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FINAL PILOT REPORT

ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF POTASSIUM PERFLUOROBUTANE SULFONATE (PFBS) IN RATS

SPONSOR'S STUDY NUMBER: T-7485.11

Author

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Study Completed On

15 October 2003
(Audited Final Pilot Report)

Performing Laboratory

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Laboratory Project ID

Argus Research, Protocol Number: 418-023P

GOOD LABORATORY PRACTICE STATEMENT

This study was conducted according to U.S. Food and Drug Administration (FDA) *Good Laboratory Practice Regulations; Final Rule* (21 CFR Part 58), the Japanese Ministry of Health and Welfare *Good Laboratory Practice Standard for Safety Studies on Drugs*, and the European Economic Community *Council decision on 28 July 1989 on the acceptance by the European Economic Community of an OECD decision/recommendation on compliance with principles of good laboratory practice or* the Organization for Economic Cooperation and Development (OECD) *Good Laboratory Practice in the Testing of Chemicals* [C(97)186/Final]. Any areas of noncompliance are documented in the study record. No deviations existed that affected the validity of the study.

15 OCT 2003

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

PROTOCOL 418-023P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF POTASSIUM PERFLUOROBUTANE SULFONATE (PFBS) IN RATS

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ARGUS RESEARCH PROTOCOL NUMBER: 418-023P
SPONSOR'S STUDY NUMBER: T-7485.11

ABSTRACT

Forty presumed pregnant Crl:CD®(SD)IGS BR VAF/Plus® female rats were randomly assigned to five dosage groups (Groups I through V), eight rats per group. Suspensions of the test substance, Potassium Perfluorobutane Sulfonate (PFBS or T-7485), or the vehicle, aqueous 0.1% carboxymethylcellulose, were administered orally (gavage) once daily to these naturally-bred female rats on days 6 through 20 of presumed gestation (DGs 6 through 20) at dosages of 0 (Vehicle), 100, 300, 1000 and 2000 mg/kg/day. The dosage volume was 10 mL/kg, adjusted daily on the basis of the individual body weights recorded immediately before administration of the test substance or vehicle.

Checks for viability were made twice daily. Clinical observations were recorded daily before dosage, approximately 60 ± 10 minutes after administration and on the day of sacrifice. Body weights were recorded daily during the dosage period and the day of sacrifice. Feed consumption values were recorded on DGs 0, 6, 9, 12, 15, 18 and 21.

All rats were sacrificed on DG 21 and examined for the number and distribution of corpora lutea, implantation sites and uterine contents. The gravid uterus was excised and weighed. A gross necropsy of the thoracic, abdominal and pelvic viscera was performed. Fetuses were weighed and examined for gross external alterations and sex.

All rats survived to scheduled sacrifice. Clinical observations considered test substance-related were limited to urine-stained abdominal fur in four rats in the 2000 mg/kg/day dosage group. Persistent adverse clinical observations were confirmed at necropsy. No additional gross lesions were identified. Rats in the 2000 mg/kg/day dosage group lost weight on DGs 6 to 9 and body weight gains were reduced at several intervals tabulated during the dosage period. Reflecting these effects of the test substance, body weight gain was reduced in the 2000 mg/kg/day dosage group for the entire treatment (DGs 6 to 21) and gestation (DGs 0 to 21) periods.

Absolute and relative feed consumption values were reduced in the 2000 mg/kg/day dosage group on DGs 6 to 9, 9 to 12, 12 to 15, 15 to 18 and 18 to 21, and for the entire treatment and gestation periods.

Fetal body weights were reduced in the 2000 mg/kg/day dosage group, as compared with the control group. No other Caesarean-sectioning or litter parameters were affected by dosages of the test substance as high as 2000 mg/kg/day. No fetal gross alterations occurred.

I. Purpose

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

II. Methods[a]

The test substance, Potassium Perfluorobutane Sulfonate (PFBS or T-7485), a white powder, was received on 14 December 2000, and was stored at room temperature. The vehicle, 0.1% carboxymethylcellulose (CMC, medium viscosity), was prepared using reverse osmosis membrane processed deionized water (R.O. deionized water). The carboxymethylcellulose, an off-white powder, was received from Sigma Chemical Company, St. Louis, Missouri, on 10 October 1999, and was stored at room temperature. Test substance and vehicle formulations were prepared approximately every 10 days and stored refrigerated (2°C to 8°C). Results of the concentration, homogeneity and stability analyses are available in ATTACHMENT 2. The 10 and 30 mg/mL samples were all found to be within ± 10% of the target concentrations; the 100 mg/mL samples were 88.9% and 105% of target and the 200 mg/mL samples were 99.2% and 76.8% of target.

Forty presumed pregnant Crl:CD®(SD)IGS BR VAF/Plus® female rats were randomly assigned to five dosage groups (Groups I through V), eight rats per group. Suspensions of the test substance or the vehicle were administered orally (gavage) once daily to these naturally-bred female rats on days 6 through 20 of presumed gestation (DGs 6 through 20) at dosages of 0 (Vehicle), 100, 300, 1000 and 2000 mg/kg/day. The dosage volume was 10 mL/kg, adjusted daily on the basis of the individual body weights recorded immediately before administration of the test substance or vehicle.

Checks for viability were made twice daily. Clinical observations were recorded daily before dosage, approximately 60 ± 10 minutes after administration and on the day of sacrifice. Body weights were recorded daily during the dosage period and the day of sacrifice. Feed consumption values were recorded on DGs 0, 6, 9, 12, 15, 18 and 21.

All rats were sacrificed on DG 21 and examined for the number and distribution of corpora lutea, implantation sites and uterine contents. The gravid uterus was excised and weighed. A gross necropsy of the thoracic, abdominal and pelvic viscera was performed. Fetuses were weighed and examined for gross external alterations and sex.

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

III. Results

A. Mortality, Clinical and Necropsy Observations (Summary - Table 1; Individual Data - Tables 8 and 9)

All rats survived to scheduled sacrifice. Clinical observations considered test substance-related were limited to urine-stained abdominal fur in four rats in the 2000 mg/kg/day dosage group. Observations of red perinasal substance, red perioral substance, excess salivation and gasping in one rat in the 2000 mg/kg/day dosage group and localized alopecia on the limbs in one rat in the 300 mg/kg/day dosage group were not considered test substance related. Persistent adverse clinical observations were confirmed at necropsy. No additional gross lesions were identified.

B. Maternal Body Weights, Body Weight Changes and Gravid Uterine Weights (Figure 1; Summaries - Tables 2 and 3; Individual Data - Table 10)

Rats in the 2000 mg/kg/day dosage group lost body weight on DGs 6 to 9 and body weight gains were reduced at several intervals tabulated during the dosage period. Reflecting these effects of the test substance, body weight gain was reduced in the 2000 mg/kg/day dosage group for the entire treatment period (calculated as DGs 6 to 21) and the entire gestation period (calculated as DGs 0 to 21), compared to control group values.

Gravid uterine weights were reduced (15.4%) for the rats in the 2000 mg/kg/day dosage group, compared to the control group. Reflecting this effect of the test substance, the corrected DG 21 body weight (DG 21 weight minus gravid uterine weight) was reduced (11.8%) in the 2000 mg/kg/day dosage group. Corrected body weight gain for the entire treatment period (calculated as DGs 6 to 21C) and the entire gestation period (calculated as DGs 0 to 21C) were also reduced in the 2000 mg/kg/day dosage group, compared to control group values.

Body weights, body weight gains and gravid uterine weights were comparable in the 0 (Vehicle), 100, 300 and 1000 mg/kg/day dosage groups.

C. Maternal Absolute (g/day) and Relative (g/kg/day) Feed Consumption Values (Summaries - Tables 4 and 5; Individual Data - Table 11)

Absolute and relative feed consumption values were reduced in the 2000 mg/kg/day dosage group on DGs 6 to 9, 9 to 12, 12 to 15, 15 to 18 and 18 to 21, compared to control group values. Reflecting this effect of the test substance, absolute feed consumption values for the entire treatment period (calculated as DGs 6 to 21) were reduced (19.2%) and the entire gestation period (calculated as DGs 0 to 21) were reduced (16.4%), compared to control group values. Relative feed consumption values for the entire treatment period were reduced (13.7%) and the entire gestation period were reduced (11.3%), compared to control group values.

Absolute and relative feed consumption values were comparable in the 0 (Vehicle), 100, 300 and 1000 mg/kg/day dosage groups.

D. Caesarean-Sectioning and Litter Observations (Summaries - Tables 6 and 7; Individual Data - Tables 12 through 14)

Caesarean-sectioning observations were based on 8 (100%), 7 (87.5%), 8 (100%), 7 (87.5%) and 8 (100%) pregnant rats in the 0 (Vehicle), 100, 300, 1000 and 2000 mg/kg/day dosage groups, respectively. Male and female fetal body weights were reduced (12.2% and 13.0%, respectively), in the 2000 mg/kg/day dosage group, as compared with the control group.

There were no other test substance-related effects on the following parameters evaluated at Caesarean-sectioning: litter averages for corpora lutea, implantations, litter sizes, live fetuses, early resorptions, percent resorbed conceptuses and percent live male fetuses. There were no dead fetuses or late resorptions, and no dams had whole litter resorptions. All placentae appeared normal.

Totals of 121, 96, 119, 101 and 118 live fetuses in the 0 (Vehicle), 100, 300, 1000 and 2000 mg/kg/day dosage groups, respectively, were examined externally for developmental alterations. No fetal gross alterations were identified.

IV. Conclusion

Based on these data dosages of 0 (Vehicle), 100, 300 and 1000 mg/kg/day of PFBS are recommended for the developmental toxicity study in rats. The 100 mg/kg/day dosage is expected to be a no-observable-adverse-effect-level (NOAEL) for both maternal and embryo-fetal toxicity, and the 1000 mg/kg/day dosage is expected to produce minimal maternal toxicity and little or no developmental toxicity.

for John F. Barnett 15 Oct 03

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

Raymond G. York 15 OCT 2003

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

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(SPONSOR'S STUDY NUMBER: T-7485.11)

MATERNAL BODY WEIGHTS
Figure 1

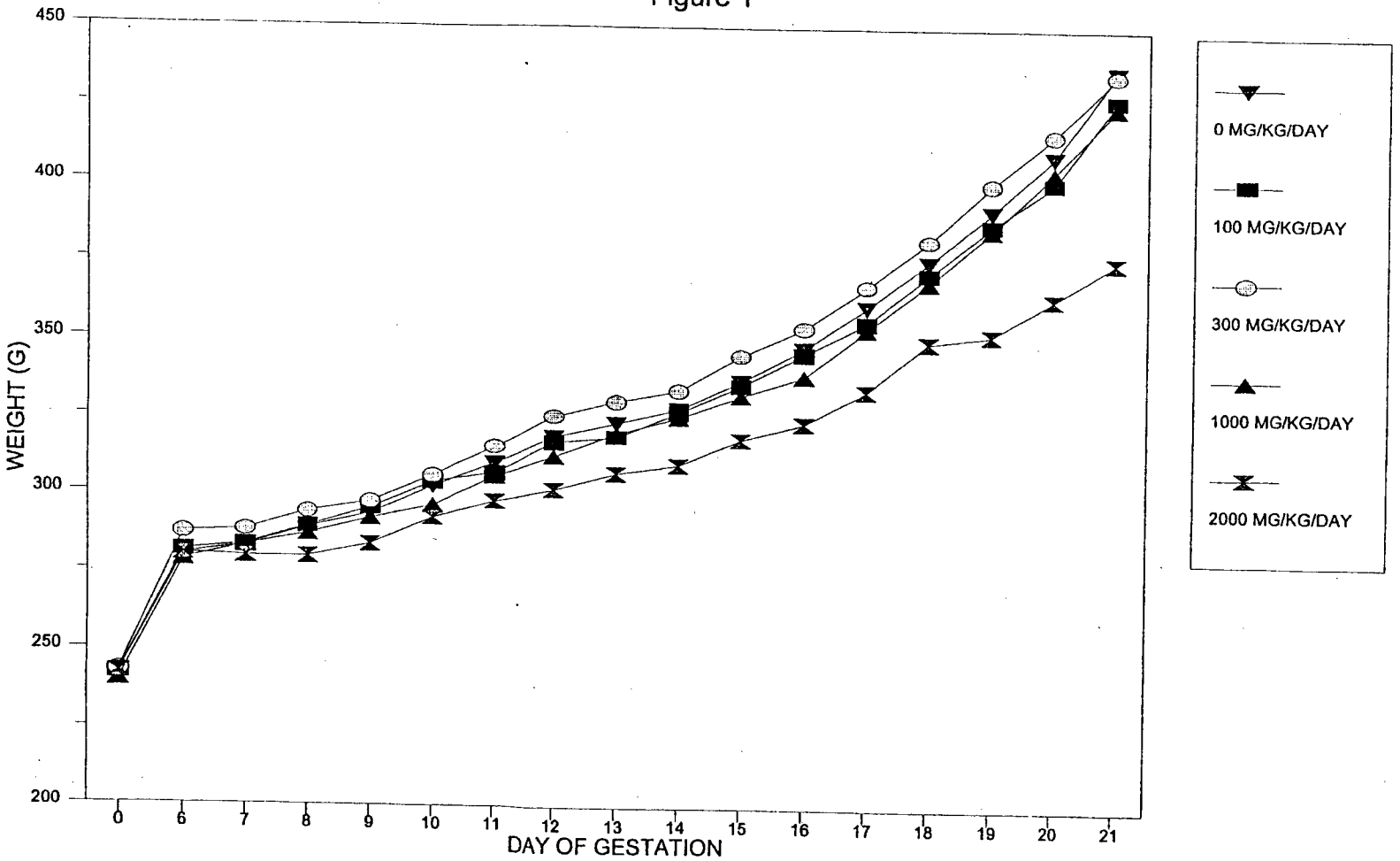

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TABLE 1 (PAGE 1): CLINICAL OBSERVATIONS AND NECROPSY - SUMMARY

GROUP DOSAGE (MG/KG/DAY)a	I 0	II 100	III 300	IV 1000	V 2000
MAXIMUM POSSIBLE INCIDENCE	128/ 8	128/ 8	128/ 8	128/ 8	128/ 8
MORTALITY	0	0	0	0	0
URINE-STAINED ABDOMINAL FUR	0/ 0	0/ 0	0/ 0	0/ 0	7/ 4
GASPING	0/ 0	0/ 0	0/ 0	0/ 0	2/ 1
RED PERINASAL SUBSTANCE	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
RED PERIORAL SUBSTANCE	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
EXCESS SALIVATION	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
LOCALIZED ALOPECIA: LIMBS	0/ 0	0/ 0	14/ 1	0/ 0	0/ 0

