	249	252	267	
	255	201	218	247	255	263	276
	256	197	228	239	239	242	
	257	215	230	240	254	256	
	258	205	224	236	234	241	
	259	201	220	223	237	243	
	260	209	235	253	256	264	

Request ID: 284397

APPENDIX 6 - continued

Bodyweight - individual values for females before pairing - F0 generation (g)

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900

Exposure level (ppm) : 0

Group /Sex	Animal Number	Day -7	Day 1	Day 8	Day 11	Day 15	Day 22	Day 29	Day 33	Day 36	Day 39	Day 43	Day 46
3F	261	205	225	231	227	235							
	262	207	237	246	255	263							
	263	209	234	238	245	250							
	264	207	214	229	242	241							
	265	198	229	236	241	242							
	266	202	213	222	225	229	230						
	267	211	237	238	236	255							
	268	199	228	230	232	245							
	269	195	215	220	225	232							
	270	192	217	231	232	247							
4F	271	218	243	206	219	230							
	272FTM	214	239	238	237	230	236	245	243	255	247	254	254
	273	208	235	217	224	219							
	274	197	204	230	238	235							
	275FTM	205	230	238	241	237	236	235	248	257	247	249	251
	276	202	223	222	232	237							
	277FTM	212	226	238	233	224	241	241	245	251	242	244	248
	278	202	221	226	233	241							
	279	195	226	221	226	229	242						
	280	218	233	235	231	234							

FTM Failed to mate

APPENDIX 6 - continued

Request ID: 284397

Bodyweight - individual values for females before pairing - F0 generation (g)

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Day	Day
4F	272FTM	252	255
	275FTM	257	262
	277FTM	242	243

FTM Failed to mate

Request ID: 284398

APPENDIX 7

Bodyweight - individual values for females after mating - F0 generation (g)

Group Compound	Exposure level (ppm)	1 Control		2-bromo-3,3,3-trifluoropropene 198		2-bromo-3,3,3-trifluoropropene 505		2-bromo-3,3,3-trifluoropropene 2900	
		Day 0	Day 3	Day 7	Day 10	Day 14	Day 17	Day 20	
1F	241	262	276	298	302	320	349	399	
	242	246	254	268	284	304	328	373	
	243	245	259	276	292	310	340	390	
	244	253	277	293	299	327	375	423	
	245	247	264	300	303	322	352	392	
	246	273	284	316	320	351	389	451	
	247	236	253	266	285	300	337	384	
	248	271	286	301	313	337	364	416	
	249	257	282	304	322	347	370	438	
	250	267	293	317	323	356	392	434	
2F	251	260	272	286	292	311	338	390	
	252	243	261	269	283	297	334	380	
	253	248	268	283	295	307	329	369	
	254	280	289	305	324	351	388	451	
	255	266	297	320	334	354	390	446	
	256	249	267	272	259	294	339	394	
	257NP	269	273	288	285	288	293	293	
	258	244	257	267	280	299	308	338	
	259	243	260	280	292	306	328	371	
	260	264	275	293	308	331	371	433	

NP Not pregnant, excluded from calculation of group means and statistical evaluation

APPENDIX 7 - continued

Request ID: 284398

Bodyweight - individual values for females after mating - F0 generation (g)

Group Compound	:	1 Control	2 2-bromo-3,3,3-trifluoropropene 198	3 2-bromo-3,3,3-trifluoropropene 505	4 2-bromo-3,3,3-trifluoropropene 2900			
Exposure level (ppm)	:	0	0	0	0			
Group /Sex	Animal Number	Day 0	Day 3	Day 7	Day 10	Day 14	Day 17	Day 20
3F	261	249	255	264	281	303	332	379
	262	267	284	296	295	332	351	395
	263U TR	266	284	286	297	308	282	287
	264	246	268	286	297	326	347	401
	265	237	259	274	285	303	322	355
	266TLL	234	263	276	280	302	305	331
	267	252	271	276	291	309	327	372
	268	254	263	281	286	313	339	389
	269	249	257	266	279	298	324	372
	270	256	266	278	291	320	350	399
4F	271TR	244	251	271	281	265	275	282
	273	227	234	239	248	272	281	316
	274TR	238	258	264	281	293	307	320
	276W	215	259	246	266	282	301	322
	278TR	256	258	272	275	302	304	300
	279W	251	262	270	280	294	289	289
	280NP	235	261	260	264	265	257	264
	U	Unilateral implantation						
TR	Total resorption, excluded from calculation of group means and statistical evaluation							
NP	Not pregnant, excluded from calculation of group means and statistical evaluation							
W	Killed for welfare reasons, excluded from calculation of group means and statistical evaluation							
TLL	Total litter loss, excluded from calculation of group means and statistical evaluation							

Request ID: 284399

APPENDIX 8

Bodyweight - individual values for females during lactation - F0 generation (g)

Group : 1 2 3 4
 Compound : Control 2-bromo-3,3,3-trifluoropropene 505 2-bromo-3,3,3-trifluoropropene 2900
 Exposure level (ppm) : 0 198

Group /Sex	Animal Number	Day	Day	Day
		1	5	10
1F	241	296	304	344
	242	292	295	304
	243	281	288	328
	244	312	352	370
	245	304	317	329
	246	327	359	374
	247	269	293	313
	248	313	342	356
	249	320	337	340
	250	327	332	357
2F	251	302	321	328
	252	279	290	284
	253	281	285	306
	254	340	356	377
	255	319	321	344
	256	296	321	327
	258	285	282	302
	259	290	306	309
	260	309	317	322

Request ID: 284399

APPENDIX 8 - continued

Bodyweight - individual values for females during lactation - F0 generation (g)

Group : 1 2 3 4
 Compound : Control 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene
 Exposure level (ppm) : 0 198 505 2900

Group /Sex	Animal Number	Day		Day	
		1	5	10	10
3F	261	284	298	312	
	262W	310	309	305	
	264	310			
	265TLL	288			
	267TLL	304			
	268	290	294	293	
4F	269	284	296	277	
	270TLL	297			
	273TLL	260			

W Killed for welfare reasons, excluded from calculation of group means and statistical evaluation
 TLL Total litter loss, excluded from calculation of group means and statistical evaluation

Request ID: 284400

APPENDIX 9

Food consumption - individual values for males and before pairing for females - F0 generation (g/animal/week)

Group /Sex	Cage Number	Week -1	1		2		3		4	
			Control	0	2-bromo-3,3,3- trifluoropropene	198	2-bromo-3,3,3- trifluoropropene	505	2-bromo-3,3,3- trifluoropropene	2900
1M	41	201	213							
	42	213	228							
2M	43	200	198							
	44	196	185							
3M	45	198	168							
	46	203	156							
4M	47	198	145							
	48	210	152							

Request ID: 284400

APPENDIX 9 - continued

Food consumption - individual values for males and before pairing for females - F0 generation (g/animal/week)

Group Compound : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm) : 0

Group /Sex	Cage Number	Week -1		Week 1		Week 2	
1F	49	135	132	132	129		
	50	139	134	134	132		
2F	51	137	117	117	122		
	52	137	118	118	126		
3F	53	137	101	101	115		
	54	136	102	102	113		
4F	55	144	82	82	96		
	56	131	90	90	101		

Request ID: 284401

APPENDIX 10

Food consumption - individual values for females after mating - F0 generation (g/animal/day)

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900
 Compound :
 Exposure level (ppm) : 0

Group /Sex	Animal Number	Day 0-2	Day 3-6	Day 7-9	Day 10-13	Day 14-16	Day 17-19
1F	241	23	27	26	25	29	25
	242	19	21	23	26	23	24
	243	22	23	25	24	24	27
	244	25	25	26	29	30	32
	245	20	27	25	27	29	27
	246	20	26	25	28	29	35
	247	28	24	26	25	29	29
	248	23	22	22	24	25	28
	249	28	31	32	31	27	33
	250	28	31	30	33	33	31
2F	251	19	20	19	22	22	28
	252	20	19	21	22	22	27
	253	21	22	22	23	23	28
	254	23	24	25	28	30	34
	255	27	25	22	26	29	30
	256	24	16	14	27	29	36
	257 NP	23	24	21	22	19	24
	258	21	20	20	24	20	27
	259	21	23	22	25	25	30
	260	20	24	24	26	26	32

NP Not pregnant, excluded from calculation of group means and statistical evaluation

Request ID: 284401

APPENDIX 10 - continued

Food consumption - individual values for females after mating - F0 generation (g/animal/day)

Group : 1 Control 2 2-bromo-3,3,3- 3 2-bromo-3,3,3- 4 2-bromo-3,3,3-
Compound : trifluoropropene 198 trifluoropropene 505 trifluoropropene 2900
Exposure level (ppm) : 0

Group /Sex	Animal Number	Day 0-2	Day 3-6	Day 7-9	Day 10-13	Day 14-16	Day 17-19
3F	261	18	20	22	21	23	29
	262	23	21	22	27	26	30
	263 U TR	19	17	20	21	16	21
	264	23	25	23	25	26	31
	265	21	24	24	22	22	28
	266	21	21	19	24	22	28
	267	22	20	20	21	20	29
	268	20	22	23	25	25	30
	269	20	20	21	24	24	27
	270	23	24	28	26	26	28
4F	271 TR	18	20	20	19	15	20
	273	15	16	17	20	21	29
	274 TR	21	21	21	23	24	24
	276 W	20	16	18	19	24	26
	278 TR	20	22	21	23	22	23
	279 W	20	21	21	23	23	22
	280 NP	23	21	20	17	18	18

U Unilateral implantation
TR Total resorption, excluded from calculation of group means and statistical evaluation
W Killed for welfare reasons, excluded from calculation of group means and statistical evaluation
NP Not pregnant, excluded from calculation of group means and statistical evaluation

Request ID: 284402

APPENDIX 11

Food consumption - individual values for females during lactation - F0 generation (g/animal/day)

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Day	
		1-4	5-9
1F	241	37	54
	242	33	47
	243	40	53
	244	48	64
	245	39	51
	246	44	64
	247	39	55
	248	38	58
	249	43	57
	250	35	57
2F	251	39	44
	252	27	31
	253	31	42
	254	36	45
	255	28	41
	256	39	42
	258	22	27
	259	29	35
	260	32	40

APPENDIX 11 - continued

Request ID: 284402

Food consumption - individual values for females during lactation - F0 generation (g/animal/day)

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group /Sex	Animal Number	Day 1-4	Day 5-9
3F	261	32	33
	264	21	23
	268	29	32
	269	31	33

Request ID: 287346

APPENDIX 12

Water consumption - individual values for males and females before pairing - F0 generation (mL/animal/day)

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900
 Compound :
 Exposure level (ppm) : 0

Group /Sex	Cage Number	Day 9	Day 10	Day 11	Day 32	Day 33	Day 34	Day 35	Day 39	Day 43	Day 44	Day 45	Day 46	Day 47
1M	41	40	43	42	41	42	36	39	39	43	35	41	41	39
	42	43	50	47	44	47	40	37	45	44	42	44	42	41
2M	43	48	52	47	44	43	40	41	45	39	41	45	42	41
	44	35	41	35	37	34	33	30	34	31	34	36	33	32
3M	45	43	44	40	43	38	38	38	42	38	39	44	36	42
	46	44	48	46	45	41	39	36	42	38	39	44	42	39
4M	47	45	50	48	42	40	39	37	42	39	40	43	42	42
	48	45	49	48	41	38	34	35	35	34	36	43	36	34

APPENDIX 12 - continued

Request ID: 287346

Water consumption - individual values for males and females before pairing - F0 generation (mL/animal/day)

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group	Cage	Day
/Sex	Number	48
1M	41	39
	42	41
2M	43	38
	44	31
3M	45	36
	46	38
4M	47	42
	48	35

Request ID: 287346

APPENDIX 12 - continued

Water consumption - individual values for males and females before pairing - F0 generation (mL/animal/day)

Group : 1
Compound : Control
Exposure level (ppm) : 0

2 2-bromo-3,3,3-trifluoropropene 198
3 2-bromo-3,3,3-trifluoropropene 505
4 2-bromo-3,3,3-trifluoropropene 2900

Group /Sex	Cage Number	Day 9	Day 10	Day 11	Day 33	Day 34	Day 35	Day 39	Day 43	Day 44	Day 45	Day 46	Day 47
1F	49	22	37	29									
	50	23	32	32									
2F	51	30	41	30									
	52	29	43	31									
3F	53	36	56	38									
	54	40	61	41									
4F	55	54	64	52	34	36	26	33	30	32	48	34	37
	56	36	54	39	7	8	14	14	11	12	10	10	8

Request ID: 287346

APPENDIX 12 - continued

Water consumption - individual values for males and females before pairing - F0 generation (mL/animal/day)

Group Compound	:	1						
	:	Control						
Exposure level (ppm)	:	0						
			2	3	4			
			2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene			
			198	505	2900			

Group /Sex	Cage Number	Day	Day
1F	49	48	53
	50		
2F	51		
	52		
3F	53		
	54		
4F	55	30	41
	56	10	13

APPENDIX 13

Request ID: 284865

Water consumption - individual values for females after mating - F0 generation (mL/animal/day)

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900

Compound : Control 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene

Exposure level (ppm) : 0 198 505 2900

Group /Sex	Animal Number	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12
1F	241	56	71	66	49	54	62	62	61	61	59	72	62	60
	242	59	82	71	52	63	68	61	62	55	65	78	65	66
	243	35	42	52	80	55	46	61	60	62	58	59	67	@
	244	60	67	66	36	33	43	38	41	47	38	84	65	67
	245	49	61	68	38	60	52	66	58	64	54	52	39	48
	246	6	63	52	63	48	65	61	61	73	68	77	75	76
	247	70	70	40	40	43	42	43	48	41	58	55	55	48
	248	57	68	66	59	55	66	59	59	56	75	68	68	74
	249	63	77	76	48	53	73	73	52	74	58	62	63	65
	250	56	67	67	54	62	61	61	57	64	58	71	71	70
2F	251	70	79	77	54	67	69	71	68	56	69	62	55	62
	252	42	49	80	79	76	48	76	72	69	71	74	79	87
	253	56	85	107	94	57	70	72	77	74	91	86	54	50
	254	31	51	81	65	42	68	54	62	60	49	61	84	77
	255	49	55	55	96	85	91	88	91	87	65	79	86	98
	256	41	43	44	36	45	66	41	72	88	82	89	85	78
	257 NP	32	36	47	44	31	57	43	43	34	37	40	69	55
	258	29	36	54	70	58	36	54	54	55	58	62	59	65
	259	43	62	59	54	54	54	54	60	58	62	75	77	75
	260	30	40	35	51	65	69	58	58	65	64	76	70	71

NP Not pregnant, excluded from calculation of group means and statistical evaluation
@ Water bottle leaked

Request ID: 284865

APPENDIX 13 - continued

Water consumption - individual values for females after mating - F0 generation (mL/animal/day)

Group Compound : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900

Exposure level (ppm) : 0

Group /Sex	Animal Number	Day 13	Day 14	Day 15	Day 16	Day 17	Day 18
1F	241	71	71	76	71	72	70
	242	69	74	71	66	77	69
	243	75	60	71	71	69	67
	244	70	73	83	76	87	86
	245	48	52	48	49	71	75
	246	67	57	78	82	63	63
	247	70	65	57	65	62	83
	248	75	67	62	79	82	79
	249	64	58	67	62	80	83
	250	80	70	68	60	57	60
2F	251	66	63	65	67	82	76
	252	77	81	85	68	88	72
	253	59	63	63	85	82	78
	254	78	85	55	59	52	76
	255	85	87	91	112	82	57
	256	89	86	95	96	87	68
	257 NP	53	46	58	53	49	40
	258	67	64	73	80	78	72
	259	90	88	86	89	71	57
	260	84	86	77	83	57	50

NP Not pregnant, excluded from calculation of group means and statistical evaluation

Request ID: 284865

APPENDIX 13 - continued

Water consumption - individual values for females after mating - F0 generation (mL/animal/day)

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900

Exposure level (ppm) : 0

Group /Sex	Animal Number	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	
3F	261	50	52	63	53	65	68	71	75	79	77	89	85	75	
	262	46	41	38	39	27	54	40	44	41	77	75	76	83	
	263 U TR	37	56	67	62	69	68	71	72	94	79	66	80	81	
	264	68	70	74	64	58	73	64	73	70	55	77	86	36	
	265	44	59	87	82	64	56	83	77	80	96	86	79	90	
	266	63	77	78	91	82	105	70	61	61	67	74	78	73	69
	267	77	89	85	72	57	64	60	61	63	58	85	85	93	83
	268	43	56	58	56	43	51	47	49	55	54	91	83	83	89
	269	35	49	58	58	66	60	60	55	63	62	64	66	66	66
	270	60	75	63	40	66	66	56	68	62	59	66	72	65	66
	4F	271 TR	74	76	70	81	75	84	72	85	70	79	63	80	68
		273	34	42	75	80	68	51	70	73	68	74	57	79	43
274 TR		56	83	96	85	65	60	68	65	76	64	64	106	@	
276 W		72	58	63	60	53	64	72	75	67	80	82	86	67	
278 TR		60	82	65	53	55	49	44	44	55	37	89	71	80	
279 W		64	39	74	63	55	68	65	57	42	42	80	83	87	
280 NP		74	82	80	60	66	69	73	79	79	78	93	70	79	

