Perfluorooctanesulfonate:

Complete Cross-Fostering Study
in Rats + Serum Analytical

FINAL REPORT

PROTOCOL 418-014

ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS

SPONSOR'S STUDY NUMBER: T-6295.13

FINAL REPORT DATE: 23 JULY 1999

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ARGUS RESEARCH LABORATORIES, INC.
PROTOCOL NUMBER: 418-014
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I. SUMMARY AND CONCLUSION

A. Methods[a]

Seventy-eight virgin female Crl:CD®BR VAF/Plus® (Sprague-Dawley) rats were assigned to two dosage groups (Groups I and II), 42 rats in the control group and 36 rats in the treated group. The rats were administered the test article, PFOS (FC-95), or the vehicle, 0.5% Tween® 80, orally (via gavage), once daily beginning 42 days before cohabitation through day 21 postpartum (DL 21). The dosage volume was 5 mL/kg. Dosages were adjusted daily for body weight changes and given at approximately the same time each day.

Rats were assigned to cross-fostering or pharmacokinetic sample collection depending on the order of delivery and the availability of rats for cross-fostering. Twenty-five litters per dosage group were assigned to cross-fostering on DL 1. The litters were assigned such that four subsets were obtained among the two dosage groups as described in the table below.

Dosage Group	Number of Mated Female Rats	Dosage (mg/kg/day)	Number of Litters Reassigned	Reassigned Litter Type (Dam Treatment)	Subset Number
I	13	0 (Vehicle)	13	Treated	A
I	12	0 (Vehicle)	12	Untreated	B
II	12	1.6	12	Treated	C
II	13	1.6	13	Untreated	D

Eight female rats from the control group and two female rats from the treated group were assigned to pharmacokinetic sample collection following delivery. These rats were not cross-fostered.

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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 APPENDIX C (PROTOCOL AND AMENDMENT).

A.1. Fo Generation Rats Assigned to Cross-Fostering:

The Fo generation female rats were observed for viability at least twice each day of the study and for clinical observations of effects of the test article, abortions, premature deliveries and/or deaths before and approximately one hour postdosage. Body weights were recorded daily during the dosage period and at sacrifice. Feed consumption values were recorded weekly to cohabitation, daily during the gestation period and on DLs 1, 4, 7, 10 and 14.

The female rats were evaluated for duration of gestation, length of parturition, litter sizes and pup viability at birth. Pups that either appeared stillborn or that died before initial examination of the litter for viability were examined for vital status at birth. Maternal behavior of the dams was evaluated daily when the pups were examined during the 21-day postpartum period. Observed maternal behavior was recorded on DLs 1, 4, 7, 14 and 21.

Twenty-four-hour urine and fecal samples were collected from DLs 21 to 22 and blood samples were collected on DL 22, via the inferior vena cava, from the maternal rats. The blood samples were centrifuged. The urine and fecal samples and the serum were shipped to the Sponsor.

All Fo generation rats assigned to cross-fostering were sacrificed on DL 22 and a gross necropsy of the thoracic, abdominal and pelvic viscera was performed. The number and distribution of implantation sites were recorded. A liver section (right lateral lobe) from each dam was collected and shipped to the Sponsor.

Rats that did not deliver a litter were sacrificed on DG 25 and examined for gross lesions. A blood sample was collected prior to sacrifice via the inferior vena cava; samples were centrifuged and serum samples were shipped to the Sponsor. A liver section (right lateral lobe) from each dam was retained and shipped to the Sponsor. Dams with no surviving pups were sacrificed after the last pup was found dead, missing or presumed cannibalized.

A.2. F1 Generation Pups Assigned to Cross-Fostering:

Day 1 of lactation (postpartum) was defined as the day of birth. Each litter was evaluated for viability at least twice each day of the postpartum period. The pups present in each litter were counted once each day. Physical signs were recorded for the pups once each day during the postpartum period. Pup body weights were recorded on DLs 1 (birth), 4, 7, 14 and 21 and at sacrifice.

Pups found dead or sacrificed because of moribundity were examined for gross lesions and for the cause of death or the moribund condition. For all pups found dead on DLs 2 to 4, the lungs and the liver were preserved. Pups with gross

lesions found on DLs 2 to 4 were preserved and for pups found dead on DLs 5 to 21, the lungs, liver and gross lesions were preserved.
On DL 4, cross-fostered F1 generation litters were culled to five male and five female pups per litter, where possible. Pups with gross lesions were preserved. The lungs and the liver were preserved. The lungs and the liver were collected from the first ten culled pups from each dosage group (irrespective of litter) from each dosage group on each day (control pool only on DL 1). The lungs and the liver were retained. Remaining culled pups were sacrificed and discarded without evaluation.

On DL 21, all pups were sacrificed via decapitation and examined for gross lesions. Gross lesions were retained. Six litters per subset were randomly selected for collection of pooled samples (per litter) of blood and liver. Blood samples were collected via the inferior vena cava from each pup, pooled (per litter) and the samples were centrifuged. The serum samples were shipped to the Sponsor.

A.3. <u>Fo Generation Rats Assigned to Pharmacokinetic Sample Collection</u>:

Viability and clinical observations, body weights, feed consumption values and delivery observations were performed as previously described for Fo generation dams assigned to cross-fostering.

Pharmacokinetic samples were collected from eight and two Fo generation rats in Groups I and II, respectively, on DL 14. Milk samples were collected approximately two to six hours postdosage on DL 14. The samples were shipped to the Sponsor. Following completion of milk sample collection, female rats were sacrificed and a gross necropsy of the thoracic, abdominal and pelvic viscera was performed. The number and distribution of implantation sites was recorded. Blood samples were collected via the inferior vena cava and centrifuged and the serum was shipped to the Sponsor. A liver section and the milk-secreting glands from the axillary, thoracic, abdominal and inguinal regions of each dam (left side only) were collected and shipped to the Sponsor.

A.4. <u>F1 Generation Pups Assigned to Pharmacokinetic Sample Collection</u>:

Viability and clinical observations, body weights and litter observations were performed as previously described for F1 generation pups assigned to cross-fostering. On DL 14, litters assigned to the pharmacokinetic sample collection were sacrificed and blood samples were collected via the inferior vena cava from each pup, pooled (per litter), centrifuged and the serum was shipped to the Sponsor. The liver from each pup was collected, pooled (per litter), and shipped to the Sponsor.

B. Results

All Fo generation female rats survived to scheduled sacrifice. All adverse clinical and necropsy observations were considered unrelated to the administration of PFOS.

Body weight gains were reduced in the 1.6 mg/kg/day dosage group during the precohabitation and gestation periods, as compared to the control group values. Maternal body weight gains were variable throughout the lactation period and body weight gains for the entire lactation period were generally comparable among the four cross-fostered subsets. Absolute body weights were slightly reduced in the 1.6 mg/kg/day dosage group beginning at the end of the precohabitation period and continuing through the gestation and lactation periods.

Absolute and relative feed consumption values were generally reduced for rats administered the 1.6 mg/kg/day dosage of PFOS during the precohabitation, gestation and lactation periods, as compared to the control group values.

The duration of gestation tended to be reduced in the 1.6 mg/kg/day dosage group. As observed in a previously conducted study (Argus Research Laboratories, Inc., Protocol 418-008), this reduction was associated with minimal preimplantation loss; the average number of implantation sites per dam was slightly reduced, resulting in a slightly reduced delivered litter size. The duration of delivery per pup (in minutes) tended to be reduced in the 1.6 mg/kg/day dosage group. The live litter size before cross-fostering in the 1.6 mg/kg/day dosage group was also slightly reduced. The gestation index was 100% in each dosage group; all pregnant rats delivered live offspring.

Pup mortality was greatest in pups from test article-treated dams fostered by test article-treated dams (subset C). Pup mortality was also increased in pups from test article-treated dams fostered by vehicle-treated dams (subset A). As a result of these increases in pup mortality, the viability indices (number of live pups on DL 4 preculling/number of pups cross-fostered DL1) were reduced, and numbers of surviving pups per litter and live litter sizes at weighing were reduced on DL 4 preculling in these two subsets. Pup mortality in pups from vehicle-treated dams fostered by test article-treated dams (subset D) was comparable to that in pups from vehicle-treated dams fostered by vehicle-treated dams (subset B). These observations indicate that *in utero* exposure to the test article is responsible for pup mortality, and that potential exposure to the test article via maternal milk did not adversely affect the viability of the pups. Pup body weights were reduced on DL 1 in both subsets of dams administered PFOS (subsets C and D), as compared to pup body weights in the subsets of dams administered the vehicle (subsets A and B). Potential exposure to the test article via maternal milk after DL1 reduced pup body weights, regardless of *in utero* exposure to the

test article or vehicle. After DL 1, pup body weights were somewhat reduced in subsets D (pups from vehicle-treated dams fostered by test article-treated dams) and A (pups from test article-treated dams fostered by vehicle-treated dams), as compared to the pups from vehicle-treated dams cross fostered to vehicle-treated dams (subset B). After DL 1, pup body weight reductions were greatest in subset C (pups from test article-treated dams fostered by test article-treated dams).

Two litters in subset A (pups from test article-treated dams cross-fostered to vehicle-treated dams) and one litter in subset C (pups from test article-treated dams cross-fostered with test article-treated dams) had pups that did not nurse; pup mortality was greatest in these two subsets. There was no milk in the stomach of 57.1%, 100% and 87.0% of the pups that were found dead and necropsied in subsets A, C and D, respectively.

Evaluation of the livers of pups that died or were sacrificed on DL 1 by electron microscopy revealed increased numbers of peroxisomes within hepatocytes of pups from dams treated with 1.6 mg/kg/day PFOS, compared with controls. Quantitation of peroxisomes indicated slightly more than twice the number of peroxisomes in treated pups. Differences in cellular membranes or mitochondria were not discernible between control and treated pups in the samples examined. Evaluation of the lungs of pups that died or were sacrificed on DL 1 with electron microscopy revealed Type II pneumocytes containing lamellar bodies in both control and 1.6 mg/kg/day dosage group pups, with an increased number of Type II pneumocytes and lamellar bodies in lungs from treated pups. Although some lamellar material (surfactant) was identifiable within alveolar lumina, no significant difference was noted between the control group and 1.6 mg/kg/day dosage group.

C. Conclusion

The 1.6 mg/kg/day dosage of PFOS caused reductions in body weight gain and reduced feed consumption values for the Fo generation dams, as occurred in a previous multigeneration study with the test article (Argus Research Laboratories, Inc., Protocol 418-008). As previously observed, the 1.6 mg/kg/day dosage of PFOS administered to the Fo generation dams in this study also reduced the durations of gestation and parturition, caused preimplantation loss and reductions in litter size and pup growth.

Cross-fostering of pups from test article treated dams and vehicle treated dams revealed that the effects on pup mortality that occurred in the previously conducted study (418-008), can be attributed to *in utero* exposure to the test article, and that potential exposure to the test article via maternal milk did not adversely affect the viability of the pups. Exposure to the test article via both *in utero* exposure and maternal milk caused reductions in pup growth.

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

23-JUL-99

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

23-JUL-99

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

II. DESCRIPTION OF TEST PROCEDURES

A. Conduct of Study:

A.1. Sponsor:

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

A.2. Testing Facility:

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

A.3. Study Number:

418-014

A.4. Sponsor's Study Number:

T-6295.13

A.5. Purpose of the Study:

The purpose of this study was to evaluate survival of F1 generation pups following PFOS treatment of Crl:CD®BR VAF/Plus® Fo generation female rats during premating, gestation and lactation. F1 generation pups were cross-fostered during the lactation period to differentiate between effects on pups exposed to the test article *in utero* and pups exposed to the test article via maternal milk. Selected pharmacokinetic samples were collected from Fo generation female rats and F1 generation pups.

A.6. Study Design:

The requirements of the U.S. Food and Drug Administration (FDA)[1] were used as the basis of study design.

A.7. Regulatory Compliance:

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

inspections during the conduct of this study are documented and have been provided to the Study Director and the Testing Facility Management.

A.8. Ownership of the Study:

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

A.9. Study Monitor:

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

A.10. Alternate Study Monitor:

Andrew M. Seacat, Ph.D.

A.11. Study Director:

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

A.12. Technical Performance:

John F. Barnett, B.S. (Director of Laboratory Operations)
Margaret M. Martin (Research Associate)
Corrie L. Pabst (Quality Control Associate)

A.13. Report Preparation:

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

A.14. Report Review:

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

A.15. Date Protocol Signed:

23 October 1998

A.16. Dates of Technical Performance:

Rat Arrival	27 OCT 98
Dosage Period (42 days before cohabitation until DL[a] 21)	02 NOV 98 - 28 JAN 99
Cohabitation Period	13 DEC 98 PM - 19 DEC 98 AM
Day 0 of Presumed Gestation (DG 0)	14 DEC 98 - 19 DEC 98
Delivery Period	04 JAN 99 - 09 JAN 99
DL 1 Culling (Control Pool)	04 JAN 99 - 09 JAN 99
DL 4 Culling (Cross-Fostered Litters)	08 JAN 99 - 11 JAN 99
DG 25 Sacrifice	08 JAN 99 - 12 JAN 99
DL 14 Pharmacokinetic Group Sacrifice	17 JAN 99 - 22 JAN 99
F1 Generation Pups Sacrifice (DL 21)	25 JAN 99 - 28 JAN 99
Fo Generation Dams Sacrifice (DL 22)	26 JAN 99 - 29 JAN 99

A.17. Records Maintained:

The original report, raw data and reserve samples of the bulk test article and vehicle components are retained in the archives of Argus Research Laboratories, Inc. Any preserved tissues are retained in the archives of the Testing Facility for one year after the mailing of the draft final report, after which the Sponsor will decide their final disposition. All unused prepared test article formulations were discarded at the Testing Facility. Unused bulk test article was returned to the Study Monitor.

B. Test Article Information:

B.1. Description:

PFOS (FC-95) - a light-colored powder

B.2. Lot/Batch Number:

217 (Expiration date: May 2000)

B.3. Date Received and Storage Conditions:

The test article was received on 21 October 1998, and stored at room temperature.

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a. DL is used as an abbreviation for day of lactation or day postpartum.

B.4. Special Handling Instructions:

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

B.5. Analysis of Activity:

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

C. Vehicle Information:

C.1. Description:

0.5% Tween® 80 in Reverse Osmosis Membrane Processed Deionized Water (R.O. Deionized Water)

C.2. Lot Numbers:

Tween® 80 - M03H05, L06662 and M29477

C.3. Dates Received and Storage Conditions:

The Tween® 80 was received on 3 December 1998 (lot M03H05), 1 September 1998 (lot L06662) and 17 September 1998 (lot M29477), from J.T. Baker, Phillipsburg, New Jersey, and was stored at room temperature. The R.O. deionized water is available from a continuous source at the Testing Facility and is maintained at room temperature.

C.4. Special Handling Instructions:

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

C.5. Analysis of Purity:

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

D. Test Article Preparation and Storage Conditions:

Suspensions were prepared daily at the Testing Facility at concentrations of 0 and 0.32 mg/mL. Records are maintained in the raw data to document how the test article formulations were prepared. Prepared suspensions were stored at room temperature.

D.1. Sample Information:

Sample Type	Size	Date Retained	Shipping/Storage Conditions	Shipped To	Date Shipped
Concentration (all levels)	2 mL[a]	01 NOV 98 27 JAN 99	Frozen on dry ice	Sponsor	02 NOV 98 27 JAN 99
Test Article Reserve	1 g	28 OCT 98	Room temperature	Testing Facility Archives	25 NOV 98
Vehicle Components Reserve					
R.O. Deionized Water	5 mL	28 OCT 98	Room temperature	Testing Facility Archives	25 NOV 98
Tween® 80					
Lot L06662	5 mL	28 OCT 98			25 NOV 98
Lot M29477	5 mL	10 NOV 98			25 NOV 98
Lot M03H05	5 mL	09 DEC 98			27 JAN 99

a. Duplicate samples were taken from the first and last preparation on the day prepared. One set of samples was sent for analysis; the remaining samples were retained at the Testing Facility as backups. Backup samples were stored (-70°C or below) and will be discarded at the Testing Facility upon request of the Sponsor.

D.2. Analytical Results:

Data verifying the stability of the test article in the vehicle for 48 hours under the conditions of administration are on file with the Sponsor. Homogeneity of the prepared formulations is on file with the Sponsor. Results of the concentration analyses have not been received.

E. Test System:

E.1. Species:

Rat

E.2. Strain:

Crl:CD®BR VAF/Plus® (Sprague-Dawley)

E.3. Supplier (Source):

Charles River Laboratories, Inc., Portgage, Michigan

E.4. Sex:

Female (Male rats of the same source and strain were used only as breeders and were not considered part of the Test System).

E.5. Rationale for Test System:

The Crl:CD®BR VAF/Plus® (Sprague-Dawley) rat was selected as the Test System because: 1) this strain of rat was used in the reproductive and developmental toxicity studies; 2) historical data and experience exist at the Testing Facility[5-7]; and 3) the test article is pharmacologically active in the species and strain.

E.6. Test System Data:

Number of Rats	86
Approximate Date of Birth	23 AUG 98
Approximate Age at Arrival	66 days
Weight (g) on the Day after Arrival	179 - 226
Weight (g) at Study Assignment	200 - 244

E.7. Breeder Male Rat Data:

Number of Rats	110
Approximate Date of Birth	13 JAN 98
Approximate Age at Arrival	77 days
Weight (g) on the Day After Arrival	317 - 352
Weight (g) at Cohabitation	514 - 866

E.8. Method of Randomization:

Upon arrival, male and female rats were assigned to individual housing on the basis of computer-generated random units. After acclimation, 78 virgin female rats were selected for study on the basis of physical appearance and body weights recorded during acclimation. The female rats were assigned to dosage groups (42 in the control group and 36 in the treated group) based on computer-generated (weight-ordered) randomization procedures.

Within each dosage group, consecutive order was used to assign female rats to cohabitation with breeder male rats, one male rat per female rat. Rats were assigned to cross-fostering or pharmacokinetic collection depending on the order

of delivery and the availability of rats for cross-fostering. Eight female rats from the control group and two female rats from the treated group were designated for pharmacokinetic sample collection following delivery; these rats were not cross-fostered[a].

Twenty-five litters per dosage group were cross-fostered on DL 1[b]. The litters were assigned such that four subsets were obtained among the two dosage groups, as described in the table below. Subset assignments were made based on order of deliveries.

Dosage Group	Number of Mated Female Rats	Dosage (mg/kg/day)	Number of Litters Reassigned	Reassigned Litter Type (Dam Treatment)	Subset Number
I	13	0 (Vehicle)	13	Treated	A
I	12	0 (Vehicle)	12	Untreated	B
II	12	1.6	12	Treated	C
II	13	1.6	13	Untreated	D

On DL 4, cross-fostered litters were culled to five male and five female pups per litter, where possible, using a table of random units.

E.9. System of Identification:

E.9.a. Fo Generation Rats:

Rats were permanently identified using Monel® self-piercing ear tag (Gey Band and Tag Co., Inc., No. MSPT 20101). Male rats were given unique permanent identification numbers upon assignment to the Testing Facility's breeder male rat population. Female rats were assigned temporary numbers at receipt and given unique permanent identification numbers when assigned to the study. Cage tags were marked with the study number, permanent rat number, sex, test article identification and dosage level.

E.9.b. F1 Generation Pups:

Pups were not individually identified during lactation; all parameters were evaluated in terms of the litter.

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a. See APPENDIX D (DEVIATIONS FROM THE PROTOCOL AND THE STANDARD OPERATING PROCEDURES OF THE TESTING FACILITY), items 1 and 2.

b. See APPENDIX D, item 3.

F. Husbandry:

F.1. Research Facility Registration:

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

F.2. Study Rooms:

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

F.3. Housing:

Fo generation rats were individually housed in stainless steel, wire-bottomed cages, except during the cohabitation and postpartum periods. During the cohabitation period, each pair of rats was housed in the male rat's cage. Beginning no later than DG 20, Fo generation female rats were individually housed in nesting boxes, except during the collection interval for urine and fecal samples. During this collection interval (DLs 21 to 22), the female rats were housed individually in metabolism cages. Each dam and assigned litter were housed in a common nesting box during the postpartum period. All cage sizes and housing conditions were in compliance with the *Guide for the Care and Use of Laboratory Animals*[8].

F.4. Lighting:

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

F.5. Sanitization:

Cage pan liners were changed approximately three times each week. Cages were changed approximately every other week. Bedding was changed as often as necessary to keep the rats dry and clean.

F.6. Feed:

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

F.7. Feed Analysis:

Analyses were routinely performed by the feed supplier. No contaminants at levels exceeding the maximum concentration limits for certified feed or deviations from expected nutritional requirements were detected by these analyses. Copies of the results of the feed analyses are available in the raw data.

Neither the Sponsor nor the Study Director was aware of any potential contaminants likely to have been present in the feed that would have interfered with the results of this study.

F.8. Water:

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

F.9. Water Analysis:

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

Neither the Sponsor nor the Study Director was aware of any potential contaminants likely to have been present in the water that would have interfered with the results of this study.

F.10. Bedding:

Bed o'cobs® was used as the nesting material (Andersons' Industrial Products Groups, Maumee, Ohio).

F.11. Bedding Analysis:

Neither the Sponsor nor the Study Director was aware of any potential contaminants likely to have been present in the bedding that would have interfered with the results of this study. Analyses for possible contamination are conducted annually and documented in the raw data.

G. Methods:

G.1. Dosage Administration:

Dosage Group	Dosage (mg/kg/day)[a]	Concentration (mg/mL)	Dosage Volume (mL/kg)
I	0 (Vehicle)	0	5
II	1.6	0.32	5

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

Dosage Group	Rats Dosed Until Cohabitation		Rats Assigned to Pharmacokinetic Evaluation	
	Number of Rats	Assigned Numbers	Number of Rats	Assigned Numbers
I	42	18901 - 18942	8	18910, 18911, 18913, 18915, 18926, 18927, 18939, 18940
II	36	18943 - 18978	2	18956, 18971

Dosage Group	Subset Number	Assigned Dam and Litter Numbers[a]	
		Dams	Litters
I	A	18903, 18907, 18908, 18909, 18918, 18920, 18924, 18929, 18934, 18936, 18937, 18941, 18942	18976, 18963, 18953, 18961, 18946, 18952, 18972, 18950, 18959, 18977, 18958, 18951, 18965
I	B	18901, 18904, 18906, 18912, 18917, 18919, 18923, 18922, 18935, 18938, 18932, 18931	18931, 18932, 18938, 18935, 18922, 18923, 18919, 18917, 18912, 18906, 18904, 18901
II	C	18943, 18947, 18948, 18957, 18960, 18964, 18967, 18974, 18969, 18970, 18973, 18968	18968, 18973, 18970, 18969, 18974, 18967, 18964, 18960, 18957, 18948, 18947, 18943
II	D	18976, 18963, 18953, 18961, 18946, 18952, 18972, 18950, 18959, 18977, 18958, 18951, 18965	18903, 18907, 18908, 18909, 18918, 18920, 18924, 18929, 18934, 18936, 18937, 18941, 18942

a. Dams and their cross-fostered litters are listed in consecutive order.

G.2. Rationale for Dosage Selection:

Dosages were selected on the basis of a previous two-generation study conducted with the test article (Argus Research Laboratories, Inc., Protocol 418-008). In this study the Fo generation maternal and paternal no-observable-effect-level (NOEL) of PFOS was 0.1 mg/kg/day (0.4 mg/kg/day and higher dosages caused reductions in body weight gain and reduced feed consumption values).

The Fo generation reproductive NOEL was greater than 3.2 mg/kg/day; no effects on mating, fertility or estrous cycling occurred. The NOEL for viability and growth in the F1 generation offspring was 0.4 mg/kg/day (1.6 mg/kg/day and higher dosages caused preimplantation loss and reductions in litter size, pup viability, growth and survival).

The F1 generation maternal and paternal NOEL of PFOS was 0.1 mg/kg/day (0.4 mg/kg/day dosage caused reductions in body weight gain and reduced feed consumption values). The F1 generation reproductive NOEL was greater than a dosage of 0.4 mg/kg/day; no effects on mating or fertility occurred. The NOEL for viability and growth in the F2 generation offspring was 0.1 mg/kg/day (0.4 mg/kg/day dosage caused stillbirths and reductions in litter size, pup viability, growth and survival).

G.3. Route of Administration:

Oral (gavage)

G.4. Rationale for Route of Administration:

The oral (gavage) route was selected for use because: 1) this was the route of administration in the developmental and reproductive toxicology studies; and 2) it is one of the possible routes of human exposure.

G.5. Frequency of Administration:

G.5.a. Fo Generation Female Rats:

Female rats were given the test article or the vehicle once daily beginning 42 days prior to cohabitation through DL 21. Dosages were adjusted daily for body weight changes and given at approximately the same time each day.

G.5.b. F1 Generation Pups:

F1 generation pups were not directly given the test article, but may have been possibly exposed to the test article during maternal gestation (*in utero* exposure) or via maternal milk during the lactation period.

G.6. Length of Study:

Approximately 3 months

G.7. Method of Study Performance:

G.7.a. Cohabitation and Cross-Fostering Procedures:

Twenty-five rats assigned to the control group were cohabited one day prior to cohabitation for rats assigned to the treated group and the cohabitation period consisted of a maximum of six days[a]. The cohabitation period for the remaining

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a. See APPENDIX D, item 4.

rats in the control group and the rats assigned to the treated group was a maximum of five days. During cohabitation, both control and PFOS-treated groups were co-housed with untreated male breeders, one male rat per one female rat. Female rats with spermatozoa observed in a smear of the vaginal contents and/or a copulatory plug observed *in situ* were considered to be at DG 0 and assigned to individual housing.

Several dams assigned to the control group that delivered on the first day of parturition occurred were allowed to deliver and retain their natural pups until needed for cross-fostering purposes. This provided a pool of control dams available for immediate cross-fostering of pups from PFOS-treated dams, thus preventing these pups from nursing from their PFOS-treated dams.

Starting with the deliveries of the dams on the second day, all pups were removed immediately (as soon as parturition was completed) from their respective dams and placed with either another dam assigned to the control group or a PFOS-treated dam. When a dam assigned to the control group was not available, then a dam from the control pool was used. The litter from that control pool dam was then sacrificed via decapitation.

This cross-fostering procedure resulted in four groups of 12 or 13 dams/pups, i.e., Control/PFOS (Subset A), Control/Control (Subset B), PFOS/PFOS (Subset C) and PFOS/Control (Subset D). This procedure allowed distinctions to be made between prenatal and postnatal effects of the continuous maternal PFOS treatment.

G.7.b. <u>Fo Generation Rats Assigned to Cross-Fostering</u>:

The Fo generation female rats were observed for viability at least twice each day of the study and for general appearance at least once during the acclimation period. The rats were also examined for clinical observations of effects of the test article, abortions, premature deliveries and/or deaths before and approximately one hour postdosage.

Body weights were recorded at least once during the acclimation period. Body weights were recorded daily during the dosage period and at sacrifice. Feed consumption values were recorded at least once during the acclimation period, weekly to cohabitation, daily during the presumed gestation period and on DLs 1, 4, 7, 10 and 14. Feed consumption was not tabulated after DL 14, when it was expected that the pups began to consume maternal feed.

The female rats were continually evaluated (24 hours per day) for clinical observations during parturition [performed under red light conditions during the dark period (time each pup was observed was recorded)], duration of gestation (DG 0 to the time the first pup was delivered), length of partuition (time of

observation of last pup minus the time of observation of the first pup divided by N-1 pups in each litter), litter sizes (defined as all pups delivered) and pup viability at birth. Pups that either appeared stillborn or that died before initial examination of the litter for viability were examined for vital status at birth. The lungs were removed and immersed in water. Pups with lungs that sank were considered stillborn; pups with lungs that floated were considered liveborn and to have died shortly after birth. Maternal behavior of the dams was evaluated daily when the pups were examined during the 21-day postpartum period. Observed maternal behavior was recorded on DLs 1, 4, 7, 14 and 21. Deviations from expected maternal behavior were recorded, if and when present, on all other days during the postpartum period.

Fo generation female rats were housed individually in metabolism cages for collection of urine and fecal samples from DLs 21 to 22. Following the 24-hour collection interval, samples were collected into centrifuge tubes, placed on dry ice, stored frozen (-70°C or below) and shipped to the Sponsor for analysis.

On DL 22, blood samples (approximately 4 mL each) were collected from the maternal rats via the inferior vena cava and transferred into serum separator tubes after removal from metabolism caging. The samples were spun in a refrigerated centrifuge. The serum was transferred into polypropylene tubes labeled with the study number, rat identification, date of collection, study day and collection timepoint. All samples were immediately frozen on dry ice, stored frozen (-70°C or below) and shipped to the Sponsor for analysis.

G.7.c. <u>F1 Generation Pups Assigned to Cross-Fostering</u>:

Day 1 of lactation (postpartum) was defined as the day of birth and was also the first day on which all pups in a litter were individually weighed.

Each litter was evaluated for viability at least twice each day of the postpartum period. Dead pups observed at these times were removed from the nesting box.

The pups present in each litter were counted once each day. Physical signs (including gross external physical anomalies) were recorded for the pups once each day during the postpartum period. Pup body weights were recorded on DLs 1 (birth), 4, 7, 14 and 21 and at sacrifice.

On DL 4, cross-fostered F1 generation litters were culled to five male and five female pups per litter, where possible.

G.7.d. Fo Generation Rats Assigned to Pharmacokinetic Sample Collection:

Viability and clinical observations, body weights, feed consumption values and delivery observations were performed, as previously described for Fo generation dams assigned to cross-fostering.

Blood, milk and liver samples were collected from eight and two Fo generation rats in Groups I and II, respectively, designated for pharmacokinetic sample collection per dosage group on DL 14. Milk samples were collected approximately two to six hours postdosage on DL 14. Each dam was removed from the nesting box and individually housed for approximately four hours. The dam was injected intravenously with one unit of oxytocin (20 USP units/mL, Lot Number 52064, expiration date July, 2000, manufactured by Osborn) approximately five minutes before milk samples (at least 100 µL per sample) were collected. The samples were immediately frozen on dry ice, stored frozen (-70°C or below) and shipped to the Sponsor.

Following milk sample collection, blood samples (approximately 4 mL each) were collected from the maternal rats via the inferior vena cava and transferred into serum separator tubes. The samples were spun in a refrigerated centrifuge. The serum was transferred into polypropylene tubes labeled with the study number, rat identification, date of collection, study day and collection timepoint. All samples were immediately frozen on dry ice, stored frozen (-70°C or below) and shipped to the Sponsor.

Following collection of milk and blood samples, a liver section (right lateral lobe) and the milk-secreting glands from the axillary, thoracic, abdominal and inguinal regions of each dam (left side only) were collected, stored frozen (-70°C or below) and shipped to the Sponsor.

G.7.e. F1 Generation Pups Assigned to Pharmacokinetic Sample Collection:

Viability and clinical observations, body weight and litter observations were performed as previously described for F1 generaton pups assigned to cross-fostering.

Caps and labeled tubes were weighed (combined weight, to the nearest 0.001 g) before and after retention of pooled pup samples for subsequent use in pharmacokinetic analyses.

Blood samples were collected via the inferior vena cava from each pup on DL 14, pooled (per litter) and transferred into serum separator tubes. The samples were spun in a refrigerated centrifuge. The serum was transferred into polypropylene tubes labeled with the study number, pup identification, date of

collection, study day and collection timepoint. All samples were immediately frozen on dry ice, stored frozen (-70°C or below) and shipped to the Sponsor for analysis.

The liver from each pup was collected, pooled (per litter), stored frozen (-70°C or below) and shipped to the Sponsor for analysis.

H. Gross Necropsy[a]:

All Fo generation rats were sacrificed by carbon dioxide asphyxiation, and a gross necropsy of the thoracic, abdominal and pelvic viscera was performed. Gross lesions were retained in neutral buffered 10% formalin for possible future evaluation. Representative photographs of maternal gross lesions are available in the raw data.

H.1. Fo Generation Rats:

The female rats were sacrificed on DL 22. The number and distribution of implantation sites were recorded. A liver section (right lateral lobe) from each dam was collected, stored frozen (-70°C or below) and shipped to the Sponsor for analysis.

Following completion of milk sample collection on DL 14, female rats assigned to pharmacokinetic collection were sacrificed. Blood and liver samples were collected as previously described. The number and distribution of implantation sites was recorded.

Rats that did not deliver a litter were sacrificed on DG 25 and examined for gross lesions. Uteri were stained with 10% ammonium sulfide to confirm the absence of implantation sites[9].

Dams with no surviving pups were sacrificed after the last pup was found dead, missing or presumed cannibalized. A blood sample (approximately 4 mL) was collected, prior to sacrifice, via the inferior vena cava and transferred into serum separator tubes. The samples were spun in a refrigerated centrifuge. The serum was transferred into a polypropylene tube labeled with study number, rat identification, date of collection, study day and collection timepoint. The samples were immediately frozen on dry ice, and stored frozen (-70°C or below) and

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a. A table of random units was used to select one Fo generation control group female rat and one F1 generation control group male and female pup from which all tissues examined at necropsy were retained, in order to provide control tissues for potential comparative histopathological evaluations.

shipped to the Sponsor for analysis. A liver section (right lateral lobe) from each dam was collected, stored frozen (-70°C or below) and shipped to the Sponsor for analysis.

H.2. F1 Generation Pups:

Pups that died before examination of the litter for pup viability were evaluated for vital status at birth, as previously described. Pups with gross lesions were preserved in Bouin's solution for possible future evaluation. The lungs were preserved in Bouin's solution, and the liver was preserved in neutral buffered 10% formalin for possible future evaluation.

Pups from dams assigned to the control pool and culled on DL 1 and all other pups culled on DL 4 were sacrificed via decapitation. The lungs and the liver were collected from the first ten culled pups from the control pool (irrespective of litter) and the first ten pups that were found dead (no autolysis) from each dosage group on DL 1. The lungs were retained in Bouin's solution, and the livers were retained in neutral buffered 10% formalin for possible future evaluation. Remaining culled pups were sacrificed and discarded without evaluation.

Pups found dead or sacrificed because of moribundity were examined for gross lesions and for the cause of death or the moribund condition. For all pups found dead on DLs 2 to 4, the lungs were preserved in Bouin's solution, and the liver was preserved in neutral buffered 10% formalin, for possible future evaluation. Pups with gross lesions found on DLs 2 to 4 were preserved in Bouin's solution for possible future evaluation. For all pups found dead on DLs 5 to 21, the lungs, liver and gross lesions were preserved in neutral buffered 10% formalin for possible future evaluation.

On DL 14, litters assigned to the pharmacokinetic sample collection and their respective dams were sacrificed by carbon dioxide asphyxiation. Individual, pooled samples (per litter) of blood and liver were collected as previously described. The pups were examined for gross lesions.

On DL 21, all pups were sacrificed via decapitation and examined for gross lesions. Gross lesions were retained in neutral buffered 10% formalin. Six litters per subset were randomly selected for collection of pooled samples (per litter) of blood and liver. Blood samples were collected via the inferior vena cava from each pup, pooled (per litter) and transferred into serum separator tubes. The samples were spun in a refrigerated centrifuge. The serum was transferred to polypropylene tubes labeled with the study number, rat identification, date of collection, study day and collection timepoint. All samples were immediately frozen on dry ice, stored frozen (-70°C or below) and shipped to the Sponsor for analysis.

All pups selected for continued observation were sacrificed via decapitation and examined for gross lesions.

I. Statistical Analyses:

Averages and percentages were calculated. Litter values were used where appropriate.

III. RESULTS

A. Mortality, Clinical and Necropsy Observations (Summaries - Tables 1 and 2; Individual Data - Tables 19 and 20)

All rats survived to scheduled sacrifice.

All adverse clinical observations during the precohabitation, gestation and lactation periods were considered unrelated to the test article because the incidences were not dosage-dependent and/or the observations are commonly seen in rats in the laboratory environment. These observations included chromorhinorrhea, scaly tail, abrasion on the head, neck, tail and/or forelimb, missing, broken and/or misaligned incisors, localized alopecia on the head, limbs, neck and/or back, chromodacryorrhea, scab on the head or tail, dehydration, perineal hernia, broken or swollen forepaw digit and protruding xiphoid.

The only necropsy observation was an inguinal mass (presumed to be a galactocele) in one control group dam assigned to pharmacokinetic sample collection on lactation day 14 (DL 14).

B. Body Weights (Figures 1 and 2; Summaries - Tables 3 through 8; Individual Data – Tables 21 through 23)

Body weight gains during the precohabitation period were reduced as compared to the control group values, beginning on days 15 to 22 of the study (DSs 15 to 2) and continuing through DSs 29 to 36. Rats in both dosage groups lost weight on DSs 36 to 43; the body weight loss was greater in the 1.6 mg/kg/day dosage group. Although calculated for a seven-day interval, the weight losses generally occurred on days 42 to 43 of the study and were associated with movement of the male breeder rats into the animal room and mating activity in the animal room when the rats were cohabited on day 42. As a result of these changes, body weight gains for the entire precohabitation period (DSs 1 to 43) were reduced and absolute body weights were slightly reduced on DS 43 (96.6% of control) in the 1.6 mg/kg/day dosage group.

Maternal body weight gains continued to be reduced in the 1.6 mg/kg/day dosage group in the first two weeks of the gestation period (days 0 to 14 of gestation, DGs 0 to 14). As a result, body weight gains were reduced for the entire gestation period (DGs 0 to 20) in the 1.6 mg/kg/day dosage group. Maternal body weights tended to be reduced in the 1.6 mg/kg/day dosage group throughout gestation.

Reduced maternal body weights persisted in the two subsets of rats administered 1.6 mg/kg/day PFOS during the lactation period (subsets C and D),

as compared to the rats in the subsets administered the vehicle (subsets A and B). Lactation body weights had the expected degree of variability but were comparable between subsets A and B (vehicle control groups) and between subsets C and D (test article-treated groups). Maternal body weight gains for the entire lactation period (DLs 1 to 22) were essentially comparable among the four subsets.

C. Absolute (g/day) and Relative (g/kg/day) Feed Consumption Values (Summaries - Tables 9 through 14; Individual Data - Tables 24 through 26)

Absolute (g/day) and relative (g/kg/day) feed consumption values were generally reduced for rats administered the 1.6 mg/kg/day dosage of PFOS during the precohabitation, gestation and lactation periods, as compared to the control group values.

D. Natural Delivery and Litter Observations (Summaries - Tables 15 and 16; Individual Data - Tables 27 through 31)

D.1. Natural Delivery Observations

The duration of gestation tended to be reduced in the 1.6 mg/kg/day dosage group, both when the duration of gestation was calculated in whole days and to the nearest tenth of a day. As previously observed, this reduction was associated with minimal preimplantation loss; the average number of implantation sites per dam was slightly reduced, resulting in a slightly reduced delivered litter size. The duration of delivery per pup (in minutes) tended to be reduced in the 1.6 mg/kg/day dosage group. The live litter size before cross-fostering in the 1.6 mg/kg/day dosage group was also slightly reduced, an observation related to total litter size and associated with stillbirths.

The gestation index was 100% in each dosage group; all pregnant rats delivered live offspring.

D.2. Cross-Fostered Litter Observations

After cross-fostering on DL 1, live litter sizes were comparable among the four subsets.

Pup mortality was greatest in subset C (pups from test article-treated dams fostered by test article-treated dams); 19.2% of the pups were found dead or presumed cannibalized on DLs 2 to 4. Pup mortality was also increased in subset A (pups from test article-treated dams fostered by vehicle-treated dams) on DLs 2 to 4; 9.0% of these pups were found dead or presumed cannibalized. As a result of these increases in pup mortality, the viability indices (number of

live pups on DL 4 preculling/number of pups cross-fostered on DL1) were reduced, and numbers of surviving pups per litter and live litter sizes at weighing were reduced on DL 4 preculling in these two subsets. Pup mortality in subset D (pups from vehicle-treated dams fostered by test article-treated dams) was comparable to that in subset B (pups from vehicle-treated dams fostered by vehicle-treated dams). These observations indicate that *in utero* exposure to the test article is responsible for pup mortality, and that potential exposure to the test article via maternal milk did not adversely affect the viability of the pups.

Pup body weight/litter were reduced on DL 1 in both subsets of pups from dams administered PFOS (subsets A and C), as compared to pup body weights in the subsets of pups from dams administered the vehicle (subsets B and D). Potential exposure to the test article via maternal milk after DL1 reduced pup body weights, regardless of *in utero* exposure to the test article or vehicle. After DL 1, pup body weights were somewhat reduced in subsets D (pups from vehicle-treated dams fostered by test article-treated dams) and A (pups from test article-treated dams fostered by vehicle-treated dams), as compared to the pups from vehicle-treated dams fostered by vehicle-treated dams (subset B). After DL 1, pup body weight reductions were greatest in subset C (pups from test article-treated dams fostered by test article-treated dams).

Sex ratios and the lactation index (number of live pups on DL 21/number of live pups on DL 4 postculling) were comparable among the four cross-fostered subsets.

E. Clinical Observations from Birth to Day 21 Postpartum and Necropsy Observations (Summaries - Tables 17 and 18; Individual Data - Tables 32 and 33)

Two litters in subset A (pups from test article-treated dams fostered by vehicle-treated dams) and one litter in subset C (pups from test article-treated dams fostered by test article-treated dams) had pups that did not nurse; pup mortality was greatest in these two subsets. There was no milk in the stomach of 57.1%, 100% and 87.0% of the pups that were found dead and necropsied in subsets A, C and D, respectively.

All other clinical and necropsy observations in the F1 generation pups were considered unrelated to the test article because: 1) the incidences were not dosage-dependent; or 2) the observation occurred in only one litter. Clinical observations included black tip of tail, labored breathing, dark in color, missing hindpaw digit and bent tail. One pup in subset A had slight dilation of the renal pelvis at necropsy on DL 21.

F. Electron Microscopic Evaluation of Liver and Lung from Day 1 Postpartum Pups (APPENDIX G)

F.1. Liver

Ultrastructurally, there were increased numbers of peroxisomes within hepatocytes of pups from dams treated with 1.6 mg/kg/day PFOS, compared with controls. Quantitation of peroxisomes indicated slightly more than twice the number of peroxisomes in treated pups. Differences in cellular membranes or mitochondria were not discernible between control and treated pups in the samples examined.

F.2. Lung

Type II pneumocytes containing lamellar bodies were identified in both control and 1.6 mg/kg/day dosage group pups; however, there appeared to be an increased number of Type II pneumocytes and lamellar bodies in lungs from treated pups. Although some lamellar material (surfactant) was identifiable within alveolar lumina, no significant difference was noted between the control group and 1.6 mg/kg/day dosage group.

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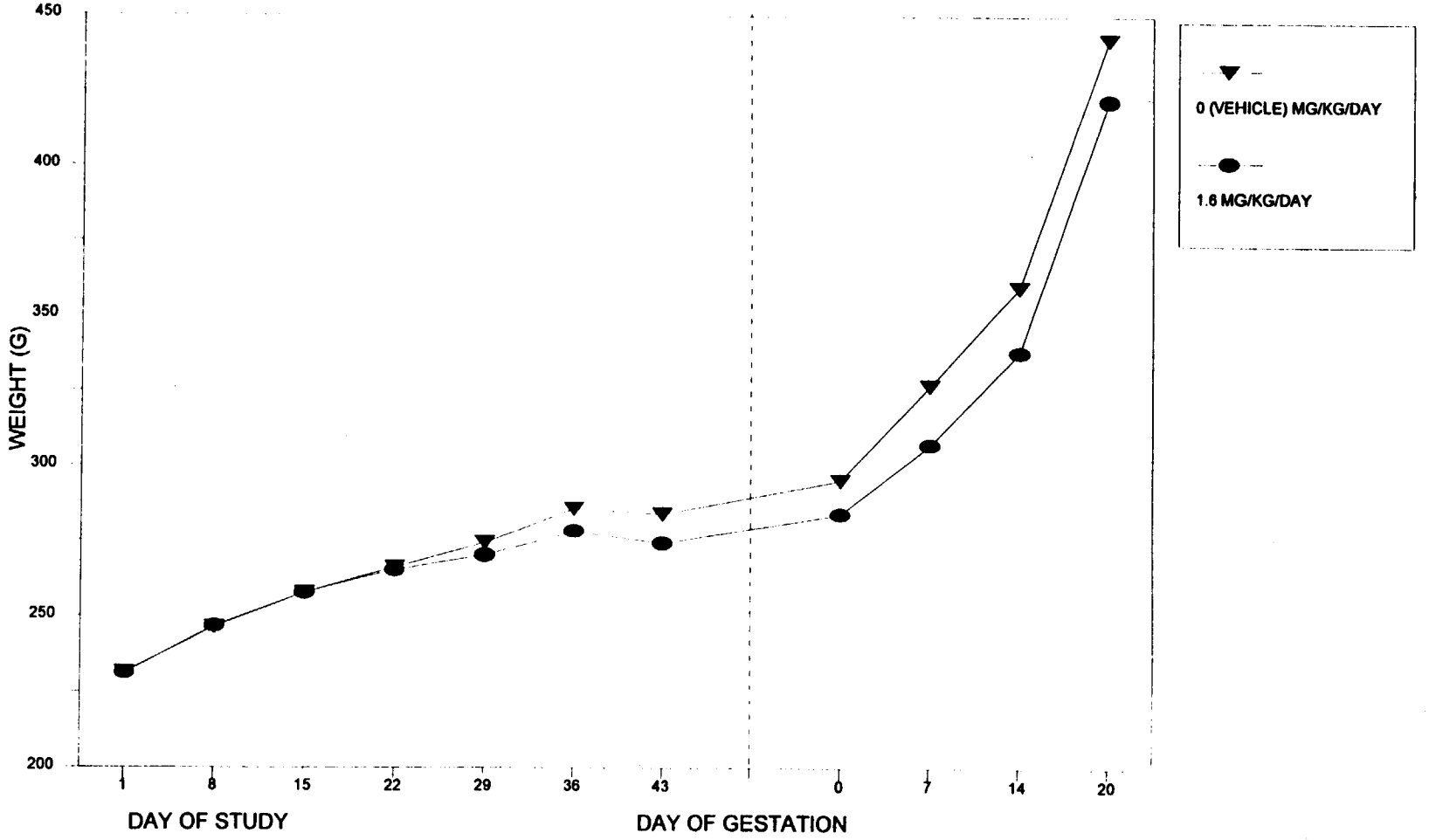
APPENDIX A

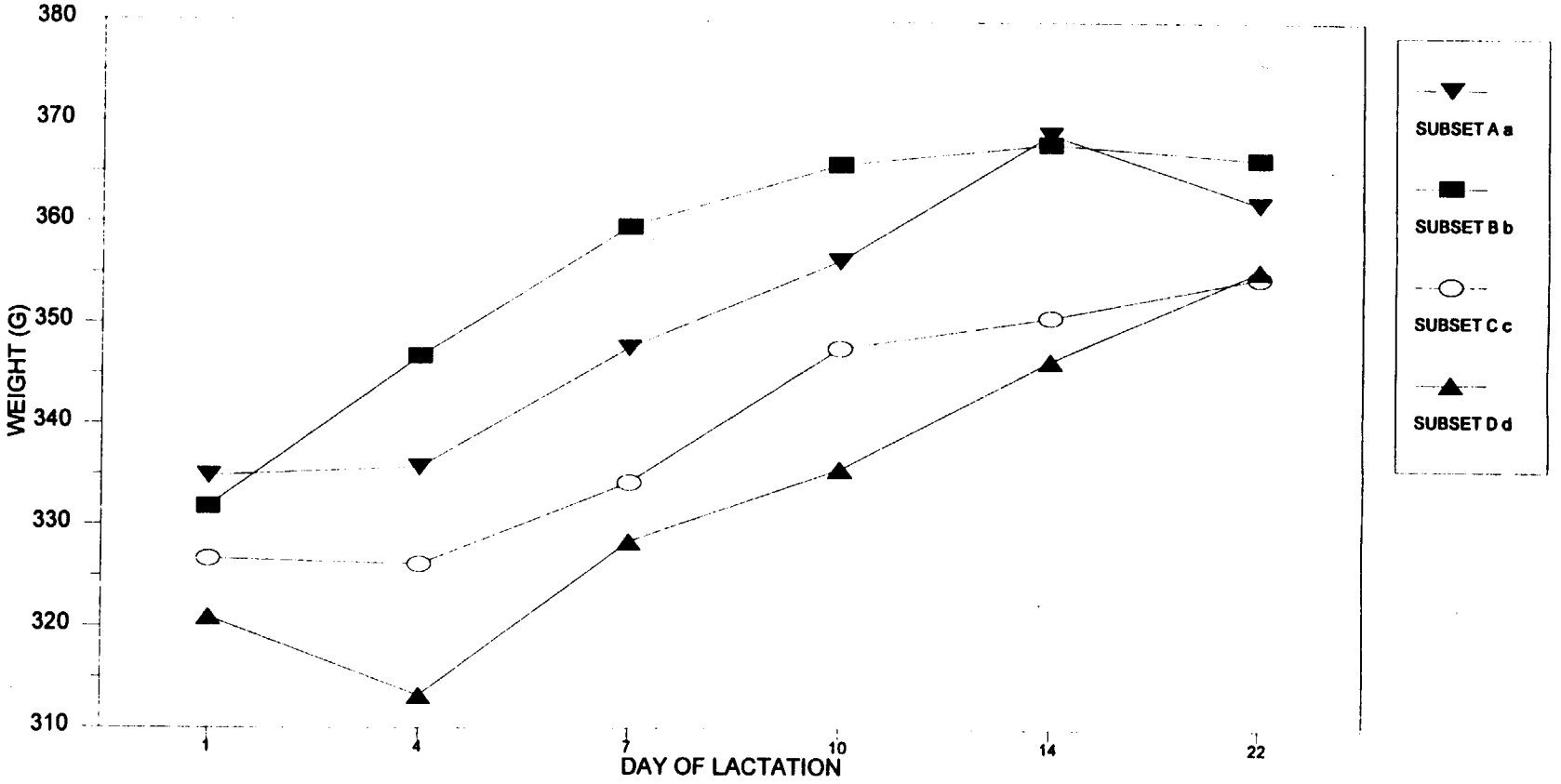
REPORT FIGURES

MATERNAL BODY WEIGHTS

Figure 1



MATERNAL BODY WEIGHTS
RATS ASSIGNED TO CROSS-FOSTERING
Figure 2



a. Vehicle control group dams cross fostered with 1.6 mg/kg/day dosage group litters.
b. Vehicle control group dams cross-fostered with vehicle control group litters.
c. 1.6 mg/kg/day dosage group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
d. 1.6 mg/kg/day dosage group dams cross-fostered with vehicle control group litters.

APPENDIX B

REPORT TABLES

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 1 (PAGE 1): CLINICAL OBSERVATIONS - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0 (VEHICLE)	II 1.6
PRECOHABITATION (DAY 1 TO 42 OF STUDY):a			
MAXIMUM POSSIBLE INCIDENCE		1764/ 42	1512/ 36
MORTALITY		0	0
CHROMORHINORRHEA		1/ 1	3/ 2
SCALY TAIL		0/ 0	35/ 1
ABRASION b		23/ 2	7/ 1
LOCALIZED ALOPECIA:	TOTAL	104/ 5	0/ 0
	HEAD	49/ 3	0/ 0
	LIMBS	57/ 2	0/ 0
	NECK	32/ 1	0/ 0
	BACK	11/ 1	0/ 0
INCISORS:	TOTAL	16/ 3	0/ 0
	MISALIGNED	14/ 2	0/ 0
	MISSING/BROKEN	2/ 1	0/ 0
CHROMODACRYORRHEA		5/ 1	0/ 0
HEAD: SCAB		2/ 1	0/ 0

MAXIMUM POSSIBLE INCIDENCE = (DAYS x RATS)/NUMBER OF RATS EXAMINED PER GROUP.
N/N = TOTAL NUMBER OF OBSERVATIONS/NUMBER OF RATS WITH OBSERVATION.
a. Day 42 of study was the first day of cohabitation for rats assigned from Group I.
b. Located on the head, neck, tail or left forelimb.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 1 (PAGE 2): CLINICAL OBSERVATIONS - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0 (VEHICLE)	II 1.6
PRESUMED GESTATION: a			
MAXIMUM POSSIBLE INCIDENCE		896/ 40	752/ 34
MORTALITY		0	0
LOCALIZED ALOPECIA:	TOTAL	21/ 2	50/ 4
	LIMBS	13/ 1	32/ 3
	NECK	0/ 0	18/ 1
	BACK	8/ 1	0/ 0
	UNDERSIDE	0/ 0	8/ 1
SCALY TAIL		0/ 0	21/ 1
INCISORS: MISALIGNED		39/ 2	0/ 0
CHROMORHINORRHEA		4/ 2	0/ 0
CHROMODACRYORRHEA		15/ 1	0/ 0
DEHYDRATION		1/ 1	0/ 0
PERINEAL HERNIA		1/ 1	0/ 0

MAXIMUM POSSIBLE INCIDENCE = (DAYS x RATS)/NUMBER OF RATS EXAMINED PER GROUP.
N/N = TOTAL NUMBER OF OBSERVATIONS/NUMBER OF RATS WITH OBSERVATION.
a. Restricted to rats with a confirmed mating date.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 1 (PAGE 3): CLINICAL OBSERVATIONS - SUMMARY - Fo GENERATION FEMALE RATS

RATS ASSIGNED TO CROSS-FOSTERING				
SUBSET	A	B	C	D
DOSAGE GROUP	I a	I b	II c	II d
DOSAGE (MG/KG/DAY)	0 (VEHICLE)	0 (VEHICLE)	1.6	1.6
LACTATION:				
MAXIMUM POSSIBLE INCIDENCE	286/ 13	264/ 12	246/ 12	267/ 13
MORTALITY	0	0	0	0
SCALY TAIL	0/ 0	0/ 0	0/ 0	22/ 1
RIGHT FOREPAW: THIRD DIGIT BROKEN	0/ 0	0/ 0	0/ 0	22/ 1
LOCALIZED ALOPECIA: LIMBS	0/ 0	0/ 0	0/ 0	7/ 1
PROTRUDING XIPHOID	0/ 0	16/ 1	0/ 0	3/ 1
TAIL: ABRASION	0/ 0	11/ 1	0/ 0	0/ 0
TAIL: SCAB	0/ 0	4/ 1	0/ 0	0/ 0
RIGHT FOREPAW: THIRD DIGIT SWOLLEN	0/ 0	2/ 1	0/ 0	0/ 0
INCISORS: MISALIGNED	22/ 1	0/ 0	0/ 0	0/ 0

MAXIMUM POSSIBLE INCIDENCE = (DAYS x RATS)/NUMBER OF RATS EXAMINED PER GROUP.
N/N = TOTAL NUMBER OF OBSERVATIONS/NUMBER OF RATS WITH OBSERVATION.
a. Vehicle control group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
b. Vehicle control group dams cross-fostered with vehicle control group litters.
c. 1.6 mg/kg/day dosage group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
d. 1.6 mg/kg/day dosage group dams cross-fostered with vehicle control group litters.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 2 (PAGE 1): NECROPSY OBSERVATIONS - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0 (VEHICLE)	II 1.6
RATS EXAMINED a	N	41b	36
MORTALITY	N	0	0
APPEARED NORMAL	N	40	36
LEFT INGUINAL AREA: MASS	N	1	0

a. Refer to the individual clinical observations table (Table B15) for external observations confirmed at necropsy.
b. Excludes values for dam 18933, which was discarded without further evaluation.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 3 (PAGE 1): BODY WEIGHTS - PRECOHABITATION - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0 (VEHICLE)	II 1.6
RATS TESTED	N	42	36
BODY WEIGHT (G)			
DAY 1	MEAN±S.D	231.4 ± 8.6	231.2 ± 9.2
DAY 8	MEAN±S.D	246.5 ± 10.0	246.8 ± 10.5
DAY 15	MEAN±S.D	257.9 ± 11.5	257.9 ± 14.1
DAY 22	MEAN±S.D	266.3 ± 14.2	265.4 ± 11.9
DAY 29	MEAN±S.D	274.7 ± 14.7	270.5 ± 12.7
DAY 36	MEAN±S.D	285.7 ± 16.5	278.3 ± 14.7
DAY 43a	MEAN±S.D	283.9 ± 12.2 [17]b	274.4 ± 15.9

DAY = DAY OF STUDY
[ ] = NUMBER OF VALUES AVERAGED
a. Last value recorded before cohabitation.
b. Excludes values for rats assigned to cohabitation on day 42 of study.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 4 (PAGE 1): BODY WEIGHT CHANGES - PRECOHABITATION - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0 (VEHICLE)	II 1.6
RATS TESTED	N	42	36
BODY WEIGHT CHANGE (G)			
DAYS 1 - 8	MEAN±S.D.	+15.1 ± 7.0	+15.6 ± 8.2
DAYS 8 - 15	MEAN±S.D.	+11.4 ± 6.3	+11.0 ± 7.5
DAYS 15 - 22	MEAN±S.D.	+8.4 ± 7.7	+7.5 ± 4.9
DAYS 22 - 29	MEAN±S.D.	+8.3 ± 4.8	+5.1 ± 5.9
DAYS 29 - 36	MEAN±S.D.	+11.0 ± 6.1	+7.8 ± 5.6
DAYS 36 - 43a	MEAN±S.D.	-2.6 ± 7.7 [17]b	-3.9 ± 6.2
DAYS 1 - 43a	MEAN±S.D.	+53.0 ± 11.4 [17]b	+43.2 ± 14.3

DAYS = DAYS OF STUDY
[ ] = NUMBER OF VALUES AVERAGED
a. Last value recorded before cohabitation.
b. Excludes values for rats assigned to cohabitation on day 42 of study.

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TABLE 5 (PAGE 1): MATERNAL BODY WEIGHTS - GESTATION - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0 (VEHICLE)	II 1.6
RATS TESTED	N	42	36
PREGNANT	N	35	27
MATERNAL BODY WEIGHT (G)			
DAY 0	MEAN±S.D.	295.1 ± 16.9	283.9 ± 14.2
DAY 7	MEAN±S.D.	326.8 ± 18.9	307.0 ± 16.2
DAY 14	MEAN±S.D.	359.5 ± 22.0	337.8 ± 17.6
DAY 20	MEAN±S.D.	442.0 ± 34.0	421.8 ± 25.5

DAY = DAY OF GESTATION

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TABLE 6 (PAGE 1): MATERNAL BODY WEIGHT CHANGES - GESTATION - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0 (VEHICLE)	II 1.6
RATS TESTED	N	42	36
PREGNANT	N	35	27
MATERNAL BODY WEIGHT CHANGE (G)			
DAYS 0 - 7	MEAN±S.D.	+31.7 ± 6.2	+23.1 ± 6.7
DAYS 7 - 14	MEAN±S.D.	+32.7 ± 7.4	+30.7 ± 8.7
DAYS 14 - 20	MEAN±S.D.	+82.5 ± 20.0	+84.1 ± 17.1
DAYS 0 - 20	MEAN±S.D.	+146.9 ± 24.8	+137.9 ± 19.9

DAYS = DAYS OF GESTATION

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TABLE 7 (PAGE 1): MATERNAL BODY WEIGHTS - LACTATION - SUMMARY - Fo GENERATION FEMALE RATS

SUBSET		A	B	C	D
DOSAGE GROUP		I a	I b	II c	II d
DOSAGE (MG/KG/DAY)		0 (VEHICLE)	0 (VEHICLE)	1.6	1.6
RATS ASSIGNED TO CROSS-FOSTERING	N	13	12	12	13
INCLUDED IN ANALYSES	N	11e	12	12	11e
MATERNAL BODY WEIGHT (G)					
DAY 1	MEAN±S.D.	334.8 ± 20.1	331.8 ± 29.9	326.6 ± 20.0	320.9 ± 20.5
DAY 4	MEAN±S.D.	335.7 ± 17.6	346.7 ± 29.5	326.1 ± 16.1 [11]f	313.2 ± 21.8
DAY 7	MEAN±S.D.	347.6 ± 11.7	359.6 ± 24.9	334.2 ± 18.2 [11]f	328.4 ± 19.0
DAY 10	MEAN±S.D.	356.3 ± 15.0	365.8 ± 26.8	347.6 ± 16.8 [11]f	335.6 ± 18.1
DAY 14	MEAN±S.D.	368.9 ± 10.5	367.9 ± 30.1	350.7 ± 18.3 [11]f	346.4 ± 20.3
DAY 22	MEAN±S.D.	362.0 ± 9.1	366.4 ± 26.0	354.7 ± 19.1	355.4 ± 18.6

DAY = DAY OF LACTATION
[ ] = NUMBER OF VALUES AVERAGED
a. Vehicle control group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
b. Vehicle control group dams cross-fostered with vehicle control litters.
c. 1.6 mg/kg/day dosage group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
d. 1.6 mg/kg/day dosage group dams cross-fostered with vehicle control group litters.
e. Excludes values for dams which had litters that were not cross-fostered.
f. Excludes values for dam 18974, which had no surviving pups on day 4 of lactation.
g. Excludes values that were associated with interrupted water access.

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TABLE 8 (PAGE 1): MATERNAL BODY WEIGHT CHANGES - LACTATION - SUMMARY - Fo GENERATION FEMALE RATS

SUBSET DOSAGE GROUP DOSAGE (MG/KG/DAY)		A I a 0 (VEHICLE)	B I b 0 (VEHICLE)	C II c 1.6	D II d 1.6
RATS ASSIGNED TO CROSS-FOSTERING	N	13	12	12	13
INCLUDED IN ANALYSES	N	11e	12	11f	11e
MATERNAL BODY WEIGHT CHANGE (G)					
DAYS 1 - 4	MEAN±S.D.	+0.9 ± 14.8	+14.9 ± 12.4	+3.0 ± 7.3	-7.7 ± 14.8
DAYS 4 - 7	MEAN±S.D.	+11.9 ± 10.7	+12.9 ± 13.0	+8.1 ± 6.7	+15.3 ± 11.0
DAYS 7 - 10	MEAN±S.D.	+8.6 ± 15.3	+6.2 ± 8.6	+13.4 ± 9.0	+7.2 ± 7.2
DAYS 10 - 14	MEAN±S.D.	+12.6 ± 16.6	+2.1 ± 13.7	+3.1 ± 9.1	+10.7 ± 9.1
DAYS 14 - 22	MEAN±S.D.	-6.9 ± 13.7	-1.5 ± 25.2	+4.0 ± 16.7	+9.0 ± 15.8
DAYS 1 - 22	MEAN±S.D.	+27.2 ± 15.1	+34.7 ± 17.5	+31.6 ± 14.6	+34.4 ± 13.5

DAYS = DAYS OF LACTATION
a. Vehicle control group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
b. Vehicle control group dams cross-fostered with vehicle control litters.
c. 1.6 mg/kg/day dosage group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
d. 1.6 mg/kg/day dosage group dams cross-fostered with vehicle control group litters.
e. Excludes values for dams which had litters that were not cross-fostered.
f. Excludes values for dam 18974, which had no surviving pups on day 4 of lactation.

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TABLE 9 (PAGE 1): ABSOLUTE FEED CONSUMPTION VALUES (G/DAY) - PRECOHABITATION - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0 (VEHICLE)	II 1.6
RATS TESTED	N	42	36
FEED CONSUMPTION (G/DAY)			
DAYS 1 - 8	MEAN±S.D.	19.5 ± 1.7 [40]a	19.7 ± 2.0 [34]a
DAYS 8 - 15	MEAN±S.D.	20.1 ± 1.7 [41]a	19.7 ± 1.6
DAYS 15 - 22	MEAN±S.D.	19.7 ± 1.8 [41]a	18.9 ± 1.3 [34]a
DAYS 22 - 29	MEAN±S.D.	19.6 ± 2.2 [40]a	18.7 ± 1.3 [34]a
DAYS 29 - 36	MEAN±S.D.	19.6 ± 2.1 [40]a	18.3 ± 1.6 [34]a
DAYS 36 - 43b	MEAN±S.D.	18.3 ± 2.4 [15]a,c	17.2 ± 1.5 [33]a
DAYS 1 - 43b	MEAN±S.D.	19.8 ± 1.6 [15]a,c	18.7 ± 1.3 [33]a

DAYS = DAYS OF STUDY
[ ] = NUMBER OF VALUES AVERAGED
a. Excludes values that were incorrectly recorded or not recorded, as well as those associated with spillage.
b. Last value recorded before cohabitation.
c. Excludes values for rats assigned to cohabitation on day 42 of study.