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

MAXIMUM POSSIBLE INCIDENCE = (DAYS x RATS)/NUMBER OF RATS EXAMINED PER GROUP ON DAYS 6 THROUGH 21 OF PRESUMED GESTATION.
N/N = TOTAL NUMBER OF OBSERVATIONS/NUMBER OF RATS WITH OBSERVATION.
a. Dosage occurred on days 6 through 20 of presumed gestation.

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

GROUP			I	II	III	IV	V
DOSAGE (MG/KG/DAY)a			0	100	300	1000	2000
RATS TESTED		N	8	8	8	8	8
PREGNANT		N	8	7	8	7	8
MATERNAL BODY WEIGHT (G)							
DAY 0		MEAN±S.D.	242.6 ± 8.5	242.4 ± 7.2	243.2 ± 8.0	240.1 ± 7.8	242.5 ± 7.5
DAY 6		MEAN±S.D.	279.9 ± 7.8	281.3 ± 5.1	287.1 ± 8.9	278.3 ± 7.6	280.0 ± 13.8
DAY 7		MEAN±S.D.	282.8 ± 7.6	283.1 ± 8.2	287.9 ± 8.1	282.8 ± 10.0	279.4 ± 18.0
DAY 8		MEAN±S.D.	288.8 ± 7.2	289.0 ± 4.7	293.9 ± 7.4	286.6 ± 9.5	279.4 ± 19.7 [7]b
DAY 9		MEAN±S.D.	293.2 ± 8.9	295.0 ± 6.8	297.2 ± 9.5	291.8 ± 9.4	283.4 ± 18.4 [7]b
DAY 10		MEAN±S.D.	302.2 ± 6.9	303.7 ± 8.4 [6]c	305.8 ± 8.1	296.1 ± 11.2	292.1 ± 18.2 [7]b
DAY 11		MEAN±S.D.	309.9 ± 6.6	306.7 ± 6.1	315.2 ± 7.7	305.6 ± 9.7	297.6 ± 13.9 [7]b
DAY 12		MEAN±S.D.	318.5 ± 8.6	316.7 ± 9.6	325.1 ± 10.4	312.1 ± 13.3	301.4 ± 23.0 [7]b
DAY 13		MEAN±S.D.	323.1 ± 9.5	318.6 ± 7.8	330.1 ± 9.3	319.8 ± 15.6	306.8 ± 21.9 [7]b
DAY 14		MEAN±S.D.	327.9 ± 9.6	326.8 ± 10.7	334.0 ± 9.4	325.0 ± 13.2	309.8 ± 21.3 [7]b
DAY 15		MEAN±S.D.	337.1 ± 11.3	335.6 ± 10.3	345.2 ± 9.4	332.3 ± 15.1	318.3 ± 21.5 [7]b
DAY 16		MEAN±S.D.	347.8 ± 10.9	346.0 ± 10.5	354.1 ± 11.8	338.7 ± 19.4	323.6 ± 23.7 [7]b
DAY 17		MEAN±S.D.	360.9 ± 11.7	356.0 ± 10.0	367.5 ± 11.0	353.7 ± 19.8	334.1 ± 22.9 [7]b
DAY 18		MEAN±S.D.	375.5 ± 11.9	371.4 ± 10.1	382.2 ± 11.2	368.8 ± 19.0	349.7 ± 21.5 [7]b
DAY 19		MEAN±S.D.	391.8 ± 9.9	387.3 ± 13.6	400.4 ± 15.4	385.8 ± 21.3	352.3 ± 27.2 [7]b

DAY = DAY OF GESTATION
[ ] = NUMBER OF VALUES AVERAGED
a. Dosage occurred on days 6 through 20 of gestation.
b. Excludes values for dam 13987 due to apparent injury.
c. Excludes a value that appeared incorrectly recorded.

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TABLE 2 (PAGE 2): MATERNAL BODY WEIGHTS AND GRAVID UTERINE WEIGHTS - SUMMARY

GROUP DOSAGE (MG/KG/DAY)a		I 0	II 100	III 300	IV 1000	V 2000
RATS TESTED	N	8	8	8	8	8
PREGNANT	N	8	7	8	7	8
MATERNAL BODY WEIGHT (G)						
DAY 20	MEAN±S.D.	409.4 ± 12.2	400.8 ± 15.2	416.4 ± 13.5	404.4 ± 22.7	363.8 ± 26.4 [7]b
DAY 21	MEAN±S.D.	436.9 ± 14.3	427.6 ± 18.5	435.6 ± 15.1	425.4 ± 19.2	375.6 ± 27.1 [7]b
GRAVID UTERINE WEIGHTS	MEAN±S.D.	111.2 ± 9.6	100.9 ± 7.3	107.9 ± 10.1	101.0 ± 14.8	94.1 ± 10.7
DAY 21C c	MEAN±S.D.	325.6 ± 13.7	326.6 ± 17.5	327.7 ± 15.1	324.4 ± 14.8	287.3 ± 26.1

DAY = DAY OF GESTATION
a. Dosage occurred on days 6 through 20 of gestation.
b. Excludes values for dam 13987 due to apparent injury.
c. 21C = Corrected maternal body weight (day 21 of gestation body weight minus the gravid uterine weight).

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

GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)a		0	100	300	1000	2000
RATS TESTED	N	8	8	8	8	8
PREGNANT	N	8	7	8	7	8
MATERNAL BODY WEIGHT CHANGE (G)						
DAYS 0 - 6	MEAN±S.D.	+37.2 ± 5.2	+38.8 ± 6.7	+43.9 ± 8.0	+38.1 ± 9.0	+37.5 ± 9.7
DAYS 6 - 9	MEAN±S.D.	+13.4 ± 2.6	+13.7 ± 3.9	+10.1 ± 10.1	+13.6 ± 7.1	+5.6 ± 10.9 [7]b
DAYS 9 - 12	MEAN±S.D.	+25.2 ± 3.6	+21.7 ± 5.1	+27.9 ± 11.9	+20.3 ± 4.7	+18.0 ± 12.4 [7]b
DAYS 12 - 15	MEAN±S.D.	+18.6 ± 3.8	+18.8 ± 5.1	+20.1 ± 5.0	+20.1 ± 7.4	+16.8 ± 6.3 [7]b
DAYS 15 - 18	MEAN±S.D.	+38.4 ± 3.6	+35.8 ± 5.3	+37.0 ± 5.5	+36.6 ± 5.9	+31.4 ± 5.7 [7]b
DAYS 18 - 21	MEAN±S.D.	+61.4 ± 6.9	+56.1 ± 9.8	+53.4 ± 13.2	+56.6 ± 3.2	+25.8 ± 25.6 [7]b
DAYS 6 - 21	MEAN±S.D.	+157.0± 10.8	+146.3± 15.9	+148.5± 14.6	+147.1± 14.5	+97.7 ± 24.5 [7]b
DAYS 0 - 21	MEAN±S.D.	+194.2± 14.2	+185.1± 17.8	+192.4± 18.1	+185.3± 20.2	+134.1± 23.1 [7]b
DAYS 6 - 21C c	MEAN±S.D.	+45.8 ± 9.2	+45.3 ± 15.7	+40.6 ± 16.0	+46.1 ± 13.2	+7.3 ± 19.8
DAYS 0 - 21C c	MEAN±S.D.	+83.0 ± 13.6	+84.2 ± 16.6	+84.5 ± 17.6	+84.3 ± 14.0	+44.8 ± 21.2

DAYS = DAYS OF GESTATION
a. Dosage occurred on days 6 through 20 of gestation.
b. Excludes values for dam 13987 due to apparent injury.
c. 21C = Corrected maternal body weight (day 21 of gestation body weight minus the gravid uterine weight).

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

GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)a		0	100	300	1000	2000
RATS TESTED	N	8	8	8	8	8
PREGNANT	N	8	7	8	7	8
MATERNAL FEED CONSUMPTION (G/DAY)						
DAYS 0 - 6	MEAN±S.D.	23.1 ± 0.8	22.8 ± 1.1	23.4 ± 1.9	22.5 ± 1.0	20.9 ± 2.9 [7]b
DAYS 6 - 9	MEAN±S.D.	24.5 ± 1.0	23.6 ± 2.2	24.6 ± 1.7	23.6 ± 2.7	22.2 ± 6.0 [7]c
DAYS 9 - 12	MEAN±S.D.	26.7 ± 1.1	24.9 ± 2.9	26.9 ± 1.6	25.0 ± 2.1	23.0 ± 2.6 [7]c
DAYS 12 - 15	MEAN±S.D.	26.0 ± 1.0	26.4 ± 2.3	26.2 ± 1.7	24.9 ± 1.4	21.4 ± 2.5 [7]c
DAYS 15 - 18	MEAN±S.D.	28.8 ± 2.2	26.6 ± 1.2	27.1 ± 2.0	26.2 ± 2.3	23.1 ± 2.5 [7]c
DAYS 18 - 21	MEAN±S.D.	26.4 ± 1.8	25.7 ± 2.5	25.8 ± 3.3	25.9 ± 2.9	17.8 ± 5.5 [7]c
DAYS 6 - 21	MEAN±S.D.	26.5 ± 0.9	25.5 ± 2.0	26.1 ± 1.3	25.1 ± 1.7	21.5 ± 2.1 [7]c
DAYS 0 - 21	MEAN±S.D.	25.5 ± 0.6	24.7 ± 1.7	25.4 ± 1.3	24.4 ± 1.2	21.3 ± 2.0 [7]c

DAYS = DAYS OF GESTATION
[ ] = NUMBER OF VALUES AVERAGED
a. Dosage occurred on days 6 through 20 of gestation.
b. Excludes a value that was associated with spillage.
c. Excludes values for dam 13987 due to apparent injury.

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

GROUP		I	II	III	IV	V
DOSAGE (MG/KG/DAY)a		0	100	300	1000	2000
RATS TESTED	N	8	8	8	8	8
PREGNANT	N	8	7	8	7	8
MATERNAL FEED CONSUMPTION (G/KG/DAY)						
DAYS 0 - 6	MEAN±S.D.	88.4 ± 3.9	87.0 ± 4.0	88.4 ± 6.7	86.7 ± 2.9	80.6 ± 12.0 [7]b
DAYS 6 - 9	MEAN±S.D.	85.7 ± 4.0	82.3 ± 6.3	84.4 ± 6.9	82.7 ± 8.6	79.0 ± 20.1 [7]c
DAYS 9 - 12	MEAN±S.D.	87.2 ± 4.0	81.4 ± 8.1	86.5 ± 4.8	82.8 ± 4.7	78.2 ± 6.9 [7]c
DAYS 12 - 15	MEAN±S.D.	79.6 ± 2.0	81.5 ± 5.7	78.4 ± 5.0	77.4 ± 1.6	69.2 ± 5.3 [7]c
DAYS 15 - 18	MEAN±S.D.	81.2 ± 6.7	75.6 ± 2.6	74.8 ± 5.1	75.0 ± 3.8	69.7 ± 5.9 [7]c
DAYS 18 - 21	MEAN±S.D.	65.5 ± 3.4	64.7 ± 5.0	63.3 ± 8.2	65.3 ± 7.3	49.2 ± 14.2 [7]c
DAYS 6 - 21	MEAN±S.D.	78.7 ± 2.5	76.2 ± 4.6	76.3 ± 4.2	75.7 ± 3.6	68.1 ± 4.4 [7]c
DAYS 0 - 21	MEAN±S.D.	77.1 ± 2.2	75.2 ± 4.1	75.4 ± 4.2	74.7 ± 2.1	68.6 ± 5.2 [7]c

DAYS = DAYS OF GESTATION
[ ] = NUMBER OF VALUES AVERAGED
a. Dosage occurred on days 6 through 20 of gestation.
b. Excludes a value that was associated with spillage.
c. Excludes values for dam 13987 due to apparent injury.