- U Unilateral implantation
- TR Total resorption, excluded from calculation of group means and statistical evaluation
- W Killed for welfare reasons, excluded from calculation of group means and statistical evaluation
- NP Not pregnant, excluded from calculation of group means and statistical evaluation
- @ Water bottle leaked

Request ID: 284865

APPENDIX 13 - continued

Water consumption - individual values for females after mating - F0 generation (mL/animal/day)

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900

Compound :
Exposure level (ppm) : 0

Group /Sex	Animal Number	Day 13	Day 14	Day 15	Day 16	Day 17	Day 18
3F	261	96	84	93	87	86	86
	262	90	71	69	90	79	85
	263 U TR	74	59	76	47	79	80
	264	68	51	54	84	80	82
	265	93	89	94	96	104	86
	266	102	98	108	97	102	107
	267	98	100	113	100	103	105
	268	94	96	96	91	100	92
	269	61	65	62	86	80	72
	270	79	84	87	86	82	84
4F	271 TR	55	66	83	82	82	100
	273	44	47	74	53	49	47
	274 TR	89	62	116	107	98	87
	276 W	95	82	89	94	87	89
	278 TR	80	91	89	81	56	47
	279 W	78	83	91	91	49	74
	280 NP	89	95	72	80	47	42

U Unilateral implantation
 TR Total resorption, excluded from calculation of group means and statistical evaluation
 W Killed for welfare reasons, excluded from calculation of group means and statistical evaluation
 NP Not pregnant, excluded from calculation of group means and statistical evaluation

APPENDIX 14

Request ID: 284866

Water consumption - individual values for females during lactation - F0 generation (mL/animal/day)

Group /Sex	Animal Number	1		2		3		4		5		6		7		8		9		
		Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	Day 15	Day 16	Day 17	Day 18	Day 19
1F	241	53	95	56	66	67	100	84	106	110										
	242	46	103	45	62	80	86	75	94	66										
	243	43	51	66	121	92	78	88	108	79										
	244	52	142	74	94	102	108	80	107	83										
	245	55	82	42	61	86	74	81	94	106										
	246	44	62	73	107	82	107	112	125	117										
	247	104	47	67	61	69	79	78	93	108										
	248	101	56	66	83	95	87	99	100	109										
	249	103	57	76	75	107	85	106	114	105										
	250	111	51	60	65	102	81	101	107	120										
2F	251	145	44	67	58	72	57	80	84	106										
	252	39	46	112	48	46	46	69	59	88										
	253	43	96	40	53	74	95	87	120	114										
	254	43	104	52	66	80	67	75	83	95										
	255	18	68	44	43	80	56	85	98	64										
	256	58	116	61	75	58	256	77	95	82										
	258	34	135	32	31	59	51	46	53	69										
	259	95	37	53	46	61	52	83	76	103										
	260	89	41	55	51	74	59	81	86	114										

Request ID: 284866

APPENDIX 14 - continued

Water consumption - individual values for females during lactation - F0 generation (mL/animal/day)

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900

Compound : Control 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene

Exposure level (ppm) : 0 198 505 2900

Group /Sex	Animal Number	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9
3F	261	39	51	56	79	53	76	83	95	93
	264	26	32	35	64	34	52	61	75	53
	268	38	43	57	49	65	106	83	89	88
	269	30	49	66	62	60	45	88	86	62
	270 TLL	96								
4F	273 TLL	111								

TLL Total litter loss, excluded from calculation of group means and statistical evaluation

APPENDIX 15

Oestrous cycle length, mating performance, fertility and gestation length - individual values - F0 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900

Exposure level (ppm) : 0

Group	Female number	Number of copulation plugs	Sperm count category ^ω	Individual cycle length (days)	Pre-coital interval (days)	Male number	Pregnancy	Gestation length (days)
1	241	4	2	4,4,4,4	3	201	+	22
	242	4	4	4,4,4,4	3	202	+	22
	243	4	4	4,4,4	1	203	+	22.5
	244	6	4	4,4,4,4	3	204	+	22.5
	245	4	4	5 [^] ,5,5,4	3	205	+	22.5
	246	3	4	5 [^] ,5,5,5	5	206	+	22
	247	5	0	4,4,4,4	4	207	+	22
	248	3	4	4,4,4,4	4	208	+	22
	249	4	3	4,4,4,4	3	209	+	23
	250	4	3	4,4,4,4	4	210	+	22

^ω 0 No sperm

1 Occasional sperm

2 Continuous few sperm

3 Many scattered sperm

4 Solid masses of sperm

[^] Estimated minimum cycle length - cycle in progress at start or end of smearing period

APPENDIX 15 - continued

Oestrous cycle length, mating performance, fertility and gestation length - individual values - F0 generation

Group : 1 2 3 4
 Compound : Control 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene
 Exposure level (ppm) : 0 198 505 2900

Group	Female number	Number of copulation plugs	Sperm count category ^ω	Individual cycle length (days)	Pre-coital interval (days)	Male number	Pregnancy	Gestation length (days)
2	251	4	3	5,5,5	3	211	+	23,5
	252	4	3	4,5,5	1	212	+	23
	253	4	2	4,5,5	2	213	+	23,5
	254	4	1	5,5,5	2	214	+	23
	255	1	2	5,4,5,5,5	10	215	+	23,5
	256	5	3	5,5,5	2	216	+	23
	257	3	1	5,5,4	2	217	-	-
	258	2	3	4,4,5	1	218	+	23,5
	259	4	4	5,5,5	3	219	+	23,5
	260	4	1	4,4,4,4	3	220	+	23

- ^ω
- 0 No sperm
 - 1 Occasional sperm
 - 2 Continuous few sperm
 - 3 Many scattered sperm
 - 4 Solid masses of sperm

APPENDIX 15 - continued

Oestrous cycle length, mating performance, fertility and gestation length - individual values - F0 generation

Group : 1 2 3 4
 Compound : Control 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene
 Exposure level (ppm) : 0 198 505 2900

Group	Female number	Number of copulation plugs	Sperm count category ^ω	Individual cycle length (days)	Pre-coital interval (days)	Male number	Pregnancy	Gestation length (days)
3	261	3	0	5,5,5	3	221	+	23.5
	262	3	3	5 [^] ,5,5,5	4	222	+	24.5
	263NLL	4	4	7,6,5	5	223	+	-
	264	3	4	12,5	4	224	+	23.5
	265	2	3	6,4,4	1	225	+	25.5
	266	3	0	5,5,6,6	8	226	+	25
	267	3	1	5,6,5	3	227	+	25.5
	268	5	0	5,5,5	3	228	+	24.5
	269	3	0	5 [^] ,5,5,5	5	229	+	23.5
	270	1	2	4,4,4,4	3	230	+	23

^ω 0 No sperm

1 Occasional sperm

2 Continuous few sperm

3 Many scattered sperm

4 Solid masses of sperm

[^] Estimated minimum cycle length - cycle in progress at start or end of smearing period

NLL No live litter - pregnancy indicated by implantation sites

APPENDIX 15 - continued

Oestrous cycle length, mating performance, fertility and gestation length - individual values - F0 generation

Group : 1 2 3 4
 Compound : Control 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene
 Exposure level (ppm) : 0 198 505 2900

Group	Female number	Number of copulation plugs	Sperm count category ^ω	Individual cycle length (days)	Pre-coital interval (days)	Male number	Pregnancy	Gestation length (days)
4	271NLL	2	3	12,6	6	231	+	-
	272	-	-	15 [^] ,6,9 [^]	FTM	-	-	-
	273	4	3	14	1	233	+	25.5
	274NLL	4	3	16	2	234	+	-
	275	-	-	7,7,5,2,8 [^]	FTM	-	-	-
	276NLL*	2	2	6,4,9 ^e	7	236	+	-
	277	-	-	16,5,6	FTM	-	-	-
	278NLL	3	2	6,5,5	3	238	+	-
	279NLL	3	4	6,6,6,5	11	239	+	-
	280	3	3	5,5,5	3	240	-	-
						232FTM		
						235FTM		
						237FTM		

^ω 0 No sperm
 1 Occasional sperm
 2 Continuous few sperm
 3 Many scattered sperm
 4 Solid masses of sperm

[^] Estimated minimum cycle length - cycle in progress at start or end of smearing period

^e Includes a period of extended oestrus (at least four consecutive days)

FTM Failed to mate
 NLL No live litter - pregnancy indicated by implantation sites
 NLL* No live litter - pregnancy indicated by late resorptions

APPENDIX 16

Litter size- individual values - F1 generation

Group : 1 Control 2-bromo-3,3,3-trifluoropropene 198 2-bromo-3,3,3-trifluoropropene 505 2-bromo-3,3,3-trifluoropropene 2900
 Compound : 1 Control 2-bromo-3,3,3-trifluoropropene 198 2-bromo-3,3,3-trifluoropropene 505 2-bromo-3,3,3-trifluoropropene 2900
 Exposure level (ppm) : 0

Group	Animal number	Implantations	Total litter size				
			Day 1	1	1	5	10
1	241	15	15	15	15	15	15
	242	15	14	14	14	14	14
	243	14	14	14	14	14	14
	244	17	16	16	16	16	16
	245	16	13	13	12	12	12
	246	18	17	17	17	16	16
	247	15	14	14	14	14	14
	248	15	15	15	15	15	15
	249	17	16	15	15	15	15
	250	17	16	16	16	16	16

APPENDIX 16 - continued

Litter size- individual values - F1 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group	Animal number	Implantations	Total litter size		Live litter size on Day			
			Day 1	Day 1	1	5	10	10
2	251	14	14	14	14	14	14	14
	252	13	12	11	9	11	9	11
	253	12	12	12	11	14	11	14
	254	16	14	14	14	14	14	14
	255	19	14	14	13	7	7	7
	256	14	14	14	13	12	12	12
257 NP	0	0	0	0	0	0	0	0
258	8	8	5	5	5	5	5	5
259	14	14	9	9	9	9	9	9
260	17	17	16	15	15	14	14	14

NP Not pregnant

APPENDIX 16 - continued

Litter size- individual values - F1 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group	Animal number	Implantations	Total litter size					Live litter size on Day					
			Day 1	1	1	5	10	1	1	5	10		
3	261	16	13	12	11	9	8						
	262 W	10	8										
	263 TR	3											
	264	17	11	11	6	6							
	265 TLL	12	5										
	266 TLL	11	4										
	267 TLL	16	2										
268	16	11	8	8	8	8	8						
269	13	12	12	12	11	11	11						
270 TLL	16	14	14	14	14	14	14						

W Killed for welfare reasons
TR Total resorption
TLL Total litter loss

APPENDIX 16 - continued

Litter size- individual values - F1 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group	Animal number	Implantations	Total litter size	Live litter size on Day				
				Day 1	1	5	10	
4	271 TR	6						
	272 FTM	0						
	273 TLL	12	3					
	274 TR	9		1				
	275 FTM	0						
	276 W	13						
	277 FTM	0						
	278 TR	8						
	279 W	9						
	280 NP	0						

TR	Total resorption
FTM	Failed to mate
TLL	Total litter loss
W	Killed for welfare reasons
NP	Not pregnant

APPENDIX 17

Offspring survival indices - individual values - F1 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group	Animal number	Post implantation survival index (%)	Live birth index (%)	Viability index (%)
1	241	100	100	100
	242	93	100	100
	243	100	100	100
	244	94	100	100
	245	81	100	92
	246	94	100	94
	247	93	100	100
	248	100	100	100
	249	94	94	100
	250	94	100	100

APPENDIX 17 - continued

Offspring survival indices - individual values - F1 generation

Group Compound	:	1 Control	2 2-bromo-3,3,3- trifluoropropene	3 2-bromo-3,3,3- trifluoropropene	4 2-bromo-3,3,3- trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group	Animal number	Post implantation survival index (%)	Live birth index (%)	Viability index (%)
2	251	100	100	100
	252	92	92	82
	253	100	100	92
	254	88	100	100
	255	74	93	54
	256	100	93	92
257 NP				
	258	63	100	100
	259	64	100	100
	260	94	94	93

NP Not pregnant

APPENDIX 17 - continued

Offspring survival indices - individual values - F1 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group	Animal number	Post implantation survival index (%)	Live birth index (%)	Viability index (%)
3	261	81	92	67
	262 W	80	0	
	263 TR	0		
	264	65	100	55
	265 TLL	42	0	
	266 TLL	36	0	
	267 TLL	13	0	
	268	69	73	100
	269	92	100	92
	270 TLL	88	100	0

W Killed for welfare reasons
TR Total resorption
TLL Total litter loss

APPENDIX 17 - continued

Offspring survival indices - individual values - F1 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group	Animal number	Post implantation survival index (%)	Live birth index (%)	Viability index (%)
4	271 TR	0		
	272 FTM			
	273 TLL	25	33	0
	274 TR	0		
	275 FTM			
	276 W	0		
	277 FTM			
	278 TR	0		
	279 W	0		
	280 NP			

TR	Total resorption
FTM	Failed to mate
TLL	Total litter loss
W	Killed for welfare reasons
NP	Not pregnant

APPENDIX 18

Sex ratio - individual values - F1 generation

Group : 1
Compound : Control
Exposure level (ppm) : 0

2-bromo-3,3,3-trifluoropropene 198
3-bromo-3,3,3-trifluoropropene 505
4-bromo-3,3,3-trifluoropropene 2900

Group	Animal number	Total on Day			Live on Day											
		1		%M	1		%M	2		%M	3		%M	4		%M
		M	F		M	F		M	F		M	F		M	F	
1	241	7	8	46.7	7	8	46.7	7	8	46.7	7	8	46.7	7	8	46.7
	242	7	7	50.0	7	7	50.0	7	7	50.0	7	7	50.0	7	7	50.0
	243	4	10	28.6	4	10	28.6	4	10	28.6	4	10	28.6	4	10	28.6
	244	8	8	50.0	8	8	50.0	8	8	50.0	8	8	50.0	8	8	50.0
	245	3	10	23.1	3	10	23.1	3	9	25.0	3	9	25.0	3	9	25.0
	246	9	8	52.9	9	8	52.9	9	8	52.9	9	8	52.9	9	7	56.3
	247	10	4	71.4	10	4	71.4	10	4	71.4	10	4	71.4	10	4	71.4
	248	8	7	53.3	8	7	53.3	8	7	53.3	8	7	53.3	8	7	53.3
	249	11	5	68.8	10	5	66.7	10	5	66.7	10	5	66.7	10	5	66.7
	250	6	10	37.5	6	10	37.5	6	10	37.5	6	10	37.5	6	10	37.5

APPENDIX 18 - continued

Sex ratio - individual values - F1 generation

Group Compound : 1 Control : 2 2-bromo-3,3,3-trifluoropropene 198 : 3 2-bromo-3,3,3-trifluoropropene 505 : 4 2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm) : 0

Group	Animal number	Total on Day 1			Live on Day 5			Live on Day 10		
		M	F	%M	M	F	%M	M	F	%M
2	251	6	8	42.9	6	8	42.9	6	8	42.9
	252	4	8	33.3	3	8	27.3	3	6	33.3
	253	8	4	66.7	8	4	66.7	7	4	63.6
	254	6	8	42.9	6	8	42.9	6	8	42.9
	255	8	6	57.1	8	5	61.5	3	4	42.9
	256	7	6	53.8	7	6	53.8	6	6	50.0
257 NP										
	258	2	3	40.0	2	3	40.0	2	3	40.0
	259	5	4	55.6	5	4	55.6	5	4	55.6
	260	11	5	68.8	10	5	66.7	10	4	71.4

NP Not pregnant

APPENDIX 18 - continued

Sex ratio - individual values - F1 generation

Group : 1
Compound : Control
Exposure level (ppm) : 0

2 2-bromo-3,3,3-trifluoropropene 198
3 2-bromo-3,3,3-trifluoropropene 505
4 2-bromo-3,3,3-trifluoropropene 2900

Group	Animal number	Total on Day			Live on Day											
		M	F	%M	1 M	1 F	%M	2 M	2 F	%M	3 M	3 F	%M	4 M	4 F	%M
3	261	4	8	33.3	4	8	33.3	3	6	33.3	3	5	37.5			
	262 W	5	3	62.5												
	263 TR	7	4	63.6	7	4	63.6	2	4	33.3	2	4	33.3			
	265 TLL	3	2	60.0												
	266 TLL	3	1	75.0												
	267 TLL	1	0	100.0												
	268	4	4	50.0	4	4	50.0	4	4	50.0	4	4	50.0			
	269	8	4	66.7	8	4	66.7	7	4	63.6	7	4	63.6			
	270 TLL	6	8	42.9	6	8	42.9									

W Killed for welfare reasons
TR Total resorption
TLL Total litter loss

APPENDIX 18 - continued

Sex ratio - individual values - F1 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group	Animal number	Total on Day			Live on Day									
		M	F	%M	M	F	%M	M	F	%M				
4	271 TR													
	272 FTM													
	273 TLL	0	1	0.0	0	1	0.0							
	274 TR													
	275 FTM													
	276 W													
	277 FTM													
	278 TR													
	279 W													
	280 NP													

TR Total resorption
 FTM Failed to mate
 TLL Total litter loss
 W Killed for welfare reasons
 NP Not pregnant

APPENDIX 19

Bodyweight - individual litter mean values for male offspring - F1 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900
Compound :
Exposure level (ppm) : 0