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TABLE 10 (PAGE 1): RELATIVE FEED CONSUMPTION VALUES (G/KG/DAY) - PRECOHABITATION - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP		I	II
DOSAGE (MG/KG/DAY)		0 (VEHICLE)	1.6
RATS TESTED	N	42	36
FEED CONSUMPTION (G/KG/DAY)			
DAYS 1 - 8	MEAN±S.D.	81.6 ± 6.1 [40]a	82.4 ± 8.1 [34]a
DAYS 8 - 15	MEAN±S.D.	79.7 ± 5.4 [41]a	78.0 ± 5.2
DAYS 15 - 22	MEAN±S.D.	75.0 ± 5.1 [41]a	72.1 ± 4.6 [34]a
DAYS 22 - 29	MEAN±S.D.	72.7 ± 6.9 [40]a	69.7 ± 3.9 [34]a
DAYS 29 - 36	MEAN±S.D.	70.0 ± 5.8 [40]a	66.8 ± 4.6 [34]a
DAYS 36 - 43b	MEAN±S.D.	63.8 ± 7.7 [15]a,c	61.9 ± 3.9 [33]a
DAYS 1 - 43b	MEAN±S.D.	74.2 ± 4.9 [15]a,c	71.7 ± 3.8 [33]a

DAYS = DAYS OF STUDY
[ ] = NUMBER OF VALUES AVERAGED
a. Excludes values that were incorrectly recorded or not recorded, as well as those associated with spillage.
b. Last value recorded before cohabitation.
c. Excludes values for rats assigned to cohabitation on day 42 of study.

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TABLE 11 (PAGE 1): MATERNAL ABSOLUTE FEED CONSUMPTION VALUES (G/DAY) - GESTATION - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0 (VEHICLE)	II 1.6
RATS TESTED	N	42	36
PREGNANT	N	35	27
MATERNAL FEED CONSUMPTION (G/DAY)			
DAYS 0 - 7	MEAN±S.D.	24.2 ± 2.7 [33]a	21.1 ± 1.5
DAYS 7 - 14	MEAN±S.D.	26.3 ± 3.0	23.7 ± 2.0
DAYS 14 - 20	MEAN±S.D.	24.8 ± 2.6	25.4 ± 2.5
DAYS 0 - 20	MEAN±S.D.	25.1 ± 2.2	23.3 ± 1.5

DAYS = DAYS OF GESTATION
[ ] = NUMBER OF VALUES AVERAGED
a. Excludes values that were associated with spillage.

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TABLE 12 (PAGE 1): MATERNAL RELATIVE FEED CONSUMPTION VALUES (G/KG/DAY) - GESTATION - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0 (VEHICLE)	II 1.6
RATS TESTED	N	42	36
PREGNANT	N	35	27
MATERNAL FEED CONSUMPTION (G/KG/DAY)			
DAYS 0 - 7	MEAN±S.D.	76.9 ± 5.8 [33]a	71.2 ± 4.2
DAYS 7 - 14	MEAN±S.D.	76.7 ± 7.8	73.8 ± 4.7
DAYS 14 - 20	MEAN±S.D.	62.8 ± 4.6	67.6 ± 6.3
DAYS 0 - 20	MEAN±S.D.	72.0 ± 4.1	70.7 ± 3.4

DAYS = DAYS OF GESTATION
[ ] = NUMBER OF VALUES AVERAGED
a. Excludes values were associated with spillage.

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TABLE 13 (PAGE 1): MATERNAL ABSOLUTE FEED CONSUMPTION VALUES (G/DAY) - LACTATION - SUMMARY - Fo GENERATION FEMALE RATS

SUBSET		A	B	C	D
DOSAGE GROUP		I a	I b	II c	II d
DOSAGE (MG/KG/DAY)		0 (VEHICLE)	0 (VEHICLE)	1.6	1.6
RATS ASSIGNED TO CROSS-FOSTERING	N	13	12	12	13
INCLUDED IN ANALYSES	N	11e	12	11f	11e
MATERNAL FEED CONSUMPTION (G/DAY)					
DAYS 1 - 4	MEAN±S.D.	19.1 ± 4.0	24.9 ± 3.6	18.8 ± 3.3	21.3 ± 3.9
DAYS 4 - 7	MEAN±S.D.	38.8 ± 2.8	42.9 ± 3.7	34.5 ± 6.4	38.5 ± 5.5
DAYS 7 - 10	MEAN±S.D.	45.0 ± 3.3 [10]g	51.3 ± 4.6 [11]g	41.2 ± 3.6	43.3 ± 3.3
DAYS 10 - 14h	MEAN±S.D.	57.8 ± 3.9	58.2 ± 4.5	52.0 ± 5.8 [10]g	53.3 ± 5.1
DAYS 1 - 14h	MEAN±S.D.	41.4 ± 2.5	45.4 ± 3.3	38.0 ± 4.4 [10]g	40.2 ± 3.7

DAYS = DAYS OF LACTATION
[ ] = NUMBER OF VALUES AVERAGED

a. Vehicle control group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
b. Vehicle control group dams cross-fostered with vehicle control litters.
c. 1.6 mg/kg/day dosage group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
d. 1.6 mg/kg/day dosage group dams cross-fostered with vehicle control group litters.
e. Excludes values for dams which had litters that were not cross-fostered.
f. Excludes values for dam 18974, which had no surviving pups on day 4 of lactation.
g. Excludes values that were associated with interrupted water access.
h. Because it is presumed that the pups begin to consume maternal feed after day 14 of lactation, maternal feed consumption values were not tabulated on days 14 to 21 of lactation.

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TABLE 14 (PAGE 1): MATERNAL RELATIVE FEED CONSUMPTION VALUES (G/KG/DAY) - LACTATION - SUMMARY - Fo GENERATION FEMALE RATS

SUBSET		A	B	C	D
DOSAGE GROUP		I a	I b	II c	II d
DOSAGE (MG/KG/DAY)		0 (VEHICLE)	0 (VEHICLE)	1.6	1.6
RATS ASSIGNED TO CROSS-FOSTERING	N	13	12	12	13
INCLUDED IN ANALYSES	N	11e	12	11f	11e
MATERNAL FEED CONSUMPTION (G/KG/DAY)					
DAYS 1 - 4	MEAN±S.D.	57.5 ± 12.5	73.8 ± 11.6	58.4 ± 11.1	67.2 ± 12.2
DAYS 4 - 7	MEAN±S.D.	113.2 ± 9.3	122.0 ± 15.1	104.4 ± 18.6	119.1 ± 12.3
DAYS 7 - 10	MEAN±S.D.	127.2 ± 10.4 [10]g	141.9 ± 14.0 [11]g	121.2 ± 12.9	129.8 ± 8.3
DAYS 10 - 14h	MEAN±S.D.	159.7 ± 12.0	159.9 ± 10.8	150.7 ± 15.8 [10]g	156.8 ± 10.1
DAYS 1 - 14h	MEAN±S.D.	118.8 ± 8.9	128.5 ± 11.4	113.8 ± 12.6 [10]g	121.9 ± 7.3

DAYS = DAYS OF LACTATION
[ ] = NUMBER OF VALUES AVERAGED

a. Vehicle control group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
b. Vehicle control group dams cross-fostered with vehicle control litters.
c. 1.6 mg/kg/day dosage group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
d. 1.6 mg/kg/day dosage group dams cross-fostered with vehicle control group litters.
e. Excludes values for dams which had litters that were not cross-fostered.
f. Excludes values for dam 18974, which had no surviving pups on day 4 of lactation.
g. Excludes values that were associated with interrupted water access.
h. Because it is presumed that the pups begin to consume maternal feed after day 14 of lactation, maternal feed consumption values were not tabulated on days 14 to 21 of lactation.

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TABLE 15 (PAGE 1): NATURAL DELIVERY OBSERVATIONS - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0 (VEHICLE)	II 1.6
RATS ASSIGNED TO CROSS-FOSTERING	N	25	25
PREGNANT	N(%)	25(100.0)	25(100.0)
DELIVERED LITTERS	N(%)	25(100.0)	25(100.0)
INCLUDED IN ANALYSES	N	23a	23a
DURATION OF GESTATION IN DAYS b	MEAN±S.D.	22.0 ± 0.5	21.6 ± 0.1
NUMBER OF DAMS DELIVERING			
DAYS 21.1 - 22.0	N(%)	14(60.9)	23(100.0)
DAYS 22.1 - 23.0	N(%)	9(39.1)	0(0.0)
DURATION OF GESTATION IN WHOLE DAYS c	MEAN±S.D.	22.4 ± 0.5	22.0 ± 0.0
NUMBER OF DAMS DELIVERING			
DAY 22	N(%)	14(60.9)	23(100.0)
DAY 23	N(%)	9(39.1)	0(0.0)
GESTATION INDEX d	%	100.0	100.0
	N/N	23/ 23	23/ 23

DAY(S) = DAY(S) OF GESTATION

a. Excludes values for dams which had litters that were not cross-fostered.
b. Calculated as the time (to the nearest tenth of a day) elapsed between confirmed mating (arbitrarily defined as 0 hour) and the time the first pup was delivered.
c. Calculated as the time (in days) elapsed between confirmed mating (arbitrarily defined as day 0) and the time (in days) the first pup was delivered.
d. Number of rats with live offspring/number of pregnant rats.

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TABLE 15 (PAGE 2): NATURAL DELIVERY OBSERVATIONS - SUMMARY - Fo GENERATION FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0 (VEHICLE)	II 1.6
RATS ASSIGNED TO CROSS-FOSTERING	N	25	25
PREGNANT	N(%)	25(100.0)	25(100.0)
DELIVERED LITTERS	N(%)	25(100.0)	25(100.0)
INCLUDED IN ANALYSES	N	23a	23a
OBSERVED DURATION OF DELIVERY PER PUP PER LITTER (MINUTES)			
TOTAL DELIVERY PERIOD OBSERVED (MINUTES) b	MEAN±S.D.	11.6 ± 4.8 [22]	9.1 ± 3.1
TOTAL OR PARTIAL DELIVERY PERIOD OBSERVED (MINUTES) b	MEAN±S.D.	11.6 ± 4.8	9.1 ± 3.1
IMPLANTATION SITES PER DELIVERED LITTER	N MEAN±S.D.	407 17.7 ± 1.8	368 16.0 ± 1.9
DELIVERED LITTER SIZE	MEAN±S.D.	16.4 ± 1.8	15.0 ± 1.8
DAMS WITH STILLBORN PUPS	N(%)	3(13.0)	1(4.3)
PUPS FOUND DEAD (PRECROSS-FOSTERING)	N/N(%)	1/373(0.3)	1/344(0.3)
LIVE LITTER SIZE c	MEAN±S.D.	16.2 ± 1.8	14.9 ± 1.8
FOSTER LITTER SIZE	MEAN±S.D.	15.2 ± 1.9	15.6 ± 1.9

[ ] = NUMBER OF VALUES AVERAGED
a. Excludes values for dams which had litters that were not cross-fostered.
b. Calculated as the time (in minutes) elapsed between delivery of the first and last pups, divided by n-1 pups.
c. Excludes values for dams with all pups dying prior to cross-fostering.

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TABLE 15 (PAGE 3): NATURAL DELIVERY OBSERVATIONS - SUMMARY - Fo GENERATION FEMALE RATS

SUBSET		A	B	C	D
DOSAGE GROUP		I a	I b	II c	II d
DOSAGE (MG/KG/DAY)		0 (VEHICLE)	0 (VEHICLE)	1.6	1.6
RATS ASSIGNED TO CROSS-FOSTERING	N	13	12	12	13
PREGNANT	N(%)	13(100.0)	12(100.0)	12(100.0)	13(100.0)
DELIVERED LITTERS	N(%)	13(100.0)	12(100.0)	12(100.0)	13(100.0)
INCLUDED IN ANALYSES	N	11e	12	12	11e
LIVE LITTER SIZE e	MEAN±S.D.	16.4 ± 1.6	15.9 ± 2.1	14.8 ± 1.9	15.1 ± 1.7
FOSTER LITTER SIZE	MEAN±S.D.	15.1 ± 1.7	15.9 ± 2.1	14.8 ± 1.9	16.4 ± 1.6
DAMS WITH ALL PUP DYING DAYS 1-4 POSTPARTUM (AFTER CROSS-FOSTERING)	N(%)	0(0.0)	0(0.0)	1(8.3)	0(0.0)
DAMS WITH ALL PUPS DYING DAYS 5-21 POSTPARTUM	N(%)	0(0.0)	0(0.0)	0(0.0)	0(0.0)

a. Vehicle control group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
b. Vehicle control group dams cross-fostered with vehicle control litters.
c. 1.6 mg/kg/day dosage group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
d. 1.6 mg/kg/day dosage group dams cross-fostered with vehicle control group litters.
e. Excludes values for dams with all pups dying prior to cross-fostering.

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TABLE 16 (PAGE 1): LITTER OBSERVATIONS (NATURALLY DELIVERED PUPS) - SUMMARY - F1 GENERATION LITTERS

SUBSET		A	B	C	D
DOSAGE GROUP		I a	I b	II c	II d
DOSAGE (MG/KG/DAY)		0 (VEHICLE)	0 (VEHICLE)	1.6	1.6
LITTERS ASSIGNED TO CROSS-FOSTERING	N	13	12	12	13
INCLUDED IN ANALYSES	N	11e	12	12	11e
PUPS CROSS-FOSTERED	N	166	191	177	181
	MEAN±S.D.	15.1 ± 1.7	15.9 ± 2.1	14.8 ± 1.9	16.4 ± 1.6
PUPS FOUND DEAD OR PRESUMED CANNIBALIZED					
DAY 1	N/N(%)	0/166(0.0)	0/191(0.0)	0/177(0.0)	0/181(0.0)
DAYS 2- 4	N/N(%)	15/166(9.0)	3/191(1.6)	34/177(19.2)	2/181(1.1)
DAYS 5- 7	N/N(%)	1/109(0.9)	0/120(0.0)	0/107(0.0)	0/110(0.0)
DAYS 8-14	N/N(%)	0/108(0.0)	0/120(0.0)	0/107(0.0)	0/110(0.0)
DAYS 15-21	N/N(%)	0/108(0.0)	0/120(0.0)	0/107(0.0)	0/110(0.0)
VIABILITY INDEX f	%	91.0	98.4	80.8	98.9
	N/N	151/166	188/191	143/177	179/181
LACTATION INDEX g	%	99.1	100.0	100.0	100.0
	N/N	108/109	120/120	107/107	110/110

DAY(S) = DAY(S) POSTPARTUM

a. Vehicle control group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
b. Vehicle control group dams cross-fostered with vehicle control litters.
c. 1.6 mg/kg/day dosage group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
d. 1.6 mg/kg/day dosage group dams cross-fostered with vehicle control group litters.
e. Excludes values for dams which had litters that were not cross-fostered.
f. Number of live pups on day 4 (preculling) postpartum/number of pups cross-fostered on day 1 postpartum.
g. Number of live pups on day 21 postpartum/number of live pups on day 4 (postculling) postpartum.

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TABLE 16 (PAGE 2): LITTER OBSERVATIONS (NATURALLY DELIVERED PUPS) - SUMMARY - F1 GENERATION LITTERS

SUBSET		A	B	C	D
DOSAGE GROUP		I a	I b	II c	II d
DOSAGE (MG/KG/DAY)		0 (VEHICLE)	0 (VEHICLE)	1.6	1.6
LITTERS ASSIGNED TO CROSS-FOSTERING	N	13	12	12	13
INCLUDED IN ANALYSES	N	11e	12	12	11e
SURVIVING PUPS/LITTER f					
DAY 1	MEAN±S.D.	15.1 ± 1.7	15.9 ± 2.1	14.8 ± 1.9	16.4 ± 1.6
DAY 4 PRECULLING	MEAN±S.D.	13.7 ± 2.3	15.7 ± 1.8	11.9 ± 4.6	16.3 ± 1.6
DAY 4 POSTCULLING	MEAN±S.D.	9.9 ± 0.3	10.0 ± 0.0	8.9 ± 2.9	10.0 ± 0.0
DAY 7	MEAN±S.D.	9.8 ± 0.6	10.0 ± 0.0	8.9 ± 2.9	10.0 ± 0.0
DAY 14	MEAN±S.D.	9.8 ± 0.6	10.0 ± 0.0	8.9 ± 2.9	10.0 ± 0.0
DAY 21	MEAN±S.D.	9.8 ± 0.6	10.0 ± 0.0	8.9 ± 2.9	10.0 ± 0.0

DAY = DAY POSTPARTUM
[ ] = NUMBER OF VALUES AVERAGED

a. Vehicle control group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
b. Vehicle control group dams cross-fostered with vehicle control litters.
c. 1.6 mg/kg/day dosage group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
d. 1.6 mg/kg/day dosage group dams cross-fostered with vehicle control group litters.
e. Excludes values for dams which had litters that were not cross-fostered.
f. Average number of live pups per litter, including litters with no surviving pups.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 16 (PAGE 3): LITTER OBSERVATIONS (NATURALLY DELIVERED PUPS) - SUMMARY - F1 GENERATION LITTERS

SUBSET DOSAGE GROUP DOSAGE (MG/KG/DAY)		A I a 0 (VEHICLE)	B I b 0 (VEHICLE)	C II c 1.6	D II d 1.6
LITTERS ASSIGNED TO CROSS-FOSTERING	N	13	12	12	13
INCLUDED IN ANALYSES	N	11e	12	12	11e
PERCENT MALE PUPS PER NUMBER OF PUPS SEXED					
DAY 1	MEAN±S.D.	46.9 ± 9.7	48.4 ± 14.4	48.8 ± 16.6	46.4 ± 8.6
DAY 4 PRECULLING	MEAN±S.D.	46.7 ± 11.0	49.1 ± 14.3	49.4 ± 21.5 [11]f	46.4 ± 9.2
DAY 4 POSTCULLING	MEAN±S.D.	48.7 ± 6.4	52.5 ± 8.7	46.0 ± 16.9 [11]f	50.0 ± 0.0
DAY 7	MEAN±S.D.	49.3 ± 7.4	52.5 ± 8.7	46.0 ± 16.9 [11]f	50.0 ± 0.0
DAY 14	MEAN±S.D.	49.3 ± 7.4	52.5 ± 8.7	46.0 ± 16.9 [11]f	50.0 ± 0.0
DAY 21	MEAN±S.D.	49.3 ± 7.4	52.5 ± 8.7	46.0 ± 16.9 [11]f	50.0 ± 0.0
LIVE LITTER SIZE AT WEIGHING					
DAY 1	MEAN±S.D.	15.1 ± 1.7	15.9 ± 2.1	14.8 ± 1.9	16.4 ± 1.6
DAY 4 PRECULLING	MEAN±S.D.	13.7 ± 2.3	15.7 ± 1.8	13.0 ± 2.9 [11]f	16.3 ± 1.6
DAY 4 POSTCULLING	MEAN±S.D.	9.9 ± 0.3	10.0 ± 0.0	9.7 ± 0.6 [11]f	10.0 ± 0.0
DAY 7	MEAN±S.D.	9.8 ± 0.6	10.0 ± 0.0	9.7 ± 0.6 [11]f	10.0 ± 0.0
DAY 14	MEAN±S.D.	9.8 ± 0.6	10.0 ± 0.0	9.7 ± 0.6 [11]f	10.0 ± 0.0
DAY 21	MEAN±S.D.	9.8 ± 0.6	10.0 ± 0.0	9.7 ± 0.6 [11]f	10.0 ± 0.0

DAY = DAY POSTPARTUM
[ ] = NUMBER OF VALUES AVERAGED

a. Vehicle control group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
b. Vehicle control group dams cross-fostered with vehicle control litters.
c. 1.6 mg/kg/day dosage group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
d. 1.6 mg/kg/day dosage group dams cross-fostered with vehicle control group litters.
e. Excludes values for dams which had litters that were not cross-fostered.
f. Excludes values for dam 18974, which had no surviving pups on day 4 postpartum.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 16 (PAGE 4): LITTER OBSERVATIONS (NATURALLY DELIVERED PUPS) - SUMMARY - F1 GENERATION LITTERS

SUBSET		A	B	C	D
DOSAGE GROUP		I a	I b	II c	II d
DOSAGE (MG/KG/DAY)		0 (VEHICLE)	0 (VEHICLE)	1.6	1.6
LITTERS ASSIGNED TO CROSS-FOSTERING	N	13	12	12	13
INCLUDED IN ANALYSES	N	11e	12	12	11e
PUP WEIGHT/LITTER (GRAMS)					
DAY 1g	MEAN±S.D.	5.6 ± 0.3	6.2 ± 0.5	5.7 ± 0.2	6.3 ± 0.6
DAY 4 PRECULLING	MEAN±S.D.	7.1 ± 0.5	8.3 ± 0.8	7.2 ± 0.8 [11]f	7.9 ± 0.6
DAY 4 POSTCULLING	MEAN±S.D.	7.3 ± 0.5	8.5 ± 0.8	7.3 ± 0.8 [11]f	8.1 ± 0.6
DAY 7	MEAN±S.D.	12.3 ± 0.9	14.1 ± 0.9	11.6 ± 1.3 [11]f	12.8 ± 0.8
DAY 14	MEAN±S.D.	26.7 ± 1.7	29.0 ± 1.5	24.6 ± 2.4 [11]f	26.2 ± 2.2
DAY 21	MEAN±S.D.	41.9 ± 1.8	46.3 ± 2.5	38.9 ± 3.8 [11]f	41.9 ± 2.1

DAY = DAY POSTPARTUM
[ ] = NUMBER OF VALUES AVERAGED

a. Vehicle control group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
b. Vehicle control group dams cross-fostered with vehicle control litters.
c. 1.6 mg/kg/day dosage group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
d. 1.6 mg/kg/day dosage group dams cross-fostered with vehicle control group litters.
e. Excludes values for dams which had litters that were not cross-fostered.
f. Excludes values for dam 18974, which had no surviving pups on day 4 postpartum.
g. Day 1 pup weights for Subsets A and C reflect pups of test article treated dams. Day 1 pup weights for Subsets B and D reflect pups of vehicle treated dams. The effects of cross-fostering are not reflected in these pup body weights.

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TABLE 17 (PAGE 1): CLINICAL OBSERVATIONS FROM BIRTH TO DAY 21 POSTPARTUM - SUMMARY - F1 GENERATION PUPS

SUBSET		A	B	C	D
DOSAGE GROUP		I a	I b	II c	II d
DOSAGE (MG/KG/DAY)		0 (VEHICLE)	0 (VEHICLE)	1.6	1.6
LITTERS EXAMINED (N)		13	12	12	13
TRANSIENT CLINICAL OBSERVATIONS: e		TOTAL FREQUENCY (DAYS x PUPS)/LITTERS WITH OBSERVATIONS			
TIP OF TAIL, BLACK	N/N	0/ 0	15/ 1	0/ 0	18/ 1
LABORED BREATHING	N/N	0/ 0	0/ 0	0/ 0	1/ 1
DARK IN COLOR	N/N	0/ 0	0/ 0	0/ 0	1/ 1
NOT NURSING	N/N	2/ 2	0/ 0	2/ 1	0/ 0
PERSISTENT CLINICAL OBSERVATIONS: e		TOTAL FREQUENCY (DAYS x PUPS)/LITTERS WITH OBSERVATIONS			
RIGHT HINDPAW, SECOND DIGIT MISSING	N/N	0/ 0	0/ 0	21/ 1	0/ 0
TAIL, BENT	N/N	0/ 0	11/ 1	0/ 0	0/ 0

N/N = TOTAL FREQUENCY (DAYS x PUPS)/LITTERS WITH OBSERVATIONS.
a. Vehicle control group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
b. Vehicle control group dams cross-fostered with vehicle control litters.
c. 1.6 mg/kg/day dosage group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
d. 1.6 mg/kg/day dosage group dams cross-fostered with vehicle control group litters.
e. Tabulation restricted to adverse observations; all other pups appeared normal.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 18 (PAGE 1): NECROPSY OBSERVATIONS - SUMMARY - F1 GENERATION PUPS

SUBSET		A	B	C	D
MATERNAL DOSAGE GROUP		I a	I b	II c	II d
MATERNAL DOSAGE (MG/KG/DAY)		0 (VEHICLE)	0 (VEHICLE)	1.6	1.6
LITTERS EXAMINED	N	13	12	12	13
PUPS FOUND DEAD e,f (AFTER CROSS-FOSTERING)	N	7	0	18	23
NO MILK IN STOMACH g	N(%)	4(57.1)	0(0.0)	18(100.0)	20(87.0)
PUPS SACRIFICED AND NECROPSIED ON 4 OR 21 POSTPARTUM f					
LITTERS EXAMINED	N	9	8	7	8
PUPS EVALUATED	N	79	75	73	92
APPEARED NORMAL					
LITTER INCIDENCE	N(%)	8(88.9)	8(100.0)	7(100.0)	8(100.0)
PUP INCIDENCE	N(%)	78(98.7)	75(100.0)	73(100.0)	92(100.0)
KIDNEYS: RIGHT, PELVIS, SLIGHT DILATION					
LITTER INCIDENCE	N(%)	1(11.1)	0(0.0)	0(0.0)	0(0.0)
PUP INCIDENCE	N(%)	1(1.3)	0(0.0)	0(0.0)	0(0.0)

a. Vehicle control group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
b. Vehicle control group dams cross-fostered with vehicle control litters.
c. 1.6 mg/kg/day dosage group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
d. 1.6 mg/kg/day dosage group dams cross-fostered with vehicle control group litters.
e. Restricted to the pups in which complete necropsies were performed. Complete necropsies were not performed on pups in which autolysis or cannibalization precluded evaluation.
f. Refer to the individual pup clinical observation table (Table B32) for external clinical observations confirmed at necropsy.
g. Analysis restricted to pups found dead and necropsied.

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TABLE 19 (PAGE 1): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP I		0 (VEHICLE) MG/KG/DAY
RAT #		DESCRIPTION
18901		NO ADVERSE FINDINGS
18902		NO ADVERSE FINDINGS
18903		NO ADVERSE FINDINGS
18904	DG(14)	CHROMORHINORRHEA
18905		NO ADVERSE FINDINGS
18906	DS(11- 17)	LOCALIZED ALOPECIA: HEAD
	DS(18)	ALOPECIA NO LONGER APPARENT
18907		NO ADVERSE FINDINGS
18908		NO ADVERSE FINDINGS
18909		NO ADVERSE FINDINGS
18910		NO ADVERSE FINDINGS
18911	DS(12- 20)	INCISORS: MISALIGNED
	DS(21)	INCISORS: REALIGNED
	DG(0- 17)	INCISORS: MISALIGNED
18912		NO ADVERSE FINDINGS
18913		NO ADVERSE FINDINGS
18914		NO ADVERSE FINDINGS
18915		NO ADVERSE FINDINGS
18916		NO ADVERSE FINDINGS
18917	DS(11- 19)	NECK: ABRASION (0.5 CM IN DIAMETER)
	DS(20)	ABRASION HEALED
18918	DG(7- 14)	LOCALIZED ALOPECIA: BACK
	DG(15)	ALOPECIA NO LONGER APPARENT
18919	DS(8- 22)	LOCALIZED ALOPECIA: HEAD
	DS(23)	ALOPECIA NO LONGER APPARENT
18920	DS(10- 44)	LOCALIZED ALOPECIA: LIMBS
	DG(0- 12)	LOCALIZED ALOPECIA: LIMBS
	DG(13)	ALOPECIA NO LONGER APPARENT
18921		NO ADVERSE FINDINGS
18922	DL(8- 18)	TAIL: ABRASION (1.0 CM IN LENGTH)
	DL(19- 22)	TAIL: SCAB (0.5 CM X 0.3 CM)
	DL(21- 22)	RIGHT FOREPAW: THIRD DIGIT SWOLLEN a
18923		NO ADVERSE FINDINGS
18924		NO ADVERSE FINDINGS
18925	DS(29- 39)	LOCALIZED ALOPECIA: BACK
18926	DG(21)	PERINEAL HERNIA
	DL(1- 14)	PERINEAL HERNIA
18927		NO ADVERSE FINDINGS

DS = DAY OF STUDY DG = DAY OF PRESUMED GESTATION
DL = DAY OF LACTATION
a. Observation confirmed at necropsy.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 19 (PAGE 2): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP I		0 (VEHICLE) MG/KG/DAY
RAT #		DESCRIPTION
18928		NO ADVERSE FINDINGS
18929		NO ADVERSE FINDINGS
18930	DS(20)	CHROMORHINORRHEA
18931		NO ADVERSE FINDINGS
18932		NO ADVERSE FINDINGS
18933		NO ADVERSE FINDINGS
18934	DS(41- 42)	INCISORS: MISSING/BROKEN
	DS(43)	INCISORS: GROWN IN
18935		NO ADVERSE FINDINGS
18936	DS(5- 14)	HEAD: ABRASION (0.5 CM IN DIAMETER)
	DS(5- 31)	LOCALIZED ALOPECIA: HEAD
	DS(11- 43)	LOCALIZED ALOPECIA: NECK
	DS(15- 16)	HEAD: SCAB (0.3 CM IN DIAMETER)
	DS(17)	SCAB HEALED
	DS(19- 43)	LOCALIZED ALOPECIA: LIMBS
	DG(0)	ALOPECIA NO LONGER APPARENT
	DS(38- 43)	CHROMODACRYORRHEA
	DS(38- 43)	INCISORS: MISALIGNED
	DS(39- 43)	TAIL: ABRASION (0.3 CM FROM TIP)
	DG(0)	ABRASION HEALED
	DG(0- 11)	CHROMODACRYORRHEA
	DG(0- 20)	INCISORS: MISALIGNED
	DG(2)	CHROMORHINORRHEA
	DG(6)	DEHYDRATION
	DG(13- 15)	CHROMODACRYORRHEA
	DG(17- 18)	CHROMORHINORRHEA
	DL(1- 22)	INCISORS: MISALIGNED a
18937		NO ADVERSE FINDINGS
18938	DL(7- 22)	PROTRUDING XIPHOID a
18939		NO ADVERSE FINDINGS
18940		NO ADVERSE FINDINGS
18941		NO ADVERSE FINDINGS
18942		NO ADVERSE FINDINGS

DS = DAY OF STUDY DG = DAY OF PRESUMED GESTATION
DL = DAY OF LACTATION
a. Observation confirmed at necropsy.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 19 (PAGE 3): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP II		1.6 MG/KG/DAY
RAT #		DESCRIPTION
18943	DS(36- 42)	LEFT FORELIMB: ABRASION (0.4 CM IN DIAMETER)
	DS(43)	ABRASION HEALED
	DS(43- 45)	LOCALIZED ALOPECIA: LIMBS
	DG(0- 4)	LOCALIZED ALOPECIA: LIMBS
	DG(5)	ALOPECIA NO LONGER APPARENT
18944		NO ADVERSE FINDINGS
18945		NO ADVERSE FINDINGS
18946		NO ADVERSE FINDINGS
18947		NO ADVERSE FINDINGS
18948		NO ADVERSE FINDINGS
18949		NO ADVERSE FINDINGS
18950		NO ADVERSE FINDINGS
18951		NO ADVERSE FINDINGS
18952	DS(17)	CHROMORHINORRHEA
18953		NO ADVERSE FINDINGS
18954		NO ADVERSE FINDINGS
18955		NO ADVERSE FINDINGS
18956		NO ADVERSE FINDINGS
18957		NO ADVERSE FINDINGS
18958	DL(1- 22)	RIGHT FOREPAW: FOURTH DIGIT BROKEN a
	DL(16- 22)	LOCALIZED ALOPECIA: LIMBS a
18959		NO ADVERSE FINDINGS
18960	DG(10- 17)	LOCALIZED ALOPECIA: UNDERSIDE
18961		NO ADVERSE FINDINGS
18962		NO ADVERSE FINDINGS
18963	DS(8- 44)	SCALY TAIL
	DG(0- 20)	SCALY TAIL
	DL(1- 22)	SCALY TAIL a
18964		NO ADVERSE FINDINGS
18965		NO ADVERSE FINDINGS
18966		NO ADVERSE FINDINGS
18967		NO ADVERSE FINDINGS
18968		NO ADVERSE FINDINGS
18969		NO ADVERSE FINDINGS
18970		NO ADVERSE FINDINGS

DS = DAY OF STUDY DG = DAY OF PRESUMED GESTATION
DL = DAY OF LACTATION
a. Observation confirmed at necropsy.

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TABLE 19 (PAGE 4): CLINICAL OBSERVATIONS - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP II		1.6 MG/KG/DAY
RAT #		DESCRIPTION
18971	DS(27- 28)	CHROMORHINORRHEA
	DG(5- 22)	LOCALIZED ALOPECIA: NECK
	DG(15- 22)	LOCALIZED ALOPECIA: LIMBS
	DL(1- 2)	LOCALIZED ALOPECIA: LIMBS
	DL(3)	ALOPECIA NO LONGER APPARENT
	DL(1- 2)	LOCALIZED ALOPECIA: NECK
	DL(3)	ALOPECIA NO LONGER APPARENT
18972		NO ADVERSE FINDINGS
18973		NO ADVERSE FINDINGS
18974		NO ADVERSE FINDINGS
18975	DG(7- 25)	LOCALIZED ALOPECIA: LIMBS
18976		NO ADVERSE FINDINGS
18977	DL(1- 3)	PROTRUDING XIPHOID a
18978		NO ADVERSE FINDINGS

DS = DAY OF STUDY DG = DAY OF PRESUMED GESTATION
DL = DAY OF LACTATION
a. Observation confirmed at necropsy.

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TABLE 20 (PAGE 1): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)	RAT NUMBER	DAY OF NECROPSY	PREGNANCY STATUS	DOSAGES ADMINISTERED	OBSERVATIONS a
I 0 (VEHICLE)	18901	DL 22	P	87	ALL TISSUES APPEARED NORMAL.
	18902	DG 25	NP	69	ALL TISSUES APPEARED NORMAL.
	18903	DL 22	P	86	ALL TISSUES APPEARED NORMAL.
	18904	DL 22	P	85	ALL TISSUES APPEARED NORMAL.
	18905	DS 72	NP	71	ALL TISSUES APPEARED NORMAL.
	18906	DL 22	P	87	ALL TISSUES APPEARED NORMAL.
	18907	DL 22	P	86	ALL TISSUES APPEARED NORMAL.
	18908	DL 22	P	87	ALL TISSUES APPEARED NORMAL.
	18909	DL 22	P	85	ALL TISSUES APPEARED NORMAL.
	18910	DL 14	P	76	ALL TISSUES APPEARED NORMAL.
	18911	DL 14	P	80	ALL TISSUES APPEARED NORMAL.
	18912	DL 22	P	87	ALL TISSUES APPEARED NORMAL.
	18913	DL 14	P	80	ALL TISSUES APPEARED NORMAL.
	18914	DG 25	NP	68	ALL TISSUES APPEARED NORMAL.
	18915	DL 14	P	76	ALL TISSUES APPEARED NORMAL.
	18916	DG 25	P	70	ALL TISSUES APPEARED NORMAL. UTERINE CONTENTS: ONE IMPLANTATIONS (ONE DEAD FETUS).b
	18917	DL 22	P	87	ALL TISSUES APPEARED NORMAL.
	18918	DL 22	P	87	ALL TISSUES APPEARED NORMAL.
	18919	DL 22	P	87	ALL TISSUES APPEARED NORMAL.
	18920	DL 22	P	86	ALL TISSUES APPEARED NORMAL.
	18922	DL 22	P	85	ALL TISSUES APPEARED NORMAL.
	18923	DL 22	P	87	ALL TISSUES APPEARED NORMAL.
	18924	DL 22	P	87	ALL TISSUES APPEARED NORMAL.
	18925	DG 26	NP	69	ALL TISSUES APPEARED NORMAL.
	18926	DL 14	P	81	LEFT INGUINAL AREA: MASS (2.5 CM X 2.0 CM X 1.5 CM).c ALL OTHER TISSUES APPEARED NORMAL.

P = PREGNANT NP = NOT PREGNANT
DS = DAY OF STUDY DG = DAY OF PRESUMED GESTATION DL = DAY OF LACTATION
a. Refer to the individual clinical observations table (Table 19) for external observations confirmed at necropsy.
b. The fetus had a large, black right hindlimb and a black tail. Evidence of compression on the abdomen and hindlimbs.
c. First observed at necropsy.

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TABLE 20 (PAGE 2): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)	RAT NUMBER	DAY OF NECROPSY	PREGNANCY STATUS	DOSAGES ADMINISTERED	OBSERVATIONS a
I					
0 (VEHICLE)	18927	DL 14	P	81	ALL TISSUES APPEARED NORMAL.
	18928	DS 72	NP	71	ALL TISSUES APPEARED NORMAL.
	18929	DL 22	P	88	ALL TISSUES APPEARED NORMAL.
	18930	DG 25	NP	72	ALL TISSUES APPEARED NORMAL.
	18931	DL 22	P	87	ALL TISSUES APPEARED NORMAL.
	18932	DL 22	P	87	ALL TISSUES APPEARED NORMAL.
	18933	DL 9	P	72	NECROPSY OBSERVATIONS WERE NOT RECORDED.
	18934	DL 22	P	86	ALL TISSUES APPEARED NORMAL.
	18935	DL 22	P	87	ALL TISSUES APPEARED NORMAL.
	18936	DL 22	P	86	ALL TISSUES APPEARED NORMAL.
	18937	DL 22	P	88	ALL TISSUES APPEARED NORMAL.
	18938	DL 22	P	87	ALL TISSUES APPEARED NORMAL.
	18939	DL 14	P	77	ALL TISSUES APPEARED NORMAL.
	18940	DL 14	P	82	ALL TISSUES APPEARED NORMAL.
	18941	DL 22	P	88	ALL TISSUES APPEARED NORMAL.
	18942	DL 22	P	88	ALL TISSUES APPEARED NORMAL.

P = PREGNANT NP = NOT PREGNANT
DS = DAY OF STUDY DG = DAY OF PRESUMED GESTATION DL = DAY OF LACTATION
a. Refer to the individual clinical observations table (Table 19) for external observations confirmed at necropsy.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 20 (PAGE 3): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)	RAT NUMBER	DAY OF NECROPSY	PREGNANCY STATUS	DOSAGES ADMINISTERED	OBSERVATIONS a
II 1.6	18943	DL 22	P	87	ALL TISSUES APPEARED NORMAL.
	18944	DG 25	NP	71	ALL TISSUES APPEARED NORMAL.
	18945	DS 72	NP	71	ALL TISSUES APPEARED NORMAL.
	18946	DL 22	P	87	ALL TISSUES APPEARED NORMAL.
	18947	DL 22	P	87	ALL TISSUES APPEARED NORMAL.
	18948	DL 22	P	87	ALL TISSUES APPEARED NORMAL.
	18949	DG 25	NP	71	ALL TISSUES APPEARED NORMAL.
	18950	DL 22	P	88	ALL TISSUES APPEARED NORMAL.
	18951	DL 22	P	88	ALL TISSUES APPEARED NORMAL.
	18952	DL 22	P	87	ALL TISSUES APPEARED NORMAL.
	18953	DL 22	P	87	ALL TISSUES APPEARED NORMAL.
	18954	DG 25	NP	69	ALL TISSUES APPEARED NORMAL.
	18955	DG 25	NP	69	ALL TISSUES APPEARED NORMAL.
	18956	DL 14	P	82	ALL TISSUES APPEARED NORMAL.
	18957	DL 22	P	87	ALL TISSUES APPEARED NORMAL.
	18958	DL 22	P	88	ALL TISSUES APPEARED NORMAL.
	18959	DL 22	P	85	ALL TISSUES APPEARED NORMAL.
	18960	DL 22	P	87	ALL TISSUES APPEARED NORMAL.
	18961	DL 22	P	86	ALL TISSUES APPEARED NORMAL.
	18962	DG 25	NP	69	ALL TISSUES APPEARED NORMAL.
	18963	DL 22	P	87	ALL TISSUES APPEARED NORMAL.
	18965	DL 22	P	88	ALL TISSUES APPEARED NORMAL.
	18966	DS 72	NP	71	ALL TISSUES APPEARED NORMAL.
	18967	DL 22	P	87	ALL TISSUES APPEARED NORMAL.
	18968	DL 22	P	86	ALL TISSUES APPEARED NORMAL.
	18969	DL 22	P	87	ALL TISSUES APPEARED NORMAL.
	18970	DL 22	P	86	ALL TISSUES APPEARED NORMAL.
	18971	DL 14	P	81	ALL TISSUES APPEARED NORMAL.
	18972	DL 22	P	87	ALL TISSUES APPEARED NORMAL.
	18973	DL 22	P	87	ALL TISSUES APPEARED NORMAL.
	18974	DL 4	P	69	ALL TISSUES APPEARED NORMAL.
	18975	DG 25	NP	71	ALL TISSUES APPEARED NORMAL.
	18976	DL 22	P	86	ALL TISSUES APPEARED NORMAL.
	18977	DL 3	P	69	ALL TISSUES APPEARED NORMAL. UTERINE CONTENTS: 2 FETUSES.b
	18978	DG 25	NP	69	ALL TISSUES APPEARED NORMAL.

P = PREGNANT NP = NOT PREGNANT
DS = DAY OF STUDY DG = DAY OF PRESUMED GESTATION DL = DAY OF LACTATION
a. Refer to the individual clinical observations table (Table 19) for external observations confirmed at necropsy.
b. Appeared normal for their developmental ages and moderate degree of autolysis at time maternal death occurred.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 21 (PAGE 1): BODY WEIGHTS - PRECOHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP I								0 (VEHICLE) MG/KG/DAY							
DAY	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
18901	221.	222.	229.	229.	232.	238.	250.	241.	239.	246.	252.	256.	255.	258.	260.	254.
18902	238.	244.	244.	233.	239.	239.	249.	237.	246.	250.	250.	248.	252.	253.	256.	250.
18903	227.	233.	232.	240.	237.	247.	257.	253.	246.	252.	260.	262.	256.	265.	269.	267.
18904	228.	226.	228.	227.	232.	234.	235.	238.	239.	243.	241.	244.	248.	248.	245.	250.
18905	214.	208.	218.	224.	223.	221.	236.	229.	226.	223.	230.	233.	236.	231.	237.	236.
18906	254.	249.	255.	260.	268.	256.	275.	271.	273.	269.	275.	280.	283.	280.	284.	289.
18907	226.	230.	236.	240.	238.	243.	250.	249.	247.	250.	255.	256.	253.	258.	259.	258.
18908	233.	222.	226.	221.	234.	233.	238.	234.	237.	232.	236.	240.	236.	237.	242.	242.
18909	226.	228.	222.	231.	237.	238.	234.	245.	244.	247.	240.	248.	250.	251.	247.	251.
18910	237.	241.	241.	235.	237.	236.	247.	238.	234.	245.	241.	242.	242.	237.	248.	244.
18911	234.	223.	237.	238.	239.	234.	249.	249.	249.	244.	253.	262.	251.	247.	257.	258.
18912	232.	224.	232.	240.	242.	235.	248.	250.	249.	243.	253.	257.	255.	251.	257.	263.
18913	214.	220.	225.	221.	226.	232.	237.	235.	242.	232.	240.	247.	252.	248.	254.	257.
18914	240.	241.	250.	255.	255.	253.	268.	272.	270.	267.	273.	272.	278.	277.	280.	286.
18915	230.	228.	234.	238.	241.	244.	248.	250.	258.	253.	256.	260.	264.	272.	262.	270.
18916	222.	231.	236.	234.	235.	247.	255.	248.	246.	254.	256.	254.	249.	259.	265.	262.
18917	219.	225.	230.	233.	231.	241.	247.	243.	244.	250.	257.	256.	258.	257.	262.	262.
18918	233.	247.	238.	232.	245.	253.	256.	239.	248.	251.	253.	240.	255.	260.	262.	253.
18919	228.	227.	232.	234.	234.	234.	246.	243.	244.	239.	247.	247.	248.	250.	250.	258.
18920	229.	238.	240.	242.	240.	251.	259.	252.	252.	258.	260.	262.	260.	265.	267.	270.
18921	228.	221.	231.	236.	237.	230.	240.	243.	238.	232.	242.	242.	239.	240.	250.	250.
18922	235.	243.	246.	239.	243.	243.	252.	251.	252.	254.	260.	261.	258.	262.	272.	268.
18923	224.	230.	229.	234.	232.	235.	246.	242.	238.	236.	242.	243.	245.	246.	253.	254.
18924	242.	238.	242.	248.	250.	250.	259.	256.	260.	255.	267.	267.	268.	260.	273.	275.
18925	233.	223.	236.	239.	239.	237.	243.	250.	243.	241.	244.	246.	248.	246.	247.	251.
18926	241.	241.	244.	251.	256.	254.	257.	256.	257.	260.	261.	265.	268.	268.	265.	270.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 21 (PAGE 2): BODY WEIGHTS - PRECOHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP I				0 (VEHICLE) MG/KG/DAY											
DAY	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
18927	231.	224.	230.	235.	230.	225.	240.	236.	237.	229.	238.	239.	239.	232.	242.	243.
18928	245.	234.	242.	248.	251.	246.	260.	256.	263.	249.	252.	260.	256.	254.	260.	265.
18929	223.	218.	222.	224.	225.	225.	237.	234.	231.	233.	239.	241.	240.	236.	244.	242.
18930	234.	235.	236.	244.	246.	250.	249.	253.	258.	262.	256.	262.	267.	270.	264.	268.
18931	234.	228.	240.	246.	247.	244.	264.	258.	257.	251.	260.	261.	262.	256.	262.	265.
18932	229.	234.	242.	240.	238.	247.	258.	243.	243.	249.	255.	259.	252.	258.	267.	265.
18933	221.	220.	216.	218.	219.	211.	225.	226.	227.	231.	229.	233.	233.	233.	233.	242.
18934	234.	241.	240.	232.	246.	250.	256.	247.	253.	260.	265.	258.	267.	273.	272.	268.
18935	228.	226.	228.	229.	232.	236.	246.	244.	244.	239.	241.	243.	245.	255.	261.	261.
18936	234.	239.	234.	241.	244.	245.	244.	243.	254.	252.	250.	256.	260.	261.	255.	261.
18937	224.	226.	225.	230.	232.	234.	236.	235.	238.	239.	241.	240.	240.	248.	240.	242.
18938	246.	234.	249.	253.	254.	248.	260.	259.	261.	253.	262.	273.	271.	269.	272.	278.
18939	230.	231.	225.	235.	243.	241.	240.	245.	244.	250.	248.	252.	257.	258.	252.	260.
18940	243.	238.	238.	247.	255.	259.	256.	258.	265.	265.	259.	270.	278.	278.	269.	278.
18941	228.	231.	237.	238.	237.	232.	246.	245.	247.	249.	243.	248.	253.	255.	254.	251.
18942	245.	250.	256.	261.	258.	249.	256.	257.	254.	247.	255.	257.	258.	254.	261.	265.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 21 (PAGE 3): BODY WEIGHTS - PRECOHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP I				0 (VEHICLE) MG/KG/DAY											
DAY	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32
18901	257.	259.	265.	260.	260.	266.	267.	267.	265.	270.	274.	277.	275.	280.	282.	278.
18902	258.	261.	260.	252.	257.	266.	269.	261.	265.	270.	271.	268.	274.	280.	277.	273.
18903	262.	268.	271.	267.	266.	277.	278.	275.	275.	282.	288.	285.	278.	285.	287.	288.
18904	254.	255.	250.	257.	255.	258.	253.	253.	257.	254.	261.	261.	262.	260.	258.	262.
18905	241.	235.	242.	239.	243.	238.	246.	246.	242.	238.	246.	252.	248.	245.	253.	258.
18906	293.	289.	300.	300.	301.	299.	307.	306.	308.	298.	309.	316.	305.	308.	317.	319.
18907	259.	264.	264.	267.	266.	271.	271.	272.	271.	275.	278.	281.	279.	283.	284.	284.
18908	240.	243.	250.	249.	248.	247.	248.	252.	250.	253.	257.	264.	261.	258.	261.	260.
18909	257.	260.	256.	251.	260.	262.	268.	255.	268.	267.	267.	266.	264.	266.	273.	272.
18910	249.	246.	246.	247.	250.	255.	252.	250.	256.	251.	251.	253.	258.	263.	264.	264.
18911	259.	253.	263.	266.	261.	262.	271.	272.	269.	271.	281.	273.	279.	274.	282.	282.
18912	262.	260.	265.	272.	271.	269.	266.	273.	278.	281.	279.	275.	284.	287.	285.	281.
18913	259.	250.	259.	263.	258.	259.	259.	260.	263.	256.	266.	271.	266.	267.	272.	278.
18914	286.	286.	290.	294.	295.	293.	292.	296.	299.	296.	302.	302.	302.	301.	307.	312.
18915	278.	277.	270.	279.	280.	285.	278.	281.	289.	290.	284.	290.	293.	294.	289.	297.
18916	259.	262.	273.	268.	266.	269.	271.	268.	260.	266.	269.	278.	269.	277.	276.	276.
18917	257.	261.	266.	256.	262.	269.	268.	266.	265.	268.	274.	275.	276.	276.	280.	282.
18918	249.	257.	262.	262.	248.	245.	256.	255.	258.	250.	262.	262.	265.	260.	256.	270.
18919	257.	255.	258.	259.	259.	260.	263.	265.	268.	264.	266.	271.	268.	265.	273.	271.
18920	262.	270.	269.	265.	267.	270.	275.	271.	271.	275.	277.	271.	270.	277.	276.	280.
18921	250.	246.	250.	254.	254.	248.	252.	254.	254.	248.	260.	262.	262.	258.	261.	265.
18922	263.	272.	276.	274.	270.	274.	278.	276.	278.	280.	282.	286.	288.	288.	288.	298.
18923	250.	249.	249.	256.	253.	257.	253.	254.	256.	256.	259.	260.	259.	263.	261.	266.
18924	276.	276.	284.	286.	286.	282.	289.	291.	287.	283.	296.	298.	293.	291.	299.	298.
18925	257.	256.	248.	254.	257.	260.	249.	252.	255.	264.	266.	261.	258.	266.	269.	269.
18926	273.	274.	271.	278.	280.	282.	276.	278.	288.	280.	284.	288.	291.	287.	288.	294.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 21 (PAGE 4): BODY WEIGHTS - PRECOHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP I				0 (VEHICLE) MG/KG/DAY											
DAY	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32
18927	241.	241.	244.	243.	243.	242.	246.	243.	243.	240.	242.	246.	244.	243.	246.	250.
18928	265.	262.	268.	271.	269.	266.	276.	273.	277.	268.	280.	284.	278.	277.	285.	288.
18929	245.	246.	252.	252.	255.	253.	261.	258.	260.	256.	260.	264.	260.	257.	263.	266.
18930	275.	272.	269.	270.	277.	277.	275.	281.	283.	283.	280.	286.	291.	288.	285.	289.
18931	264.	261.	270.	265.	273.	268.	266.	268.	270.	270.	278.	280.	278.	278.	283.	285.
18932	262.	266.	267.	267.	263.	266.	270.	270.	265.	270.	278.	278.	274.	279.	280.	282.
18933	246.	247.	240.	248.	249.	254.	252.	254.	258.	254.	247.	256.	262.	260.	259.	263.
18934	280.	284.	281.	276.	288.	292.	290.	283.	294.	296.	295.	292.	297.	304.	300.	298.
18935	254.	256.	263.	269.	267.	263.	267.	264.	271.	262.	270.	275.	274.	272.	275.	275.
18936	262.	267.	260.	265.	272.	272.	268.	275.	276.	274.	271.	284.	282.	285.	278.	286.
18937	240.	246.	250.	250.	247.	246.	249.	249.	254.	247.	246.	249.	252.	256.	250.	259.
18938	279.	272.	277.	278.	276.	278.	278.	283.	283.	276.	284.	290.	290.	279.	292.	293.
18939	265.	263.	263.	268.	270.	269.	268.	271.	279.	277.	272.	278.	280.	278.	276.	282.
18940	286.	286.	279.	282.	293.	293.	279.	285.	301.	294.	284.	295.	300.	302.	294.	302.
18941	257.	263.	260.	254.	255.	262.	266.	269.	270.	262.	272.	275.	275.	274.	273.	278.
18942	263.	262.	266.	268.	271.	262.	269.	272.	271.	262.	275.	274.	272.	266.	276.	279.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 21 (PAGE 5): BODY WEIGHTS - PRECOHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP I				0 (VEHICLE) MG/KG/DAY						
DAY	33	34	35	36	37	38	39	40	41	42	43a
18901	284.	284.	293.	294.	291.	294.	295.	293.	288.	290.	b
18902	279.	283.	285.	279.	285.	286.	282.	278.	277.	282.	b
18903	282.	292.	296.	295.	291.	297.	296.	294.	287.	295.	299.
18904	267.	269.	265.	268.	271.	272.	270.	271.	271.	272.	b
18905	252.	252.	260.	258.	260.	251.	258.	259.	255.	250.	b
18906	320.	317.	325.	328.	331.	320.	324.	332.	326.	319.	b
18907	287.	287.	299.	288.	286.	287.	292.	291.	282.	284.	b
18908	261.	261.	266.	266.	262.	257.	264.	264.	262.	258.	b
18909	274.	275.	274.	281.	287.	283.	276.	281.	280.	280.	b
18910	260.	264.	273.	273.	269.	263.	269.	269.	268.	267.	b
18911	283.	277.	292.	286.	291.	277.	287.	291.	280.	280.	b
18912	278.	286.	290.	287.	290.	286.	293.	296.	294.	287.	288.
18913	277.	270.	286.	289.	285.	271.	280.	286.	284.	277.	283.
18914	310.	307.	316.	318.	317.	311.	314.	318.	316.	314.	b
18915	297.	299.	296.	301.	304.	302.	299.	305.	310.	308.	b
18916	278.	277.	288.	288.	286.	290.	292.	290.	281.	290.	287.
18917	275.	282.	286.	289.	283.	280.	287.	284.	280.	286.	b
18918	275.	273.	268.	262.	276.	278.	276.	266.	260.	271.	268.
18919	273.	274.	275.	280.	279.	274.	279.	278.	276.	272.	272.
18920	273.	285.	285.	280.	278.	281.	285.	281.	278.	285.	287.
18921	268.	262.	275.	273.	273.	266.	268.	271.	269.	263.	262.
18922	302.	306.	302.	303.	305.	305.	303.	300.	309.	310.	b
18923	265.	267.	273.	268.	269.	266.	273.	273.	268.	271.	268.
18924	297.	298.	303.	307.	305.	297.	307.	311.	307.	301.	b
18925	260.	273.	279.	272.	267.	270.	276.	274.	266.	276.	b
18926	292.	293.	293.	299.	300.	299.	300.	299.	302.	301.	303.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Last value recorded before cohabitation.
b. Rat assigned to cohabitation on day 42 of study.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 21 (PAGE 6): BODY WEIGHTS - PRECOHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP I				0 (VEHICLE) MG/KG/DAY						
DAY	33	34	35	36	37	38	39	40	41	42	43a
18927	250.	247.	254.	258.	259.	252.	258.	259.	255.	251.	b
18928	283.	281.	292.	297.	289.	285.	292.	294.	289.	284.	b
18929	266.	266.	268.	273.	274.	268.	274.	273.	270.	267.	b
18930	294.	292.	291.	295.	299.	298.	298.	299.	304.	303.	290.
18931	283.	285.	290.	294.	290.	283.	287.	297.	288.	287.	289.
18932	277.	281.	291.	291.	286.	288.	290.	290.	286.	292.	b
18933	268.	264.	261.	262.	272.	272.	268.	271.	278.	269.	b
18934	303.	310.	312.	305.	315.	315.	315.	308.	318.	323.	b
18935	278.	272.	285.	286.	285.	283.	286.	285.	285.	278.	278.
18936	286.	289.	285.	291.	293.	262.	263.	263.	263.	267.	271.
18937	255.	260.	259.	254.	264.	267.	263.	262.	259.	260.	b
18938	297.	290.	293.	304.	303.	298.	296.	296.	300.	298.	294.
18939	287.	285.	280.	294.	290.	290.	289.	291.	299.	292.	b
18940	308.	303.	298.	302.	314.	307.	298.	305.	310.	313.	299.
18941	276.	283.	284.	278.	284.	286.	289.	285.	285.	284.	288.
18942	275.	273.	282.	282.	287.	276.	282.	282.	281.	278.	b

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Last value recorded before cohabitation.
b. Rat assigned to cohabitation on day 42 of study.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 21 (PAGE 7): BODY WEIGHTS - PRECOHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP II				1.6 MG/KG/DAY											
DAY	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
18943	218.	217.	227.	226.	232.	224.	234.	236.	234.	229.	238.	240.	236.	233.	238.	240.
18944	256.	266.	271.	270.	263.	267.	266.	263.	261.	268.	270.	268.	262.	272.	272.	271.
18945	234.	231.	229.	238.	238.	244.	236.	242.	246.	247.	240.	249.	253.	249.	244.	250.
18946	236.	238.	245.	248.	238.	236.	241.	244.	242.	238.	246.	247.	248.	245.	252.	254.
18947	211.	221.	228.	230.	228.	239.	241.	245.	239.	246.	250.	253.	252.	257.	261.	263.
18948	250.	246.	261.	257.	261.	255.	264.	268.	261.	250.	253.	270.	262.	263.	269.	266.
18949	228.	221.	216.	224.	231.	229.	226.	232.	237.	237.	233.	245.	246.	243.	237.	248.
18950	234.	230.	236.	243.	245.	239.	249.	251.	257.	248.	257.	262.	264.	253.	262.	266.
18951	227.	227.	225.	229.	233.	237.	229.	236.	239.	232.	228.	232.	240.	238.	236.	236.
18952	238.	244.	249.	251.	244.	259.	258.	261.	255.	265.	268.	269.	262.	279.	281.	280.
18953	235.	228.	237.	242.	241.	237.	242.	244.	240.	240.	249.	250.	248.	248.	249.	253.
18954	238.	233.	234.	241.	245.	247.	241.	249.	250.	249.	247.	245.	251.	256.	254.	253.
18955	225.	225.	220.	228.	233.	236.	227.	233.	231.	234.	232.	240.	242.	239.	240.	244.
18956	241.	239.	235.	243.	242.	246.	239.	247.	251.	250.	252.	255.	261.	261.	255.	262.
18957	226.	237.	242.	240.	234.	249.	249.	249.	242.	252.	258.	254.	254.	258.	265.	262.
18958	232.	234.	229.	241.	247.	246.	245.	254.	258.	259.	251.	260.	264.	268.	258.	267.
18959	222.	219.	226.	228.	231.	230.	230.	241.	240.	244.	240.	237.	247.	248.	246.	243.
18960	246.	245.	255.	254.	262.	261.	269.	272.	272.	272.	275.	279.	277.	277.	293.	291.
18961	222.	225.	226.	222.	234.	236.	235.	231.	236.	241.	244.	237.	245.	249.	250.	238.
18962	225.	231.	232.	241.	236.	246.	252.	253.	252.	259.	260.	259.	258.	263.	272.	269.
18963	217.	227.	230.	226.	221.	233.	241.	238.	233.	240.	242.	241.	232.	243.	242.	248.
18964	237.	240.	240.	234.	244.	247.	244.	237.	243.	240.	242.	242.	248.	253.	251.	246.
18965	224.	224.	224.	232.	230.	233.	229.	236.	232.	232.	236.	237.	238.	238.	233.	240.
18966	238.	239.	244.	242.	253.	246.	248.	254.	254.	259.	252.	252.	256.	262.	267.	261.
18967	226.	223.	235.	238.	236.	233.	246.	251.	249.	244.	257.	259.	258.	252.	261.	266.
18968	239.	246.	247.	243.	255.	256.	259.	254.	266.	264.	268.	262.	270.	273.	277.	272.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 21 (PAGE 8): BODY WEIGHTS - PRECOHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP II				1.6 MG/KG/DAY											
DAY	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
18969	229.	225.	235.	242.	237.	236.	243.	246.	247.	244.	252.	259.	256.	253.	262.	261.
18970	224.	234.	235.	238.	233.	240.	248.	245.	243.	245.	254.	254.	249.	256.	261.	258.
18971	224.	222.	231.	233.	235.	234.	243.	243.	245.	239.	245.	252.	250.	246.	251.	253.
18972	234.	239.	245.	247.	243.	250.	253.	250.	254.	259.	260.	264.	262.	267.	273.	272.
18973	230.	227.	236.	240.	238.	236.	243.	247.	244.	242.	249.	252.	249.	249.	256.	259.
18974	236.	240.	250.	250.	246.	254.	262.	263.	259.	263.	271.	272.	269.	276.	278.	276.
18975	234.	231.	245.	242.	246.	242.	254.	256.	257.	250.	263.	266.	266.	263.	274.	280.
18976	232.	240.	247.	249.	246.	253.	246.	229.	242.	241.	241.	243.	249.	256.	258.	258.
18977	222.	229.	228.	224.	234.	236.	236.	235.	238.	242.	243.	240.	245.	243.	247.	247.
18978	234.	244.	243.	240.	252.	252.	254.	251.	255.	253.	254.	252.	261.	260.	259.	256.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 21 (PAGE 9): BODY WEIGHTS - PRECOHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP II				1.6 MG/KG/DAY											
DAY	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32
18943	240.	235.	241.	244.	243.	246.	249.	252.	250.	248.	252.	252.	250.	249.	255.	258.
18944	272.	272.	277.	274.	276.	280.	287.	284.	278.	287.	290.	290.	290.	288.	293.	300.
18945	253.	247.	247.	251.	255.	251.	246.	250.	257.	253.	250.	253.	254.	256.	255.	257.
18946	253.	256.	260.	263.	260.	264.	261.	269.	266.	264.	269.	272.	272.	269.	269.	272.
18947	258.	269.	268.	265.	262.	269.	268.	265.	262.	264.	265.	268.	262.	269.	271.	269.
18948	266.	260.	266.	267.	268.	271.	273.	278.	279.	272.	280.	279.	279.	274.	279.	286.
18949	250.	247.	247.	250.	259.	252.	253.	257.	259.	258.	253.	262.	264.	258.	257.	264.
18950	266.	261.	270.	270.	270.	266.	268.	268.	271.	266.	270.	275.	272.	267.	270.	270.
18951	243.	238.	236.	242.	243.	244.	241.	246.	249.	246.	246.	251.	254.	256.	253.	255.
18952	270.	283.	287.	277.	268.	286.	284.	283.	276.	283.	287.	289.	282.	292.	295.	294.
18953	257.	254.	254.	258.	262.	259.	264.	267.	269.	269.	278.	278.	279.	274.	280.	279.
18954	253.	256.	261.	259.	258.	257.	258.	261.	258.	257.	266.	261.	261.	259.	258.	264.
18955	243.	244.	240.	246.	252.	253.	251.	255.	258.	258.	254.	263.	263.	263.	262.	264.
18956	268.	266.	263.	269.	267.	267.	265.	268.	272.	270.	271.	272.	280.	276.	277.	280.
18957	254.	264.	264.	260.	255.	266.	263.	262.	258.	265.	268.	265.	263.	273.	272.	267.
18958	274.	270.	265.	269.	275.	274.	268.	272.	275.	276.	268.	278.	280.	279.	275.	280.
18959	243.	249.	253.	253.	250.	250.	252.	254.	256.	250.	250.	255.	257.	256.	254.	254.
18960	285.	282.	296.	288.	290.	288.	293.	294.	296.	291.	299.	303.	298.	297.	305.	303.
18961	251.	253.	252.	249.	252.	258.	252.	244.	252.	257.	258.	258.	261.	262.	260.	255.
18962	269.	273.	276.	272.	272.	278.	271.	273.	269.	282.	287.	287.	283.	290.	290.	287.
18963	241.	252.	253.	249.	241.	254.	256.	254.	248.	251.	259.	257.	248.	259.	259.	257.
18964	255.	258.	258.	250.	261.	260.	258.	246.	257.	263.	263.	261.	263.	262.	260.	261.
18965	242.	239.	237.	246.	242.	242.	238.	244.	242.	244.	242.	248.	245.	247.	244.	250.
18966	259.	265.	267.	268.	270.	267.	270.	272.	269.	271.	274.	275.	274.	276.	274.	280.
18967	262.	261.	264.	266.	266.	266.	274.	275.	273.	272.	274.	276.	277.	276.	282.	287.
18968	279.	281.	280.	270.	275.	280.	276.	273.	285.	279.	284.	278.	286.	289.	286.	284.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 21 (PAGE 10): BODY WEIGHTS - PRECOHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP II				1.6 MG/KG/DAY											
DAY	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32
18969	260.	258.	267.	264.	265.	266.	271.	274.	271.	271.	274.	276.	279.	270.	277.	279.
18970	256.	261.	265.	264.	258.	268.	271.	266.	263.	272.	274.	272.	269.	275.	276.	279.
18971	253.	250.	255.	259.	262.	262.	260.	261.	264.	263.	268.	268.	267.	264.	268.	274.
18972	271.	273.	278.	276.	276.	279.	284.	282.	281.	278.	285.	289.	286.	288.	290.	295.
18973	260.	254.	257.	259.	259.	261.	262.	262.	265.	262.	266.	270.	267.	261.	272.	269.
18974	266.	274.	274.	276.	272.	280.	284.	282.	279.	281.	289.	283.	278.	288.	286.	285.
18975	281.	273.	280.	286.	285.	282.	282.	291.	290.	287.	290.	296.	291.	288.	297.	299.
18976	258.	260.	262.	261.	260.	271.	268.	264.	265.	271.	270.	270.	267.	280.	279.	275.
18977	253.	254.	250.	248.	258.	263.	255.	252.	261.	263.	262.	255.	265.	264.	266.	262.
18978	266.	268.	264.	261.	274.	275.	266.	266.	273.	273.	270.	269.	272.	275.	274.	274.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 21 (PAGE 11): BODY WEIGHTS - PRECOHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP II				1.6 MG/KG/DAY						
DAY	33	34	35	36	37	38	39	40	41	42	43a
18943	257.	252.	263.	262.	259.	250.	258.	257.	251.	248.	252.
18944	296.	295.	295.	304.	309.	302.	300.	305.	303.	298.	292.
18945	257.	255.	257.	259.	267.	264.	256.	261.	262.	261.	253.
18946	271.	278.	275.	280.	281.	274.	277.	283.	282.	280.	281.
18947	265.	274.	276.	274.	267.	275.	276.	273.	267.	273.	271.
18948	282.	284.	288.	289.	286.	280.	280.	290.	281.	279.	288.
18949	271.	263.	260.	269.	272.	265.	267.	270.	271.	268.	263.
18950	270.	266.	265.	273.	276.	272.	266.	270.	271.	271.	269.
18951	255.	256.	251.	260.	258.	255.	250.	253.	252.	252.	245.
18952	288.	295.	301.	299.	291.	295.	299.	294.	284.	291.	288.
18953	283.	280.	283.	287.	288.	280.	288.	286.	287.	283.	280.
18954	268.	270.	268.	264.	266.	265.	266.	262.	258.	261.	254.
18955	262.	263.	261.	265.	266.	258.	257.	259.	259.	259.	253.
18956	286.	281.	283.	283.	287.	283.	279.	282.	288.	283.	275.
18957	271.	275.	276.	273.	271.	275.	277.	280.	272.	278.	275.
18958	285.	280.	279.	282.	284.	284.	279.	285.	284.	281.	270.
18959	261.	261.	264.	264.	266.	272.	268.	268.	270.	274.	271.
18960	309.	303.	314.	315.	310.	307.	313.	313.	308.	307.	310.
18961	264.	270.	270.	265.	270.	269.	264.	262.	266.	270.	269.
18962	288.	288.	293.	288.	290.	289.	293.	289.	287.	291.	290.
18963	253.	263.	267.	266.	263.	265.	265.	263.	256.	258.	259.
18964	267.	271.	268.	265.	267.	266.	262.	258.	260.	261.	252.
18965	252.	246.	247.	250.	248.	249.	246.	246.	252.	248.	240.
18966	280.	280.	278.	274.	284.	282.	282.	279.	282.	287.	281.
18967	283.	284.	288.	292.	294.	287.	292.	291.	290.	285.	288.
18968	292.	299.	296.	286.	295.	292.	294.	289.	293.	299.	286.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Last value recorded before cohabitation.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 21 (PAGE 12): BODY WEIGHTS - PRECOHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP II				1.6 MG/KG/DAY						
DAY	33	34	35	36	37	38	39	40	41	42	43a
18969	276.	275.	286.	286.	286.	281.	288.	291.	287.	285.	284.
18970	272.	279.	285.	282.	277.	280.	281.	281.	274.	281.	282.
18971	272.	270.	280.	280.	277.	271.	276.	276.	274.	275.	275.
18972	291.	289.	295.	297.	296.	293.	297.	298.	295.	289.	291.
18973	268.	268.	276.	276.	277.	269.	274.	275.	270.	269.	275.
18974	282.	284.	285.	282.	284.	286.	292.	284.	278.	286.	288.
18975	302.	295.	308.	309.	305.	299.	301.	302.	305.	301.	301.
18976	275.	281.	279.	281.	278.	279.	283.	278.	274.	280.	280.
18977	271.	272.	276.	267.	274.	276.	275.	267.	272.	276.	273.
18978	278.	277.	275.	272.	284.	276.	276.	265.	276.	276.	275.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Last value recorded before cohabitation.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 22 (PAGE 1): MATERNAL BODY WEIGHTS - PRESUMED GESTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP I	0 (VEHICLE) MG/KG/DAY										
PREGNANCY STATUS	DAY 0	1	2	3	4	5	6	7	8	9	10	11	12
18901 P	293.	309.	311.	312.	321.	316.	323.	327.	326.	330.	328.	339.	345.
18902 NP	288.	300.	299.	303.	308.	314.	316.	318.	317.	321.	320.	318.	327.
18903 P	296.	307.	313.	316.	325.	329.	333.	330.	335.	342.	346.	353.	360.
18904 P	276.	280.	286.	292.	294.	299.	301.	307.	304.	308.	314.	316.	321.
18905 NP	MATING NOT CONFIRMED												
18906 P	334.	348.	359.	366.	370.	373.	378.	377.	384.	386.	392.	393.	409.
18907 P	301.	317.	320.	319.	318.	330.	329.	327.	333.	336.	342.	352.	357.
18908 P	276.	287.	282.	287.	292.	291.	304.	302.	307.	308.	316.	324.	332.
18909 P	290.	300.	305.	304.	308.	310.	317.	320.	321.	325.	330.	340.	345.
18910 P	270.	280.	287.	286.	293.	295.	299.	301.	304.	306.	311.	313.	316.
18911 P	293.	308.	308.	310.	318.	316.	322.	327.	330.	335.	333.	337.	345.
18912 P	302.	312.	316.	319.	321.	328.	328.	337.	335.	340.	348.	350.	361.
18913 P	291.	299.	306.	306.	300.	300.	302.	314.	309.	313.	326.	329.	334.
18914 NP	307.	317.	332.	329.	335.	342.	350.	350.	350.	356.	365.	355.	343.
18915 P	320.	326.	327.	335.	335.	340.	346.	345.	354.	358.	367.	377.	382.
18916 P a	286.	296.	296.	296.	310.	306.	308.	310.	317.	323.	321.	333.	329.
18917 P	298.	308.	305.	308.	314.	317.	323.	326.	328.	330.	334.	345.	348.
18918 P	279.	292.	293.	299.	301.	312.	319.	322.	321.	331.	332.	342.	340.
18919 P	286.	300.	300.	304.	306.	315.	320.	320.	329.	326.	341.	350.	353.
18920 P	294.	299.	303.	307.	310.	315.	316.	319.	317.	322.	327.	336.	344.
18921 NP	269.	266.	262.	265.	267.	263.	259.	262.	263.	263.	260.	266.	266.
18922 P	310.	320.	318.	325.	329.	336.	341.	345.	352.	357.	367.	370.	378.
18923 P	276.	282.	287.	291.	296.	298.	299.	302.	301.	305.	310.	318.	321.
18924 P	323.	333.	341.	346.	355.	347.	351.	360.	356.	360.	364.	380.	376.
18925 NP	284.	278.	284.	288.	284.	275.	289.	285.	287.	280.	283.	291.	291.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Dam 18916 did not deliver a litter; only one dead fetus was present in utero on day 25 of gestation.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 22 (PAGE 2): MATERNAL BODY WEIGHTS - PRESUMED GESTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP I	0 (VEHICLE) MG/KG/DAY											
	PREGNANCY STATUS	DAY 0	1	2	3	4	5	6	7	8	9	10	11	12
18926	P	317.	320.	327.	328.	332.	332.	337.	340.	344.	345.	355.	360.	371.
18927	P	273.	288.	293.	298.	303.	304.	304.	315.	313.	317.	320.	327.	327.
18928	NP	MATING NOT CONFIRMED												
18929	P	292.	302.	305.	308.	320.	317.	323.	330.	329.	335.	349.	352.	358.
18930	NP	312.	324.	329.	332.	334.	334.	336.	338.	337.	344.	343.	344.	352.
18931	P	298.	300.	310.	314.	320.	322.	330.	336.	331.	336.	348.	351.	356.
18932	P	290.	294.	304.	307.	312.	315.	316.	316.	321.	328.	330.	340.	344.
18933	P	288.	289.	293.	300.	306.	303.	304.	312.	319.	322.	330.	325.	335.
18934	P	315.	327.	336.	340.	341.	351.	349.	354.	361.	368.	368.	375.	373.
18935	P	295.	292.	297.	306.	319.	321.	330.	326.	327.	330.	336.	336.	340.
18936	P	270.	272.	279.	278.	277.	278.	277.	291.	305.	313.	312.	318.	324.
18937	P	265.	274.	284.	289.	294.	300.	296.	301.	304.	300.	309.	312.	317.
18938	P	306.	317.	328.	329.	328.	334.	335.	341.	343.	351.	358.	361.	366.
18939	P	302.	310.	313.	323.	324.	326.	326.	330.	334.	336.	346.	345.	356.
18940	P	329.	333.	340.	346.	357.	369.	363.	360.	362.	370.	376.	383.	390.
18941	P	300.	308.	315.	326.	327.	333.	335.	338.	343.	347.	356.	360.	364.
18942	P	294.	302.	305.	312.	315.	321.	321.	330.	325.	328.	337.	341.	346.