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

GROUP DOSAGE (MG/KG/DAY)a		I 0	II 100	III 300	IV 1000	V 2000
RATS TESTED	N	8	8	8	8	8
PREGNANT	N(%)	8(100.0)	7(87.5)	8(100.0)	7(87.5)	8(100.0)
RATS PREGNANT AND CAESAREAN-SECTIONED ON DAY 21 OF GESTATION	N	8	7	8	7	8
CORPORA LUTEA	MEAN±S.D.	19.5 ± 2.5	18.6 ± 4.4	19.6 ± 2.3	19.1 ± 4.4	17.6 ± 1.5
IMPLANTATIONS	MEAN±S.D.	15.5 ± 1.7	13.7 ± 1.1	15.4 ± 1.6	14.6 ± 2.6	14.9 ± 0.8
LITTER SIZES	MEAN±S.D.	15.1 ± 1.4	13.7 ± 1.1	14.9 ± 1.6	14.4 ± 2.5	14.8 ± 0.9
LIVE FETUSES	N	121	96	119	101	118
	MEAN±S.D.	15.1 ± 1.4	13.7 ± 1.1	14.9 ± 1.6	14.4 ± 2.5	14.8 ± 0.9
DEAD FETUSES	N	0	0	0	0	0
RESORPTIONS	MEAN±S.D.	0.4 ± 0.5	0.0 ± 0.0	0.5 ± 1.1	0.1 ± 0.4	0.1 ± 0.4
EARLY RESORPTIONS	N	3	0	4	1	1
	MEAN±S.D.	0.4 ± 0.5	0.0 ± 0.0	0.5 ± 1.1	0.1 ± 0.4	0.1 ± 0.4
LATE RESORPTIONS	N	0	0	0	0	0
DAMS WITH ANY RESORPTIONS	N(%)	3(37.5)	0(0.0)	2(25.0)	1(14.3)	1(12.5)
DAMS WITH ALL CONCEPTUSES RESORBED	N(%)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
DAMS WITH VIABLE FETUSES	N(%)	8(100.0)	7(100.0)	8(100.0)	7(100.0)	8(100.0)
PLACENTAE APPEARED NORMAL	N(%)	8(100.0)	7(100.0)	8(100.0)	7(100.0)	8(100.0)

a. Dosage occurred on days 6 through 20 of gestation.

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

GROUP DOSAGE (MG/KG/DAY)a		I 0	II 100	III 300	IV 1000	V 2000
LITTERS WITH ONE OR MORE LIVE FETUSES	N	8	7	8	7	8
IMPLANTATIONS	MEAN±S.D.	15.5 ± 1.7	13.7 ± 1.1	15.4 ± 1.6	14.6 ± 2.6	14.9 ± 0.8
LIVE FETUSES	N	121	96	119	101	118
	MEAN±S.D.	15.1 ± 1.4	13.7 ± 1.1	14.9 ± 1.6	14.4 ± 2.5	14.8 ± 0.9
LIVE MALE FETUSES	N	47	47	52	58	59
% LIVE MALE FETUSES/LITTER	MEAN±S.D.	39.2 ± 11.1	48.7 ± 7.2	44.2 ± 10.8	58.0 ± 15.6	50.7 ± 18.8
LIVE FETAL BODY WEIGHTS (GRAMS)/LITTER	MEAN±S.D.	5.30 ± 0.22	5.38 ± 0.40	5.25 ± 0.20	5.21 ± 0.36	4.64 ± 0.35
MALE FETUSES	MEAN±S.D.	5.43 ± 0.24	5.54 ± 0.41	5.40 ± 0.22	5.30 ± 0.38	4.77 ± 0.40
FEMALE FETUSES	MEAN±S.D.	5.22 ± 0.21	5.22 ± 0.43	5.14 ± 0.22	5.12 ± 0.38	4.54 ± 0.34
% RESORBED CONCEPTUSES/LITTER	MEAN±S.D.	2.2 ± 3.1	0.0 ± 0.0	3.1 ± 6.7	0.9 ± 2.3	0.8 ± 2.4

NO FETAL ALTERATIONS WERE IDENTIFIED AT GROSS EXTERNAL EXAMINATION

a. Dosage occurred on days 6 through 20 of gestation.

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TABLE 8 (PAGE 1): CLINICAL OBSERVATIONS - INDIVIDUAL DATA

RAT #		DESCRIPTION
GROUP I		0 MG/KG/DAY
13951		NO ADVERSE FINDINGS
13952		NO ADVERSE FINDINGS
13953		NO ADVERSE FINDINGS
13954		NO ADVERSE FINDINGS
13955		NO ADVERSE FINDINGS
13956		NO ADVERSE FINDINGS
13957		NO ADVERSE FINDINGS
13958		NO ADVERSE FINDINGS
GROUP II		100 MG/KG/DAY
13959		NO ADVERSE FINDINGS
13960		NO ADVERSE FINDINGS
13961		NO ADVERSE FINDINGS
13962		NO ADVERSE FINDINGS
13963		NO ADVERSE FINDINGS
13964		NO ADVERSE FINDINGS
13965		NO ADVERSE FINDINGS
13966		NO ADVERSE FINDINGS
GROUP III		300 MG/KG/DAY
13967		NO ADVERSE FINDINGS
13968		NO ADVERSE FINDINGS
13969	DG(8- 21)	LOCALIZED ALOPECIA: LIMBS a
13971		NO ADVERSE FINDINGS
13972		NO ADVERSE FINDINGS
13973		NO ADVERSE FINDINGS
13974		NO ADVERSE FINDINGS

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

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(SPONSOR'S STUDY NUMBER: T-7485.11)

TABLE 8 (PAGE 2): CLINICAL OBSERVATIONS - INDIVIDUAL DATA

RAT #		DESCRIPTION
GROUP IV		1000 MG/KG/DAY
13975		NO ADVERSE FINDINGS
13977		NO ADVERSE FINDINGS
13978		NO ADVERSE FINDINGS
13979		NO ADVERSE FINDINGS
13980		NO ADVERSE FINDINGS
13981		NO ADVERSE FINDINGS
13982		NO ADVERSE FINDINGS
GROUP V		2000 MG/KG/DAY
13983	DG(20- 21)	URINE-STAINED ABDOMINAL FUR
13984	DG(9)	EXCESS SALIVATION
	DG(13)	URINE-STAINED ABDOMINAL FUR
13985		NO ADVERSE FINDINGS
13986		NO ADVERSE FINDINGS
13987	DG(8)	RED PERINASAL SUBSTANCE
	DG(8)	RED PERIORAL SUBSTANCE
	DG(8- 9)	GASPING
	DG(9- 11)	URINE-STAINED ABDOMINAL FUR
13988	DG(21)	URINE-STAINED ABDOMINAL FUR
13989		NO ADVERSE FINDINGS
13990		NO ADVERSE FINDINGS

DG = DAY OF PRESUMED GESTATION

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

GROUP DOSAGE (MG/KG/DAY)	RAT NUMBER	DAY OF NECROPSY	PREGNANCY STATUS	DOSAGES ADMINISTERED	OBSERVATIONS a
I					
0	13951	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13952	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13953	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13954	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13955	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13956	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13957	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13958	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
II					
100	13959	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13960	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13961	DG 21	NP	15	ALL TISSUES APPEARED NORMAL.
	13962	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13963	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13964	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13965	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13966	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
III					
300	13967	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13968	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13969	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13970	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13971	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13972	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13973	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13974	DG 21	P	15	ALL TISSUES APPEARED NORMAL.

DG = DAY OF PRESUMED GESTATION
P = PREGNANT NP = NOT PREGNANT
a. Refer to the individual clinical observations table (Table 8) for external observations confirmed at necropsy.

PROTOCOL 418-023P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF POTASSIUM PERFLUOROBUTANE SULFONATE (PFBS) IN RATS
(SPONSOR'S STUDY NUMBER: T-7485.11)

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

GROUP DOSAGE (MG/KG/DAY)	RAT NUMBER	DAY OF NECROPSY	PREGNANCY STATUS	DOSAGES ADMINISTERED	OBSERVATIONS a
IV					
1000	13975	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13976	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13977	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13978	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13979	DG 21	NP	15	ALL TISSUES APPEARED NORMAL.
	13980	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13981	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13982	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
V					
2000	13983	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13984	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13985	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13986	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13987	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13988	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13989	DG 21	P	15	ALL TISSUES APPEARED NORMAL.
	13990	DG 21	P	15	ALL TISSUES APPEARED NORMAL.

DG = DAY OF PRESUMED GESTATION
P = PREGNANT NP = NOT PREGNANT
a. Refer to the individual clinical observations table (Table 8) for external observations confirmed at necropsy.

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TABLE 10 (PAGE 1): MATERNAL BODY WEIGHTS AND GRAVID UTERINE WEIGHTS - INDIVIDUAL DATA

RAT #		GROUP I				0 MG/KG/DAY							
	PREGNANCY STATUS	DAY 0	6	7	8	9	10	11	12	13	14	15	16	17
13951	P	227.	272.	282.	283.	288.	302.	311.	317.	323.	327.	338.	348.	367.
13952	P	240.	278.	289.	290.	290.	300.	307.	313.	322.	318.	327.	336.	347.
13953	P	249.	288.	281.	292.	299.	310.	313.	330.	338.	342.	356.	362.	381.
13954	P	236.	267.	269.	275.	278.	289.	297.	305.	307.	314.	321.	331.	347.
13955	P	249.	290.	294.	298.	308.	310.	320.	331.	333.	339.	349.	361.	371.
13956	P	244.	278.	277.	288.	290.	298.	308.	316.	322.	328.	335.	348.	358.
13957	P	242.	282.	284.	289.	297.	304.	310.	317.	316.	324.	332.	344.	358.
13958	P	254.	284.	286.	295.	296.	305.	313.	319.	324.	331.	339.	352.	358.

	DAY 18	19	20	21	GRAVID UTERINE WEIGHTS
13951 P	377.	390.	406.	432.	111.2
13952 P	359.	377.	388.	423.	90.2
13953 P	394.	409.	427.	460.	115.3
13954 P	361.	385.	403.	426.	122.5
13955 P	388.	400.	422.	453.	115.8
13956 P	375.	396.	415.	434.	115.8
13957 P	376.	386.	410.	445.	111.4
13958 P	374.	391.	404.	422.	107.6

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

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TABLE 10 (PAGE 2): MATERNAL BODY WEIGHTS AND GRAVID UTERINE WEIGHTS - INDIVIDUAL DATA

RAT #		GROUP II				100 MG/KG/DAY							
	PREGNANCY STATUS	DAY 0	6	7	8	9	10	11	12	13	14	15	16	17
13959	P	252.	291.	294.	295.	306.	316.	310.	332.	326.	345.	347.	358.	371.
13960	P	245.	280.	281.	286.	290.	296.	305.	311.	317.	326.	330.	341.	352.
13961	NP	243.	297.	302.	304.	306.	311.	304.	315.	304.	303.	308.	302.	300.
13962	P	237.	285.	289.	291.	296.	307.	308.	316.	323.	324.	334.	344.	364.
13963	P	243.	281.	288.	294.	302.	309.	314.	322.	328.	336.	350.	357.	360.
13964	P	231.	277.	269.	282.	287.	272.a	297.	304.	306.	313.	327.	337.	347.
13965	P	240.	278.	283.	289.	292.	300.	312.	323.	318.	326.	339.	354.	356.
13966	P	249.	277.	278.	286.	292.	294.	301.	309.	312.	318.	322.	331.	342.

	DAY 18	19	20	21	GRAVID UTERINE WEIGHTS
13959 P	390.	411.	420.	460.	103.1
13960 P	363.	368.	374.	403.	90.5
13961 NP	308.	311.	309.	307.	-----
13962 P	370.	384.	405.	418.	112.7
13963 P	376.	392.	412.	438.	100.7
13964 P	366.	389.	395.	425.	94.3
13965 P	375.	391.	408.	434.	105.4
13966 P	360.	376.	392.	415.	99.9

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

PROTOCOL 418-023P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF POTASSIUM PERFLUOROBUTANE SULFONATE (PFBS) IN RATS
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TABLE 10 (PAGE 3): MATERNAL BODY WEIGHTS AND GRAVID UTERINE WEIGHTS - INDIVIDUAL DATA

RAT #	GROUP III				300 MG/KG/DAY								
PREGNANCY STATUS	DAY 0	6	7	8	9	10	11	12	13	14	15	16	17
13967 P	239.	286.	283.	288.	299.	301.	316.	325.	330.	342.	347.	361.	375.
13968 P	230.	275.	280.	286.	294.	296.	305.	311.	319.	327.	336.	345.	362.
13969 P	237.	287.	292.	303.	280.	306.	319.	334.	336.	336.	349.	368.	371.
13970 P	247.	289.	288.	295.	300.	307.	317.	325.	332.	335.	347.	353.	369.
13971 P	245.	300.	294.	295.	297.	311.	320.	330.	337.	342.	357.	361.	375.
13972 P	251.	279.	279.	287.	301.	304.	311.	328.	329.	330.	348.	356.	368.
13973 P	242.	282.	284.	291.	293.	299.	306.	309.	315.	316.	327.	330.	343.
13974 P	255.	299.	303.	306.	314.	322.	328.	339.	343.	344.	351.	359.	377.