Group	Animal number	Day of age					
		1		5		10	
		Mean	SD	Mean	SD	Mean	SD
1	241	6.6	0.2	10.5	0.4	16.1	0.8
	242	6.7	0.4	10.7	0.5	16.7	1.2
	243	7.4	0.1	11.7	0.4	18.3	0.8
	244	6.9	0.3	10.9	0.8	18.3	2.0
	245	6.5	0.2	11.1	0.1	18.7	0.1
	246	6.9	0.4	11.1	1.0	18.6	1.4
	247	6.8	0.3	10.6	0.6	17.2	1.3
	248	6.8	0.3	10.7	0.3	16.9	0.8
	249	7.1	0.6	11.7	1.0	18.2	2.0
	250	6.5	0.5	9.9	0.9	16.1	1.0

APPENDIX 19 - continued

Bodyweight - individual litter mean values for male offspring - F1 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900
 Compound :
 Exposure level (ppm) : 0

Group	Animal number	Day of age					
		1		5		10	
		Mean	SD	Mean	SD	Mean	SD
2	251	7.3	0.5	11.1	0.7	16.7	0.5
	252	7.3	0.3	11.1	0.6	16.5	0.7
	253	7.6	0.3	11.4	0.3	17.5	0.6
	254	7.2	0.3	9.8	0.9	15.5	1.4
	255	7.0	0.4	10.6	1.4	18.1	2.8
	256	6.6	0.6	10.5	0.7	15.6	0.9
257 NP							
	258	8.5	0.1	13.3	0.4	18.7	0.5
	259	8.0	0.4	12.0	1.2	18.1	1.4
	260	6.8	0.3	10.4	0.6	16.0	1.5

NP Not pregnant

APPENDIX 19 - continued

Bodyweight - individual litter mean values for male offspring - F1 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900
 Compound :
 Exposure level (ppm) : 0

Group	Animal number	Day of age					
		1		5		10	
		Mean	SD	Mean	SD	Mean	SD
3	261	7.3	0.4	11.3	0.4	17.2	0.5
	262 W						
	263 TR						
	264	5.9	0.6	7.9	0.6	12.0	1.1
	265 TLL						
	266 TLL						
	267 TLL						
	268	6.8	0.4	11.8	0.6	18.0	0.7
	269	7.6	0.4	11.4	0.5	16.8	0.7
	270 TLL	6.4	0.8				

W Killed for welfare reasons
 TR Total resorption
 TLL Total litter loss

APPENDIX 19 - continued

Bodyweight - individual litter mean values for female offspring - F1 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900

Compound :
Exposure level (ppm) : 0

Group	Animal number	Day of age					
		1		5		10	
		Mean	SD	Mean	SD	Mean	SD
1	241	6.1	0.3	9.8	0.7	15.4	1.1
	242	6.2	0.4	10.4	0.5	16.0	0.8
	243	6.6	0.2	10.5	0.6	16.8	0.5
	244	6.5	0.4	10.2	1.2	17.1	2.5
	245	6.2	0.3	10.4	0.6	17.6	0.7
	246	6.2	0.4	10.7	0.9	18.0	1.3
	247	6.5	0.2	10.4	0.2	17.1	0.3
	248	6.4	0.1	10.2	0.4	15.6	0.9
	249	7.2	0.3	11.6	0.5	18.3	1.2
	250	6.0	0.5	9.5	0.9	15.3	1.7

APPENDIX 19 - continued

Bodyweight - individual litter mean values for female offspring - F1 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group	Animal number	Day of age					
		1		5		10	
		Mean	SD	Mean	SD	Mean	SD
2	251	6.7	0.5	10.2	0.7	15.8	0.9
	252	7.2	0.4	11.4	0.8	16.6	1.0
	253	6.7	0.5	10.1	1.2	15.5	2.2
	254	7.1	0.4	10.0	0.7	15.3	0.9
	255	6.8	0.4	11.1	0.9	18.0	2.5
	256	6.2	0.3	9.8	0.7	14.7	0.9
257 NP							
	258	7.7	0.8	13.1	1.2	18.6	1.3
	259	7.4	0.6	11.5	0.6	17.6	0.6
	260	6.9	0.5	10.6	0.6	13.8	3.7

NP Not pregnant

APPENDIX 19 - continued

Bodyweight - individual litter mean values for female offspring - F1 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group	Animal number	Day of age					
		1		5		10	
		Mean	SD	Mean	SD	Mean	SD
3	261	6.3	0.7	10.0	1.6	16.1	2.2
	262 W						
	263 TR	6.0	0.3	7.5	0.4	11.6	0.2
	264						
	265 TLL						
	266 TLL						
	267 TLL						
	268	6.2	0.4	11.0	1.3	17.5	1.9
	269	6.5	0.6	10.2	0.9	15.1	1.1
	270 TLL	6.3	0.3				

W	Killed for welfare reasons
TR	Total resorption
TLL	Total litter loss

APPENDIX 19 - continued

Body weight - individual litter mean values for female offspring - F1 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group	Animal number	Day of age	
		1	SD
4	271 TR		
	272 FTM		
	273 TLL	5.5	-
	274 TR		
	275 FTM		
	276 W		
	277 FTM		
	278 TR		
	279 W		
	280 NP		

TR	Total resorption
FTM	Failed to mate
TLL	Total litter loss
W	Killed for welfare reasons
NP	Not pregnant

APPENDIX 20

Clinical signs - individual observations for offspring - F1 generation

Group	:	1				4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900	2900

Group	Dam number	Number/Sex of offspring	Observation	Day of age
1	241	7M & 8F	Cold to touch	1
	250	1F	Pale	1
2	251	6M & 8F	Cold to touch	1
	252	1F	Darker in colour than other pups Found dead	1 2
	253	1M 1M	Bruising on head Bruising on hindlimb, Right	1 1
	254	1M 1M	Bruising on head Small amount of milk seen in abdomen Bruising on head	1 1 1
	255	3M & 4F 4M 1F 1M	Cold to touch Cold to touch Pups missing Cold to touch Pup missing Cold to touch Found dead	1 1 2 1 2 1 2

Only animals with observations are presented

APPENDIX 20 - continued

Clinical signs - individual observations for offspring - F1 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Group	Dam number	Number/Sex of offspring	Observation	Day of age
2	256	1F	Bruising on head	1
	260	1F	Pale	1
			Cold to touch	1
			Pup missing	3
3	261	3M & 5F	Dark in colour	1
			Underactive	1
			Cold to touch	1-2
			Slightly cold to touch	3
		1F	Dark in colour	1
			Underactive	1
			Cold to touch	1
			Pup missing	2
		1M & 1F	Dark in colour	1
			Underactive	1
			Cold to touch	1-2
			Pups missing	3
		1F	Dark in colour	1
			Underactive	1
			Cold to touch	1-2
			Slightly cold to touch	3
			Pup missing	9

Only animals with observations are presented

APPENDIX 20 - continued

Clinical signs - individual observations for offspring - F1 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Group	Dam number	Number/Sex of offspring	Observation	Day of age
3	262 W	3F	Cold to touch No milk present in stomach Dark in colour Underactive Dam and pups killed for welfare reasons	1 1 1 1 1
	264	2M & 4F 2M	Cold to touch Cold to touch Pups missing	2 2 3
	266 TLL	1M	Cold to touch Dark in colour Inactive Killed for welfare reasons	1 1 1 1
	267 TLL	1M	No food present in stomach Dark in colour Underactive Killed for welfare reasons	1 1 1 1

Only animals with observations are presented

W Killed for welfare reasons
TLL Total litter loss

APPENDIX 20 - continued

Clinical signs - individual observations for offspring - F1 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group	Dam number	Number/Sex of offspring	Observation	Day of age		
3	269	7M & 4F	Cold to touch	1		
			Milk present in stomach	1		
			Cold to touch	1		
			Milk present in stomach	1		
			Found dead	2		
270 TLL		3M & 3F	Cold to touch	1		
			Pups missing	2		
		1M	Cold to touch	1		
			Pale	1		
		1M & 2F	Pup missing	2		
			Cold to touch	1		
		1M & 3F	Found dead	2		
			Cold to touch	1		
					Dark, underactive, little milk present in stomach	2
					Killed for welfare reasons	2

Only animals with observations are presented
TLL Total litter loss

APPENDIX 21

Macropathology - individual findings for offspring killed or dying before scheduled termination - F1 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Group	F0 Female Number	Death Code	Day of age	Sex of offspring	Macroscopic observation
1	245	F	5	F	Milk in stomach
	246	F	6	F	No milk in stomach
2	252	F	<1	M	Milk in stomach
		F	2	F	Liver, Mottled, Pale No milk in stomach
	255	F	<1	F	No milk in stomach
		F	2	M	No milk in stomach

APPENDIX 21 - continued

Macropathology - individual findings for offspring dying before scheduled termination (F1)

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group	F0 Female Number	Death Code	Day of age	Sex of offspring	Macroscopic observation
3	261	F	<1	F	No milk in stomach
		F	1	F	Milk in stomach
262		W	<1	M	No milk in stomach
		W	<1	F	Milk in stomach
		F	<1	3 x M: 2 x F	No milk in stomach
		F	<1	M	A small amount of milk in stomach
265	F	<1	3 x M: 2 x F	No milk in stomach	
266		W	<1	M	No milk in stomach
		F	<1	2 x M	No milk in stomach
		F	<1	F	Milk in stomach
267	W	<1	M	No milk in stomach	
269		F	2	M	Milk in stomach
		F	2	1 x M: 2 x F	No milk in stomach
270		W	2	1 x M: 3 x F	No milk in stomach

Only animals with abnormalities presented

APPENDIX 22

Macropathology - individual findings for offspring killed at scheduled termination - F1 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group	F0 Female Number	Sex of offspring	Macroscopic observation
2	254	F	Left forepaw, third digit; pale swelling underlying tattoo, 4 mm

Only animals with abnormalities presented

APPENDIX 23

Sperm analysis - individual values - F0 generation

Group Compound	:	1	2	3	4
	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group number	Animal number	Motile sperm (%)	Progressively motile sperm (%)	----- Cauda epididymis -----		----- Testis -----	
				Weight (g)	Sperm count (millions/g)	Weight (g)	Sperm count (millions/g)
1	201	94	50	0.236	1169	2.00	202
	202	97	26	0.255	333	1.96	199
	203	97	65	0.238	1237	1.61	220
	204	95	79	0.254	955	1.71	196
	205	91	64	0.252	1203	1.87	115
	206	92	68	0.282	1526	1.93	241
	207	89	64	0.183	1196	1.82	175
	208	99	53	0.236	1080	1.73	249
	209	97	74	0.247	1032	1.65	187
	210	90	51	0.218	1169	1.75	208
					Total (million)	Total (million)	
				276	430	404	404
				85	219	391	391
				294	255	353	353
				243	255	335	335
				303	255	216	216
				430	255	466	466
				219	255	318	318
				255	255	430	430
				255	255	309	309
				255	255	364	364

B Excluded from group mean cauda epididymal count values, suspected sample preparation/dilution error

APPENDIX 23 - continued

Sperm analysis - individual values - F0 generation

Group Compound	Exposure level (ppm)	1 Control	2 2-bromo-3,3,3- trifluoropropene 198	3 2-bromo-3,3,3- trifluoropropene 505	4 2-bromo-3,3,3- trifluoropropene 2900	----- Cauda epididymis -----		----- Testis -----	
						Progressively motile sperm (%)	Weight (g)	Sperm count (millions/g)	Total (million)
2	211	91	43	1081	240	1.76	149	262	
	212	95	54	1377	325	1.74	147	255	
	213	99	22	877	218	1.91	294	561	
	214	95	55	1256	281	1.94	281	545	
	215	92	75	1490	326	1.89	251	474	
	216	99	19	1056	279	1.87	210	393	
	217	99	41	963	236	1.78	175	311	
	218	86	43	1133	286	1.68	125	211	
	219	100	75	1173	257	1.85	107	197	
	220	95	48	1041	247	2.00	208	416	

APPENDIX 24

Sperm motion data - individual values - F0 generation

Group	1	2	3	4									
Compound	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900									
Exposure level (ppm)	0												
Group number	VAP (um/s)	VSL (um/s)	VCL (um/s)	ALH (um)	BCF (Hz)	STR (%)	LIN (%)	Elongation (%)	Area (um sq)	Rapid (%)	Medium (%)	Slow (%)	Static (%)
1	201	138	94	287	23	26	69	34	439	62	3	29	6
	202	124	85	260	25	28	69	35	438	32	7	59	3
	203	138	107	289	21	25	77	38	399	71	3	23	3
	204	144	110	303	21	22	77	37	492	85	0	9	5
	205	124	96	267	20	22	77	36	442	71	5	14	9
	206	143	103	323	23	24	72	32	444	76	2	14	8
	207	137	107	303	21	25	78	36	477	68	2	20	11
	208	142	98	309	24	29	69	33	730	64	5	30	1
	209	151	111	339	23	25	74	33	557	84	2	10	3
	210	138	108	313	23	26	77	35	448	55	2	33	10

APPENDIX 24 - continued

Sperm motion data - individual values - F0 generation

Group Compound : : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900

Exposure level (ppm) : 0

Group number	Animal number	VAP (um/s)	VSL (um/s)	VCL (um/s)	ALH (um)	BCF (Hz)	STR (%)	LIN (%)	Elongation (%)	Area (um sq)	Rapid (%)	Medium (%)	Slow (%)	Static (%)
2	211	116	85	238	21	27	73	38	20	406	49	4	39	9
	212	143	100	291	22	25	70	35	27	553	63	2	30	5
	213	120	83	268	24	29	69	33	29	469	27	6	65	1
	214	145	104	297	23	27	72	36	24	481	64	5	27	5
	215	123	99	264	19	24	80	38	17	388	77	5	10	8
	216	110	79	229	24	30	72	37	32	661	24	7	67	1
	217	132	99	273	23	27	75	39	25	420	47	6	46	1
	218	120	84	260	21	23	70	33	23	435	51	7	28	14
	219	137	106	284	21	24	78	38	23	473	82	2	16	0
	220	113	83	245	20	29	73	36	27	777	56	9	30	5

APPENDIX 24 - continued

Sperm motion data - individual values - F0 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900

Exposure level (ppm) : 0

Group number	Animal number	VAP (um/s)	VSL (um/s)	VCL (um/s)	ALH (um)	BCF (Hz)	STR (%)	LIN (%)	Elongation (%)	Area (um sq)	Rapid (%)	Medium (%)	Slow (%)	Static (%)
3	221	106	74	215	22	32	70	37	27	442	14	3	82	1
	222	133	102	273	19	27	76	39	26	521	68	5	21	6
	223	127	87	253	22	21	69	35	24	413	78	2	11	9
	224	132	98	272	22	28	73	37	27	482	62	6	32	1
	225	115	76	224	19	22	68	36	21	349	65	5	26	4
	226	124	86	239	22	27	70	39	27	478	43	6	48	2
	227	125	91	247	23	25	73	38	26	502	44	5	45	5
	228	90	59	182	19	24	68	35	23	275	13	9	41	37
	229	125	93	258	19	23	75	38	22	543	77	5	15	3
	230	0	0	0	0	0	0	0	0	0	0	0	0	100

A Few sperm in sample, excluded from group mean values

APPENDIX 24 - continued

Sperm motion data - individual values - F0 generation

Group : 1 Control 2 2-bromo-3,3,3-trifluoropropene 198 3 2-bromo-3,3,3-trifluoropropene 505 4 2-bromo-3,3,3-trifluoropropene 2900

Exposure level (ppm) : 0

Group number	Animal number	VAP (um/s)	VSL (um/s)	VCL (um/s)	ALH (um)	BCF (Hz)	STR (%)	LIN (%)	Elongation (%)	Area (um sq)	Rapid (%)	Medium (%)	Slow (%)	Static (%)
4	231	146	102	320	22	27	70	34	27	780	71	3	23	4
	232	143	115	290	20	28	80	41	19	374	60	4	21	16
	233	102	69	206	22	29	69	36	30	534	30	9	50	10
	234	128	95	258	21	28	74	38	24	415	63	6	25	6
	235	124	82	257	21	28	68	34	30	787	61	6	28	4
	236	114	87	226	20	28	76	40	23	364	47	9	38	6
	237	124	86	265	21	28	71	35	27	551	43	5	40	12
	238	123	86	259	22	29	70	35	22	435	45	6	39	10
	239	114	80	247	22	31	71	36	29	578	40	11	46	3
	240	130	95	271	24	29	73	36	27	429	46	7	42	6

APPENDIX 25

Sperm morphology - individual values - F0 generation

Group : 1
Compound : Control
Exposure level (ppm) : 0

Group number	Animal number	Number of sperm examined	Normal		Total abnormal		Decapitate		Head abnormal		Detached/broken		Other abnormality	
			number	%	number	%	number	%	number	%	number	%	number	%
1	201	200	197	98.5	3	1.5	2	1.0	1	0.5	0	0.0	0	0.0
	202	200	199	99.5	1	0.5	0	0.0	0	0.0	0	0.0	1	0.5
	203	200	197	98.5	3	1.5	1	0.5	2	1.0	0	0.0	0	0.0
	204	200	197	98.5	3	1.5	1	0.5	2	1.0	0	0.0	0	0.0
	205	200	196	98.0	4	2.0	1	0.5	1	0.5	2	1.0	0	0.0
	206	200	199	99.5	1	0.5	0	0.0	0	0.0	0	0.0	1	0.5
	207	200	198	99.0	2	1.0	1	0.5	1	0.5	0	0.0	0	0.0
	208	200	193	96.5	7	3.5	7	3.5	0	0.0	0	0.0	0	0.0
	209	200	199	99.5	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0
	210	200	196	98.0	4	2.0	1	0.5	2	1.0	0	0.0	2	1.0