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

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 22 (PAGE 3): MATERNAL BODY WEIGHTS - PRESUMED GESTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP I	0 (VEHICLE) MG/KG/DAY											
	PREGNANCY STATUS	DAY 13	14	15	16	17	18	19	20	21	22	23	24	25
18901	P	344.	353.	358.	374.	379.	400.	417.	436.	455.				
18902	NP	325.	315.	310.	309.	309.	307.	300.	304.	313.	314.	306.	303.	315.
18903	P	361.	367.	380.	392.	402.	426.	452.	470.	488.				
18904	P	322.	326.	335.	356.	371.	387.	406.	427.	450.	304.			
18905	NP	MATING NOT CONFIRMED												
18906	P	422.	414.	426.	440.	460.	483.	499.	523.	526.				
18907	P	354.	363.	376.	380.	396.	414.	436.	456.	478.				
18908	P	333.	339.	348.	363.	377.	397.	413.	443.	459.				
18909	P	349.	356.	362.	378.	394.	395.	414.	427.	445.	429.			
18910	P	320.	319.	324.	333.	342.	346.	355.	357.	369.				
18911	P	355.	354.	365.	374.	392.	409.	424.	455.	464.	329.			
18912	P	366.	373.	374.	388.	406.	427.	444.	467.	480.				
18913	P	343.	343.	352.	368.	383.	404.	409.	434.	443.	457.			
18914	NP	340.	347.	341.	342.	346.	349.	346.	340.	350.	347.	351.	350.	350.
18915	P	389.	397.	406.	426.	436.	452.	478.	491.	525.				
18916	P a	331.	339.	340.	334.	334.	340.	347.	341.	341.	336.	322.	324.	327.
18917	P	347.	358.	365.	372.	386.	396.	412.	428.	444.	438.			
18918	P	359.	354.	366.	369.	378.	395.	413.	425.	442.	431.			
18919	P	366.	367.	366.	382.	394.	413.	434.	454.	463.				
18920	P	348.	356.	364.	372.	383.	406.	428.	434.	451.				
18921	NP	265.	259.	268.	267.	263.	258.	263.	270.	271.	268.	277.	280.	286.
18922	P	374.	383.	394.	404.	415.	431.	442.	465.	477.				
18923	P	325.	333.	341.	348.	359.	376.	394.	405.	412.				
18924	P	393.	388.	394.	398.	403.	421.	442.	468.	476.				
18925	NP	280.	288.	294.	289.	287.	286.	287.	298.	298.	294.	292.	288.	290.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAY = DAY OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Dam 18916 did not deliver a litter; only one dead fetus was present in utero on day 25 of gestation.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 22 (PAGE 4): MATERNAL BODY WEIGHTS - PRESUMED GESTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP I	0 (VEHICLE) MG/KG/DAY											
	PREGNANCY STATUS	DAY 13	14	15	16	17	18	19	20	21	22	23	24	25
18926	P	373.	370.	375.	389.	406.	420.	443.	450.	465.				
18927	P	339.	339.	336.	353.	364.	385.	402.	429.	443.				
18928	NP	MATING NOT CONFIRMED												
18929	P	370.	375.	373.	382.	405.	423.	437.	470.	478.	477.			
18930	NP	338.	329.	329.	335.	335.	328.	334.	335.	327.	322.	336.	338.	330.
18931	P	357.	357.	360.	371.	389.	405.	405.	428.	434.				
18932	P	348.	354.	366.	368.	383.	398.	421.	434.	457.	449.			
18933	P	337.	340.	350.	370.	384.	396.	421.	442.	468.				
18934	P	384.	385.	401.	410.	413.	434.	455.	475.	480.				
18935	P	358.	359.	370.	382.	392.	417.	425.	450.	457.				
18936	P	319.	330.	343.	352.	357.	370.	389.	398.	413.				
18937	P	323.	324.	328.	343.	359.	374.	394.	418.	427.	433.			
18938	P	378.	382.	385.	401.	417.	438.	446.	472.	474.				
18939	P	358.	360.	366.	376.	389.	395.	409.	428.	462.				
18940	P	390.	392.	393.	408.	425.	435.	456.	468.	469.				
18941	P	372.	370.	377.	393.	400.	424.	436.	466.	470.				
18942	P	353.	364.	365.	373.	386.	401.	420.	437.	445.	310.			

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

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 22 (PAGE 5): MATERNAL BODY WEIGHTS - PRESUMED GESTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP II	1.6 MG/KG/DAY											
	PREGNANCY STATUS	DAY 0	1	2	3	4	5	6	7	8	9	10	11	12
18943	P	261.	272.	270.	272.	274.	276.	276.	276.	282.	282.	295.	297.	303.
18944	NP	307.	319.	322.	326.	326.	322.	334.	340.	329.	333.	340.	348.	349.
18945	NP	MATING NOT CONFIRMED												
18946	P	291.	295.	302.	303.	304.	298.	311.	323.	314.	315.	320.	325.	333.
18947	P	282.	286.	293.	292.	297.	300.	304.	309.	313.	318.	321.	319.	330.
18948	P	292.	300.	304.	302.	313.	314.	317.	327.	325.	329.	342.	349.	354.
18949	NP	278.	279.	280.	284.	284.	280.	279.	287.	283.	277.	278.	282.	279.
18950	P	287.	290.	294.	296.	299.	296.	303.	300.	309.	307.	317.	320.	320.
18951	P	264.	264.	272.	273.	273.	275.	280.	284.	285.	289.	294.	299.	302.
18952	P	296.	307.	307.	310.	316.	319.	323.	320.	330.	329.	331.	342.	341.
18953	P	295.	305.	306.	309.	304.	308.	316.	316.	320.	320.	329.	337.	339.
18954	NP	266.	268.	266.	261.	258.	263.	265.	263.	261.	265.	263.	266.	260.
18955	NP	261.	266.	267.	264.	269.	272.	268.	264.	267.	271.	271.	267.	273.
18956	P	288.	296.	298.	293.	295.	290.	296.	299.	303.	305.	309.	313.	318.
18957	P	289.	288.	293.	295.	296.	297.	301.	301.	308.	313.	317.	324.	327.
18958	P	289.	304.	306.	308.	311.	310.	310.	313.	316.	322.	330.	336.	344.
18959	P	270.	273.	280.	283.	280.	287.	284.	290.	293.	296.	301.	306.	310.
18960	P	316.	331.	327.	336.	338.	334.	337.	341.	338.	346.	352.	356.	360.
18961	P	273.	279.	281.	291.	298.	294.	302.	304.	302.	304.	314.	317.	322.
18962	NP	290.	283.	287.	288.	282.	281.	282.	284.	280.	275.	281.	282.	282.
18963	P	266.	268.	277.	281.	288.	292.	293.	296.	302.	305.	313.	320.	328.
18964	P	259.	267.	272.	272.	272.	276.	279.	284.	291.	287.	294.	295.	302.
18965	P	264.	268.	269.	271.	272.	278.	275.	280.	281.	285.	293.	302.	306.
18966	NP	MATING NOT CONFIRMED												
18967	P	285.	282.	299.	303.	307.	302.	301.	306.	309.	310.	323.	327.	332.

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

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 22 (PAGE 6): MATERNAL BODY WEIGHTS - PRESUMED GESTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP II	1.6 MG/KG/DAY											
	PREGNANCY STATUS	DAY 0	1	2	3	4	5	6	7	8	9	10	11	12
18968	P	302.	302.	307.	306.	311.	310.	318.	328.	327.	331.	324.	335.	341.
18969	P	294.	306.	306.	305.	310.	311.	310.	322.	316.	322.	331.	340.	334.
18970	P	286.	292.	295.	297.	294.	298.	301.	300.	310.	309.	316.	320.	323.
18971	P	282.	288.	288.	290.	291.	303.	300.	309.	303.	304.	315.	312.	326.
18972	P	298.	309.	309.	314.	315.	315.	321.	324.	335.	328.	337.	344.	349.
18973	P	268.	279.	276.	282.	280.	288.	288.	293.	291.	294.	303.	308.	314.
18974	P	297.	305.	305.	306.	312.	319.	319.	319.	330.	328.	334.	344.	348.
18975	NP	313.	315.	318.	324.	315.	316.	325.	330.	326.	326.	333.	341.	337.
18976	P	292.	296.	295.	294.	302.	306.	306.	311.	318.	320.	328.	330.	335.
18977	P	280.	285.	283.	289.	294.	299.	308.	315.	316.	315.	322.	329.	337.
18978	NP	283.	285.	284.	288.	290.	292.	296.	298.	302.	301.	294.	293.	283.

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

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 22 (PAGE 7): MATERNAL BODY WEIGHTS - PRESUMED GESTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP II			1.6 MG/KG/DAY								
PREGNANCY STATUS	DAY 13	14	15	16	17	18	19	20	21	22	23	24	25
18943 P	302.	307.	324.	339.	354.	374.	394.	417.	424.				
18944 NP	353.	336.	334.	327.	328.	326.	321.	325.	327.	325.	322.	329.	328.
18945 NP	MATING NOT CONFIRMED												
18946 P	335.	334.	343.	365.	375.	394.	418.	444.	450.				
18947 P	327.	342.	346.	356.	374.	394.	405.	412.	431.				
18948 P	362.	359.	359.	385.	402.	424.	443.	458.	470.				
18949 NP	279.	281.	275.	280.	272.	281.	277.	280.	271.	272.	276.	275.	278.
18950 P	318.	335.	341.	355.	375.	394.	410.	419.	442.				
18951 P	306.	309.	317.	330.	346.	359.	375.	393.	406.				
18952 P	340.	354.	359.	364.	386.	402.	420.	430.	446.				
18953 P	348.	351.	349.	366.	370.	401.	413.	444.	442.				
18954 NP	255.	265.	264.	265.	259.	255.	263.	266.	254.	266.	255.	254.	264.
18955 NP	273.	272.	270.	272.	268.	266.	296.	269.	273.	274.	269.	271.	277.
18956 P	320.	324.	330.	337.	353.	366.	380.	395.	412.	416.			
18957 P	330.	338.	345.	350.	369.	389.	401.	413.	420.				
18958 P	346.	349.	356.	367.	385.	403.	421.	426.	443.				
18959 P	320.	320.	332.	341.	351.	361.	376.	394.	406.				
18960 P	367.	362.	371.	388.	406.	425.	438.	449.	461.				
18961 P	333.	328.	340.	352.	357.	382.	401.	417.	436.				
18962 NP	279.	280.	284.	284.	285.	288.	288.	290.	288.	293.	294.	297.	293.
18963 P	329.	339.	345.	355.	365.	380.	378.	391.	406.				
18964 P	304.	309.	319.	323.	338.	361.	374.	391.	399.				
18965 P	310.	316.	332.	345.	371.	384.	407.	411.					
18966 NP	MATING NOT CONFIRMED												
18967 P	345.	349.	352.	368.	388.	406.	425.	445.	457.				

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

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 22 (PAGE 8): MATERNAL BODY WEIGHTS - PRESUMED GESTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP II	1.6 MG/KG/DAY											
	PREGNANCY STATUS	DAY 13	14	15	16	17	18	19	20	21	22	23	24	25
18968	P	342.	351.	366.	373.	387.	407.	426.	447.	452.				
18969	P	345.	350.	364.	372.	386.	415.	434.	459.	472.				
18970	P	327.	333.	334.	346.	362.	374.	391.	406.	406.				
18971	P	322.	320.	324.	319.	332.	340.	345.	354.	355.	356.	318.		
18972	P	365.	365.	365.	383.	398.	422.	437.	460.	468.				
18973	P	321.	321.	329.	341.	355.	387.	398.	422.	420.				
18974	P	354.	367.	374.	378.	396.	410.	433.	440.	469.				
18975	NP	326.	315.	316.	324.	317.	313.	318.	329.	309.	309.	297.	320.	311.
18976	P	338.	343.	352.	360.	372.	389.	404.	423.	456.				
18977	P	341.	345.	358.	370.	380.	394.	414.	430.	461.				
18978	NP	278.	281.	291.	284.	274.	287.	291.	288.	283.	295.	294.	291.	290.

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

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 23 (PAGE 1): MATERNAL BODY WEIGHTS - LACTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RATS ASSIGNED TO CROSS-FOSTERING

RAT #	DOSAGE GROUP I a			0 (VEHICLE) MG/KG/DAY				SUBSET A					
	DAY 1	2	3	4	5	6	7	8	9	10	11	12	13
18903	353.	342.	337.	333.	338.	341.	336.	345.	346.	365.	363.	368.	358.
18907	337.	334.	329.	328.	345.	338.	346.	341.	353.	366.	357.	325.	356.
18908	318.	311.	324.	321.	318.	319.	328.	336.	339.	342.	341.	337.	365.
18909	319.	319.	317.	321.	337.	336.	347.	362.	345.	359.	350.	355.	345.
18918b	300.	309.	321.	341.	345.	343.	353.	360.	350.	356.	347.	351.	370.
18920	325.	325.	320.	319.	338.	339.	345.	342.	307.c	345.	360.	360.	350.
18924	351.	343.	318.	356.	361.	360.	369.	368.	370.	379.	387.	373.	376.
18929	330.	337.	344.	348.	353.	354.	350.	354.	365.	371.	356.	373.	375.
18934	362.	353.	358.	365.	365.	373.	363.	369.	367.	335.	369.	378.	379.
18936b	315.	302.	310.	314.	303.	306.	326.	335.	332.	343.	333.	334.	334.
18937	294.	303.	304.	324.	328.	340.	344.	358.	361.	342.	342.	362.	371.
18941	354.	356.	348.	358.	358.	360.	356.	357.	365.	371.	383.	374.	374.
18942	340.	332.	337.	320.	345.	347.	340.	354.	347.	344.	350.	368.	361.

	DAY 14	15	16	17	18	19	20	21	22
18903	374.	386.	378.	388.	383.	399.	390.	377.	364.
18907	355.	346.	353.	370.	358.	351.	355.	349.	358.
18908	364.	370.	368.	368.	367.	379.	374.	379.	372.
18909	353.	373.	371.	384.	373.	376.	379.	386.	353.
18918	377.	363.	374.	382.	386.	388.	397.	365.	360.
18920	360.	371.	366.	363.	367.	369.	374.	370.	362.
18924	370.	388.	404.	394.	403.	396.	398.	389.	365.
18929	383.	388.	383.	390.	394.	380.	379.	380.	354.
18934	370.	380.	381.	390.	381.	381.	372.	361.	375.
18936	330.	350.	348.	352.	313.	335.	326.	349.	353.
18937	381.	371.	377.	368.	377.	369.	392.	384.	346.
18941	382.	383.	375.	376.	403.	391.	374.	371.	373.
18942	366.	378.	383.	372.	361.	371.	372.	364.	360.

DAY = DAY OF LACTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Vehicle control group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
b. Litter was not cross-fostered; values excluded from group averages.
c. Water access was interrupted; value excluded from group averages.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 23 (PAGE 2): MATERNAL BODY WEIGHTS - LACTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RATS ASSIGNED TO CROSS-FOSTERING

RAT #	DOSAGE GROUP I a			0 (VEHICLE) MG/KG/DAY				SUBSET B					
	DAY 1	2	3	4	5	6	7	8	9	10	11	12	13
18901	313.	338.	343.	351.	366.	368.	370.	355.	359.	375.	374.	366.	371.
18904	311.	314.	313.	314.	330.	345.	353.	362.	353.	341.	316.b	337.	337.
18906	399.	394.	407.	420.	426.	420.	417.	391.	405.	430.	412.	426.	440.
18912	347.	355.	355.	361.	363.	362.	368.	374.	376.	383.	363.	366.	367.
18917	325.	331.	338.	343.	349.	352.	357.	362.	362.	370.	368.	362.	369.
18919	338.	324.	344.	355.	354.	357.	357.	349.	369.	359.	352.	353.	375.
18922	366.	362.	370.	363.	367.	341.	372.	377.	371.	374.	372.	378.	386.
18923	280.	292.	300.	307.	314.	317.	330.	323.	330.	344.	346.	336.	328.
18931	324.	322.	331.	340.	345.	358.	356.	361.	362.	354.	355.	357.	363.
18932	320.	322.	337.	344.	342.	334.	341.	348.	355.	359.	354.	349.	347.
18935	320.	313.	320.	316.	339.	334.	319.	327.	328.	323.	326.	325.	343.
18938	338.	339.	346.	346.	351.	366.	375.	370.	382.	378.	384.	375.	392.

	DAY 14	15	16	17	18	19	20	21	22
18901	384.	376.	375.	372.	388.	385.	395.	380.	358.
18904	315.	333.	343.	350.	352.	352.	351.	358.	356.
18906	436.	438.	456.	457.	441.	443.	448.	437.	406.
18912	379.	382.	372.	378.	380.	389.	398.	385.	345.
18917	370.	366.	377.	364.	374.	372.	383.	377.	376.
18919	372.	380.	374.	374.	380.	385.	366.	380.	375.
18922	377.	387.	389.	385.	389.	390.	392.	401.	420.
18923	331.	339.	340.	343.	339.	346.	334.	334.	324.
18931	366.	367.	363.	362.	372.	373.	375.	370.	358.
18932	353.	352.	367.	362.	375.	363.	368.	353.	368.
18935	351.	343.	346.	352.	348.	352.	333.	340.	349.
18938	381.	388.	397.	390.	395.	397.	383.	365.	362.

DAY = DAY OF LACTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Vehicle control group dams cross-fostered with vehicle control litters.
b. Water access was interrupted; value excluded from group averages.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 23 (PAGE 3): MATERNAL BODY WEIGHTS - LACTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RATS ASSIGNED TO CROSS-FOSTERING

RAT #	DOSAGE GROUP II a			1.6 MG/KG/DAY				SUBSET C					
	DAY 1	2	3	4	5	6	7	8	9	10	11	12	13
18943	291.	297.	307.	310.	325.	320.	324.	322.	326.	331.	316.	324.	346.
18947	324.	318.	325.	322.	334.	338.	326.	344.	348.	344.	347.	350.	346.
18948	345.	344.	343.	341.	346.	350.	353.	364.	357.	363.	363.	357.	366.
18957	318.	316.	313.	312.	317.	326.	325.	323.	332.	345.	337.	338.	341.
18960	345.	349.	341.	352.	351.	354.	361.	364.	380.	376.	380.	376.	330.b
18964	313.	302.	313.	312.	319.	304.	317.	325.	334.	330.	327.	329.	321.
18967	331.	327.	335.	342.	336.	331.	338.	361.	345.	360.	348.	367.	368.
18968	331.	327.	331.	332.	324.	340.	348.	344.	337.	347.	358.	353.	359.
18969	336.	334.	334.	338.	342.	339.	352.	347.	358.	351.	354.	357.	366.
18970	324.	311.	316.	324.	326.	329.	332.	345.	345.	359.	348.	355.	340.
18973	296.	292.	294.	302.	300.	290.	300.	304.	312.	318.	317.	306.	314.
18974	360.	353.	338.	336.	NO SURVIVING PUPS ON DAY 4 OF LACTATION								

	DAY 14	15	16	17	18	19	20	21	22
18943	344.	334.	362.	358.	353.	356.	289.b	322.	339.
18947	359.	359.	368.	376.	372.	368.	367.	371.	339.
18948	374.	378.	385.	372.	380.	378.	326.	292.b	353.
18957	349.	361.	357.	360.	366.	366.	353.	352.	350.
18960	381.	380.	380.	395.	399.	397.	407.	396.	390.
18964	329.	343.	348.	348.	353.	351.	363.	361.	329.
18967	346.	374.	374.	379.	383.	383.	383.	357.	366.
18968	350.	364.	363.	377.	381.	373.	388.	385.	374.
18969	360.	369.	365.	371.	372.	371.	361.	368.	376.
18970	350.	358.	364.	374.	370.	371.	376.	344.b	343.
18973	316.	314.	315.	324.	327.	332.	332.	317.	343.
18974	NO SURVIVING PUPS ON DAY 4 OF LACTATION								

DAY = DAY OF LACTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. 1.6 mg/kg/day dosage group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
b. Water access was interrupted; value excluded from group averages.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 23 (PAGE 4): MATERNAL BODY WEIGHTS - LACTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RATS ASSIGNED TO CROSS-FOSTERING

RAT #	DOSAGE GROUP II a			1.6 MG/KG/DAY				SUBSET D				
DAY	1	2	3	4	5	6	7	8	9	10	11	12	13
18946b	325.	321.	320.	322.	329.	334.	342.	320.	343.	346.	352.	341.	348.
18950	332.	326.	319.	317.	328.	344.	332.	342.	351.	335.	337.	349.	354.
18951	299.	298.	300.	300.	307.	305.	305.	309.	311.	311.	309.	317.	325.
18952	328.	331.	333.	335.	350.	355.	350.	358.	355.	360.	360.	365.	357.
18953	325.	320.	323.	318.	316.	315.	321.	332.	327.	339.	348.	331.	340.
18958	333.	327.	327.	324.	316.	316.	321.	326.	329.	331.	329.	335.	338.
18959	307.	295.	291.	290.	291.	306.	315.	323.	318.	309.	318.	315.	306.
18961	327.	311.	315.	286.	306.	320.	320.	327.	324.	330.	341.	343.	335.
18963	298.	293.	298.	296.	309.	308.	311.	324.	324.	328.	340.	325.	342.
18965	286.	295.	305.	295.	308.	321.	323.	328.	330.	332.	322.	344.	291.
18972	349.	344.	351.	356.	363.	370.	368.	366.	368.	368.	370.	372.	372.
18976	346.	323.	325.	328.	342.	348.	347.	349.	358.	349.	339.	350.	355.
18977b	354.	338.	334.	NO SURVIVING PUPS ON DAY 3 OF LACTATION									

DAY	14	15	16	17	18	19	20	21	22
18946b	350.	354.	357.	343.	351.	352.	354.	365.	338.
18950	353.	353.	365.	354.	362.	358.	365.	361.	361.
18951	334.	335.	338.	346.	346.	345.	320.	330.	347.
18952	360.	364.	351.	365.	348.	338.	352.	362.	344.
18953	340.	347.	356.	368.	358.	358.	363.	360.	360.
18958	344.	343.	352.	347.	368.	367.	359.	361.	371.
18959	310.	319.	319.	334.	336.	337.	340.	335.	346.
18961	334.	342.	341.	354.	354.	357.	354.	353.	333.
18963	346.	352.	352.	352.	351.	354.	362.	362.	340.
18965	334.	345.	347.	352.	344.	348.	348.	336.	337.
18972	385.	376.	386.	389.	393.	400.	328.	310.	380.
18976	370.	362.	361.	387.	368.	384.	373.	374.	390.
18977b	NO SURVIVING PUPS ON DAY 3 OF LACTATION								

DAY = DAY OF LACTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. 1.6 mg/kg/day dosage group dams cross-fostered with vehicle control group litters.
b. Litter was not cross-fostered; values excluded from group averages.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 23 (PAGE 5): MATERNAL BODY WEIGHTS - LACTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RATS ASSIGNED TO PHARMACOKINETIC EVALUATION

RAT #	DOSAGE GROUP I				0 (VEHICLE) MG/KG/DAY								
	DAY 1	2	3	4	5	6	7	8	9	10	11	12	13
18910	311.	297.	296.	303.	313.	317.	330.	329.	330.	338.	329.	338.	335.
18911	348.	347.	348.	352.	369.	380.	371.	370.	368.	355.	362.	365.	366.
18913	320.	323.	328.	324.	348.	354.	336.	345.	339.	342.	350.	350.	356.
18915	380.	365.	370.	370.	374.	379.	395.	406.	393.	396.	408.	399.	394.
18926	371.	364.	366.	375.	376.	376.	374.	386.	397.	393.	401.	401.	401.
18927	312.	309.	322.	322.	331.	330.	333.	337.	344.	348.	330.	344.	341.
18939	341.	328.	339.	342.	350.	352.	359.	357.	352.	357.	365.	367.	367.
18940	343.	357.	351.	370.	376.	353.	358.	365.	372.	373.	368.	391.	398.

	DAY 14
18910	332.
18911	363.
18913	368.
18915	370.
18926	389.
18927	345.
18939	361.
18940	403.

DAY = DAY OF LACTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 23 (PAGE 6): MATERNAL BODY WEIGHTS - LACTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RATS ASSIGNED TO PHARMACOKINETIC EVALUATION

RAT #	DOSAGE GROUP II	1.6 MG/KG/DAY										
DAY	1	2	3	4	5	6	7	8	9	10	11	12	13
18956	320.	318.	319.	320.	323.	321.	333.	335.	286.	331.	337.	347.	359.
18971	311.	311.	309.	312.	311.	311.	317.	315.	316.	318.	320.	328.	328.

DAY	14	15	16	17	18	19	20	21	22
18956	353.								
18971	325.								

DAY = DAY OF LACTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 24 (PAGE 1): FEED CONSUMPTION VALUES - PRECOHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP I					0 (VEHICLE) MG/KG/DAY
DAYS	1- 8	8- 15	15- 22	22- 29	29- 36	36- 43a
18901	147.	146.	137.	143.	147.	b
18902	123.	135.	124.	140.	134.	b
18903	c	152.	144.	178.	158.	140.
18904	c	131.	128.	128.	125.	b
18905	133.	138.	130.	c	129.	b
18906	144.	149.	150.	c	160.	b
18907	147.	148.	144.	147.	152.	b
18908	116.	129.	126.	136.	122.	b
18909	132.	138.	133.	132.	133.	b
18910	122.	c	130.	162.	135.	b
18911	137.	133.	127.	129.	143.	b
18912	136.	139.	139.	134.	140.	118.
18913	118.	139.	150.	129.	124.	124.
18914	152.	153.	157.	161.	126.	b
18915	147.	148.	153.	104.	188.	b
18916	145.	138.	136.	154.	125.	135.
18917	142.	148.	135.	134.	141.	b
18918	127.	137.	114.	106.	121.	125.
18919	123.	129.	132.	133.	130.	c
18920	136.	134.	126.	127.	128.	128.
18921	130.	128.	132.	132.	129.	119.
18922	129.	154.	146.	138.	148.	b
18923	139.	127.	133.	132.	c	d
18924	159.	160.	165.	162.	159.	b
18925	142.	144.	144.	133.	147.	b
18926	143.	139.	137.	136.	134.	126.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Last value recorded before cohabitation.
b. Rat assigned to cohabitation on day 43 of gestation.
c. Spilled feed precluded the calculation of this value.
d. Value was not recorded.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 24 (PAGE 2): FEED CONSUMPTION VALUES - PRECOHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP I				0 (VEHICLE) MG/KG/DAY	
DAYS	1- 8	8- 15	15- 22	22- 29	29- 36	36- 43a
18927	115.	115.	113.	111.	115.	b
18928	139.	133.	132.	133.	131.	b
18929	121.	126.	127.	134.	125.	b
18930	151.	165.	165.	158.	155.	150.
18931	162.	162.	153.	150.	161.	151.
18932	131.	134.	129.	139.	140.	b
18933	108.	124.	131.	122.	123.	b
18934	148.	166.	155.	157.	c	b
18935	148.	146.	145.	141.	134.	134.
18936	141.	145.	143.	138.	136.	80.
18937	136.	145.	c	125.	120.	b
18938	138.	148.	140.	141.	141.	131.
18939	137.	145.	141.	142.	142.	b
18940	146.	155.	162.	149.	146.	138.
18941	134.	131.	124.	129.	119.	126.
18942	145.	125.	129.	132.	130.	b

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Last value recorded before cohabitation.
b. Rat assigned to cohabitation on day 42 of study.
c. Spilled feed precluded the calculation of this value.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 24 (PAGE 3): FEED CONSUMPTION VALUES - PRECOHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP II			1.6 MG/KG/DAY		
DAYS	1- 8	8- 15	15- 22	22- 29	29- 36	36- 43a
18943	131.	126.	123.	126.	121.	109.
18944	150.	137.	133.	145.	144.	134.
18945	b	149.	b	136.	b	b
18946	129.	126.	131.	130.	124.	122.
18947	182.	140.	147.	b	131.	122.
18948	156.	131.	121.	128.	131.	122.
18949	113.	139.	134.	124.	123.	122.
18950	140.	140.	130.	121.	111.	106.
18951	124.	121.	124.	125.	118.	101.
18952	145.	144.	137.	135.	c	118.
18953	134.	138.	135.	132.	136.	122.
18954	127.	127.	118.	119.	115.	105.
18955	b	135.	b	b	124.	106.
18956	114.	129.	130.	130.	120.	114.
18957	142.	139.	129.	125.	136.	120.
18958	141.	142.	138.	124.	120.	114.
18959	133.	139.	130.	127.	127.	131.
18960	145.	154.	142.	142.	135.	125.
18961	130.	139.	132.	129.	138.	126.
18962	135.	134.	130.	134.	131.	124.
18963	138.	126.	124.	124.	125.	116.
18964	125.	120.	125.	122.	117.	105.
18965	113.	112.	115.	117.	106.	104.
18966	130.	132.	126.	126.	118.	121.
18967	150.	151.	147.	152.	147.	140.
18968	139.	157.	133.	136.	134.	127.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Last value recorded before cohabitation.
b. Spilled feed precluded the calculation of this value.
c. Value appeared incorrectly recorded and was excluded from group averages.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 24 (PAGE 4): FEED CONSUMPTION VALUES - PRECOHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP II			1.6 MG/KG/DAY		
DAYS	1- 8	8- 15	15- 22	22- 29	29- 36	36- 43a
18969	151.	151.	149.	151.	141.	142.
18970	132.	133.	129.	129.	125.	119.
18971	148.	148.	134.	132.	124.	117.
18972	139.	159.	139.	142.	137.	130.
18973	137.	135.	130.	129.	125.	113.
18974	161.	146.	118.	124.	120.	121.
18975	152.	156.	154.	153.	156.	140.
18976	130.	129.	137.	130.	141.	b
18977	134.	138.	139.	128.	142.	b
18978	145.	145.	139.	126.	125.	128.

DAY = DAY OF STUDY
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Last value recorded before cohabitation.
b. Spilled feed precluded the calculation of this value.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 25 (PAGE 1): MATERNAL FEED CONSUMPTION VALUES - PRESUMED GESTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP I					0 (VEHICLE) MG/KG/DAY						
PREGNANCY STATUS	DAYS 0 - 1	1 - 2	2 - 3	3 - 4	4 - 5	5 - 6	6 - 7	7 - 8	8 - 9	9 - 10	10 - 11	11 - 12	12 - 13
18901 P	26.	21.	21.	27.	19.	21.	26.	21.	26.	24.	22.	27.	25.
18902 NP	23.	20.	21.	26.	26.	24.	25.	22.	23.	26.	19.	24.	24.
18903 P	25.	26.	30.	29.	29.	27.	23.	18.	31.	29.	27.	34.	30.
18904 P	20.	21.	22.	22.	25.	24.	25.	20.	21.	23.	20.	24.	20.
18905 NP	MATING NOT CONFIRMED												
18906 P	28.	31.	25.	29.	28.	28.	27.	31.	49.	6.	28.	32.	35.
18907 P	27.	26.	28.	25.	29.	19.	26.	21.	29.	39.	15.	31.	26.
18908 P	25.	22.	21.	22.	20.	26.	20.	28.	79.	a	30.	28.	27.
18909 P	25.	23.	23.	21.	25.	24.	26.	25.	25.	24.	28.	27.	26.
18910 P	22.	24.	21.	24.	29.	26.	b	23.	21.	18.	27.	25.	24.
18911 P	27.	26.	26.	23.	18.	23.	25.	27.	24.	21.	30.	25.	29.
18912 P	25.	24.	24.	24.	23.	22.	22.	28.	24.	23.	28.	28.	29.
18913 P	22.	24.	23.	20.	18.	20.	23.	20.	21.	23.	24.	22.	26.
18914 NP	18.	23.	23.	25.	23.	28.	26.	28.	28.	27.	28.	16.	18.
18915 P	25.	28.	27.	26.	30.	30.	29.	27.	29.	25.	34.	32.	28.
18916 P	21.	17.	19.	24.	21.	20.	17.	25.	24.	22.	25.	23.	20.
18917 P	26.	22.	20.	21.	26.	24.	24.	24.	26.	22.	25.	26.	24.
18918 P	22.	19.	22.	20.	28.	26.	28.	24.	28.	27.	27.	26.	31.
18919 P	25.	23.	21.	b	23.	23.	20.	24.	26.	25.	28.	30.	28.
18920 P	21.	22.	22.	22.	25.	20.	22.	20.	24.	22.	24.	27.	27.
18921 NP	18.	8.	17.	18.	16.	16.	14.	17.	17.	14.	19.	17.	22.
18922 P	23.	23.	26.	28.	27.	29.	27.	28.	28.	30.	28.	29.	29.
18923 P	22.	24.	23.	22.	24.	27.	b	19.	22.	23.	26.	c	25.
18924 P	31.	31.	28.	30.	25.	27.	26.	37.	32.	26.	33.	32.	36.
18925 NP	17.	23.	23.	22.	14.	25.	21.	22.	12.	23.	25.	19.	15.

P = PREGNANT NP = NOT PREGNANT (VALUES EXCLUDED FROM AVERAGES)
DAYS = DAYS OF PRESUMED GESTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. Value could not be calculated.
b. Spilled feed precluded the calculation of this value.
c. Value was not recorded.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 25 (PAGE 2): MATERNAL FEED CONSUMPTION VALUES - PRESUMED GESTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP I	0 (VEHICLE) MG/KG/DAY											
PREGNANCY STATUS	DAYS	0 - 1	1 - 2	2 - 3	3 - 4	4 - 5	5 - 6	6 - 7	7 - 8	8 - 9	9 - 10	10 - 11	11 - 12	12 - 13
18926 P		19.	25.	25.	23.	22.	21.	26.	23.	22.	27.	25.	26.	26.
18927 P		26.	26.	26.	26.	24.	24.	23.	29.	23.	22.	26.	23.	26.
18928 NP		MATING NOT CONFIRMED												
18929 P		24.	26.	24.	27.	23.	26.	22.	26.	29.	26.	32.	29.	31.
18930 NP		27.	28.	29.	27.	28.	24.	32.	30.	30.	32.	27.	31.	25.
18931 P		24.	27.	26.	29.	28.	30.	24.	31.	28.	30.	31.	23.	32.
18932 P		19.	24.	24.	25.	22.	23.	25.	20.	28.	26.	25.	29.	24.
18933 P		26.	25.	25.	25.	24.	24.	25.	29.	29.	24.	24.	26.	24.
18934 P		27.	27.	29.	26.	30.	30.	38.	32.	28.	32.	26.	24.	31.
18935 P		14.	18.	22.	28.	27.	26.	21.	19.	25.	24.	25.	24.	30.
18936 P		16.	16.	16.	15.	13.	14.	24.	28.	22.	21.	28.	21.	20.
18937 P		20.	26.	24.	23.	23.	24.	18.	26.	20.	23.	24.	22.	24.
18938 P		23.	28.	25.	25.	27.	25.	27.	26.	25.	28.	29.	26.	30.
18939 P		25.	26.	22.	26.	26.	24.	26.	25.	26.	25.	28.	24.	21.
18940 P		23.	26.	31.	30.	34.	23.	29.	29.	29.	33.	27.	30.	27.
18941 P		23.	24.	27.	27.	24.	24.	23.	27.	27.	26.	28.	23.	28.
18942 P		24.	23.	22.	24.	27.	24.	25.	24.	25.	24.	27.	26.	26.

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

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 25 (PAGE 3): MATERNAL FEED CONSUMPTION VALUES - PRESUMED GESTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP I						0 (VEHICLE) MG/KG/DAY					
PREGNANCY STATUS	DAYS 13 - 14	14 - 15	15 - 16	16 - 17	17 - 18	18 - 19	19 - 20	20 - 21	21 - 22	22 - 23	23 - 24	24 - 25
18901 P	20.	23.	21.	20.	22.	25.	25.	29.				
18902 NP	17.	15.	18.	11.	15.	11.	13.	16.	19.	17.	10.	16.
18903 P	29.	26.	20.	28.	26.	30.	25.					
18904 P	28.	21.	30.	25.	19.	27.	21.					
18905 NP	MATING NOT CONFIRMED											
18906 P	28.	15.	30.	31.	31.	28.	39.					
18907 P	31.	28.	24.	28.	27.	27.	25.					
18908 P	28.	19.	26.	25.	30.	20.	33.					
18909 P	32.	25.	33.	31.	16.	28.	21.	22.	3.			
18910 P	28.	23.	25.	28.	19.	24.	19.	19.				
18911 P	22.	20.	25.	23.	27.	19.	32.	19.				
18912 P	23.	20.	25.	29.	31.	21.	35.					
18913 P	21.	17.	27.	27.	24.	20.	24.	22.				
18914 NP	a	19.	18.	23.	15.	19.	13.	18.	11.	22.	18.	12.
18915 P	35.	30.	39.	32.	29.	36.	29.					
18916 P	25.	21.	15.	23.	21.	18.	13.	21.	14.	4.	16.	17.
18917 P	28.	25.	20.	26.	26.	24.	23.	29.				
18918 P	22.	28.	17.	25.	25.	25.	20.	23.				
18919 P	26.	16.	27.	24.	32.	24.	39.					
18920 P	24.	22.	18.	26.	27.	30.	21.					
18921 NP	12.	17.	16.	9.	11.	16.	16.	11.	16.	23.	8.	17.
18922 P	25.	29.	31.	19.	29.	27.	27.	20.				
18923 P	24.	24.	16.	24.	23.	22.	16.	18.				
18924 P	28.	17.	27.	26.	33.	20.	36.					
18925 NP	19.	25.	20.	12.	14.	18.	17.	16.	14.	16.	8.	18.

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

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 25 (PAGE 4): MATERNAL FEED CONSUMPTION VALUES - PRESUMED GESTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE

RAT #	DOSAGE GROUP I							0 (VEHICLE) MG/KG/DAY					
PREGNANCY STATUS	DAYS 13 - 14	14 - 15	15 - 16	16 - 17	17 - 18	18 - 19	19 - 20	20 - 21	21 - 22	22 - 23	23 - 24	24 - 25	
18926 P	16.	21.	26.	27.	23.	40.	32.	16.					
18927 P	22.	13.	22.	20.	27.	17.	34.	25.					
18928 NP	MATING NOT CONFIRMED												
18929 P	31.	13.	27.	28.	27.	22.	36.	27.					
18930 NP	10.	19.	20.	19.	12.	23.	19.	3.	11.	23.	18.	16.	
18931 P	27.	14.	29.	27.	31.	20.	32.						
18932 P	25.	24.	19.	23.	25.	26.	19.	28.					
18933 P	25.	23.	32.	25.	25.	32.	28.						
18934 P	27.	31.	27.	19.	26.	28.	27.	18.					
18935 P	27.	23.	30.	28.	28.	21.	29.						
18936 P	26.	29.	25.	24.	22.	27.	19.	19.					
18937 P	20.	12.	21.	22.	24.	19.	28.	25.					
18938 P	28.	13.	26.	26.	26.	20.	29.						
18939 P	28.	24.	25.	31.	18.	23.	25.	28.					
18940 P	17.	20.	22.	23.	17.	28.	26.	7.					
18941 P	23.	19.	31.	26.	29.	22.	36.	29.					
18942 P	27.	15.	17.	31.	26.	19.	28.	13.					

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

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 25 (PAGE 5): MATERNAL FEED CONSUMPTION VALUES - PRESUMED GESTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP II	1.6 MG/KG/DAY										
PREGNANCY STATUS	DAYS 0 - 1	1 - 2	2 - 3	3 - 4	4 - 5	5 - 6	6 - 7	7 - 8	8 - 9	9 - 10	10 - 11	11 - 12	12 - 13
18943 P	20.	19.	18.	21.	19.	7.	19.	21.	23.	22.	22.	24.	22.
18944 NP	26.	29.	25.	23.	21.	29.	23.	26.	26.	29.	29.	24.	28.
18945 NP	MATING NOT CONFIRMED												
18946 P	19.	22.	21.	22.	19.	23.	27.	19.	19.	23.	24.	23.	44.
18947 P	20.	21.	22.	20.	22.	22.	21.	23.	25.	25.	24.	30.	22.
18948 P	19.	27.	20.	20.	23.	27.	22.	26.	27.	24.	25.	26.	29.
18949 NP	20.	20.	19.	19.	14.	18.	17.	22.	13.	18.	20.	17.	15.
18950 P	20.	19.	21.	23.	21.	17.	21.	27.	20.	22.	21.	21.	20.
18951 P	17.	20.	21.	20.	22.	21.	25.	26.	19.	27.	22.	22.	24.
18952 P	23.	20.	23.	24.	21.	24.	23.	21.	25.	21.	26.	25.	20.
18953 P	21.	23.	25.	22.	20.	25.	20.	21.	21.	23.	25.	25.	25.
18954 NP	19.	15.	12.	14.	17.	17.	15.	15.	17.	19.	17.	12.	13.
18955 NP	20.	18.	14.	23.	24.	19.	13.	19.	18.	26.	16.	22.	21.
18956 P	21.	20.	17.	15.	15.	20.	22.	23.	19.	21.	21.	20.	22.
18957 P	17.	23.	21.	21.	22.	22.	20.	26.	25.	23.	25.	23.	25.
18958 P	23.	22.	22.	23.	21.	20.	21.	20.	25.	26.	24.	27.	27.
18959 P	17.	20.	20.	18.	22.	19.	22.	23.	21.	24.	25.	23.	25.
18960 P	22.	22.	23.	23.	19.	22.	21.	25.	27.	21.	26.	27.	25.
18961 P	19.	22.	22.	24.	22.	23.	23.	21.	20.	27.	26.	24.	29.
18962 NP	13.	18.	18.	12.	13.	17.	17.	15.	11.	18.	19.	17.	13.
18963 P	17.	20.	22.	22.	23.	22.	22.	23.	26.	25.	27.	27.	25.
18964 P	20.	21.	19.	20.	23.	20.	23.	24.	19.	23.	20.	20.	24.
18965 P	21.	22.	17.	21.	18.	17.	26.	18.	20.	24.	21.	23.	23.
18966 NP	MATING NOT CONFIRMED												
18967 P	14.	24.	23.	25.	20.	18.	20.	30.	24.	27.	32.	19.	31.

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

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 25 (PAGE 6): MATERNAL FEED CONSUMPTION VALUES - PRESUMED GESTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP II				1.6 MG/KG/DAY							
PREGNANCY STATUS DAYS	0 - 1	1 - 2	2 - 3	3 - 4	4 - 5	5 - 6	6 - 7	7 - 8	8 - 9	9 - 10	10 - 11	11 - 12	12 - 13
18968 P	18.	22.	18.	22.	19.	23.	25.	24.	24.	21.	25.	25.	27.
18969 P	28.	25.	21.	26.	21.	25.	25.	28.	23.	27.	29.	26.	31.
18970 P	20.	18.	22.	19.	a	21.	22.	23.	25.	21.	24.	23.	23.
18971 P	21.	17.	17.	20.	27.	20.	23.	20.	20.	23.	21.	22.	20.
18972 P	20.	18.	22.	21.	23.	24.	23.	25.	24.	25.	26.	27.	30.
18973 P	18.	18.	17.	17.	20.	18.	17.	19.	19.	23.	23.	21.	25.
18974 P	23.	20.	18.	21.	24.	24.	25.	25.	25.	23.	24.	29.	27.
18975 NP	22.	22.	22.	19.	19.	23.	23.	22.	24.	26.	26.	23.	19.
18976 P	18.	20.	20.	24.	23.	23.	27.	22.	31.	20.	26.	27.	28.
18977 P	19.	20.	21.	23.	24.	25.	26.	26.	22.	25.	24.	27.	28.
18978 NP	17.	16.	20.	20.	20.	25.	21.	24.	20.	19.	22.	10.	12.

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 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 25 (PAGE 7): MATERNAL FEED CONSUMPTION VALUES - PRESUMED GESTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP II			1.6 MG/KG/DAY								
PREGNANCY STATUS	DAYS 13 - 14	14 - 15	15 - 16	16 - 17	17 - 18	18 - 19	19 - 20	20 - 21	21 - 22	22 - 23	23 - 24	24 - 25
18943 P	20.	24.	31.	30.	27.	26.	33.					
18944 NP	18.	5.	17.	15.	11.	8.	21.	18.	7.	12.	21.	16.
18945 NP	MATING NOT CONFIRMED											
18946 P	18.	18.	26.	26.	23.	28.	32.					
18947 P	7.	29.	22.	32.	30.	25.	13.					
18948 P	23.	14.	32.	32.	36.	21.	39.					
18949 NP	19.	9.	16.	9.	17.	12.	17.	9.	7.	18.	16.	12.
18950 P	16.	22.	26.	30.	20.	35.	29.					
18951 P	15.	25.	26.	29.	22.	37.	28.					
18952 P	24.	26.	13.	26.	24.	23.	20.					
18953 P	24.	16.	26.	25.	28.	23.	34.					
18954 NP	16.	15.	18.	7.	12.	16.	14.	10.	15.	14.	5.	14.
18955 NP	20.	14.	18.	10.	15.	13.	18.	13.	18.	15.	7.	15.
18956 P	16.	19.	21.	27.	23.	34.	30.	14.	18.			
18957 P	25.	27.	17.	31.	27.	27.	20.					
18958 P	20.	26.	25.	27.	25.	38.	33.	13.				
18959 P	24.	23.	29.	15.	23.	29.	27.	19.				
18960 P	23.	14.	23.	25.	27.	24.	30.					
18961 P	19.	21.	24.	19.	28.	27.	24.	24.				
18962 NP	17.	19.	18.	8.	16.	15.	15.	8.	18.	19.	8.	12.
18963 P	28.	28.	19.	26.	27.	20.	15.					
18964 P	20.	25.	24.	22.	29.	28.	24.	23.				
18965 P	15.	26.	26.	30.	21.	34.	25.					
18966 NP	MATING NOT CONFIRMED											
18967 P	28.	10.	27.	29.	29.	27.	39.					

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

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 25 (PAGE 8): MATERNAL FEED CONSUMPTION VALUES - PRESUMED GESTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RAT #	DOSAGE GROUP II	1.6 MG/KG/DAY										
PREGNANCY STATUS	DAYS 13 - 14	14 - 15	15 - 16	16 - 17	17 - 18	18 - 19	19 - 20	20 - 21	21 - 22	22 - 23	23 - 24	24 - 25
18968 P	23.	28.	29.	24.	29.	29.	24.	20.				
18969 P	23.	20.	27.	31.	31.	21.	42.					
18970 P	20.	21.	17.	24.	22.	26.	20.					
18971 P	21.	14.	19.	20.	20.	18.	25.	21.	9.			
18972 P	28.	18.	29.	27.	31.	25.	37.					
18973 P	24.	15.	22.	21.	27.	22.	26.					
18974 P	30.	29.	18.	30.	26.	30.	23.					
18975 NP	15.	10.	20.	16.	11.	14.	24.	14.	9.	15.	20.	15.
18976 P	27.	24.	21.	25.	24.	23.	18.					
18977 P	26.	31.	31.	19.	21.	28.	29.	28.				
18978 NP	16.	26.	18.	3.	22.	21.	19.	6.	27.	22.	9.	11.

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

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 26 (PAGE 1): MATERNAL FEED CONSUMPTION VALUES - LACTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RATS ASSIGNED TO CROSS-FOSTERING

DAYS	1 - 4	4 - 7	7 - 10	10 - 14a
RAT #	DOSAGE GROUP I b		0 (VEHICLE) MG/KG/DAY	SUBSET A
18903	47.	109.	130.	232.
18907	51.	117.	135.	235.
18908	48.	104.	138.	243.
18909	48.	121.	149.	207.
18918c	82.	145.	156.	264.
18920	63.	124.	116.d	226.
18924	48.	124.	134.	218.
18929	69.	127.	147.	257.
18934	49.	108.	114.	215.
18936c	46.	117.	148.	183.
18937	62.	123.	130.	250.
18941	61.	104.	132.	219.
18942	85.	120.	140.	239.
RAT #	DOSAGE GROUP I e		0 (VEHICLE) MG/KG/DAY	SUBSET B
18901	96.	135.	174.	255.
18904	71.	143.	160.d	200.
18906	90.	128.	168.	248.
18912	64.	122.	154.	246.
18917	80.	134.	147.	240.
18919	74.	130.	147.	227.
18922	62.	117.	145.	227.
18923	82.	149.	177.	242.
18931	72.	130.	148.	244.
18932	74.	118.	145.	203.
18935	60.	110.	133.	218.
18938	70.	128.	156.	243.

DAYS = DAYS OF LACTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. It is presumed that the pups begin to consume the maternal feed after day 14 of lactation.
b. Vehicle control group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
c. Litter was not cross-fostered; values excluded from group averages.
d. Water access was interrupted; values excluded from group averages.
e. Vehicle control group dams cross-fostered with vehicle control litters.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 26 (PAGE 2): MATERNAL FEED CONSUMPTION VALUES - LACTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RATS ASSIGNED TO CROSS-FOSTERING

DAYS	1 - 4	4 - 7	7 - 10	10 - 14a
RAT #	DOSAGE GROUP II b	1.6 MG/KG/DAY		SUBSET C
18943	73.	123.	141.	240.
18947	68.	113.	126.	211.
18948	48.	95.	106.	193.
18957	51.	112.	128.	208.
18960	46.	102.	116.	191.c
18964	54.	98.	126.	182.
18967	68.	112.	138.	243.
18968	50.	108.	125.	197.
18969	63.	116.	128.	231.
18970	54.	109.	114.	191.
18973	45.	51.	113.	182.
18974	31.	NO SURVIVING PUPS ON DAY 4 OF LACTATION		
RAT #	DOSAGE GROUP II d	1.6 MG/KG/DAY		SUBSET D
18946e	29.	76.	77.	124.
18950	68.	121.	135.	227.
18951	67.	99.	115.	205.
18952	74.	140.	138.	215.
18953	59.	104.	127.	203.
18958	51.	87.	119.	202.
18959	46.	104.	135.	179.
18961	64.	119.	134.	201.
18963	48.	114.	127.	233.
18965	82.	116.	133.	209.
18972	77.	140.	148.	258.
18976	66.	127.	118.	213.
18977e	NO SURVIVING PUPS ON DAY 3 OF LACTATION			

DAYS = DAYS OF LACTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).
a. It is presumed that the pups begin to consume the maternal feed after day 14 of lactation.
b. 1.6 mg/kg/day dosage group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
c. Water access was interrupted; value excluded from group averages.
d. 1.6 mg/kg/day dosage group dams cross-fostered with vehicle control group litters.
e. Litters were not cross-fostered; values excluded from group averages.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 26 (PAGE 3): MATERNAL FEED CONSUMPTION VALUES - LACTATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RATS ASSIGNED TO PHARMACOKINETIC EVALUATION

DAYS	1 - 4	4 - 7	7 - 10	10 - 14
RAT #	DOSAGE GROUP I			0 (VEHICLE) MG/KG/DAY
18910	61.	73.	114.	145.
18911	107.	149.	148.	251.
18913	68.	134.	140.	261.
18915	88.	138.	216.	246.
18926	97.	131.	181.	300.
18927	66.	119.	137.	231.
18939	86.	120.	154.	230.
18940	82.	106.	141.	265.
RAT #	DOSAGE GROUP II			1.6 MG/KG/DAY
18956	73.	97.	122.	258.
18971	31.	44.	57.	77.

DAYS = DAYS OF LACTATION
ALL WEIGHTS WERE RECORDED IN GRAMS (G).