	DAY 18	19	20	21	GRAVID UTERINE WEIGHTS
13967 P	388.	412.	431.	449.	120.3
13968 P	369.	380.	401.	420.	113.0
13969 P	394.	414.	420.	447.	107.1
13970 P	374.	389.	406.	436.	97.5
13971 P	391.	412.	426.	459.	115.7
13972 P	387.	408.	422.	432.	108.6
13973 P	365.	378.	396.	426.	89.3
13974 P	390.	410.	429.	416.	111.8

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

PROTOCOL 418-023P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF POTASSIUM PERFLUOROBUTANE SULFONATE (PFBS) IN RATS
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TABLE 10 (PAGE 4): MATERNAL BODY WEIGHTS AND GRAVID UTERINE WEIGHTS - INDIVIDUAL DATA

RAT #		GROUP IV				1000 MG/KG/DAY							
	STATUS	DAY 0	6	7	8	9	10	11	12	13	14	15	16	17
13975	P	227.	276.	285.	285.	293.	296.	306.	314.	330.	330.	342.	346.	365.
13976	P	239.	288.	272.	282.	288.	294.	312.	308.	323.	330.	339.	350.	362.
13977	P	248.	288.	302.	305.	309.	318.	319.	337.	340.	341.	350.	360.	374.
13978	P	234.	274.	276.	280.	287.	291.	301.	311.	312.	326.	330.	341.	355.
13979	NP	258.	299.	304.	307.	308.	315.	325.	328.	294.	290.	295.	301.	299.
13980	P	249.	279.	287.	293.	299.	302.	313.	318.	332.	334.	341.	351.	368.
13981	P	241.	267.	276.	277.	281.	284.	294.	296.	297.	304.	309.	311.	326.
13982	P	243.	276.	282.	284.	286.	288.	294.	301.	305.	310.	315.	312.	326.

	DAY 18	19	20	21	GRAVID UTERINE WEIGHTS
13975 P	374.	392.	411.	430.	107.4
13976 P	380.	401.	417.	435.	105.0
13977 P	388.	407.	430.	450.	105.7
13978 P	374.	396.	415.	431.	118.4
13979 NP	297.	297.	304.	316.	-----
13980 P	382.	394.	413.	434.	101.0
13981 P	341.	356.	374.	400.	70.5
13982 P	343.	355.	371.	398.	99.0

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

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TABLE 10 (PAGE 5): MATERNAL BODY WEIGHTS AND GRAVID UTERINE WEIGHTS - INDIVIDUAL DATA

RAT #	GROUP V				2000 MG/KG/DAY								
PREGNANCY STATUS	DAY 0	6	7	8	9	10	11	12	13	14	15	16	17
13983 P	240.	268.	243.	242.	251.	263.	280.	284.	294.	293.	299.	309.	318.
13984 P	241.	286.	284.	291.	297.	302.	302.	317.	324.	332.	336.	340.	360.
13985 P	244.	271.	279.	281.	285.	295.	296.	302.	311.	314.	325.	325.	338.
13986 P	254.	293.	286.	292.	293.	302.	309.	315.	321.	323.	337.	352.	352.
13987 P	250.	295.	300.	282.a	247.a	245.a	260.a	282.a	298.a	299.a	310.a	326.a	342.a
13988 P	245.	294.	297.	302.	305.	318.	318.	330.	323.	332.	338.	345.	355.
13989 P	231.	274.	278.	280.	285.	289.	297.	301.	312.	299.	310.	307.	314.
13990 P	235.	259.	268.	268.	268.	276.	281.	261.	263.	276.	283.	287.	302.

	DAY 18	19	20	21	GRAVID UTERINE WEIGHTS
13983 P	338.	316.	323.	342.	81.8
13984 P	374.	356.	371.	392.	105.0
13985 P	352.	375.	386.	382.	112.5
13986 P	367.	379.	400.	424.	95.2
13987 P	358.a	380.a	402.a	422.a	95.5
13988 P	368.	381.	373.	356.	82.5
13989 P	333.	329.	345.	360.	86.9
13990 P	316.	330.	349.	373.	93.5

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Value was excluded from group averages and statistical analyses due to apparent injury.

PROTOCOL 418-023P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF POTASSIUM PERFLUOROBUTANE SULFONATE (PFBS) IN RATS
(SPONSOR'S STUDY NUMBER: T-7485.11)

TABLE 11 (PAGE 1): MATERNAL FEED CONSUMPTION VALUES - INDIVIDUAL DATA

PREGNANCY STATUS	DAYS 0 - 6	6 - 9	9 - 12	12 - 15	15 - 18	18 - 21
RAT #	GROUP I			0 MG/KG/DAY		
13951 P	130.	73.	85.	77.	88.	77.
13952 P	141.	77.	82.	75.	79.	81.
13953 P	137.	74.	81.	84.	90.	89.
13954 P	142.	74.	78.	78.	96.	76.
13955 P	140.	78.	82.	81.	87.	83.
13956 P	141.	73.	81.	76.	82.	78.
13957 P	144.	71.	77.	76.	77.	79.
13958 P	133.	68.	74.	77.	93.	71.
RAT #	GROUP II			100 MG/KG/DAY		
13959 P	134.	76.	79.	79.	80.	79.
13960 P	135.	67.	73.	75.	76.	63.
13961 NP	150.	75.	73.	57.	55.	a
13962 P	141.	75.	78.	79.	79.	77.
13963 P	147.	79.	86.	94.	87.	88.
13964 P	126.	59.	58.	73.	78.	77.
13965 P	137.	72.	77.	81.	82.	80.
13966 P	138.	69.	72.	75.	78.	76.
RAT #	GROUP III			300 MG/KG/DAY		
13967 P	140.	76.	80.	80.	80.	77.
13968 P	137.	80.	76.	78.	75.	72.
13969 P	140.	65.	89.	76.	91.	79.
13970 P	136.	73.	76.	76.	73.	74.
13971 P	157.	72.	86.	90.	87.	92.
13972 P	118.	70.	77.	74.	81.	77.
13973 P	149.	81.	78.	78.	83.	89.
13974 P	148.	73.	83.	76.	80.	60.

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

PROTOCOL 418-023P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF POTASSIUM PERFLUOROBUTANE SULFONATE (PFBS) IN RATS
(SPONSOR'S STUDY NUMBER: T-7485.11)

TABLE 11 (PAGE 2): MATERNAL FEED CONSUMPTION VALUES - INDIVIDUAL DATA

PREGNANCY STATUS	DAYS 0 - 6	6 - 9	9 - 12	12 - 15	15 - 18	18 - 21
RAT #	GROUP IV			1000 MG/KG/DAY		
13975 P	132.	75.	75.	75.	77.	68.
13976 P	139.	57.	71.	76.	80.	80.
13977 P	138.	81.	86.	80.	86.	90.
13978 P	132.	64.	78.	75.	81.	76.
13979 NP	159.	79.	84.	28.	57.	52.
13980 P	141.	71.	78.	79.	85.	77.
13981 P	123.	76.	70.	70.	74.	86.
13982 P	139.	71.	67.	69.	66.	66.
RAT #	GROUP V			2000 MG/KG/DAY		
13983 P	118.	30.	70.	63.	71.	32.
13984 P	140.	73.	77.	73.	78.	45.
13985 P	132.	72.	68.	66.	61.	59.
13986 P	136.	66.	73.	73.	79.	78.
13987 P	a	37.b	40.b	73.b	82.b	82.b
13988 P	89.	71.	75.	65.	71.	39.
13989 P	134.	90.	67.	55.	60.	51.
13990 P	129.	65.	53.	55.	65.	70.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAYS = DAYS OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Spilled feed precluded the calculation of this value.
b. Value was excluded from group averages and statistical analyses due to apparent injury.

PROTOCOL 418-023P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF POTASSIUM PERFLUOROBUTANE SULFONATE (PFBS) IN RATS
(SPONSOR'S STUDY NUMBER: T-7485.11)

TABLE 12 (PAGE 1): CAESAREAN-SECTIONING OBSERVATIONS - INDIVIDUAL DATA

			VIABLE FETUSES			DEAD FETUSES			EARLY RESORPTIONS			LATE RESORPTIONS			IMPLANTATION SITES			CORPORA LUTEA		
	SEX		RIGHT	LEFT		RIGHT	LEFT		RIGHT	LEFT		RIGHT	LEFT		RIGHT	LEFT		RIGHT	LEFT	
RAT #	M	F	HORN		TOTAL	HORN		TOTAL	HORN		TOTAL	HORN		TOTAL	HORN		TOTAL	OVARY		TOTAL
GROUP I						0 MG/KG/DAY														
13951	4	11	7	8	15	0	0	0	0	0	0	0	0	0	7	8	15	10	8	18
13952	6	6	6	6	12	0	0	0	0	0	0	0	0	0	6	6	12	7	10	17
13953	3	13	5	11	16	0	0	0	0	0	0	0	0	0	5	11	16	6	16	22
13954	8	9	6	11	17	0	0	0	0	1	1	0	0	0	6	12	18	6	15	21
13955	7	8	8	7	15	0	0	0	0	1	1	0	0	0	8	8	16	8	10	18
13956	6	10	6	10	16	0	0	0	0	0	0	0	0	0	6	10	16	10	12	22
13957	7	8	8	7	15	0	0	0	0	0	0	0	0	0	8	7	15	8	8	16
13958	6	9	6	9	15	0	0	0	0	1	1	0	0	0	6	10	16	10	12	22
GROUP II						100 MG/KG/DAY														
13959	7	7	9	5	14	0	0	0	0	0	0	0	0	0	9	5	14	18	8	26
13960	7	6	4	9	13	0	0	0	0	0	0	0	0	0	4	9	13	6	10	16
13961	NOT PREGNANT																			
13962	7	7	8	6	14	0	0	0	0	0	0	0	0	0	8	6	14	10	8	18
13963	5	8	4	9	13	0	0	0	0	0	0	0	0	0	4	9	13	6	12	18
13964	5	7	4	8	12	0	0	0	0	0	0	0	0	0	4	8	12	4	8	12
13965	7	8	6	9	15	0	0	0	0	0	0	0	0	0	6	9	15	6	12	18
13966	9	6	6	9	15	0	0	0	0	0	0	0	0	0	6	9	15	9	13	22
GROUP III						300 MG/KG/DAY														
13967	5	12	7	10	17	0	0	0	0	0	0	0	0	0	7	10	17	7	15	22
13968	6	9	7	8	15	0	0	0	0	0	0	0	0	0	7	8	15	9	11	20
13969	9	6	8	7	15	0	0	0	0	0	0	0	0	0	8	7	15	9	12	21
13970	5	8	4	9	13	0	0	0	1	2	3	0	0	0	5	11	16	10	12	22
13971	6	10	7	9	16	0	0	0	1	0	1	0	0	0	8	9	17	8	9	17
13972	6	9	6	9	15	0	0	0	0	0	0	0	0	0	6	9	15	7	10	17
13973	7	5	3	9	12	0	0	0	0	0	0	0	0	0	3	9	12	5	12	17
13974	8	8	5	11	16	0	0	0	0	0	0	0	0	0	5	11	16	6	15	21

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

PROTOCOL 418-023P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF POTASSIUM PERFLUOROBUTANE SULFONATE (PFBS) IN RATS
(SPONSOR'S STUDY NUMBER: T-7485.11)

TABLE 12 (PAGE 2): CAESAREAN-SECTIONING OBSERVATIONS - INDIVIDUAL DATA

			VIABLE FETUSES			DEAD FETUSES			EARLY RESORPTIONS			LATE RESORPTIONS			IMPLANTATION SITES			CORPORA LUTEA		
	SEX		RIGHT	LEFT		RIGHT	LEFT		RIGHT	LEFT		RIGHT	LEFT		RIGHT	LEFT		RIGHT	LEFT	
RAT #	M	F	HORN		TOTAL	HORN		TOTAL	HORN		TOTAL	HORN		TOTAL	HORN		TOTAL	OVARY		TOTAL
GROUP IV						1000 MG/KG/DAY														
13975	9	7	9	7	16	0	0	0	0	0	0	0	0	0	9	7	16	12	11	23
13976	11	5	10	6	16	0	0	0	0	0	0	0	0	0	10	6	16	17	10	27
13977	10	5	5	10	15	0	0	0	0	0	0	0	0	0	5	10	15	5	11	16
13978	5	11	6	10	16	0	0	0	0	0	0	0	0	0	6	10	16	6	12	18
13979	NOT PREGNANT																			
13980	6	8	9	5	14	0	0	0	0	0	0	0	0	0	9	5	14	10	6	16
13981	6	3	2	7	9	0	0	0	0	0	0	0	0	0	2	7	9	6	9	15
13982	11	4	3	12	15	0	0	0	0	1	1	0	0	0	3	13	16	5	14	19
GROUP V						2000 MG/KG/DAY														
13983	9	5	7	7	14	0	0	0	0	0	0	0	0	0	7	7	14	8	9	17
13984	4	12	7	9	16	0	0	0	0	0	0	0	0	0	7	9	16	7	10	17
13985	5	11	6	10	16	0	0	0	0	0	0	0	0	0	6	10	16	6	11	17
13986	8	6	6	8	14	0	0	0	0	0	0	0	0	0	6	8	14	6	10	16
13987	10	5	8	7	15	0	0	0	0	0	0	0	0	0	8	7	15	10	11	21
13988	11	3	9	5	14	0	0	0	0	0	0	0	0	0	9	5	14	10	7	17
13989	6	9	7	8	15	0	0	0	0	0	0	0	0	0	7	8	15	9	9	18
13990	6	8	10	4	14	0	0	0	1	0	1	0	0	0	11	4	15	12	6	18