APPENDIX 25 - continued

Sperm morphology - individual values - F0 generation

Group Compound	1 Control	2 2-bromo-3,3,3- trifluoropropene 198	3 2-bromo-3,3,3- trifluoropropene 505	4 2-bromo-3,3,3- trifluoropropene 2900
Exposure level (ppm)	0			

Group number	Animal number	Number of sperm examined	Normal		Total abnormal		Decapitate		Head abnormal		Detached/broken neck/midpiece/tail		Other abnormality	
			number	%	number	%	number	%	number	%	number	%	number	%
2	211	200	186	93.0	14	7.0	2	1.0	11	5.5	0	0.0	1	0.5
	212	200	198	99.0	2	1.0	1	0.5	1	0.5	0	0.0	0	0.0
	213	200	197	98.5	3	1.5	2	1.0	1	0.5	0	0.0	0	0.0
	214	200	198	99.0	2	1.0	0	0.0	2	1.0	0	0.0	0	0.0
	215	200	194	97.0	6	3.0	4	2.0	1	0.5	1	0.5	0	0.0
	216	200	195	97.5	5	2.5	1	0.5	2	1.0	1	0.5	1	0.5
	217	200	188	94.0	12	6.0	10	5.0	0	0.0	2	1.0	0	0.0
	218	200	196	98.0	4	2.0	1	0.5	1	0.5	1	0.5	1	0.5
	219	200	192	96.0	8	4.0	4	2.0	3	1.5	1	0.5	1	0.5
	220	213	200	93.9	13	6.1	5	2.3	8	3.8	0	0.0	0	0.0

APPENDIX 25 - continued

Sperm morphology - individual values - F0 generation

Group : 1
Compound : Control 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene 2-bromo-3,3,3-trifluoropropene
Exposure level (ppm) : 0 198 505 2900

Group number	Animal number	Number of sperm examined	Normal		Total abnormal		Decapitate		Head abnormal		Detached/broken		Other abnormality	
			number	%	number	%	number	%	number	%	number	%	number	%
3	221	200	195	97.5	5	2.5	4	2.0	1	0.5	0	0.0	0	0.0
	222	200	197	98.5	3	1.5	0	0.0	2	1.0	2	1.0	0	0.0
	223	200	186	93.0	14	7.0	12	6.0	1	0.5	2	1.0	0	0.0
	224	200	191	95.5	9	4.5	6	3.0	3	1.5	0	0.0	0	0.0
	225	200	193	96.5	7	3.5	4	2.0	3	1.5	0	0.0	0	0.0
	226	200	187	93.5	13	6.5	10	5.0	1	0.5	2	1.0	0	0.0
	227	10	8	80.0	2	20.0	2	20.0	0	0.0	0	0.0	0	A
	228	200	194	97.0	6	3.0	2	1.0	1	0.5	3	1.5	0	0.0
	229	200	190	95.0	10	5.0	0	0.0	9	4.5	1	0.5	1	0.5
	230	0												A

A Few / no sperm in sample, excluded from group mean values

APPENDIX 25 - continued

Sperm morphology - individual values - F0 generation

Group : 1
Compound : Control
Exposure level (ppm) : 0

2 2-bromo-3,3,3-trifluoropropene 198

3 2-bromo-3,3,3-trifluoropropene 505

4 2-bromo-3,3,3-trifluoropropene 2900

Group number	Animal number	Number of sperm examined	Normal		Total abnormal		Decapitate		Head abnormal		Detached/broken		Other abnormality	
			number	%	number	%	number	%	number	%	number	%	number	%
4	231	200	189	94.5	11	5.5	4	2.0	3	1.5	3	1.5	1	0.5
	232	200	160	80.0	40	20.0	15	7.5	18	9.0	8	4.0	2	1.0
	233	200	161	80.5	39	19.5	31	15.5	5	2.5	5	2.5	1	0.5
	234	200	186	93.0	14	7.0	8	4.0	6	3.0	1	0.5	1	0.5
	235	200	177	88.5	23	11.5	15	7.5	3	1.5	3	1.5	3	1.5
	236	200	191	95.5	9	4.5	5	2.5	3	1.5	2	1.0	1	0.5
	237	200	191	95.5	9	4.5	3	1.5	4	2.0	2	1.0	1	0.5
	238	200	184	92.0	16	8.0	5	2.5	11	5.5	1	0.5	1	0.5
	239	200	173	86.5	27	13.5	15	7.5	10	5.0	2	1.0	1	0.5
	240	200	193	96.5	7	3.5	2	1.0	5	2.5	0	0.0	0	0.0

APPENDIX 26

Request ID: 284410

Organ weights - individual absolute values (g) for males - F0 generation

Group Compound	1 Control	2 2-bromo-3,3,3- trifluoropropene 198	3 2-bromo-3,3,3- trifluoropropene 505	4 2-bromo-3,3,3- trifluoropropene 2900				
Exposure level (ppm)	0							
Group Animal Number	Terminal Bodyweight	Lt. Epididymis	Rt. Epididymis	Pituitary	Prostate	Seminal Vesicles	Lt. Testis	Rt. Testis
1M	201 533	0.667	0.648	0.014	1.538	1.405	2.00	1.99
	202 485	0.759	0.699	0.013	1.428	1.376	1.96	1.86
	203 518	0.618	0.550	0.015	1.261	1.180	1.61	1.69
	204 561	0.689	0.705	0.016	1.510	2.251	1.71	1.68
	205 582	0.731	0.667	0.020	1.493	1.523	1.87	1.85
	206 589	0.799	0.745	0.015	1.233	2.418	1.93	1.96
	207 537	0.592	0.638	0.012	1.393	1.338	1.82	1.88
	208 542	0.641	0.668	0.016	1.453	1.890	1.73	1.68
	209 564	0.705	0.666	0.016	1.335	1.588	1.65	1.63
	210 518	0.603	0.580	0.012	0.998	1.697	1.75	1.70
2M	211 503	0.585	0.584	0.011	0.964	1.692	1.76	1.77
	212 407	0.700	0.651	0.009	1.022	1.910	1.74	1.74
	213 511	0.648	0.588	0.012	1.178	1.164	1.91	1.82
	214 564	0.642	0.665	0.012	1.028	1.254	1.94	1.94
	215 515	0.651	0.629	0.011	1.085	1.517	1.89	1.96
	216 553	0.683	0.597	0.014	0.999	1.356	1.87	1.79
	217 471	0.686	0.592	0.008	0.968	0.849	1.78	1.77
	218 437	0.636	0.604	0.010	0.891	1.554	1.68	1.67
	219 439	0.636	0.626	0.009	0.972	1.279	1.85	1.91
	220 436	0.650	0.637	0.011	0.975	0.996	2.00	1.98

Request ID: 284410

APPENDIX 26 - continued

Organ weights - individual absolute values (g) for males - F0 generation

Group Compound	1 Control	2 2-bromo-3,3,3- trifluoropropene 198	3 2-bromo-3,3,3- trifluoropropene 505	4 2-bromo-3,3,3- trifluoropropene 2900					
Exposure level (ppm)	: 0								
Group /Sex	Animal Number	Terminal Bodyweight	Lt. Epididymis	Rt. Epididymis	Pituitary	Prostate	Seminal Vesicles	Lt. Testis	Rt. Testis
3M	221	465	0.604	0.554	0.010	0.726	1.434	1.82	1.82
	222	410	0.671	0.641	0.010	0.712	1.174	2.12	2.15
	223	425	0.578	0.529	0.013	0.687	1.236	1.57	1.57
	224	438	0.687	0.617	0.010	0.821	1.191	1.81	1.84
	225	470	0.631	0.656	0.013	1.160	1.259	1.83	1.94
	226	441	0.652	0.644	0.011	1.460	0.959	1.77	1.75
	227	511	0.677	0.692	0.012	0.891	0.883	1.90	1.89
	228	452	0.627	0.591	0.011	0.855	0.925	1.73	1.69
	229	446	0.631	0.605	0.009	0.894	1.187	1.72	1.65
	230	469	0.207	0.652	0.009	1.167	1.034	0.31	2.13
4M	231	469	0.618	0.585	0.011	0.463	1.601	1.79	1.79
	232	409	0.532	0.636	0.012	0.264	0.899	1.85	1.78
	233	380	0.602	0.565	0.009	0.627	1.320	1.65	1.64
	234	414	0.595	0.595	0.008	0.636	0.925	1.72	1.68
	235	452	0.595	0.623	0.008	0.781	0.924	1.78	1.77
	236	453	0.559	0.552	0.006	0.843	1.253	1.74	1.72
	237	403	0.582	0.590	0.011	0.643	1.139	1.59	1.56
	238	387	0.573	0.547	0.009	0.540	1.468	1.72	1.65
	239	444	0.494	0.559	0.009	0.730	0.963	1.63	1.58
	240	423	0.620	0.620	0.011	0.722	0.759	1.95	1.99

APPENDIX 27

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 201 Sex: Male Dose Group: 1 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 532.9 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED ***ANIMAL HAS NO MICROSCOPIC FINDINGS RECORDED***

The following examined tissues had no gross observations and no findings microscopically:
 Prostate, Rt. Epididymis, Rt. Testis

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 202 Sex: Male Dose Group: 1 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 484.9 g

MACROPATHOLOGY

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED

ANIMAL HAS NO MICROSCOPIC FINDINGS RECORDED

The following examined tissues had no gross observations and no findings microscopically:
 Prostate, Rt. Epididymis, Rt. Testis

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 203 Sex: Male Dose Group: 1 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 518.0 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED

Prostate
 Interstitial Inflammation, Minimal

The following examined tissues had no gross observations and no findings microscopically:
 Rt. Epididymis, Rt. Testis

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Animal Number: 204 Sex: Male Dose Group: 1 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 560.5 g

MACROPATHOLOGY

PATHOLOGY OBSERVATIONS

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED ***ANIMAL HAS NO MICROSCOPIC FINDINGS RECORDED***

The following examined tissues had no gross observations and no findings microscopically:
 Prostate, Rt. Epididymis, Rt. Testis

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 205 Sex: Male Dose Group: 1 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 581.7 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED ***ANIMAL HAS NO MICROSCOPIC FINDINGS RECORDED***

The following examined tissues had no gross observations and no findings microscopically:
 Prostate, Rt. Epididymis, Rt. Testis

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 206 Sex: Male Dose Group: 1 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 589.0 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED

Prostate
 Acinar Cell Atrophy, Focal, Minimal

The following examined tissues had no gross observations and no findings microscopically:
 Rt. Epididymis, Rt. Testis

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 207 Sex: Male Dose Group: 1 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 537.4 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED ***ANIMAL HAS NO MICROSCOPIC FINDINGS RECORDED***

The following examined tissues had no gross observations and no findings microscopically:
 Prostate, Rt. Epididymis, Rt. Testis

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 208 Sex: Male Dose Group: 1 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 541.8 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED

Prostate
 Interstitial Inflammation, Slight

The following examined tissues had no gross observations and no findings microscopically:
 Rt. Epididymis, Rt. Testis

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Animal Number: 209 Sex: Male Dose Group: 1 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 563.6 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED ***ANIMAL HAS NO MICROSCOPIC FINDINGS RECORDED***

The following examined tissues had no gross observations and no findings microscopically:
 Prostate, Rt. Epididymis, Rt. Testis

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 210 Sex: Male Dose Group: 1 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 517.7 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Teeth

Incisor(s) pale, Lower, Right

The following examined tissues had no gross observations and no findings microscopically:
 Prostate, Rt. Epididymis, Rt. Testis

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 211 Sex: Male Dose Group: 2 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 502.5 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED ***ANIMAL HAS NO MICROSCOPIC FINDINGS RECORDED***

The following examined tissues had no gross observations and no findings microscopically:
 Prostate

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	1	2	3	4
Compound	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	0	198	505	2900

Animal Number: 212 Sex: Male Dose Group: 2 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 407.0 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

Spleen
 Capsule thickened, Multiple, areas.

Spleen
 Capsular/Subcapsular Inflammation, Slight
 Adhesions/Inflammation/Fibrosis, Minimal

HISTOPATHOLOGY

The following examined tissues had no gross observations and no findings microscopically:
 Prostate

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 213 Sex: Male Dose Group: 2 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 510.5 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED

Prostate
 Interstitial Inflammation, Focal, Minimal

The following examined tissues had no gross observations and no findings microscopically:

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 214 Sex: Male Dose Group: 2 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 564.1 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Spleen Capsule thickened, Posterior pole, A few, areas, Imm.
 Prostate Interstitial Inflammation, Minimal
 Spleen Capsular/Subcapsular Inflammation, Minimal
 Adhesions/Inflammation/Fibrosis, Minimal

The following examined tissues had no gross observations and no findings microscopically:

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	1	2	3	4
Compound	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	0	198	505	2900

Animal Number: 215 Sex: Male Dose Group: 2 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 514.5 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Spleen

Capsule thickened, areas.
 Adhesions, Anterior pole, capsule to adipose tissue.

Spleen

Capsular/Subcapsular Inflammation, Slight
 Capsular Thickening, Minimal
 Adhesions/Inflammation/Fibrosis, Slight

The following examined tissues had no gross observations and no findings microscopically:
 Prostate

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 216 Sex: Male Dose Group: 2 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 553.1 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Skin

Hair loss, Side(s) of face, diffuse.

Spleen

Capsule thickened, Multiple, areas.
 Adhesions, capsule to adipose tissue.

Spleen

Capsular/Subcapsular Inflammation, Slight
 Capsular Thickening, Minimal
 Adhesions/Inflammation/Fibrosis, Slight

The following examined tissues had no gross observations and no findings microscopically:
 Prostate

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	1	2	3	4
Compound	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	0	198	505	2900

Animal Number: 217 Sex: Male Dose Group: 2 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 471.2 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Spleen
 Capsule thickened, Multiple, areas.

Spleen
 Capsular/Subcapsular Inflammation, Minimal
 Adhesions/Inflammation/Fibrosis, Minimal

The following examined tissues had no gross observations and no findings microscopically:
 Prostate

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 218 Sex: Male Dose Group: 2 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 436.6 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Prostate
Small

Prostate
No significant lesions

Spleen
Capsule thickened, Multiple, areas.

Spleen
Capsular/Subcapsular Inflammation, Minimal
Capsular Thickening, Minimal

The following examined tissues had no gross observations and no findings microscopically:

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 219 Sex: Male Dose Group: 2 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 438.7 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Spleen
Capsule thickened, areas.

Spleen
Capsular/Subcapsular Inflammation, Minimal
Capsular Thickening, Minimal

The following examined tissues had no gross observations and no findings microscopically:
Prostate

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 220 Sex: Male Dose Group: 2 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 435.5 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Spleen Spleen
 Capsule thickened, Anterior pole, A few, areas. Capsular/Subcapsular Inflammation, Focal, Minimal

The following examined tissues had no gross observations and no findings microscopically:
 Prostate

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 221 Sex: Male Dose Group: 3 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 464.6 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Prostate Prostate
 Small No significant lesions

The following examined tissues had no gross observations and no findings microscopically:

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 222 Sex: Male Dose Group: 3 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 410.2 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Prostate	Prostate
Small	No significant lesions
Spleen	Spleen
Capsule thickened, Punctate, A few, areas.	Capsular/Subcapsular Inflammation, Focal, Minimal
Teeth	
Incisor(s) pale, Lower	

The following examined tissues had no gross observations and no findings microscopically:

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 223 Sex: Male Dose Group: 3 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 425.4 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Prostate
Small

Prostate
Interstitial Inflammation, Minimal
Acinar Cell Atrophy, Focal, Slight

Skin
Hair loss, Side(s) of face, Right
Scab(s), Side(s) of face, Right, One, 1mm.

Skin
Scab(s), Present
Epidermal Hyperplasia, Minimal

The following examined tissues had no gross observations and no findings microscopically:

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Animal Number: 224 Sex: Male Dose Group: 3 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 437.8 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Prostate	Small	Prostate	Abscessation, Focal, Minimal
Skin	Hair loss, Side(s) of face, Right, diffuse.		
Spleen	Capsule thickened, Anterior pole, an area. Adhesions, Anterior pole, capsule to adipose tissue.	Spleen	Capsular/Subcapsular Inflammation, Minimal Capsular Thickening, Minimal Adhesions/Inflammation/Fibrosis, Minimal
Teeth	Incisor(s) pale, Lower		

The following examined tissues had no gross observations and no findings microscopically:

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 225 Sex: Male Dose Group: 3 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 470.2 g

MACROPATHOLOGY

PATHOLOGY OBSERVATIONS

HISTOPATHOLOGY

Prostate
 Interstitial Inflammation, Minimal

Teeth
 Incisor(s) pale, Lower

The following examined tissues had no gross observations and no findings microscopically:

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 226 Sex: Male Dose Group: 3 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 440.5 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Spleen
 Adhesions, Multiple, diffuse.

Spleen
 Capsular/Subcapsular Inflammation, Slight
 Capsular Thickening, Slight
 Adhesions/Inflammation/Fibrosis, Slight

The following examined tissues had no gross observations and no findings microscopically:
 Prostate

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 227 Sex: Male Dose Group: 3 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 511.2 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Prostate
Small

Prostate
Interstitial Inflammation, Slight

Spleen
Capsule thickened, A few, areas.
Adhesions, Anterior pole, capsule to adipose tissue.