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 27 (PAGE 1): NATURAL DELIVERY, IMPLANTATION SITES, AND PUP VIABILITY AND SEX - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS/F1 GENERATION LITTERS

RATS ASSIGNED TO CROSS-FOSTERING

RAT/ LITTER NUMBER	LITTER DELIVERED LIVE BORN N	STILL-BORN N	TOTAL BORN N	TOTAL IMPLAN-TATIONS N	FOSTER LITTER #	PUPS CROSS-FOSTERED N	NUMBER OF LIVE FOSTER PUPS AT COMPLETION OF DAY POSTPARTUM 1 M	1 F	4a M	4a F	4b M	4b F	7 M	7 F	14 M	14 F	21 M	21 F
MATERNAL DOSAGE GROUP I c				0 (VEHICLE) MG/KG/DAY			SUBSET A											
18903	18	0	18	18	18976	15	7	8	6	7	5	5	5	5	5	5	5	5
18907	19	0	19	20	18963	13	5	8	5	7	5	5	5	5	5	5	5	5
18908	16	0	16	17	18953	16	4	12	3	12	3	7	3	7	3	7	3	7
18909	16	0	16	17	18961	16	8	8	7	8	5	5	5	5	5	5	5	5
18918d	15	0	15	16	18946	17	9	8	7	8	5	5	5	5	5	5	5	5
18920	17	0	17	17	18952	15	8	7	8	5	5	5	5	5	5	5	5	5
18924	16	0	16	17	18972	17	9	8	8	7	5	5	5	5	5	5	5	5
18929	18	0	18	18	18950	16	8	8	7	8	5	5	5	5	5	5	5	5
18934	16	0	16	18	18959	14	7	7	7	6	5	5	5	5	5	5	5	5
18936d	12(1)	0	12	15	18977	12	7	5	7	4	6	4	6	4	6	4	6	4
18937	14	1	15	18	18958	13	5	8	5	8	5	5	5	5	5	5	5	5
18941	14	0	14	17	18951	13	8	5	5	4	5	4	5	3	5	3	5	3
18942	17	0	17	17	18965	18	9	9	9	9	5	5	5	5	5	5	5	5
MATERNAL DOSAGE GROUP I e				0 (VEHICLE) MG/KG/DAY			SUBSET B											
18901	16	0	16	17	18923	16	6	10	6	10	5	5	5	5	5	5	5	5
18904	15	3	18	20	18922	15	7	8	7	8	5	5	5	5	5	5	5	5
18906	16	0	16	19	18935	19	8	11	8	10	5	5	5	5	5	5	5	5
18912	15	1	16	16	18938	20	11	9	11	8	5	5	5	5	5	5	5	5
18917	14	0	14	17	18932	16	9	7	9	7	5	5	5	5	5	5	5	5
18919	17	0	17	18	18931	12	7	5	7	5	5	5	5	5	5	5	5	5
18922	15	0	15	18	18904	15	5	10	5	10	5	5	5	5	5	5	5	5
18923	17(1)	0	17	17	18901	16	6	10	6	9	5	5	5	5	5	5	5	5
18931	12	0	12	12	18919	17	7	10	7	10	5	5	5	5	5	5	5	5
18932	16	0	16	18	18917	14	6	8	6	8	5	5	5	5	5	5	5	5
18935	19	0	19	21	18906	16	7	9	7	9	5	5	5	5	5	5	5	5
18938	20	0	20	20	18912	15	13	2	13	2	8	2	8	2	8	2	8	2

M = MALE F = FEMALE
( ) = NUMBER OF PUPS DYING PRIOR TO CROSS-FOSTERING ON DAY 1 POSTPARTUM
a. Number of live pups preculling.
b. Number of live pups postculling.
c. Vehicle control group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
d. Litter were not cross-fostered; values excluded from group averages.
e. Vehicle control group dams cross-fostered with vehicle control litters.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 27 (PAGE 2): NATURAL DELIVERY, IMPLANTATION SITES, AND PUP VIABILITY AND SEX - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS/F1 GENERATION LITTERS

RATS ASSIGNED TO CROSS-FOSTERING

RAT/ LITTER NUMBER	LITTER DELIVERED LIVE BORN N	STILL-BORN N	TOTAL BORN N	TOTAL IMPLAN-TATIONS N	FOSTER LITTER #	PUPS CROSS-FOSTERED N	NUMBER OF LIVE FOSTER PUPS AT COMPLETION OF DAY POSTPARTUM 1 M	1 F	4a M	4a F	4b M	4b F	7 M	7 F	14 M	14 F	21 M	21 F
MATERNAL DOSAGE GROUP II c				1.6 MG/KG/DAY			SUBSET C											
18943	16	0	16	16	18967	15	5	10	5	10	5	5	5	5	5	5	5	5
18947	15	0	15	16	18974	14	8	6	8	6	5	5	5	5	5	5	5	5
18948	17	0	17	19	18969	17	11	6	6	2	6	2	6	2	6	2	6	2
18957	15	0	15	15	18970	13	4	9	3	8	3	7	3	7	3	7	3	7
18960	15	0	15	17	18973	15	5	10	3	8	3	7	3	7	3	7	3	7
18964	10	0	10	13	18968	15	8	7	7	7	5	5	5	5	5	5	5	5
18967	15	0	15	17	18943	16	9	7	9	7	5	5	5	5	5	5	5	5
18968	15	0	15	16	18964	10	2	8	1	8	1	8	1	8	1	8	1	8
18969	17	0	17	19	18948	17	12	5	12	5	5	5	5	5	5	5	5	5
18970	13	0	13	13	18957	15	9	6	9	5	5	5	5	5	5	5	5	5
18973	16(1)	0	16	16	18960	15	10	5	10	4	6	4	6	4	6	4	6	4
18974	14	0	14	17	18947	15	6	9	-	-	-	-	-	-	-	-	-	-
MATERNAL DOSAGE GROUP II d				1.6 MG/KG/DAY			SUBSET D											
18946e	17	0	17	17	18918	15	9	8	3	1	3	1	2	1	2	1	2	1
18950	16	0	16	17	18929	18	8	10	8	10	5	5	5	5	5	5	5	5
18951	13	0	13	13	18941	14	8	6	8	6	5	5	5	5	5	5	5	5
18952	15	2	17	17	18920	17	8	9	8	9	5	5	5	5	5	5	5	5
18953	16	0	16	18	18908	16	8	8	8	8	5	5	5	5	5	5	5	5
18958	13	0	13	14	18937	14	6	8	6	8	5	5	5	5	5	5	5	5
18959	14	0	14	15	18934	16	9	7	9	6	5	5	5	5	5	5	5	5
18961	16	0	16	16	18909	16	5	11	5	11	5	5	5	5	5	5	5	5
18963	13	0	13	13	18907	19	11	8	11	8	5	5	5	5	5	5	5	5
18965	18	0	18	18	18942	17	6	11	6	11	5	5	5	5	5	5	5	5
18972	17	0	17	18	18924	16	7	9	7	9	5	5	5	5	5	5	5	5
18976	15	0	15	15	18903	18	8	10	7	10	5	5	5	5	5	5	5	5
18977e	12	0	12	16	18936	12	7	4	-	-	-	-	-	-	-	-	-	-

M = MALE F = FEMALE

( ) = NUMBER OF PUPS DYING PRIOR TO CROSS-FOSTERING ON DAY 1 POSTPARTUM

a. Number of live pups preculling.

b. Number of live pups postculling.

c. 1.6 mg/kg/day dosage group dams cross-fostered with 1.6 mg/kg/day dosage group litters.

d. 1.6 mg/kg/day dosage group dams cross-fostered with vehicle control group litters.

e. Litter were not cross-fostered; values excluded from group averages.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 27 (PAGE 3): NATURAL DELIVERY, IMPLANTATION SITES, AND PUP VIABILITY AND SEX - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS/F1 GENERATION LITTERS

RATS ASSIGNED TO PHARMACOKINETIC EVALUATION

RAT/ LITTER NUMBER	LITTER DELIVERED LIVE BORN N	STILL-BORN N	TOTAL BORN N	NUMBER OF LIVE PUPS AT COMPLETION OF DAY POSTPARTUM 1 M	1 F	4 M	4 F	7 M	7 F	14 M	14 F	TOTAL IMPLAN-TATIONS N
MATERNAL DOSAGE GROUP I				0 (VEHICLE) MG/KG/DAY								
18910	5	0	5	3	2	3	2	3	2	3	2	8
18911	16	0	16	11	5	11	5	11	4	11	4	16
18913	18	0	18	16	2	15	2	14	2	14	2	19
18915	15	2	17	4	11	4	11	4	11	4	11	17
18926	12	0	12	6	6	6	6	6	6	6	6	13
18927	17	0	17	8	9	8	8	8	8	8	7	17
18939	15	0	15	7	8	7	8	7	8	7	8	15
18940	16	0	16	10	6	10	6	10	6	10	6	18
MATERNAL DOSAGE GROUP II				1.6 MG/KG/DAY								
18956	12	1	13	5	7	5	7	5	7	5	7	16
18971	1	2	3	-	1	-	1	-	1	-	1	3

M = MALE F = FEMALE

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 28 (PAGE 1): DURATION OF GESTATION AND AVERAGE DURATION OF DELIVERY (MINUTES) PER PUP PER LITTER - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RATS ASSIGNED TO CROSS-FOSTERING			
RAT/ LITTER NUMBER	DURATION OF GESTATION (DAYS) a N	DURATION OF GESTATION (WHOLE DAYS) N	AVERAGE DURATION OF DELIVERY PER PUP (MINUTES) b
MATERNAL DOSAGE GROUP I c	0 (VEHICLE) MG/KG/DAY		SUBSET A
18903	21.6	22	16.9
18907	21.5	22	14.5
18908	21.7	22	8.5
18909	22.5	23	15.5
18918d	22.6	23	7.2
18920	21.6	22	9.1
18924	21.6	22	6.5
18929	22.4	23	6.7
18934	21.5	22	5.1
18936d	21.7	22	25.1
18937	22.5	23	23.2
18941	22.4	23	15.3
18942	21.8	22	9.5
MATERNAL DOSAGE GROUP I e	0 (VEHICLE) MG/KG/DAY		SUBSET B
18901	22.3	23	21.8
18904	22.6	23	11.4
18906	21.6	22	8.8
18912	21.6	22	12.7
18917	22.5	23	13.4
18919	21.7	22	9.1
18922	21.6	22	13.3
18923	22.8	23	11.7f
18931	21.6	22	12.4
18932	22.5	23	7.2
18935	21.6	22	7.4
18938	21.6	22	6.4

a. Calculated to the nearest tenth of a day.
b. Calculated as the time (in minutes) elapsed between delivery of the first and last pup, divided by n-1 pups.
c. Vehicle control group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
d. Vehicle control group dams cross-fostered with vehicle control litters.
e. Litters were not cross-fostered; values excluded from group averages.
f. Partuition period only partially observed.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 28 (PAGE 2): DURATION OF GESTATION AND AVERAGE DURATION OF DELIVERY (MINUTES) PER PUP PER LITTER - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RATS ASSIGNED TO CROSS-FOSTERING			
RAT/ LITTER NUMBER	DURATION OF GESTATION (DAYS) a N	DURATION OF GESTATION (WHOLE DAYS) N	AVERAGE DURATION OF DELIVERY PER PUP (MINUTES) b
MATERNAL DOSAGE GROUP II c	1.6 MG/KG/DAY		SUBSET C
18943	21.5	22	4.9
18947	21.5	22	10.8
18948	21.6	22	11.2
18957	21.6	22	11.1
18960	21.6	22	3.1
18964	21.8	22	9.9
18967	21.5	22	4.6
18968	21.7	22	9.5
18969	21.6	22	11.2
18970	21.7	22	8.3
18973	21.5	22	11.0
18974	21.5	22	8.6
MATERNAL DOSAGE GROUP II d	1.6 MG/KG/DAY		SUBSET D
18946e	21.5	22	12.3f
18950	21.5	22	8.3
18951	21.6	22	11.2
18952	21.5	22	13.2
18953	21.7	22	14.1
18958	21.7	22	5.5
18959	21.5	22	9.2
18961	21.5	22	7.9
18963	21.6	22	11.2
18965	21.4	22	6.4
18972	21.7	22	4.4
18976	21.7	22	13.8
18977e	21.6	22	24.4

a. Calculated to the nearest tenth of a day.
b. Calculated as the time (in minutes) elapsed between delivery of the first and last pup, divided by n-1 pups.
c. 1.6 mg/kg/day dosage group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
d. 1.6 mg/kg/day dosage group dams cross-fostered with vehicle control group litters.
e. Litters were not cross-fostered; values excluded from group averages.
f. Partuition period only partially observed.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 28 (PAGE 3): DURATION OF GESTATION AND AVERAGE DURATION OF DELIVERY (MINUTES) PER PUP PER LITTER - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

RATS ASSIGNED TO PHARMACOKINETIC EVALUATION

RAT/ LITTER NUMBER	DURATION OF GESTATION (DAYS) a N	DURATION OF GESTATION (WHOLE DAYS) N	AVERAGE DURATION OF DELIVERY PER PUP (MINUTES) b
MATERNAL DOSAGE GROUP I	0 (VEHICLE) MG/KG/DAY		
18910	21.7	22	14.8
18911	21.8	22	14.9
18913	22.4	23	6.1
18915	21.6	22	30.4
18926	22.4	23	5.2
18927	22.3	23	9.5
18939	21.9	22	9.6
18940	21.7	22	9.2d
MATERNAL DOSAGE GROUP II	1.6 MG/KG/DAY		
18956	22.5	23	8.2
18971	c	24	c

a. Calculated to the nearest tenth of a day.
b. Calculated as the time (in minutes) elapsed between delivery of the first and last pup, divided by n-1 pups.
c. Partuition period not observed.
d. Partuition period only partially observed.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 29 (PAGE 1): PUP BODY WEIGHT LITTER AVERAGES FROM BIRTH TO DAY 21 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION LITTERS

RATS ASSIGNED TO CROSS-FOSTERING

RAT/ FOSTER LITTER #	DAY 1			DAY 4a			DAY 4b			DAY 7			DAY 14			DAY 21		
	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T
MATERNAL DOSAGE GROUP I c				0 (VEHICLE) MG/KG/DAY						SUBSET A								
18903	5.6	5.2	5.4	5.9	5.9	5.9	6.1	5.9	6.0	10.5	9.6	10.0	24.7	23.2	24.0	41.1	38.2	39.7
18907	6.1	5.8	5.9	7.8	7.4	7.6	7.8	7.6	7.7	13.0	12.6	12.8	27.9	27.1	27.5	44.2	42.6	43.4
18908	5.8	5.4	5.5	7.1	7.0	7.0	7.1	7.2	7.2	12.6	11.7	11.9	26.8	26.2	26.4	42.1	39.9	40.6
18909	5.5	5.5	5.5	7.4	7.2	7.3	7.7	7.7	7.7	13.4	13.4	13.4	28.1	27.8	28.0	42.7	40.5	41.6
18918d	5.6	5.1	5.3	10.0	9.2	9.6	10.0	9.1	9.6	16.5	15.0	15.8	33.0	30.6	31.8	50.0	49.9	50.0
18920	5.3	5.2	5.3	6.7	7.0	6.8	7.3	7.0	7.1	12.3	11.8	12.0	25.0	24.5	24.7	41.4	40.5	40.9
18924	5.7	5.5	5.6	7.5	6.7	7.1	7.5	7.3	7.4	12.5	12.0	12.3	25.9	25.3	25.6	41.2	40.9	41.0
18929	5.6	5.3	5.4	7.6	7.2	7.4	8.1	7.4	7.8	13.7	12.5	13.1	30.2	27.9	29.0	47.2	43.8	45.5
18934	5.8	5.4	5.6	7.4	7.0	7.2	7.6	7.0	7.3	13.0	12.4	12.7	27.6	26.3	27.0	42.0	40.2	41.1
18936d	6.2	5.8	6.1	8.7	7.7	8.3	8.6	7.7	8.2	13.1	12.0	12.7	25.1	23.0	24.2	39.9	36.6	38.6
18937	6.0	5.5	5.7	8.0	7.3	7.6	8.0	7.5	7.7	11.9	11.5	11.7	24.9	25.2	25.1	40.3	41.0	40.7
18941	6.2	5.9	6.1	8.2	6.9	7.6	8.2	6.9	7.6	12.8	12.7	12.8	28.2	29.2	28.6	44.5	45.4	44.8
18942	5.3	5.1	5.2	7.0	7.0	7.0	7.2	7.3	7.3	12.4	12.5	12.4	28.0	28.4	28.2	41.7	41.6	41.6
MATERNAL DOSAGE GROUP I e				0 (VEHICLE) MG/KG/DAY						SUBSET B								
18901	6.7	6.2	6.4	9.4	8.6	8.9	9.5	8.5	9.0	15.6	14.3	15.0	31.7	30.1	30.9	50.0	46.4	48.2
18904	5.9	5.6	5.7	7.6	7.0	7.3	8.0	7.4	7.7	14.2	12.6	13.4	28.9	26.5	27.7	44.4	41.5	43.0
18906	5.8	5.5	5.6	8.2	7.6	7.9	8.4	8.1	8.3	13.5	13.4	13.4	28.7	28.3	28.5	49.9	47.9	48.9
18912	5.5	5.2	5.4	6.8	6.2	6.6	7.0	6.3	6.6	12.5	12.7	12.6	29.8	27.5	28.6	48.6	44.7	46.7
18917	7.0	6.7	6.9	8.7	8.4	8.5	8.6	8.4	8.5	13.8	13.6	13.7	28.9	28.4	28.6	45.3	45.7	45.5
18919	6.4	6.3	6.4	9.5	9.3	9.4	9.3	9.3	9.3	15.6	15.1	15.4	30.9	29.9	30.4	49.0	47.8	48.4
18922	6.8	6.4	6.5	8.9	8.5	8.6	8.9	8.9	8.9	15.5	15.1	15.3	30.8	31.0	30.9	48.7	48.4	48.5
18923	7.0	6.7	6.8	9.6	8.9	9.2	9.8	8.8	9.3	16.1	14.3	15.2	30.5	28.1	29.3	50.4	46.1	48.3
18931	6.4	6.0	6.2	8.3	8.0	8.1	8.2	8.2	8.2	13.8	13.8	13.8	30.6	30.5	30.6	48.9	47.7	48.3
18932	6.8	6.2	6.4	9.1	8.6	8.8	9.2	8.7	8.9	14.5	13.9	14.2	27.4	26.9	27.2	43.7	43.5	43.6
18935	6.3	5.8	6.0	8.4	7.7	8.0	8.5	8.1	8.3	13.5	13.0	13.2	26.2	25.9	26.0	42.3	41.5	41.9
18938	6.1	5.8	6.1	8.5	8.4	8.5	8.7	8.4	8.6	13.8	13.8	13.8	29.2	29.0	29.1	44.5	43.8	44.3

M = MALE F = FEMALE T = TOTAL (SUM OF PUP WEIGHTS/NUMBER OF LIVE PUPS) DAY = DAY POSTPARTUM
ALL WEIGHTS WERE RECORDED IN GRAMS (G). MEAN LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.

a. Preculling
b. Postculling
c. Vehicle control group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
d. Litters were not cross-fostered; values excluded from group averages.
e. Vehicle control group dams cross-fostered with vehicle control litters.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 29 (PAGE 2): PUP BODY WEIGHT LITTER AVERAGES FROM BIRTH TO DAY 21 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION LITTERS

RATS ASSIGNED TO CROSS-FOSTERING

RAT/ FOSTER LITTER #	DAY 1			DAY 4a			DAY 4b			DAY 7			DAY 14			DAY 21		
	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T
MATERNAL DOSAGE GROUP II c				1.6 MG/KG/DAY						SUBSET C								
18943	5.8	5.6	5.7	8.0	8.1	8.0	8.0	8.2	8.1	12.9	13.0	13.0	28.4	28.1	28.2	43.1	42.0	42.5
18947	5.8	5.6	5.7	7.6	7.1	7.4	7.8	7.2	7.5	12.5	11.7	12.1	26.4	24.2	25.3	43.1	39.7	41.4
18948	5.8	5.4	5.7	6.3	5.8	6.2	6.3	5.8	6.2	10.1	9.0	9.8	23.7	20.8	23.0	36.8	33.6	36.0
18957	6.2	5.7	5.9	7.6	7.4	7.5	7.6	7.5	7.6	12.3	12.3	12.3	24.9	25.4	25.2	39.7	39.8	39.8
18960	5.4	5.3	5.4	6.8	6.2	6.3	6.8	6.4	6.5	10.3	9.3	9.6	22.9	20.4	21.2	35.9	32.4	33.4
18964	6.1	6.0	6.0	6.6	6.7	6.6	6.6	6.9	6.8	10.3	11.0	10.7	21.4	22.3	21.8	33.9	35.0	34.4
18967	5.8	5.5	5.7	8.0	7.2	7.6	8.3	7.0	7.7	14.0	11.3	12.6	29.5	24.9	27.2	47.1	41.1	44.1
18968	6.6	6.2	6.3	10.4	8.7	8.9	10.4	8.7	8.9	15.4	13.4	13.6	30.4	26.6	27.1	50.7	42.9	43.8
18969	5.6	5.6	5.6	7.4	7.5	7.4	7.7	7.5	7.6	12.7	11.9	12.3	27.0	25.6	26.3	40.5	38.2	39.4
18970	5.7	5.4	5.6	7.1	5.6	6.6	7.4	5.6	6.5	12.6	9.4	11.0	25.1	20.0	22.5	39.9	33.0	36.4
18973	5.6	5.4	5.6	7.4	7.2	7.3	7.5	7.2	7.4	11.4	10.9	11.2	23.0	22.9	23.0	36.6	36.6	36.6
18974	5.7	5.3	5.4	NO SURVIVING PUPS														
MATERNAL DOSAGE GROUP II d				1.6 MG/KG/DAY						SUBSET D								
18946e	6.9	6.4	6.7	6.3	5.2	6.0	6.3	5.2	6.0	12.4	7.8	10.8	30.3	19.3	26.6	48.8	36.3	44.6
18950	7.1	6.3	6.7	8.1	7.3	7.7	8.4	7.6	8.0	13.3	12.3	12.8	26.9	25.4	26.1	44.5	39.7	42.1
18951	7.8	7.5	7.6	8.8	8.4	8.6	9.0	8.4	8.7	12.6	11.2	11.9	24.2	21.6	22.9	39.4	36.5	38.0
18952	6.4	5.9	6.1	8.2	7.4	7.8	8.7	7.6	8.2	14.8	13.3	14.0	30.7	28.1	29.4	47.1	43.4	45.3
18953	7.0	6.5	6.8	8.2	8.2	8.2	8.6	8.5	8.6	12.7	11.9	12.3	25.4	24.8	25.1	41.6	40.3	41.0
18958	7.2	6.4	6.7	9.2	8.1	8.6	9.1	8.4	8.7	12.9	12.3	12.6	24.7	24.0	24.4	40.2	39.5	39.8
18959	6.0	5.4	5.8	8.2	7.6	8.0	8.0	7.7	7.8	13.0	12.5	12.7	27.1	26.2	26.6	42.8	42.1	42.5
18961	6.3	6.1	6.2	8.3	7.7	7.9	8.3	8.5	8.4	13.3	13.1	13.2	26.3	25.7	26.0	42.0	40.1	41.1
18963	5.8	5.4	5.6	7.1	6.4	6.8	7.3	6.6	6.9	12.2	11.7	12.0	26.8	25.9	26.4	43.2	41.7	42.5
18965	6.0	5.7	5.8	8.1	7.6	7.8	8.2	7.7	8.0	12.7	12.3	12.5	25.6	24.9	25.2	44.0	42.3	43.1
18972	6.4	5.8	6.0	9.0	8.1	8.5	9.0	8.3	8.7	14.8	14.0	14.4	31.4	29.9	30.6	46.1	43.7	44.9
18976	6.2	5.9	6.0	7.4	7.1	7.2	7.6	7.2	7.4	12.8	12.5	12.6	26.2	24.8	25.5	41.7	39.6	40.6
18977e	6.7	6.1	6.5	NO SURVIVING PUPS														

M = MALE F = FEMALE T = TOTAL (SUM OF PUP WEIGHTS/NUMBER OF LIVE PUPS) DAY = DAY POSTPARTUM
ALL WEIGHTS WERE RECORDED IN GRAMS (G). MEAN LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.

a. Preculling
b. Postculling
c. 1.6 mg/kg/day dosage group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
d. 1.6 mg/kg/day dosage group dams cross-fostered with vehicle control group litters.
e. Litters were not cross-fostered; values excluded from group averages.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 29 (PAGE 3): PUP BODY WEIGHT LITTER AVERAGES FROM BIRTH TO DAY 21 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION LITTERS

RATS ASSIGNED TO PHARMACOKINETIC EVALUATION

RAT/ LITTER NUMBER	DAY 1			DAY 4			DAY 7			DAY 14		
	M	F	T	M	F	T	M	F	T	M	F	T
MATERNAL DOSAGE GROUP I				0 (VEHICLE) MG/KG/DAY								
18910	7.4	7.1	7.3	a	a	a	17.5	16.4	17.1	33.8	32.1	33.1
18911	6.6	6.5	6.6	8.9	8.4	8.8	12.4	12.5	12.4	23.7	24.1	23.8
18913	6.2	5.7	6.2	8.0	7.6	8.0	10.9	10.6	10.9	21.2	19.6	21.0
18915	6.4	6.1	6.2	a	a	a	12.6	13.0	12.9	24.5	25.3	25.0
18926	7.0	7.0	7.0	11.9	12.4	12.2	15.9	15.6	15.8	30.0	29.4	29.7
18927	6.6	6.1	6.3	8.8	8.2	8.5	12.3	10.8	11.5	22.4	20.6	21.6
18939	6.4	6.0	6.2	a	a	a	12.9	12.5	12.7	23.6	22.6	23.1
18940	6.2	5.8	6.1	8.5	8.3	8.4	10.8	10.8	10.8	19.8	18.8	19.4
MATERNAL DOSAGE GROUP II				1.6 MG/KG/DAY								
18956	6.4	6.0	6.2	9.3	8.8	9.0	13.1	12.1	12.5	24.2	23.4	23.8
18971	---	7.6	7.6	---	9.1	9.1	---	9.2	9.2	---	11.7	11.7

M = MALE F = FEMALE T = TOTAL (SUM OF PUP WEIGHTS/NUMBER OF LIVE PUPS) DAY = DAY POSTPARTUM
ALL WEIGHTS WERE RECORDED IN GRAMS (G). MEAN LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.
a. Values were not recorded.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 30 (PAGE 1): PUP BODY WEIGHTS FROM BIRTH TO DAY 21 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

RATS ASSIGNED TO CROSS-FOSTERING

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP I [a]						0 (VEHICLE) MG/KG/DAY					SUBSET A		POSTPARTUM DAY 1						
18903	5.6	6.1	5.3	5.5	5.6	5.3	5.7	4.9	5.0	5.4	5.4	5.5	5.6	5.2	5.0					
18907	6.2	6.0	5.8	6.1	6.3	5.9	5.8	5.7	5.8	5.9	5.8	5.5	6.2							
18908	6.0	5.9	6.0	5.4	5.8	5.2	5.1	5.5	5.5	5.8	4.9	5.4	5.1	5.4	5.3	5.8				
18909	5.2	5.7	5.4	5.2	6.0	5.3	5.8	5.6	5.5	5.2	5.5	5.2	5.6	5.6	5.7	5.4				
18918b	5.2	5.3	5.5	5.5	5.7	5.4	5.5	5.3	6.7	5.5	5.1	5.0	5.1	5.0	5.0	4.9	5.2			
18920	5.6	5.1	5.3	5.2	5.3	5.6	5.2	5.4	5.2	5.0	5.5	5.4	5.0	5.1	5.2					
18924	5.6	5.3	5.8	5.9	5.7	6.0	5.9	5.8	5.0	5.5	5.7	5.4	5.5	5.4	5.0	5.7	5.5			
18929	5.6	6.1	5.6	5.5	5.5	5.6	5.5	5.6	5.4	5.5	4.9	5.0	5.3	5.5	5.3	5.2				
18934	5.6	5.7	5.6	6.0	5.8	6.2	5.7	5.3	5.6	5.3	5.5	5.3	5.4	5.5						
18936b	6.4	6.3	5.9	6.6	6.0	6.2	6.4	5.9	5.7	5.9	5.9	5.8								
18937	6.2	5.9	6.0	6.2	5.8	5.6	5.1	5.5	5.7	5.5	5.7	5.6	5.6							
18941	6.3	5.9	6.3	6.4	6.8	6.3	6.0	5.5	5.6	6.0	5.7	6.6	5.8							
18942	5.3	5.2	5.1	4.9	5.3	5.5	5.6	5.5	5.6	5.5	5.0	5.0	4.9	4.4	5.3	5.3	5.4	5.0		
RAT/ LITTER #	MATERNAL DOSAGE GROUP I [c]						0 (VEHICLE) MG/KG/DAY					SUBSET B		POSTPARTUM DAY 1						
18901	6.4	6.7	6.7	6.9	7.1	6.2	6.3	6.7	6.5	6.4	6.6	6.2	5.4	5.8	5.8	6.2				
18904	5.2	6.4	6.5	6.1	5.6	6.0	5.5	5.3	5.9	6.1	5.3	5.7	5.4	6.1	5.1					
18906	6.1	5.8	5.7	6.1	5.0	5.9	6.1	5.6	5.6	5.4	4.9	5.7	5.1	5.7	5.5	5.5	5.8	5.8	5.3	
18912	5.7	5.2	5.9	5.8	5.2	5.6	5.6	5.4	5.6	5.6	5.3	5.1	5.6	5.1	5.5	5.2	4.8	4.8	5.0	5.6
18917	7.2	6.9	6.7	6.9	7.3	6.5	7.5	6.5	7.3	6.8	6.6	7.0	6.9	6.5	6.9	6.4				
18919	6.0	6.3	6.4	6.2	6.9	6.5	6.5	6.4	6.2	6.3	6.4	6.1								
18922	7.3	6.7	6.8	5.9	7.4	6.3	6.7	7.0	5.7	5.7	6.0	6.9	6.4	6.5	6.7					
18923	7.3	6.7	6.9	7.0	7.2	6.9	6.5	6.3	6.4	6.7	7.2	6.3	6.8	6.9	6.9	6.8				
18931	6.4	6.3	6.7	6.3	6.7	6.6	6.1	6.4	6.2	6.2	6.1	5.9	6.0	6.3	5.3	5.9	6.1			
18932	6.8	6.8	6.3	7.0	7.0	6.9	6.0	5.7	6.5	6.5	6.1	6.1	6.3	6.3						
18935	6.3	6.3	6.2	6.3	6.5	5.9	6.6	5.7	5.7	6.0	5.5	6.4	6.1	4.7	5.8	6.0				
18938	5.9	6.1	6.3	6.1	6.3	6.3	5.9	6.2	6.4	6.2	6.1	5.8	6.2	5.9	5.8					

ALL WEIGHTS WERE RECORDED IN GRAMS (G).
FIRST LETTER -- M-MALE, F-FEMALE
SECOND LETTER -- A-ALIVE, S-STILLBORN, D-DIED, C-CULLED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.
a. Vehicle control group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
b. Litters were not cross-fostered; values excluded from group averages.
c. Vehicle control group dams cross-fostered with vehicle control litters.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 30 (PAGE 2): PUP BODY WEIGHTS FROM BIRTH TO DAY 21 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

RATS ASSIGNED TO CROSS-FOSTERING

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP II a						1.6 MG/KG/DAY					SUBSET C			POSTPARTUM DAY 1					
18943	5.7	5.8	6.1	5.7	5.8	5.7	6.0	5.4	5.7	5.3	5.7	5.6	5.6	5.5	5.8					
18947	5.6	5.4	6.1	5.9	5.9	5.8	5.8	6.2	5.4	5.7	5.6	5.7	5.5	5.7						
18948	6.1	5.5	5.9	5.8	5.9	5.8	5.5	6.1	5.8	6.2	5.6	5.8	4.4	5.5	5.9	5.2	5.7			
18957	6.2	6.7	6.2	5.6	6.1	5.8	5.8	5.9	5.8	5.6	5.7	5.5	5.5							
18960	5.2	5.5	5.4	5.2	5.7	5.3	5.2	5.6	5.4	5.4	5.2	5.3	5.7	5.5	4.7					
18964	6.0	6.4	6.2	6.3	6.0	5.9	6.0	5.9	6.1	5.8	5.6	6.5	5.8	5.8	6.1					
18967	6.2	6.2	5.8	5.9	5.9	5.9	5.8	5.5	5.5	5.7	5.5	5.6	5.8	5.4	5.1	5.2				
18968	7.3	6.0	6.3	6.1	6.0	5.6	6.6	6.9	6.1	5.9										
18969	5.9	5.6	5.8	5.6	6.0	5.7	5.5	5.3	5.5	5.6	5.8	5.6	5.7	5.6	5.4	5.6	5.7			
18970	5.7	5.5	5.8	5.7	5.8	5.8	5.6	5.4	6.0	5.6	5.3	5.4	5.6	5.1	5.3					
18973	5.8	5.9	5.3	5.2	6.1	5.4	5.8	5.4	5.6	5.7	5.4	5.5	5.2	5.6	5.5					
18974	5.6	5.5	5.9	5.9	5.6	5.5	5.4	5.2	5.3	5.4	5.3	4.6	5.4	5.3	5.6					
RAT/ LITTER #	MATERNAL DOSAGE GROUP II b						1.6 MG/KG/DAY					SUBSET D			POSTPARTUM DAY 1					
18946c	7.0	7.2	6.6	6.8	6.7	7.0	7.3	6.6	6.6	6.4	6.6	6.1	6.2	6.4	6.7	d	d			
18950	6.5	6.7	7.0	7.0	7.9	7.3	7.3	7.1	6.3	7.0	6.4	6.6	6.0	6.4	5.7	6.2	6.1	6.6		
18951	8.4	7.7	7.2	7.8	7.9	7.8	7.3	7.9	7.4	7.6	7.6	7.8	7.0	7.7						
18952	5.6	6.3	6.6	6.4	6.5	6.8	6.3	6.4	5.7	6.1	6.1	6.1	5.7	5.9	6.2	5.8	5.8			
18953	6.9	7.1	6.7	7.3	7.2	6.9	6.7	7.3	6.9	6.1	7.1	6.8	6.4	6.1	6.3	6.6				
18958	7.1	7.4	6.8	7.1	7.3	7.2	6.3	5.5	6.4	6.8	6.7	6.5	7.2	6.0						
18959	6.1	6.2	6.0	6.0	6.4	6.0	5.9	5.8	6.0	5.5	5.3	5.9	5.8	5.5	6.1	4.1				
18961	6.1	6.2	6.9	6.1	6.2	6.5	5.8	6.1	6.4	6.3	6.3	6.4	6.2	5.4	5.5	6.0				
18963	6.1	5.6	5.6	5.7	5.9	6.0	5.8	5.5	6.0	5.7	5.6	5.2	5.8	5.5	5.6	5.5	5.0	5.4	4.9	
18965	6.4	6.0	6.1	5.9	5.8	5.9	5.5	5.9	6.1	5.4	5.2	5.3	6.0	5.9	5.8	5.9	6.0			
18972	6.4	6.1	6.2	6.4	6.4	6.7	6.3	5.7	6.2	5.9	6.1	5.7	5.4	5.6	5.9	5.6				
18976	6.2	6.0	6.1	5.9	6.0	6.3	6.3	6.5	5.8	5.9	6.2	5.9	5.4	5.7	6.0	6.1	5.9	5.9		
18977c	6.7	7.1	6.1	6.5	6.4	7.0	7.0	6.1	5.9	6.3	6.1	FD 1								

ALL WEIGHTS WERE RECORDED IN GRAMS (G).
FIRST LETTER -- M-MALE, F-FEMALE
SECOND LETTER -- A-ALIVE, S-STILLBORN, D-DIED, C-CULLED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.
a. 1.6 mg/kg/day dosage group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
b. 1.6 mg/kg/day dosage group dams cross-fostered with vehicle control group litters.
c. Litters were not cross-fostered; values excluded from group averages.
d. Value was not recorded.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 30 (PAGE 3): PUP BODY WEIGHTS FROM BIRTH TO DAY 21 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

RATS ASSIGNED TO CROSS-FOSTERING

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP I a						0 (VEHICLE) MG/KG/DAY					SUBSET A		POSTPARTUM DAY 4 PRECULLING						
18903	4.7	5.9	5.7	6.5	6.5	6.0	MM 3	6.8	6.5	6.5	5.3	6.0	5.8	4.6	FM 3					
18907	8.0	6.7	8.8	7.3	8.4	7.7	8.1	5.3	8.2	7.4	6.7	8.1	FD 4							
18908	7.0	6.7	7.5	MM 4	7.4	7.6	5.7	7.2	6.8	7.6	6.5	6.3	7.0	8.0	7.3	6.5				
18909	7.6	7.7	5.3	7.9	7.6	7.8	7.8	MD 4	8.0	8.1	7.0	7.5	4.6	7.0	7.3	7.8				
18918b	10.5	9.2	9.7	9.5	10.6	10.1	10.4	MM 2	MM 2	9.7	9.0	9.3	9.2	9.0	9.5	9.0	8.7			
18920	7.2	4.1	6.9	7.4	7.1	6.2	7.7	7.0	7.0	7.6	7.1	7.1	6.2	FM 3	FD 2					
18924	8.2	8.4	7.3	7.5	7.7	6.5	7.0	MM 3	7.2	7.0	7.7	7.6	6.8	5.4	7.3	4.9	FD 4			
18929	5.6	7.0	8.6	8.0	7.5	7.9	8.7	MM 3	7.3	6.0	6.8	7.5	6.4	8.2	7.4	7.9				
18934	8.0	7.5	6.2	7.1	8.3	7.0	7.4	6.8	7.1	7.4	7.5	7.1	5.9	FD 2						
18936b	8.4	9.2	9.2	8.9	8.4	8.2	8.6	7.2	8.1	7.7	7.8	FM 2								
18937	8.1	8.2	8.3	7.7	7.7	7.4	7.1	7.7	7.4	7.1	7.7	6.4	7.8							
18941	8.7	8.2	8.2	7.1	9.0	MM 3	MM 3	MD 2	9.3	6.1	8.7	3.6	FD 2							
18942	5.7	7.6	7.9	6.5	7.2	7.3	7.1	6.8	6.7	6.9	6.9	6.1	7.2	6.4	7.9	6.9	7.3	7.6		
RAT/ LITTER #	MATERNAL DOSAGE GROUP I c						0 (VEHICLE) MG/KG/DAY					SUBSET B		POSTPARTUM DAY 4 PRECULLING						
18901	8.7	8.8	9.5	10.7	9.5	9.2	8.3	8.3	8.6	8.4	9.6	8.8	8.9	8.0	7.9	9.3				
18904	6.8	6.5	9.2	7.8	7.9	7.7	7.2	6.3	6.8	8.6	7.5	7.7	6.4	6.8	6.3					
18906	8.0	8.3	8.8	6.7	8.4	7.7	9.0	8.4	7.7	6.0	8.8	6.7	7.9	7.6	7.8	8.4	8.0	7.6	FD 4	
18912	6.5	7.2	5.5	7.0	6.5	7.4	6.9	7.3	7.4	7.4	6.1	6.8	5.9	6.8	6.1	6.7	6.0	6.3	4.7	FM 4
18917	9.3	9.0	9.0	8.2	7.1	9.1	8.7	8.3	9.3	8.9	8.4	8.6	8.1	7.7	8.5	8.5				
18919	10.2	9.6	8.7	9.4	9.0	10.1	9.3	9.5	9.1	9.5	9.3	9.1								
18922	8.1	10.1	8.8	8.7	8.7	8.0	8.5	8.3	8.7	9.2	9.4	9.5	8.4	7.3	7.9					
18923	9.9	9.9	8.4	9.3	10.6	9.5	9.4	8.1	9.3	8.6	9.4	9.7	9.2	7.6	9.2	FM 3				
18931	8.3	7.7	8.6	8.2	8.3	8.6	8.2	8.5	7.5	7.9	8.3	8.2	8.0	7.2	7.6	8.7	8.2			
18932	9.3	8.9	9.8	9.0	8.8	9.0	8.5	9.2	8.5	8.4	8.5	8.5	8.7	8.2						
18935	9.0	8.7	7.8	8.8	8.7	8.0	7.5	8.7	8.2	8.2	8.0	4.6	8.2	8.7	7.5	7.3				
18938	8.5	9.5	8.5	8.9	8.5	8.1	8.2	9.1	8.1	7.7	9.1	8.6	7.4	8.2	8.5					

ALL WEIGHTS WERE RECORDED IN GRAMS (G).
FIRST LETTER -- M-MALE, F-FEMALE
SECOND LETTER -- A-ALIVE, S-STILLBORN, D-DIED, C-CULLED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.
a. Vehicle control group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
b. Litters were not cross-fostered; values excluded from group averages.
c. Vehicle control group dams cross-fostered with vehicle control litters.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 30 (PAGE 4): PUP BODY WEIGHTS FROM BIRTH TO DAY 21 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

RATS ASSIGNED TO CROSS-FOSTERING

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP II a						1.6 MG/KG/DAY					SUBSET C			POSTPARTUM DAY 4 PRECULLING					
18943	7.1	7.8	8.7	7.5	8.8	8.2	8.6	8.8	7.3	8.2	8.2	8.5	7.6	6.9	8.4					
18947	7.6	8.0	7.7	7.4	7.0	7.9	7.9	7.4	6.3	7.6	7.7	7.0	7.1	6.7						
18948	6.1	7.1	6.1	7.1	4.4	7.2	MM 4	MM 3	MD 2	MD 2	MD 2	6.5	5.1	FD 3	FD 3	FM 3	FM 3			
18957	8.8	7.0	7.1	MM 3	6.9	6.8	6.9	7.3	8.7	7.7	7.6	7.7	FM 3							
18960	6.6	7.3	6.5	MM 4	MM 4	6.0	6.4	7.4	6.5	6.5	6.6	4.6	5.2	FM 4	FM 4					
18964	6.9	6.6	6.6	6.5	7.1	6.2	MM 3	6.3	6.0	7.4	6.3	6.1	7.0	7.6	6.6					
18967	9.0	8.6	7.8	6.7	8.3	9.0	7.7	6.6	8.1	7.5	7.3	7.7	7.9	7.6	6.1	6.0				
18968	10.4	MD 2	9.3	8.3	9.4	9.4	9.1	8.5	7.6	8.0										
18969	7.4	7.9	6.8	7.2	7.6	7.6	6.8	7.3	7.4	7.5	6.9	8.2	7.9	7.5	7.8	8.2	6.3			
18970	7.6	7.1	7.1	7.8	6.2	6.9	7.7	6.1	7.7	6.9	4.3	3.9	6.0	6.7	FM 3					
18973	6.1	8.7	7.7	7.8	7.3	6.7	7.0	7.8	7.8	6.8	6.2	7.5	7.2	7.8	FD 2					
18974	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	FM 4	FM 3	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2					
RAT/ LITTER #	MATERNAL DOSAGE GROUP II b						1.6 MG/KG/DAY					SUBSET D			POSTPARTUM DAY 4 PRECULLING					
18946c	8.7	6.0	4.3	MD 4	MD 4	MM 3	MD 2	MD 2	MD 2	5.2	FM 3	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2			
18950	7.3	7.9	7.5	8.3	8.7	7.8	8.3	9.1	6.7	7.2	6.7	8.8	7.4	7.4	7.3	6.3	7.8	7.4		
18951	8.8	8.9	8.0	8.6	8.9	9.6	8.8	8.6	8.9	8.3	8.1	7.5	8.7	8.6						
18952	8.7	6.3	8.9	8.5	8.3	7.8	8.9	8.4	7.1	6.6	7.8	7.5	7.6	7.7	7.7	7.4	7.4			
18953	8.0	8.7	5.5	8.8	8.3	8.4	9.1	8.9	8.8	7.4	8.0	9.0	7.8	7.8	8.3	8.9				
18958	9.3	7.8	10.0	8.9	9.5	9.5	7.8	8.1	8.7	8.4	8.8	6.9	8.5	7.7						
18959	8.4	8.0	8.0	8.1	7.8	8.5	8.0	8.3	8.8	8.0	7.3	7.3	8.4	7.8	7.0	FM 3				
18961	7.8	8.9	8.4	8.0	8.5	6.0	9.1	7.1	6.8	8.5	7.6	7.5	8.1	8.3	8.3	7.7				
18963	7.1	7.0	6.8	7.4	7.0	7.3	6.5	6.7	8.0	7.1	7.3	6.5	5.6	6.4	6.9	6.8	6.1	6.6	6.2	
18965	8.2	8.5	8.4	7.3	8.1	8.0	7.5	8.2	8.2	7.4	7.3	6.3	7.2	7.2	7.6	8.0	8.6			
18972	8.6	8.5	9.7	9.1	8.7	9.1	9.1	8.3	8.5	7.4	8.1	8.2	7.4	7.2	8.6	9.0				
18976	8.0	8.0	6.8	7.0	7.7	7.3	7.3	MD 2	7.6	6.7	6.6	6.4	7.0	7.4	7.4	7.4	7.0	7.2		
18977c	MD 3	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	FD 2	FD 2	FD 2	FD 2	FD 1								

ALL WEIGHTS WERE RECORDED IN GRAMS (G).
FIRST LETTER -- M-MALE, F-FEMALE
SECOND LETTER -- A-ALIVE, S-STILLBORN, D-DIED, C-CULLED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.
a. 1.6 mg/kg/day dosage group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
b. 1.6 mg/kg/day dosage group dams cross-fostered with vehicle control group litters.
c. Litters were not cross-fostered; values excluded from group averages.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 30 (PAGE 5): PUP BODY WEIGHTS FROM BIRTH TO DAY 21 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

RATS ASSIGNED TO CROSS-FOSTERING

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP I [a]						0 (VEHICLE) MG/KG/DAY					SUBSET A			POSTPARTUM DAY 4 POSTCULLING					
18903	MC 4	5.9	5.7	6.5	6.5	6.0	MM 3	6.8	FC 4	6.5	FC 4	6.0	5.8	4.6	FM 3					
18907	8.0	6.7	8.8	7.3	8.4	7.7	8.1	FC 4	8.2	7.4	6.7	FC 4	FD 4							
18908	7.0	6.7	7.5	MM 4	7.4	7.6	FC 4	7.2	FC 4	FC 4	6.5	FC 4	FC 4	8.0	7.3	6.5				
18909	7.6	7.7	MC 4	7.9	7.6	MC 4	7.8	MD 4	8.0	8.1	7.0	7.5	FC 4	FC 4	FC 4	7.8				
18918b	10.5	MC 4	9.7	9.5	MC 4	10.1	10.4	MM 2	MM 2	FC 4	9.0	9.3	FC 4	FC 4	9.5	9.0	8.7			
18920	7.2	MC 4	6.9	7.4	7.1	MC 4	7.7	MC 4	7.0	7.6	7.1	7.1	6.2	FM 3	FD 2					
18924	MC 4	8.4	7.3	7.5	MC 4	MC 4	7.0	MM 3	7.2	7.0	7.7	7.6	6.8	FC 4	7.3	FC 4	FD 4			
18929	MC 4	MC 4	8.6	8.0	7.5	7.9	8.7	MM 3	7.3	FC 4	FC 4	FC 4	6.4	8.2	7.4	7.9				
18934	8.0	7.5	MC 4	7.1	8.3	7.0	MC 4	FC 4	7.1	7.4	7.5	7.1	5.9	FD 2						
18936b	8.4	9.2	MC 4	8.9	8.4	8.2	8.6	7.2	8.1	7.7	7.8	FM 2								
18937	8.1	8.2	8.3	7.7	7.7	7.4	FC 4	7.7	7.4	7.1	7.7	FC 4	FC 4							
18941	8.7	8.2	8.2	7.1	9.0	MM 3	MM 3	MD 2	9.3	6.1	8.7	3.6	FD 2							
18942	MC 4	7.6	7.9	MC 4	MC 4	MC 4	7.1	6.8	6.7	6.9	FC 4	FC 4	7.2	FC 4	7.9	6.9	FC 4	7.6		
RAT/ LITTER #	MATERNAL DOSAGE GROUP I [c]						0 (VEHICLE) MG/KG/DAY					SUBSET B			POSTPARTUM DAY 4 POSTCULLING					
18901	MC 4	8.8	9.5	10.7	9.5	9.2	8.3	8.3	8.6	FC 4	FC 4	FC 4	FC 4	FC 4	7.9	9.3				
18904	MC 4	MC 4	9.2	7.8	7.9	7.7	7.2	FC 4	FC 4	8.6	7.5	7.7	FC 4	6.8	6.3					
18906	MC 4	8.3	8.8	MC 4	MC 4	7.7	9.0	8.4	FC 4	FC 4	8.8	FC 4	7.9	7.6	7.8	8.4	FC 4	FC 4	FD 4	
18912	MC 4	7.2	MC 4	7.0	6.5	MC 4	6.9	MC 4	MC 4	7.4	MC 4	6.8	FC 4	6.8	FC 4	6.7	FC 4	6.3	4.7	FM 4
18917	9.3	9.0	MC 4	MC 4	7.1	9.1	8.7	MC 4	MC 4	8.9	FC 4	8.6	8.1	7.7	FC 4	8.5				
18919	MC 4	MC 4	8.7	9.4	9.0	10.1	9.3	9.5	9.1	9.5	9.3	9.1								
18922	8.1	10.1	8.8	8.7	8.7	FC 4	FC 4	FC 4	8.7	9.2	9.4	9.5	FC 4	FC 4	7.9					
18923	9.9	9.9	MC 4	9.3	10.6	9.5	FC 4	FC 4	9.3	8.6	FC 4	FC 4	9.2	7.6	9.2	FM 3				
18931	8.3	7.7	8.6	MC 4	8.3	MC 4	8.2	8.5	FC 4	7.9	FC 4	FC 4	FC 4	FC 4	7.6	8.7	8.2			
18932	9.3	MC 4	9.8	9.0	8.8	9.0	8.5	9.2	8.5	FC 4	8.5	FC 4	8.7	FC 4						
18935	9.0	8.7	MC 4	8.8	8.7	MC 4	7.5	8.7	FC 4	8.2	FC 4	FC 4	FC 4	8.7	7.5	7.3				
18938	8.5	9.5	8.5	MC 4	MC 4	8.1	MC 4	9.1	8.1	MC 4	9.1	8.6	MC 4	8.2	8.5					

ALL WEIGHTS WERE RECORDED IN GRAMS (G).
FIRST LETTER -- M-MALE, F-FEMALE
SECOND LETTER -- A-ALIVE, S-STILLBORN, D-DIED, C-CULLED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.
a. Vehicle control group dams cross-fostered 1.6 mg/kg/day dosage group litters.
b. Litters were not cross-fostered; values excluded from group averages.
c. Vehicle control group dams cross-fostered vehicle control litters.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 30 (PAGE 6): PUP BODY WEIGHTS FROM BIRTH TO DAY 21 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

RATS ASSIGNED TO CROSS-FOSTERING

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP II a						1.6 MG/KG/DAY					SUBSET C			POSTPARTUM DAY 4 POSTCULLING					
18943	7.1	7.8	8.7	7.5	8.8	FC 4	FC 4	8.8	7.3	8.2	8.2	FC 4	FC 4	FC 4	8.4					
18947	7.6	8.0	MC 4	MC 4	MC 4	7.9	7.9	7.4	FC 4	7.6	7.7	7.0	7.1	6.7						
18948	6.1	7.1	6.1	7.1	4.4	7.2	MM 4	MM 3	MD 2	MD 2	MD 2	6.5	5.1	FD 3	FD 3	FM 3	FM 3			
18957	8.8	7.0	7.1	MM 3	FC 4	6.8	6.9	7.3	8.7	7.7	7.6	7.7	FM 3							
18960	6.6	7.3	6.5	MM 4	MM 4	6.0	6.4	7.4	6.5	6.5	6.6	FC 4	5.2	FM 4	FM 4					
18964	6.9	6.6	MC 4	MC 4	7.1	6.2	MM 3	6.3	FC 4	7.4	FC 4	6.1	7.0	7.6	6.6					
18967	9.0	8.6	MC 4	MC 4	8.3	MC 4	7.7	MC 4	8.1	7.5	FC 4	FC 4	7.9	7.6	6.1	6.0				
18968	10.4	MD 2	9.3	8.3	9.4	9.4	9.1	8.5	7.6	8.0										
18969	MC 4	7.9	MC 4	MC 4	MC 4	7.6	MC 4	7.3	MC 4	7.5	MC 4	8.2	7.9	7.5	7.8	8.2	6.3			
18970	MC 4	MC 4	7.1	7.8	MC 4	6.9	7.7	MC 4	7.7	6.9	4.3	3.9	6.0	6.7	FM 3					
18973	MC 4	8.7	MC 4	MC 4	7.3	6.7	MC 4	7.8	7.8	6.8	6.2	7.5	7.2	7.8	FD 2					
18974	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	FM 4	FM 3	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2					
RAT/ LITTER #	MATERNAL DOSAGE GROUP II b						1.6 MG/KG/DAY					SUBSET D			POSTPARTUM DAY 4 POSTCULLING					
18946c	8.7	6.0	4.3	MD 4	MD 4	MM 3	MD 2	MD 2	MD 2	5.2	FM 3	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2			
18950	MC 4	MC 4	7.5	8.3	8.7	MC 4	8.3	9.1	FC 4	7.2	6.7	8.8	FC 4	7.4	FC 4	FC 4	7.8	FC 4		
18951	8.8	8.9	MC 4	MC 4	8.9	9.6	8.8	MC 4	8.9	8.3	FC 4	7.5	8.7	8.6						
18952	8.7	MC 4	8.9	8.5	8.3	MC 4	8.9	MC 4	FC 4	FC 4	7.8	FC 4	7.6	7.7	7.7	7.4	FC 4			
18953	8.0	8.7	MC 4	8.8	MC 4	8.4	9.1	MC 4	8.8	FC 4	8.0	9.0	FC 4	7.8	FC 4	8.9				
18958	9.3	7.8	10.0	8.9	MC 4	9.5	7.8	8.1	8.7	FC 4	8.8	FC 4	8.5	FC 4						
18959	MC 4	8.0	8.0	8.1	7.8	MC 4	8.0	MC 4	MC 4	8.0	FC 4	7.3	8.4	7.8	7.0	FM 3				
18961	7.8	8.9	8.4	8.0	8.5	FC 4	9.1	FC 4	FC 4	8.5	FC 4	FC 4	8.1	8.3	8.3	FC 4				
18963	MC 4	7.0	6.8	7.4	MC 4	7.3	MC 4	MC 4	8.0	MC 4	MC 4	6.5	FC 4	FC 4	6.9	6.8	6.1	6.6	FC 4	
18965	8.2	8.5	8.4	MC 4	8.1	8.0	7.5	8.2	FC 4	FC 4	FC 4	FC 4	7.2	FC 4	7.6	8.0	FC 4			
18972	8.6	MC 4	9.7	MC 4	8.7	9.1	9.1	8.3	FC 4	7.4	8.1	FC 4	FC 4	FC 4	8.6	9.0				
18976	8.0	8.0	6.8	MC 4	7.7	MC 4	7.3	MD 2	7.6	6.7	FC 4	FC 4	FC 4	FC 4	7.4	FC 4	7.0	7.2		
18977c	MD 3	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	FD 2	FD 2	FD 2	FD 2	FD 1								

ALL WEIGHTS WERE RECORDED IN GRAMS (G).
FIRST LETTER -- M-MALE, F-FEMALE
SECOND LETTER -- A-ALIVE, S-STILLBORN, D-DIED, C-CULLED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.
a. 1.6 mg/kg/day dosage group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
b. 1.6 mg/kg/day dosage group dams cross-fostered with vehicle control group litters.
c. Litters were not cross-fostered; values excluded from group averages.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 30 (PAGE 7): PUP BODY WEIGHTS FROM BIRTH TO DAY 21 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

RATS ASSIGNED TO CROSS-FOSTERING

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP I a						0 (VEHICLE) MG/KG/DAY					SUBSET A			POSTPARTUM DAY 7					
18903	MC 4	10.9	11.4	10.5	9.5	10.0	MM 3	10.2	FC 4	8.1	FC 4	10.2	11.5	8.2	FM 3					
18907	14.9	11.2	13.9	13.8	11.4	13.4	12.0	FC 4	11.8	11.5	14.3	FC 4	FD 4							
18908	12.8	12.2	12.7	MM 4	10.9	10.6	FC 4	12.4	FC 4	FC 4	11.7	FC 4	FC 4	12.7	12.1	11.3				
18909	14.0	13.0	MC 4	13.0	13.2	MC 4	13.6	MD 4	14.5	13.7	12.9	14.2	FC 4	FC 4	FC 4	11.8				
18918b	16.7	MC 4	17.1	15.6	MC 4	16.7	16.5	MM 2	MM 2	FC 4	15.3	15.6	FC 4	FC 4	13.7	15.1	15.2			
18920	12.6	MC 4	11.5	12.3	12.5	MC 4	12.4	MC 4	12.0	11.4	10.4	11.9	13.1	FM 3	FD 2					
18924	MC 4	13.6	12.6	11.0	MC 4	MC 4	13.0	MM 3	12.3	12.3	11.6	12.0	11.5	FC 4	12.7	FC 4	FD 4			
18929	MC 4	MC 4	14.2	13.9	13.3	14.6	12.5	MM 3	10.8	FC 4	FC 4	FC 4	12.2	13.0	12.5	13.8				
18934	14.5	11.9	MC 4	13.2	13.9	11.5	MC 4	FC 4	13.6	10.4	12.5	13.5	12.1	FD 2						
18936b	13.5	13.1	MC 4	13.0	12.9	12.8	13.3	12.7	12.5	11.2	11.8	FM 2								
18937	12.2	12.4	12.2	11.0	11.7	11.6	FC 4	11.7	11.2	11.1	11.8	FC 4	FC 4							
18941	10.3	12.5	12.7	14.6	14.1	MM 3	MM 3	MD 2	9.1	13.7	15.2	FM 5	FD 2							
18942	MC 4	12.5	12.7	MC 4	MC 4	MC 4	12.2	11.5	13.0	12.1	FC 4	FC 4	12.2	FC 4	12.2	13.5	FC 4	12.6		
RAT/ LITTER #	MATERNAL DOSAGE GROUP I c						0 (VEHICLE) MG/KG/DAY					SUBSET B			POSTPARTUM DAY 7					
18901	MC 4	15.0	14.7	15.8	17.4	15.3	13.6	13.2	14.2	FC 4	FC 4	FC 4	FC 4	FC 4	15.5	14.9				
18904	MC 4	MC 4	16.0	14.1	14.2	13.5	13.3	FC 4	FC 4	11.4	11.6	14.2	FC 4	12.3	13.3					
18906	MC 4	13.7	12.6	MC 4	MC 4	13.7	13.9	13.6	FC 4	FC 4	13.8	FC 4	12.9	12.6	13.9	13.8	FC 4	FC 4	FD 4	
18912	MC 4	11.1	MC 4	13.5	12.3	MC 4	12.8	MC 4	MC 4	12.8	MC 4	12.1	FC 4	12.8	FC 4	12.8	FC 4	13.7	12.1	FM 4
18917	14.1	12.3	MC 4	MC 4	14.1	13.9	14.6	MC 4	MC 4	14.0	FC 4	14.6	13.0	13.1	FC 4	13.3				
18919	MC 4	MC 4	14.0	17.7	14.7	16.1	15.7	15.4	14.7	15.1	15.4	15.0								
18922	15.0	15.8	15.0	14.5	17.1	FC 4	FC 4	FC 4	16.0	16.4	15.0	13.7	FC 4	FC 4	14.3					
18923	15.8	15.7	MC 4	16.3	17.6	15.1	FC 4	FC 4	15.2	14.5	FC 4	FC 4	13.9	12.8	15.0	FM 3				
18931	12.5	14.2	14.1	MC 4	14.5	MC 4	13.7	14.5	FC 4	14.2	FC 4	FC 4	FC 4	FC 4	13.6	12.4	14.3			
18932	15.3	MC 4	14.5	14.8	14.0	13.9	13.5	13.9	14.0	FC 4	13.7	FC 4	14.4	FC 4						
18935	13.5	12.2	MC 4	13.8	14.1	MC 4	14.1	14.0	FC 4	11.9	FC 4	FC 4	FC 4	12.4	13.2	13.3				
18938	13.2	12.8	14.7	MC 4	MC 4	14.5	MC 4	14.3	13.5	MC 4	13.4	14.2	MC 4	13.4	14.2					

ALL WEIGHTS WERE RECORDED IN GRAMS (G).
FIRST LETTER -- M-MALE, F-FEMALE
SECOND LETTER -- A-ALIVE, S-STILLBORN, D-DIED, C-CULLED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.
a. Vehicle control group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
b. Litters were not cross-fostered; values excluded from group averages.
c. Vehicle control group dams cross-fostered with vehicle control litters.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 30 (PAGE 8): PUP BODY WEIGHTS FROM BIRTH TO DAY 21 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

RATS ASSIGNED TO CROSS-FOSTERING

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP II a					1.6 MG/KG/DAY						SUBSET C			POSTPARTUM DAY 7					
18943	14.1	12.0	12.4	13.6	12.6	FC 4	FC 4	12.9	14.7	12.7	12.5	FC 4	FC 4	FC 4	12.4					
18947	12.2	13.3	MC 4	MC 4	MC 4	12.5	11.9	12.7	FC 4	12.7	12.7	11.0	11.7	10.3						
18948	6.0	9.6	9.9	11.7	11.7	11.5	MM 4	MM 3	MD 2	MD 2	MD 2	9.7	8.2	FD 3	FD 3	FM 3	FM 3			
18957	14.1	11.5	11.3	MM 3	FC 4	12.7	11.7	14.0	12.2	11.5	11.6	12.7	FM 3							
18960	9.9	9.5	11.5	MM 4	MM 4	8.6	8.6	9.4	9.7	10.4	7.3	FC 4	11.2	FM 4	FM 4					
18964	11.0	9.7	MC 4	MC 4	9.9	10.6	MM 3	10.4	FC 4	11.5	FC 4	10.5	11.4	10.3	11.3					
18967	14.8	14.4	MC 4	MC 4	13.4	MC 4	13.4	MC 4	14.1	11.8	FC 4	FC 4	12.4	9.9	12.8	9.5				
18968	15.4	MD 2	13.1	14.2	14.2	12.2	13.9	12.0	13.1	14.6										
18969	MC 4	12.2	MC 4	MC 4	MC 4	12.6	MC 4	12.4	MC 4	12.6	MC 4	13.5	12.3	10.6	11.5	13.3	11.9			
18970	MC 4	MC 4	13.3	13.4	MC 4	12.5	11.4	MC 4	12.3	10.6	11.5	6.9	6.3	11.8	FM 3					
18973	MC 4	13.1	MC 4	MC 4	10.8	12.0	MC 4	9.9	12.0	10.5	10.7	12.7	10.8	9.4	FD 2					
18974	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	FM 4	FM 3	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2					
RAT/ LITTER #	MATERNAL DOSAGE GROUP II b					1.6 MG/KG/DAY						SUBSET D			POSTPARTUM DAY 7					
18946c	10.1	14.6	MD 5	MD 4	MD 4	MM 3	MD 2	MD 2	MD 2	7.8	FM 3	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2			
18950	MC 4	MC 4	13.7	11.8	12.9	MC 4	14.3	13.8	FC 4	12.4	14.2	11.7	FC 4	11.8	FC 4	FC 4	11.2	FC 4		
18951	12.8	12.9	MC 4	MC 4	12.8	11.9	12.7	MC 4	11.8	10.0	FC 4	12.2	10.4	11.7						
18952	14.6	MC 4	15.3	14.5	14.7	MC 4	14.7	MC 4	FC 4	FC 4	13.6	FC 4	13.5	13.3	13.5	12.4	FC 4			
18953	11.7	12.7	MC 4	13.1	MC 4	13.1	12.7	MC 4	12.2	FC 4	11.8	12.5	FC 4	11.7	FC 4	11.5				
18958	11.0	12.8	13.6	13.6	MC 4	13.5	11.3	12.4	12.5	FC 4	12.4	FC 4	12.9	FC 4						
18959	MC 4	13.3	12.2	13.1	13.1	MC 4	13.2	MC 4	MC 4	13.1	FC 4	12.3	12.4	13.1	11.5	FM 3				
18961	14.2	13.7	13.2	12.4	12.9	FC 4	12.9	FC 4	FC 4	13.2	FC 4	FC 4	13.9	12.7	13.0	FC 4				
18963	MC 4	13.6	12.5	10.3	MC 4	12.4	MC 4	MC 4	12.1	MC 4	MC 4	11.7	FC 4	FC 4	11.8	12.5	11.7	10.9	FC 4	
18965	13.0	12.7	12.5	MC 4	13.0	12.2	12.0	12.2	FC 4	FC 4	FC 4	FC 4	11.9	FC 4	13.2	12.0	FC 4			
18972	13.4	MC 4	13.7	MC 4	15.7	15.5	15.7	12.0	FC 4	15.6	15.1	FC 4	FC 4	FC 4	14.3	12.8				
18976	12.9	13.5	12.2	MC 4	11.8	MC 4	13.4	MD 2	11.4	11.4	FC 4	FC 4	FC 4	FC 4	13.7	FC 4	13.1	12.8		
18977c	MD 3	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	FD 2	FD 2	FD 2	FD 2	FD 1								

ALL WEIGHTS WERE RECORDED IN GRAMS (G).
FIRST LETTER -- M-MALE, F-FEMALE
SECOND LETTER -- A-ALIVE, S-STILLBORN, D-DIED, C-CULLED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.
a. 1.6 mg/kg/day dosage group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
b. 1.6 mg/kg/day dosage group dams cross-fostered with vehicle control group litters.
c. Litters were not cross-fostered; values excluded from group averages.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 30 (PAGE 9): PUP BODY WEIGHTS FROM BIRTH TO DAY 21 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

RATS ASSIGNED TO CROSS-FOSTERING

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP I a						0 (VEHICLE) MG/KG/DAY					SUBSET A			POSTPARTUM DAY 14					
18903	MC 4	26.5	23.4	23.2	26.2	24.4	MM 3	24.8	FC 4	22.4	FC 4	24.9	20.3	23.8	FM 3					
18907	26.4	29.3	30.2	26.4	27.2	27.3	30.5	FC 4	26.4	25.8	25.7	FC 4	FD 4							
18908	25.8	27.2	27.5	MM 4	23.7	26.6	FC 4	25.3	FC 4	FC 4	28.0	FC 4	FC 4	26.1	25.4	28.1				
18909	27.8	28.2	MC 4	28.1	28.8	MC 4	27.8	MD 4	29.8	26.8	28.1	29.4	FC 4	FC 4	FC 4	25.1				
18918b	33.2	MC 4	33.9	31.0	MC 4	33.7	33.4	MM 2	MM 2	FC 4	32.3	30.3	FC 4	FC 4	30.6	28.7	31.0			
18920	26.1	MC 4	25.4	26.4	24.3	MC 4	22.7	MC 4	24.9	26.7	24.4	24.4	22.0	FM 3	FD 2					
18924	MC 4	23.5	27.2	25.5	MC 4	MC 4	25.9	MM 3	27.4	26.0	25.6	25.8	25.1	FC 4	23.9	FC 4	FD 4			
18929	MC 4	MC 4	33.0	29.8	29.4	31.9	26.8	MM 3	28.6	FC 4	FC 4	FC 4	27.3	26.3	29.4	27.8				
18934	28.7	24.4	MC 4	28.0	30.1	26.9	MC 4	FC 4	29.1	24.8	28.0	22.5	27.0	FD 2						
18936b	25.1	25.5	MC 4	24.8	25.8	24.5	24.8	21.7	22.5	24.0	23.7	FM 2								
18937	27.0	25.5	24.5	25.2	22.5	24.5	FC 4	23.5	27.1	25.6	25.4	FC 4	FC 4							
18941	30.8	31.3	28.2	27.1	23.7	MM 3	MM 3	MD 2	33.3	22.5	31.7	FM 5	FD 2							
18942	MC 4	26.4	29.3	MC 4	MC 4	MC 4	26.6	29.1	28.5	26.7	FC 4	FC 4	28.1	FC 4	28.8	31.0	FC 4	27.5		
RAT/ LITTER #	MATERNAL DOSAGE GROUP I c						0 (VEHICLE) MG/KG/DAY					SUBSET B			POSTPARTUM DAY 14					
18901	MC 4	35.0	29.9	31.2	30.5	31.7	28.9	27.8	31.0	FC 4	FC 4	FC 4	FC 4	FC 4	31.6	31.1				
18904	MC 4	MC 4	27.2	28.1	32.1	28.5	28.6	FC 4	FC 4	27.1	29.1	25.8	FC 4	24.9	25.7					
18906	MC 4	27.9	29.0	MC 4	MC 4	30.4	28.7	27.3	FC 4	FC 4	27.5	FC 4	28.3	28.7	29.5	27.5	FC 4	FC 4	FD 4	
18912	MC 4	25.8	MC 4	30.8	30.0	MC 4	30.3	MC 4	MC 4	31.9	MC 4	29.9	FC 4	29.9	FC 4	27.9	FC 4	26.6	23.0	FM 4
18917	29.5	29.7	MC 4	MC 4	28.2	26.7	30.3	MC 4	MC 4	29.6	FC 4	30.3	26.6	28.3	FC 4	27.3				
18919	MC 4	MC 4	28.6	31.3	30.2	33.3	31.3	30.6	30.6	30.6	28.9	28.8								
18922	32.4	29.3	31.4	29.9	30.9	FC 4	FC 4	FC 4	29.1	32.6	32.6	29.1	FC 4	FC 4	31.8					
18923	31.6	28.5	MC 4	30.1	31.0	31.2	FC 4	FC 4	25.7	28.7	FC 4	FC 4	30.5	28.7	26.8	FM 3				
18931	31.5	30.9	29.9	MC 4	29.4	MC 4	31.5	32.3	FC 4	29.5	FC 4	FC 4	FC 4	FC 4	30.5	31.8	28.5			
18932	27.1	MC 4	27.2	28.2	27.4	27.2	26.4	26.7	26.6	FC 4	27.7	FC 4	27.1	FC 4						
18935	27.4	26.8	MC 4	27.7	26.6	MC 4	22.4	25.6	FC 4	26.4	FC 4	FC 4	FC 4	26.1	26.7	24.5				
18938	28.2	30.1	29.5	MC 4	MC 4	27.9	MC 4	28.5	32.0	MC 4	29.1	27.9	MC 4	28.9	29.0					