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

PROTOCOL 418-023P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF POTASSIUM PERFLUOROBUTANE SULFONATE (PFBS) IN RATS
(SPONSOR'S STUDY NUMBER: T-7485.11)

TABLE 13 (PAGE 1): LITTER OBSERVATIONS (CAESAREAN-DELIVERED FETUSES) - INDIVIDUAL DATA

	NUMBER OF LIVE FETUSES			AVERAGE FETAL BODY WEIGHT (G)			---- CONCEPTUSES ------ RESORBED		
RAT #	MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL a	N	N	%
GROUP I			0 MG/KG/DAY						
13951	4	11	15	5.52	5.29	5.35	15	0	0.0
13952	6	6	12	5.36	5.06	5.22	12	0	0.0
13953	3	13	16	5.29	5.07	5.11	16	0	0.0
13954	8	9	17	5.27	5.10	5.18	18	1	5.6
13955	7	8	15	5.86	5.66	5.75	16	1	6.2
13956	6	10	16	5.47	5.04	5.20	16	0	0.0
13957	7	8	15	5.60	5.37	5.48	15	0	0.0
13958	6	9	15	5.08	5.19	5.14	16	1	6.2
GROUP II			100 MG/KG/DAY						
13959	7	7	14	5.40	5.27	5.34	14	0	0.0
13960	7	6	13	5.25	4.96	5.12	13	0	0.0
13961	NOT PREGNANT								
13962	7	7	14	6.03	5.66	5.85	14	0	0.0
13963	5	8	13	5.93	5.52	5.68	13	0	0.0
13964	5	7	12	5.92	5.71	5.80	12	0	0.0
13965	7	8	15	5.22	4.84	5.02	15	0	0.0
13966	9	6	15	5.04	4.62	4.87	15	0	0.0
GROUP III			300 MG/KG/DAY						
13967	5	12	17	5.20	4.94	5.02	17	0	0.0
13968	6	9	15	5.62	5.36	5.46	15	0	0.0
13969	9	6	15	5.16	5.04	5.11	15	0	0.0
13970	5	8	13	5.59	5.34	5.43	16	3	18.8
13971	6	10	16	5.75	5.36	5.50	17	1	5.9
13972	6	9	15	5.26	5.10	5.17	15	0	0.0
13973	7	5	12	5.34	5.17	5.27	12	0	0.0
13974	8	8	16	5.24	4.77	5.01	16	0	0.0

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

PROTOCOL 418-023P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF POTASSIUM PERFLUOROBUTANE SULFONATE (PFBS) IN RATS
(SPONSOR'S STUDY NUMBER: T-7485.11)

TABLE 13 (PAGE 2): LITTER OBSERVATIONS (CAESAREAN-DELIVERED FETUSES) - INDIVIDUAL DATA

	NUMBER OF LIVE FETUSES			AVERAGE FETAL BODY WEIGHT (G)			---- CONCEPTUSES ------ RESORBED		
RAT #	MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL a	N	N	%
GROUP IV			1000 MG/KG/DAY						
13975	9	7	16	4.99	4.76	4.89	16	0	0.0
13976	11	5	16	4.81	4.57	4.74	16	0	0.0
13977	10	5	15	5.41	5.32	5.38	15	0	0.0
13978	5	11	16	5.59	5.20	5.32	16	0	0.0
13979	NOT PREGNANT								
13980	6	8	14	5.48	5.30	5.38	14	0	0.0
13981	6	3	9	5.82	5.70	5.78	9	0	0.0
13982	11	4	15	4.97	4.97	4.97	16	1	6.2
GROUP V			2000 MG/KG/DAY						
13983	9	5	14	4.37	4.19	4.30	14	0	0.0
13984	4	12	16	4.94	4.63	4.71	16	0	0.0
13985	5	11	16	5.46	5.20	5.28	16	0	0.0
13986	8	6	14	5.17	4.73	4.98	14	0	0.0
13987	10	5	15	4.46	4.43	4.45	15	0	0.0
13988	11	3	14	4.38	4.28	4.36	14	0	0.0
13989	6	9	15	4.53	4.20	4.33	15	0	0.0
13990	6	8	14	4.84	4.64	4.72	15	1	6.7

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

PROTOCOL 418-023P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF POTASSIUM PERFLUOROBUTANE SULFONATE (PFBS) IN RATS
(SPONSOR'S STUDY NUMBER: T-7485.11)

TABLE 14 (PAGE 1): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

GROUP I 0 MG/KG/DAY

RAT #	CLs	FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
13951	10/ 8		FA	FA	MA	MA	FA	FA	FA / MA		FA	FA	FA	FA	FA	MA	FA								
			5.37	5.19	5.69	5.63	5.31	5.46	5.43	5.24	5.38	4.91	5.42	4.75	5.60	5.51	5.34								
13952	7/10		MA	FA	MA	FA	MA	MA / FA		MA	MA	FA	FA	FA											
			5.12	4.66	5.42	5.11	5.25	5.66	5.04	5.24	5.50	5.38	5.05	5.15											
13953	6/16		FA	FA	FA	FA	FA / FA		MA	FA	FA	MA	FA	MA	FA	FA	FA	FA							
			4.99	4.86	4.97	5.46	4.96	5.22	5.09	5.07	5.03	5.33	4.96	5.44	4.89	5.01	5.35	5.14							
13954	6/15		FA	MA	FA	MA	MA	FA / E		FA	MA	MA	FA	FA	FA	FA	MA	MA	MA	FA					
			4.75	4.86	4.82	5.39	5.54	5.37		5.20	5.63	5.43	5.08	5.40	5.14	4.88	5.32	4.98	5.04	5.25					
13955	8/10		MA	FA	MA	FA	FA	FA	MA	FA / MA		FA	MA	E	FA	MA	FA	MA							
			5.81	5.65	5.93	5.55	5.75	5.66	6.19	5.46	5.67	5.65	5.80		5.82	5.75	5.72	5.86							
13956	10/12		FA	FA	FA	FA	FA	MA / MA		MA	FA	FA	FA	FA	MA	FA	MA	MA							
			5.07	5.14	4.98	5.01	5.09	5.48	5.20	5.44	5.03	5.20	5.32	4.58	5.27	5.03	5.47	5.97							
13957	8/ 8		FA	MA	MA	MA	MA	MA	FA	FA / MA		FA	MA	FA	FA	FA	FA								
			5.57	5.64	5.60	5.50	5.66	5.45	5.05	5.50	5.58	5.27	5.75	5.69	5.40	5.28	5.23								
13958	10/12		MA	FA	FA	MA	MA	MA / FA		FA	E	FA	MA	FA	FA	FA	MA	FA							
			4.44	5.38	5.49	5.16	5.32	5.36	4.76	5.04		5.50	5.15	5.04	4.97	5.11	5.02	5.40							

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

PROTOCOL 418-023P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF POTASSIUM PERFLUOROBUTANE SULFONATE (PFBS) IN RATS
(SPONSOR'S STUDY NUMBER: T-7485.11)

TABLE 14 (PAGE 2): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

GROUP II 100 MG/KG/DAY

RAT #	CLs	FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
13959	18/ 8		MA	MA	FA	MA	FA	FA	FA	FA	MA / MA		FA	FA	MA	MA									
			5.64	5.25	5.39	5.44	5.38	5.53	5.28	5.33	5.20	5.31	5.15	4.85	5.37	5.59									
13960	6/10		FA	FA	MA	MA / MA		MA	FA	MA	FA	MA	FA	MA	FA										
			4.89	5.10	5.44	5.74	5.09	4.80	4.84	5.24	5.00	5.25	4.80	5.22	5.11										
13961			NOT PREGNANT																						
13962	10/ 8		FA	FA	MA	FA	FA	MA	FA	MA / MA		MA	MA	MA	FA	FA									
			5.41	5.61	6.32	5.89	5.79	6.02	5.53	6.09	6.16	6.08	5.69	5.88	5.58	5.84									
13963	6/12		FA	MA	FA	MA / MA		FA	FA	FA	FA	MA	MA	FA	FA										
			5.47	5.90	5.62	6.18	6.03	5.17	5.34	5.46	5.58	6.08	5.47	5.75	5.81										
13964	4/ 8		FA	FA	MA	FA / MA		FA	FA	MA	MA	MA	FA	FA											
			5.76	5.65	6.13	5.75	5.65	5.62	5.78	6.03	6.06	5.72	5.59	5.83											
13965	6/12		MA	FA	FA	FA	MA	MA / FA		FA	FA	MA	FA	MA	FA	MA	MA								
			5.15	5.11	5.08	4.79	5.06	5.39	4.41	4.59	4.84	5.13	4.82	5.20	5.12	5.18	5.46								
13966	9/13		MA	FA	MA	FA	MA	MA / MA		FA	FA	MA	MA	FA	MA	FA	MA								
			5.28	4.62	5.07	4.73	5.15	5.11	4.95	4.62	4.34	5.27	5.03	4.95	4.49	4.46	5.05								

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

PROTOCOL 418-023P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF POTASSIUM PERFLUOROBUTANE SULFONATE (PFBS) IN RATS (SPONSOR'S STUDY NUMBER: T-7485.11)

TABLE 14 (PAGE 3): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

GROUP III		300 MG/KG/DAY																						
	FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
RAT #	CLs																							
13967	7/15	MA	FA	FA	FA	FA	FA	FA / MA		FA	FA	MA	FA	FA	FA	MA	MA	FA						
		5.27	5.06	4.89	4.94	5.07	4.86	5.09	5.15	4.77	4.89	5.34	4.86	4.81	4.96	5.38	4.84	5.08						
13968	9/11	FA	FA	FA	MA	FA	FA	FA / MA		FA	FA	MA	FA	MA	MA	MA								
		5.34	5.49	5.65	5.71	5.02	5.28	5.52	5.79	5.14	5.46	5.60	5.30	5.75	5.46	5.38								
13969	9/12	MA	MA	FA	MA	FA	FA	MA	FA / FA		FA	MA	MA	MA	MA	MA								
		5.16	5.01	5.30	5.12	5.33	4.92	5.24	5.02	4.86	4.83	4.88	4.96	5.27	5.51	5.26								
13970	10/12	MA	E	MA	FA	FA / FA		FA	FA	MA	E	FA	MA	E	MA	FA	FA							
		5.63		5.72	5.48	5.39	5.33	5.50	5.15	5.56		5.38	5.82		5.20	4.89	5.58							
13971	8/ 9	FA	MA	FA	FA	MA	E	MA	MA / FA		MA	FA	FA	FA	MA	FA	FA	FA						
		5.13	5.43	5.29	5.45	5.85		6.03	5.86	4.74	5.64	5.81	5.30	5.13	5.70	5.40	5.72	5.61						
13972	7/10	FA	MA	MA	FA	MA	FA / FA		FA	FA	FA	FA	MA	MA	FA	MA								
		5.16	5.39	5.61	5.19	4.90	5.15	4.76	5.27	5.18	5.19	4.79	5.29	5.18	5.25	5.19								
13973	5/12	MA	FA	FA / FA		FA	MA	FA	MA	MA	MA	MA	MA											
		5.27	5.37	5.14	5.18	4.77	5.12	5.37	5.15	5.50	5.83	5.36	5.15											
13974	6/15	MA	FA	MA	FA	FA / FA		MA	FA	MA	FA	FA	MA	FA	MA	MA	MA							
		5.33	4.86	5.42	5.15	4.91	4.33	5.04	4.49	5.17	4.75	4.97	5.33	4.73	5.22	5.39	5.03							

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

PROTOCOL 418-023P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF POTASSIUM PERFLUOROBUTANE SULFONATE (PFBS) IN RATS
(SPONSOR'S STUDY NUMBER: T-7485.11)