Spleen
Capsular/Subcapsular Inflammation, Slight
Capsular Thickening, Minimal

The following examined tissues had no gross observations and no findings microscopically:

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 228 Sex: Male Dose Group: 3 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 451.8 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Prostate
Small

Prostate
No significant lesions

Spleen
Capsule thickened

Spleen
Capsular/Subcapsular Inflammation, Moderate
Capsular Thickening, Slight
Adhesions/Inflammation/Fibrosis, Moderate

Teeth
Incisor(s) pale, Lower

The following examined tissues had no gross observations and no findings microscopically:

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 229 Sex: Male Dose Group: 3 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 445.8 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Prostate	Small	Prostate	Acinar Cell Atrophy, Focal, Slight
Spleen	Capsule thickened, Anterior pole, areas.	Spleen	Capsular Thickening, Focal, Minimal
Teeth	Incisor(s) pale, Lower		

The following examined tissues had no gross observations and no findings microscopically:

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Animal Number: 230 Sex: Male Dose Group: 3 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 468.6 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Lt. Epididymis
Small

Lt. Epididymis
No significant lesions

Spleen
Capsule thickened, Multiple, areas.

Spleen
Capsular/Subcapsular Inflammation, Minimal
Capsular Thickening, Minimal
Adhesions/Inflammation/Fibrosis, Minimal

Lt. Testis
Small
Prominent tubules, A few

Lt. Testis
No significant lesions

Teeth
Incisor(s) pale, Lower

The following examined tissues had no gross observations and no findings microscopically:
Prostate

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 231 Sex: Male Dose Group: 4 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 468.5 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Prostate	Small	Prostate	No significant lesions
Skin	Hair loss, cranial region and sides of face, diffuse.		
Spleen	Capsule thickened, Anterior pole, areas.	Spleen	Capsular/Subcapsular Inflammation, Focal, Minimal
Teeth	Incisor(s) pale, Lower		

The following examined tissues had no gross observations and no findings microscopically:
 Rt. Epididymis, Rt. Testis

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 232 Sex: Male Dose Group: 4 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 409.3 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Prostate
Small

Prostate
No significant lesions

Spleen
Capsule thickened
Adhesions, to adipose tissue.

Spleen
Capsular/Subcapsular Inflammation, Slight
Capsular Thickening, Moderate
Adhesions/Inflammation/Fibrosis, Moderate

Teeth
Incisor(s) pale, Lower

Rt. Testis
Spermatocytes Degeneration, Minimal

The following examined tissues had no gross observations and no findings microscopically:
Rt. Epididymis

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 233 Sex: Male Dose Group: 4 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 379.5 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Prostate	Small	Prostate	No significant lesions
Skin	Hair loss, cranial region extending to dorsal cervical region and sides of face.		
Spleen	Capsule thickened, Anterior pole, two areas.	Spleen	No significant lesions
Teeth	Incisor(s) pale, Lower		

The following examined tissues had no gross observations and no findings microscopically:
 Rt. Epididymis, Rt. Testis

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	1	2	3	4
Compound	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	0	198	505	2900

Animal Number: 234 Sex: Male Dose Group: 4 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 414.2 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Prostate
Small

Prostate
Interstitial Inflammation, Slight

Skin

Hair loss, cranial region and ventral cervical region.

Spleen

Capsule thickened, areas, up to 1mm.

Spleen

Capsular Thickening, Focal, Minimal

Teeth

Incisor(s) pale, Lower

The following examined tissues had no gross observations and no findings microscopically:

Rt. Epididymis, Rt. Testis

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 235 Sex: Male Dose Group: 4 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 452.2 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Prostate
Small

Prostate
No significant lesions

Spleen
Capsule thickened
Adhesions, capsulat to adipose tissue.

Spleen
Capsular/Subcapsular Inflammation, Moderate
Capsular Thickening, Slight
Adhesions/Inflammation/Fibrosis, Slight

Teeth
Incisor(s) pale, Lower

The following examined tissues had no gross observations and no findings microscopically:
Rt. Epididymis, Rt. Testis

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 236 Sex: Male Dose Group: 4 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 453.1 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Prostate	Prostate
Small	Interstitial Inflammation, Minimal
Spleen	Spleen
Capsule thickened, a few areas.	Capsular/Subcapsular Inflammation, Minimal
Adhesions, Anterior pole, capsule to adipose tissue.	Capsular Thickening, Slight
	Adhesions/Inflammation/Fibrosis, Minimal
Teeth	
Incisor(s) pale, Lower	

The following examined tissues had no gross observations and no findings microscopically:
 Rt. Epididymis, Rt. Testis

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 237 Sex: Male Dose Group: 4 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 403.2 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Prostate
 Small Prostate
 No significant lesions

Teeth
 Incisor(s) pale, Lower

The following examined tissues had no gross observations and no findings microscopically:
 Rt. Epididymis, Rt. Testis

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 238 Sex: Male Dose Group: 4 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 386.6 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Prostate
Small

Prostate
Abscessation, Focal, Slight

Spleen
Capsule thickened
Adhesions, capsule to abdominal wall.

Spleen
Capsular/Subcapsular Inflammation, Moderate
Capsular Thickening, Slight
Adhesions/Inflammation/Fibrosis, Slight

Teeth
Incisor(s) pale, Lower

The following examined tissues had no gross observations and no findings microscopically:
Rt. Epididymis, Rt. Testis

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 239 Sex: Male Dose Group: 4 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 444.0 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Prostate	Small	Prostate	Interstitial Inflammation, Focal, Minimal
Skin	Hair loss, Cranial region, diffuse.		
Spleen	Capsule thickened, Multiple, areas.	Spleen	Capsular/Subcapsular Inflammation, Slight Capsular Thickening, Slight Adhesions/Inflammation/Fibrosis, Slight
Teeth	Incisor(s) pale, Lower		

The following examined tissues had no gross observations and no findings microscopically:
 Rt. Epididymis, Rt. Testis

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 240 Sex: Male Dose Group: 4 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 51 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 422.6 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Prostate	Prostate
Small	No significant lesions
Spleen	Spleen
Capsule thickened, Multiple, areas.	Capsular/Subcapsular Inflammation, Minimal Capsular Thickening, Minimal Adhesions/Inflammation/Fibrosis, Minimal
Teeth	
Incisor(s) pale, Lower	

The following examined tissues had no gross observations and no findings microscopically:
 Rt. Epididymis, Rt. Testis

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 241 Sex: Female Dose Group: 1 Phase: Lactation Sacrifice Status: Final phase sacrifice
 Date of Death: 05-Sep-12 Day of Death: 10 Week of Death: 2 Subgroup: 1 Terminal Bodyweight: 339.8 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED ***ANIMAL HAS NO MICROSCOPIC FINDINGS RECORDED***

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 242 Sex: Female Dose Group: 1 Phase: Lactation Sacrifice Status: Final phase sacrifice
 Date of Death: 05-Sep-12 Day of Death: 10 Week of Death: 2 Subgroup: 1 Terminal Bodyweight: 310.0 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED ***ANIMAL HAS NO MICROSCOPIC FINDINGS RECORDED***

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 243 Sex: Female Dose Group: 1 Phase: Lactation Sacrifice Status: Final phase sacrifice
 Date of Death: 03-Sep-12 Day of Death: 10 Week of Death: 2 Subgroup: 1 Terminal Bodyweight: 318.7 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED ***ANIMAL HAS NO MICROSCOPIC FINDINGS RECORDED***

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Animal Number: 244 Sex: Female Dose Group: 1 Phase: Lactation Sacrifice Status: Final phase sacrifice
 Date of Death: 05-Sep-12 Day of Death: 10 Week of Death: 2 Subgroup: 1 Terminal Bodyweight: 380.3 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED ***ANIMAL HAS NO MICROSCOPIC FINDINGS RECORDED***

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Animal Number: 245 Sex: Female Dose Group: 1 Phase: Lactation Sacrifice Status: Final phase sacrifice
 Date of Death: 05-Sep-12 Day of Death: 10 Week of Death: 2 Subgroup: 1 Terminal Bodyweight: 336.3 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED ***ANIMAL HAS NO MICROSCOPIC FINDINGS RECORDED***

The following examined tissues had no gross observations and no findings microscopically:
Ovaries

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 246 Sex: Female Dose Group: 1 Phase: Lactation Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 10 Week of Death: 2 Subgroup: 1 Terminal Bodyweight: 378.7 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED ***ANIMAL HAS NO MICROSCOPIC FINDINGS RECORDED***

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 247 Sex: Female Dose Group: 1 Phase: Lactation Sacrifice Status: Final phase sacrifice
 Date of Death: 06-Sep-12 Day of Death: 10 Week of Death: 2 Subgroup: 1 Terminal Bodyweight: 306.8 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED ***ANIMAL HAS NO MICROSCOPIC FINDINGS RECORDED***

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 248 Sex: Female Dose Group: 1 Phase: Lactation Sacrifice Status: Final phase sacrifice
 Date of Death: 06-Sep-12 Day of Death: 10 Week of Death: 2 Subgroup: 1 Terminal Bodyweight: 349.7 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Skin

Hair loss, Forelimb(s)

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 249 Sex: Female Dose Group: 1 Phase: Lactation Sacrifice Status: Final phase sacrifice
 Date of Death: 06-Sep-12 Day of Death: 10 Week of Death: 2 Subgroup: 1 Terminal Bodyweight: 340.9 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED ***ANIMAL HAS NO MICROSCOPIC FINDINGS RECORDED***

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 250 Sex: Female Dose Group: 1 Phase: Lactation Sacrifice Status: Final phase sacrifice
 Date of Death: 06-Sep-12 Day of Death: 10 Week of Death: 2 Subgroup: 1 Terminal Bodyweight: 354.6 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Skin

Hair loss, Forelimb(s)

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 251 Sex: Female Dose Group: 2 Phase: Lactation Sacrifice Status: Final phase sacrifice
 Date of Death: 06-Sep-12 Day of Death: 10 Week of Death: 2 Subgroup: 1 Terminal Bodyweight: 323.5 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED ***ANIMAL HAS NO MICROSCOPIC FINDINGS RECORDED***

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 252 Sex: Female Dose Group: 2 Phase: Lactation Sacrifice Status: Final phase sacrifice
 Date of Death: 04-Sep-12 Day of Death: 10 Week of Death: 2 Subgroup: 1 Terminal Bodyweight: 292.3 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED ***ANIMAL HAS NO MICROSCOPIC FINDINGS RECORDED***

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 253 Sex: Female Dose Group: 2 Phase: Lactation Sacrifice Status: Final phase sacrifice
 Date of Death: 05-Sep-12 Day of Death: 10 Week of Death: 2 Subgroup: 1 Terminal Bodyweight: 300.9 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED

ANIMAL HAS NO MICROSCOPIC FINDINGS RECORDED

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Animal Number: 254 Sex: Female Dose Group: 2 Phase: Lactation Sacrifice Status: Final phase sacrifice
 Date of Death: 05-Sep-12 Day of Death: 10 Week of Death: 2 Subgroup: 1 Terminal Bodyweight: 370.5 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED ***ANIMAL HAS NO MICROSCOPIC FINDINGS RECORDED***

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 255 Sex: Female Dose Group: 2 Phase: Lactation Sacrifice Status: Final phase sacrifice
 Date of Death: 13-Sep-12 Day of Death: 10 Week of Death: 2 Subgroup: 1 Terminal Bodyweight: 339.8 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Skin

Hair loss, Ventral surface, Patchy

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 256 Sex: Female Dose Group: 2 Phase: Lactation Sacrifice Status: Final phase sacrifice
 Date of Death: 05-Sep-12 Day of Death: 10 Week of Death: 2 Subgroup: 1 Terminal Bodyweight: 331.2 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Kidneys
Pelvic dilatation

Kidneys
Cortical Tubular Basophilia, Bilateral, Slight
Cortical Tubular Dilatation, Unilateral, Minimal
Pelvic Dilatation, Present

The following examined tissues had no gross observations and no findings microscopically:
Ovaries

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 257 Sex: Female Dose Group: 2 Phase: Gestation Sacrifice Status: Final phase sacrifice
 Date of Death: 29-Aug-12 Day of Death: 25 Week of Death: 4 Subgroup: 1 Terminal Bodyweight: 285.4 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED

Ovaries
 Reduced Size of Corpora Lutea, Slight

The following examined tissues had no gross observations and no findings microscopically:

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 258 Sex: Female Dose Group: 2 Phase: Lactation Sacrifice Status: Final phase sacrifice
 Date of Death: 05-Sep-12 Day of Death: 10 Week of Death: 2 Subgroup: 1 Terminal Bodyweight: 301.2 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Stomach Stomach
 Cyst(s), Limiting ridge, Pale, Two, up to 2mm. Squamous Cyst - Limiting Ridge, Focal, Moderate

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 259

Sex: Female

Dose Group: 2

Phase: Lactation

Sacrifice Status: Final phase sacrifice

Date of Death: 06-Sep-12

Day of Death: 10

Week of Death: 2

Subgroup: 1

Terminal Bodyweight: 308.4 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Skin

Hair loss, ventral cervical to abdominal region and forelimbs.

The following examined tissues had no gross observations and no findings microscopically:
Ovaries

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Animal Number: 260 Sex: Female Dose Group: 2 Phase: Lactation Sacrifice Status: Final phase sacrifice
 Date of Death: 06-Sep-12 Day of Death: 10 Week of Death: 2 Subgroup: 1 Terminal Bodyweight: 318.9 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED ***ANIMAL HAS NO MICROSCOPIC FINDINGS RECORDED***

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 261 Sex: Female Dose Group: 3 Phase: Lactation Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 10 Week of Death: 2 Subgroup: 1 Terminal Bodyweight: 309.5 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Spleen
 Capsule thickened
 Adhesions, capsule to adipose tissue.

Spleen
 Capsular/Subcapsular Inflammation, Minimal
 Capsular Thickening, Slight
 Adhesions/Inflammation/Fibrosis, Minimal

Teeth
 Incisor(s) pale, Lower, Patchy, slight.

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Animal Number: 262 Sex: Female Dose Group: 3 Phase: Lactation Sacrifice Status: Killed for welfare reasons
 Date of Death: 30-Aug-12 Day of Death: 1 Week of Death: 1 Subgroup: 1 Terminal Bodyweight: 304.0 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED

Fac con to death
 Limited Tissues Examined, Present

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 263 Sex: Female Dose Group: 3 Phase: Gestation Sacrifice Status: Final phase sacrifice
 Date of Death: 01-Sep-12 Day of Death: 25 Week of Death: 4 Subgroup: 1 Terminal Bodyweight: 295.4 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED ***ANIMAL HAS NO MICROSCOPIC FINDINGS RECORDED***

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Animal Number: 264 Sex: Female Dose Group: 3 Phase: Lactation Sacrifice Status: Final phase sacrifice
 Date of Death: 07-Sep-12 Day of Death: 10 Week of Death: 2 Subgroup: 1 Terminal Bodyweight: 303.4 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED ***ANIMAL HAS NO MICROSCOPIC FINDINGS RECORDED***

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 265 Sex: Female Dose Group: 3 Phase: Lactation Sacrifice Status: Total litter loss
 Date of Death: 28-Aug-12 Day of Death: 1 Week of Death: 1 Subgroup: 1 Terminal Bodyweight: 295.1 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED ***ANIMAL HAS NO MICROSCOPIC FINDINGS RECORDED***

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	1	2	3	4
Compound	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	0	198	505	2900

Animal Number: 266 Sex: Female Dose Group: 3 Phase: Gestation Sacrifice Status: Total litter loss
 Date of Death: 04-Sep-12 Day of Death: 25 Week of Death: 4 Subgroup: 1 Terminal Bodyweight: 282.0 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Teeth

Incisor(s) pale, Lower

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 268 Sex: Female Dose Group: 3 Phase: Lactation Sacrifice Status: Final phase sacrifice
 Date of Death: 08-Sep-12 Day of Death: 10 Week of Death: 2 Subgroup: J Terminal Bodyweight: 288.7 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Teeth

Incisor(s) pale, Lower

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 269 Sex: Female Dose Group: 3 Phase: Lactation Sacrifice Status: Final phase sacrifice
 Date of Death: 08-Sep-12 Day of Death: 10 Week of Death: 2 Subgroup: 1 Terminal Bodyweight: 277.9 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

ANIMAL HAS NO MACROSCOPIC FINDINGS RECORDED ***ANIMAL HAS NO MICROSCOPIC FINDINGS RECORDED***

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 270 Sex: Female Dose Group: 3 Phase: Lactation Sacrifice Status: Total litter loss
 Date of Death: 29-Aug-12 Day of Death: 2 Week of Death: 1 Subgroup: 1 Terminal Bodyweight: 304.1 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Ovaries Ovaries
 Cyst(s), Left, Dark fluid, One, 8mm. Cyst(s), Present

The following examined tissues had no gross observations and no findings microscopically:

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 271 Sex: Female Dose Group: 4 Phase: Gestation Sacrifice Status: Final phase sacrifice
 Date of Death: 02-Sep-12 Day of Death: 25 Week of Death: 4 Subgroup: 1 Terminal Bodyweight: 271.1 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Kidneys

Irregular surface, Left
 Pale area(s), Left, A few, subcapsular, diffuse.