ALL WEIGHTS WERE RECORDED IN GRAMS (G).
FIRST LETTER -- M-MALE, F-FEMALE
SECOND LETTER -- A-ALIVE, S-STILLBORN, D-DIED, C-CULLED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.
a. Vehicle control group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
b. Litters were not cross-fostered; values excluded from group averages.
c. Vehicle control group dams cross-fostered with vehicle control litters.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 30 (PAGE 10): PUP BODY WEIGHTS FROM BIRTH TO DAY 21 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

RATS ASSIGNED TO CROSS-FOSTERING

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP II a					1.6 MG/KG/DAY						SUBSET C			POSTPARTUM DAY 14					
18943	29.8	26.8	28.7	27.2	29.3	FC 4	FC 4	27.9	31.4	27.7	26.6	FC 4	FC 4	FC 4	27.1					
18947	25.5	25.5	MC 4	MC 4	MC 4	28.0	27.0	25.9	FC 4	23.4	25.9	22.3	25.5	23.8						
18948	23.4	26.3	27.5	24.0	26.6	14.2	MM 4	MM 3	MD 2	MD 2	MD 2	22.5	19.1	FD 3	FD 3	FM 3	FM 3			
18957	23.6	27.0	24.1	MM 3	FC 4	24.1	25.1	23.9	26.3	24.6	25.8	27.7	FM 3							
18960	25.2	22.1	21.4	MM 4	MM 4	24.1	19.1	19.2	21.2	22.1	16.4	FC 4	21.1	FM 4	FM 4					
18964	21.8	21.0	MC 4	MC 4	20.1	23.1	MM 3	20.9	FC 4	21.9	FC 4	22.9	20.7	23.8	22.3					
18967	30.1	29.9	MC 4	MC 4	29.8	MC 4	28.8	MC 4	28.8	28.8	FC 4	FC 4	25.7	23.3	21.6	24.9				
18968	30.4	MD 2	26.0	25.6	24.6	27.9	30.1	27.6	27.0	24.4										
18969	MC 4	26.4	MC 4	MC 4	MC 4	26.5	MC 4	27.6	MC 4	26.0	MC 4	28.3	24.3	25.6	27.9	24.9	25.3			
18970	MC 4	MC 4	25.5	26.1	MC 4	24.8	22.8	MC 4	26.2	24.4	24.0	22.1	15.1	14.3	FM 3					
18973	MC 4	26.3	MC 4	MC 4	22.4	23.9	MC 4	20.0	23.8	21.5	24.3	23.4	21.3	22.7	FD 2					
18974	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	FM 4	FM 3	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2					
RAT/ LITTER #	MATERNAL DOSAGE GROUP II b					1.6 MG/KG/DAY						SUBSET D			POSTPARTUM DAY 14					
18946c	35.4	25.2	MD 5	MD 4	MD 4	MM 3	MD 2	MD 2	MD 2	19.3	FM 3	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2			
18950	MC 4	MC 4	24.0	28.4	28.6	MC 4	25.0	28.4	FC 4	23.0	24.5	25.3	FC 4	25.9	FC 4	FC 4	28.3	FC 4		
18951	24.6	23.6	MC 4	MC 4	24.1	24.6	24.3	MC 4	20.6	21.6	FC 4	23.4	22.7	19.9						
18952	32.4	MC 4	28.7	31.5	29.8	MC 4	31.0	MC 4	FC 4	FC 4	28.0	FC 4	27.5	28.0	28.9	28.3	FC 4			
18953	25.9	22.0	MC 4	25.8	MC 4	25.5	27.6	MC 4	24.5	FC 4	25.5	24.5	FC 4	25.3	FC 4	24.3				
18958	26.3	21.5	24.2	25.1	MC 4	26.6	24.9	24.5	22.0	FC 4	24.0	FC 4	24.5	FC 4						
18959	MC 4	26.9	26.1	27.6	27.5	MC 4	27.3	MC 4	MC 4	26.7	FC 4	26.0	24.9	25.4	28.0	FM 3				
18961	26.4	26.9	26.8	25.6	25.6	FC 4	26.1	FC 4	FC 4	23.7	FC 4	FC 4	25.7	27.3	25.6	FC 4				
18963	MC 4	28.7	26.5	27.5	MC 4	24.8	MC 4	MC 4	26.7	MC 4	MC 4	27.1	FC 4	FC 4	24.8	25.7	26.1	25.7	FC 4	
18965	26.4	24.9	25.8	MC 4	25.3	25.5	24.7	24.3	FC 4	FC 4	FC 4	FC 4	24.7	FC 4	26.1	24.6	FC 4			
18972	29.2	MC 4	29.2	MC 4	33.8	33.7	31.2	30.7	FC 4	28.1	33.6	FC 4	FC 4	FC 4	30.6	26.4				
18976	27.2	25.8	24.7	MC 4	26.2	MC 4	27.0	MD 2	24.3	23.4	FC 4	FC 4	FC 4	FC 4	25.1	FC 4	26.6	24.7		
18977c	MD 3	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	FD 2	FD 2	FD 2	FD 2	FD 1								

ALL WEIGHTS WERE RECORDED IN GRAMS (G).
FIRST LETTER -- M-MALE, F-FEMALE
SECOND LETTER -- A-ALIVE, S-STILLBORN, D-DIED, C-CULLED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.
a. 1.6 mg/kg/day dosage group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
b. 1.6 mg/kg/day dosage group dams cross-fostered with vehicle control group litters.
c. Litters were not cross-fostered; values excluded from group averages.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 30 (PAGE 11): PUP BODY WEIGHTS FROM BIRTH TO DAY 21 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

RATS ASSIGNED TO CROSS-FOSTERING

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP I a						0 (VEHICLE) MG/KG/DAY					SUBSET A			POSTPARTUM DAY 21					
18903	MC 4	44.8	41.8	40.2	39.6	39.2	MM 3	37.3	FC 4	38.7	FC 4	40.1	39.5	35.5	FM 3					
18907	41.8	46.3	45.8	43.3	43.7	40.5	42.1	FC 4	46.1	42.1	42.3	FC 4	FD 4							
18908	40.9	42.9	42.4	MM 4	42.6	42.4	FC 4	36.6	FC 4	FC 4	39.3	FC 4	FC 4	37.3	39.9	41.3				
18909	43.2	43.9	MC 4	44.1	41.8	MC 4	40.6	MD 4	41.1	38.9	37.6	43.5	FC 4	FC 4	FC 4	41.2				
18918b	53.9	MC 4	57.2	53.2	MC 4	56.0	29.7	MM 2	MM 2	FC 4	49.3	51.5	FC 4	FC 4	47.5	51.2	50.2			
18920	43.5	MC 4	43.2	41.4	37.9	MC 4	40.8	MC 4	40.6	42.9	41.2	40.6	37.3	FM 3	FD 2					
18924	MC 4	42.6	39.8	40.4	MC 4	MC 4	39.2	MM 3	44.0	40.9	41.3	41.0	41.7	FC 4	39.6	FC 4	FD 4			
18929	MC 4	MC 4	49.2	47.3	42.7	46.7	50.1	MM 3	41.2	FC 4	FC 4	FC 4	45.2	42.2	43.2	47.0				
18934	43.5	41.5	MC 4	38.6	44.1	42.5	MC 4	FC 4	43.3	40.8	40.9	38.9	37.3	FD 2						
18936b	38.7	39.8	MC 4	39.5	40.4	41.6	39.2	35.6	35.1	39.2	36.4	FM 2								
18937	42.5	37.5	40.1	39.9	41.7	43.3	FC 4	41.1	40.2	39.3	41.1	FC 4	FC 4							
18941	41.7	40.3	45.4	47.6	47.3	MM 3	MM 3	MD 2	48.8	48.0	39.4	FM 5	FD 2							
18942	MC 4	43.0	42.9	MC 4	MC 4	MC 4	40.0	41.7	40.7	41.0	FC 4	FC 4	41.8	FC 4	44.5	39.2	FC 4	41.7		
RAT/ LITTER #	MATERNAL DOSAGE GROUP I c						0 (VEHICLE) MG/KG/DAY					SUBSET B			POSTPARTUM DAY 21					
18901	MC 4	50.2	49.9	48.9	54.6	46.6	44.2	47.5	42.5	FC 4	FC 4	FC 4	FC 4	FC 4	48.8	48.8				
18904	MC 4	MC 4	41.1	44.5	45.2	48.7	42.6	FC 4	FC 4	39.8	41.3	42.2	FC 4	43.9	40.2					
18906	MC 4	49.6	53.0	MC 4	MC 4	50.6	48.3	48.2	FC 4	FC 4	48.8	FC 4	49.8	47.3	46.8	46.8	FC 4	FC 4	FD 4	
18912	MC 4	48.7	MC 4	44.3	50.9	MC 4	48.4	MC 4	MC 4	50.9	MC 4	49.6	FC 4	47.1	FC 4	43.3	FC 4	44.6	38.8	FM 4
18917	42.3	43.4	MC 4	MC 4	47.2	47.3	46.4	MC 4	MC 4	45.7	FC 4	48.5	45.8	43.9	FC 4	44.6				
18919	MC 4	MC 4	47.2	45.4	51.8	51.1	49.5	49.4	50.0	49.1	46.7	43.9								
18922	49.2	48.2	51.1	49.7	45.3	FC 4	FC 4	FC 4	50.6	45.3	50.8	45.0	FC 4	FC 4	50.2					
18923	49.6	50.6	MC 4	50.3	50.2	51.4	FC 4	FC 4	44.7	49.3	FC 4	FC 4	44.9	46.2	45.5	FM 3				
18931	50.5	50.2	45.9	MC 4	49.5	MC 4	48.2	50.9	FC 4	46.9	FC 4	FC 4	FC 4	FC 4	48.4	44.0	48.5			
18932	43.4	MC 4	43.8	44.3	44.4	42.8	44.0	43.7	42.2	FC 4	44.2	FC 4	43.2	FC 4						
18935	44.2	42.2	MC 4	44.0	45.2	MC 4	36.1	41.1	FC 4	41.0	FC 4	FC 4	FC 4	42.9	39.9	42.8				
18938	45.4	44.8	43.2	MC 4	MC 4	43.5	MC 4	46.6	45.9	MC 4	43.0	43.3	MC 4	45.5	42.0					

ALL WEIGHTS WERE RECORDED IN GRAMS (G).
FIRST LETTER -- M-MALE, F-FEMALE
SECOND LETTER -- A-ALIVE, S-STILLBORN, D-DIED, C-CULLED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.
a. Vehicle control group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
b. Litters were not cross-fostered; values excluded from group averages.
c. Vehicle control group dams cross-fostered with vehicle control litters.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 30 (PAGE 12): PUP BODY WEIGHTS FROM BIRTH TO DAY 21 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

RATS ASSIGNED TO CROSS-FOSTERING

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP II a					1.6 MG/KG/DAY						SUBSET C			POSTPARTUM DAY 21					
18943	42.8	42.3	45.8	39.8	44.7	FC 4	FC 4	41.8	41.6	42.1	37.9	FC 4	FC 4	FC 4	46.4					
18947	45.4	41.5	MC 4	MC 4	MC 4	40.8	45.0	42.7	FC 4	41.9	38.3	36.1	40.4	41.7						
18948	40.7	36.5	37.9	40.7	39.5	25.8	MM 4	MM 3	MD 2	MD 2	MD 2	36.3	30.9	FD 3	FD 3	FM 3	FM 3			
18957	42.5	39.1	37.4	MM 3	FC 4	41.4	40.1	38.0	38.8	37.7	43.9	39.0	FM 3							
18960	34.1	39.5	34.1	MM 4	MM 4	33.4	35.6	36.9	27.0	33.2	30.4	FC 4	30.3	FM 4	FM 4					
18964	33.1	32.0	MC 4	MC 4	35.2	35.0	MM 3	34.3	FC 4	35.1	FC 4	33.7	35.7	35.6	34.8					
18967	45.8	46.5	MC 4	MC 4	47.9	MC 4	47.8	MC 4	47.7	40.7	FC 4	FC 4	39.3	39.2	45.1	41.1				
18968	50.7	MD 2	38.0	44.1	48.1	45.7	40.5	43.5	43.1	40.2										
18969	MC 4	40.9	MC 4	MC 4	MC 4	39.2	MC 4	42.4	MC 4	40.0	MC 4	40.2	37.6	37.2	40.2	38.0	38.1			
18970	MC 4	MC 4	39.8	41.4	MC 4	40.6	37.0	MC 4	40.7	37.0	27.0	37.5	36.1	27.2	FM 3					
18973	MC 4	37.2	MC 4	MC 4	42.2	33.1	MC 4	34.1	37.4	35.3	38.0	37.8	37.4	33.2	FD 2					
18974	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	FM 4	FM 3	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2					
RAT/ LITTER #	MATERNAL DOSAGE GROUP II b					1.6 MG/KG/DAY						SUBSET D			POSTPARTUM DAY 21					
18946c	55.0	42.5	MD 5	MD 4	MD 4	MM 3	MD 2	MD 2	MD 2	36.3	FM 3	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2			
18950	MC 4	MC 4	47.3	42.8	39.9	MC 4	47.7	44.6	FC 4	40.3	37.7	37.0	FC 4	44.1	FC 4	FC 4	39.6	FC 4		
18951	39.7	40.3	MC 4	MC 4	38.9	40.4	37.9	MC 4	34.5	38.5	FC 4	36.3	38.7	34.6						
18952	49.8	MC 4	48.7	46.7	44.3	MC 4	46.1	MC 4	FC 4	FC 4	43.6	FC 4	43.1	44.3	41.6	44.4	FC 4			
18953	44.8	37.3	MC 4	41.0	MC 4	44.0	40.9	MC 4	40.4	FC 4	42.9	38.6	FC 4	39.0	FC 4	40.7				
18958	42.8	41.4	42.1	34.2	MC 4	40.6	41.5	39.0	39.9	FC 4	40.5	FC 4	36.4	FC 4						
18959	MC 4	42.6	42.6	43.6	43.1	MC 4	42.3	MC 4	MC 4	39.8	FC 4	40.5	45.6	43.7	40.9	FM 3				
18961	42.4	40.8	42.5	42.4	41.9	FC 4	41.0	FC 4	FC 4	42.6	FC 4	FC 4	39.8	36.8	40.5	FC 4				
18963	MC 4	42.8	46.2	43.0	MC 4	41.6	MC 4	MC 4	42.4	MC 4	MC 4	40.7	FC 4	FC 4	42.8	41.7	41.9	41.5	FC 4	
18965	45.5	44.1	43.0	MC 4	43.6	43.6	43.6	41.2	FC 4	FC 4	FC 4	FC 4	42.7	FC 4	43.0	41.0	FC 4			
18972	43.6	MC 4	49.7	MC 4	42.0	46.8	48.5	43.4	FC 4	44.5	47.0	FC 4	FC 4	FC 4	42.7	40.7				
18976	40.3	42.4	42.5	MC 4	40.7	MC 4	42.6	MD 2	39.0	42.3	FC 4	FC 4	FC 4	FC 4	39.9	FC 4	39.0	37.7		
18977c	MD 3	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	FD 2	FD 2	FD 2	FD 2	FD 1								

ALL WEIGHTS WERE RECORDED IN GRAMS (G).
FIRST LETTER -- M-MALE, F-FEMALE
SECOND LETTER -- A-ALIVE, S-STILLBORN, D-DIED, C-CULLED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.
a. 1.6 mg/kg/day dosage group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
b. 1.6 mg/kg/day dosage group dams cross-fostered with vehicle control group litters.
c. Litters were not cross-fostered; values excluded from group averages.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 30 (PAGE 13): PUP BODY WEIGHTS FROM BIRTH TO DAY 21 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

RATS ASSIGNED TO PHARAMACOKINETIC EVALUATION

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP I							0 (VEHICLE) MG/KG/DAY							POSTPARTUM DAY 1					
18910	7.3	7.4	7.6	7.2	7.0															
18911	6.6	5.9	7.1	7.0	7.0	6.2	7.5	6.3	6.8	6.4	6.3	6.8	6.2	6.4	6.3	6.6				
18913	6.2	6.8	6.8	6.5	5.3	6.9	6.4	6.2	6.1	5.9	5.9	5.6	6.3	5.9	7.0	6.0	6.0	5.4		
18915	6.3	6.3	6.8	6.0	5.9	6.1	6.1	5.5	6.5	5.5	6.2	6.5	6.0	6.3	6.4	FS	FS			
18926	7.2	7.2	7.4	7.4	6.2	6.7	7.2	6.7	6.7	7.2	7.4	6.5								
18927	6.5	6.1	7.1	6.8	6.8	6.1	7.2	6.4	6.8	5.1	6.3	6.4	5.8	6.2	6.2	5.5	6.5			
18939	6.0	6.4	6.3	6.0	6.6	6.8	6.6	5.9	5.9	5.7	6.0	5.9	6.4	5.8	6.1					
18940	6.9	6.2	6.5	6.3	6.2	6.2	6.5	6.1	5.5	5.8	6.0	5.8	5.6	6.1	6.2	5.4				
RAT/ LITTER #	MATERNAL DOSAGE GROUP II							1.6 MG/KG/DAY							POSTPARTUM DAY 1					
18956	6.7	6.4	6.2	6.3	6.6	MS	6.1	6.0	6.9	6.3	6.7	4.3	6.1							
18971	MS	7.6	FS																	

ALL WEIGHTS WERE RECORDED IN GRAMS (G).
FIRST LETTER -- M-MALE, F-FEMALE
SECOND LETTER -- A-ALIVE, S-STILLBORN, D-DIED, C-CULLED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 30 (PAGE 14): PUP BODY WEIGHTS FROM BIRTH TO DAY 21 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

RATS ASSIGNED TO PHARAMACOKINETIC EVALUATION

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP I						0 (VEHICLE) MG/KG/DAY								POSTPARTUM DAY 4					
18910	NO PUP WEIGHTS RECORDED																			
18911	8.4	9.5	9.5	9.1	10.3	7.9	7.4	7.9	9.5	9.3	9.5	8.8	8.6	8.7	8.8	7.2				
18913	9.9	7.4	8.7	7.6	7.9	6.5	6.7	7.2	8.2	8.6	8.2	7.2	8.6	8.8	8.8	MD 4	7.6	7.6		
18915	NO PUP WEIGHTS RECORDED																			
18926	10.6	11.6	15.7	13.0	11.4	9.3	11.9	12.9	13.9	11.4	11.5	12.6								
18927	8.4	8.8	8.6	9.1	8.8	9.3	8.3	9.2	8.7	7.5	8.2	7.0	9.0	8.0	7.6	9.3	FM 4			
18939	NO PUP WEIGHTS RECORDED																			
18940	9.5	8.5	9.2	7.1	8.5	8.2	8.5	8.2	9.1	7.8	7.4	8.9	8.7	8.5	7.0	9.3				
RAT/ LITTER #	MATERNAL DOSAGE GROUP II						1.6 MG/KG/DAY								POSTPARTUM DAY 4					
18956	8.8	9.3	9.2	9.6	9.6	MS	9.1	8.9	9.2	6.7	8.9	9.6	9.4							
18971	MS	9.1	FS																	

ALL WEIGHTS WERE RECORDED IN GRAMS (G).
FIRST LETTER -- M-MALE, F-FEMALE
SECOND LETTER -- A-ALIVE, S-STILLBORN, D-DIED, C-CULLED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 30 (PAGE 15): PUP BODY WEIGHTS FROM BIRTH TO DAY 21 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

RATS ASSIGNED TO PHARAMACOKINETIC EVALUATION

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP I						0 (VEHICLE) MG/KG/DAY								POSTPARTUM DAY 7					
18910	18.8	16.5	17.1	16.0	16.9															
18911	13.2	12.0	13.7	9.9	11.2	9.9	11.7	13.7	12.7	13.8	14.5	13.0	12.7	12.0	12.3	FM 7				
18913	14.1	12.6	9.7	10.0	9.3	11.1	9.8	11.7	12.1	11.5	13.2	9.7	10.4	7.3	MD 6	MD 4	10.2	11.1		
18915	13.6	12.4	11.3	13.3	12.4	13.5	10.6	9.2	14.2	14.9	13.1	14.1	13.4	14.5	12.6	FS	FS			
18926	16.4	15.9	16.1	16.6	15.4	14.9	15.4	14.8	15.9	16.2	15.1	16.5								
18927	12.3	12.0	12.2	12.7	11.7	12.9	11.9	12.4	10.7	10.8	12.4	9.4	10.2	11.0	12.4	9.1	FM 4			
18939	12.2	13.5	14.1	12.9	13.2	12.7	12.0	12.4	11.9	12.9	13.3	12.2	13.1	13.3	11.1					
18940	10.3	12.2	11.8	11.1	8.5	12.1	10.8	10.0	10.3	11.0	12.0	10.3	11.6	12.0	10.8	7.9				
RAT/ LITTER #	MATERNAL DOSAGE GROUP II						1.6 MG/KG/DAY								POSTPARTUM DAY 7					
18956	13.4	13.2	13.0	13.2	12.7	MS	12.9	12.4	12.4	13.3	12.1	11.8	9.7							
18971	MS	9.2	FS																	

ALL WEIGHTS WERE RECORDED IN GRAMS (G).
FIRST LETTER -- M-MALE, F-FEMALE
SECOND LETTER -- A-ALIVE, S-STILLBORN, D-DIED, C-CULLED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 30 (PAGE 16): PUP BODY WEIGHTS FROM BIRTH TO DAY 21 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

RATS ASSIGNED TO PHARAMACOKINETIC EVALUATION

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAT/ LITTER #	MATERNAL DOSAGE GROUP I							0 (VEHICLE) MG/KG/DAY							POSTPARTUM DAY 14					
18910	35.7	32.7	32.9	33.7	30.5															
18911	26.7	25.3	24.0	22.1	17.8	23.0	26.8	19.2	24.2	25.3	26.4	22.7	25.0	25.2	23.4	FM 7				
18913	19.8	24.2	21.9	20.5	20.2	19.9	23.3	23.0	25.1	20.8	24.1	20.4	18.7	14.9	MD 6	MD 4	21.7	17.6		
18915	24.6	23.5	25.2	24.6	25.9	24.8	20.5	27.8	26.9	20.7	27.8	25.2	25.3	27.8	25.2	FS	FS			
18926	29.7	31.3	31.3	29.4	28.8	29.5	29.9	29.2	27.8	32.0	30.0	27.8								
18927	22.6	23.2	23.8	21.7	22.5	20.8	23.7	21.3	21.2	22.6	20.6	19.5	22.7	18.0	20.0	FM10	FM 4			
18939	24.9	23.1	23.7	21.6	26.0	23.2	23.1	22.1	25.0	24.1	23.0	21.4	24.8	21.5	18.8					
18940	18.3	16.0	22.3	24.5	16.6	20.2	17.4	18.9	23.7	20.3	13.1	20.6	20.0	19.2	19.0	20.9				
RAT/ LITTER #	MATERNAL DOSAGE GROUP II							1.6 MG/KG/DAY							POSTPARTUM DAY 14					
18956	24.1	23.7	24.4	24.1	24.9	MS	23.7	22.9	24.9	23.7	24.3	23.6	20.7							
18971	MS	11.7	FS																	

ALL WEIGHTS WERE RECORDED IN GRAMS (G).
FIRST LETTER -- M-MALE, F-FEMALE
SECOND LETTER -- A-ALIVE, S-STILLBORN, D-DIED, C-CULLED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 31 (PAGE 1): PUP VITAL STATUS AND SEX FROM BIRTH TO DAY 21 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

RATS ASSIGNED TO CROSS-FOSTERING

PUP #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
RAT/ LITTER #	MATERNAL DOSAGE GROUP I a										0 (VEHICLE) MG/KG/DAY										SUBSET A		
18903	MC 4	M A	M A	M A	M A	M A	MM 3	F A	FC 4	F A	FC 4	F A	F A	F A	FM 3								
18907	M A	M A	M A	M A	M A	F A	F A	FC 4	F A	F A	F A	FC 4	FD 4										
18908	M A	M A	M A	MM 4	F A	F A	FC 4	F A	FC 4	FC 4	F A	FC 4	FC 4	F A	F A	F A							
18909	M A	M A	MC 4	M A	M A	MC 4	M A	MD 4	F A	F A	F A	F A	FC 4	FC 4	FC 4	F A							
18918b	M A	MC 4	M A	M A	MC 4	M A	M A	MM 2	MM 2	FC 4	F A	F A	FC 4	FC 4	F A	F A	F A						
18920	M A	MC 4	M A	M A	M A	MC 4	M A	MC 4	F A	F A	F A	F A	F A	FM 3	FD 2								
18924	MC 4	M A	M A	M A	MC 4	MC 4	M A	MM 3	M A	F A	F A	F A	F A	FC 4	F A	FC 4	FD 4						
18929	MC 4	MC 4	M A	M A	M A	M A	M A	MM 3	F A	FC 4	FC 4	FC 4	F A	F A	F A	F A							
18934	M A	M A	MC 4	M A	M A	M A	MC 4	FC 4	F A	F A	F A	F A	F A	FD 2									
18936b	M A	M A	MC 4	M A	M A	M A	M A	F A	F A	F A	F A	FM 2											
18937	M A	M A	M A	M A	M A	F A	FC 4	F A	F A	F A	F A	FC 4	FC 4										
18941	M A	M A	M A	M A	M A	MM 3	MM 3	MD 2	F A	F A	F A	FM 5	FD 2										
18942	MC 4	M A	M A	MC 4	MC 4	MC 4	M A	M A	M A	F A	FC 4	FC 4	F A	FC 4	F A	F A	FC 4	F A					
RAT/ LITTER #	MATERNAL DOSAGE GROUP I c										0 (VEHICLE) MG/KG/DAY										SUBSET B		
18901	MC 4	M A	M A	M A	M A	M A	F A	F A	F A	FC 4	FC 4	FC 4	FC 4	FC 4	F A	F A							
18904	MC 4	MC 4	M A	M A	M A	M A	M A	FC 4	FC 4	F A	F A	F A	FC 4	F A	F A								
18906	MC 4	M A	M A	MC 4	MC 4	M A	M A	M A	FC 4	FC 4	F A	FC 4	F A	F A	F A	F A	FC 4	FC 4	FD 4				
18912	MC 4	M A	MC 4	M A	M A	MC 4	M A	MC 4	MC 4	M A	MC 4	F A	FC 4	F A	FC 4	F A	F A	FM 4					
18917	M A	M A	MC 4	MC 4	M A	M A	M A	MC 4	MC 4	F A	FC 4	F A	F A	F A	FC 4	F A							
18919	MC 4	MC 4	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A											
18922	M A	M A	M A	M A	M A	FC 4	FC 4	FC 4	F A	F A	F A	F A	FC 4	FC 4	F A								
18923	M A	M A	MC 4	M A	M A	M A	FC 4	FC 4	F A	F A	FC 4	FC 4	F A	F A	F A	FM 3							
18931	M A	M A	M A	MC 4	M A	MC 4	M A	F A	FC 4	F A	FC 4	FC 4	FC 4	FC 4	F A	F A	F A						
18932	M A	MC 4	M A	M A	M A	M A	F A	F A	F A	FC 4	F A	FC 4	F A	FC 4									
18935	M A	M A	MC 4	M A	M A	MC 4	M A	F A	FC 4	F A	FC 4	FC 4	F A	F A	F A								
18938	M A	M A	M A	MC 4	MC 4	M A	MC 4	M A	M A	MC 4	M A	M A	MC 4	F A	F A								

FIRST LETTER -- M-MALE, F-FEMALE
SECOND LETTER -- A-ALIVE, S-STILLBORN, D-DIED, C-CULLED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.
a. Vehicle control group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
b. Litters were not cross-fostered; values excluded from group averages.
c. Vehicle control group dams cross-fostered with vehicle control litters.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 31 (PAGE 2): PUP VITAL STATUS AND SEX FROM BIRTH TO DAY 21 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

RATS ASSIGNED TO CROSS-FOSTERING

RAT/ LITTER #	PUP # 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
MATERNAL DOSAGE GROUP II a																							
18943	M A	M A	M A	M A	M A	FC 4	FC 4	F A	F A	F A	F A	FC 4	FC 4	FC 4	F A								
18947	M A	M A	MC 4	MC 4	MC 4	M A	M A	M A	M A	FC 4	F A	F A	F A	F A	F A								
18948	M A	M A	M A	M A	M A	M A	M A	MM 4	MM 3	MD 2	MD 2	MD 2	F A	F A	FD 3	FD 3	FM 3	FM 3					
18957	M A	M A	M A	MM 3	FC 4	F A	F A	F A	F A	F A	F A	F A	F A	FM 3									
18960	M A	M A	M A	MM 4	MM 4	F A	F A	F A	F A	F A	F A	F A	FC 4	F A	FM 4	FM 4							
18964	M A	M A	MC 4	MC 4	M A	M A	MM 3	M A	FC 4	F A	FC 4	F A	F A	F A	F A								
18967	M A	M A	MC 4	MC 4	M A	MC 4	M A	MC 4	M A	F A	FC 4	FC 4	F A	F A	F A	F A							
18968	M A	MD 2	F A	F A	F A	F A	F A	F A	F A	F A													
18969	MC 4	M A	MC 4	MC 4	MC 4	M A	MC 4	M A	MC 4	M A	MC 4	M A	F A	F A	F A	F A	F A	F A					
18970	MC 4	MC 4	M A	M A	MC 4	M A	M A	MC 4	M A	F A	F A	F A	F A	F A	FM 3								
18973	MC 4	M A	MC 4	MC 4	M A	M A	MC 4	M A	M A	M A	F A	F A	F A	F A	FD 2								
18974	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	FM 4	FM 3	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2								
DOSAGE GROUP II b																							
18946c	M A	M A	MD 5	MD 4	MD 4	MM 3	MD 2	MD 2	MD 2	F A	FM 3	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2						
18950	MC 4	MC 4	M A	M A	M A	MC 4	M A	M A	FC 4	F A	F A	F A	FC 4	F A	FC 4	FC 4	F A	FC 4					
18951	M A	M A	MC 4	MC 4	M A	M A	M A	MC 4	F A	F A	FC 4	F A	F A	F A									
18952	M A	MC 4	M A	M A	M A	MC 4	M A	MC 4	FC 4	FC 4	F A	FC 4	F A	F A	F A	F A	FC 4						
18953	M A	M A	MC 4	M A	MC 4	M A	M A	MC 4	F A	FC 4	F A	F A	FC 4	F A	FC 4	F A							
18958	M A	M A	M A	M A	MC 4	M A	F A	F A	F A	FC 4	F A	FC 4	F A	FC 4									
18959	MC 4	M A	M A	M A	M A	MC 4	M A	MC 4	MC 4	F A	FC 4	F A	F A	F A	F A	FM 3							
18961	M A	M A	M A	M A	M A	FC 4	F A	FC 4	FC 4	F A	FC 4	FC 4	F A	F A	F A	FC 4							
18963	MC 4	M A	M A	M A	MC 4	M A	MC 4	MC 4	M A	MC 4	MC 4	F A	FC 4	FC 4	F A	F A	F A	F A	FC 4				
18965	M A	M A	M A	MC 4	M A	M A	F A	F A	FC 4	FC 4	FC 4	FC 4	F A	FC 4	F A	F A	FC 4						
18972	M A	MC 4	M A	MC 4	M A	M A	M A	F A	FC 4	F A	F A	FC 4	FC 4	FC 4	F A	F A							
18976	M A	M A	M A	MC 4	M A	MC 4	M A	MD 2	F A	F A	FC 4	FC 4	FC 4	FC 4	F A	FC 4	F A	F A					
18977c	MD 3	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	FD 2	FD 2	FD 2	FD 2	FD 1											

FIRST LETTER -- M-MALE, F-FEMALE
SECOND LETTER -- A-ALIVE, S-STILLBORN, D-DIED, C-CULLED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.
a. 1.6 mg/kg/day dosage group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
b. 1.6 mg/kg/day dosage group dams cross-fostered with vehicle control group litters.
c. Litters were not cross-fostered; values excluded from group averages.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 31 (PAGE 3): PUP VITAL STATUS AND SEX FROM BIRTH TO DAY 21 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

RATS ASSIGNED TO PHARMACOKINETIC EVALUATION

RAT/ LITTER #	PUP # 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
MATERNAL DOSAGE GROUP I																				0 (VEHICLE) MG/KG/DAY			
18910	MA	MA	MA	FA	FA																		
18911	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	FA	FA	FA	FA	FM 7							
18913	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MD 6	MD 4	FA	FA				
18915	MA	MA	MA	MA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FA	FS	FS					
18926	MA	MA	MA	MA	MA	MA	FA	FA	FA	FA	FA	FA	FA										
18927	MA	MA	MA	MA	MA	MA	MA	MA	MA	FA	FA	FA	FA	FA	FA	FA	FM10	FM 4					
18939	MA	MA	MA	MA	MA	MA	MA	MA	FA	FA	FA	FA	FA	FA	FA	FA							
18940	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	MA	FA	FA	FA	FA	FA	FA						
MATERNAL DOSAGE GROUP II																				1.6 MG/KG/DAY			
18956	MA	MA	MA	MA	MA	MS	FA	FA	FA	FA	FA	FA	FA										
18971	MS	FA	FS																				

FIRST LETTER -- M-MALE, F-FEMALE
SECOND LETTER -- A-ALIVE, S-STILLBORN, D-DIED, C-CULLED, M-MISSING (PRESUMED CANNIBALIZED)
NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 32 (PAGE 1): CLINICAL OBSERVATIONS FROM BIRTH TO DAY 21 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

RATS ASSIGNED TO CROSS-FOSTERING

SUBSET MATERNAL DOSAGE GROUP MATERNAL DOSAGE (MG/KG/DAY)	FOSTER LITTER #	DAY(S) POSTPARTUM	OBSERVATIONS a
A I b 0 (VEHICLE)	18920	3	1/14 PUPS: NOT NURSING.
	18941	4	1/9 PUPS: NOT NURSING.
B I c 0 (VEHICLE)	18932	7-10	1/10 PUPS: TIP OF TAIL, BLACK.
		11-21	1/10 PUPS: TIP OF TAIL, BLACK. TAIL, BENT (DID NOT EXCEED 2.5 CM FROM BASE OF TAIL).d
C II e 1.6	18968	1- 2	1/10 PUPS: RIGHT HINDPAW, SECOND DIGIT MISSING.
		3-21	1/9 PUPS: RIGHT HINDPAW, SECOND DIGIT MISSING.d
	18974	2	2/2 PUPS: NOT NURSING.
D II f 1.6	18950	7-15	2/10 PUPS: TIP OF TAIL, BLACK.
	18953	1	1/16 PUPS: LABORED BREATHING. DARK IN COLOR.

a. Tabulation restricted to adverse observations; all other pups appeared normal.
b. Vehicle control group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
c. Vehicle control group dams cross-fostered with vehicle control group litters.
d. Observation confirmed at necropsy.
e. 1.6 mg/kg/day dosage group dams cross-fostered with 1.6 mg/kg/day dosage group litters.
f. 1.6 mg/kg/day dosage group dams cross-fostered with vehicle control group litters.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 32 (PAGE 2): CLINICAL OBSERVATIONS FROM BIRTH TO DAY 21 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

RATS ASSIGNED TO PHARMACOKINETIC EVALUATION

MATERNAL DOSAGE GROUP MATERNAL DOSAGE (MG/KG/DAY)	LITTER NUMBER	DAY(S) POSTPARTUM	OBSERVATIONS a
I 0 (VEHICLE)	18911	14	1/15 PUPS: MOUTH, MASS (0.2 CM X 0.2 CM X 0.2 CM).
	18913	6	1/17 PUPS: NOT NURSING.

a. Tabulation restricted to adverse observations; all other pups appeared normal.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 33 (PAGE 1): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

PUPS DYING PRIOR TO CROSS-FOSTERING

MATERNAL DOSAGE GROUP MATERNAL DOSAGE (MG/KG/DAY)	LITTER NUMBER	DAY(S) POSTPARTUM	OBSERVATIONS a
I 0 (VEHICLE)	18904	1	3 PUPS: STILLBORN.
	18912	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL.
	18923	1	1 PUP: FOUND DEAD.
	18937	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL.
II 1.6	18952	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL.
	18973	1	1 PUP: FOUND DEAD. NO MILK IN STOMACH. BACK: RAISED AREA (2.0 CM X 1.3 CM X 0.3 CM), CONTAINED GAS.

a. Complete necropsies were not performed on pups in which autolysis or cannibalization precluded evaluation. Refer to the individual pup clinical observations table (Table 32) for external observations confirmed at necropsy.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 33 (PAGE 2): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

RATS ASSIGNED TO CROSS-FOSTERING

SUBSET MATERNAL DOSAGE GROUP MATERNAL DOSAGE (MG/KG/DAY)	FOSTER LITTER #	DAY(S) POSTPARTUM	OBSERVATIONS a
A I b 0 (VEHICLE)	18903	4,21	ALL PUPS APPEARED NORMAL.
	18907	4	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		21	ALL PUPS APPEARED NORMAL.
	18908	4	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
	18909	4	ALL PUPS APPEARED NORMAL.
	18918	21	ALL PUPS APPEARED NORMAL.
	18920	2	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		4	ALL PUPS APPEARED NORMAL.
	18924	4	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		21	ALL PUPS APPEARED NORMAL.
	18934	2	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		21	ALL PUPS APPEARED NORMAL.
	18936	21	ALL PUPS APPEARED NORMAL.
	18941	2	2 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
	18942	4	ALL PUPS APPEARED NORMAL.

a. Complete necropsies were not performed on pups in which autolysis or cannibalization precluded evaluation. Refer to the individual pup clinical observations table (Table 32) for external observations confirmed at necropsy.
b. Vehicle control group dams cross-fostered 1.6 mg/kg/day dosage group litters.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 33 (PAGE 3): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

RATS ASSIGNED TO CROSS-FOSTERING

SUBSET MATERNAL DOSAGE GROUP MATERNAL DOSAGE (MG/KG/DAY)	FOSTER LITTER #	DAY(S) POSTPARTUM	OBSERVATIONS a
B I b 0 (VEHICLE)	18901	4,21	ALL PUPS APPEARED NORMAL.
	18904	4	ALL PUPS APPEARED NORMAL.
	18906	4	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
	18917	21	ALL PUPS APPEARED NORMAL.
	18922	21	ALL PUPS APPEARED NORMAL.
	18923	21	ALL PUPS APPEARED NORMAL.
	18931	21	ALL PUPS APPEARED NORMAL.
	18932	4	ALL PUPS APPEARED NORMAL.
	18935	21	ALL PUPS APPEARED NORMAL.

a. Complete necropsies were not performed on pups in which autolysis or cannibalization precluded evaluation. Refer to the individual pup clinical observations table (Table 32) for external observations confirmed at necropsy.
b. Vehicle control group dams cross-fostered vehicle control group litters.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 33 (PAGE 4): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

RATS ASSIGNED TO CROSS-FOSTERING

SUBSET MATERNAL DOSAGE GROUP MATERNAL DOSAGE (MG/KG/DAY)	FOSTER LITTER #	DAY(S) POSTPARTUM	OBSERVATIONS a
C II b 1.6	18943	21	ALL PUPS APPEARED NORMAL.
	18947	4	ALL PUPS APPEARED NORMAL.
	18948	2	3 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		3	2 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
	19857	4,21	ALL PUPS APPEARED NORMAL.
	19860	21	ALL PUPS APPEARED NORMAL.
	19864	4,21	ALL PUPS APPEARED NORMAL.
	19868	2	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
	19870	21	ALL PUPS APPEARED NORMAL.
	18973	2	1 PUP: FOUND DEAD. NO MILK IN STOMACH.
		4,21	ALL PUPS APPEARED NORMAL.
	18974	2	13 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.

a. Complete necropsies were not performed on pups in which autolysis or cannibalization precluded evaluation. Refer to the individual pup clinical observations table (Table 32) for external observations confirmed at necropsy.
b. 1.6 mg/kg/day dosage group dams cross-fostered with 1.6 mg/kg/day dosage group litters.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 33 (PAGE 5): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

RATS ASSIGNED TO CROSS-FOSTERING

SUBSET MATERNAL DOSAGE GROUP MATERNAL DOSAGE (MG/KG/DAY)	FOSTER LITTER #	DAY(S) POSTPARTUM	OBSERVATIONS a
D II b 1.6	18946	2	2 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
			7 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		5	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
	18951	21	ALL PUPS APPEARED NORMAL.
	18952	21	ALL PUPS APPEARED NORMAL.
	18953	4,21	ALL PUPS APPEARED NORMAL.
	18958	4,21	ALL PUPS APPEARED NORMAL.
	18961	4,21	ALL PUPS APPEARED NORMAL.
	18963	4	ALL PUPS APPEARED NORMAL.
	18965	4	ALL PUPS APPEARED NORMAL.
	18972	21	ALL PUPS APPEARED NORMAL.
	18976	2	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
	18977	2	11 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		3	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.

a. Complete necropsies were not performed on pups in which autolysis or cannibalization precluded evaluation. Refer to the individual pup clinical observations table (Table 32) for external observations confirmed at necropsy.
b. 1.6 mg/kg/day dosage group dams cross-fostered with vehicle control group litters.

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS (SPONSOR'S STUDY NUMBER: T-6295.13)

TABLE 33 (PAGE 6): NECROPSY OBSERVATIONS INDIVIDUAL DATA - F1 GENERATION PUPS

RATS ASSIGNED TO PHARMACOKINETIC EVALUATION

MATERNAL DOSAGE GROUP MATERNAL DOSAGE (MG/KG/DAY)	LITTER NUMBER	DAY(S) POSTPARTUM	OBSERVATIONS a
I			
0 (VEHICLE)	18910	14	ALL PUPS APPEARED NORMAL.
	18911	14	ALL PUPS APPEARED NORMAL.
	18913	4	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		14	ALL PUPS APPEARED NORMAL.
	18915	1	2 PUPS: STILLBORN.
		14	ALL PUPS APPEARED NORMAL.
	18926	14	ALL PUPS APPEARED NORMAL.
	18927	14	ALL PUPS APPEARED NORMAL.
	18939	14	ALL PUPS APPEARED NORMAL.
	18940	14	ALL PUPS APPEARED NORMAL.
II			
1.6	18956	14	ALL PUPS APPEARED NORMAL.
	18971	14	ALL PUPS APPEARED NORMAL.

a. Complete necropsies were not performed on pups in which autolysis or cannibalization precluded evaluation. Refer to the individual pup clinical observations table (Table 32) for external observations confirmed at necropsy.

APPENDIX C

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 418-014

SPONSOR'S STUDY NUMBER: T-6295.13

STUDY TITLE: Oral (Gavage) Cross-Fostering Study of PFOS in Rats

PURPOSE: The purpose of this study is to evaluate pup survival of F1 rats following PFOS treatment of Crl:CD®BR VAF/Plus® female rats during premating, gestation and lactation. F1 pups will be cross-fostered during the lactation period to differentiate via maternal milk the differences for *in utero* exposure and exposure through maternal milk. Selected pharmacokinetic samples will be collected from Fo generation females and F1 generation pups.

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

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

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

STUDY MONITOR: Marvin T. Case, D.V.M., Ph.D.
Telephone: (651) 733-5180
Telefax: (651) 733-1773

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

REGULATORY CITATIONS:

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

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

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

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

REGULATORY COMPLIANCE:

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

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

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

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

SCHEMATIC OF STUDY DESIGN AND STUDY SCHEDULE:

See ATTACHMENT 1 to the protocol.

TEST ARTICLE AND VEHICLE:

Identification:

Test Article:

Name:	PFOS (Synonym: FC-95).
Physical Description:	Light-colored powder.
Lot/Batch Number:	217.
Specific Gravity:	~0.6.
Purity:	98.9%.
Expiration Date:	May 2000.

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

Vehicle:

0.5% Tween® 80 in Reverse Osmosis Membrane Processed Deionized Water (R.O. Deionized Water). Supplier and lot identification of Tween® 80 to be documented in the raw data.

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

Safety Precautions:

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

Storage:

Bulk Test Article:	Room temperature.
Vehicle Components:	Room temperature.
Prepared Vehicle:	Room temperature.
Prepared Formulations:	Room temperature.

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

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

FORMULATION:

Frequency of Preparation:

Formulations (suspensions) will be prepared daily at the Testing Facility. Data verifying the stability of the test article in the vehicle for 48 hours under the conditions of administration are on file with the Sponsor.

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

Adjustment for Purity:

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

Testing Facility Reserve Samples:

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

ANALYSES:

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

Bulk Test Article Sampling:

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

Analyses of Prepared Formulations:

Homogeneity and stability of prepared formulations is on file with the Sponsor. However, records will be maintained to document how the test article formulations were prepared.

Concentration of Test Article Formulations:

Concentration of the prepared formulations will be verified during the course of this study. Duplicate samples (2 mL each) will be taken from the first and last preparation on the day prepared. One sample of each set will be shipped for analysis; the remaining samples will be retained at the Testing Facility as backup samples. Backup samples will be stored frozen (-70°C or below) and discarded at the Testing Facility upon request of the Sponsor.

Shipping Instructions:

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

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

The recipient will be notified in advance of sample shipment.

DISPOSITION:

Prepared formulations will be discarded at the Testing Facility. All remaining bulk test article will be returned to the Study Monitor at the previously cited address upon completion of all work with the test article.

TEST SYSTEM:

Species/Strain and Reason for Selection:

The Crl:CD®BR VAF/Plus® (Sprague-Dawley) rat was selected as the Test System because: 1) this strain of rat was used in the reproductive and developmental toxicity studies; 2) historical data and experience exist at the Testing Facility[1-3]; and 3) the test article is pharmacologically active in the species and strain.

Number:

Initial population acclimated:	86 virgin female rats.
Population selected for study:	54 mated female rats (30 in the control group and 24 in the treated group).
Population selected for pharmacokinetic sample collection (day 14 postpartum):	12 mated female rats (six per dosage group).

Body Weight and Age:

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

Sex:

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

Source:

Charles River Laboratories, Inc.

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

Identification:

Fo Generation:

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.

F1 Generation:

Pups will not be individually identified during lactation; all parameters will be evaluated in terms of the litter.

ANIMAL HUSBANDRY:

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

Housing:

Fo Generation Rats/F1 Generation Litters:

Fo generation rats will be individually housed in stainless steel, wire-bottomed cages, except during the cohabitation and postpartum periods. During cohabitation, each pair of rats will be housed in the male rat's cage. Beginning no later than day 20 of presumed gestation, Fo generation female rats will be individually housed in nesting boxes, except during collection intervals for urine and fecal samples. During these collection intervals, the female rats will be housed individually in metabolism cages. Each dam and assigned litter will be housed in a common nesting box during the postpartum period.

Nesting Material:

Bedding material (bed-o'cobs®) will be provided.

Bedding will be changed as often as necessary to keep the animals dry and clean. Analyses for possible contamination are conducted annually and documented in the raw data.

Room Air, Temperature and Humidity:

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

Light:

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

Diet:

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

Water:

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

Contaminants:

Neither the Sponsor nor the Study Director is aware of any potential contaminants likely to be present in the certified diet, the drinking water or the nesting material 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, COHABITATION AND CROSS-FOSTERING PROCEDURES:

Upon arrival, male and female rats will be assigned to individual housing on the basis of computer-generated random units. After acclimation, 78 virgin female rats will be selected for study on the basis of physical appearance and body weights recorded during acclimation. The female rats will be assigned to dosage groups (42 in the control group and 36 in the treated group) based on computer-generated (weight-ordered) randomization procedures and treated with either the vehicle or the test article for 42 days prior to cohabitation.

Within each dosage group, consecutive order will be used to assign female rats to cohabitation with breeder male rats, one male rat per female rat. The rats assigned to the control group will be cohabited one day prior to cohabitation for rats assigned to the treated group. 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.

Mated female rats (those with confirmed evidence of mating) will be assigned as follows: of the 42 female rats assigned to the control group, 30 mated female rats will be assigned to the control group for cross-fostering purposes; of the 36 female rats assigned to the treated group, 24 mated female rats will be assigned to the treated group for cross-fostering purposes. An additional six mated female rats from each dosage group will be designated for pharmacokinetic sample collection (as described below) following delivery, but these rats will not be cross-fostered. Finally, any remaining female rats with confirmed evidence of mating that were assigned to the control group prior to cohabitation will be assigned to the control pool for cross-fostering

purposes. Any remaining female rats with confirmed evidence of mating that were assigned to the treated group prior to cohabitation will be sacrificed and discarded without further evaluation at the discretion of the Study Director and the Study Monitor.

Day 1 of lactation (postpartum) is defined as the day of birth and is also the first day on which all pups in a litter are individually weighed (pup body weights will be recorded after all pups in a litter are delivered and groomed by the dam).

Twelve dams and their respective litters will be selected and assigned to the pharmacokinetic sample collection (six dams and litters per dosage group). These litters will not be cross-fostered.

Up to 24 litters per dosage group will be reassigned for cross-fostering on day 1 postpartum. The litters will be assigned such that four subsets are obtained among the two dosage groups as described in the table below.

Dosage Group	Number of Mated Female Rats	Dosage (mg/kg/day)	Number of Litters Reassigned	Reassigned Litter Type (Dam Treatment)	Subset Number
I	12	0 (Vehicle)	12	Treated	A
I	12	0 (Vehicle)	12	Untreated	B
II	12	1.6	12	Treated	C
II	12	1.6	12	Untreated	D

Detailed procedures for reassignment of litters for cross-fostering are attached to this protocol (ATTACHMENT 4).

On day 1 postpartum, pups from dams assigned to the control pool will be culled, sacrificed via decapitation and handled as described in ATTACHMENT 4.

On day 4 postpartum, cross-fostered litters will be culled to five male and five female pups per litter, where possible. Pups not selected for continued evaluation will be sacrificed via decapitation; the lungs (saved in Bouin's solution) and the liver (saved in neutral buffered 10% formalin) will be collected from the first ten culled pups from each dosage group (irrespective of litter) determined to be at day 4 postpartum and preserved for possible future histopathological evaluation. Remaining culled pups will be sacrificed via decapitation and discarded without necropsy evaluation.

ADMINISTRATION:

Route and Reason for Choice:

The oral (gavage) route was selected for use because: 1) this was the route of administration in the developmental and reproductive toxicology studies; and 2) it is one of the possible routes of human exposure.

Method and Frequency:

Fo Generation Female Rats:

Female rats will be given the test article or the vehicle once daily beginning 42 days prior to cohabitation through day 21 postpartum. Dosages will be adjusted daily for body weight changes and given at approximately the same time each day.

F1 Generation Pups:

F1 generation pups will not be directly given the test article, but may be possibly exposed to the test article during maternal gestation (*in utero* exposure) or via maternal milk during the lactation period.

Rationale for Dosage Selection:

Dosages were selected on the basis of a previous study conducted with the test article (Argus Research Laboratories, Inc., Protocol 418-008).

Dosage Levels, Concentrations and Volumes:

Dosage Group	Number of Mated Female Rats	Dosage (mg/kg/day)	Concentration (mg/mL)	Dosage Volume (mL/kg)	Argus Batch Number
I	30 + 6[a]	0 (Vehicle)	0	5	B-418-014-A(Day.Month.Year)
II	24 + 6[a]	1.6	0.32	5	B-418-014-B(Day.Month.Year)

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

a. Samples for analysis of pharmacokinetics will be collected from six dams and their respective litters on day 14 postpartum. These dams and their respective litters will be sacrificed following sample collection.

TESTS, ANALYSES AND MEASUREMENTS - Fo GENERATION:

Viability:

All Periods: At least twice daily.

Clinical Observations and/or General Appearance:

Acclimation Period:	At least once.
Dosage Period:	Twice daily. Prior to administration and once approximately one hour postdosage.
Maternal Behavior:	Days 1, 4, 7, 14 and 21 postpartum. Observed abnormal behavior will be recorded daily.

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

Body Weights:

Acclimation Period:	At least once.
Dosage Period:	Daily.
Sacrifice:	Terminal weight.

Feed Consumption Values (recorded and tabulated):

Acclimation Period:	At least once.
Dosage Period:	Weekly to cohabitation. Daily during presumed gestation and days 1, 4, 7, 10 and 14 postpartum. Feed consumption will not be tabulated after day 14 postpartum, when it is expected that pups will begin to consume maternal feed.

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*.

Natural Delivery:

Female rats will be evaluated for:

Clinical Observations During Parturition [to be performed under red light conditions during the dark period (time each pup is observed will be recorded)].

Duration of Gestation (day 0 of presumed gestation to the time the first pup is observed).

Length of Parturition (time of observation of last pup minus the time of observation of the first pup divided by N-1 pups in each litter).

Litter Size (defined as all pups delivered).

Pup Viability at Birth.

Pharmacokinetic Sample Collection:

Caps and labeled tubes will be weighed (combined weight, to the nearest .001 gram) before and after retention of pooled pup samples for subsequent use in pharmacokinetic analyses. These weights will be documented in the raw data, and copies of these weights will be included with the packing list prior to shipment.

Blood, Milk and Liver Samples - Fo Generation Rats:

Blood, milk and liver samples will be collected from six maternal rats designated for pharmacokinetic sample collection per dosage group on day 14 postpartum. The time of sample collections (blood and milk) will be recorded in the raw data.

Milk samples will be collected approximately two to six hours postdosage on day 14 postpartum. Each dam will be removed from the nesting box and individually housed for approximately four hours. The dam will be injected intravenously with one unit of oxytocin approximately five minutes before milk samples (at least 100 µL per sample) are collected. The samples will be immediately frozen on dry ice and maintained frozen (-70°C or below) until shipment to the Sponsor for analysis.

Following milk sample collection, blood samples (approximately 4 mL each) will be collected from the maternal rats via the inferior vena cava and transferred into serum separator tubes. The samples will be spun in a refrigerated centrifuge. The serum will be transferred into polypropylene tubes labeled with the study number, animal identification, date of collection, study day and collection timepoint. All samples will be immediately frozen on dry ice and maintained frozen (-70°C or below) until shipment to the Sponsor for analysis.

Following collection of milk and blood samples, a liver section (right lateral lobe) and the milk-secreting glands from the axillary, thoracic, abdominal and inguinal regions of each dam (left side only) will be collected, frozen and stored (-70°C or below) until shipment to the Sponsor for analysis.

Blood and Liver Samples - F1 Generation Pups:

Blood samples will be collected via the inferior vena cava from each pup on day 14 postpartum, pooled (per litter) and transferred into serum separator tubes. The samples will be spun in a refrigerated centrifuge. The serum will be transferred into polypropylene tubes labeled with the study number, animal identification, date of collection, study day and collection timepoint. All samples will be immediately frozen on dry ice and maintained frozen (-70°C or below) until shipment to the Sponsor for analysis.

The liver from each pup will be collected, pooled (per litter), frozen and stored (-70°C or below) until shipment to the Sponsor for analysis.

Shipping Instructions:

All samples will be maintained frozen (-70°C or below) until shipment for analysis. Samples will be shipped on frozen on dry ice via overnight mail. A packing list will be included with the samples and sent to Kris J. Hansen, Ph.D., at the previously cited address. Both the recipient and the Study Monitor will be notified in advance of sample shipment.

Urine and Fecal Sample Collection:

Fo generation female rats will be housed individually in metabolism cages for collection of urine and fecal samples from days 21 to 22 postpartum. Following the 24-hour collection interval, samples will be collected into centrifuge tubes, placed on dry ice and stored frozen (-70°C or below) until shipment for analysis.

Shipping Instructions:

All samples will be maintained frozen (-70°C or below) until shipment for analysis. Samples will be shipped on frozen on dry ice via overnight mail. A packing list will be included with the samples and sent to Kris J. Hansen, Ph.D., at the previously cited address. Both the recipient and the Study Monitor will be notified in advance of sample shipment.

METHOD OF SACRIFICE - Fo GENERATION RATS:

Rats will be sacrificed by carbon dioxide asphyxiation.

NECROPSY - Fo GENERATION RATS:

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

Rats Not Delivering a Litter:

Rats that do not deliver a litter will be sacrificed on day 25 of presumed gestation and examined for gross lesions. Uteri will be stained with 10% ammonium sulfide to confirm the absence of implantation sites[5].

Scheduled Sacrifice - Rats Assigned to Pharmacokinetic Sample Collection:

On day 14 postpartum, milk and blood samples, a liver section (right lateral lobe) and the milk-secreting glands from the axillary, thoracic, abdominal and inguinal regions of each dam (left side only) will be collected as described previously, frozen and stored (-70°C or below) until shipment to the Sponsor for analysis. Following the completion of pharmacokinetic sample collection, Fo generation female rats will be sacrificed, and a gross necropsy of the thoracic, abdominal and pelvic viscera will be performed. The number and distribution of implantation sites will be recorded.

Scheduled Sacrifice - Day 22 Postpartum:

On day 22 postpartum, blood samples will be collected from the Fo generation female rats following removal from metabolism caging.

Blood samples (approximately 4 mL each) will be collected from the maternal rats via the inferior vena cava and transferred into serum separator tubes. The samples will be spun in a refrigerated centrifuge. The serum will be transferred into polypropylene tubes labeled with the study number, animal identification, date of collection, study day and collection timepoint. All samples will be immediately frozen on dry ice and maintained frozen (-70°C or below) until shipment to the Sponsor for analysis.

The female rats will then be sacrificed, and a gross necropsy of the thoracic, abdominal and pelvic viscera will be performed. The number and distribution of implantation sites will be recorded. A liver section (right lateral lobe) from each dam will be collected, frozen and stored (-70°C or below) until shipment to the Sponsor for analysis.

Dams with No Surviving Pups:

Dams with no surviving pups will be sacrificed after the last pup is found dead, missing or presumed cannibalized.

Prior to sacrifice, a blood sample (approximately 4 mL) will be collected from the maternal rat via the inferior vena cava and transferred into serum separator tubes. The sample will be spun in a refrigerated centrifuge. The serum will be transferred into a polypropylene tube labeled with the study number, animal identification, date of collection, study day and collection timepoint. The sample will be immediately frozen on dry ice and maintained frozen (-70°C or below) until shipment to the Sponsor for analysis.

A gross necropsy of the thoracic, abdominal and pelvic viscera will be performed. A liver section (right lateral lobe) from each dam will be collected, frozen and stored (-70°C or below) until shipment to the Sponsor for analysis. Postpartum data for these dams will be excluded from summary tables.

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. A liver section (right lateral lobe) from each dam will be collected, frozen and stored (-70°C or below) until shipment to the Sponsor for analysis. Pregnancy status and uterine contents of female rats will be recorded. Aborted fetuses and/or delivered pups will be examined to the extent possible. Uteri of apparently nonpregnant rats will be stained with 10% ammonium sulfide to confirm the absence of implantation sites[5].

Shipping Instructions:

All samples will be maintained frozen (-70°C or below) until shipment for analysis. Samples will be shipped frozen on dry ice via overnight mail. A packing list will be included with the samples and sent to Kris J. Hansen, Ph.D., at the previously cited address. Both the recipient and the Study Monitor will be notified in advance of sample shipment.

TESTS, ANALYSES AND MEASUREMENTS - F1 GENERATION:

Viability:

Postpartum Period:	Litters will be observed for dead pups at least twice daily. The pups in each litter will be counted once daily.

Clinical Observations and/or General Appearance:

Postpartum Period: Once daily.

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

Body Weights:

Postpartum Period: Days 1 (birth), 4, 7, 14 and 21 postpartum.

Sacrifice: Terminal weight.

METHOD OF SACRIFICE - F1 GENERATION RATS:

As previously cited for Fo generation rats. Culled pups will be sacrificed via decapitation.

NECROPSY - F1 GENERATION RATS:

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

As described previously, caps and labeled tubes will be weighed (combined weights, to the nearest .001 gram) before and after retention of pooled pup samples. These weights will be documented in the raw data, and copies of these weights will be included with the packing list prior to shipment.

Pups Found Dead on Day 1 Postpartum:

Pups that die before examination of the litter for pup viability will be evaluated for vital status at birth. The lungs will be removed and immersed in water. Pups with lungs that sink will be identified as stillborn; pups with lungs that float will be identified as liveborn, and to have died shortly after birth. Pups with gross lesions will be preserved in Bouin's solution for possible future evaluation. The lungs will be preserved in Bouin's solution and the liver will be preserved in neutral buffered 10% formalin for possible future evaluation.

Pups Found Dead or Moribund on Days 2 to 21 Postpartum:

Pups found dead or sacrificed because of moribundity will be examined for gross lesions and for the cause of death or the moribund condition. Pups with gross lesions found on days 2 to 4 postpartum will be preserved in Bouin's solution for possible future evaluation; gross lesions of pups found on days 5 to 21 postpartum will be preserved in neutral buffered 10% formalin.

For all pups found dead on days 2 to 4 postpartum, the lungs will be preserved in Bouin's solution and the liver will be preserved in neutral buffered 10% formalin for possible future evaluation. For all pups found dead on days 5 to 21 postpartum, the lungs and the liver will be preserved in neutral buffered 10% formalin for possible future evaluation.

Pups Not Selected for Continued Observation - Days 1 and 4 Postpartum:

All pups culled on day 1 postpartum (pups from dams assigned to the control pool) and day 4 postpartum (all other culled pups) will be sacrificed via decapitation. The lungs and the liver will be collected from the first ten pups culled (irrespective of litter) from each dosage group on each day (control pool only on day 1 postpartum); the lungs will be retained in Bouin's solution, and the livers will be retained in neutral buffered 10% formalin for possible future evaluation. Remaining culled pups will be sacrificed and discarded without evaluation.

Scheduled Sacrifice - Litters Assigned to Pharmacokinetic Sample Collection:

On day 14 postpartum, litters assigned to the pharmacokinetic sample collection will be sacrificed with their respective dams. Individual, pooled samples (per litter) of blood and liver will collected as described previously. The pups will be examined for gross lesions.

Scheduled Sacrifice - Litters Assigned to Sacrifice on Day 21 Postpartum:

On day 21 postpartum, six litters per subset will be randomly selected for collection of pooled samples (per litter) of blood and liver.

Blood samples will be collected via the inferior vena cava from each pup, pooled (per litter) and transferred into serum separator tubes. The samples will be spun in a refrigerated centrifuge. The serum will be transferred into polypropylene tubes labeled with the study number, animal identification, date of collection, study day and collection timepoint. All samples will be immediately frozen on dry ice and maintained frozen (-70°C or below) until shipment to the Sponsor for analysis.

The pups will be examined for gross lesions. The liver from each pup will be collected, pooled (per litter), frozen and stored (-70°C or below) until shipment to the Sponsor for analysis.

All other remaining pups will be sacrificed and discarded without further evaluation.

Shipping Instructions:

All samples will be maintained frozen (-70°C or below) until shipment for analysis. Samples will be shipped frozen on dry ice via overnight mail. A packing list will be included with the samples and sent to Kris J. Hansen, Ph.D., at the previously cited address. Both the recipient and the Study Monitor will be notified in advance of sample shipment.

STATISTICAL EVALUATION:

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

DATA ACQUISITION, VERIFICATION AND STORAGE:

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

RECORDS TO BE MAINTAINED:

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

KEY PERSONNEL:

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

FINAL REPORT:

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

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

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE STATEMENT:

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

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

REFERENCES:

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

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

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

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

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

PROTOCOL APPROVAL:

FOR THE TESTING FACILITY

22-Oct-98

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

Date

23-Oct-98

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

Date

22 Oct 98

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

Date

FOR THE SPONSOR

27 Oct 98

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

Date

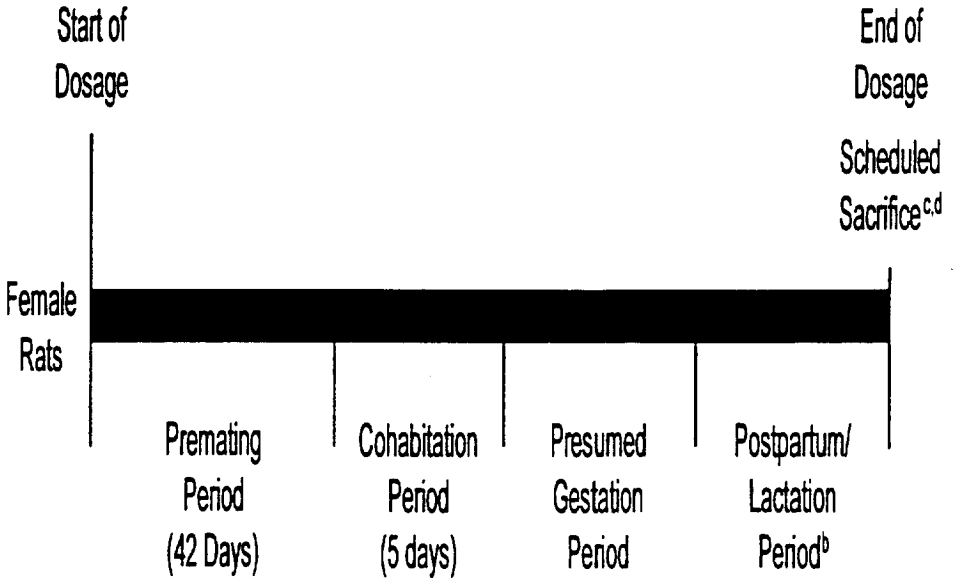
ATTACHMENT 1

SCHEMATIC OF STUDY DESIGN AND STUDY SCHEDULE

ATTACHMENT 1

STUDY SCHEMATIC

CROSS-FOSTERING STUDY[a]



Dosage Period.