TABLE 14 (PAGE 4): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

GROUP IV 1000 MG/KG/DAY

FETUS #		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
RAT #	CLs																							
13975	12/11	MA	MA	FA	MA	FA	FA	MA	FA	MA / MA		MA	FA	FA	MA	MA	FA							
		5.00	5.02	4.97	5.07	4.77	4.70	5.15	4.56	5.25	5.14	4.73	4.68	4.60	4.79	4.77	5.06							
13976	17/10	MA	FA	FA	MA	MA	FA	MA	MA	MA	MA / MA		FA	FA	MA	MA	MA							
		4.50	4.66	4.46	5.22	4.84	4.81	4.33	4.80	4.60	4.78	4.98	4.64	4.27	5.14	4.88	4.85							
13977	5/11	FA	MA	MA	MA	FA / MA		MA	MA	FA	MA	MA	FA	FA	MA	MA								
		5.43	5.21	5.41	5.68	5.66	5.54	5.38	5.29	5.16	5.36	5.24	5.02	5.33	5.54	5.43								
13978	6/12	FA	MA	FA	FA	FA	FA / MA		MA	FA	FA	FA	MA	FA	FA	MA	FA							
		5.28	5.45	5.16	5.49	5.19	5.15	5.74	5.52	5.18	5.09	5.13	5.55	5.00	5.16	5.69	5.35							
13979		NOT PREGNANT																						
13980	10/ 6	FA	FA	MA	MA	FA	MA	MA	FA	MA / FA		FA	MA	FA	FA									
		5.06	5.16	5.40	5.46	5.29	5.52	5.31	5.26	5.56	5.02	5.65	5.66	5.24	5.69									
13981	6/ 9	MA	MA / FA		MA	FA	MA	FA	MA	MA														
		5.97	5.87	5.56	5.99	5.80	5.87	5.74	5.53	5.66														
13982	5/14	MA	FA	FA / MA		FA	MA	FA	MA	MA	E	MA	MA	MA	MA	MA	MA							
		5.50	5.39	5.17	4.13	4.63	4.95	4.70	5.08	4.82		4.97	5.09	4.89	5.12	4.85	5.24							

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

PROTOCOL 418-023P: ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF POTASSIUM PERFLUOROBUTANE SULFONATE (PFBS) IN RATS
(SPONSOR'S STUDY NUMBER: T-7485.11)

TABLE 14 (PAGE 5): FETAL SEX, VITAL STATUS AND BODY WEIGHT - INDIVIDUAL DATA

GROUP V 2000 MG/KG/DAY

FETUS #		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
RAT #	CLs																							
13983	8/ 9	MA	MA	MA	MA	FA	FA	MA / MA		MA	FA	MA	FA	FA	MA									
		4.10	4.48	4.52	4.71	4.13	3.95	4.29	4.17	4.30	4.35	4.43	4.22	4.29	4.34									
13984	7/10	FA	FA	FA	FA	FA	MA	MA / FA		FA	FA	MA	FA	FA	MA	FA	FA							
		4.28	4.87	4.32	4.97	4.63	4.91	5.07	4.65	4.55	4.53	5.16	4.40	4.66	4.64	4.86	4.82							
13985	6/11	MA	MA	FA	FA	FA	FA / MA		FA	FA	FA	MA	MA	FA	FA	FA	FA							
		5.92	5.62	5.42	4.99	5.41	4.98	5.51	5.04	5.04	5.13	5.02	5.23	5.35	5.15	5.31	5.35							
13986	6/10	MA	MA	MA	MA	FA	MA / FA		MA	FA	FA	FA	FA	MA	MA									
		5.39	5.35	5.44	5.11	4.71	5.10	4.87	5.03	4.97	4.63	4.42	4.80	4.96	4.98									
13987	10/11	MA	FA	MA	MA	FA	MA	FA	FA / MA		MA	MA	MA	MA	FA	MA								
		5.01	4.70	4.58	4.15	4.62	4.18	4.33	4.12	4.59	4.46	4.17	4.38	4.25	4.39	4.84								
13988	10/ 7	MA	MA	MA	MA	FA	FA	FA	MA	MA / MA		MA	MA	MA	MA									
		4.51	4.19	4.53	4.36	4.43	4.36	4.04	4.06	4.25	4.69	4.13	4.44	4.35	4.65									
13989	9/ 9	FA	MA	FA	FA	FA	FA	FA / MA		MA	FA	MA	FA	MA	FA	MA								
		4.53	4.91	4.50	4.56	4.44	4.41	2.66	4.82	4.40	4.54	4.93	4.17	3.26	3.95	4.86								
13990	12/ 6	E	FA	FA	FA	FA	MA	MA	MA	MA	FA	FA / MA		MA	FA	FA								
			4.82	4.74	4.41	4.49	4.87	4.75	4.74	4.56	4.38	4.93	5.24	4.86	4.94	4.40								

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

ATTACHMENT 1

PROTOCOL AND AMENDMENT

PRIMEDICA

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

PROTOCOL 418-023P

SPONSOR'S STUDY NUMBER: T-7485.11

STUDY TITLE: Oral (Gavage) Dosage-Range Developmental Toxicity Study of Potassium Perfluorobutane Sulfonate (PBSF) in Rats

PURPOSE: The purpose of this study is to provide information for the selection of dosages to be used in the developmental toxicity (embryo-fetal toxicity and teratogenic potential) study of Potassium Perfluorobutane Sulfonate (PBSF) administered orally via gavage to Crl:CD®(SD)IGS BR VAF/Plus® presumed pregnant female rats.

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

STUDY DIRECTOR: Raymond G. York, Ph.D., DABT
Associate Director of Research
raymond.york@primedica.com

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

STUDY MONITOR: Ph.D., DABT
3M Corporate Toxicology
3M Medical Department
Telephone:
Telefax:

REGULATORY CITATIONS:

U.S. Environmental Protection Agency (1998). Health Effects Test Guidelines; Prenatal Developmental Toxicity Study. Office of Prevention, Pesticides and Toxic Substances (OPPTS) 870.3700, August, 1998.

U.S. Environmental Protection Agency (1997). Toxic Substances Control Act (TSCA) Test Guidelines; Final Rule. Prenatal Developmental Toxicity, 799.9370 (cross-referenced to OPPTS 870.3700). *Federal Register*, August 15, 1997.

Organization for Economic Cooperation and Development (1981). *OECD Guidelines for Testing of Chemicals*. Section 4, No. 414: Teratogenicity, adopted 12 May 1981.

Japanese Ministry of Agriculture, Forestry and Fisheries (1985). *Guidance on Toxicology Study Data for Application of Agricultural Chemical Registration*. 59 NohSan No. 4200.

U.S. Environmental Protection Agency. Toxic Substances Control Act (TSCA); Good Laboratory Practice Standards; Final Rule. 40 CFR Part 792.

U.S. Environmental Protection Agency. Federal Insecticide, Fungicide and Rodenticide Act (FIFRA); Good Laboratory Practice Standards; Final Rule. 40 CFR Part 160.

Organization for Economic Cooperation and Development (1998). The Revised OECD Principles of Good Laboratory Practices [C(97)186/Final].

Japanese Ministry of Agriculture, Forestry and Fisheries (1984). *Good Laboratory Practice Standards*. 59 NohSan No. 3850.

REGULATORY COMPLIANCE:

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

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

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

Should any portion of the study be conducted by a subcontractor or by the Sponsor, the QAU for that facility will conduct critical phase inspections and audit respective results and reports for that study portion according to the SOPs of that facility. Such critical phase inspection reports and report audits will be submitted by that facility to the Study

Director. The dates of the inspections and report submissions will be incorporated into a QAU Statement generated by that facility and provided to the Testing Facility for inclusion in the final report.

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

SCHEMATIC OF STUDY DESIGN AND STUDY SCHEDULE:

See ATTACHMENT 1 to the protocol.

TEST SUBSTANCE AND VEHICLE:

Identification:

Test Substance:

Potassium Perfluorobutane Sulfonate (PBSF or T-7485). Lot number will be documented in the raw data.

The Sponsor will provide to the Testing Facility documentation or certification of the identity, composition, method of synthesis, strength and purity of the test substance.

Vehicle:

Aqueous 0.1% carboxymethylcellulose (CMC) (medium viscosity) prepared using reverse osmosis membrane processed deionized water (R.O. deionized water). Lot number will be documented in the raw data.

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

Safety Precautions:

Gloves, dust-mist/HEPA-filtered mask, appropriate eye protection and uniform/lab coat to be worn during formulation preparation and dosage. In addition, Tyvek sleeves and a half-face respirator will be worn and preparation will be conducted in a chemical fume hood when using the bulk test substance. The Material Safety Data Sheet (MSDS) is attached to the protocol (ATTACHMENT 2).

Storage:

Bulk Test Substance:	Room temperature.
Bulk Vehicle Components:	Room temperature
Prepared Test Article and Vehicle Formulations:	2°C to 8°C

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

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

FORMULATION:

Frequency of Preparation:

Formulations (suspensions) will be prepared (approximately every 10 days) at the Testing Facility.

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

Adjustment for Purity:

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

Testing Facility Reserve Samples:

The Testing Facility will reserve a sample (1 g) of each lot of bulk test substance and bulk vehicle component used during the course of the study. Samples will be stored under the previously cited conditions.

ANALYSES:

Results of required analyses will be provided to the Testing Facility for inclusion in the study report.

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

Bulk Test Substance Sampling:

A sample (1g) of the test substance will be taken on the last day of treatment and sent (ambient conditions) to the Sponsor for analysis.

This sample will be sent to:

, Ph.D.
3M Environmental Technology & Safety Services
935 Bush Avenue
Building 2-3E-09
St. Paul, Minnesota 55133-3331

Telephone:
Telefax:

The recipient will be notified in advance of sample shipment.

Analyses of Prepared Formulations:

Homogeneity:

Homogeneity analyses of the prepared formulations will not be conducted. Information is on file with the Sponsor to document the homogeneity of the test substance in the prepared vehicle over the range of concentrations to be used in this study. This information will be provided to the Study Director for inclusion in the final report.

Concentration:

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

Stability:

Stability data for prepared formulations bracketing the range of concentrations in this study are on file with the Sponsor and will not be determined during the conduct of this study. This information will be provided to the Study Director for inclusion in the final report.

Shipping Instructions:

Samples to be analyzed will be shipped (on cold packs) to Ph.D., at the previously cited address.

The recipient will be notified in advance of sample shipment.

DISPOSITION:

Prepared formulations will be discarded at the Testing Facility. All remaining bulk test substance will be returned to:

3M SMMG EHS&R
3M Center
Building 236-1B-10
St. Paul, MN 55144-1000

TEST SYSTEM:

Species/Strain and Reason for Selection:

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

Number:

Initial population acclimated: 60 virgin female rats.
Population selected for study: 40 mated female rats (8 per dosage group).

Body Weight and Age:

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

Sex:

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

Source:

Charles River Laboratories, Inc.

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

Identification:

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

ANIMAL HUSBANDRY:

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

Housing:

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

Room Air, Temperature and Humidity:

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

Light:

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

Diet:

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

Water:

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

Contaminants:

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

RANDOMIZATION AND COHABITATION:

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

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

ADMINISTRATION:

Route and Reason for Choice:

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

Method and Frequency:

Female rats will be given the test substance once daily on days 6 through 20 of presumed gestation. Dosages will be adjusted daily for body weight changes and given at approximately the same time each day.

Rationale for Dosage Selection:

Dosages were selected on the basis of a 28-day (gavage) study of T-7485 in rats (Redfield Laboratories Study Number 132-007) with an approximate 14-day recovery period which resulted in no mortality or abnormal clinical observations as well as no changes in body weights, body weight changes, feed consumption, peripheral neuropathy, motor activity, audio/visual response, hematology, clinical chemistry, gross pathology and histopathology. The administration of 900 mg/kg/day T-7485 resulted in significant increases in male liver and female kidney weights when compared to control animals and establishes the no-observable-adverse-effect-level (NOAEL) at 300 mg/kg/day T-7485.

The highest dosage level selected should induce some overt developmental and/or maternal mortality. The intermediate dosage levels should produce minimal observed toxic effects. The lowest dosage level should not produce any evidence of either maternal or developmental toxicity.

Dosage Levels, Concentrations and Volumes:

Group	Number of Rats	Dosage (mg/kg/day)	Concentration (mg/mL)	Volume (mL/kg)	Argus Batch Number
I	8	0	0	10	B-418-023P-A(Day.Month.Year)
II	8	100	10	10	B-418-023P-B(Day.Month.Year)
III	8	300	30	10	B-418-023P-C(Day.Month.Year)
IV	8	1000	100	10	B-418-023P-D(Day.Month.Year)
V	8	2000	200	10	B-418-023P-E(Day.Month.Year)

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

TESTS, ANALYSES AND MEASUREMENTS:

Viability:

All Periods: At least twice daily.

Clinical Observations and/or General Appearance:

Acclimation Period: Weekly.

Predosage Period: Day 0 of presumed gestation.

Dosage Period: Daily before dosage. Postdosage observations will be recorded approximately 60±10 minutes after administration.

Day of Sacrifice: Once.

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

Body Weights:

Acclimation Period:	Weekly.
Predosage Period:	Day 0 of presumed gestation.
Dosage Period:	Daily.
Day of Sacrifice:	Prior to sacrifice.

Feed Consumption Values (recorded and tabulated):

Predosage Period:	Day 0 of presumed gestation.
Dosage Period:	Days 6, 9 12, 15, 18 and 21 of presumed gestation.
Day of Sacrifice:	Feed left recorded.