Kidneys

Cortical Tubular Basophilia, Unilateral, Moderate
 Cortical Tubular Dilatation, Unilateral, Moderate

Spleen

Adhesions, to abdominal wall and surrounding adipose tissue.

Spleen

Capsular Thickening, Focal, Minimal
 Adhesions/Inflammation/Fibrosis, Minimal

Teeth

Incisor(s) pale

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 272 Sex: Female Dose Group: 4 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 10-Sep-12 Day of Death: 54 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 252.2 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Kidneys

Pelvic dilatation, Right

Kidneys

Cortical Tubular Dilatation, Unilateral, Minimal
 Pelvic Dilatation, Unilateral, Present

Spleen

Capsule thickened, Multiple, areas.
 Adhesions, Anterior pole, capsule to adipose tissue.

Spleen

Capsular/Subcapsular Inflammation, Minimal
 Capsular Thickening, Slight
 Adhesions/Inflammation/Fibrosis, Slight

Teeth

Incisor(s) pale, Lower

The following examined tissues had no gross observations and no findings microscopically:

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 273 Sex: Female Dose Group: 4 Phase: Lactation Sacrifice Status: Total litter loss
 Date of Death: 29-Aug-12 Day of Death: 2 Week of Death: 1 Subgroup: 1 Terminal Bodyweight: 260.1 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Teeth

Incisor(s) pale, Lower

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 275 Sex: Female Dose Group: 4 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 10-Sep-12 Day of Death: 54 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 241.6 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Liver
Pale

Liver
No significant lesions

Spleen
Capsule thickened, Multiple, areas, up to 1mm.

Ovaries
Reduced Size of Corpora Lutea, Slight

Teeth
Incisor(s) pale, Lower

Spleen
Capsular/Subcapsular Inflammation, Focal, Minimal
Capsular Thickening, Focal, Minimal

The following examined tissues had no gross observations and no findings microscopically:

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 276 Sex: Female Dose Group: 4 Phase: Gestation Sacrifice Status: Killed for welfare reasons
 Date of Death: 02-Sep-12 Day of Death: 24 Week of Death: 4 Subgroup: 1 Terminal Bodyweight: 271.1 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Fac con to death
 Limited Tissues Examined, Present

Kidneys
 Pelvic dilatation, Left
 Pale area(s), Left, Punctate, Multiple, subcapsular.

Kidneys
 Cortical Tubular Basophilia, Unilateral, Slight
 Cortical Tubular Dilatation, Unilateral, Slight
 Pelvic Dilatation, Unilateral, Present
 Cortical Tubular Necrosis, Focal, Minimal

Teeth
 Incisor(s) pale, Lower

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	1	2	3	4
Compound	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	0	198	505	2900

Animal Number: 277 Sex: Female Dose Group: 4 Phase: Treatment Sacrifice Status: Final phase sacrifice
 Date of Death: 10-Sep-12 Day of Death: 54 Week of Death: 8 Subgroup: 1 Terminal Bodyweight: 250.4 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Ovaries

Reduced Size of Corpora Lutea, Slight

Spleen

Capsule thickened
 Adhesions, capsule to adipose tissue.

Spleen

Capsular/Subcapsular Inflammation, Slight
 Capsular Thickening, Moderate
 Adhesions/Inflammation/Fibrosis, Slight

Teeth

Incisor(s) pale, Lower

The following examined tissues had no gross observations and no findings microscopically:

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 278 Sex: Female Dose Group: 4 Phase: Gestation Sacrifice Status: Final phase sacrifice
 Date of Death: 30-Aug-12 Day of Death: 25 Week of Death: 4 Subgroup: 1 Terminal Bodyweight: 280.8 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Spleen
 Adhesions, to omental adipose tissue.

Spleen
 Capsular/Subcapsular Inflammation, Minimal
 Capsular Thickening, Minimal
 Adhesions/Inflammation/Fibrosis, Slight
 Extramedullary Haemopoiesis, Slight

Teeth
 Incisor(s) pale, Lower

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

APPENDIX 27 - continued

Request ID: 289382

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 279 Sex: Female Dose Group: 4 Phase: Gestation Sacrifice Status: Killed for welfare reasons
 Date of Death: 06-Sep-12 Day of Death: 24 Week of Death: 4 Subgroup: 1 Terminal Bodyweight: 286.2 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Fac con to death
 Limited Tissues Examined, Present

Spleen
 Adhesions, to surrounding adipose tissue and pancreas.
 Spleen
 Capsular Thickening, Minimal
 Adhesions/Inflammation/Fibrosis, Minimal
 Extramedullary Haemopoiesis, Slight

Teeth
 Incisor(s) pale, Lower

The following examined tissues had no gross observations and no findings microscopically:
 Ovaries

Request ID: 289382

APPENDIX 27 - continued

Macropathology and histopathology - individual findings - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Animal Number: 280 Sex: Female Dose Group: 4 Phase: Gestation Sacrifice Status: Final phase sacrifice
 Date of Death: 30-Aug-12 Day of Death: 25 Week of Death: 4 Subgroup: 1 Terminal Bodyweight: 259.9 g

PATHOLOGY OBSERVATIONS

MACROPATHOLOGY

HISTOPATHOLOGY

Ovaries
 Reduced Size of Corpora Lutea, Slight

Teeth
 Incisor(s) pale, Lower

The following examined tissues had no gross observations and no findings microscopically:

APPENDIX 28

Primordial ovarian follicle counts - individual values - F0 generation

Group	1	2	3	4																
Compound	Control	2-bromo-3,3,3-trifluoropropene																		
Exposure level (ppm)	0	198	505	2900																
Group	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Animal	241	242	243	244	245	246	247	248	249	250	251	252	253	254	255	256	257	258	259	260
Ovary	1	2	1	1	2	1	1	2	1	2	1	2	1	2	1	2	1	2	1	2
Section No.																				
1	3	14	26	23	16	19	4	2	8	34	16	27	28	14	14	14	14	14	14	50
Mean	8.5	24.5	17.5	3.0	21.0	21.5	21.0	21.0	21.0	21.0	21.5	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	32.0
SD	7.78	2.12	2.12	1.41	18.38	7.78	9.90	9.90	9.90	9.90	7.78	7.78	9.90	9.90	9.90	9.90	9.90	9.90	9.90	25.46
N	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2

APPENDIX 28 - continued

Primordial ovarian follicle counts - individual values - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group	1	1
Animal	249	250
Ovary	1	2
Section No.	1	2

1	19	3	10	6
Mean	11.0		8.0	
SD	11.31		2.83	
N	2		2	

APPENDIX 28 - continued

Primordial ovarian follicle counts - individual values - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group	2	2
Animal	259	260
Ovary	1	2
Section No.	1	2

1	12	14	26	23
---	----	----	----	----

Mean	13.0	24.5
SD	1.41	2.12
N	2	2

APPENDIX 28 - continued

Primordial ovarian follicle counts - individual values - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene	2-bromo-3,3,3-trifluoropropene
Exposure level (ppm)	:	0	198	505	2900

Group	3	3
Animal	269	270
Ovary	1	2
Section No.	1	2

1	15	3	19	10
Mean	9.0		14.5	
SD	8.49		6.36	
N	2		2	

APPENDIX 28 - continued

Primordial ovarian follicle counts - individual values - F0 generation

Group	1	2	3	4															
Compound	Control	2-bromo-3,3,3-trifluoropropene																	
Exposure level (ppm)	0	198	505	2900															
Group	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
Animal	271	272	273	274	275	276	277	278	279	280	281	282	283	284	285	286	287	288	289
Ovary	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1
Section No.																			
1	6	13	9	5	20	7	11	5	40	11	20	18	15	18	3	13			
Mean	9.5	7.0	13.5	8.0	25.5	19.0	16.5	8.0											
SD	4.95	2.83	9.19	4.24	20.51	1.41	2.12	7.07											
N	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2

APPENDIX 28 - continued

Primordial ovarian follicle counts - individual values - F0 generation

Group	:	1	2	3	4
Compound	:	Control	2-bromo-3,3,3-trifluoropropene 198	2-bromo-3,3,3-trifluoropropene 505	2-bromo-3,3,3-trifluoropropene 2900
Exposure level (ppm)	:	0			

Group	4			
Animal	279	280		
Ovary	1	2	1	2
Section No.				

1	19	28	28	18
---	----	----	----	----

Mean	23.5	23.0
SD	6.36	7.07
N	2	2

Annex 1 Certificate of analysis



Phone (435) 865 - 5000

AMERICAN PACIFIC CORPORATION - UTAH OPERATIONS
10622 W 6400 N
CEDAR CITY, UTAH 84720

Fax (435) 865 - 5029

CERTIFICATE OF ANALYSIS

MATERIAL: Stabilized 2-Bromo-3,3,3-trifluoropropene
(2-BTP)

CUSTOMER: Huntingdon Life Sciences Ltd.

QUANTITY: 2827 kg

LOT #: WNCC-BTP111128

P.O. NUMBER: 72032.2

O.I.D. NUMBER: 170588

LINE ITEM NUMBER: 1

SPECIFICATION: AMP-QSP-072, Rev 00

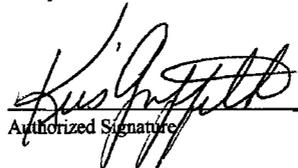
DATE OF MANUFACTURE: November 2011

DATE: 02 April 2012

<u>PROPERTY</u>	<u>CERTIFIED VALUE</u>	<u>SPECIFICATION</u>
Assay	>99.6	99.0% Min
Water-ppm	<10	15 ppm Max
Acidity (by weight as HBr)	2.3	3 ppm Max
Non Volatile Residue	960	4000 ppm Max
Appearance (Color)	Light Yellow, < 200	200 Color Units Max
Appearance (Clarity)	< 15	15 NTU Max

The signing of this document by an authorized representative of the Quality Assurance department indicates that the material is in conformance with specified requirements. Information contained in this report applies only to the material related to the specified lot number. This report shall not be reproduced, except in full, without written approval from AMPAC.

Where references to NELAC accreditation is made on any certificate or report, all requirements of the associated standard regarding information on the report will be met.


Authorized Signature

4/2/12
Date

Director Analytical Laboratories
Title

Doc ID: 002910
HI-LAB-090-FM-06

Rev: 00

Effective Date: 06 November 2007
Page 1 of 1

Annex 2 Aerosol technology and inhalation analysis report

Huntingdon Life Sciences

Working for a better future

Aerosol Technology Report

HLS study number:	WAG0015
Author	A Allen
Version ID:	Draft
Issue date:	28 Sept 2012

Table of Contents

Signature Page	399
1. Pre-study Atmosphere Characterization	400
2. Test Article Handling and Processing for Inhalation Generation	400
3. Exposure System	400
4. Administration	401
5. Atmosphere Analysis.....	401
5.1 Vapour Concentration	401
5.2 Flow diagram of the analytical method for the analysis of 2-bromo-3,3,3-trifluoropropene in test atmosphere samples	401
5.3 Nominal Concentration.....	402
5.4 Chamber Temperature	402
5.5 Chamber Humidity	402
6. Data and Calculations	402
7. Results and Discussion	402
7.1 Aerosol Concentrations.....	402
7.2 Chamber Temperature	403
7.3 Chamber Humidity	403

List of Tables

Table 1	Chamber atmosphere concentration of 2-bromo-3,3,3-trifluoropropene – daily means and individual exposure values – Group 2.....	404
Table 2	Chamber atmosphere concentration of 2-bromo-3,3,3-trifluoropropene – daily means and individual exposure values – Group 3.....	406
Table 3	Chamber atmosphere concentration of 2-bromo-3,3,3-trifluoropropene - daily means and individual exposure values – Group 4.....	408
Table 4	Chamber Temperatures - daily mean values.....	410
Table 5	Chamber Humidity - daily mean values.....	412

List of Figures

Figure 1	Schematic of Inhalation Exposure System	414
----------	---	-----

Signature Page

Aerosol Technology Report



Andrew Allen
Senior Aerosol Technologist
Huntingdon Life Sciences

18 OCT 2012

Date

1. Pre-study Atmosphere Characterization

Inhalation exposure system characterized including determinations of:

- Achieved vapour concentration
- Spatial distribution around the chamber

2. Test Article Handling and Processing for Inhalation Generation

As supplied, 2-Bromo-3,3,3-trifluoro-1-propene was easily vapourised using warmed air through a sintered glass vapouriser.

3. Exposure System

A schematic of the exposure system is presented in Figure 1. Components of the exposure system:

- Directed flow Whole body exposure chamber:
 - 0.75 m³ chamber of stainless steel and glass construction
- Animal Restraint:
 - Wire mesh modular caging
- Aerosol Generator:
 - Sintered glass vaporiser for Groups 2 to 4 all in a water bath set at 40°C
 - Syringe driver, polypropylene syringe for Group 2
 - Liquid reservoir and feed rate used to alter concentration Groups 3 and 4
 - Test groups - 30 L/min
- Diluent Airflow:
 - From in-house compressed air system – breathing quality
 - Group 1 - 149 L/min
 - Group 2 to 4 - 119 L/min
- Extract Airflow:
 - Drawn by a fan extract system
 - Drawn from base of exposure system
 - Controlled by a gate clamp situated at the rear of the chamber
- Airflow Monitoring:
 - In-line flowmeters monitored continuously for generation and diluent airflows
 - Chamber pressure differential monitored by Magnahelic set at -1 to -5 mm H₂O to ensure a slight negative pressure within the chamber ~ 150 L/min.

4. Administration

Animals exposed for 6 hours per day, 7 days a week
Exposure system operational parameters monitored continuously
Airflows documented initially and monitored during exposure

5. Atmosphere Analysis

5.1 Vapour Concentration

Vapour samples collected as follows:

Sample frequency – minimum of 3 samples/group/exposure

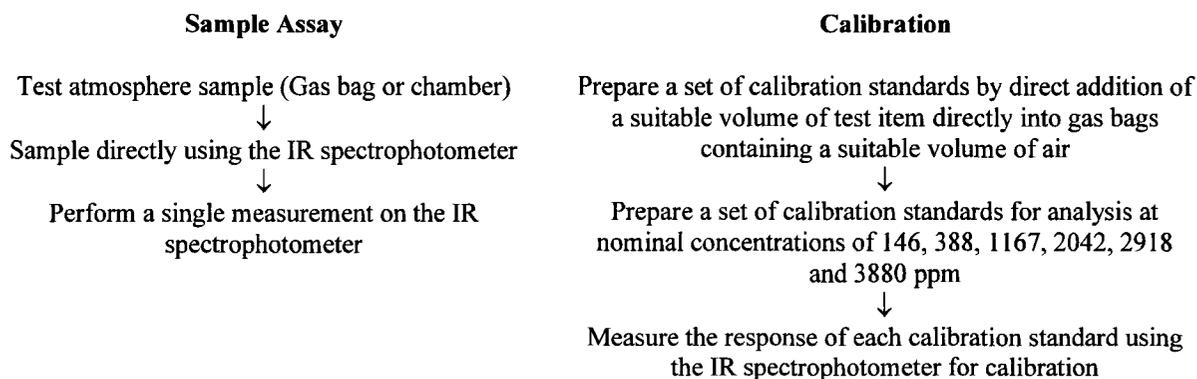
Sample location – representative animal level

Sample position remained constant

Sample analysis

Infra-red spectrophotometer

5.2 Flow diagram of the analytical method for the analysis of 2-bromo-3,3-trifluoropropene in test atmosphere samples



IR conditions

Instrument: MIRAN SapphIRe model 205B

Path length: Short (0.5m)

Wavelength: 10.699 μm

The IR spectrophotometer was calibrated using external standards. Absorbance measurements acquired by the IR spectrophotometer were used to calculate analysed concentration (ppm) using a 2nd order fit subjected to least squares regression analysis.

Standards were shared with another concurrent and related study.

5.3 Nominal Concentration

A mean daily nominal concentration was calculated for all test groups from the mass of test article used over the exposure period and the airflow through the exposure chamber. The ideal gas equation was used with the molecular weight of the test article and the measured chamber conditions to compute the volume of vapour produced from the mass of test article used. This data is not reported but retained in the raw data.

5.4 Chamber Temperature

Monitored using a liquid in glass thermometer.

5.5 Chamber Humidity

Monitored using wet and dry liquid in glass thermometers, with humidity calculated using proprietary tables.

6. Data and Calculations

To minimize the cumulative errors from repeated rounding of numbers, data in this report has been calculated continuously using unrounded numbers and only rounded for printing. Consequently, presented data may include rounding errors in the last significant figure.

All data not presented in this report is retained in the study data files and archives.

7. Results and Discussion

7.1 Aerosol Concentrations

Individual exposure concentrations and daily means are presented in Tables 1 to 3 and summarized below:

Group	Concentration (ppm)	
	Target	Mean
2	200	198
3	500	505
4	3000	2900

All groups were close to target.

Additional samples were taken for confirmation of atypical results and after minor generation rate adjustments.

All samples collected for Group 1 were negative for the presence of test article. This information is not tabulated but is retained in the study data files.

7.2 Chamber Temperature

The chamber temperature was monitored continuously for all groups and recorded at 30 minute intervals. Daily means are presented in Table 4 and were within expected parameters for this type of exposure system.

7.3 Chamber Humidity

The chamber humidity was derived from wet and dry bulb thermometers for all groups. These temperatures were recorded at 30 minute intervals and the subsequent humidity determined from propriatory tables. Daily means are presented in Table 5 and were within expected parameters for this type of exposure system.