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

b. F1 generation pups will be cross-fostered beginning on day 1 postpartum and continuing until day 21 postpartum.

c. F1 generation pups will be sacrificed on day 21 postpartum. Fo generation dams will be sacrificed on day 22 postpartum.

d. Samples for analysis of pharmacokinetics will be collected from six dams and their respective litters on day 14 postpartum. These litters will not be cross-fostered and will be sacrificed following sample collection.

SCHEDULE[a]

27 OCT 98	Animals Arrive - Acclimation Begins.
02 NOV 98	Dosage Period - Female Rats (42 days prior to cohabitation until day 21 postpartum).
13 DEC 98 PM - 19 DEC 98 AM	Cohabitation Period.
14 DEC 98	First Possible Day 0 of Presumed Gestation.
19 DEC 98	Last Possible Day 0 of Presumed Gestation.
04 JAN 99	First Possible Delivery (Day 21 of presumed gestation).
13 JAN 99	Last Possible Delivery (Day 25 of presumed gestation).
04 JAN 99	First Possible Day 1 Postpartum Culling - Control Pool Only.
12 JAN 99	Last Possible Day 1 Postpartum Culling - Control Pool Only.
08 JAN 99	First Possible Day 4 Postpartum Culling - Cross-Fostered Litters.
16 JAN 99	Last Possible Day 4 Postpartum Culling - Cross-Fostered Litters.
08 JAN 99	First Possible Day 25 of Presumed Gestation Female Sacrifice.
13 JAN 99	Last Possible Day 25 of Presumed Gestation Female Sacrifice.
17 JAN 99	First Possible Day 14 Postpartum Pharmacokinetic Sacrifice.
26 JAN 99	Last Possible Day 14 Postpartum Pharmacokinetic Sacrifice.
24 JAN 99 - 02 FEB 99	Scheduled Sacrifice - F1 Generation Pups (Day 21 postpartum).
25 JAN 99 - 03 FEB 99	Scheduled Sacrifice - Fo Generation Dams (Day 22 postpartum).
08 JUN 99	Draft Final Report.

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

ATTACHMENT 2

MATERIAL SAFETY DATA SHEET

MATERIAL SAFETY DATA SHEET

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

DIVISION: 3M CHEMICALS
TRADE NAME:
FC-95 FLUORAD Brand Fluorochemical Surfactant
ID NUMBER/U.P.C.:
98-0207-0103-7 00-51135-09054-1 98-0207-0104-5 00-51135-09055-8
98-0211-0888-5 00-51135-09362-7 98-0211-3916-1 00-51135-02311-2
ZF-0002-1044-1 - - -
ISSUED: January 29, 1998
SUPERSEDES: November 05, 1997
DOCUMENT: 10-3796-9

1. INGREDIENT

INGREDIENT	C.A.S. NO.	PERCENT
POTASSIUM PERFLUOROALKYL SULFONATE.....	2795-39-3	82 - 86
POTASSIUM PERFLUOROALKYL SULFONATE.....	3871-99-6	3 - 8
POTASSIUM PERFLUOROALKYL SULFONATE.....	29420-49-3	3 - 7
POTASSIUM PERFLUOROALKYL SULFONATE.....	60270-55-5	2 - 6
POTASSIUM PERFLUOROALKYL SULFONATE.....	3872-25-1	1 - 3

2. PHYSICAL DATA

BOILING POINT:..... N/A
VAPOR PRESSURE:..... N/A
VAPOR DENSITY:..... N/A
EVAPORATION RATE:..... N/A
SOLUBILITY IN WATER:..... slight
SPECIFIC GRAVITY:..... ca. 0.6 Water=1 (Bulk)
PERCENT VOLATILE:..... 0 %
pH:..... 7 - 8 (0.1% Aqueous)
VISCOSITY:..... N/D
MELTING POINT:..... N/D

APPEARANCE AND ODOR:
Light colored, free flowing powder.

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

3. FIRE AND EXPLOSION HAZARD DATA

FLASH POINT:..... None
FLAMMABLE LIMITS - LEL:..... N/A
FLAMMABLE LIMITS - UEL:..... N/A
AUTOIGNITION TEMPERATURE:..... N/A

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

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

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

4. REACTIVITY DATA

STABILITY: Stable

INCOMPATIBILITY - MATERIALS/CONDITIONS TO AVOID:
Not applicable.

HAZARDOUS POLYMERIZATION: Hazardous polymerization will not occur.

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

5. ENVIRONMENTAL INFORMATION

SPILL RESPONSE:
Observe precautions from other sections. Vacuum, use wet sweeping compound or water to avoid dusting. CAUTION! A vacuum cleaner could be an ignition source. Clean up residue with water. Place in an approved metal container. Seal the container.

RECOMMENDED DISPOSAL:
Do not release to waterways or sewer. Do not use in products or processes that could result in aquatic concentrations greater than 1/10 of the lowest EC50 or LC50 concentration. 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

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5. ENVIRONMENTAL INFORMATION (continued)

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accept chemical waste.

ENVIRONMENTAL DATA:
96-Hr. Aquatic Fish LC50, Fathead Minnow(Pimephales promelas)=38 mg/l, Bluegill Sunfish(Lepomis macrochirus)=68 mg/l, Rainbow Trout(Salmo gairdneri)=11 mg/l; 48-Hr. EC50, Daphnia Magna = 50 mg/l; COD=.004 g/g; BOD20 = Nil.

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

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

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

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

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6. SUGGESTED FIRST AID

EYE CONTACT:
Immediately flush eyes with large amounts of water for at least 15 minutes. Get immediate medical attention.

SKIN CONTACT:
Immediately flush skin with large amounts of water. Remove contaminated clothing. If irritation persists, call a physician. Wash contaminated clothing before reuse.

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

IF SWALLOWED:
Drink two glasses of water. Call a physician.

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7. PRECAUTIONARY INFORMATION

EYE PROTECTION:
Avoid eye contact. Wear vented goggles.

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7. PRECAUTIONARY INFORMATION (continued)

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

RECOMMENDED VENTILATION:
Use with appropriate local exhaust ventilation. Use in a well-ventilated area. 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 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, half-mask supplied air respirator, full-face dust and mist respirator, full-face supplied air respirator.

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

RECOMMENDED STORAGE:
Keep container dry. Keep container closed when not in use.

FIRE AND EXPLOSION AVOIDANCE:
Nonflammable.

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

HMIS HAZARD RATINGS: HEALTH: 2 FLAMMABILITY: 0 REACTIVITY: 0
PERSONAL PROTECTION: X (See precautions, section 7.)

EXPOSURE LIMITS

INGREDIENT	VALUE	UNIT	TYPE	AUTH	SKIN*
POTASSIUM PERFLUOROALKYL SULFONATE...	0.1	MG/M3	TWA	3M	Y
POTASSIUM PERFLUOROALKYL SULFONATE...	0.1	MG/M3	TWA	3M	Y
POTASSIUM PERFLUOROALKYL SULFONATE...	0.1	MG/M3	TWA	3M	Y
POTASSIUM PERFLUOROALKYL SULFONATE...	0.1	MG/M3	TWA	3M	Y

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

EXPOSURE LIMITS (continued)

INGREDIENT	VALUE	UNIT	TYPE	AUTH	SKIN*
POTASSIUM PERFLUOROALKYL SULFONATE...	0.1	MG/M3	TWA	3M	Y

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

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

8. HEALTH HAZARD DATA

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

SKIN CONTACT:
Mild Skin Irritation (after prolonged or repeated contact): signs/symptoms can include redness, swelling, and itching.

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

INHALATION:
May be harmful if inhaled.

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

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

Illness may result from a single swallowing of a moderate quantity of this material.

May be harmful if swallowed.

MUTAGENICITY:
Mutagenicity assays indicate the product is not mutagenic.

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8. HEALTH HAZARD DATA (continued)

REPRODUCTIVE/DEVELOPMENTAL TOXINS:
Not teratogenic in the rat at oral doses below maternally toxic levels.

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

A Product Toxicity Summary Sheet is available.

SECTION CHANGE DATES

HEADING	SECTION CHANGED SINCE November 05, 1997 ISSUE

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

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ATTACHMENT 3

TEST ARTICLE PREPARATION PROCEDURE

ATTACHMENT 3

TEST ARTICLE PREPARATION PROCEDURE

Test Article: PFOS.

Vehicle: 0.5% Tween® 80 in R.O. Deionized Water.

A. Purpose: The purpose of this procedure is to provide a method for the preparation of dosage suspensions of PFOS and the vehicle for oral administration to rats on Argus Study 418-014.

B. General Information:

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

2. Suspensions will be prepared:
   _X_ Daily ___ Weekly __ For____ days of use

3. Vehicle will be prepared:
   ____ Daily _X_ Weekly __ For____ days of use

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

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

6. Dosage solutions adjusted for Free base and % Purity.
   __ Yes _X_ No (Calculations based on 100%)
   ___ Free Base ___ Purity

7. Sampling requirements: Cited in protocol.

8. Storage: Cited in protocol.

ATTACHMENT 3

TEST ARTICLE PREPARATION PROCEDURE

NOTE: Once the final volumes are achieved, stir bars are to be added to the containers; mixing should occur during sampling and/or administration.

C. Preparation of Vehicle:

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

D. Test Article Suspension Preparation:

1. To prepare the suspension for the high dosage group, add the required amount of test article (See TEST ARTICLE CALCULATIONS) into an appropriately sized, labeled container. QS ad to the required amount with vehicle, add a stir bar and heat the mixture to 80°C, ±5°C, in a water bath for approximately 30 minutes or until the test article dissolves.

2. Once the test article has dissolved, remove the suspension from the water bath and spin the suspension while it cools. (Be sure there is a visible vortex, this will achieve the desired emulsion. This may be prepared the day before use.)

Written by: _____

Approved by: _____ Date: 23-OCT-98

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

Initial/Date : _____

ATTACHMENT 4

CROSS-FOSTERING PROCEDURE

ATTACHMENT 4

CROSS-FOSTERING PROCEDURE

The cohabitation period will begin one day earlier for the rats assigned to the control group. Dams assigned to the control group that mate on the first day will be allowed to deliver and will retain their natural pups until needed for cross-fostering purposes. This will provide a pool of control dams available for immediate cross-fostering to pups from PFOS-treated dams, thus preventing these pups from nursing from their PFOS-treated dams.

On the remaining days of cohabitation, both control and PFOS-treated groups will be co-housed with male breeders, one male rat to one female rat. Starting with this set of deliveries, all pups will be removed immediately (as soon as parturition is complete) from their respective dams and placed with either another dam assigned to the control group or a PFOS-treated dam. If a dam assigned to the control group is not available, then a dam from the control pool will be used. The litter from that control pool dam will then be sacrificed via decapitation.

The first ten pups from the control pool (irrespective of litter) determined to be at day 1 postpartum will be decapitated, and the lungs (saved in Bouin's solution) and the liver (saved in neutral buffered 10% formalin) will be collected and preserved for possible future histopathological evaluation. The remaining pups from the control pool dams will be sacrificed via decapitation and discarded without necropsy evaluation.

This cross-fostering procedure will result in four groups of 12 dams/pups, i.e., Control/Control (Subset A), Control/PFOS (Subset B), PFOS/Control (Subset C) and PFOS/PFOS (Subset D). This procedure will allow distinctions to be made between prenatal and postnatal effects of the continuous maternal PFOS treatment.

PRIMEDICA

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

PROTOCOL 418-014

Oral (Gavage) Cross-Fostering Study of PFOS in Rats

SPONSOR'S STUDY NUMBER: T-6295.13

Amendment 1 – 4 January 1999

---

1. Cross-Fostering Procedure (Paragraph 3 of Attachment 4 to the protocol):

The first ten pups from the control pool (irrespective of litter) and the first ten pups that are found dead (no autolysis present) per dosage group determined to be at day 1 postpartum will be decapitated at approximately 1 to 3 hours after birth, and the lungs and the liver will be retained. Several (minimum of two) sections (approximately 1 mm thick) of the lung and the liver will be removed using a scalpel and will be retained in McDowell-Trump's Fixative [preparation procedure provided by the Sponsor is documented in the raw data (stored under refrigeration in scintillation vials) (see attached)] for future evaluation. The remaining lung and liver samples will be retained in Bouin's solution or neutral buffered 10% formalin, respectively, for possible future evaluation. The remaining pups from the control group dams will be sacrificed via decapitation and discarded without necropsy evaluation.

The liver sections in McDowell-Trump's Fixative will be shipped (on cold packs), for evaluation by electron microscopy, to:

Jeanne deWard
Pathology Associates International
4915 D Prospectus Drive
Durham, North Carolina 27713
Telephone: (919) 544-5257
Telefax: (919) 544-3218

The remaining samples will be shipped (ambient conditions) to the Kris J. Hansen, Ph.D., at the address cited in the protocol for histopathological and biochemical evaluation.

Reason for Change:

The Sponsor has requested that these additional samples be retained for continued evaluation of the reasons for reduced pup survival observed in previous studies.

2. Cross-Fostering Procedure (Paragraph 4 of Attachment 4 to the protocol):

The fourth paragraph of the Cross-Fostering procedure has been changed to read:

This cross-fostering procedure will result in four groups of 12 dams/pups, i.e., Control/Control (Subset B), Control/PFOS (Subset A), PFOS/Control (Subset D) and PFOS/PFOS (Subset C). This Procedure will allow distinctions to be made between prenatal and postnatal effect of the continuous maternal PFOS treatment.

Reason for Change:

This corrects the protocol.

04 Jan 99	04-JAN-99
Alan M. Hoberman, Ph.D., DABT Date Director of Research	Raymond G. York, Ph.D., DABT Date Associate Director of Research and Study Director
04 Jan 99	04 Jan 99
Dena C. Lebo, V.M.D. Date Chairperson, Institutional Animal Care and Use Committee	Marvin T. Case, D.V.M., Ph.D. Date Study Monitor

FIXATIVE PREPARATION PROCEDURE

Fixative : McDowell-Trump's Fixative

A. Purpose:

The purpose of this procedure is to provide a method for the preparation of McDowell-Trump's Fixative for tissue samples for study 418-014.

B. General Information:

1. All solution containers will be labeled. Each label will specify the protocol number, fixative identification, preparation date, expiration date and storage conditions.

2. Fixative will be prepared:

__ Daily __ Weekly __x__ Once

3. Safety:
__X__ Gloves, lab coat, goggles or safety glasses and face shield
__X__ Dust-Mist Respirator
__X__ Half-Face Respirator
__ Full-Face Respirator/Positive Pressure Hood
__ Tyvek Suit/Apron
__X__ Other: Chemical Fume Hood

4. Dosage suspensions adjusted for % Activity/Purity or Correction Factor:

__ Yes __X__ No (Calculations based on 100%)

5. Sampling requirements: Cited in protocol.

7. Storage: Room temperature

FIXATIVE PREPARATION PROCEDURE

C. Preparation of Fixative:

McDowell-Trump's Fixative

1. Add 860 mLs of R.O. Deionized water into an appropriately labeled container.
2. Add 100 mLs of 37% Formaldehyde to the container and stir until uniform.
3. Add 40 mLs of Gluteraldehyde to the container and stir until uniform.
4. Add 11.6g of Sodium Phosphate Monobasic to the container and stir until uniform.
5. Add 2.70g of Sodium Hydroxide to the vessel and stir until uniform.

[NOTE: The final solution should have a pH of approximately 7.3.]

Written By: Christopher K. Rapp

Approved by: [signature] Date: 2/28/98

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

Initials/Date: Christopher K. Rapp 2/10/99

APPENDIX D

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

APPENDIX E

TEMPERATURE AND RELATIVE HUMIDITY REPORTS

ARGUS

Temperature and Relative Humidity Report
Location: Room 04

Protocol Number: 418-014

Range of Dates: 27-Oct-1998 13:15 to 23-Nov-1998 15:49

	Temperature		Relative Humidity	
Target Range:	64°F to 79°F		30% to 70%	
Species: Rat				
Total Number of Days:	28		28	
Total Number of Hours:	650.51		650.51	
Total Number of Data Points:	634		634	
Mean (± SD):	69.1	(± 1.9)	53.2	(± 8.0)
Maximum:	76.4		66.2	
Median:	68.4		57.2	
Minimum:	66.5		28.6	
Number of Points in Range (%):	634	(100.0)	633	(99.8)
Number of Points High (%):	0	(0.0)	0	(0.0)
Number of Points Low (%):	0	(0.0)	1	(0.2)

Report Generated: 04-Feb-1999 at 17:26

COMMENTS: _____

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REVIEWED BY: M. Martin **DATE:** 2·8 99

ARGUS

Temperature and Relative Humidity Report
Location: Room 27

Protocol Number: 418-014

Range of Dates: 23-Nov-1998 15:49 to 31-Dec-1998 14:10

	Temperature		Relative Humidity	
Target Range:	64°F to 79°F		30% to 70%	
Species: Rat				
Total Number of Days:	39		39	
Total Number of Hours:	910.01		910.01	
Total Number of Data Points:	913		913	
Mean (± SD):	70.9	(± 0.7)	57.1	(± 6.1)
Maximum:	72.6		69.2	
Median:	71.0		58.3	
Minimum:	69.0		36.0	
Number of Points in Range (%):	913	(100.0)	913	(100.0)
Number of Points High (%):	0	(0.0)	0	(0.0)
Number of Points Low (%):	0	(0.0)	0	(0.0)

Report Generated: 04-Feb-1999 at 17:28

COMMENTS: _____

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REVIEWED BY: M. Martin **DATE:** 2.8.99

ARGUS

Temperature and Relative Humidity Report
Location: Room 35-37

Protocol Number: 418-014

Range of Dates: 31-Dec-1998 14:10 to 18-Jan-1999 08:45

	Temperature		Relative Humidity	
Target Range:	64°F to 79°F		30% to 70%	
Species: Rat				
Total Number of Days:	19		19	
Total Number of Hours:	426.24		426.24	
Total Number of Data Points:	427		427	
Mean (± SD):	75.6	(± 1.7)	50.1	(± 7.4)
Maximum:	78.3		56.1	
Median:	76.4		51.6	
Minimum:	68.5		5.0	
Number of Points in Range (%):	427	(100.0)	417	(97.7)
Number of Points High (%):	0	(0.0)	0	(0.0)
Number of Points Low (%):	0	(0.0)	10	(2.3)

Report Generated: 04-Feb-1999 at 17:30

COMMENTS: _____

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REVIEWED BY: M. Martin **DATE:** 2-8-99

ARGUS

Temperature and Relative Humidity Report
Location: Room 27

Protocol Number: 418-014

Range of Dates: 18-Jan-1999 08:45 to 29-Jan-1999 09:57

	Temperature		Relative Humidity	
Target Range:	64°F to 79°F		30% to 70%	
Species: Rat				
Total Number of Days:	12		12	
Total Number of Hours:	265.0		265.0	
Total Number of Data Points:	266		266	
Mean (± SD):	70.4	(± 0.5)	54.3	(± 8.3)
Maximum:	72.0		70.4	
Median:	70.4		56.4	
Minimum:	69.1		33.1	
Number of Points in Range (%):	266	(100.0)	265	(99.6)
Number of Points High (%):	0	(0.0)	1	(0.4)
Number of Points Low (%):	0	(0.0)	0	(0.0)

Report Generated: 04-Feb-1999 at 17:33

COMMENTS: _____

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REVIEWED BY: M. Martin **DATE:** 2.8.99

ARGUS

Relative Humidity Deviations Report
Location: Room 04

Protocol Number: 418-014

Range of Dates: 27-Oct-1998 13:15 to 23-Nov-1998 15:49

Humidity Target Range: 30% to 70%
Species: rat

Date	Time	R.H.	Date	Time	R.H.
03-Nov-1998	14:00	28.6 L			

H = Value out of range - High L = Value out of range - Low
R.H. = Relative Humidity (%)

Report Generated: 13-May-1999 at 10:45

✓ These deviations did not adversely affect the outcome or interpretation of the study.

_____ The following deviation(s) impacted on the outcome of the study as described:

Study Director: [signature] Date: 13-MAY-99

ARGUS

Relative Humidity Deviations Report
Location: Room 35-37

Protocol Number: 418-014

Range of Dates: 31-Dec-1998 14:10 to 18-Jan-1999 08:45

Humidity Target Range: 30% to 70%
Species: rat

Date	Time	R.H.	Date	Time	R.H.
05-Jan-1999	21:00	5.8 L			
05-Jan-1999	22:00	5.1 L			
05-Jan-1999	23:00	5.0 L			
06-Jan-1999	00:00	5.1 L			
06-Jan-1999	01:00	5.1 L			
06-Jan-1999	02:00	5.2 L			
06-Jan-1999	03:00	5.3 L			
06-Jan-1999	04:00	5.5 L			
06-Jan-1999	05:00	5.6 L			
06-Jan-1999	06:00	5.6 L			

H = Value out of range - High L = Value out of range - Low
R.H. = Relative Humidity (%)

Report Generated: 13-May-1999 at 10:50

✓ These deviations did not adversely affect the outcome or interpretation of the study.

_____ The following deviation(s) impacted on the outcome of the study as described:

Study Director: _____ Date: 13-May-99

ARGUS

Relative Humidity Deviations Report
Location: Room 27

Protocol Number: 418-014

Range of Dates: 18-Jan-1999 08:45 to 29-Jan-1999 09:57

Humidity Target Range: 30% to 70%
Species: rat

Date	Time	R.H.	Date	Time	R.H.
24-Jan-1999	06:00	70.4 H			

H = Value out of range - High L = Value out of range - Low
R.H. = Relative Humidity (%)

Report Generated: 13-May-1999 at 10:54

✓ These deviations did not adversely affect the outcome or interpretation of the study.

_____ The following deviation(s) impacted on the outcome of the study as described:

Study Director: _____ Date: 13 MAY 99

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

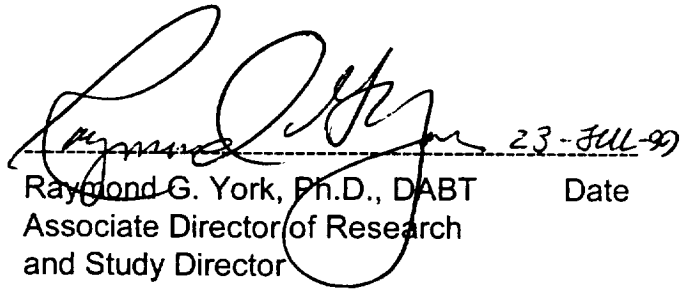
1. Two extra female from the treated group (Group II) were used for pharmacokinetic sample collection on day 14 of lactation (DL 14), 22 January 1999. These two female rats in turn received all collections and were sacrificed on DL 14. This deviation did not adversely affect the outcome of the study because the pharmacokinetic samples were not analyzed.

2. Eight female rats rather than six female rats from the control group (Group I) were used for pharmacokinetic sample collection on DL 14, 17 January 1999, 21 January 1999 and 22 January 1999. The two extra female rats received all sample collections and were sacrificed on DL 14. This deviation did not adversely affect the outcome of the study because the pharmacokinetic samples were not analyzed.

3. A total of 25 litters from the control (Group I) and treated (Group II) groups were cross-fostered rather than 24 litters. This deviation did not adversely affect the outcome of the study because only one additional litter was added to each dosage group.

4. Twenty-five female rats rather than all of the rats in the control group (Group I) were placed into cohabitation on 13 December 1998. The cohabitation period for these rats lasted six days rather than five days. This deviation did not adversely affect the outcome of the study because it provided sufficient mated rats for cross-fostering.

   All deviations are documented in the raw data.



23-JUL-99

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

APPENDIX F

PATHOLOGY REPORT

Pathology Associates International
A Company of Science Applications International Corporation
An Employee-Owned Company

PATHOLOGY REPORT
(ANCILLARY STUDY)

ELECTRON MICROSCOPIC EVALUATION OF LIVER AND LUNG IN CRL:CD®BR VAF/PLUS® RATS)

ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS

CLIENT STUDY NUMBER 418-014
PAI STUDY NUMBER EM 99.46

Prepared by:

James B. Nold, D.V.M., Ph.D., Diplomate, A.C.V.P.

Pathology Associates International
4915-D Prospectus Drive
Durham, NC 27713

April 5, 1999

PREPARED FOR 3M CORPORATE TOXICOLOGY,
3M CENTER, ST. PAUL, MN 55144-1000

I. Pathology Narrative

PATHOLOGY REPORT
(ANCILLARY STUDY)

ELECTRON MICROSCOPIC EVALUATION OF LIVER AND LUNG IN CRL:CD®BR VAF/PLUS® RATS)

ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS

CLIENT STUDY NUMBER 418-014
PAI STUDY NUMBER EM 99.46

SUMMMARY

Ultrastructurally, there were increased numbers of peroxisomes within hepatocytes of neonatal rat pup livers from dams treated with 1.6 mg/kg/day (high-dose) PFOS compared with controls. Quantitation of peroxisomes indicated slightly more than twice the number of peroxisomes in treated animals. Differences in cellular membranes or mitochondria were not discernible between control and treated animals in the samples examined. Type II pneumocytes containing lamellar bodies were identified in both controls and high-dose animals; however, there appeared to be an increased number of type II pneumocytes and lamellar bodies in lungs from treated samples. Although some lamellar material (surfactant) was identifiable within alveolar lumina, no significant difference was noted between control and treated samples.

PROCEDURES

The objective of this study was to examine by electron microscopy the livers and lungs from selected day-1 postpartum rat pups in an oral (gavage) cross-fostering study of PFOS. In addition to a general qualitative evaluation for differences between control and treated animals, the ultrastructural endpoints included quantitation of peroxisomes within hepatocytes, membrane and mitochondrial changes in hepatocytes, and the quantitation of surfactant lamellar bodies in the lung.

For the cross-fostering study, 66 female Crl:CD®BR VAF/PLUS® rats were given the test article or the vehicle once daily beginning 42 days prior to cohabitation with a male through day 21 postpartum according to Text Table 1.

Text Table 1. Dosage Levels, Concentrations and Volumes

Dosage Group	Number of Mated Female Rats	PFOS Dosage (mg/kg/day)	PFOS Concentration (mg/mL)	Dosage Volume (mL/kg)
I	30 + 6[a]	0 (Vehicle)	0	5
II	24 + 6a	1.6	0.32	5

a Samples for analysis of pharmacokinetics were collected from 6 dams and their respective litters on day 14 postpartum. These dams and their respective litters were sacrificed following sample collection.

The first ten pups from the control pool (irrespective of litter) and the first 10 pups that were found dead (no autolysis present) from the treated group determined to be at day 1 postpartum were decapitated at approximately 1-3 hours after birth, and the lungs and liver were collected. Samples of lung and liver were thin-sliced and placed in McDowell-Trump fixative (McDowell EM, 1976), and submitted to this laboratory for electron microscopy processing and evaluation.

Per sponsor request, tissue samples from selected pups were processed and evaluated ultrastructurally (Text Table 2). Pup numbers were assigned by this laboratory because submitted samples were identified by dam number only. The five digit number is the dam number; the suffix 1 or 2 denotes the pup number from that dam's litter.

Text Table 2. Animals Selected for Electron Microscopy

Control (0 mg/kg/day)	High-Dose (1.6 mg/kg/day)
18904-1	18952-1
18904-2	18952-2
18915-1	18956-1
18915-2	18973-1
18912-1	

The lungs and livers were then processed into Spurr's resin for ultrastructural examination. Thick (1μ) sections were cut, stained with toluidine blue, and examined to select representative areas for further electron microscopy processing. Thin sections (approximately 90 nm) were cut, mounted on 200-mesh copper grids, stained with 5% methanolic uranyl acetate and Reynold's lead citrate, and examined on a Zeiss 900 transmission electron microscope. Centrilobular hepatocytes, where clearly identifiable in liver sections, were preferentially examined. Representative electron photomicrographs of liver and lung were taken and significant ultrastructural features were summarized for each photograph and animal on a designated transmission electron micrograph interpretation form. The number of peroxisomes in hepatocytes was manually counted for each center photographed hepatocyte and recorded.

RESULTS AND DISCUSSION

Individual interpretations of light and electron micrographs for each animal are shown in Section II. Selected representative electron photomicrographs were labeled and are shown in Section III.

Fixation of the tissues was less than optimal for electron microscopy. This was especially evident in the liver compared with the lung. Lung is inherently less dense than liver and allows better infiltration of the fixative into the tissue. Suboptimal fixation was characterized by discontinuous plasma membranes, loss of detail of cytoplasmic organelles, dilatation of endoplasmic reticulum and the nuclear envelope, and dilatation of mitochondrial cristae. Fixation, however, was still considered adequate to assess for

the presence of peroxisomes in the hepatocytes and lamellar bodies in the lung and to make general comparisons between control and treated samples.

LIVER

Control (0 mg/kg/day). Subcellular features of control hepatocytes are demonstrated in Figures 1 and 2. Hepatocytes characteristically contain numerous mitochondria and prominent endoplasmic reticulum. In these cells rough endoplasmic reticulum was evident, but smooth endoplasmic reticulum was not because of suboptimal fixation. Mitochondria generally appeared dark and contained scattered dense deposits and some dilated cristae, both artifacts due to suboptimal fixation. Dilatation of endoplasmic reticulum and the nuclear envelope were additional artifacts of poor fixation. Fine granular material in the cytoplasm is consistent with glycogen particles. Peroxisomes were identified and quantitated in from representative hepatocytes. For the control livers, the average number of peroxisomes counted per hepatocyte photograph was 7 peroxisomes per cell (Text Table 3). Fetal and neonatal rat liver is a hematopoietic tissue, and numerous hematopoietic cells were evident within the liver sinusoids.

Text Table 3. Quantitation of Hepatocellular Peroxisomes

Control (0 mg/kg/day)		High-Dose (1.6 mg/kg/day)	
Animal Number	Number of Peroxisomes per Hepatocyte	Animal Number	Number of Peroxisomes per Hepatocyte
18904-1	4.6	18952-1	16.0
18904-2	6.2	18952-2	17.0
18912-1	9.0	18956-1	17.25
18915-1	8.8	18973-1	14.0
18915-2	6.4		
Mean Control =	7.0	Mean High-Dose =	16.1

High-Dose (1.6 mg/kg/day). The average number of peroxisomes per hepatocyte (14.7) was higher in the high-dose animals compared with controls (Text Table 3). Otherwise, general ultrastructural morphology was similar in high-dose livers compared with control livers. Figures 3-5 illustrate representative hepatocytes from several high-dose animals. Differences in mitochondria and cellular membranes were not discernible between high-dose and control livers. However, suboptimal fixation of the tissue precluded detailed evaluation of these organelles.

LUNG

Control (0 mg/kg/day). Lung samples were atelectatic and not inflated with fixative. Therefore most alveoli and alveolar septa were collapsed with poor delineation of alveolar and airway spaces. Figures 6-8 illustrate some normal cellularity and ultrastructural pulmonary anatomy. Type II pneumocytes (PN2) were infrequently identified lining alveoli, terminal bronchioles, or within collapsed septa. Type II pneumocytes were identified by the presence of lamellar bodies, which are cytoplasmic

vacuoles containing electron-dense laminated membrane-like profiles. Lamellar bodies represent the material secreted into the alveolar spaces as surfactant. Surfactant or lamellar material within airway spaces was very rarely identified in control lungs. The type I pneumocyte (PN1) is characteristically flattened and lines the alveolar space as a thin margin of cytoplasm. Type I pneumocytes differentiate from type II pneumocytes. Many pneumocytes appeared to be cuboidal without distinctive lamellar bodies, and may represent a transition stage between PN2s and PN1s, especially since these lungs were neonatal and had not been fully expanded with air. Additionally, some cuboidal epithelial cells represented terminal bronchiolar epithelium.

Type II pneumocytes and lamellar bodies were infrequently identified in these control lungs and no reliable quantitation could be assessed of them. Some lamellar-like bodies were also present within capillary lumina.

High-Dose (1.6 mg/kg/day). Ultrastructural pathology of the high-dose lungs was essentially similar to control samples. There appeared, however, to be increased numbers of type II pneumocytes and lamellar bodies; at least, identifying them for illustrative purposes was easier than in control samples. The collapsed nature of most of the alveoli and septa made definitive quantitation impractical. Some lamellar bodies were identified within capillary lumina and only a small number were seen within alveoli. Figures 9-12 illustrate some representative lung fields from the high-dose animals.

CONCLUSION

Ultrastructural evaluation of liver and lungs of rat pups from dams treated with 0 (control) or 1.6 mg/kg/day (high-dose) PFOS identified increased numbers of peroxisomes within hepatocytes of high-dose rat pup livers. Quantitation of peroxisomes indicated slightly more than twice the number of peroxisomes in treated animals. Differences in cellular membranes or mitochondria were not discernible between control and treated animals in the samples examined. In lung samples the presence of type II pneumocytes and lamellar bodies was evaluated. Type II pneumocytes containing lamellar bodies were identified in both controls and high-dose animals; however, there appeared to be an increased number of type II pneumocytes and lamellar bodies in lungs from treated samples. Some lamellar bodies and lamellar myelin-like figures were extracellular and within capillary lumina. Although some lamellar material (surfactant) was identifiable within alveolar lumina, no significant difference was noted between control and treated samples.

SIGNATURE OF AUTHOR

James B. Nold

James B. Nold, D.V.M., Ph.D.,
Diplomate, A.C.V.P.

April 5, 1999
Date

REFERENCES

McDowell, EM and Trump, BF: Histologic fixative for routine diagnostic light and electron microscopy. *Arch. Pathol. Lab. Med.*, 100:405-414, 1976.

II. Transmission Electron Micrograph Interpretation Forms[1]

[1] Forms are typographically corrected versions of signed/dated raw data sheets maintained in archived study file.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-014; EM-99.46

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 18904-1

Tissue: Liver

Treatment Group: 0 mg/kg Control

Block No(s).: 99.46-1

Sex: non applicable

Photo/Negative No(s).: Z15683, Z15684, Z15686-88

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15683:- Hepatocyte, several erythrocytes in sinusoid, and nucleus of probable endothelial cell on right side of photograph. Six (6) peroxisomes evident in large central hepatocyte. Dilated blebs in RER are pseudo-peroxisomes. Abundant fine granular material, glycogen, in cytosol. Dense mitochondria with some granular deposits and dilated cristae. Poor definition of endothelial cells.
Z15684: Several hepatocytic nuclei present, but poor cytoplasmic margin definition. Some swelling of mitochondria. Dilated blebs in RER. Bile canaliculus in lower left corner. Two (2) peroxisomes in central cell. In adjacent two cells only single peroxisomes are clearly evident.
Z15686: Single hepatocyte surrounded by erythrocytes. No clear definition of endothelial cells. Distended cytosol with glycogen-like granular particles. Abundant mitochondria and RER. Mitochondria have some granular densities and dilated cristae. Dilated blebs in RER. Ten (10) peroxisomes evident.
Z15687: Single hepatocyte. Granulocytic cell (hematopoietic) present in bottom left corner. Distended cytosol with granular material. Dense mitochondria with some granular deposits. Two (2) peroxisomes evident in central hepatocyte.
Z15688: Hepatocyte. Erythroid precursor present in lower left sinusoid. Dilated blebs in RER. Cytosol expanded with fine granular material, probably glycogen. Three (3) peroxisomes present.

Conclusions: Normal hepatocytes. 23/5 = 4.6 peroxisomes per hepatocyte evident. Plasma membranes poorly defined. Dense mitochondria with some granular deposits and dilated cristae. Suboptimal fixation.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-014; EM-99.46

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 18904-1

Tissue: Lung

Treatment Group: 0 mg/kg Control

Block No(s).: 99.46-2

Sex: non applicable

Photo/Negative No(s).: Z15689 - Z15693

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15689: Capillary with three endothelial cell nuclei. In lumen of capillary is a lamellar-like body. Several type 1 pneumocytes (PN1) present surrounding capillary. No pneumocyte lamellar bodies present.
Z15690: Type 2 pneumocyte (PN2) present, containing multiple lamellar bodies (~7). Beneath the PN2 is a capillary containing an erythrocyte, platelet, and endothelial cell nuclei. PN1 to right side of photograph with more translucent cytoplasm.
Z15691: Collapsed alveolar septa. On top is a PN1 with flattened cytoplasm and large round nucleus. Other cells less clearly defined, but appear to be primarily PN1s in collapsed septa. No pneumocyte lamellar bodies evident.
Z15692: Collapsed alveolar septa. On top is a thin-layered PN1, and in the bottom left is larger profile of a PN1. Centrally appears to be a capillary lumen containing some lamellar debris and two leucocytes. Also some lipid debris is present in the capillary lumen. Endothelial cell cytoplasm is evident, but no endothelial cell nucleus. No pneumocyte lamellar bodies identified.
Z15693: Collapsed alveolar septa. At top is a profile of a PN1 in the alveolar space. Beneath it is a thin-layered PN1, and to the left side of photo is a PN1. Subjacent nuclei are probably endothelial cell nuclei. At bottom left is an erythrocyte. Just to the right is a collapsed alveoli and thin-line PN1. No pneumocyte lamellar bodies identified.

Conclusions: Normal lung tissue. Fixation adequate. Only one PN2 identified.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-014; EM-99.46

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 18904-2

Tissue: Liver

Treatment Group: 0 mg/kg/ Control

Block No(s).: 99.46-3

Sex: non applicable

Photo/Negative No(s).: Z15694 - Z15698

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15694: Hepatocyte. Multiple mitochondria, some RER and multiple rounded blebs of RER. Cytoplasm full of granular glycogen. Poor endothelial cell definition in sinusoids. Nucleated erythrocyte in bottom left. Mitochondria appear dense with some granular deposits and dilated cristae. Three (3) peroxisomes identified.
Z15695: Hepatocyte. Dilated RER. Multiple dense mitochondria with granular deposits and dilated cristae. Cytoplasmic margins and endothelial cells poorly defined. Six (6) peroxisomes identified.
Z15696: Hepatocyte. Many dilated blebs of RER. Dense mitochondria with granular deposits and dilated cristae. Top left hepatocyte has swollen, less dense, mitochondria. Twelve (12) peroxisomes identified.
Z15697: Several poorly-fixed hepatocytes. Many light and dark dilated blebs of RER, which are difficult to differentiate from peroxisomes. Five (5) peroxisomes identified in single more-circumscribed hepatocyte.
Z15698: Hepatocyte. Large clear areas in cell contain fine granular material consistent with glycogen. Five (5) peroxisomes evident.

Conclusions: Normal hepatocytes. Suboptimal fixation. 31/5 = 6.2 peroxisomes per cell.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-014; EM-99.46

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 18904-2

Tissue: Lung

Treatment Group: 0 mg/kg Control

Block No(s).: 99.46-4

Sex: non applicable

Photo/Negative No(s).: 15699 - Z15704

Significant Lesions (check one): _____ Yes X No

Interpreting Pathologist (signature and date): _____

Features: Z15699: Alveolus containing several cuboidal pneumocyte cells. The lower cell appears to contain a couple small lamellar bodies, probably a PN2. The other two large cuboidal cells do not contain any lamellar bodies, but appear to be pneumocytes which haven't flattened out into PN1s or are terminal bronchiolar epithelia. At the left and bottom are capillaries lined by endothelial cells. The flattened PN1 at the bottom contains a segment of luminal surface with some dense electron-dense material. Some dilated cristae in mitochondria.
Z15700: Alveolar space with capillary/erythrocyte at left and pneumocytes around top and right. Top left pneumocyte contains three "empty" vacuoles, possibly extruded lamellar bodies. PN1 at right is slightly more electron dense.
Z15701: Multiple PN1s lining alveolar spaced. No lamellar bodies or PN2s evident. Capillary at lower right with endothelial cells.
Z15702: Cell type containing central lamellar body not clearly discernible. It appears to be outside the capillary and endothelial cell at top left, but compressed between the pneumocyte on right and lower central cell. This is an area of collapsed alveolar septa.
Z15703: Alveolus and lining cells. Large PN1 appears to contain a single lamellar body in center of photograph. Capillary and endothelium at left of photograph. Collapsed alveolar septa in bottom center and right. Dilated cristae in some mitochondria.
Z15704: Alveolus with lining pneumocytes. Cell in lower left corner contains partially-empty vacuole containing some lamellar material. Denser cell at center left contains a couple clear vacuoles, although this cell is lined by a flattened PN1.

Conclusions: Normal lung and alveoli. A few lamellar bodies identified.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-014; EM-99.46

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 18912-1

Tissue: Liver

Treatment Group: 0 mg/kg, Control

Block No(s).: 99.46-5

Sex: non applicable

Photo/Negative No(s).: Z15773 - Z15777

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15773: Hepatocyte. Some segments of hematopoietic cells are present in the upper right corner. Endothelial cell details are indistinct, and fixation is poor. There is dilation and blebbing of the RER and some dilation of the nuclear envelope. Six (6) peroxisomes counted.
Z15774: Hepatocyte surrounded by some hematopoietic cells. Marked dilation and blebbing of RER. Four (4) peroxisomes counted.
Z15775: Hepatocyte with canaliculus at the bottom and sinusoidal erythrocyte at top right. Endothelial cells poorly-defined and fixation is suboptimal. Eleven (11) peroxisomes counted.
Z15776: Hepatocyte is poorly-fixed and disrupted. Marked dilation and blebbing of the RER. Mitochondria are dense and contain some granular deposits and dilated cristae. Seven (7) peroxisomes counted.
Z15777: Hepatocyte appears similar to those described above. It is poorly fixed and RER and nuclear envelope are dilated. Seventeen (17) peroxisomes counted.

Conclusions: Suboptimal fixation. Nine (9) peroxisomes/hepatocyte (average of 5 cells)

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-014; EM-99.46

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 18912-1

Tissue: Lung

Treatment Group: 0 mg/kg, Control

Block No(s).: 99.46-6

Sex: non applicable

Photo/Negative No(s).: Z15768 - Z15772

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15768: A row of cuboidal epithelial cells, probably bronchiolar epithelium. The central smaller cell contains several empty vacuoles which may have been lamellar bodies, suggestive of a PN2. Some distended cristae in mitochondria.
Z15769: Again, several cuboidal epithelial cells, consistent with bronchiolar epithelium. The two central cells contain a few lamellar bodies and are probably PN2s. The smaller darker cell appears to be a basal cell.
Z15770: Alveolus with lining cells and underlying collapsed alveolar septa. The small dark lining cell contains four lamellar bodies and is a PN2. The other two lining cells are PN1s.
Z15771: Area seems to be a terminal bronchiole junctioning with an alveolar area with a flattened PN1 (lower right). Center top is a PN2 with five lamellar bodies. It appears to squeeze in between two cuboidal epithelial cells. At the right and left are capillaries. The right one contains a lamellar body in its lumen.
Z15772: Two large cuboidal epithelial cells or pneumocytes and a PN1 lining cell (bottom). Some dilated cristae in mitochondria noted.

Conclusions: Appears normal. A few random PN2s with lamellar bodies noted.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-014; EM-99.46

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 18915-1

Tissue: Liver

Treatment Group: 0 mg/kg, Control

Block No(s).: 99.46-7

Sex: non applicable

Photo/Negative No(s).: Z15763 - Z15767

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15763: Hepatocyte in photograph has a large area of cytoplasm filled with abundant glycogen-like material. Plasma membranes and endothelial cells are poorly-defined due to poor fixation. Mitochondria are dense and contain some dense deposits and dilated cristae. There is dilation of the RER, showing as round blebs on cross-section. A bile canaliculus is present in lower left. Fourteen (14) peroxisomes counted.
Z15764: Hepatocyte, similar to Z15763. Five (5) peroxisomes counted.
Z15765: Hepatocyte. Poor fixation clearly evidenced by loss of endothelial cells lining sinusoids. Eight (8) peroxisomes counted.
Z15766: Six (6) peroxisomes counted. Much of the cytoplasm contains fine dispersed granules, probably mostly glycogen, but also consistent with poor fixation.
Z15767: Hepatocyte similar to those described above. Many dilated blebs of RER. Eleven (11) peroxisomes counted.

Conclusions: Suboptimal fixation of tissue. Number of peroxisomes counted: 8.8/cell (five counted).

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-014; EM-99.46

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 18915-1

Tissue: Lung

Treatment Group: 0 mg/kg, Control

Block No(s).: 99.46-8

Sex: non applicable

Photo/Negative No(s).: Z15758 - 15762

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15758: Collapsed alveolar septa. Air space at bottom is lined by a thin electron-dense cytoplasmic margin containing a few organelles and a large dilated bleb. Two capillaries in the collapsed area contain some lamellar structures free within the lumina. Lamellar bodies within pneumocytes or free in the air spaces are not evident.
Z15759: Alveolus and septa, mostly collapsed. PN1s line air spaces. Capillary at top left appears to contain a lamellar body within the endothelial cell cytoplasm. Smaller dark nucleus in the center appears to be a nucleus of a PN1.
Z15760: Area of collapsed septa, with air space to left. The space is lined by thin margin of PN1. Subjacent to this space is a capillary containing a large lamellar body within the lumen. At top right is a cell, probably a PN2, which contains a single lamellar body in its cytoplasm. The clear cell in the center appears to be a pneumocyte.
Z15761: Photograph contains several capillaries in the collapsed septa. The large lumen at the bottom contains some pale-staining lipid material intermixed with endothelial cell cytoplasm. Air space is lined by flattened PN1 cytoplasm. No lamellar bodies noted in pneumocytes. This profile in lumen may be tubular surfactant (lamellar body).
Z15762: Central dark cell appears to be a PN2 with a few lamellar bodies in its cytoplasm. Flattened PN1 cytoplasm lines the remainder of the air space. Two capillary lumina, dorsal to and to the right of this PN2, contain some lamellar material. A focus of lamellar material is in the airway lumen.

Conclusions: Normal fetal lung. One PN2 was identified with some lamellar bodies. Other lamellar like structures were free within capillary lumina, and a single focus of lamellar material was present in airway lumen.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-014; EM-99.46

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 18915-2

Tissue: Liver

Treatment Group: 0 mg/kg, Control

Block No(s).: 99.46-9

Sex: non applicable

Photo/Negative No(s).: Z15753 - Z15757

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15753: Hepatocyte with numerous dilated blebs of RER present. Some dilatations noted in nuclear envelope. Abundant granular glycogen in cytoplasm. Mitochondria appear dense with some granular densities and some dilated cristae. Nine (9) peroxisomes counted.
Z15754: Hepatocyte surrounded by erythrocytes and hematopoietic cells. Endothelial cells are poorly defined due to poor fixation. Hepatocyte contains many dilated segments and blebs of RER and nuclear envelope. Five (5) peroxisomes counted.
Z15755: Large central hepatocyte with abundant glycogen. Blebbing of RER abundant. Two (2) peroxisomes counted.
Z15756: Field with several hepatocytes, however, only one at top center with nucleus is a complete cell. Cells has numerous dilated blebs of RER, some dark and some light staining. Some dilated cristae noted in mitochondria. Four (4) peroxisomes counted. The cell at lower right appears to have more peroxisomes, but is an incomplete cell for counting.
Z15757: Several hepatocytes, although center cell with nucleus is only complete cell. It has dense mitochondria with granular densities and numerous dilated blebs of RER. Twelve (12) peroxisomes counted.

Conclusions: Average number of peroxisomes = 6.4 (5 cells counted). Suboptimal fixation.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-014; EM-99.46

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 18915-2

Tissue: Lung

Treatment Group: 0 mg/kg, control

Block No(s).: 99.46-10

Sex: non applicable

Photo/Negative No(s).: Z15748 - Z15752

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15748: Two alveoli with intervening septum and capillary. PN1s line the septum, and there is a large cell attached to the right. This cell has minimal cytoplasmic organelles, might be a lymphocyte. Some lamellar material is present within the capillary lumen, but is not present in pneumocytes in this photograph.
Z15049: Alveolus, lining cells, and collapsed septa. Lining pneumocyte contains a single lamellar body in its cytoplasm just beneath the nucleus. At central top are several lamellar bodies with cytoplasm of probably PN2s.
Z15750: Cuboidal epithelium of probably bronchiole. Centrally is a PN2 with 5 lamellar bodies.
Z15751: Alveolus and lining PM1s. At lower right is a capillary with a lamellar body in the lumen of the capillary. At top left, in collapsed septal area, is a PM2 with several lamellar bodies.
Z15752: Alveolus on left with lining pneumocytes is free of lamellar bodies. At top right is a single cell with three vacuoles which appear to have lamellar structures in them. Two capillaries at center and lower right.

Conclusions: Several PN2 and lamellar bodies identified. Some lamellar bodies were in capillary lumina.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-014; EM-99.46

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 18952-1

Tissue: Liver

Treatment Group: 1.6 mg/kg, high-dose

Block No(s).: 99.46-15

Sex: non applicable

Photo/Negative No(s).: Z15722 - Z15726

Significant Lesions (check one): X Yes _____ No

Interpreting Pathologist (signature and date): _____

Features: Z15722: Hepatocyte. Cytoplasm contains abundant fine granular material, glycogen. Some dilated blebs of RER. Mitochondria appear dense with granular deposits and some dilated cristae. Twenty (20) peroxisomes identified. Adjacent endothelial cell is poorly-defined (poor fixation).
Z15723: Similar to Z15722. Numerous round dilated blebs of RER. Bile canaliculus present in bottom of photograph. Ten (10) peroxisomes counted.
Z15724: Sinusoid containing several erythrocytes. Segment of hematopoietic granulocytic cell in top left. Endothelial cell and lipid-containing perisinusoidal cell are poorly fixed. Two incomplete hepatocytes on right. A few peroxisomes are noted, but not counted.
Z15725: Hepatocyte. Bile canaliculus at top; sinusoid in lower right of photograph. Numerous dilated blebs of RER. Fifteen (15) peroxisomes counted.
Z15726: Hepatocyte. Bile canaliculi at top right and left. Numerous, variably-sized dilated blebs of RER. Nineteen (19) peroxisomes counted.

Conclusions: Increased numbers of peroxisomes. Average 16 peroxisomes/hepatocyte (4 cells counted). Suboptimal fixation.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-014; EM-99.46

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 18952-1

Tissue: Lung

Treatment Group: 1.6 mg/kg, high-dose

Block No(s).: 99.46-16

Sex: non applicable

Photo/Negative No(s).: Z15717 - Z15721

Significant Lesions (check one): X Yes _____ No

Interpreting Pathologist (signature and date): _____

Features: 15717: Alveolus with lining cells. Two large PN1s are present and appear to have a PN2 between them. However, a PN1 margin still separates the PN2 from the sinusoid. Several lamellar bodies are present associated with the PN2, and some of them appear to be extracellular. The PN1 on the left contains abundant fine granular material in its cytoplasm, consistent with glycogen.
Z15718: Collapsed area of alveolar septa. Two central cells contain lamellar bodies, three (3) in one, and seven (7) in the other. Both cells appear to be PN2s, although normal pulmonary architecture is unclear because of the collapsed state.
Z15719: Two cells with abundant centrioles appear to represent bronchiolar cells, and the centrioles are associated with cilia. Centrally are two cuboidal cells. One contains multiple (5) lamellar bodies. This cell appears to be a PN2. A large lamellar body is associated with the left cell, but it may be extracellular. Both cells contain abundant granular material, consistent with glycogen.
Z15720: Alveolus and lining cells. Two cells contain lamellar bodies, six in one and eight in the other. Some lamellar material appears to be extracellular.
Z15721: Alveolus, five lining cells, and a capillary in top right of photograph. This is possibly a junction with a terminal bronchiole. Two of the pneumocytes contain multiple lamellar bodies, and appear to be PN2s.

Conclusions: There appear to be increased numbers of PN2s containing lamellar bodies. Some extracellular lamellar material noted.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-014; EM-99.46

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 18952-2

Tissue: Liver

Treatment Group: 1.6 mg/kg, high-dose

Block No(s).: 99.46-17

Sex: non applicable

Photo/Negative No(s).: Z15712 - Z15716

Significant Lesions (check one): X Yes _____ No

Interpreting Pathologist (signature and date): _____

Features: Z15712: Hepatocyte. Poorly-defined sinusoids and endothelium at top right and bottom of photograph. The hepatocyte cytoplasm appears voluminous with abundant fine granular material consistent with glycogen. Mitochondria appear dense and have some granular deposits and dilated cristae. Some dilated blebs of RER. Eight (8) peroxisomes identified.
Z15713: Hepatocyte. Hematopoietic cell to right. Bile canaliculus present in lower right. Abundant fine granular material, glycogen, in cytoplasm. Appear to be increased numbers of peroxisomes. Twenty-seven (27) peroxisomes present.
Z15714: Hepatocyte. Many dilated blebs of RER and abundant glycogen particles in cytoplasm. Fourteen (14) peroxisomes identified in this cell.
Z15715: Hepatocyte. Many dilated blebs of RER and abundant glycogen particles in cytoplasm. Mitochondria with some granular deposits and dilated cristae. Nineteen (19) peroxisomes identified in this cell.
Z15716: Sinusoid with lining endothelial cell. Cellular fixation is poor. Adjacent hepatocytes contain many mitochondria, RER and glycogen-like particles. Dilated blebs of RER are present. Multiple peroxisomes are present, but not counted because whole hepatocytes are not in photograph.

Conclusions: Hepatocytes appear to contain increased numbers of peroxisomes, average 17/hepatocyte (4 cells counted). Cells contain abundant glycogen. Suboptimal cellular fixation.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-014; EM-99.46

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 18952-2

Tissue: Lung

Treatment Group: 1.6 mg/kg, high-dose

Block No(s).: 99.46-18

Sex: non applicable

Photo/Negative No(s).: Z15707 - Z15711

Significant Lesions (check one): X Yes _____ No

Interpreting Pathologist (signature and date): _____

Features: 15707: Single PN2 lining alveolus. Cell contains multiple mitochondria around the nucleus, and also multiple clear vacuoles, which are mostly empty of contents. These were probably lamellar bodies which were extruded into the alveolar space. These vacuoles are lined by a single membrane, whereas the mitochondria have a double membrane.
15708: Collapsed alveolar septa. A thin layered PN1 covers the surface. Beneath is an endothelial cell with many pinocytotic vesicles, one a single lamellar body. Centrally is an area of flattened basement membrane material containing many collagen fibrils. A dark cell is present in the upper right, which contains many mitochondria. To the left of this cell are two lamellar bodies, although they appear to be in a cytoplasmic extension of an unidentified cell.
Z15709: A nucleated PN2 containing multiple lamellar bodies (5) appears to be overlain by a PN1 lining the alveolus.
Z15710: Alveolar space in top right is lined by a thin PN1 cell. Adjacent to this PN1 and covered by it's cytoplasm is an extracellular area with several (3) lamellar bodies. A capillary is dorsal containing an erythrocyte and endothelial cell. Several cells within collapsed septa are not clearly identifiable as to cell type.
Z15711: A single dark PN2 is squeezed between two PN1s. Its cytoplasm contains several empty vacuoles, which have apparently extruded lamellar bodies. To the right of this cell are two large lamellar bodies within some lipid-like material. These bodies may be in the adjacent PN1, macrophage, or may be extracellular. A small capillary is in the lower right margin of the photograph.

Conclusions: There appear to be increased numbers of type II pneumocytes (PN2s), and more lamellar bodies were seen in this sample. Otherwise, cellular morphology appeared essentially normal. Fixation appeared satisfactory.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-014; EM-99.46

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 18956-1

Tissue: Liver

Treatment Group: 1.6 mg/kg, high-dose

Block No(s).: 99.46-13

Sex: non applicable

Photo/Negative No(s).: Z15732 - Z15736

Significant Lesions (check one): X Yes _____ No

Interpreting Pathologist (signature and date): _____

Features: Z15732: Hepatic sinusoid containing nucleated erythroycte and a couple mature erythrocytes. Some lamellar debris is present in the sinusoid. Two endothelial cell nuclei are present. There are no complete hepatocytes in this photograph.
Z15733: Hepatocyte contains abundant granular particles consistent with glycogen, and numerous RER palisades. Mitochondria appear dense and have some granular deposits and dilated cristae. Eleven (11) peroxisomes counted. A bile canaliculus is present between two hepatocytes.
Z15734: Hepatocyte. Similar to Z15733. Numerous dilated blebs of RER are present. Twenty-four (24) peroxisomes.
Z15735: Hepatocyte with similar morphology as described for above cells. Sixteen (16) peroxisomes counted.
Z15736: Hepatocyte. Dilated blebs of RER present. Mitochondria are dense with granular deposits and dilated cristae. Eighteen (18) peroxisomes.

Conclusions: Increased numbers of peroxisomes per hepatocyte. 17.25 peroxisomes per hepatocyte (average of four counted cells). Suboptimal fixation.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-014; EM-99.46

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 18956-1

Tissue: Lung

Treatment Group: 1.6 mg/kg, high-dose

Block No(s).: 99.46-14

Sex: non applicable

Photo/Negative No(s).: Z15727 - Z15731

Significant Lesions (check one): X Yes _____ No

Interpreting Pathologist (signature and date): _____

Features: 15727: Alveolus with adjacent collapsed septa. The two bottom pneumocytes are PN2 with lamellar bodies. Some of the bodies are partially empty, and in one cell appear to be extruding material extracellularly with other lipid material. At the top is a large PN1. At the left is a capillary with a nucleated erythrocyte.
Z15728: Collapsed alveolar septa. Several cells contain lamellar bodies. At left one lamellar body appears to be within the lumen of a capillary.
Z15729: Somewhat T-shaped capillary containing an electron-dense erythrocyte. The endothelial cell nucleus is ventral to the erythrocyte. Within the lumen of the capillary are several lamellar bodies. At left of field is the thin cytoplasmic lining of a PN1. The other cells appear to be sections through pneumocytes at various angles.
Z15730: Alveolar lumen and lining cells. Centrally is a small PN2 containing a couple small lamellar bodies next to its nucleus. The dark-staining cytoplasm to the right of this cell appears to be an extension from an alveolar macrophage. To the left are a couple pneumocytes, and they contain a couple lamellar bodies.
Z15731: Alveolar lumen and lining cells. Top left cell is a PN2 with two lamellar bodies. A right central, pale-staining, pneumocyte also contains several small lamellar bodies. The septa are collapsed in this area.

Conclusions: Increased number of pneumocytes containing lamellar bodies. Some lamellar bodies noted in capillaries.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-014; EM-99.46

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 18973-1

Tissue: Liver

Treatment Group: 1.6 mg/kg, high-dose

Block No(s).: 99.46-11

Sex: non applicable

Photo/Negative No(s).: Z15742 - Z15747

Significant Lesions (check one): X Yes _____ No

Interpreting Pathologist (signature and date): _____

Features: Z15742: Hepatocyte contains abundant fine granular material consistent with glycogen in the cytoplasm. There are numerous dilated blebs of RER on cross section. Mitochondria appear dense and have some granular deposits. Seventeen (17) peroxisomes counted. Some lamellar material noted extracellularly and possibly within clear spaces in the left portion of the hepatocyte.
Z15743: Hepatocyte, overall similar to Z15742, although fixation appears better. Nine (9) peroxisomes counted. Lamellar material at top appears to be extracellular.
Z15744: Hepatocyte. At left is a hematopoietic cell in sinusoid and at upper right appears to be a dilated bile canaliculus. Abundant area of glycogen in cytoplasm. Nineteen (19) peroxisomes counted.
Z15745: Sinusoid, endothelial cell and incomplete portions of a couple hepatocytes. Centrally is a clear cytoplasmic area with many dilated blebs of RER. A few peroxisomes are present. No peroxisome count made.
Z1546: Hepatocyte contains abundant fine granular material consistent with glycogen in the cytoplasm. There are numerous dilated blebs of RER on cross section. Mitochondria appear dense and have some granular deposits and some dilated cristae. Eleven (11) peroxisomes counted.
Z15747: No photograph. Negative was too dark. With five photographs already evaluated, it is not necessary to retake or try to print this image.

Conclusions: Appear to be increased peroxisomes per hepatocyte. Average 14/cell (four cells counted. Suboptimal fixation.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-014; EM-99.46

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 18973-1

Tissue: Lung

Treatment Group: 1.6 mg/kg, high-dose

Block No(s).: 99.46-12

Sex: non applicable

Photo/Negative No(s).: Z15737 - Z15741

Significant Lesions (check one): X Yes _____ No

Interpreting Pathologist (signature and date): _____

Features: Z15737: Collapsed alveolar septa. Centrally is a PN2 with approximately eight lamellar bodies, of which several appear to be releasing their contents into the extracellular space. Ventrally are also segments of a cell's cytoplasm that appears to contain some lamellar body vacuoles. A couple PN1s are present adjacent to the PN2, and a capillary with erythrocyte and endothelial cell is present in lower left central area of photograph.
Z15738: Alveolus with lining cells. The large nucleus belongs to a PN1 whose cytoplasm lines the air space. Beneath this cell and just to the right are several lamellar bodies, although it's in a subjacent capillary. To the middle left is a capillary with an eyrthrocyte that does contain some lamellar debris in the lumen.
Z15739: Alveolus and collapsed septa. Similar to Z15738, some lamellar bodies appear to be within the lumen of a capillary. PN1s line the alveolar space.
Z15740: Large capillary with several erythrocytes to the right. Left of this is a cellular extension, probably a PN2, that contains a distinct lamellar body. A thin layer of PN1 lines the alveolar space.
Z15741: Alveolar space contains abundant lamellar material. Several PN1s are present along the lining, but no PN2 are present. Lamellar bodies are present in one capillary lumen and in some interstitial spaces in the right side of the photograph.

Conclusions: Appear to be increased lamellar bodies in the tissue compared with control sample, although many were in capillary lumina and some in alveolar and interstitial spaces.

III. Transmission Electron Micrographs

NOTE:

The original glossy figure photographs (Figures 1- 12) were delivered to Dr. Marvin T. Case with the draft pathology report on March 19, 1999.

Figure Legends

Figure 1. Liver. Hepatocyte showing normal cytoplasmic organelles. White spots within mitochondria represent some dilatation of cristae. Some peroxisomes are identified. To the right is an endothelial cell and erythrocytes of adjacent sinusoid. Animal No. 18904-1, 0 mg/kg/day (control), 11,200X magnification.

Figure 2. Liver. Hepatocyte. Dilatation of nuclear envelope and rough endoplasmic reticulum (blebbing) indicates suboptimal fixation. Mitochondria are dense and show some granular deposits and dilated cristae. Some representative peroxisomes are labeled. Hematopoietic cells are present in sinusoid at upper right of photograph. Animal No. 18912-1, 0 mg/kg/day (control), 11,200X magnification.

Figure 3. Liver. Cellular morphology is similar to Figure 2. Some peroxisomes are labeled, and appear more numerous than in controls. A bile canaliculus is present in upper right of photograph and hematopoietic cells are present in sinusoid at upper left. Animal No. 18952-2, 1.6 mg/kg/day (high-dose), 11,200X magnification.

Figure 4. Liver. Dilatation of rough endoplasmic reticulum is evident. Some peroxisomes, increased in number, are labeled. Animal No.18956-1, 1.6 mg/kg/day (high-dose), 11,200X magnification.

Figure 5. Liver. Hepatocyte demonstrating somewhat better fixation with more even dispersion of organelles. Clear space at top of cell, which contains some membranous debris, appears to be extracellular in the perisinusoidal space. Animal No. 18973-1, 1.6 mg/kg/day (high-dose), 11,200X magnification.

Figure 6. Lung. Type II pneumocyte is present along the alveolar wall, adjacent to type I pneumocyte. Lamellar bodies within the cytoplasm identify this cells as a type II pneumocyte. Animal No. 18904-1, 0 mg/kg/day (control), 15,680X magnification.

Figure 7. Lung. Three cuboidal pneumocytes line this airway space. A flattened type I pneumocyte is evident along the ventral portion of the airway space. Two small lamellar bodies in one cuboidal cell suggest this is a type II pneumocyte which has secreted most of its lamellar bodies and is destined to become a type I pneumocyte. Animal No. 18904-2, 0 mg/kg/day (control), 11,200X magnification.

Figure 8. Lung. A more densely-staining type II pneumocyte, containing two lamellar bodies, appears squeezed between two type I pneumocytes. Some lamellar material is also present within the capillary lumen of the septal wall both above and to the right of the type II pneumocyte. Animal No. 18915-1, 0 mg/kg/day (control), 11,200X magnification.