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

Mating Performance:

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

Caesarean-Sectioning Observations:

Rats will be Caesarean-sectioned on day 21 of presumed gestation. To minimize bias, Caesarean-sectioning and subsequent fetal observations will be conducted without knowledge of dosage group. The gravid uterus will be excised and weighed. The fetuses will be removed from the uterus and placed in individual containers. The rats will be examined for number and distribution of:

Corpora Lutea.

Implantation Sites.

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

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

Fetal Observations:

To minimize bias, fetal observations will be conducted without knowledge of dosage group.

Fetuses will be examined for sex and for gross external alterations. Late resorptions and dead fetuses will be examined for gross external alterations to the extent possible. The body weight of each fetus will be recorded. Only body weights of live fetuses will be used to determine litter fetal body weight averages. Fetuses with gross external alterations will be fixed in Bouin's solution; all other fetuses will be discarded. Representative photographs of fetal gross external alterations will be taken.

METHOD OF SACRIFICE:

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

NECROPSY:

Gross lesions will be retained in neutral buffered 10% formalin for possible future evaluation. Unless specifically cited below, all other tissues will be discarded.

Scheduled Sacrifice:

On day 21 of presumed gestation, female rats will be Caesarean-sectioned, and a gross necropsy of the thoracic, abdominal and pelvic viscera will be performed. The gravid uterus will be excised and weighed. Uteri of apparently nonpregnant rats will be examined while being pressed between glass plates to confirm the absence of implantation sites.

Rats Found Dead or Moribund:

Rats that die or are sacrificed because of moribund condition, abortion or premature delivery will be examined for the cause of death or moribund condition on the day the observation is made. The rats will be examined for gross lesions. Pregnancy status and uterine contents of female rats will be recorded. Gravid uterine weights will not be recorded if precluded by autolysis. Aborted fetuses, delivered pups and/or concepti *in uteri* will be examined to the extent possible, using the methods described above. Uteri of apparently nonpregnant rats will be examined while being pressed between glass plates to confirm the absence of implantation sites.

STATISTICAL EVALUATION:

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

DATA ACQUISITION, VERIFICATION AND STORAGE:

Data generated during the course of this study will be recorded either by hand or using the *Primedica Argus Automated Data Collection and Management System* and the *Vivarium Temperature and Relative Humidity Monitoring System.* All data will be tabulated, summarized and/or statistically analyzed using the *Primedica Argus Automated Data Collection and Management System*, the *Vivarium Temperature and Relative Humidity Monitoring System, Microsoft Excel* [part of Microsoft Office 97 (version SR-2)] and/or *The SAS System* (version 6.12).

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

RECORDS TO BE MAINTAINED:

Protocol and Amendments.
Test Substance, Vehicle and/or Reagent Receipt, Preparation and Use.
Animal Acquisition.
Randomization Schedules.
Mating History.
Treatment (if prescribed by Staff Veterinarian).
General Comments.
Clinical Observations and/or General Appearance.
Blood Sample Collection, Processing and Shipment (if required).

Body Weights.
Feed Consumption Values.
Caesarean-Sectioning and Fetal Observations.
Gross Necropsy Observations.
Organ Weights (if required).
Photographs (if required).
Study Maintenance (room and environmental records).
Feed and Water Analyses.
Packing and/or Shipment Lists.

KEY PERSONNEL:

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

REPORT:

The Study Director may provide periodic updates of study progress to the Sponsor. Draft summary tables of unaudited computer-recorded data may accompany these updates. Statistical analyses will not be performed on these interim data.

An unaudited letter report for the purpose of dosage selection for the full study will be prepared immediately following completion of the in-life phase.

An audited report will be prepared including: abstract, summaries of the methods, results and conclusion; table of contents; Study Director's GLP compliance statement; copy of the protocol; amendments; QAU statement; summary and individual tables; and reports of supporting data (if appropriate). The report **(will be included) (will not be included)** as an appendix to the full study report. The Sponsor will receive one copy of the draft report and two copies of the final report.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE STATEMENT:

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

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

REFERENCES:

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

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

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

4. Institute of Laboratory Animal Resources (1996). *Guide for the Care and Use of Laboratory Animals.* National Academy Press, Washington, D.C.

PROTOCOL APPROVAL:

FOR THE TESTING FACILITY

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

22-Dec-00
Date

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

22-Dec-00
Date

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

22 Dec 00
Date

FOR THE SPONSOR

, Ph.D., DABT
Study Monitor
Sponsor's Representative

27 Dec-2000
Date

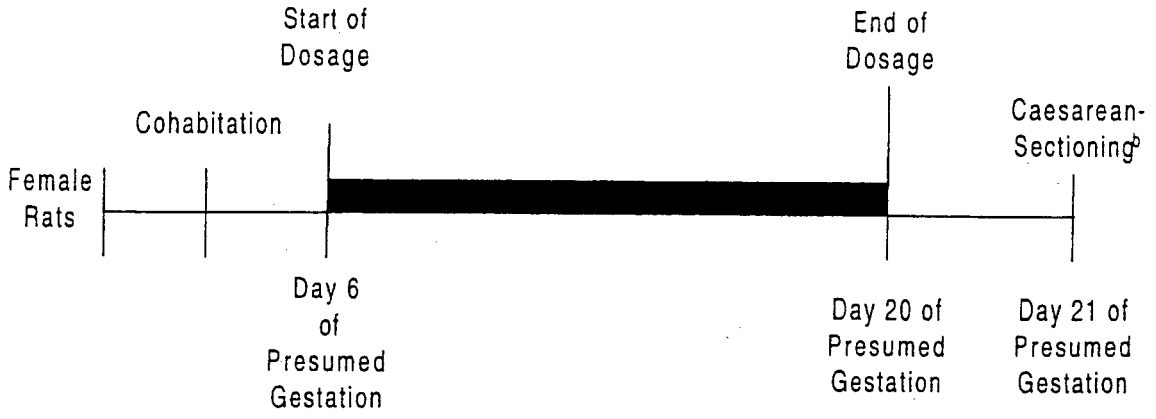
ATTACHMENT 1

SCHEMATIC OF STUDY DESIGN AND STUDY SCHEDULE

ATTACHMENT 1

STUDY SCHEMATIC

DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY[a]



Dosage Period.

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

b. Fetal evaluations (all fetuses - external examinations).

SCHEDULE[a]

19 DEC 00	Animals Arrive - Acclimation Begins.
24 DEC 00 PM – 29 DEC 00 AM	Cohabitation Period.
25 DEC 00	First Possible Day 0 of Presumed Gestation.
29 DEC 00	Last Possible Day 0 of Presumed Gestation.
31 DEC 00 – 18 JAN 01	Dosage Period (Days 6 through 20 of presumed gestation).
15 JAN 01 –19 JAN 01	Caesarean-Sectioning Period (Day 21 of presumed gestation).
26 JAN 01	Unaudited Letter Report.
29 MAR 01	Audited Summary Report.

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a. The study initiation date is the date the Study Director signs the protocol.

ATTACHMENT 2

MATERIAL SAFETY DATA SHEET

T-7485

MATERIAL SAFETY DATA SHEET (Experimental)

3M
3M Center
St. Paul, Minnesota
55144-1000
1-800-364-3577 or (651) 737-6501 (24 hours)

DIVISION: 3M SPECIALTY MATERIALS
MATERIAL:
L-7038 DEVELOPMENTAL MATERIAL
ISSUED: December 08, 2000
SUPERSEDES: October 11, 2000
DOCUMENT: 04-4734-2

1. INGREDIENT

INGREDIENT	C.A.S. NO.	PERCENT
POTASSIUM NONAFLUOROBUTANESULFONATE.....	29420-49-3	~ 98
POTASSIUM GAMMAHYDRO OCTAFLUOROBUTANE SULFONATE.....	Unknown	~ 2

The components of this product are in compliance with the chemical notification requirements of TSCA. All applicable chemical ingredients in this material are listed on the European Inventory of Existing Chemical Substances (EINECS), or are exempt polymers whose monomers are listed on EINECS.

2. PHYSICAL DATA

BOILING POINT:..... N/A
VAPOR PRESSURE:..... N/A
VAPOR DENSITY:..... N/A
EVAPORATION RATE:..... N/A
SOLUBILITY IN WATER:..... 5 %
SPECIFIC GRAVITY:..... ca. 0.54 Water=1
Bulk Density 7-8 lb/gal
PERCENT VOLATILE:..... N/A
pH:..... 5.5 - 7.5
(5% Aqueous)
VISCOSITY:..... N/A
MELTING POINT:..... 265 C

APPEARANCE AND ODOR:
Solid, white, odorless, granular

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

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3. FIRE AND EXPLOSION HAZARD DATA

FLASH POINT:..... Non-Flammable
FLAMMABLE LIMITS - LEL:..... N/A
FLAMMABLE LIMITS - UEL:..... N/A
AUTOIGNITION TEMPERATURE:..... N/A

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

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

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

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4. REACTIVITY DATA

STABILITY: Stable

INCOMPATIBILITY - MATERIALS/CONDITIONS TO AVOID:
None known.

HAZARDOUS POLYMERIZATION: Hazardous polymerization will not occur.

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

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5. ENVIRONMENTAL INFORMATION

SPILL RESPONSE:
Observe precautions from other sections. Ventilate area. Collect spilled material. Use wet sweeping compound or water to avoid dusting. Clean up residue. Place in a closed container.

RECOMMENDED DISPOSAL:
Incinerate in an industrial or commercial facility in the presence of a combustible material. Combustion products will include HF. Disposal alternative: Dispose of waste product in a facility permitted to accept chemical waste.

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5. ENVIRONMENTAL INFORMATION (continued)

ENVIRONMENTAL DATA:
Not determined.

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

Since regulations vary, consult applicable regulations or authorities before disposal. U.S. EPA Hazardous Waste Number = None (Not U.S. EPA Hazardous).

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

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6. SUGGESTED FIRST AID

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

SKIN CONTACT:
Wash affected area with soap and water.

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

IF SWALLOWED:
If swallowed, call a physician immediately. Only induce vomiting at the instruction of a physician. Never give anything by mouth to an unconscious person.

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7. PRECAUTIONARY INFORMATION

EYE PROTECTION:
Avoid eye contact. The following should be worn alone or in combination, as appropriate, to prevent eye contact: Wear vented goggles. Wear safety glasses with side shields.

SKIN PROTECTION:
Avoid skin contact. Wear appropriate gloves when handling this material. A pair of gloves made from the following material(s) are recommended: neoprene, nitrile rubber. Use one or more of the following personal protection items as necessary to prevent skin contact: head covering, coveralls. Protective garments (other than gloves) should be made of either of the following materials:

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7. PRECAUTIONARY INFORMATION (continued)

Plain Tyvek or coated Tyvek or similar disposable coverall.

RECOMMENDED VENTILATION:
Provide appropriate local exhaust when product is heated. Provide appropriate local exhaust ventilation at transfer points. Provide sufficient ventilation to maintain emissions below recommended exposure limits. If exhaust ventilation is not adequate, use appropriate respiratory protection.

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

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

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

FIRE AND EXPLOSION AVOIDANCE:
Not applicable. Nonflammable.

OTHER PRECAUTIONARY INFORMATION:
No smoking: Smoking while using this product can result in contamination of the tobacco and/or smoke and lead to the formation of the hazardous decomposition products mentioned in the Reactivity Data section of this MSDS. Store work clothes separately from other clothing, food and tobacco products.

EXPOSURE LIMITS

INGREDIENT	VALUE	UNIT	TYPE	AUTH	SKIN*
POTASSIUM NONAFLUOROBUTANESULFONATE.....	0.1	MG/M3	TWA	3M	Y
POTASSIUM GAMMAHYDRO OCTAFLUOROBUTANE SULFONATE.....	NONE	NONE	NONE	NONE	

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

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

EXPOSURE LIMITS (continued)

INGREDIENT	VALUE	UNIT	TYPE	AUTH	SKIN*

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

- NONE: None Established

8. HEALTH HAZARD DATA

EYE CONTACT:
Moderate Eye Irritation: signs/symptoms can include redness, swelling, pain, tearing, and hazy vision.

SKIN CONTACT:
Contact with the skin during product use is not expected to result in significant irritation.

INHALATION:
Single overexposure, above recommended guidelines, may cause:

Irritation (upper respiratory): signs/symptoms can include soreness of the nose and throat, coughing and sneezing.

IF SWALLOWED:
May be harmful if swallowed.

SECTION CHANGE DATES

PHYSICAL DATA	SECTION CHANGED SINCE October 11, 2000	ISSUE
FIRE AND EXPL.	SECTION CHANGED SINCE October 11, 2000	ISSUE
ENVIRONMENTAL INFO.	SECTION CHANGED SINCE October 11, 2000	ISSUE
PRECAUTIONARY INFO.	SECTION CHANGED SINCE October 11, 2000	ISSUE

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ATTACHMENT 3

TEST SUBSTANCE PREPARATION PROCEDURE

ATTACHMENT 3

TEST SUBSTANCE PREPARATION PROCEDURE

Test Substance: PBSF
Vehicle: Aqueous 0.1% CMC (medium viscosity)

A. Purpose:

The purpose of this procedure is to provide a method for the preparation of dosage suspensions of PBSF for oral (gavage) administration to rats on Primedica Argus Research Laboratories, Inc., Study 418-023P.