Table 1 Chamber atmosphere concentration of 2-bromo-3,3,3-trifluoropropene – daily means and individual exposure values – Group 2

Exposure Week/ Day	Chamber concentration (ppm)						Daily mean
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6	
1.1	63	92	115	147	147	178	124
1.2	166	92	187	174			155
1.3	153	138	126	71	246	178	152
1.4	263	206	210				226
1.5	201	206	212				206
1.6	115	203	212				177
1.7	189	206	208				201
2.1	86	176	195	187			161
2.2	199	180	203				194
2.3	203	203	206				204
2.4	191	208	210				203
2.5	201	206	206				204
2.6	183	192	194				190
2.7	188	190	190				189
3.1	181	194	196				190
3.2	186	192	196				191
3.3	183	186	196				188
3.4	181	186	192				186
3.5	181	192	194				189
3.6	190	192	192				191
3.7	192	192	192				192
4.1	190	195	197				194
4.2	188	195	195				193
4.3	188	190	197				192
4.4	186 ¹	188 ¹	190 ¹				188 ¹
4.5	190	190	197				192
4.6	192	194	180				189
4.7	202	209	207				206
5.1	213	215	213				214
5.2	205	211	217				211
5.3	192	211	204				202
5.4	180 ¹	180 ¹	182 ¹				181 ¹
5.5	202	215	219				212
5.6	211	217	219				216
5.7	215	215	221				217
6.1	191	197	209				199
6.2	189	201	203				198
6.3	194	190	188				191
6.4	190	192	192				191
6.5	200	204	206				203
6.6	208	210	214				211
6.7	202	204	212				206
7.1	202	206	204				204
7.2	204	210	212				209
7.3	202	206	208				205
7.4	204	208	218				210
7.5	206	208	204				206
7.6	205	220	216				214

Table 1 Chamber atmosphere concentration of 2-bromo-3,3,3-trifluoropropene – daily means and individual exposure values – Group 2 (continued)

Exposure Week/Day	Chamber concentration (ppm)						Daily mean
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6	
7.7	207	212	216				212
8.1	203	210	218				210
8.2	216	216	220				217
8.3	216	220	220				219
8.4	223	229	203				218
8.5	205	220	225				217
8.6	203	207	210				207
8.7	175	193	201				190
Mean							198
sd							18.2
CV (%)							9.2

1 For exposures 4.4 and 5.4 the samples have been excluded due to standard check bag failures. The samples and test article usage were within expected tolerances.

sd Standard deviation

CV (%) Coefficient of variation ($sd \times 100/\text{mean}$)

Table 2 Chamber atmosphere concentration of 2-bromo-3,3,3-trifluoropropene – daily means and individual exposure values – Group 3

Exposure Week/ Day	Chamber concentration (ppm)							Daily mean
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6	Sample 7	
1.1	308	299	786	571	499	471	839	539
1.2	417	551	456					475
1.3	242	425	523					397
1.4	471	619	518					536
1.5	346	299	735					460
1.6	394	456	469					440
1.7	490	566	516					524
2.1	458	486	490					478
2.2	503	392	564					486
2.3	559	551	499					536
2.4	546	469	518					511
2.5	407	687	531	467				523
2.6	462	522	518					501
2.7	495	409	608	362				469
3.1	329	453	453					412
3.2	475	469	608					517
3.3	493	437	545					492
3.4	471	424	587					494
3.5	460	489	531					493
3.6	549	505	539					531
3.7	489	354	503	539				471
4.1	483	451	489					474
4.2	517	567	580					555
4.3	549	555	551					552
4.4	510 ¹	480 ¹	505 ¹					498 ¹
4.5	430	517	535	537				505
4.6	453	453	578					495
4.7	476	566	615					552
5.1	498	459	541					499
5.2	512	516	549					526
5.3	413	465	472	539				472
5.4	611 ¹	533 ¹	508 ¹	482 ¹				534 ¹
5.5	613	615	642	599	586	541	506	586
5.6	111	548	409	475	437	810	756	507
5.7	347	488	453					429
6.1	465	455	518					479
6.2	536	494	500					510
6.3	458	461	535					485
6.4	513	605	607	542	537			561
6.5	517	495	482					498
6.6	517	493	503					504
6.7	511	466	501					493
7.1	451	507	619	557				534
7.2	491	852	575	509				607
7.3	540	476	476					497
7.4	478	474	511					488
7.5	501	466	523					497
7.6	540	500	487					509

Table 2 Chamber atmosphere concentration of 2-bromo-3,3,3-trifluoropropene – daily means and individual exposure values (continued) – Group 3

Exposure Week/ Day	Chamber concentration (ppm)							Daily mean
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6	Sample 7	
7.7	743	511	481	571				577
8.1	716	593	558	520				597
8.2	476	476	450					467
Mean								505
sd								43.1
CV (%)								8.5

1 For exposures 4.4 and 5.4 the samples have been excluded due to standard check bag failures. The samples and test article usage were within expected tolerances.

sd Standard deviation

CV (%) Coefficient of variation ($sd \times 100/\text{mean}$)

Table 3 Chamber atmosphere concentration of 2-bromo-3,3,3-trifluoropropene - daily means and individual exposure values – Group 4

Exposure Week/Day	Chamber concentration (ppm)						Daily mean
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6	
1.1	3175	3332	3191	3092	2817		3121
1.2	2860	2584	2362				2602
1.3	2000	2303	2444				2249
1.4	4184	3939	2303	2110			3134
1.5	1990	2293	3007				2430
1.6	3095	2975	3356				3142
1.7	2697	2944	2707				2783
2.1	2046	2224	2771	2278			2330
2.2	2586	386 ¹	3148	3228			2987
2.3	3372	3413	2238				3008
2.4	3645	3252	2631	3276			3201
2.5	2871	3856	3268	1575	2864		2887
2.6	3274	3030	3111				3138
2.7	3030	3415	3518	3184			3287
3.1	2426	3316	3297				3013
3.2	3297	3027	3349				3224
3.3	3067	2806	2788				2887
3.4	2469	2955	2437				2620
3.5	2845	3200	3168				3071
3.6	3043	2858	3095				2999
3.7	3422	3016	1707	2994	2888		2805
4.1	2301	3087	2745				2711
4.2	2977	3696	2734				3136
4.3	2828	3303	3068				3066
4.4	2983 ²	2193 ²	2729 ²	3071 ²			2744
4.5	2615	2745	3040	2874			2819
4.6	2711	2795	3377				2961
4.7	2766	3262	2401	3341			2943
5.1	2908	2751	3256				2972
5.2	3224	3243	3181				3216
5.3	2876	2737	2795				2803
5.4	2213 ²	2861 ²	2809 ²	3150 ²			2758
5.5	2483	3181	2714	2546	3458		2876
5.6	719	2939	2550	3526	3387	2958	2680
5.7	2345	2435	3136	2917			2708
6.1	2476	2936	2721	2606	2684		2685
6.2	2338	2710	2826				2625
6.3	2126	3448	3376	3025	2998		2995
6.4	2764	2912	3112				2929
6.5	2623	2885	2610				2706
6.6	2620	2699	2919				2746
6.7	2717	3088	2880				2895
7.1	2638	2707	3287				2877
7.2	3214	3106	2955				3092
7.3	3472	2924	2727	2709			2958
7.4	2722	2725	2725				2724
7.5	4103	3168	2717	2702			3173
7.6	3217	2953	2783				2984

Table 3 Chamber atmosphere concentration of 2-bromo-3,3,3-trifluoropropene - daily means and individual exposure values (continued) – Group 4

Exposure Week/Day	Chamber concentration (ppm)						Daily mean
	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6	
7.7	3209	2796	2791				2932
8.1	2877	3179	2806				2954
8.2	3017	2882	2838				2912
8.3	2793	2801	2827				2807
8.4	2958	3136	2927				3007
Mean							2899
sd							223
CV (%)							7.7

1 Value omitted from daily mean due to sample taken when pressure vessel was empty, vessel refilled and sample repeated.

2 For exposures 4.4 and 5.4 the samples have been excluded due to standard check bag failures. The samples and test article usage were within expected tolerances.

sd Standard deviation

CV (%) Coefficient of variation ($sd \times 100/\text{mean}$)

Table 4 Chamber Temperatures - daily mean values

Exposure Week/Day	Chamber Temperature (°C)			
	Group 1	Group 2	Group 3	Group 4
1.1	25.9	23.9	23.0	23.8
1.2	24.8	23.9	23.5	23.6
1.3	22.7	22.5	21.5	20.8
1.4	22.8	22.0	22.0	21.0
1.5	26.0	23.7	23.0	24.3
1.6	24.7	23.4	23.2	24.2
1.7	24.1	22.5	22.7	24.3
2.1	24.9	22.8	21.9	23.7
2.2	25.3	22.9	21.8	23.4
2.3	20.7	20.7	19.5	19.2
2.4	21.3	20.7	19.6	20.7
2.5	25.0	23.8	22.8	24.2
2.6	25.4	24.0	23.6	24.4
2.7	24.8	24.3	23.2	24.3
3.1	25.1	24.5	23.3	24.2
3.2	24.8	24.2	23.3	25.0
3.3	22.3	23.5	22.8	23.5
3.4	23.0	23.2	22.8	23.2
3.5	25.6	24.8	23.4	24.2
3.6	25.2	24.3	23.8	24.4
3.7	25.3	24.6	23.7	24.8
4.1	25.5	24.8	23.9	25.0
4.2	25.9	24.5	23.6	24.4
4.3	22.2	22.7	22.2	22.9
4.4	22.4	22.8	22.3	22.9
4.5	25.5	24.9	23.9	24.7
4.6	25.5	24.3	23.8	25.4
4.7	25.7	23.8	23.4	24.8
5.1	25.4	23.8	23.0	25.3
5.2	25.3	24.3	22.9	24.6
5.3	22.5	20.5	20.9	22.6
5.4	22.2	21.8	21.7	21.9
5.5	26.2	23.8	22.9	24.6
5.6	25.7	22.7	22.4	24.9
5.7	25.8	22.6	22.8	25.0
6.1	26.2	23.8	23.4	24.0
6.2	25.8	23.6	23.2	23.8
6.3	23.1	21.3	20.4	22.0
6.4	21.8	21.3	20.6	21.3
6.5	25.6	24.1	23.4	25.3
6.6	26.1	24.3	24.3	25.8
6.7	25.8	23.8	23.8	24.9
7.1	25.8	23.8	23.7	24.5
7.2	26.5	24.7	23.3	25.0
7.3	23.9	23.1	22.0	23.0
7.4	24.1	23.8	22.5	22.9
7.5	26.6	24.7	26.6	24.3
7.6	25.9	24.0	25.9	24.9

Table 4 Chamber Temperatures - daily mean values (continued)

Exposure Week/Day	Chamber Temperature (°C)			
	Group 1	Group 2	Group 3	Group 4
7.7	25.5	23.7	25.5	24.4
8.1	25.6	24.0	25.6	25.1
8.2		22.3	24.7	24.2
8.3		20.2		21.9
8.4		21.1		22.1
8.5		25.6		
8.6		24.2		
8.7		25.0		
Mean	24.7	23.4	23.0	23.8
sd	1.5	1.3	1.4	1.4
CV (%)	6.1	5.4	6.0	5.9

sd Standard deviation
CV (%) Coefficient of variation (sd × 100/mean)

Table 5 Chamber Humidity - daily mean values

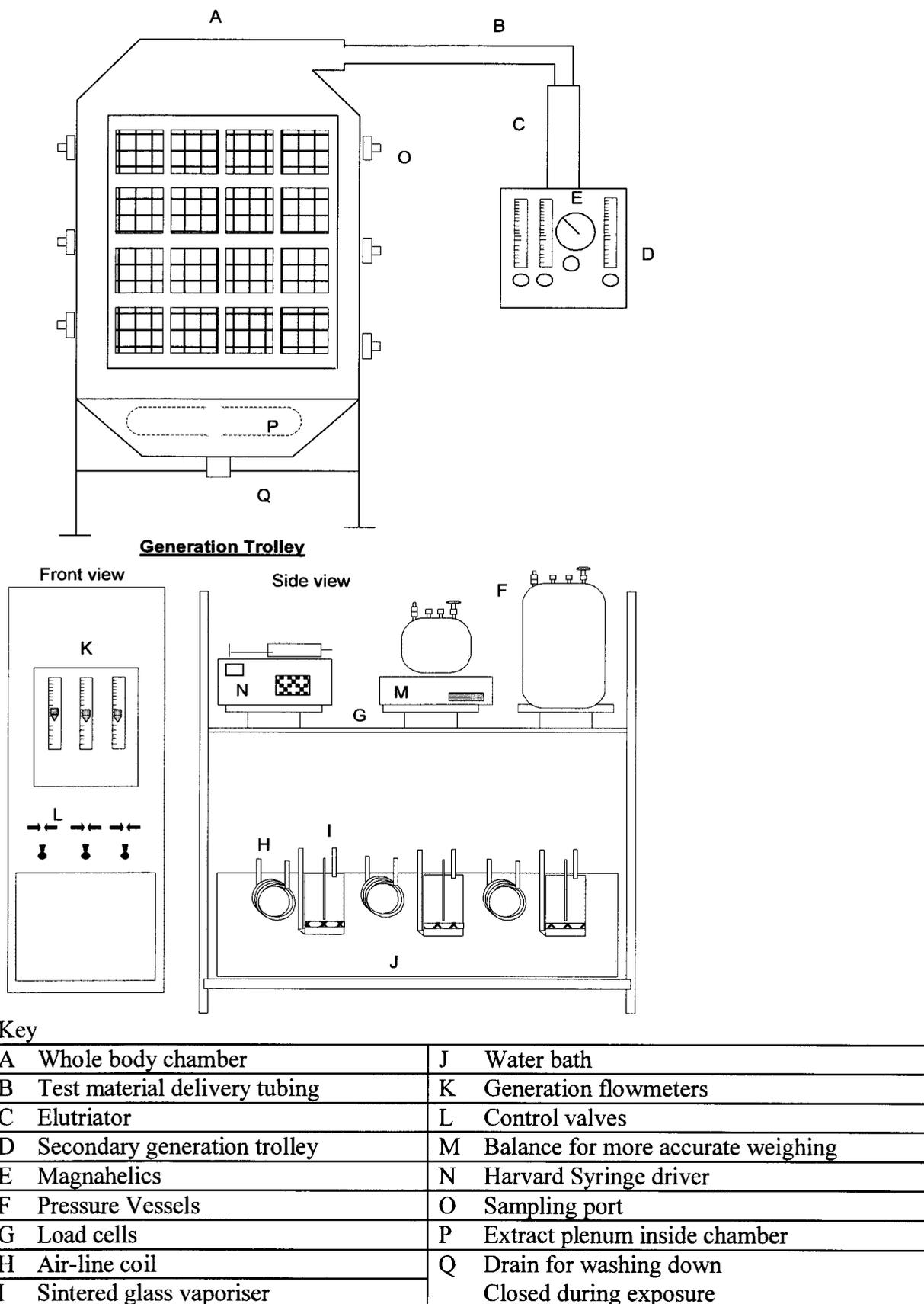
Exposure Week/Day	Chamber Humidity (%)			
	Group 1	Group 2	Group 3	Group 4
1.1	30.9	49.6	32.9	47.2
1.2	52.0	51.2	29.9	51.2
1.3	41.2	53.8	53.8	64.8
1.4	28.5	42.7	30.6	60.3
1.5	30.2	37.5	40.2	39.2
1.6	72.5	46.2	48.6	60.2
1.7	50.9	48.0	40.2	53.1
2.1	34.5	50.1	48.9	78.0
2.2	35.8	36.5	51.2	68.1
2.3	29.1	41.9	50.5	63.0
2.4	29.5	43.6	49.8	55.3
2.5	49.9	31.6	41.6	51.6
2.6	28.3	37.1	47.8	53.1
2.7	44.2	29.1	38.1	64.4
3.1	35.8	30.8	47.9	50.9
3.2	41.5	36.5	44.0	54.9
3.3	31.1	24.1	34.5	43.9
3.4	27.7	28.6	33.8	42.9
3.5	34.5	30.7	44.6	57.0
3.6	39.7	35.2	47.7	49.9
3.7	36.7	38.5	44.8	49.8
4.1	34.8	38.0	49.4	48.2
4.2	39.0	35.0	44.4	57.7
4.3	39.8	24.4	37.9	44.4
4.4	35.8	25.2	33.8	44.3
4.5	33.5	32.0	41.6	50.2
4.6	33.0	39.0	42.9	50.7
4.7	31.5	36.8	49.2	53.8
5.1	34.0	39.6	38.3	41.8
5.2	40.8	38.3	42.4	47.8
5.3	34.6	35.8	60.2	35.5
5.4	31.9	37.8	33.2	55.6
5.5	35.2	43.5	41.2	56.5
5.6	29.8	51.4	60.1	44.7
5.7	29.5	51.6	53.8	45.5
6.1	28.7	41.3	46.3	63.8
6.2	32.1	43.8	50.0	61.0
6.3	26.9	64.0	64.0	26.9
6.4	31.0	57.4	57.4	31.0
6.5	29.2	32.2	43.6	47.8
6.6	25.9	29.0	38.5	48.4
6.7	29.8	37.0	38.1	49.3
7.1	27.3	32.6	41.1	55.5
7.2	31.3	30.2	40.6	48.4
7.3	28.3	32.7	32.7	47.8
7.4	27.3	23.3	37.0	55.2
7.5	33.0	33.0	44.1	54.7
7.6	29.0	38.4	44.4	47.2

Table 5 Chamber Humidity - daily mean values (continued)

Exposure Week/Day	Chamber Humidity (%)			
	Group 1	Group 2	Group 3	Group 4
7.7	32.1	32.5	50.1	58.9
8.1	32.6	29.2	40.3	44.5
8.2		27.8	39.6	42.6
8.3		45.2		44.4
8.4		29.5		43.0
8.5		26.8		
8.6		49.5		
8.7		32.7		
Mean	34.6	37.9	43.9	51.1
sd	8.2	9.0	7.8	9.1
CV (%)	23.6	23.8	17.7	17.8

sd Standard deviation
CV (%) Coefficient of variation (sd × 100/mean)

Figure 1 Schematic of Inhalation Exposure System



Annex 3 Pathology report

PATHOLOGY REPORT

**2-bromo-3,3,3-trifluoropropene: Reproductive/Developmental
Toxicity Screening Study in the CD Rat by Inhalation
Administration**

HLS study number:	WAG0015
Version ID:	1
Issue date:	13 November 2012

Signature Page

PATHOLOGY REPORT

2-bromo-3,3,3-trifluoropropene: Reproductive/Developmental Toxicity Screening Study in the CD Rat by Inhalation Administration



Miledi Azzalin DVM, MRCVS
Pathologist
Huntingdon Life Sciences

13 Nov. 2012
13 November 2012

Table of Contents

Signature Page	2
1. Introduction	4
1.1 Objective	4
2. Results	4
2.1 Decedents	4
2.2 Macroscopic Pathology	5
2.2.1 Animals killed after scheduled treatment period	5
2.3 Microscopic Pathology	6
2.3.1 Animals killed after scheduled treatment period	6
3. Discussion	7
4. Conclusion	8
5. Appendix I	9

1. Introduction

1.1 Objective

Initial screening assessment of the influence of 2-bromo-3,3,3-trifluoropropene when administered by inhalation administration on reproductive performance and development in the CD rat.