Figure 9. Lung. Dense-staining cell is a type II pneumocyte positioned between two type I pneumocytes. Four distinct lamellar bodies are present in the cytoplasm of the type II pneumocyte, although the lamellar material is partially washed out in these vacuoles. To the right of this cell are two dark lamellar-type bodies surrounded by some lipid. This appears to be within a cell in a collapsed area of septa, and may be a macrophage. Animal No. 18952-2, 1.6 mg/kg/day (high-dose), 11,200X magnification.

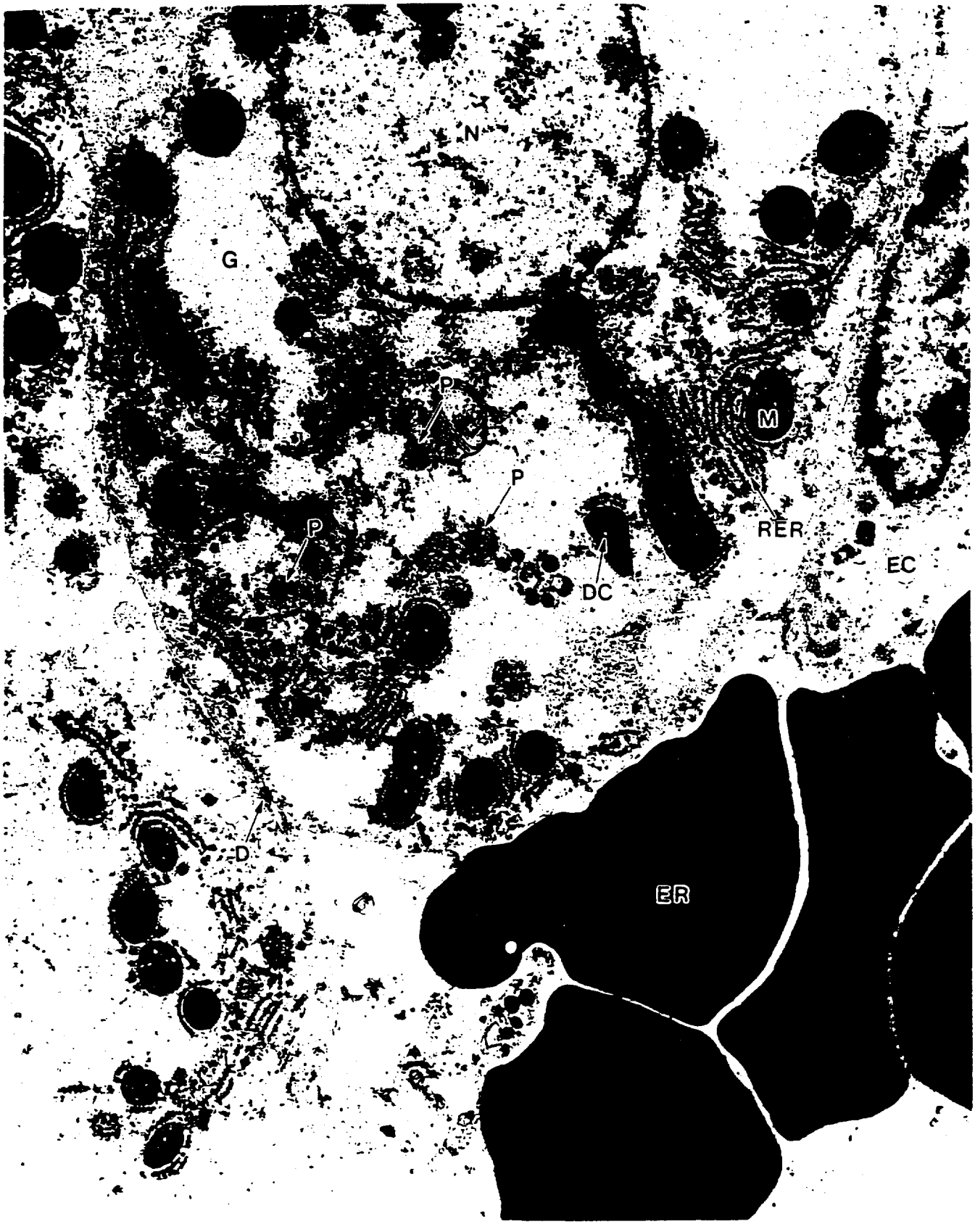
Figure 10. Lung. Collapsed area of septa showing two type II pneumocytes containing lamellar bodies. A type I pneumocyte is to the left of these cells. Capillaries and adjacent alveolar cells are present dorsally and to the right of the photograph. Animal No. 18952-1, 1.6 mg/kg/day (high-dose), 11,200X magnification.

Figure 11. Lung. Centrally is a cell containing several lamellar-like structures which appears to be a type II pneumocyte. Glycogen-like material appears to fill much of the cytoplasm. Adjacent cells to the right contain centrioles and represent ciliated bronchiolar cells. Cuboidal epithelial cells are to the left and ventral to the type II pneumocyte. Animal No. 18952-1, 1.6 mg/kg/day (high-dose), 11,200X magnification.

Figure 12. Lung. Alveolar space contains abundant lamellar-like material, which is consistent with surfactant secreted from type II pneumocytes. A type I pneumocyte lines the space on the left and right. Two cuboidal cells containing glycogen-like granular material appear to be pneumocytes, probably type IIs which have released their lamellar bodies. Animal No. 18973-1, 1.6 mg/kg/day (high-dose), 11,200X magnification.

Index of Labels for Ultrastructural Structures

Abbreviation	Structure
A	Alveolar space
BC	Bile canaliculus
BE	Bronchiolar epithelium
CL	Capillary lumen
Cap	Capillary
CN	Centrioles
CP	Cuboidal pneumocyte
D	Desmosome
DD	Dense deposits
DC	Dilated cristae
DN	Dilated nuclear envelope
DR	Dilated RER
EC	Endothelial cell
ER	Erythrocyte
G	Glycogen
HC	Hematopoietic cells
L	Lipid droplet
LB	Lamellar body
M	Mitochondria
N	Nucleus
P	Peroxisome
PN1	Type I pneumocyte
PN2	Type II pneumocyte
PM	Plasma membrane
RER	Rough endoplasmic reticulum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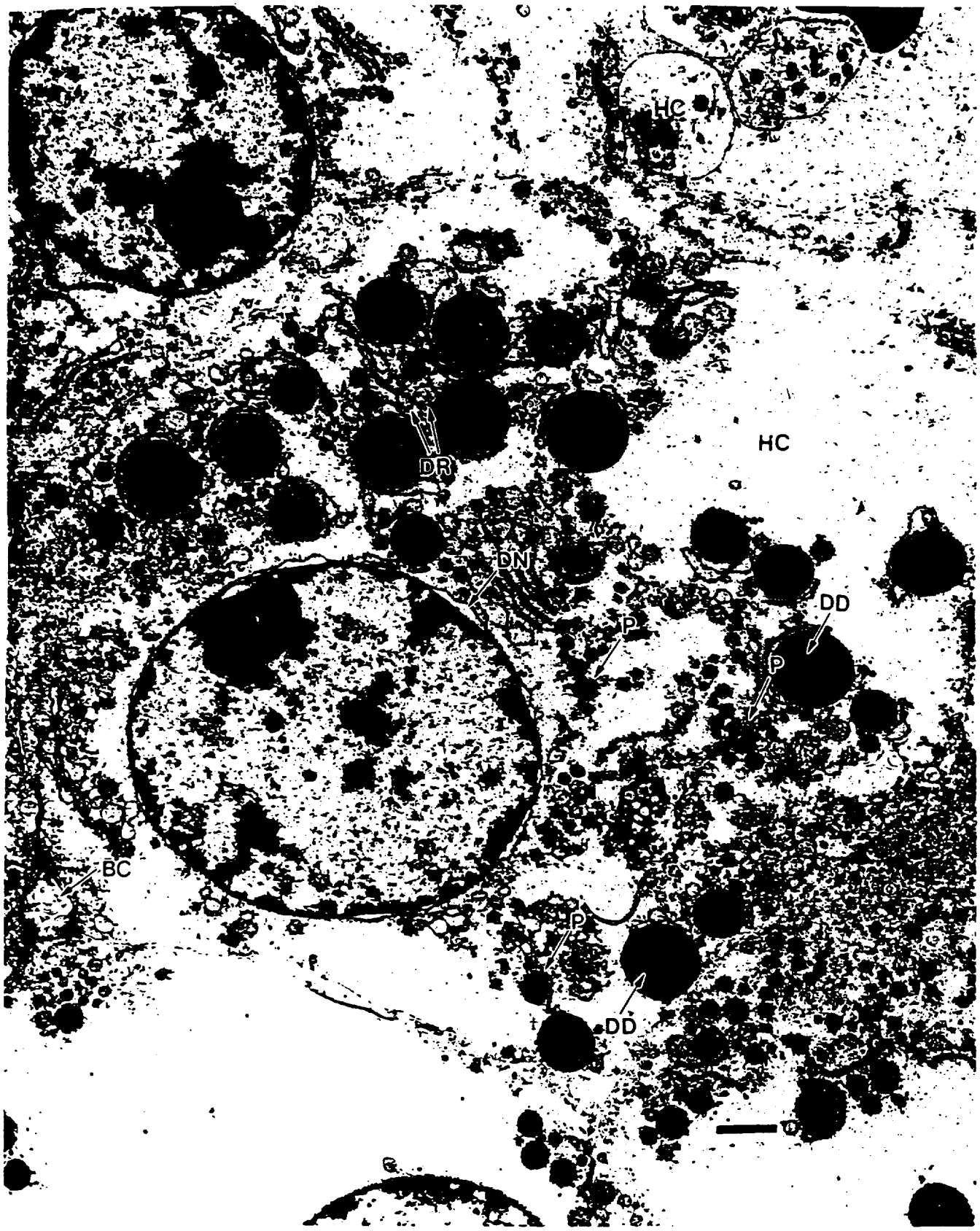
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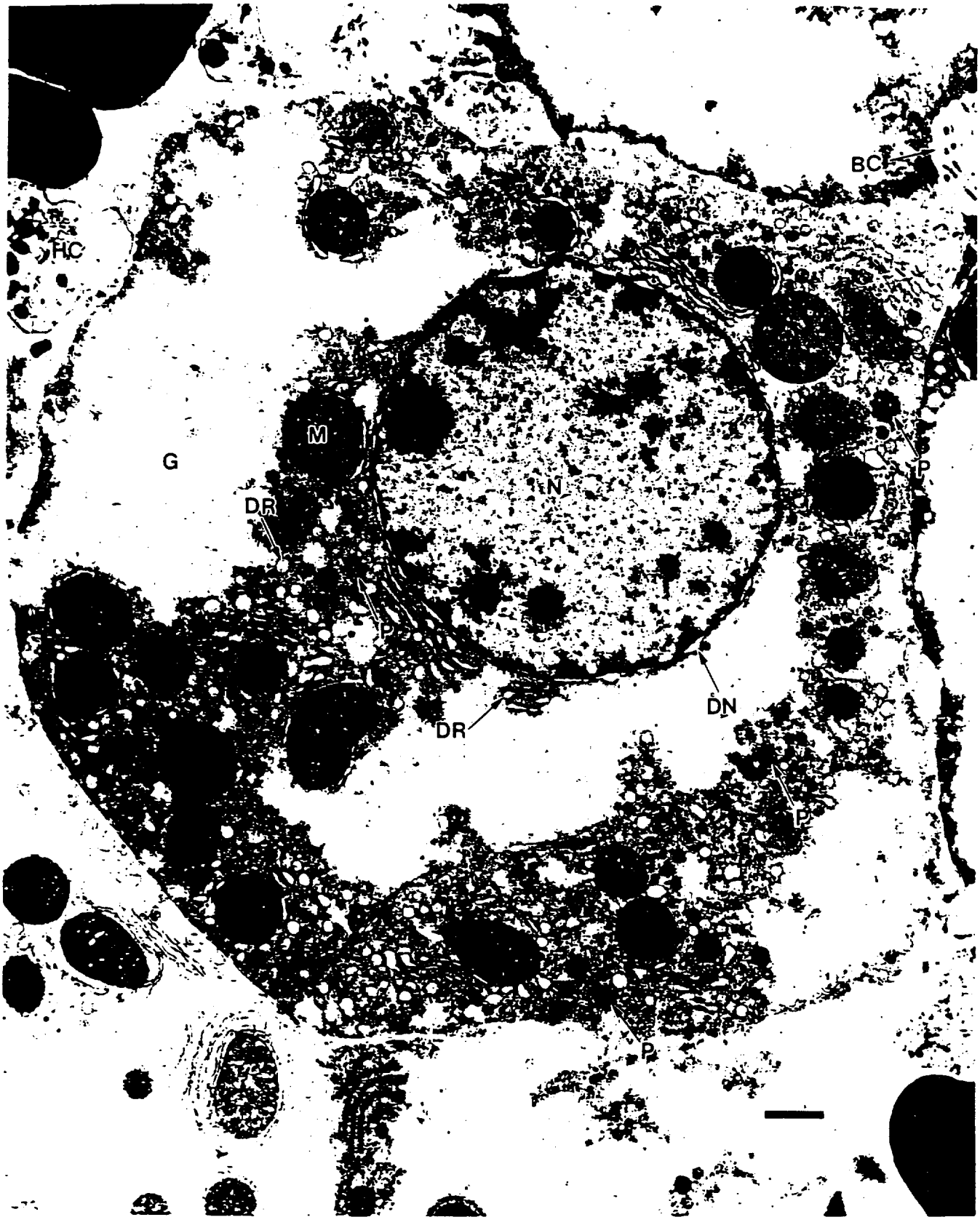
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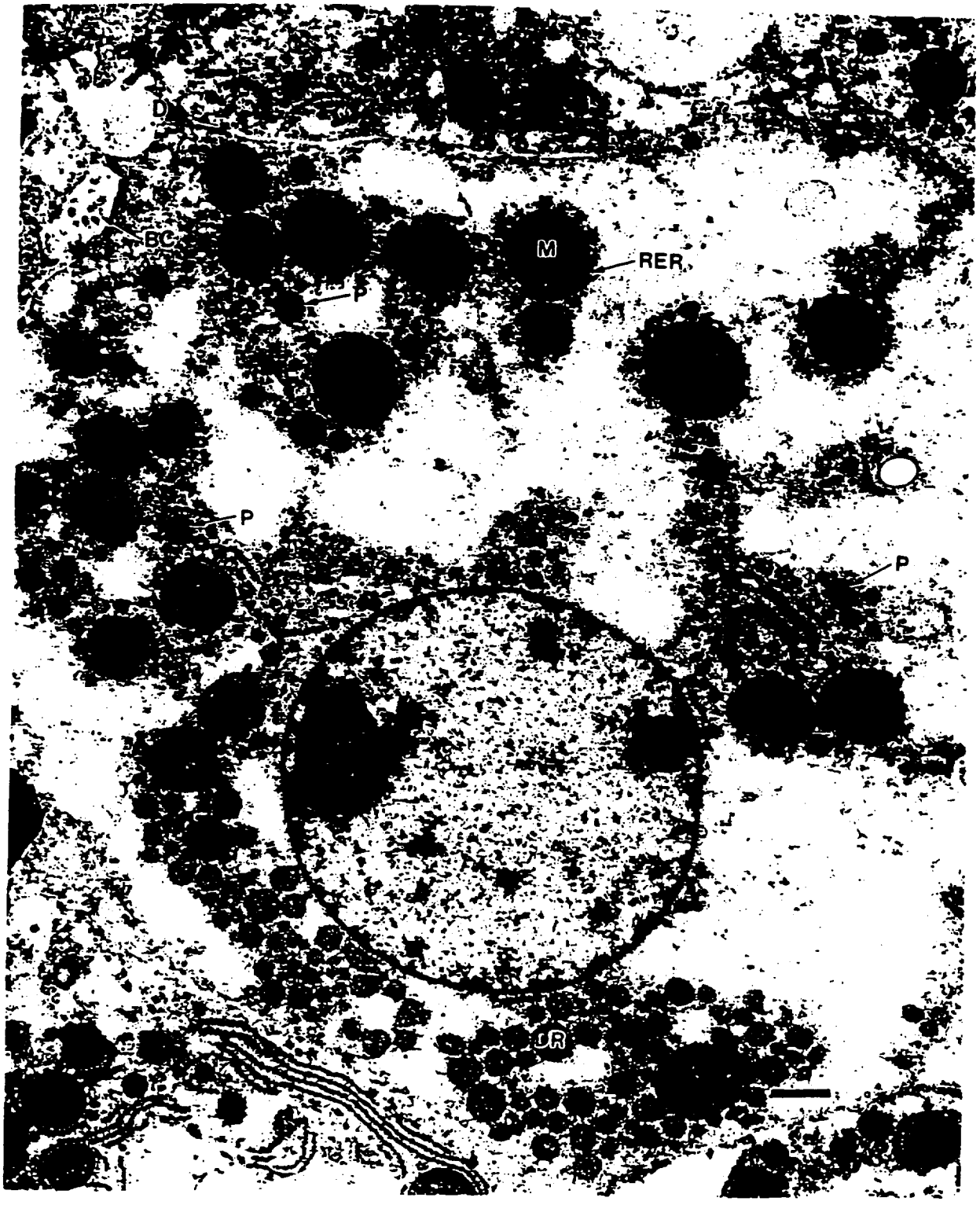
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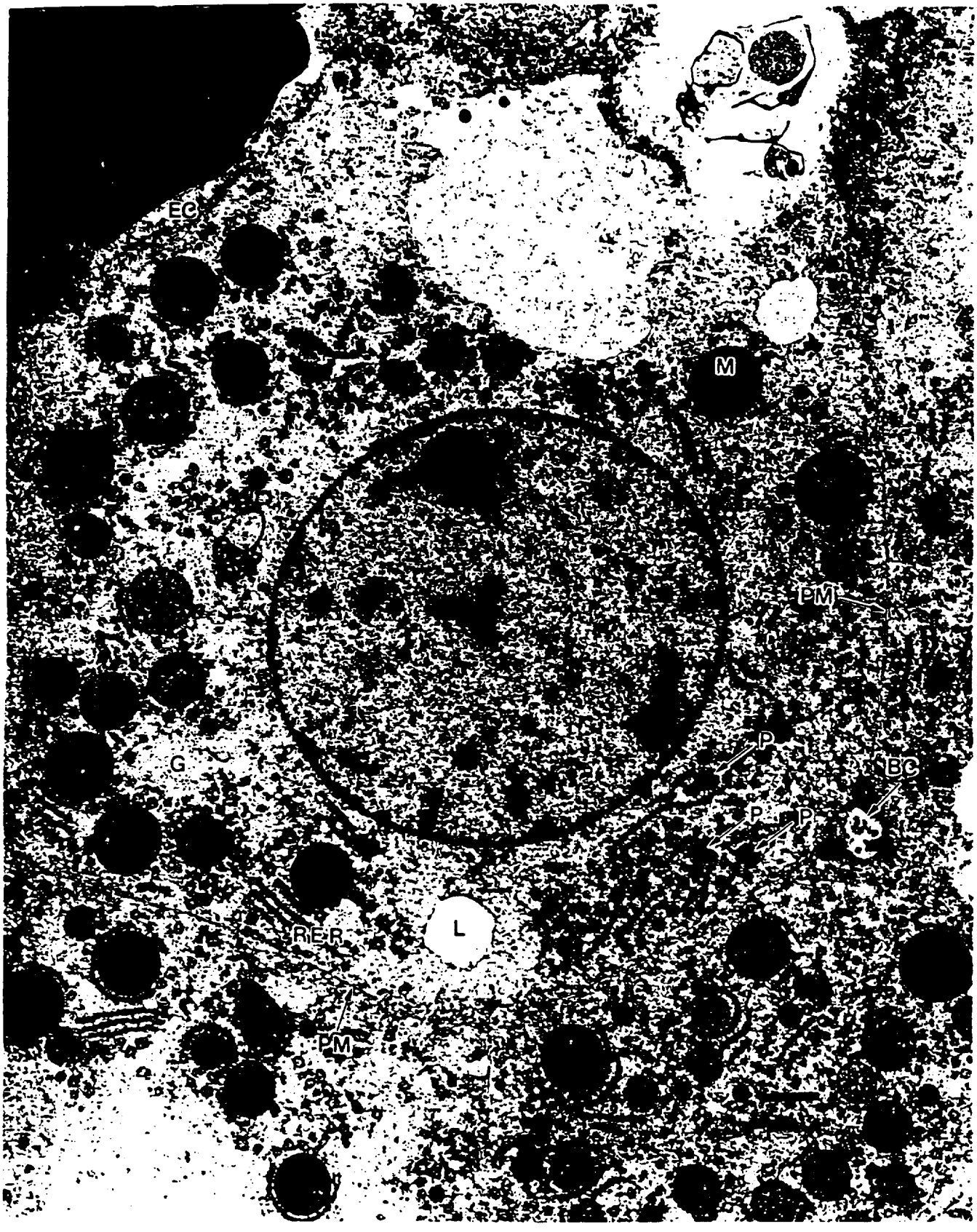
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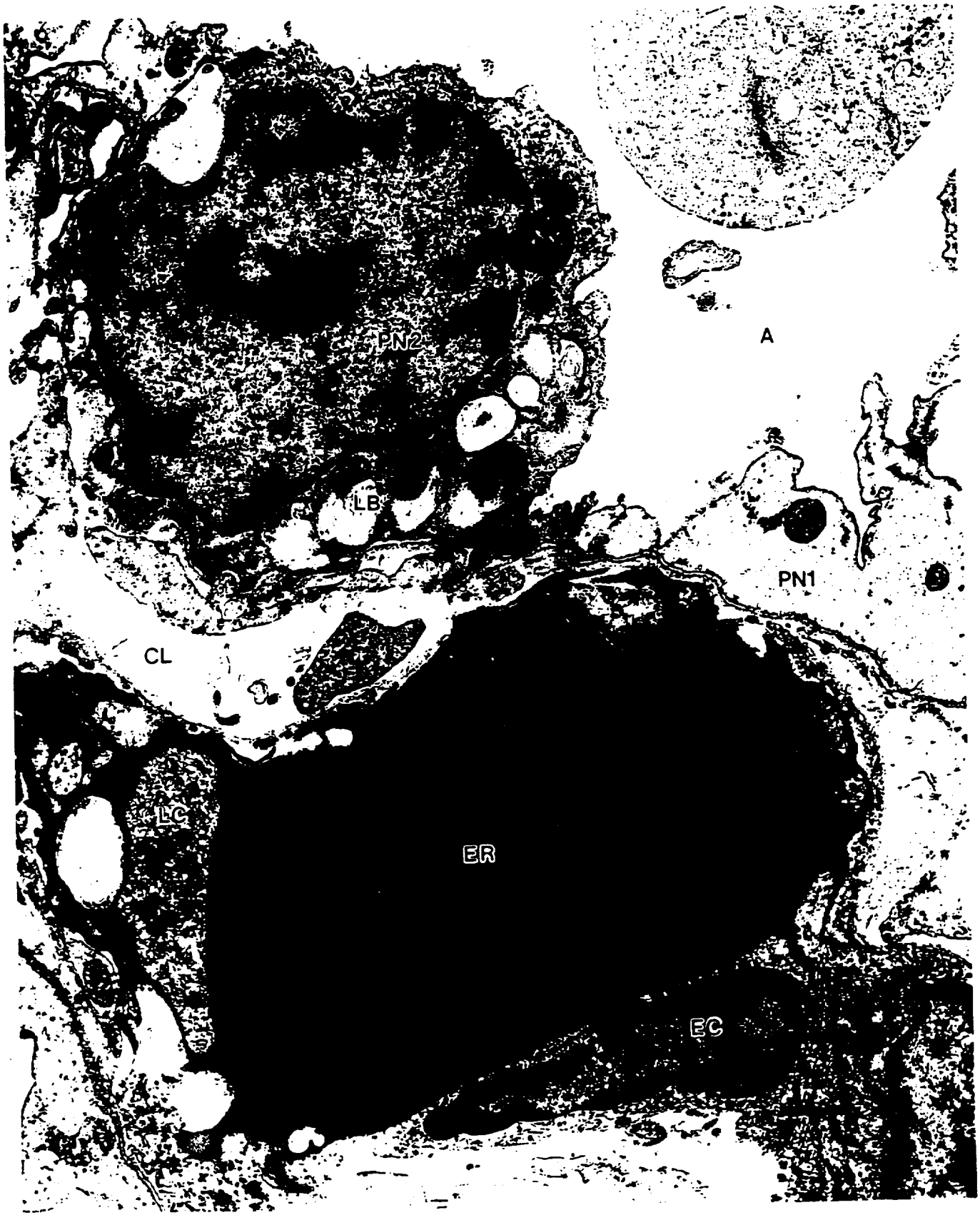
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PN1
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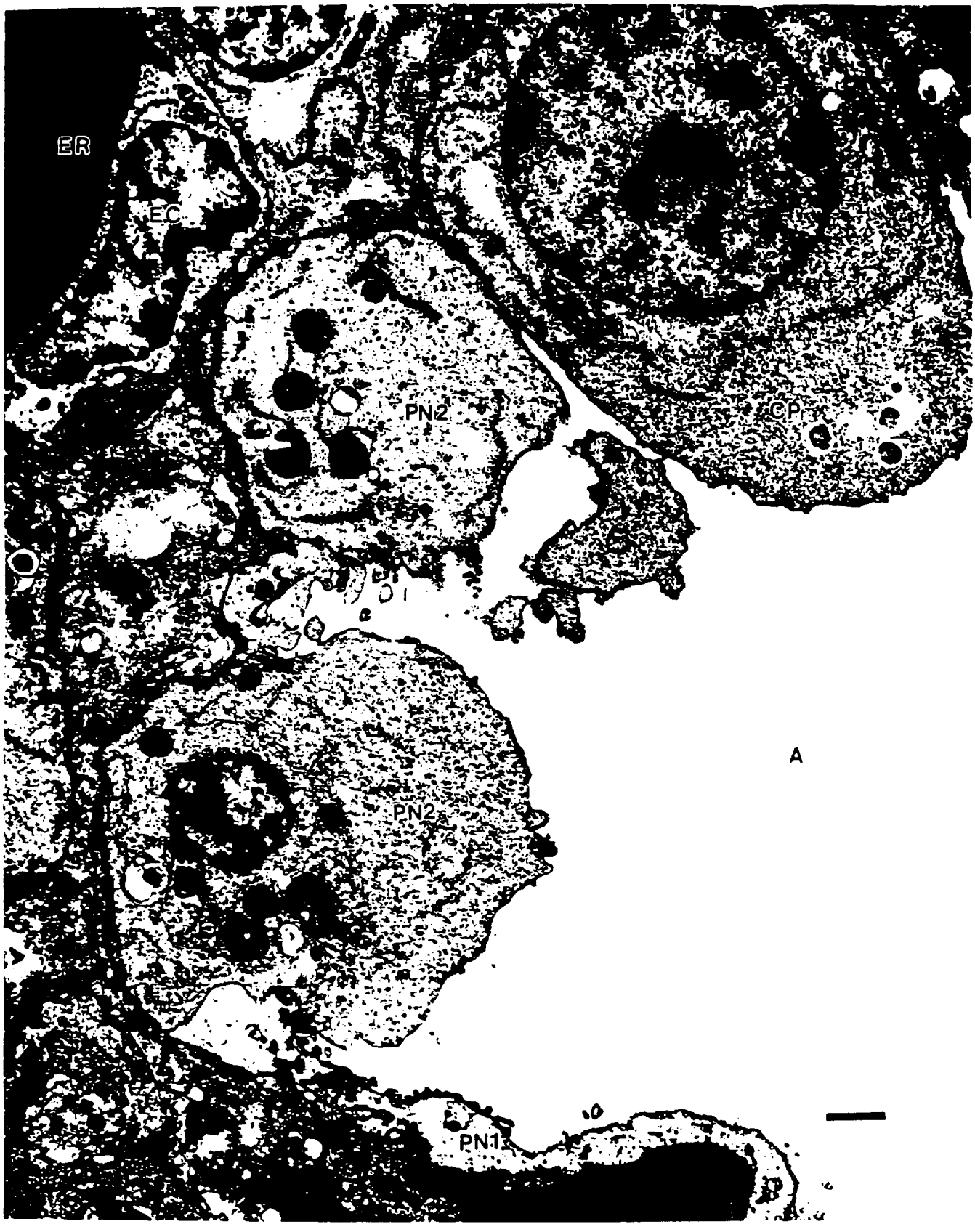
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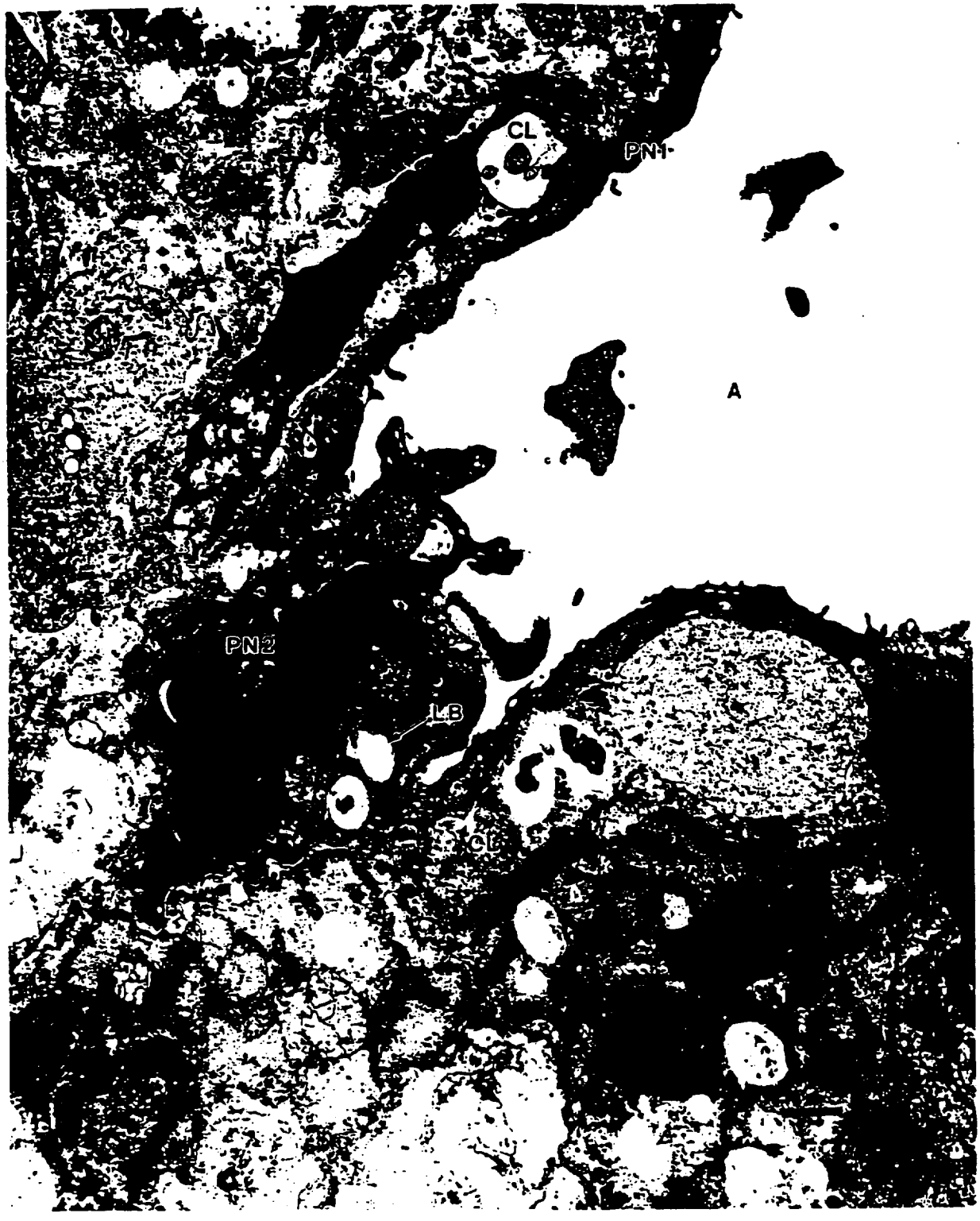
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PN2
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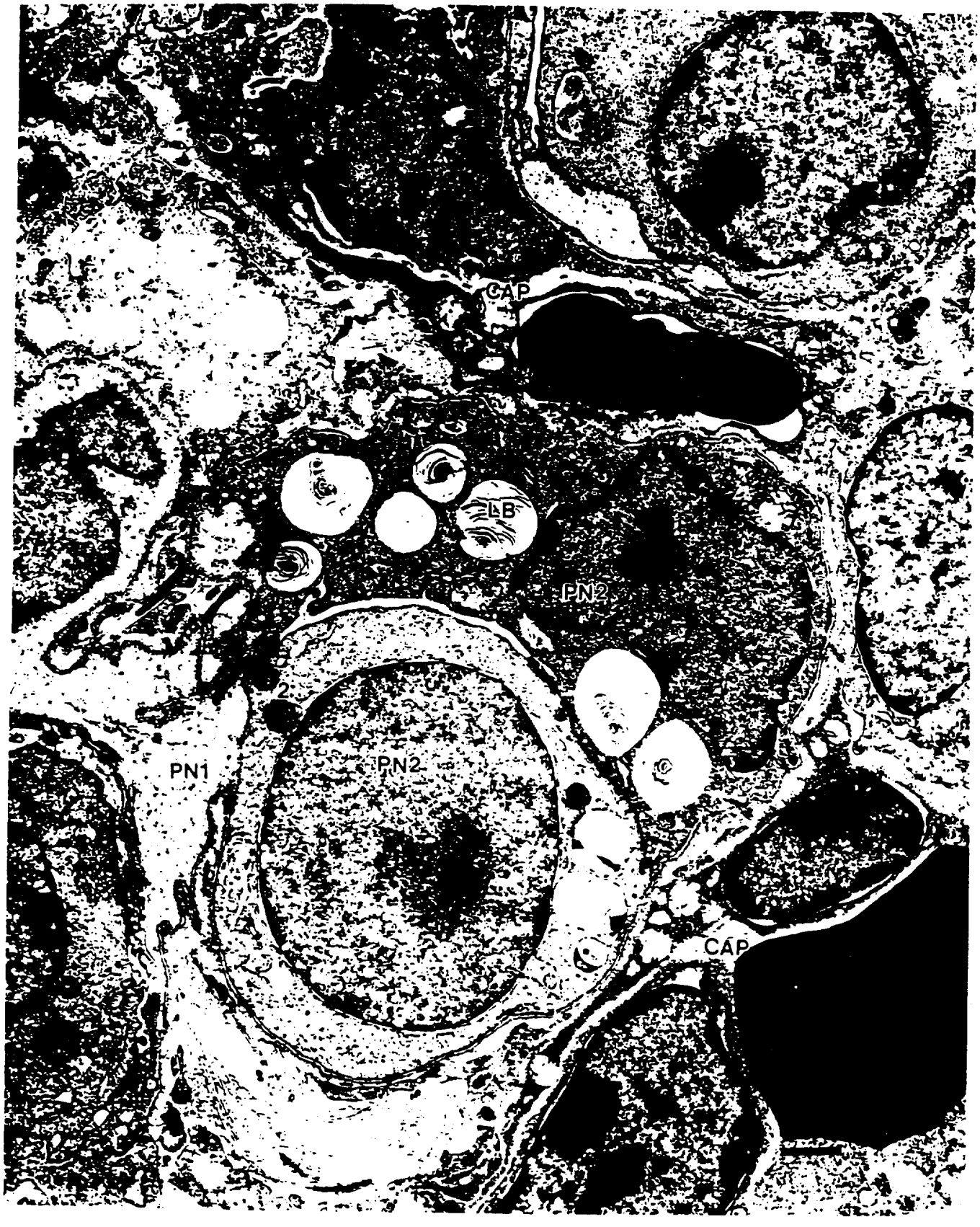
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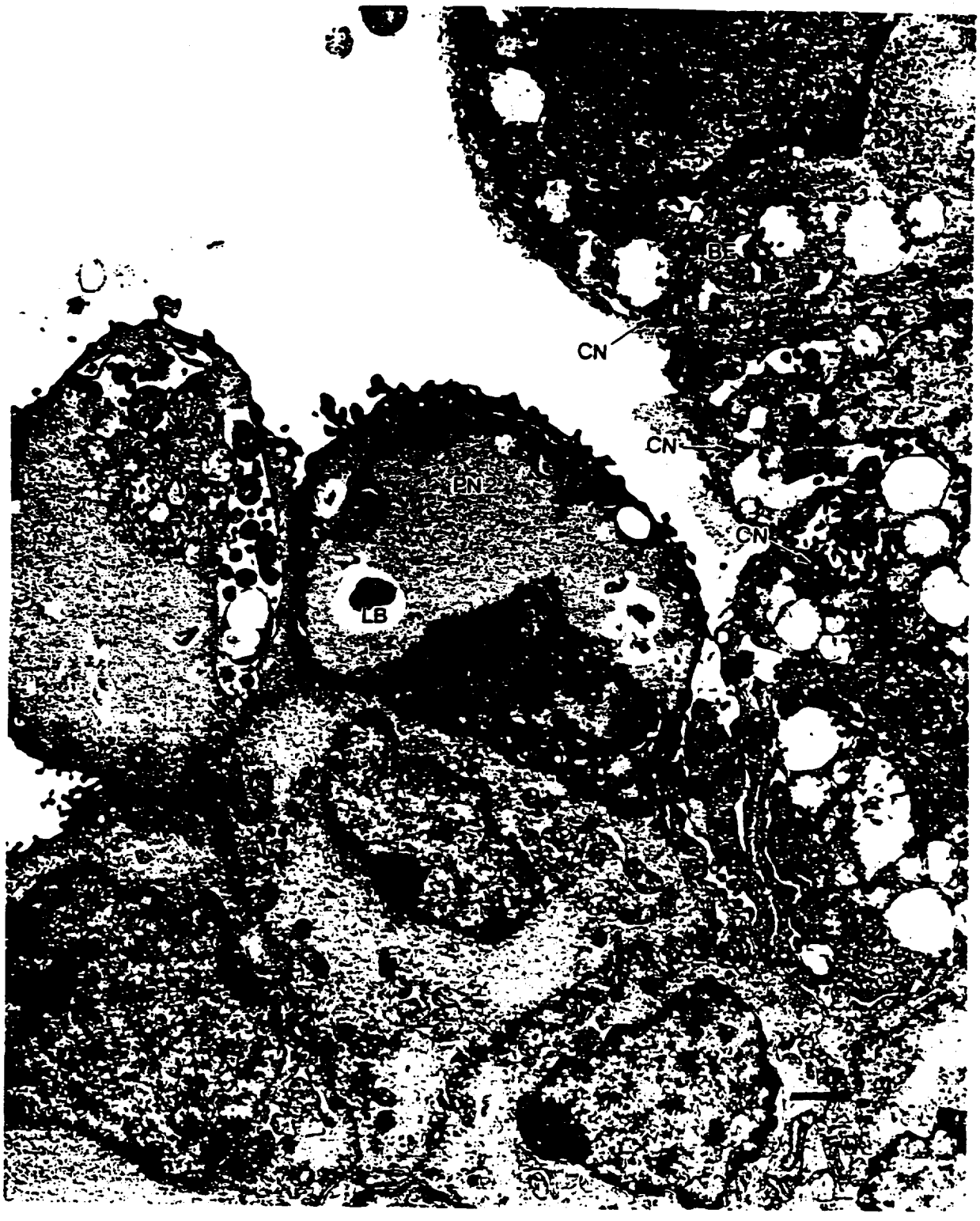
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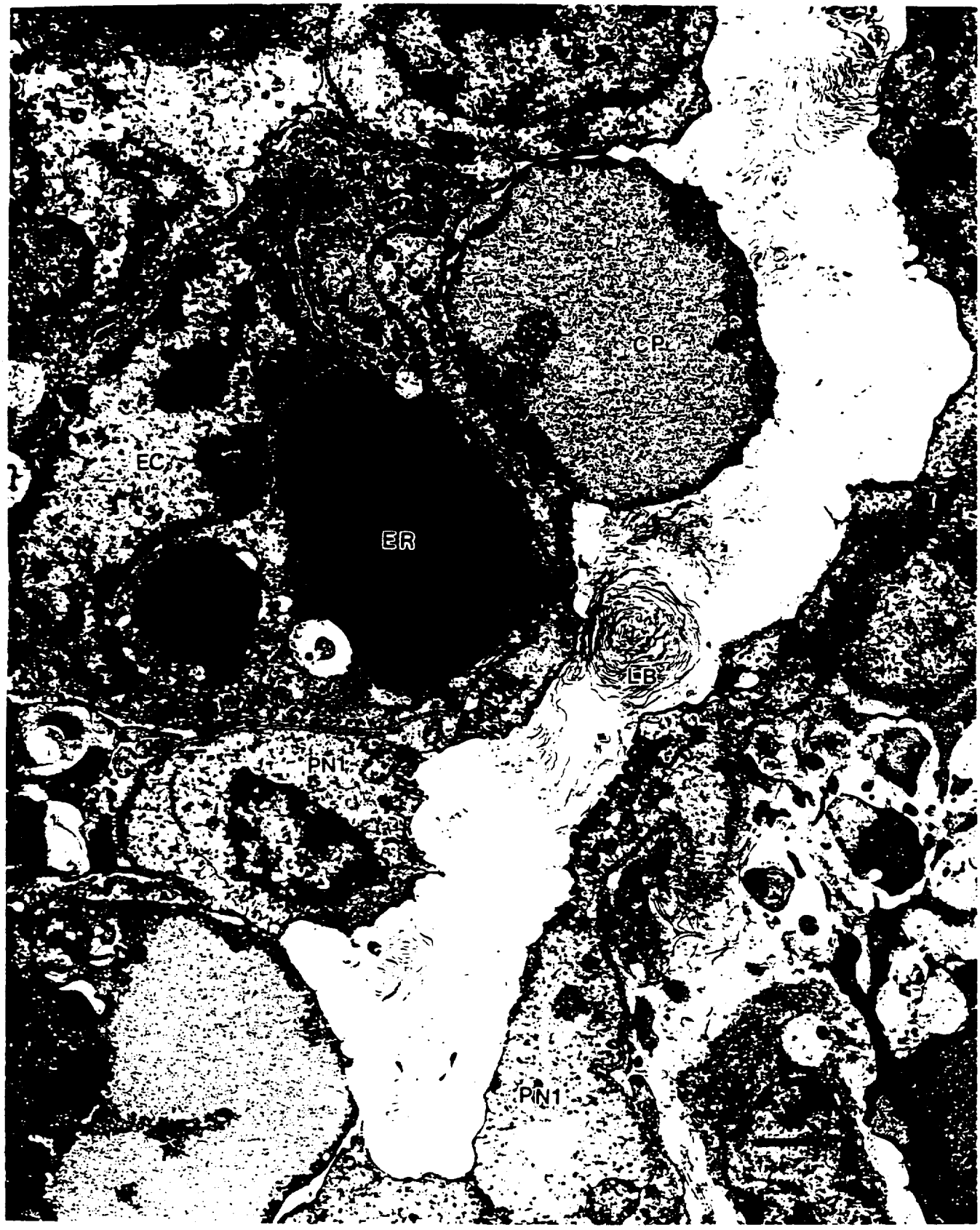
CP
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PN1

IV. Quality Assurance Statement

Pathology Associates International
A Company of Science Applications International Corporation
An Employee-Owned Company

QUALITY ASSURANCE STATEMENT

This electron microscopy study has been inspected and audited by the Quality Assurance Unit as required by the Good Laboratory Practices Regulations promulgated by the U.S. Food and Drug Administration. PAI has a functioning and responsive Quality Assurance Unit which reports directly to management. The following is a record of inspections/audits and their resulting reports:

Date of Inspection	Phase Inspected	Date Findings Reported to Management and Study Director
2/18, 19/99	Processing and Embedding	2/19/99
3/16/99	Data Audit	3/17/99
3/17/99	Draft Report Audit	3/17/99
4/5/99	Final Report Audit	4/5/99

Jeanne deWard, B.S., RQAP-GLP
Quality Assurance Specialist

4/5/99
Date

Sponsor: 3M Corporate Toxicology

Test Article: PFOS

Study Number: 418-014, PAI Study EM-99.46

APPENDIX G

STATEMENT OF THE STUDY DIRECTOR

PRIMEDICA

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

PROTOCOL 418-014: ORAL (GAVAGE) CROSS-FOSTERING STUDY OF PFOS IN RATS
SPONSOR'S STUDY NUMBER: T-6295.13

STATEMENT OF THE STUDY DIRECTOR

This final report accurately reflects the raw data obtained during the performance of the study. No deviations from the U.S. Food and Drug Administration (FDA) Good Laboratory Practice Regulations; Final Rule[a], the Japanese Ministry of Health and Welfare (MHW) *Good Laboratory Practice Standard for Safety Studies on Drugs*[b] and the European Economic Community (EEC) *Council decision on 28 July 1989 on the acceptance by the European Economic Community of an OECD decision/recommendation on compliance with principles of good laboratory practice*[c] occurred that affected the quality or integrity of the study.

23 JUL - 99

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

---

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

b. Japanese Ministry of Health and Welfare (1988). *Good Laboratory Practice Standard for Safety Studies on Drugs*, MHW Ordinance Number 21, March 26, 1997.

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

APPENDIX H

QUALITY ASSURANCE UNIT FINAL REPORT STATEMENT

PRIMEDICA

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

QUALITY ASSURANCE UNIT FINAL REPORT STATEMENT

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

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

Protocol 418-014: Oral (Gavage) Cross-Fostering Study of PFOS in Rats
Sponsor's Study Number: T-6295.13

The draft protocol for this study was audited for adherence to U.S. Food and Drug Administration (FDA) Good Laboratory Practice Regulations, Japanese Ministry of Health and Welfare (MHW); Good Laboratory Practice Standard for Safety Studies on Drugs, and European Economic Community (1989) council decision on 28 July 1989 on the acceptance by the European Economic Community of an OECD decision/recommendation on compliance with principles of good laboratory practice on 19 OCT 98.

Critical phases of this study were inspected nine times; study information and raw data were audited twice (see tables 1 and 2 for dates and phases/data).

The draft final report and the raw data for this study were compared and audited for accuracy, for adherence to protocol requirements, and for adherence to U.S. Food and Drug Administration (FDA) Good Laboratory Practice Regulations, Japanese Ministry of Health and Welfare (MHW); Good Laboratory Practice Standard for Safety Studies on Drugs, and European Economic Community (1989) council decision on 28 July 1989 on the acceptance by the European Economic Community of an OECD decision/recommendation on compliance with principles of good laboratory practice between 21 MAY 99 and 10 JUN 99, and for revisions requested by the Sponsor on 20 JUL 99, 22 JUL 99, and for finalization on 23 JUL 99.

This study was conducted according to U.S. Food and Drug Administration (FDA) Good Laboratory Practice Regulations, Japanese Ministry of Health and Welfare (MHW); Good Laboratory Practice Standard for Safety Studies on Drugs, and European Economic Community (1989) council decision on 28 July 1989 on the acceptance by the European Economic Community of an OECD decision/recommendation on compliance with principles of good laboratory practice.

Nancy J. Gongliewski 23Jul99

Nancy J. Gongliewski Date
Quality Assurance Manager

Heather L. Rabuttino 23Jul 99

Heather L. Rabuttino, M.S. Date
Quality Assurance Supervisor
and Principal Auditor

TABLE 1

CRITICAL PHASES INSPECTED

Test Article Administration - Gavage

Date of inspection: 03 NOV 98

Date results reported to the Study Director and Management: 06 NOV 98

Test Article Preparation

Date of inspection: 03 NOV 98

Date results reported to the Study Director and Management: 06 NOV 98

Cohabitation

Date of inspection: 17 DEC 98

Date results reported to the Study Director and Management: 18 DEC 98

Natural Delivery/Litter Observations

Date of inspection: 06 JAN 99

Date results reported to the Study Director and Management: 19 JAN 99

Blood Collection - Dams and Pups

Dates of inspection: 28 JAN 99, 28 JAN 99

Dates results reported to the Study Director and Management: 02 FEB 99, 02 FEB 99

Fecal and Urine Collection

Date of inspection: 28 JAN 99

Date results reported to the Study Director and Management:
02 FEB 99

Scheduled Sacrifice - Dams and Pups

Dates of inspection: 28 JAN 99, 28 JAN 99

Dates results reported to the Study Director and Management:
02 FEB 99, 02 FEB 99

TABLE 2

RAW DATA AUDIT(S)

The following study information and raw data were audited from 26 FEB 99 to 10 MAR 99:

Animal receipt, randomization, physical examination and acclimation.
In-life transaction record.
Feed consumption.
Cohabitation.
Natural delivery observations.
Litter observations.
Pup body weights and status.
Table of random units.
Milk collection data and packing lists.
Blood and liver collection data and packing lists.
Urine and fecal collection data and packing lists.
Necropsy.
Tissue packing lists.
Male breeder colony records.
General comments.
Study maintenance records.
Temperature and relative humidity reports.
Feed, water and bedding analyses.
Edit requests.
Dosage volumes.
Data review pages.

The results of this audit were reported to the Study Director and Management on 12 MAR 99.

The following study information and raw data were audited from 26 FEB 99 to 10 MAR 99:

Vehicle receipt, preparation and use.
Test article receipt, preparation and use.
Test article packing lists.

The results of this audit were reported to the Study Director and Management on 12 MAR 99.

PATHOLOGY REPORT
(ANCILLARY STUDY)

ELECTRON MICROSCOPIC EVALUATION OF LIVER AND LUNG AND LIGHT MICROSCOPIC EVALUATION OF LIVER IN CRL:CD®BR VAF/PLUS® RATS)

ORAL (GAVAGE) PHARMACOKINETIC STUDY OF PFOS IN RATS

CLIENT STUDY NUMBER 418-013
PAI STUDY NUMBER 99-11 (EM 99.39)

Prepared by:

James B. Nold, D.V.M., Ph.D., Diplomate, A.C.V.P.

Pathology Associates International
4915-D Prospectus Drive
Durham, NC 27713

April 5, 1999

PREPARED FOR 3M CORPORATE TOXICOLOGY,
3M CENTER, ST. PAUL, MN 55144-1000

I. Pathology Narrative

PATHOLOGY REPORT
(ANCILLARY STUDY)

ELECTRON MICROSCOPIC EVALUATION OF LIVER AND LUNG AND LIGHT MICROSCOPIC EVALUATION OF LIVER IN CRL:CD®BR VAF/PLUS® RATS)

ORAL (GAVAGE) PHARMACOKINETIC STUDY OF PFOS IN RATS

CLIENT STUDY NUMBER 418-013
PAI STUDY NUMBER 99-11 (EM 99.39)

SUMMMARY

Ultrastructural evaluation of liver and lungs of rat pups from dams treated with 0 (control), 0.4, 1.6, or 3.2 mg/kg/day (high-dose) PFOS identified increased numbers of peroxisomes within hepatocytes of high-dose rat pup livers. Quantitation of peroxisomes indicated at least twice the number of peroxisomes in animals treated with 0.4 mg/kg/day and triple the number in those given 1.6 or 3.2 mg/kg/day. Differences in cellular membranes or mitochondria were not discernible between control and treated animals in the samples examined; however, suboptimal fixation precluded a detailed evaluation of these organelles. In lung samples, the presence of type II pneumocytes and lamellar bodies was evaluated. No significant ultrastructural differences were identified between lung from control and treated rats. Random type II pneumocytes containing lamellar bodies were identified in all lungs examined ultrastructurally.

PROCEDURES

The objective of this study was to examine by electron microscopy the livers and lungs from selected day-21 gestation rat fetuses in an oral (gavage) pharmacokinetic study of PFOS. In addition to a general qualitative evaluation for differences between control and treated animals, the ultrastructural endpoints included quantitation of peroxisomes within hepatocytes, membrane and mitochondrial changes in hepatocytes, and the quantitation of surfactant lamellar bodies in the lung. Light microscopy of paraffin-embedded liver sections was also performed.

For the pharmacokinetic study, 90 female Crl:CD®BR VAF/PLUS® rats were given the test article or the vehicle once daily beginning 42 days prior to cohabitation with a male through day 20 postpartum according to Text Table 1.

Text Table 1. Dosage Levels, Concentrations and Volumes				
Dosage Group	Number of Mated Female Rats	PFOS Dosage (mg/kg/day)	PFOS Concentration (mg/mL)	Dosage Volume (mL/kg)
I	16	0 (Vehicle)	0	5
II	16	0.1	0.02	5
III	16	0.4	0.08	5
IV	16	1.6	0.32	5
V	16	3.2	0.64	5

At Caesarean-sectioning on day 21 of presumed gestation, lung and liver samples were collected from three fetuses per litter from five litters per dosage group. Samples of lung and liver from selected fetuses for Groups I, III, IV, and V were thin-sliced and placed in McDowell-Trump fixative (McDowell EM, 1976) and submitted to this laboratory for electron microscopy processing and evaluation. Sections of liver from these same animals were immersion-fixed in neutral buffered formalin and submitted along with electron microscopy samples.

Per sponsor request, tissue samples from selected pups were processed and evaluated (Text Table 2). The five digit number is the dam number; the suffixes 1-4 denotes the pup number from that dam's litter.

Text Table 2. Animals Selected for Electron Microscopy			
Group I Control (0 mg/kg/day)	Group III 0.4 mg/kg/day	Group IV 1.6 mg/kg/day	Group V 3.2 mg/kg/day
19504-3	19534-1	19560-1	19568-2
19505-1	19536-3	19560-2	19569-1
19506-4	19543-4	19560-3	19572-1
19509-1	19546-1	19562-2	19577-4
19516-2	19546-2	19562-3	19579-3

The lungs and livers were then processed into Spurr's resin for ultrastructural examination. Thick (1μ) sections were cut, stained with toluidine blue, and examined to select representative areas for further electron microscopy processing. Thin sections (approximately 90 nm) were cut, mounted on 200-mesh copper grids, stained with 5% methanolic uranyl acetate and Reynold's lead citrate, and examined on a Zeiss 900 transmission electron microscope. Centrilobular hepatocytes, where clearly identifiable in liver sections, were preferentially examined. Representative electron photomicrographs of liver and lung were taken and significant ultrastructural features were summarized for each photograph and animal on a designated transmission electron micrograph interpretation form. The number of peroxisomes in hepatocytes was manually counted for each center photographed hepatocyte and recorded.

For light microscopy, formalin-fixed liver samples were processed and embedded in paraffin, cut at approximately five microns, stained with hematoxylin and eosin, and evaluated.

RESULTS AND DISCUSSION

Individual interpretations of light microscopy slides and electron micrographs for each animal are shown in Section II. Selected representative electron photomicrographs were labeled and are shown in Section III.

Light Microscopy

A summary of the incidence and severity of light microscopic findings in the liver is shown in Text Table 3. There was an increased incidence and severity of eosinophilic granularity of the cytoplasm of hepatocytes in treated rats compared with control rat livers. The severity of this finding increased in a dose-related fashion. Hepatocellular eosinophilic granularity was diffusely distributed in most animals given 1.6 or 3.2 mg/kg/day of PFOS, but was predominantly periportal in 1 animal given 1.6 and in 3 animals given 0.4 mg/kg/day. Cytoplasmic clearing of hepatocytes was prominent in control livers. This morphological description is usually associated with the normal accumulation of glycogen in hepatocytes. In this study, the incidence and severity of cytoplasmic clearing was almost inversely proportional to the occurrence of eosinophilic granularity.

The liver is a hematopoietic organ in rat fetuses and neonates. Thus, large numbers of hematopoietic cells are present within the sinusoids throughout the liver. Extramedullary hematopoiesis (EMH) occurred in all animals, including controls, and was uniformly graded as moderate to moderately-severe. The severity of EMH was increased in the treated groups. Random mitoses of hepatocytes are normal in rat livers, especially in fetuses and neonates. There appeared to be a slight increase in hepatocellular mitotic figures in the animals given 3.2 mg/kg/day PFOS.

Text Table 3. Incidence and Severity of Light Microscopic Liver Findings

Microscopic Finding		PFOS Dose Levels (mg/kg/day)			
		0	0.4	1.6	3.2
(number examined)		(5)	(5)	(5)	(5)
Eosinophilic granularity, cytoplasmic, increased	minimal	2	2	1	-
	slight	-	3	3	1
	moderate	-	-	1	4
Cytoplasmic clearing	minimal	-	1	2	-
	slight	-	4	1	-
	moderate	5	-	1	-
Extramedullary hematopoiesis	moderate	5	4	1	-
	moderately-severe	-	1	4	5
Mitotic figures, increased	minimal	2	1	2	2
	slight	-	-	-	2

Electron Microscopy

Fixation of the tissues was less than optimal for electron microscopy. This was especially evident in the liver compared with the lung. Lung is inherently less dense than liver and allows better infiltration of the fixative into the tissue. Suboptimal fixation was characterized by clumping of large organelles, discontinuous plasma membranes, loss of detail of cytoplasmic organelles, dilatation of endoplasmic reticulum and the nuclear envelope, granular deposits in the mitochondrial matrix, and dilatation of mitochondrial cristae. The poor fixation of membranes made ultrastructural assessment of these structures impossible. Fixation, however, was still considered adequate to assess for the presence of peroxisomes in the hepatocytes and lamellar bodies in the lung and to make general comparisons between control and treated samples.

LIVER

Control (0 mg/kg/day). Subcellular features of control hepatocytes are demonstrated in Figures 1 and 2. Hepatocytes characteristically contain numerous mitochondria and prominent endoplasmic reticulum. Clumping of the large organelles (mitochondria, rough endoplasmic reticulum and peroxisomes) is indicative of poor fixation. In these cells rough endoplasmic reticulum was evident, but smooth endoplasmic reticulum was not because of suboptimal fixation. Mitochondria generally appeared dark and contained scattered dense deposits and some dilated cristae, both artifacts due to suboptimal fixation. Dilatation of endoplasmic reticulum and the nuclear envelope were additional artifacts of poor fixation. The fine granular material in the cytoplasm is consistent with glycogen particles. Peroxisomes were identified and quantitated in from representative hepatocytes. For the control livers, the average number of peroxisomes counted per hepatocyte photographed was 4.2 peroxisomes per cell (Text Table 4). Fetal and neonatal rat liver is a hematopoietic tissue, and numerous hematopoietic cells were evident within the liver sinusoids.

Text Table 4. Quantitation of Hepatocellular Peroxisomes

0 mg/kg		0.4 mg/kg		1.6 mg/kg		3.2 mg/kg	
Animal Number	Number[1] of Peroxisomes	Animal Number	Number of Peroxisomes	Animal Number	Number of Peroxisomes	Animal Number	Number of Peroxisomes
19504-3	3.2	19534-1	12.0	19560-1	11.6	19568-2	6.0
19505-1	3.0	19536-3	12.2	19560-2	12.8	19569-1	10.6
19506-4	4.4	19543-4	8.0	19560-3	10.2	19572-1	13.2
19509-1	5.2	19546-1	13.0	19562-2	10.6	19577-4	11.2
19516-2	5.0	19546-2	5.4	19562-3	20.0	19579-3	21.8
Mean =	4.2	Mean =	10.1	Mean =	13.0	Mean =	12.6

[1] Average number of peroxisomes per hepatocyte for five hepatocytes counted per animal.

0.4 mg/kg/day. The average number of peroxisomes per hepatocyte (10.1) was higher in the animals given 0.4 mg/kg/day PFOS compared with controls (Text Table 4). A representative hepatocyte is shown in Figure 3. Qualitatively, there were no identifiable

ultrastructural differences between the hepatocytes treated with 0 (control) and 0.4 mg/kg/day.

1.6 mg/kg/day. For animals given 1.6 mg/kg/day, the average number of peroxisomes per hepatocyte was 13.0. Figure 4 illustrates a representative hepatocyte from this treatment group. Otherwise, general ultrastructural morphology was similar in high-dose livers compared with control livers.

High-Dose (3.2 mg/kg/day). The average number of peroxisomes per hepatocyte (12.6) was higher in the high-dose animals compared with controls (Text Table 4). Figures 5 and 6 illustrate representative hepatocytes from high-dose animals. Differences in mitochondria and cellular membranes were not discernible between treated and control livers. Suboptimal fixation, however, of the tissues precluded detailed evaluation of these organelles.

LUNG

0 mg/kg/day (Control). Lung samples were atelectatic and not inflated with fixative. Therefore, most alveoli and alveolar septa were collapsed with poor delineation of alveolar and airway spaces. Figures 7-9 illustrate some normal cellularity and ultrastructural pulmonary anatomy. Type II pneumocytes (PN2) were randomly identified lining alveoli, terminal bronchioles, or within collapsed septa. Type II pneumocytes were identified by the presence of lamellar bodies, which are cytoplasmic vacuoles containing electron-dense laminated membrane-like profiles. Lamellar bodies represent the material secreted into the alveolar spaces as surfactant. Occasionally some lamellar body vacuoles were empty, as if the lamellar material had washed out or been secreted. Surfactant or lamellar material within airway spaces was only occasionally identified in control lungs or treated lungs. The type I pneumocyte (PN1) is characteristically flattened and lines the alveolar space as a thin margin of cytoplasm. Type I pneumocytes differentiate from type II pneumocytes. Many pneumocytes appeared to be cuboidal without distinctive lamellar bodies, and may represent a transition stage between PN2s and PN1s, especially since these lungs were fetal and had not been expanded with air. Additionally, some cuboidal epithelial cells represented terminal bronchiolar epithelium.

Type II pneumocytes and lamellar bodies were randomly identified in these control lungs. Some lamellar-like bodies were also present within capillary lumina, although in the control sections examined no lamellar bodies were clearly identified in the alveolar lumina.

0.4 mg/kg/day. Qualitatively, the lung samples from animals given 0.4 mg/kg/day appeared essentially the same as control samples. A representative sample is shown in Figure 10. Random type II pneumocytes containing lamellar bodies were identified, and only occasionally some lamellar material was seen within alveolar lumina.

1.6 mg/kg/day. Figures 11 and 12 illustrate some representative ultrastructural features from rat fetal lung samples given 1.6 mg/kg/day. These were considered essentially similar to the control and other treated samples. Lamellar bodies were identified within type II pneumocytes and, occasionally, within alveoli.

3.2 mg/kg/day (High-Dose). Ultrastructural pathology of the high-dose lungs was essentially similar to control, low- and mid-dose samples. The collapsed nature of most of the alveoli and septa made definitive quantitation impractical. Some lamellar bodies were identified within capillary lumina and only a small amount was seen within alveoli. Figures 13 and 14 illustrate some representative lung fields from the high-dose animals.

CONCLUSION

Ultrastructural evaluation of liver and lungs of rat pups from dams treated with 0 (control), 0.4, 1.6, or 3.2 mg/kg/day (high-dose) PFOS identified increased numbers of peroxisomes within hepatocytes of rat pup livers from dams given 1.6 or 3.2 mg/kg/day. Quantitation of peroxisomes indicated at least twice the number of peroxisomes in animals treated with 0.4 mg/kg/day and triple the number in those given 1.6 or 3.2 mg/kg/day. Differences in cellular membranes or mitochondria were not discernible between control and treated animals in the samples examined; however, suboptimal fixation precluded a detailed evaluation of these organelles.

In lung samples, the presence of type II pneumocytes and lamellar bodies was evaluated. No significant ultrastructural differences were identified between lung from control and treated rats. Random type II pneumocytes containing lamellar bodies were identified in all lungs examined ultrastructurally. Although some lamellar material (surfactant) was morphologically identifiable within alveolar lumina, no significant differences were noted between control and treated samples.

SIGNATURE OF AUTHOR

James B. Nold

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April 19 1999
Date

REFERENCES

McDowell, EM and Trump, BF: Histologic fixative for routine diagnostic light and electron microscopy. *Arch. Pathol. Lab. Med.*, 100:405-414, 1976.

II. Light Microscopy and Transmission Electron Micrograph Interpretation Forms [1]

[1] Forms are typographically corrected versions of signed/dated raw data sheets maintained in archived study file.