B. General Information:

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

2. Suspensions will be prepared:
   __ Daily __ Weekly __ For_ days of use
   _X_ Approximately every ten days __ By Sponsor

3. Suspensions will be prepared at a final dosage volume of _10_ mL/kg.

4. Safety:
   _X_ Nitrile or neoprene gloves, uniform/lab coat, goggles or safety glasses with side shields
   _X_ Dust-Mist Respirator if used in a chemical fume hood
   _X_ Half-Face Respirator if not used in a chemical fume hood
   __ Full-Face Respirator/Positive Pressure Hood
   _X_ Tyvek Suit or tyvek apron and sleeves

5. Dosage suspensions adjusted for % Activity/Purity or Correction Factor:
   __ Yes _X_ No (Calculations based on 100%)
   __ % Activity __ % Purity __ Correction Factor

6. Sampling requirements: Cited in protocol

7. Storage: Cited in protocol

ATTACHMENT 3

TEST SUBSTANCE PREPARATION PROCEDURE

NOTE: Prior to test substance preparation accurately measure the required amount of the appropriate vehicle (R.O. deionized water should be used for calibration purposes) in a graduated cylinder, pour the required amount of vehicle into a beaker. Carefully mark each beaker at the meniscus. This mark will be used during the preparation to bring the test substance slurry up to volume.

C. Dosage Suspension Preparation:

1. Weigh the required amount of test substance on a piece of weigh paper or into an appropriately sized mortar (see PREPARATION CALCULATIONS).

2. If weigh paper is used, transfer the test substance to an appropriately sized mortar. If necessary, grind the test substance into a fine powder. Slowly add a small amount of vehicle and grind. Continue to add vehicle slowly and grind the vehicle and the test substance together to form a fine slurry. Transfer the vehicle/test substance slurry to a marked beaker.

3. Rinse the mortar and pestle with additional vehicle to remove any remaining test substance. Transfer rinse to beaker.

4. Add additional vehicle to the beaker to bring volume up to the mark. Place on magnetic stir plate and agitate prior to and during administration and/or sampling.

5. Repeat steps (1) through (4) for each concentration.

Written By: Mary A. Coker

Approved by: [signature] Date: 22-DEC-00

Clarification: ✓ No ___ Yes [see attached clarification form]

Initial/Date : [signature] 1/25/01

PRIMEDICA

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

PROTOCOL 418-023P

ORAL (GAVAGE) DOSAGE-RANGE DEVELOPMENTAL TOXICITY STUDY OF POTASSIUM PERFLUOROBUTANE SULFONATE (PFBS) IN RATS

SPONSOR'S STUDY NUMBER: T-7485.11

Amendment 1 - 26 February 2001

1. Study Title (page 1 and citations throughout the protocol):

The abbreviation for potassium perfluorobutane sulfonate is PFBS, rather than PBSF.

Reason for Change:

This change corrects the protocol.

for George E. Boulware 26 Feb 01 Raymond G. York 26-FEB-01

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

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

Theresa H. Woodard 26 FEB 01 1-Oct-03

Theresa H. Woodard, D.V.M. Date
Chairperson, Institutional Animal Care and Use Committee

Ph.D., DABT Date
Study Monitor
Sponsor's Representative

Any revisions made to this finalized amendment must be made by subsequent amendment.

ATTACHMENT 2

ANALYTICAL REPORT

ANALYSIS OF DOSING SOLUTIONS USED AT ARGUS RESEARCH LABORATORY FOR SPONSOR'S STUDY NUMBERS T-7485.11, T-7485.12, AND T-7485.13 (ARGUS RESEARCH LABORATORY PROTOCOL NUMBERS: 418-023P, 418-023 AND 418-021)

STUDY ID: A343.1

SPONSOR STUDY NOS. T-7485.11
T-7485.12
T-7485.13

Southern Research Institute
2000 Ninth Avenue South
P.O. Box 55305
Birmingham, AL 35255-5305

SUMMARY

A total of 30 formulated dose samples including blanks and vehicles ranging in concentration from 3 to 200 mg/mL were analyzed by analytical method BACG 3533 to determine the concentration of perfluorobutanesulfonate (PFBS) in the formulated mixture. All dose formulations were found to be within ± 10% of the reported concentration except for four samples, 100 mg/mL dated 1/11/01, 100 mg/mL dated 2/23/01, 100 mg/mL date 9/4/01 and 200 mg/mL dated 1/11/01. These three samples were found to have measured concentrations of 88.9 %, 86.3 %, 76.6% and 76.8 % of target values, respectively.

KEY PERSONNEL

Raymond G. York, Ph.D., D.A.B.T.
Study Director
Argus Research Laboratories

James D. Johnson, M.S., MBA
Manager
Bioanalytical Chemistry Group

Gregory S. Gorman, Ph.D.
Staff Chemist
Bioanalytical Chemistry Group

Lara Cook, M.S.
Research Associate II
Bioanalytical Chemistry Group

1. OBJECTIVE

The objective of this study was to determine the dose concentration of PFBS in the supplied dosing solutions received from the sponsor.

2. SAFETY

All necessary procedures to ensure safety of the analysts were based on information contained in the Material Safety and Data Sheets (MSDS), provided by the producer of the test article and the study director.

3. Compliance

The study described in this final report was conducted in accordance with the EPA Good Laboratory Practice Regulations (40 CFR Part 160 and 792), OECD Principles of Good Laboratory Practice [C(97)186/Final]. For studies 418-023 and 418-023P Good Laboratory Practice Standards (1984) for MAFF 59 Nohsan No. 3850 were met. The final report accurately reflects the raw data obtained during the performance of the study. There were no adverse circumstances that affected the quality or integrity of the study.

4. EXPERIMENTAL

4.1 Analytical Procedures

The sample preparation and analysis procedures as described in the analytical method BACG 3533 were employed for all analyses. Each sample was allowed to warm to room temperature and was then vortexed well before being sampled. An aliquot was taken from each and diluted as described in the method. (Note: the 66.7 mg/mL and higher concentrated samples often were suspensions and the entire sample volume in some cases were diluted to the target range). Multiple calibration curves were prepared over a concentration range of 500 to 10,000 ng/mL and analyzed along with the samples as described in the method. The correlation coefficient for each curve was greater than 0.9982.

4.2 Results

The results of the analysis are presented in the Tables I-III corresponding to the sponsors study number at the end of the report.

5.0 Conclusion

A total of 30 dose formulation samples ranging in concentration from 3 to 200 mg/mL were analyzed by BACG 3533. All samples except for four, 100 mg/mL dated 1/11/01, 100 mg/mL dated 2/23/01, 100 mg/mL dated 9/4/01 and 200 mg/mL dated 1/11 were found to be within ± 10 % of the reported concentration.

Table I
Dose Formulation Analysis of PFBS in 0.1% CMC
Sponsor Study Number T-7485.13

Dose (mg/mL)	Target Dilution	Measured Conc. (ng/mL)	Dose Conc.(mg/mL)	% Theoretical
0 (12/25)	no dilution	not detected	------	------
0 (9/4)	no dilution	792.3[1]	0.001	------
3 (12/25)	3192	3441	3.2	108
3 (9/4)	3192	3454	3.2	108
10 (12/25)	3200	3165	9.9	98.9
10 (9/4)	3200	3408	10.7	107
30 (12/25)	3192	3239	30.4	101
30 (9/4)	3192	3165	29.7	99.2
66.7 (5/17)	3200	3139[2]	65.4	98.4
66.7 (4/18)	3200	2997[2]	61.9	92.8
100 (9/4)	3200	2451[2]	76.6	76.6
100 (12/25)	3200	3171	99.1	99.1

[1]Small amount of material detected in the undiluted sample is considered insignificant when compared to amount found in diluted samples and is believed to be the result of carry-over from a previously run standard injection.

[2]Average of two results.

Table II
Dose Formulation Analysis of PFBS in 0.1% CMC
Sponsor Study Number T-7485.12

	Target	Measured	Dose	
Dose (mg/mL)	Dilution	Conc. (ng/mL)	Conc.(mg/mL)	% Theoretical
0 (2/23)	no dilution	not detected	------	------
0 (3/8)	no dilution	not detected	------	------
10 (2/23)	3200	3311	10.3	103
10 (3/8)	3200	3207	10.0	100
30 (2/23)	3192	3112	29.2	97.5
30 (3/8)	3192	3154	29.6	98.8
100 (2/23)	3200	2760	86.3	86.3
100 (3/8)	3200	3383	106	106

Table III
Dose Formulation Analysis of PFBS in 0.1% CMC
Sponsor Study Number T-7485.11

Dose (mg/mL)	Target Dilution	Measured Conc. (ng/mL)	Dose Conc.(mg/mL)	% Theoretical
0 (12/27)	no dilution	not detected	------	------
0 (1/11)	no dilution	not detected	------	------
10 (12/27)	3200	3282	10.3	103
10 (1/11)	3200	3266	10.2	102
30 (12/27)	3192	3302	31.0	103
30 (1/11)	3192	3353	31.5	105
100(1/11)	3200	2845	88.9	88.9
100 (12/27)	3200	3362	105	105
200 (12/27)	3200	3174	198	99.2
200 (1/11)	3200	2457	154	76.8

6.0 Approvals

Lara Cook, M.S.
Research Associate II
Bioanalytical Chemistry Group

1-30-02
Date

Gregory S. Gorman, Ph.D.
Staff Chemist
Bioanalytical Chemistry Group

1-30-02
Date

Tina Rogers, Ph.D.
Director
Safety Assessment Department

1/30/02
Date

Raymond G. York, Ph.D., D.A.B.T.
Study Director
Argus Research Laboratories

13 FEB 2002
Date

Quality Assurance Statement

Final Report On

Analysis of Dosing Solutions Used at Argus Research Laboratory for Sponsor's Study Numbers T-7485.11, T-7485.12, and T-7485.13 (Argus Research Laboratory Protocol Numbers: 418-023P, 418-023, and 418-021)

A343.1

Listed below are the phases and/or procedures performed by Southern Research Institute that were inspected and audited by the Quality Assurance Unit during the study described in the report. Findings were reported to the study director and management periodically.

Phases/Procedures	*Inspection/ Audit Date*	*Date Management Notified*	*Date Study Director Notified*[1]
Protocol Review	5/14/01	5/14/01	1/18/02
Dose Formulation Concentration Analysis	5/14/01	6/14/01	1/18/02
Data Audit and Draft Report Review	12/3/01-12/6/01; 1/14/02-1/17/02	1/18/02	1/18/02
Final Report	1/30/02	1/30/02	1/30/02

[1] The study director is off-site.

C.L. Marsh, Manager, Quality Assurance/Quality Control

1/30/02
Date

ATTACHMENT 3

QUALITY ASSURANCE STATEMENT

905 Sheehy Drive, Bldg. A
Horsham, PA 19044
Telephone: (215) 443-8710
Telefax: (215) 443-8587

ARGUS RESEARCH
Charles River Laboratories
Discovery and Development Services

QUALITY ASSURANCE STATEMENT

Argus Protocol: 418-023P

Sponsor's Study Number: T-7485.11

Study Director: Raymond G. York, Ph.D., DABT

The protocol, critical phases, raw data and pilot report were inspected by the Quality Assurance Unit (QAU), to assure conformance with:

U.S. Environmental Protection Agency. Toxic Substances Control Act (TSCA); Good Laboratory Practice Standards; Final Rule. 40 CFR Part 792.

U.S. Environmental Protection Agency. Federal Insecticide, Fungicide and Rodenticide Act (FIFRA); Good Laboratory Practice Standards; Final Rule. 40 CFR Part 160.

Organization for Economic Cooperation and Development (1998). The Revised OECD Principles of Good Laboratory Practices [C(97)186/Final].

Japanese Ministry of Agriculture, Forestry and Fisheries (1984). Good Laboratory Practice Standards. 59 NohSan No. 3850.

The undersigned indicate that the report is an accurate representation of the raw data. Data provided by the Sponsor or a subcontractor were not audited by the Primedica Argus Quality Assurance Unit.

The QAU inspection and report audit dates are listed below:

Inspection Phase	Inspection Date(s)	Date(s) Findings Submitted to Study Director	Date(s) Findings Submitted to Management
Protocol	21 DEC 00	21 DEC 00	21 DEC 00
Test Substance Administration	05 JAN 01	17 JAN 01	17 JAN 01
Test Substance Formulation	11 JAN 01	11 JAN 01	11 JAN 01
Caesarean-Sectioning	16 JAN 01	17 JAN 01	17 JAN 01
In-Life Raw Data	29-31 JAN 01	31 JAN 01	31 JAN 01
Formulation Data	21 FEB 01	21 FEB 01	21 FEB 01
Report Tables	21,22 MAR 01	22 MAR 01	22 MAR 01
Report Text	27 MAR 01	27 MAR 01	27 MAR 01

Cynthia M Kelsch 15 Oct 03

for Matthew J. Vaneman, B.S. Date
Senior Manager, Regulatory Compliance