Group	Treatment	Achieved concentration (ppm)	Number of animals	
			Male	Female
1	Control	0	10	10
2	2-bromo-3,3,3-trifluoropropene	198	10	10
3	2-bromo-3,3,3-trifluoropropene	505	10	10
4	2-bromo-3,3,3-trifluoropropene	2900	10	10

2. Results

2.1 Decedents

Two females exposed to 2900 ppm, animals 276 and 279, were killed for welfare reasons on Day 24 of the gestation phase and one female exposed to 505 ppm, animal 262, was killed for welfare reasons on Day 1 of the lactation phase. No histopathological findings were seen in the ovaries of these three animals. Animal 276 had multiple but unilateral histopathological changes in the kidney and animal 279 had capsular thickening, adhesions/inflammation/fibrosis of the spleen; in both cases the findings observed could not be considered as a factor contributing to death.

2.2 Macroscopic Pathology

2.2.1 Animals killed after scheduled treatment period

The macroscopic examinations performed in the F0 animals revealed intergroup differences in the prostate, spleen, incisor teeth and skin.

Prostate

A reduction in size of the prostate was seen in all males exposed to 2900 ppm, in the majority of males exposed to 505 ppm and in one male exposed to 198 ppm.

Summary of findings in the prostate of F0 animals after scheduled treatment period

Group/sex Exposure Level (ppm)	1M 0	2M 198	3M 505	4M 2900
Small	0	1	7	10
Number of animals examined	10	10	10	10

Spleen

Capsular thickening was seen in the spleen of the majority of males exposed to 2900, 505 or 198 ppm and in occasional females exposed to 2900 or 505 ppm. Capsular adhesions were seen in occasional treated males across all groups, in a few females exposed to 2900 ppm and one female exposed to 505 ppm.

Summary of findings in the spleen of F0 animals after scheduled treatment period

Group/sex Exposure Level (ppm)	1M 0	2M 198	3M 505	4M 2900	1F 0	2F 198	3F 505	4F 2900
Capsule thickened	0	8	6	9	0	0	2	3
Adhesions	0	2	3	4	0	0	1	4
Number of animals examined	10	10	10	10	10	10	9	8

Teeth

Pale incisor teeth were seen in all male and female animals exposed to 2900 ppm, in the majority of males and three females exposed to 505 ppm and in one control male.

Summary of findings in the teeth of F0 animals after scheduled treatment period

Group/sex Exposure Level (ppm)	1M 0	2M 198	3M 505	4M 2900	1F 0	2F 198	3F 505	4F 2900
Incisor(s) pale	1	0	6	10	0	0	3	8
Number of animals examined	10	10	10	10	10	10	9	8

Skin

An increased incidence of hair loss was noted in occasional males exposed to 2900ppm.

Summary of findings in the skin of F0 animals after scheduled treatment period

Group/sex	1M	2M	3M	4M	1F	2F	3F	4F
Exposure Level (ppm)	0	198	505	2900	0	198	505	2900
Hair loss	0	1	2	4	2	2	0	0
Number of animals examined	10	10	10	10	10	10	9	8

The nature and incidence of all other findings were consistent with the common background of macroscopic changes seen at these laboratories.

2.3 Microscopic Pathology

2.3.1 Animals killed after scheduled treatment period

Treatment related findings

Changes related to treatment with 2-bromo-3,3,3-trifluoropropene were seen in the F0 ovaries.

Ovary

A slight reduction in the size of corpora lutea was seen in the ovaries of 4 females exposed to 2900 ppm and in a single female exposed to 198 ppm.

Summary of findings in the ovary of F0 animals after scheduled treatment period

Group/sex	1F	2F	3F	4F
Exposure Level (ppm)	0	198	505	2900
Reduced Size of Corpora Lutea				
Slight	0	1	0	4
Total	0	1	0	4
Number of tissues examined	10	10	9	8

Findings of an uncertain relationship to treatment

Findings of an uncertain relationship to treatment were identified in the spleen. This tissue was examined microscopically only when macroscopic abnormalities had been observed at necropsy. No spleen from control animals was examined.

Spleen

Minimal to moderate capsular/subcapsular inflammation and/or capsular thickening and/or adhesions/inflammation/fibrosis were observed in the majority of treated males exposed to 198, 505 or 2900 ppm and in occasional females exposed to 505 or 2900 ppm.

Summary of findings of an uncertain relationship to treatment in the spleen of F0 animals after scheduled treatment period

Group/sex Exposure Level (ppm)	1M 0	2M 198	3M 505	4M 2900	1F 0	2F 198	3F 505	4F 2900
Capsular/Subcapsular Inflammation								
Minimal	0	5	3	3	0	0	1	3
Slight	0	3	2	2	0	0	0	1
Moderate	0	0	1	2	0	0	0	0
Total	0	8	6	7	0	0	1	4
Capsular Thickening								
Minimal	0	4	4	2	0	0	0	4
Slight	0	0	2	4	0	0	2	1
Moderate	0	0	0	1	0	0	0	1
Total	0	4	6	7	0	0	2	6
Adhesions/Inflammation/Fibrosis								
Minimal	0	3	2	2	0	0	2	1
Slight	0	2	1	3	0	0	0	3
Moderate	0	0	1	1	0	0	0	0
Total	0	5	4	6	0	0	2	4
Number of tissues examined	0	8	7	9	0	0	2	6

The incidence and distribution of all other findings were consistent with the common background seen at these laboratories.

3. Discussion

All females exposed to 2900 ppm and half of those exposed to 505 ppm were killed at a different time during the study as they failed to mate (sacrificed on Day 25 after the last paring) or failed to litter (sacrificed on Day 25 after mating) or lost the litter post-partum (sacrificed on the Day of litter loss); therefore, none performed as expected up to the end of the study on Day 10 of lactation.

The examination of the ovaries from the F0 generation females revealed the presence of histopathological changes attributable to treatment. A reduction in size of corpora lutea was observed in the ovaries of four females exposed to 2900 ppm and one female exposed to 198 ppm. The corpora lutea were quite small and appeared to be not newly formed. As this change was not consistent with the increasing exposure level across the treated groups, the presence in a single female exposed to 198 ppm was considered to be incidental.

There was no apparent difference in the average number of corpora lutea in the treated groups when compared with controls, as reported in Appendix I. This count did not take account of differences in size of corpora lutea, however, as has been reported. No histopathological findings were seen to account for the irregular oestrus cycle or the prolonged gestation length as reported in the in life phase.

The histopathological examination of testes and epididymides from the F0 generation animals performed after scheduled treatment period revealed no findings attributable to treatment with the test article 2-bromo-3,3,3-trifluoropropene.

The seminiferous tubules were evaluated with respect to their stage in the spermatogenic cycle and the integrity of the various cell types present within the different stages. No significant cell or stage-specific abnormalities were seen in the sections of testes either stained with haematoxylin & eosin (H&E) or periodic acid Schiff (PAS).

Evaluation of the epididymides did not reveal any changes in leukocyte infiltration, cell populations, or sperm numbers. There were no findings to correlate with the organ weight variation reported at necropsy.

An increased incidence of small prostates was observed at the macroscopic examination. This was consistent with a reduction in prostate weight seen with increasing exposure level. No microscopic correlate for the small prostates could be identified. A low incidence of inflammatory changes was observed in all groups including controls and was considered to be incidental as these types of changes are occasionally seen in rats of this age.

Capsular thickening and adhesions were observed in the spleen of the majority of treated males and occasional treated females at the macroscopic examination. Most of these macroscopic observations correlated with findings of capsular/subcapsular inflammation and/or capsular thickening and/or adhesions/inflammation/fibrosis seen at the microscopic examination and are likely to be related to treatment. However, as no controls and only tissues with macroscopic changes were sampled and microscopically examined, conclusions as to the significance of these changes could not be made.

The significance of the increased incidence of pale incisors and hair loss of the skin observed at the macroscopic examination could not be clarified as these lesions were not examined microscopically.

Pale incisors and hair loss of the skin are not routinely presented for microscopic evaluation as such changes do not usually correlate with changes seen histopathologically. These tissues are also not routinely required to be examined for reproductive developmental screening studies.

4. Conclusion

The microscopic evaluation on this study revealed the presence of histopathological changes related to 2-bromo-3,3,3-trifluoropropene only in the ovaries of animals exposed to 2900 ppm.

5. Appendix I

Corpora Lutea Counts

Group/ Animal No.	L Ovary Level 1	R Ovary Level 1	Total CL
1F/241	4	9	13
1F/242	9	11	20
1F/243	7	12	19
1F/244	3	13	16
1F/245	8	11	19
1F/246	12	14	26
1F/247	5	5	10
1F/248	5	13	18
1F/249	13	9	22
1F/250	11	8	19

2F/251	10	16	26
2F/252	15	6	21
2F/253	8	11	19
2F/254	21	13	34
2F/255	5	15	20
2F/256	12	13	25
2F/257	16	18	34
2F/258	18	18	36
2F/259	17	11	28
2F/260	15	7	22

3F/261	12	7	19
3F/262	8	8	16
3F/263	12	13	25
3F/264	9	12	21
3F/265	3	2	5
3F/266	4	9	13
3F/267	4	14	18
3F/268	11	12	23
3F/269	13	6	19
3F/270	12	8	20

4F271	9	11	20
4F272	16	11	27
4F273	6	4	10
4F274	8	5	13
4F275	5	13	18
4F276	4	11	15
4F277	7	10	17
4F278	8	5	13
4F279	5	7	12
4F280	12	16	28

Key:

L= Refer to the ovary on the Left of each slide;
R= Refer to the ovary on the Right of each slide.
CL= Corpora Lutea

Annex 4 GLP compliance statements

HUNTINGDON RESEARCH CENTRE GLP COMPLIANCE STATEMENT 2011



**THE DEPARTMENT OF HEALTH OF THE GOVERNMENT
OF THE UNITED KINGDOM**

GOOD LABORATORY PRACTICE

**STATEMENT OF COMPLIANCE
IN ACCORDANCE WITH DIRECTIVE 2004/9/EC**

TEST FACILITY

Huntingdon Life Sciences
Woolley Road
Alconbury
Huntingdon
Cambridgeshire
PE28 4HS

TEST TYPE(S)

Analytical/Clinical Chemistry
Environmental Fate
Environmental Toxicity
Ecosystems
Toxicology

DATE OF INSPECTION

23 August 2011

An inspection for compliance with the Principles of Good Laboratory Practice was carried out at the above test facility as part of the UK Good Laboratory Practice Compliance Monitoring Programme.

This statement confirms that, on the date of issue, the UK Good Laboratory Practice Monitoring Authority were satisfied that the above test facility was operating in compliance with the OECD Principles of Good Laboratory Practice.

This statement constitutes a Good Laboratory Practice Instrument (as defined in the UK Good Laboratory Practice Regulations 1999).

A handwritten signature in black ink, appearing to read 'A. Gray', with the date '12/12/11' written below it.

Dr. Andrew J. Gray
Head, UK GLP Monitoring Authority



EYE RESEARCH CENTRE GLP COMPLIANCE STATEMENT 2012



**THE DEPARTMENT OF HEALTH OF THE GOVERNMENT
OF THE UNITED KINGDOM**

GOOD LABORATORY PRACTICE

**STATEMENT OF COMPLIANCE
IN ACCORDANCE WITH DIRECTIVE 2004/9/EC**

TEST FACILITY	TEST TYPE(S)
Huntingdon Life Sciences Eye Research Centre Occold Eye Suffolk IP23 7PX	Analytical/Clinical Chemistry Environmental Fate Environmental Toxicity Ecosystems Phys.Chem. Testing Residue studies Mutagenicity Toxicology

DATE OF INSPECTION

18th – 20th June 2012

An inspection for compliance with the Principles of Good Laboratory Practice was carried out at the above test facility as part of the UK Good Laboratory Practice Compliance Monitoring Programme.

This statement confirms that, on the date of issue, the UK Good Laboratory Practice Monitoring Authority were satisfied that the above test facility was operating in compliance with the OECD Principles of Good Laboratory Practice.

This statement constitutes a Good Laboratory Practice Instrument (as defined in the UK Good Laboratory Practice Regulations 1999).

A handwritten signature in black ink, followed by the date '19/9/12' written below it.

Dr. Andrew J. Gray
Head, UK GLP Monitoring Authority



From: (702) 699-4171
Brad Colton
American Pacific Corp
3883 Howard Hughes Pkwy.
Suite 700
Las Vegas, NV 89169

Origin ID: FLXA



J12201209200325

Ship Date: 16JAN13
ActWgt: 2.0 LB
CAD: 5430836/NET3300

Delivery Address Bar Code

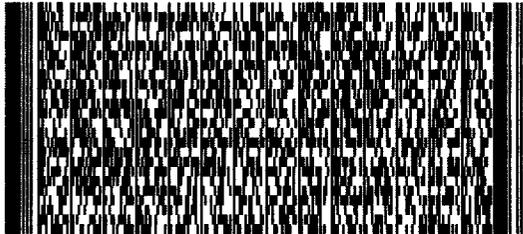


SHIP TO: (202) 564-8940 **BILL SENDER**
EPA East-Room 6428 Attn: Sectn 8(e)
US EPA
1200 PENNSYLVANIA AVE NW
TSCA CONFIDENTIAL BUS. INFO. CTR
WASHINGTON, DC 20460

Ref # TSCA Submittal
Invoice #
PO #
Dept #

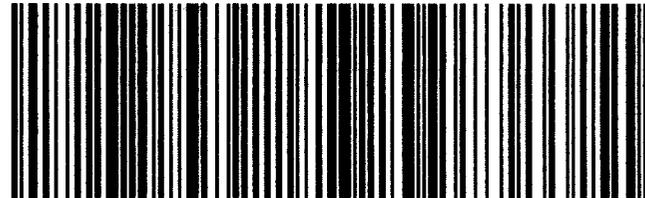
THU - 17 JAN A1
STANDARD OVERNIGHT

TRK# **7945 3668 7278**
0201



XC RDVA

20460
DC-US
DCA



515G2/7813/AA44

After printing this label:

1. Use the 'Print' button on this page to print your label to your laser or inkjet printer.
2. Fold the printed page along the horizontal line.
3. Place label in shipping pouch and affix it to your shipment so that the barcode portion of the label can be read and scanned.

Warning: Use only the printed original label for shipping. Using a photocopy of this label for shipping purposes is fraudulent and could result in additional billing charges, along with the cancellation of your FedEx account number

Use of this system constitutes your agreement to the service conditions in the current FedEx Service Guide, available on fedex.com. FedEx will not be responsible for any claim in excess of \$100 per package, whether the result of loss, damage, delay, non-delivery, misdelivery, or misinformation, unless you declare a higher value, pay an additional charge, document your actual loss and file a timely claim. Limitations found in the current FedEx Service Guide apply. Your right to recover from FedEx for any loss, including intrinsic value of the package, loss of sales, income interest, profit, attorney's fees, costs, and other forms of damage whether direct, incidental, consequential, or special is limited to the greater of \$100 or the authorized declared value. Recovery cannot exceed actual documented loss. Maximum for items of extraordinary value is \$1,000, e.g. jewelry, precious metals, negotiable instruments and other items listed in our ServiceGuide. Written claims must be filed within strict time limits, see current FedEx Service Guide.