LIGHT MICROSCOPIC EVALUATION

Study No.: 418-013 (PAI 99-11)

Species/Strain: Crl:CD®BR VAF/Plus® Rats, Term Fetuses

Animal No: see below

Tissue: Liver

Sex: n/a

Interpreting Pathologist (signature and date): _____

Dose	Animal Number	Microscopic Findings and Comments
0 mg/kg	19504-3	1. Extramedullary hematopoiesis (EMH), diffuse, moderate 2. Cytoplasmic clearing, diffuse, moderate 3. Mitotic figures, minimal, multifocal
	19505-1	1. EMH, diffuse, moderate 2. Cytoplasmic clearing, diffuse, moderate
	19506-4	1. EMH, diffuse, moderate 2. Cytoplasmic clearing, diffuse, moderate 3. Eosinophilic granularity, cytoplasmic, increased, periportal, minimal
	19509-1	1. EMH, diffuse, moderate 2. Cytoplasmic clearing, diffuse, moderate 3. Eosinophilic granularity, cytoplasmic, increased, periportal, minimal
	19516-2	1. EMH, diffuse, moderate 2. Cytoplasmic clearing, diffuse, moderate 3. Mitotic figures, minimal, multifocal
0.4 mg/kg	19534-1	1. EMH, diffuse, moderate 2. Cytoplasmic clearing, diffuse, minimal 3. Eosinophilic granularity, cytoplasmic, increased, diffuse, minimal
	19536-3	1. EMH, diffuse, moderate 2. Cytoplasmic clearing, diffuse, slight 3. Eosinophilic granularity, cytoplasmic, increased, periportal, slight
	19543-4	1. EMH, diffuse, moderate 2. Cytoplasmic clearing, diffuse, slight 3. Eosinophilic granularity, cytoplasmic, increased, periportal, slight
	19546-1	1. EMH, diffuse, moderate 2. Cytoplasmic clearing, diffuse, slight 3. Eosinophilic granularity, cytoplasmic, increased, diffuse, minimal
	19546-2	1. EMH, diffuse, moderately-severe 2. Cytoplasmic clearing, diffuse, slight 3. Eosinophilic granularity, cytoplasmic, increased, periportal, slight 4. Mitotic figures, minimal, multifocal

Dose	Animal Number	Microscopic Findings and Comments
1.6 mg/kg	19560-1	1. Eosinophilic granularity, cytoplasmic, increased, moderate, diffuse 2. EMH, diffuse, moderately-severe
	19560-2	1. EMH, diffuse, moderately-severe 2. Cytoplasmic clearing, diffuse, minimal 3. Eosinophilic granularity, cytoplasmic, increased, diffuse, slight 4. Mitotic figures, minimal, multifocal
	19560-3	1. EMH, diffuse, moderate 2. Cytoplasmic clearing, diffuse, moderate 3. Eosinophilic granularity, cytoplasmic, increased, periportal, minimal 4. Mitotic figures, minimal, multifocal
	19562-2	1. EMH, diffuse, moderately-severe 2. Cytoplasmic clearing, diffuse, slight 3. Eosinophilic granularity, cytoplasmic, increased, diffuse, slight
	19562-3	1. EMH, diffuse, moderately-severe 2. Cytoplasmic clearing, diffuse, minimal 3. Eosinophilic granularity, cytoplasmic, increased, diffuse, slight
3.2 mg/kg	19568-2	1. Eosinophilic granularity, cytoplasmic, increased, moderate, diffuse 2. EMH, diffuse, moderately-severe 3. Mitotic figures, slight, multifocal
	19569-1	1. Eosinophilic granularity, cytoplasmic, increased, slight diffuse 2. EMH, diffuse, moderately-severe 3. Mitotic figures, slight, multifocal
	19572-1	1. Eosinophilic granularity, cytoplasmic, increased, moderate, diffuse 2. EMH, diffuse, moderately-severe 3. Mitotic figures, minimal, multifocal
	19577-4	1. Eosinophilic granularity, cytoplasmic, increased, moderate, diffuse 2. EMH, diffuse, moderately-severe 3. Mitotic figures, minimal, multifocal
	19579-3	1. Eosinophilic granularity, cytoplasmic, increased, moderate, diffuse 2. EMH, diffuse, moderately-severe

Incidence and Severity of Light Microscopic Liver Findings				
Microscopic Finding	PFOS Dose Levels (mg/kg/day)			
	0	0.4	1.6	3.2
(number examined)	(5)	(5)	(5)	(5)
Eosinophilic granularity, cytoplasmic, increased				
minimal	2	2	1	-
slight	-	3	3	1
moderate	-	-	1	4
Cytoplasmic clearing				
minimal	-	1	2	-
slight	-	4	1	-
moderate	5	-	1	-
Extramedullary hematopoiesis				
moderate	5	4	1	-
moderately-severe	-	1	4	5
Mitotic figures, increased				
minimal	2	1	2	2
slight	-	-	-	2

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013; EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19504-3

Tissue: Liver

Treatment Group: 0 mg/kg, Control

Block No(s).: 99.39-1

Sex: non applicable

Photo/Negative No(s).: Z15778 - Z15782

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____ 3-10-99

Features: Z15778. Liver. Hepatocyte adjacent to central vein at left and bottom. Bile canaliculus at top. Cytoplasmic organelles are clumped together with intervening spaces of fine granular material. Mitochondria appear dense and have some dilated cristae. Five (5) peroxisomes counted.
Z15779. Liver. Hepatocyte exhibiting similar cellular details as Z15778. Zero (0) peroxisomes clearly identified.
Z15780. Liver. Hepatocyte appears similar to above examples with clumped organelles. A hematopoietic cell is in the top right sinusoid and a bile canaliculus is present in the lower left. Mitochondria appear dense and have some dilated cristae. Three (3) peroxisomes counted.
Z15781. Liver. Hepatocyte and adjacent sinusoid containing two nucleated red blood cells. Mitochondria appear dense with some granular deposits and dilated cristae. Few numbers of peroxisomes identified, although poor fixation makes their clear identification difficult. Four (4) peroxisomes counted.
Z15782. Liver. Center hepatocyte is surrounded by several other hepatocytes, with a sinusoid containing a nucleated erythrocyte in bottom right and a bile canaliculus in top portion of photograph. Mitochondria appear dense with some granular deposits and dilated cristae. Four (4) peroxisomes counted.

Conclusions: Normal hepatocyte. Suboptimal fixation. Average 3.2 peroxisomes per hepatocyte.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013; EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19504-3

Tissue: Lung

Treatment Group: 0 mg/kg, control

Block No(s).: 99.39-2

Sex: non applicable

Photo/Negative No(s).: Z15783 - Z15787

Significant Lesions (check one): _____ Yes ____X__ No

Interpreting Pathologist (signature and date): _____

Features: Z15783. Lung. Dark lining cell is a type II pneumocyte (PN2) which contains four lamellar bodies. Adjacent lining cells are cuboidal with abundant granular material in their cytoplasm consistent with glycogen. Subjacent to the surface is a capillary and endothelial cell and a cell with an oblong nucleus and abundant lipid-like material in its cytoplasm, probably a macrophage.
Z1584. Lung. Central dark lining cell is a PN2 with several lamellar bodies. A large area of granular material in this cell is probably glycogen. Adjacent lining cells contain abundant fine granular material, probably glycogen as well. Dorsally is an isolated cell, with numerous mitochondria and some endoplasmic reticulum and several dense granules, probably a macrophage. A capillary and endothelial cell is to the right of the PN2.
Z15785. Lung. A cluster of cuboidal epithelial cells with abundant granular material in their cytoplasm, apparently glycogen. This may be a terminal bronchiole or an alveolus whose lining cells have not flattened out. Subjacent to these is a capillary, lining endothelial cell and a macrophage, whose cytoplasm contains abundant lipid-like droplets.
Z15786. Lung. An alveolus with several cuboidal lining cells. All appear to be unflattened PN1s. The central cell contains several vacuoles which may represent empty lamellar bodies suggestive of a PN2. The long cleft is probably an artifact. Dorsally is a capillary and a couple endothelial cells.
Z15787. Lung. Area of collapsed alveoli and capillaries. Erythrocytes within capillaries. Flattened PN1s line the alveolar spaces. No lamellar bodies evident.

Conclusions: Normal lung. Few type II pneumocytes and lamellar bodies identified.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013; EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19505-1

Tissue: Liver

Treatment Group: 0 mg/kg, control

Block No(s).: 99.39-3

Sex: non applicable

Photo/Negative No(s).: Z15788 - Z15792

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15788. Liver. Hepatocyte contains abundant fine granular material and some clumping of mitochondria and endoplasmic reticulum. Mitochondria are dense and contain some dilated cristae. Few peroxisomes are noted, four (4) counted.
Z15789. Liver. Hepatocyte appears similar to Z15788, with fine granular cytoplasmic material and clumping of larger organelles. Four (4) peroxisomes counted.
Z15790. Liver. Hepatocyte. Ventrally is a large sinusoid with a Kupffer cell among several erythrocytes. A hematopoietic cell is on the lower right. Some dilated blebs of rough endoplasmic reticulum (RER) are evident in the center hepatocyte. . Mitochondria appear dense with some granular deposits and dilated cristae. One (1) peroxisome counted.
Z15791. Liver. Hepatocyte appear partially detached from adjacent cells and suboptimally fixed. . Mitochondria appear dense with some granular deposits and dilated cristae. Two (2) peroxisomes counted.
Z15792. Liver. Hepatocyte appears essentially similar to those described above. Abundant fine granular material in cytoplasm. . Mitochondria appear dense with some granular deposits and dilated cristae. Some dilated blebs of RER noted. Four (4) peroxisomes counted.

Conclusions: Normal hepatocyte. Suboptimal fixation. Average 3.0 peroxisomes per hepatocyte.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013; EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19505-1

Tissue: Lung

Treatment Group: 0 mg/kg, Control

Block No(s).: 99.39-4

Sex: non applicable

Photo/Negative No(s).: Z15793 - Z15797

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15793. Lung. Alveolus with lining cells. Two cuboidal pneumocytes with fine granular cytoplasm. Top cell has an extended flattened portion that contains a lamellar-like structure, and may be a PN2 that is becoming a PN1. Normal, more flattened PN1s are present adjacent to these two central cells.
Z15794. Lung. Two of four cuboidal lining cells have lamellar bodies characteristic of PN2. Smaller and darker cells has a microvillous border than contains a lamellar structure, probably alveolar surfactant.
Z15795. Lung. Alveolus with lining cells. Dark cuboidal cell is a PN2 and contains several lamellar bodies. Some flattened PN1s are present as well as another cuboidal pneumocyte. A capillary containing erythrocytes is within the alveolar septum.
Z15796. Lung. Alveolus and area of collapsed septa. Two PN2s are present, both containing two to six lamellar bodies. No alveolar luminal lamellar structures are evident.
Z15797. Lung. Alveolus and lining cells. The dark columnar cell is a PN2 and contains several lamellar bodies. The left adjacent pneumocytes appear not to have flattened out as more differentiated PN1s. A second PN2 is just to the right of the central PN2, and contains several small lamellar bodies. Subjacent tot he alveolus is a capillary containing a leucocyte and endothelial cell.

Conclusions: Normal lung. A moderate number of type II pneumocytes were identifiable, and contained lamellar bodies.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013; EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19506-4

Tissue: Liver

Treatment Group: 0 mg/kg, control

Block No(s).: 99.39-5

Sex: non applicable

Photo/Negative No(s).: Z15808 - Z15812

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15808. Liver. Hepatocyte contains abundant fine granular cytoplasmic material and some clumping of predominantly mitochondria and rough endoplasmic reticulum. Five (5) peroxisomes counted.
Z15809. Liver. Hepatocyte appears similar to Z15808. Some dilated blebs of RER are noted. Six (6) peroxisomes counted.
Z15810. Liver. Hepatocyte has a washed-out appearance to much of its cytoplasm, and is surrounded by hematopoietic cells ventrally. Endothelial cells are incompletely defined. At the top left of the photograph is a bile canaliculus. Two (2) peroxisomes are counted.
Z15811. Liver. Hepatocyte with prominent bile canaliculus at lower left and sinusoid on right margin of photograph. Mitochondria are dense and contain some dense deposit and dilated cristae. Six (6) peroxisomes counted.
Z15812. Liver. Hepatocyte contains abundant washed-out cytoplasm and clumping of RER and mitochondria. At the top are two hematopoietic cells and a bile canaliculus is present in lower right of photograph. Three (3) peroxisomes counted.

Conclusions: Normal liver. Suboptimal fixation. Average 4.4 peroxisomes per hepatocyte

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013; EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19506-4

Tissue: Lung

Treatment Group: 0 mg/kg, control

Block No(s).: 99.39-6

Sex: non applicable

Photo/Negative No(s).: Z15818 - Z15822

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15818. Lung. Dark cell with round nucleus in the center is a PN2 which partially lines the alveolar space. Several lamellar bodies are within its cytoplasm. The large clear cytoplasm represents an adjacent PN1. A capillary containing an erythrocyte within the septum is immediately adjacent the PN2. The remainder of the tissue is collapsed alveoli and septa.
Z15819. Lung. A thin-margin of PN1 surrounds a protruding septum and capillary in the middle of the photograph. Two endothelial cells appear to line the capillary, which contains an erythrocyte. To the right is a somewhat darker PN2, which contains several lamellar bodies. In the central bottom is a large type I pneumocyte, with a large polygonal nucleus and mostly clear cytoplasm.
Z15820. Lung. PN1s line several septa in this photograph. Dorsally, the septal capillary contains a lymphocyte and a nucleated erythrocyte. In the center capillary a granulocytic cell is evident. No discernible PN2s or lamellar bodies are evident.
Z15821. Lung. Alveolus and lining cells. A PN2 is present lining the alveolus. It is the darker cell with several dilated lamellar bodies. Most of the lamellar material in these bodies is missing. Two PN1s are evident on the right margin of this alveolar space. Large nucleus on the left appears to belong to an endothelial cell lining a septal capillary.
Z15822. Lung. Alveolus and several lining cells. Most appear to be PN1s with abundant somewhat clear cytoplasm, which hasn't completely flattened out. No definitive PN2s are evident, although two small vacuoles in a lining pneumocyte at the bottom of the photograph may represent lamellar bodies. A capillary containing two nucleated cells occupies the right side of the photograph.

Conclusions: Normal lung. Occasional type II pneumocytes containing lamellar bodies identified. No lamellar material noted within alveolar spaces.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013; EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19509-1

Tissue: Liver

Treatment Group: 0 mg/kg, control

Block No(s).: 99.39-7

Sex: non applicable

Photo/Negative No(s).: Z15823 - Z15827

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15823. Liver. Hepatocyte bordered by sinusoid containing nucleated erythrocyte on left and other hepatocytes on bottom and right. An endothelial cell is in the upper left portion of the photograph. There is clumping of the mitochondria and RER with an intervening open area or areas filled with fine granular material. The RER is dilated. Mitochondria contain some granular deposits. Five (5) peroxisomes counted.
Z15824. Liver. Hepatocyte. At the top is a nucleated erythrocyte. Sinusoidal endothelium is poorly delineated. The RER shows some blebbing and dilatation, and mitochondria have some dense deposits and some dilatation of cristae. Five (5) peroxisomes counted.
Z15825. Liver. Hepatocyte surrounded by hematopoietic cells. The RER and nuclear envelope shows some dilatation and blebbing. Mitochondria appear dense and have some granular deposits and dilated cristae. Seven (7) peroxisomes counted.
Z15826. Liver. Hepatocyte appears essentially similar to above described cells with clumping of major organelles. Five (5) peroxisomes counted.
Z15827. Liver. Hepatocyte surrounded by hematopoietic cells. A single larger vacuole is present in the cytoplasm and contains a flocculent like material. Four (4) peroxisomes counted.

Conclusions: Normal hepatocyte. Suboptimal fixation. Average 5.2 peroxisomes per hepatocyte.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013; EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19509-1

Tissue: Lung

Treatment Group: 0 mg/kg, control

Block No(s).: 99.39-8

Sex: non applicable

Photo/Negative No(s).: Z15828 - Z15832

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15828. Lung. Alveolus and lining cells. The darker cuboidal cell is a PN2 and contains several lamellar bodies. An erythrocyte is immediately to the left of the PN2 and appears to be within the alveolus. At top left is a pneumocyte which has two small lamellar-like bodies and is probably a PN2 in transition to a PN1. A flattened PN1 is immediately on top and to the right of the dark PN2. Beneath these cells the septa are collapsed together.
Z15829. Lung. Alveolus and lining cells. The smaller dark cell is a PN2 with several lamellar bodies. To its right is a flattened PN1 and to its left is a cuboidal PN1. The lamellar or myelin-like material to the right of the PN2 appears to be within a capillary lumen. At the bottom right is a thin-walled septum containing a capillary and erythrocyte.
Z15830. Lung. Two erythrocytes are within the capillary lumen. The lining pneumocytes are flattened and appear to contain several vacuoles that may have contained lamellar bodies. Subjacent are collapsed septa and a mixture of septal cells including pneumocytes and endothelial cells.
Z15831. Lung. Area of collapsed alveolar septa. At the left middle and right middle-top are dark cells which contain lamellar bodies and are PN2s. Other cells are compressed pneumocytes, endothelial cells, and blood cells within capillaries. Some lamellar debris appears to be within capillary lumina.
Z15832. Lung. Area of collapsed septa. The large round clear cell is a cuboidal pneumocyte. Dorsal to this are endothelial cells lining a capillary. The lamellar structure appears to be within the lumen of the capillary.

Conclusions: Normal lung. Scattered type II pneumocytes present. Some lamellar material also present within capillaries. No lamellar bodies noted in alveolar spaces.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013; EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19516-2

Tissue: Lung

Treatment Group: 0 mg/kg, control

Block No(s).: 99.39-10

Sex: non applicable

Photo/Negative No(s).: Z15838 - Z15842

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15838. Lung. Two pneumocytes at the bottom are PN2 and contain some lamellar bodies. Dorsal to them are collapsed septa containing primarily pneumocytes and endothelial cells.
Z15839. Lung. Several pneumocytes are present. Central pneumocyte contains several lamellar bodies and is a PN2. Flattened PN1s line the protruding septum which contains a capillary, endothelial cell and leucocyte within the capillary.
Z15840. Lung. Single septum lined by PN1s on either side. On the right top is a PN2 with several lamellar bodies. The right lower pneumocyte also contains a single lamellar body. The septal capillary and endothelium are also evident.
Z15841. Lung. Area of collapsed septa. At right are two pneumocytes which contain multiple lamellar bodies. Other compressed septal cells appear to be pneumocytes and endothelial cells.
Z15842. Lung. Area of collapsed septa. Several cuboidal pneumocytes are present . Centrally is a capillary containing an erythrocyte. Next to it is a couple lamellar structures that appear to be within the capillary lumen.

Conclusions: Normal lung. Random type II pneumocytes containing lamellar bodies were identified. No lamellar bodies were clearly identified within alveolar spaces.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013; EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19516-2

Tissue: Liver

Treatment Group: 0 mg/kg, control

Block No(s).: 99.39-9

Sex: non applicable

Photo/Negative No(s).: Z15833 - Z15837

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15833. Liver. Hepatocyte with a sinusoid at lower right and a bile canaliculus on the left. Cell has abundant washed-out cytoplasm and clumping of mitochondria and RER. There is dilatation of RER and the nuclear envelope. Mitochondria contain some granular deposits and some dilated cristae. Plasma membranes and sinusoidal endothelial cells are poorly delineated. Five (5) peroxisomes counted.
Z15834. Liver. Dilation and blebbing of RER. Some granular deposits present in mitochondria. Nine (9) peroxisomes counted.
Z15835. Liver. Mitochondria contain some dense deposits and dilated cristae. There is blebbing of the RER. Plasma membranes are poorly defined. Five (5) peroxisomes counted.
Z15836. Liver. Hepatocellular morphology essentially similar as those described above. Four (4) peroxisomes counted.
Z15837. Liver. Mitochondria contain some dense deposits and dilated cristae. Plasma membranes are poorly defined. A multivesicular body is present to the right of the nucleus. Cell at lower left appears to be an endothelial cell, but may be a hematopoietic cell in the sinusoids. Two (2) peroxisomes counted.

Conclusions: Normal liver. Suboptimal fixation. Average 5.0 peroxisomes per hepatocyte.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013 EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19534-1

Tissue: Liver

Treatment Group: 0.4 mg/kg

Block No(s).: 99.39-31

Sex: non applicable

Photo/Negative No(s).: Z15935 - Z15939

Significant Lesions (check one): X Yes _____ No

Interpreting Pathologist (signature and date): _____

Features: Z15935. Liver. Hepatocyte with poorly-defined plasma membrane and no surrounding endothelial cells. Some hematopoietic cells are around this hepatocyte. Mitochondria contain some granular deposits and some dilated cristae. RER is dilated and shows some blebbing. Four (4) peroxisomes counted.
Z15936. Liver. Hepatocyte shows marked dilation of RER and poor delineation of the plasma membrane. The nuclear envelope is also dilated. A large clear vacuole is present in the right side of the cell. Eighteen (18) peroxisomes counted.
Z15937. Liver. Hepatocyte with clumping of organelles and intervening washed-out areas of cytoplasm. Mitochondria contain some granular deposits and some dilated cristae. RER is dilated and shows some blebbing. Eleven (11) Peroxisomes counted.
Z15938. Liver. Hepatocyte shows similar ultrastructural morphology as those described above, with suboptimal fixation. A multivesicular body is present to the right of the nucleus. Eleven (11) peroxisomes counted.
Z15939. Liver. Hepatocyte with clumping of organelles and intervening washed-out areas of cytoplasm. Plasma membrane is indistinct. A hematopoietic cell is at the bottom of the photograph. Mitochondria contain some granular deposits and some dilated cristae. RER is dilated and shows some blebbing. Sixteen (16) peroxisomes counted.

Conclusions: There appears to be increased numbers of peroxisomes per hepatocyte compared with control liver. Average 12.0 peroxisomes per hepatocyte. Cellular fixation suboptimal.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013 EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19534-1

Tissue: Lung

Treatment Group: 0.4 mg/kg

Block No(s).: 99.39-32

Sex: non applicable

Photo/Negative No(s).: Z15941 - 15945

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15941. Lung. Alveolus and lining cells. All the lining cells appear to be type I pneumocytes (PN1s). Beneath the PN1s is a round to polygonal cell containing 5 lamellar bodies in its cytoplasm; this is a type II pneumocyte (PN2). This is probably a lining cell, and the plane of section is somewhat flat through the septal wall.
Z15942. Lung. Alveolar space and lining cells. The dark and somewhat flattened lining cell is a PN2 and contains several vacuoles empty of contents. These appear to be "empty" lamellar bodies. The lighter-staining pneumocyte at the far left also contains two similar-appearing vacuoles.
Z15943. Lung. Alveolus and lining cells. The dark nucleus is part of a flattened pneumocyte, but also attaches with two adjacent more lucent PN1s. No lamellar bodies noted in this photograph, although a vacuole adjacent to the top left nucleus may be an "empty" lamellar body. Septal walls and alveoli are collapsed and normal pulmonary architecture is indistinct.
Z15944. Lung. The dark lining cell on the right contains several lamellar bodies and is a PN2. The other lining cells, although cuboidal, appear to be pneumocytes which have not flattened out in the characteristic type I pneumocyte fashion.
Z15945. Lung. Alveolus and lining cells. The two dark lining cells both appear flattened along the septal wall and are PN1s. No lamellar bodies are seen in these lining cells. The top cell in the photograph appears detached and surrounded by some extracellular lipid-like material. Its identity is unclear, but may be a macrophage or endothelial cell. A capillary is present at the top left.

Conclusions: Essentially normal fetal lung. Random type II pneumocytes with lamellar bodies identified. No remarkable abnormalities noted.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013 EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19536-3

Tissue: Liver

Treatment Group: 0.4 mg/kg

Block No(s).: 99.39-33

Sex: non applicable

Photo/Negative No(s).: Z15946 - Z15950

Significant Lesions (check one): X Yes _____ No

Interpreting Pathologist (signature and date): _____

Features: Z15946. Liver. Hepatocyte. There is dilatation of RER and of the nuclear envelope. Some granular deposits are evident within some mitochondria. Four (4) peroxisomes counted.
Z15947. Liver. Hepatocyte. There is some clumping of organelles. The RER and nuclear envelope are dilated. Seventeen (17) peroxisomes counted.
Z15948. Liver. Hepatocyte. There is poor definition of the plasma membrane. RER and the nuclear envelope are dilated. Fourteen (14) peroxisomes counted.
Z15949. Liver. Hepatocyte appears similar to those described above. Eighteen (18) peroxisomes counted.
Z15950. Liver. Hepatocyte. At the top is an endothelial cell and several adjacent erythrocytes and one nucleated erythrocyte. The plasma membrane of the hepatocyte is indistinct and organelles are clumped in the cytoplasm. RER is dilated. Eight (8) peroxisomes counted.

Conclusions: Increased number of peroxisomes per hepatocyte compared with control samples. Average 12.2 peroxisomes per hepatocyte. Suboptimal fixation.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013 EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19536-3

Tissue: Lung

Treatment Group: 0.4 mg/kg

Block No(s).: 99.39-34

Sex: non applicable

Photo/Negative No(s).: Z15951 - Z15955

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15951. Lung. Alveolus and area of collapsed septa. The bottom alveolus contains debris including some lamellar material consistent with secreted lamellar bodies (surfactant) from PN2s. The lining pneumocytes are all flattened and appear to be PN1s. No PN2s are identified. At least two capillaries are present in the collapsed septal area.
Z15952. Lung. Alveolus and lining cells. PN1s line the alveolar space and are flattened. On the right the nucleus and cell beneath the PN1 contains a single dark lamellar body, which suggest this cell maybe a PN2. Other cells in the photograph are endothelial cells, granulocyte in a capillary and some nonidentified cells. No lamellar bodies are present in the alveolar lumen.
Z15953. Lung. The prominent dark lamellar or myelin-like body in the center of the photograph is within a capillary space. Type 1 pneumocytes are flattened and line the alveolar space. At the bottom of the photograph in the collapsed septal area is a cell which contains two lamellar bodies, a PN2. No abnormalities noted.
Z15954. Lung. Alveolus and lining cells. A small central dark cell contains 3-4 lamellar bodies and is a PN2. The adjacent cell is cuboidal, but appears to be a pneumocyte which has not flattened out. A capillary containing several erythrocytes and a lining endothelial cell is prominent in the center of the photograph. Some debris is present in the alveolar lumen, and some may be fine lamellar material. The nucleated cell at the top contains two lamellar bodies and is also a PN2.
Z15955. Lung. Lamellar bodies within a PN2 line the alveolar space. Collapsed alveoli and septa fill the top of the page. No abnormalities noted.

Conclusions: Essentially normal fetal lung. Some type II pneumocytes identified containing lamellar bodies. Some lamellar bodies present within alveoli.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013 EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19543-4

Tissue: Liver

Treatment Group: 0.4 mg/kg

Block No(s).: 99.39-35

Sex: non applicable

Photo/Negative No(s).: Z15956 - Z15960

Significant Lesions (check one): X Yes _____ No

Interpreting Pathologist (signature and date): _____

Features: Z15956. Liver. Hepatocyte with clumping of RER and mitochondria. Plasma membranes are indistinct. Cross-sections of RER appear dark. A bile canaliculus is present at the top right. Several hematopoietic cells are around the periphery. Mitochondria contain some dilated cristae. Eight (8) peroxisomes counted.
Z15957. Liver. Hepatocyte morphology appears similar to Z15956. Organelles are clumped in the cytoplasm; intervening spaces contain fine granular material which is probably glycogen and cytosolic debris. Five (5) peroxisomes counted.
Z15958. Liver. Hepatocyte with bile canaliculi present at top and bottom of cell. Fifteen (15) peroxisomes counted. Fixation is very poor.
Z15959. Liver. Hepatocyte with marked clumping of organelles. Two hematopoietic cells are present at the bottom of the photograph. Three (3) peroxisomes counted.
Z15960. Liver. Hepatocyte surrounded primarily by hematopoietic cells. Sinusoidal endothelial cells are absent due to poor fixation. Hepatocytic mitochondria contain some granular deposits and dilated cristae. Nine (9) peroxisomes counted.

Conclusions: Section of liver exhibits suboptimal to poor fixation. Numbers of peroxisome per hepatocyte only very slightly higher than control values. Average 8.0 peroxisomes per hepatocyte.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013 EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19543-4

Tissue: Lung

Treatment Group: 0.4 mg/kg

Block No(s).: 99.39-36

Sex: non applicable

Photo/Negative No(s).: Z15961 - Z15965

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15961. Lung. Alveolus and lining cells. Lining cells appear cuboidal, and may be a terminal bronchiole. The central cuboidal cell contains several lamellar bodies within a fine granular cytoplasmic background. On either side are two darker compressed cells which contain apical vacuoles. Some lamellar material is present in the alveolar space.
Z15962. Lung. Several cuboidal pneumocytes line this airway or alveolar space. They all contain abundant granular material in their cytoplasm, which is consistent with glycogen. No PN2s are evident. A flattened PN1 is present at the right top of the alveolar space. Two septal capillaries are present, one dorsally and one ventrally. Both contain some lamellar myelin-like material in their lumina.
Z15963. Lung. Photograph shows several cuboidal pneumocytes, the top cell of which contains a clear vacuole suggestive of an "empty" lamellar body. A dark erythrocyte is present in the capillary to the left of the lining cells. The cell at the bottom left contains a few small lamellar bodies and is probably a PN2. No lamellar bodies noted in alveoli, and no abnormalities noted.
Z15964. Lung. Alveolus and lining cells. The lining cells are predominantly flattened and appear to be differentiated PN1s. Several mitochondria and a dark vacuole are present in the central lining cell. The dark vacuole may represent a depleted lamellar body. The dark lamellar myelin-like structure near the top is within a capillary space with a collapsed septum.
Z15965. Lung. The cell at the bottom of the photograph contains several lamellar bodies and is a PN2 within the collapsed septum. PN1s line the air space on the right. Two capillaries containing dark erythrocytes are beneath the surface epithelium. No abnormalities are noted.

Conclusions: Essentially normal fetal lung. Several type II pneumocytes identified with lamellar bodies. Also, some lamellar structures noted within alveolar spaces.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013 EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19546-1

Tissue: Liver

Treatment Group: 0.4 mg/kg

Block No(s).: 99.39-37

Sex: non applicable

Photo/Negative No(s).: Z15966 - Z15970

Significant Lesions (check one): X Yes _____ No

Interpreting Pathologist (signature and date): _____

Features: Z15966. Liver. Hepatocyte. Plasma membrane is indistinct and cytoplasmic organelles are clumped together. Mitochondria show some dense deposits and dilated cristae. Fifteen (15) peroxisomes counted.
Z15967. Liver. Hepatocyte appears morphologically similar to Z15966, with clumping of organelles, indistinct plasma membranes, and mitochondrial changes. RER appears dilated. Seven (7) peroxisomes counted.
Z15968. Liver. Hepatocyte. A prominent bile canaliculus is present in the bottom right corner. Organelles are clumped with large intervening spaces of fine granular material. Mitochondria show some dense deposits and dilated cristae. Twenty (20) peroxisomes counted.
Z15969. Liver. Hepatocyte appears essentially similar to Z15968. Fixation is poor. Eleven (11) peroxisomes counted.
Z15970. Liver. RER is dilated and plasma membranes are indistinct. An endothelial cell is not present at sinus at top. Mitochondria show some dense deposits and dilated cristae. Twelve (12) peroxisomes counted.

Conclusions: Liver exhibits poor fixation. There appears to be increased numbers of peroxisomes per hepatocyte. Average 13.0 peroxisomes per hepatocyte.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013 EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19546-1

Tissue: Lung

Treatment Group: 0.4 mg/kg

Block No(s).: 99.39-38

Sex: non applicable

Photo/Negative No(s).: Z15971 - Z15975

Significant Lesions (check one): _____ Yes __X__ No

Interpreting Pathologist (signature and date): _____

Features: Z15971. Lung. Alveolus and lining cells. Several lining cells contain lamellar bodies, most predominantly the center cell with at least nine lamellar bodies. This is a distinctive PN2. The three cells at the top of the photograph appear to be pneumocytes whose alveoli are out of plane of section or are collapsed.
Z15972. Lung. Photograph slightly out of focus. An unattached PN2 is present in the alveolar space. Both sides of the septum are lined by flattened PN1s. A capillary and endothelial cell are evident within the septum. No lamellar material is present in the alveoli.
Z15973. Lung. Alveoli and septum. The dark cell on the top left is a PN2 with several "empty" lamellar bodies. The other lining cells are PN1s. A capillary with a luminal erythrocyte is present in the center of the septum. No lamellar material is present in the alveoli.
Z15974. Lung. Alveolus and lining cells. A flattened PN1 lines the bottom margin of the alveolus. Next to it is a cuboidal pneumocyte with several clear vacuoles, a PN2. The vacuoles are "empty" lamellar bodies. The central cell with a microvillous border, dilated nuclear envelope and distended endoplasmic reticulum is a cuboidal pneumocyte exhibiting some elements of suboptimal fixation. No lamellar bodies noted in the alveoli.
Z15975. Lung. Cuboidal lining cell in center right and cell at center left both contain one or two vacuoles which appear to be lamellar bodies. These cells are probably PN2s converting to PN1s after expressing their lamellar (surfactant) material. No lamellar material noted in the alveoli.

Conclusions: Essentially normal fetal lung. Scattered type II pneumocytes with lamellar bodies identified. No lamellar material is present in the alveoli.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013 EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19546-2

Tissue: Liver

Treatment Group: 0.4 mg/kg

Block No(s).: 99.39-39

Sex: non applicable

Photo/Negative No(s).: Z15976 - Z15980

Significant Lesions (check one): _____ Yes X No

Interpreting Pathologist (signature and date): _____

Features: Z15976. Liver. Hepatocyte exhibits a poorly-defined plasma membrane. The organelles are clumped and the mitochondria show dilated cristae. At top right is an interstitial cell surrounded by collagen, probably a fibroblast. At the lower left are some hematopoietic cells within a sinusoid. Four (4) peroxisomes counted.
Z15977. Liver. Two hepatocytes with an intervening bile canaliculus. Hematopoietic cells are present in the upper right and lower left sinusoids. The larger cytoplasmic organelles are clumped together and the cytosol appears washed-out or contains a fine granular material. The mitochondria show some dilated cristae. The hepatocyte (bottom cell) contains seven (7) peroxisomes.
Z15978. Liver. Central hepatocyte in photograph appears similar to those described above, fixation is poor. Two (2) peroxisomes counted.
Z15979. Liver. Hepatocyte, whose morphology is similar to those described above. Five (5) peroxisomes counted.
Z15980. Liver. Hepatocyte exhibits a poorly-defined plasma membrane. The organelles are clumped and the mitochondria show dilated cristae. RER is dilated. Nine (9) peroxisomes counted.

Conclusions: Essentially normal liver. Poor cellular fixation. Average 5.4 peroxisomes per hepatocyte.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013 EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19546-2

Tissue: Lung

Treatment Group: 0.4 mg/kg

Block No(s).: 99.39-40

Sex: non applicable

Photo/Negative No(s).: Z15981 - Z15985

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15981. Lung. Alveolus and lining cells. A partially detached pneumocyte is present in the air space. Large right central cell contains a single lamellar body near its top margin. The other dark organelles appear to be predominantly mitochondria. The cytoplasm of these cuboidal pneumocytes contains a fine granular material suggestive of glycogen.
Z15982. Lung. Central cell contains multiple lamellar bodies and is the cytoplasm of a PN2. This is in an area of collapsed alveoli and septa. A capillary and endothelial cell are at the left of the photograph. The two dark cells on either side of the PN2 are not clearly identifiable. The bottom right cell is a PN1. No abnormalities described.
Z15983. Lung. Two columnar cells on the right both contain lamellar bodies, although the majority of their cytoplasm consist of fine granular material. PN1s appear to be at the bottom of the photograph and a capillary and endothelial cell are at the left.
Z15984. Lung. An area of collapsed alveoli and septa. At the top and bottom are two round to polygonal cells that contain some lamellar bodies consistent with type II pneumocytes (PN2s). Some lamellar material appears to be extracellular adjacent to the bottom PN2. The central cells all appear to be PN1s. At the bottom right is a capillary, endothelial cell and erythrocyte. No lamellar bodies noted in alveoli.
Z15985. Lung. At the top right is a cuboidal PN2 lining the alveolus. This cell contains several lamellar bodies, and sits next to a more flattened PN1. Centrally is a capillary containing two large endothelial cell nuclei and an erythrocyte.

Conclusions: Essentially normal fetal lung. Random type II pneumocytes (PN2s) containing lamellar bodies were identified. Some extracellular lamellar material identified outside one type II pneumocyte.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013 EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19560-1

Tissue: Liver

Treatment Group: 1.6 mg/kg

Block No(s).: 99.39-21

Sex: non applicable

Photo/Negative No(s).: Z15884 - Z15888

Significant Lesions (check one): X Yes _____ No

Interpreting Pathologist (signature and date): _____

Features: Z15884. Liver. Hepatocyte. Plasma membranes and adjacent endothelial cells are indistinct, consistent with suboptimal fixation. Dilation of RER with some blebs. Some dilated cristae in mitochondria. A single clear vacuole is present in the cytoplasm on the right side of the cell. Fifteen (15) peroxisomes counted.
Z15885. Liver. Some granular deposits present in mitochondria and dilatation of RER. Twenty-one (21) peroxisomes counted.
Z15886. Liver. Hepatocyte in center of photograph with hematopoietic cells at top. Some clumping of mitochondria and RER. Dilated RER. Six (6) peroxisomes counted.
Z15887. Liver. Hepatocyte containing a single large lipid droplet in dorsal cytoplasm. At top right is a hematopoietic cell and at lower left is a bile canaliculus. There is clumping of cytoplasmic organelles. RER and nuclear envelope appear dilated. Five (5) peroxisomes counted.
Z15888. Liver. Hepatocyte similar to those described above. Some stain precipitate is present on photograph. Eleven (11) peroxisomes counted.

Conclusions: There appears to be increased numbers of peroxisomes per hepatocyte compared with control samples. Average 11.6 peroxisomes per hepatocyte. Suboptimal tissue fixation.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013 EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19560-1

Tissue: Lung

Treatment Group: 1.6 mg/kg

Block No(s).: 99.39-22

Sex: non applicable

Photo/Negative No(s).: Z15889 - Z15893

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15889. Lung. Alveolus and lining cells. Top cell with darker cytoplasm is a PN2 and contains two lamellar bodies. The lower cell also contains two prominent vacuoles, which are probably expressed lamellar bodies even though the lamellar material is no longer evident. The central cell is a PN1. Beneath the PN1 is an extension of an unidentified cell out of plane of section. A capillary is present at the bottom left of the photograph. No lamellar material is present in the alveolar space.

Z15890. Lung. Three lining cells and a capillary are evident. The central dark cell with an oblong nucleus is a PN2, and it contains 3 discernible lamellar bodies. At the top left and to the right of the PN2 are PN1s with more lucent cytoplasm. The capillary and lining endothelial cell are at the top right. A dark erythrocyte is present in the capillary.

Z15891. Lung. Alveolus, lining cells, and capillaries. Centrally is a PN2 somewhat sandwiched in between two flattened PN1s lining the alveolus. The PN2 contains several lamellar bodies within its cytoplasm. Capillaries containing dark erythrocytes and lined by endothelium are present at the upper left and lower right of the photograph. No lamellar material is present in the alveolar space.

Z15892. Lung. Features are similar to those described for Z15891. A single PN2 is present between two PN1s lining the alveolus. The PN2 contains several lamellar bodies. The cell beneath the PN2 has an irregular nucleus, some prominent RER and is surrounded by some collagen; this appears to be a fibroblast.

Z15893. Lung. Alveolus with several cuboidal pneumocytes. There are not clearly distinctive PN2s in this photograph. The capillary at the bottom contains a lamellar myelin-line structure within its lumen. No lamellar material is present in the alveolar space.

Conclusions: Essentially normal lung. Several type II pneumocytes with lamellar bodies were identified. Fixation was considered acceptable.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013 EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19560-2

Tissue: Liver

Treatment Group: 1.6 mg/kg

Block No(s).: 00.39-23

Sex: non applicable

Photo/Negative No(s).: Z15894 - Z15898

Significant Lesions (check one): X Yes _____ No

Interpreting Pathologist (signature and date): _____

Features: Z15894. Liver. Hepatocyte with surrounding hematopoietic cells. This cell appears partially detached from adjacent hepatocytes, although two hepatocytes are present in the lower right of photograph, all three sharing a common bile canaliculus. There is clumping of mitochondria, RER and some peroxisomes. Some dilatation of cristae is noted. Thirteen (13) peroxisomes counted.
Z15895. Liver. Hepatocyte appears similar to cell described in Z15894 with clumping of organelles. Some granular deposits noted in mitochondria. Fourteen (14) peroxisomes counted.
Z15896. Liver. Hepatocyte has clumping of organelles with intervening cytoplasm filled with fine granular material, probably predominantly glycogen. Mitochondria appear dense and contain some granular deposits and dilated cristae. Ten (10) peroxisomes counted.
Z15897. Liver. Hepatocyte appears similar to those described above. Plasma membranes are indistinct. A hematopoietic cell is at the bottom of the photograph. Fourteen (14) peroxisomes are counted.
Z15898. Liver. Hepatocyte morphology essentially same as above. A bile canaliculus serves four attached hepatocytes in the top center of the photograph. Thirteen (13) peroxisomes counted.

Conclusions: There appear to be increased numbers of peroxisomes per hepatocyte. Average 12.8 per hepatocyte. Suboptimal fixation of tissue.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013 EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19560-2

Tissue: Lung

Treatment Group: 1.6 mg/kg

Block No(s).: 99.39-24

Sex: non applicable

Photo/Negative No(s).: Z15899 - Z15903

Significant Lesions (check one): X Yes _____ No

Interpreting Pathologist (signature and date): _____

Features: Z15899. Lung. Alveolus and lining cells. Central cell is a PN2 with several basilar lamellar bodies. Adjacent lining cells appear to be PN1s. A free erythrocyte is present in the alveolar space. At the left of the photograph is a small capillary containing a luminal erythrocyte. No abnormalities noted.
Z15900. Lung. Alveolus and lining cells. At top center is a single PN2 which contains five lamellar bodies. Two lamellar myelin-like structures in middle left of photograph are within capillary lumina. No lamellar material is identified within alveolar spaces.
Z15901. Lung. Alveolus and lining cells. Nucleated cell free in alveolus appears to be a lymphocyte. Two center lining cells both contain lamellar bodies and are PN2s even though one is "light" and one is "dark". Large cuboidal pneumocyte at lower left contains some lamellar bodies and connects to the next flattened PN1 segment.
Z15902. Lung. A cluster of pneumocytes, four of which contain lamellar bodies characteristic of PN2s. No lamellar material is identified within alveolar spaces.
Z15903. Lung. A group of cuboidal and flattened pneumocytes and ventral capillary within a septal wall. Two cells contain clefts, but none contain definitive lamellar bodies. No abnormalities noted.

Conclusions: Type II pneumocytes fairly easily identified in this animal, and at least one cluster of PN2, possibly suggestive of increased numbers of PN2. Otherwise ultra-structural morphology appeared essentially similar to control sections.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013 EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19560-3

Tissue: Liver

Treatment Group: 1.6 mg/kg

Block No(s).: 99.39-25

Sex: non applicable

Photo/Negative No(s).: Z15904 - Z15908

Significant Lesions (check one): X Yes _____ No

Interpreting Pathologist (signature and date): _____

Features: Z15904. Liver. Hepatocyte bordered by hepatocytes on three sides and sinusoid with hematopoietic cell on right. Bile canaliculi at top and on left. There is clumping of larger organelles within the cytoplasm. Mitochondria contain some dilated cristae. Ten (10) peroxisomes counted.
Z15905. Liver. Hepatocyte with clumping of organelles. The RER appears dilated. Seven (7) peroxisomes counted.
Z15906. Liver. Hepatocyte with hematopoietic cells along top, left, and bottom. There is clumping of the larger organelles. Mitochondria contain some dense deposits and dilated cristae. Fifteen (15) peroxisomes counted. Some peroxisomes exhibit marked degeneration.
Z15907. Liver. Hepatocyte morphology essentially same as described above. Seven (7) peroxisomes counted.
Z15908. Liver. Hepatocyte adjacent to central vein. Appears similar to previously described cells with clumping of mitochondria and RER. Twelve (12) peroxisomes counted.

Conclusions: Cellular fixation suboptimal to poor. There appears to be slightly increased numbers of peroxisomes compared with control liver. Average 10.2 peroxisomes per hepatocyte.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013 EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19560-3

Tissue: Lung

Treatment Group: 1.6 mg/kg

Block No(s).: 99.39-26

Sex: non applicable

Photo/Negative No(s).: Z15910 - Z15914

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15910. Lung. Alveolus and lining cells. All pneumocytes are cuboidal in this photograph. The second cell from the right contains several lamellar bodies and is a PN2. The third cell also contains two small lamellar bodies. No other remarkable features noted.
Z15911. Lung. The dark cuboidal lining cell contains multiple cytoplasmic vacuoles and appears to be a PN2 although definitive lamellar structures are not within the vacuoles. The pneumocyte at top right also contains 1-2 vacuoles which probably are/were lamellar bodies.
Z15912. Lung. Alveolus and lining cells. Along the alveolus pneumocytes all appear flattened and to be PN1s. At bottom of photograph in collapsed septal area is a cell containing multiple lamellar structures, cytoplasm of a PN2. No lamellar structures are present in the alveolar space.
Z15913. Lung. At top center a large PN2 contains multiple lamellar bodies. A dark thin PN1 lines the remainder of the airway space. At bottom right a capillary contains a large white blood cell. Dorsal to this is an unidentified cell with dilated endoplasmic reticulum and nuclear envelope.
Z15914. Lung. Alveolar space and lining cells. Within the alveolus are multiple extracellular lamellar bodies. Lining pneumocytes in this region all appear to be PN1s. Several capillaries are present in the photograph.

Conclusions: Essentially normal fetal lung. Some type II pneumocytes and lamellar bodies identified. Some lamellar bodies were occasionally present in alveoli.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013 EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19562-2

Tissue: Liver

Treatment Group: 1.6 mg/kg

Block No(s).: 99.39-27

Sex: non applicable

Photo/Negative No(s).: Z15915 - Z15919

Significant Lesions (check one): X Yes _____ No

Interpreting Pathologist (signature and date): _____

Features: Z15915. Liver. Hepatocyte and surrounding hematopoietic cells. Sinusoidal endothelium and plasma membranes are indistinct, but cytoplasmic organelles are fairly evenly dispersed. Dilated cristae are present in the mitochondria. Nine (9) peroxisomes counted.
Z15916. Liver. Hepatocyte and surrounding hematopoietic cells. Dilated cristae are present in the mitochondria. Sinusoidal endothelium and plasma membranes are indistinct. Dilatation of RER. Eleven (11) peroxisomes counted.
Z15917. Liver. Hepatocyte with clumping of organelles and washed-out appearance of much of the cytoplasm. Plasma membrane is indistinct. Twelve (12) peroxisomes counted.
Z15918. Liver. Hepatocyte morphology similar to those described above. Mitochondria contain some dense deposits and dilated cristae. Eight (8) peroxisomes counted.
Z15919. Liver. Hepatocyte contains multiple clear vacuoles and marked dilation of RER. Mitochondria contain some dense deposits and dilated cristae. Thirteen (13) peroxisomes counted.

Conclusions: Poor cellular fixation of liver tissue. There appears to be a slight increase in the number of peroxisomes per hepatocyte. Average 10.6 peroxisomes per hepatocyte.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013 EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19562-2

Tissue: Lung

Treatment Group: 1.6 mg/kg

Block No(s).: 99.39-28

Sex: non applicable

Photo/Negative No(s).: Z15920 - Z15924

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15920. Lung. Alveolus and lining cells. At center right is a rounded lining cell which contains two distinct vacuoles, and appears to be a PN2. These appear consistent with "empty" lamellar body vacuoles. The lining cells on either side of this round cell are flattened PN1s. Similarly, at left central is a cuboidal cell protruding into the lumen which contains two vacuoles which appeared to be empty lamellar bodies. The columnar cell at the lower left is a pneumocyte without remarkable distinguishing feature, and is probably a PN1 which hasn't flattened out.
Z15921. Lung. Alveolus and collapsed septa. At bottom right is an oval cell whose cytoplasm contains one round vacuole and multiple open clefts that appear to be "empty" lamellar bodies. The dark oblong nucleus to its top left is an endothelial cell of a capillary containing a dark erythrocyte. Lining the septum on top of this is a flattened PN1. Another capillary is in the center of the collapsed area.
Z15922. Lung. Alveolus and lining cells. The central dark lining cell contains many prominent mitochondria, but also contains a few vacuoles which may be lamellar bodies. A larger PN1 is just to the left of this cell. At the top is an endothelial cell nucleus.
Z15923. Lung. In the center of the photograph is a scrolled lamellar or myelin-like figure that appears to be extracellularly within a capillary space. Dorsally and ventrally are capillaries containing erythrocytes and a lymphocyte (ventrally). To its right is a lining PN1.
Z15924. Alveolus and lining cells. A single dark type II pneumocyte is present, which contains multiple lamellar bodies. It is bounded on either side by flattened PN1s. Capillaries lined by endothelial cells and containing erythrocytes are present at top right and lower left. No lamellar bodies evident within alveolar spaces.

Conclusions: Essentially normal fetal lung. Some random type II pneumocytes containing lamellar bodies were identified. No lamellar bodies were seen in alveolar spaces.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013 EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 15962-3

Tissue: Liver

Treatment Group: 1.6 mg/kg

Block No(s).: 99.39-29

Sex: non applicable

Photo/Negative No(s).: Z15925 - Z15929

Significant Lesions (check one): X Yes _____ No

Interpreting Pathologist (signature and date): _____

Features: Z15925. Liver. Hepatocyte surrounded by other hepatocytes and a hematopoietic cell on the right. There is clumping of the cytoplasmic organelles and large areas of washed out cytoplasm. Mitochondria appear to have some granular densities and some dilated cristae. There is dilatation and blebbing of RER. Twenty-six (26) peroxisomes counted.
Z15926. Liver. Hepatocyte appears similar to hepatocyte in Z15925. There are hematopoietic cells on the left and bottom. Twenty-three (23) peroxisomes counted.
Z15927. Liver. Hepatocyte with indistinct cytoplasmic borders. There is dilatation and blebbing of RER. Mitochondria appear to have some granular densities and some dilated cristae. Twenty-one (21) peroxisomes counted.
Z15928. Liver. Hepatocyte appears essentially similar to above cells. Fixation is suboptimal. Twelve (12) peroxisomes counted.
Z15929. Liver. Hepatocyte with indistinct cytoplasmic borders. There is dilatation of RER. Mitochondria appear to have some granular densities and some dilated cristae. Eighteen (18) peroxisomes counted.

Conclusions: Increased numbers of peroxisomes per hepatocyte. Average 20.0 peroxisomes per hepatocyte. Poor, suboptimal fixation.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013 EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19562-3

Tissue: Lung

Treatment Group: 1.6 mg/kg

Block No(s).: 99.39-30

Sex: non applicable

Photo/Negative No(s).: Z15930 - Z15934

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15930. Lung. Alveolus and lining cells. Two PN2s with lamellar bodies are present. One PN2 exhibits pseudopodia of cytoplasm extending into the alveolus. The other PN2 contains several large cytoplasmic vacuoles. Some small tubular surfactant bodies are present in the alveolar lumen. Capillaries with endothelial cells and erythrocytes are present beneath the lining cells.
Z15931. Lung. Alveolus and lining cells. Centrally is a dark PN2 which contains one distinct lamellar body dorsal to its nucleus. The cell immediately on top of this dark cell contains an open-faced nucleus but also contains several lamellar bodies, a PN2. The other lining cells appear to be PN1s.
Z15932. Lung. Alveolus and lining cells. Within the alveolus is a free and unattached cell which is not clearly identified as to cell type. All the lining pneumocytes appear to be flattened, but the one on the lower and middle right appears to contains several vacuoles and one distinct lamellar body, i.e., a PN2 which has differentiated into a PN1. No lamellar bodies noted in alveolar lumen.
Z15933. Lung. Alveolus and lining cells. The middle lining cell with only a small portion of nucleus showing contains several vacuoles, which appear to be "empty" lamellar bodies. The angular nucleus above it is a PN1 nucleus. The large dorsal clear pneumocyte has not flattened and may contain a couple empty lamellar vacuoles. The oblong nucleus beneath the PN2 is an endothelial cell nucleus. Some small tubular structures in the lumen of the alveolus may be released lamellar surfactant.
Z15934. Lung. Alveolus, lining cells and collapsed alveolar septa. The lining pneumocytes all appear flattened. No lamellar bodies are present. At the top is a large endothelial cell nucleus and erythrocyte adjacent to it. No unusual findings noted.

Conclusions: Several type II pneumocytes with lamellar bodies seen. Also, some lamellar substance within alveoli noted.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013; EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19568-2

Tissue: Liver

Treatment Group: 3.2 mg/kg, high-dose

Block No(s).: 99.39-11

Sex: non applicable

Photo/Negative No(s).: Z15799 - Z15802, Z15909

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15799. Liver. Hepatocyte with sinusoid containing hematopoietic cell at top and longitudinal segment of bile canaliculus at bottom right. Hepatocyte contains one distinct multivesicular body. Numerous mitochondria show some slight dilation of cristae, and there is some dilated blebbing of RER. Sinusoidal endothelial cell at top is poorly defined, suggestive of suboptimal fixation. Five (5) peroxisomes counted.
Z15800. Liver. Hepatocyte surrounded by hematopoietic cells. Six (6) peroxisomes counted.
Z15801. Liver. Hepatocyte surrounded by hematopoietic cells. Plasma membrane of the hepatocyte is indistinct and fixation is poor. . Mitochondria appear dense with some granular deposits and dilated cristae. Dilated blebs of RER are noted. Three (3) peroxisomes counted.
Z15802. Liver. Similar overall cellular morphology to Z15801. Plasma membrane is indistinct. . Mitochondria appear dense with some granular deposits and dilated cristae. Seven (7) peroxisomes counted.
Z15909. Liver. Hepatocyte with granular cytoplasm intermixed with mitochondria, RER, and random peroxisomes. . Mitochondria appear dense with some granular deposits and dilated cristae. Nine (9) peroxisomes counted.
Z15798: Liver. No negative; no print developed.

Conclusions: Normal hepatocyte. Suboptimal fixation. Average 6 peroxisomes per hepatocyte.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013; EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19568-2

Tissue: Lung

Treatment Group: 3.2 mg/kg, high-dose

Block No(s).: 99.39-12

Sex: non applicable

Photo/Negative No(s).: Z15803 - Z15807

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15803. Lung. Air space lined by several cuboidal epithelial cells. These cells appear to be pneumocytes which have not flattened out into differentiated PN1s. They have fine granular cytoplasm without many distinct organelles. Dorsally are two blood vessels lined by endothelial cells. No lamellar bodies noted.
Z15804. Lung. Alveolus and lining cells. Two cuboidal pneumocytes are PN2s and contain lamellar bodies. Two adjacent PN1s are associated with these cells. Adjacent tissue is collapsed septa and cell types are less clearly definable.
Z15805. Lung. A cluster of cuboidal pneumocytes similar to those described in Z15803. To the left is a capillary lined by an endothelial cell. Within the capillary are two lamellar-like structures that appear to be extracellular. No PN2s or alveolar lamellar bodies noted.
Z15806. Lung. Alveolus with lining cells. Pneumocytes are low cuboidal and appear to be PN1s, although not completely flattened out. No PN2s noted. The cell to the right with an oblong nucleus appears to be a fibroblast. It contains numerous RER and some collagen fibrils are present extracellulary.
Z15807. Lung. Alveolus with two PN1s, although cells are not flattened. Adjacent tissue is collapsed septa and interstitium. No PN2s or alveolar lamellar bodies noted.

Conclusions: Occasional type II pneumocytes noted. Some intravascular lamellar-like material also present. Many type I pneumocytes have apparently not flattened out, probably normal fetal lung.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013; EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19569-1

Tissue: Liver

Treatment Group: 3.2 mg/kg, high-dose

Block No(s).: 99.39-13

Sex: non applicable

Photo/Negative No(s).: Z15843 - Z15847

Significant Lesions (check one): X Yes _____ No

Interpreting Pathologist (signature and date): _____

Features: Z15843. Liver. Hepatocyte adjacent to central vein. Abundant numbers of mitochondria and RER are present, but plasma membranes and sinusoidal endothelium are poorly delineated. Cristae are dilated and broken up in some mitochondria. Multivesicular body present. Eleven (11) peroxisomes counted.
Z15844. Liver. Hepatocyte with some rarefaction of cytoplasm. Dilated RER are evident and some granular deposits are present in mitochondria. Eleven (11) peroxisomes are counted.
Z15845. Liver. Hepatocyte with hematopoietic cell in sinusoid at lower left of photograph. Mitochondria in hepatocyte contain dilated cristae. Two multivesicular bodies are present in the cytoplasm. The RER appears dilated with some blebbing. Cytosol appears rarefied and plasma membrane is poorly defined. Eleven (11) peroxisomes counted.
Z15846. Liver. Hepatocyte surrounded by hematopoietic cells. Morphology similar to those described above. A golgi associated with multivesicular body is present. The mitochondria contain multiple granular deposits and dilated cristae. Eleven (11) peroxisomes counted.
Z15847. Liver. Hepatocyte, similar to above descriptions. Plasma membrane is poorly defined and fixation is suboptimal. The mitochondria contain multiple granular deposits and dilated cristae. Nine (9) peroxisomes counted.

Conclusions: Hepatocytes appear to contain slightly more peroxisomes. Average 10.6 peroxisomes per hepatocyte. Suboptimal fixation. No other difference noted compared with control.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013; EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19569-1

Tissue: Lung

Treatment Group: 3.2 mg/kg, high-dose

Block No(s).: 99.39-14

Sex: non applicable

Photo/Negative No(s).: Z15848 - Z15852

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15848. Lung. Alveolus with lining cells. Several cuboidal pneumocytes are present. The central cell has two basilar vacuoles which probably represent lamellar bodies, although the lamellar material is absent in them. A small portion of a septal capillary is present at left.
Z15849. Lung. Section shows several cuboidal to columnar epithelial cells. The central cell appears to contain two small vacuoles, one with some lipid-like material, possibly a lamellar body. To the lower right of this cell is a cell with an irregular nucleus and several lipid or lamellar vacuoles; this cell appears to be a macrophage. A capillary is in the center of the photograph with an endothelial lining cells.
Z15850. Lung. A cluster of cuboidal pneumocytes, with mostly cytoplasm containing a fine granular material. No characteristic lamellar bodies are present in these pneumocytes or in the alveolar space. An interstitial cell contains a single myelin-like or lamellar body, but this cell is not clearly identified as to cell type.
Z15851. Lung. Two PN2s are present and they contain multiple lamellar bodies. A fibroblast appears to contain the elongated nucleus to the right of these PN2s.
Z15852. Lung. A cluster of pneumocytes or epithelial cells as described in above photographs. The top cell contains a couple lamellar bodies and is a PN2. The cells appear to be pneumocytes (PN1s) which haven't flattened out, or PN2s in transition to PN1s.

Conclusions: Essentially normal lung. Some random PN2s were identified. There are numerous cuboidal pneumocytes which appear to not have flattened out.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013; EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19572-1

Tissue: Liver

Treatment Group: 3.2 mg/kg, high-dose

Block No(s).: 99.39-15

Sex: non applicable

Photo/Negative No(s).: Z15853 - Z15857

Significant Lesions (check one): X Yes _____ No

Interpreting Pathologist (signature and date): _____

Features: Z15853. Liver. Plasma membranes are poorly defined and many cytoplasmic details are apparently lost. Membranes and cristae within mitochondria are indistinct. Nine (9) peroxisomes counted.
Z15854. Liver. Similar to Z15853, plasma and cellular membranes are poorly defined due to poor fixation. RER appears markedly dilated. Thirteen (13) peroxisomes counted.
Z15855. Liver. Hepatocyte with hematopoietic cells to the right margin and another hepatocyte and bile canaliculus at the top. RER profiles are dilated and plasma membranes are indistinct. Twelve (12) peroxisomes counted.
Z15856. Liver. Hepatocellular morphology is similar to cells described above. Fourteen (14) peroxisomes counted.
Z15857. Liver. Hepatocyte and surrounding hematopoietic cells. Plasma and cellular membranes are poorly defined. Eighteen (18) peroxisomes counted.

Conclusions: Hepatocytes poorly fixed. There are higher numbers of peroxisomes within hepatocytes as compared with controls. Average 13.2 peroxisomes per hepatocyte.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013; EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19572-1

Tissue: Lung

Treatment Group: 3.2 mg/kg, high-dose

Block No(s).: 99.39-16

Sex: non applicable

Photo/Negative No(s).: Z15858 - Z15863

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15858. Lung. Alveolus and lining cells. Central lining cell appears to contain one lamellar body to the right of its nucleus, a PN2. To its left is a capillary containing an erythrocyte and lining endothelial cell. Plasma and cellular membranes are poorly defined due to suboptimal fixation. Some cellular debris is present in the alveolar space.
Z15859. Lung. Alveolus and predominantly cuboidal lining cells. Lining cell on right and bottom right both contain some lamellar body vacuoles and appear to be PN2s. The other two pneumocytes appear to be PN1s. No specific abnormalities noted.
Z15860. Lung. Collapsed septum and lining cells. Most appear to be type I pneumocytes, although not flattened out. No lamellar bodies identified. Fixation is poor.
Z15861. Lung. Large top center cell is a pneumocyte. At its dorsal margin is vacuole that may be an "empty" lamellar body. Other lining cells appear to be type I pneumocytes. At bottom right is a small portion of a cell with some lysosomes that appear to contain some crystals or possibly lamellar debris. This cell may be a PN2 or a macrophage. The cell at top right with numerous cytoplasmic inclusions is a granulocyte within a capillary, its endothelial nucleus directly below the granulocyte.
Z15862. Lung. Collapsed septa. Lining this are several flattened pneumocytes, both dark and light. The collapsed area contains several light-staining pneumocytes and endothelial cells. A granulocyte is present in the capillary at the right. The oval nucleus next to this vessel appears to belong to a fibroblast. No abnormalities noted. No lamellar bodies clearly evident in this photograph.
Z15863. Lung. Collapsed septal area. The lamellar myelin-like material in the top center is within a capillary lumen. The top air space is lined by a flattened PN1. Some lamellar material may be present in the alveolus. At the bottom left is a darker cell which contains a lamellar body.

Conclusions: Essentially normal fetal lung. Some lamellar bodies noted in type II pneumocytes. Fixation was suboptimal.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013; EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19577-4

Tissue: Liver

Treatment Group: 3.2 mg/kg, high-dose

Block No(s).: 99.39-17 Z15864 - Z15868

Sex: non applicable

Photo/Negative No(s).: Z15940

Significant Lesions (check one): X Yes _____ No

Interpreting Pathologist (signature and date): _____

Features: Z15864. Liver. Hepatocyte with surrounding erythrocytes in sinusoids. Plasma and cellular membranes are indistinct due to poor fixation. Mitochondria show some granular deposits and dilated cristae. Three (3) peroxisomes counted.
Z15865. Liver. Hepatocyte surrounded by adjacent hepatocytes and hematopoietic cells. A bile canaliculus is present at the bottom of the photograph. Eleven (11) peroxisomes counted.
Z15866. No negative.
Z15867. Liver. The plasma membrane is indistinct. Eleven (11) peroxisomes counted.
Z15568. Liver. Hepatocyte and adjacent hematopoietic cells. Dilation and blebbing of RER. Plasma membranes are indistinct. Sixteen (16) peroxisomes counted. Some of the peroxisomes show advanced degeneration.
Z15940. Liver. Hepatocyte with poorly-defined plasma membranes. Mitochondria show dilatation of cristae. Fifteen (15) peroxisomes counted.

Conclusions: Hepatocytes exhibit features of poor fixation. There appears to be a slight increase in the number of peroxisomes per hepatocyte. Average 11.2 peroxisomes per hepatocyte.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013; EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19577-4

Tissue: Lung

Treatment Group: 3.2 mg/kg, high-dose

Block No(s).: 99.39-18

Sex: non applicable

Photo/Negative No(s).: Z15869 - Z15873

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15869. Lung. Alveolar space and lining cells. Central pneumocyte on right contains several lamellar bodies and is a PN2. A detached cell is just above this one and may be a pneumocyte or possibly a lymphocyte. At the top left is a capillary with an oblong endothelial cell nucleus.
Z15870. Lung. Area of collapsed alveolar septa. Centrally is a dark cell that contains several cytoplasmic vacuoles, two of which contain lamellar body material. Two cell beneath this cell also contain similar cytoplasmic vacuoles and may be PN2s. Other cells with abundant more clear cytoplasm appear to be type I pneumocytes, although they are not flattened.
Z15871. Lung. Ventrally a PN1 lines the airway space. The smaller dark cell adjacent to and covered by it contains multiple small clear vacuoles, but lamellar material is not clearly evident. Dorsally the tissue contains collapsed septa with a mixture of endothelial cells, capillary lumen, pneumocytes, and interstitium. No abnormalities noted.
Z15872. Lung. Area of collapsed alveoli and septa. Centrally are two PN2s containing vacuoles and lamellar bodies. Ventrally is a capillary containing a lamellar-type body within its lumen.
Z15873. Lung. Ventrally are several cuboidal pneumocytes lining an alveolar space. The central cell contains a couple small lamellar-type structures in its cytoplasm. To the right and top right are capillaries containing some lamellar material in their lumina. At the top is a flattened pneumocyte.

Conclusions: Normal lung. Some type II pneumocytes identified. Some lamellar structures present within capillary lumina.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013 EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19579-3

Tissue: Liver

Treatment Group: 3.2 mg/kg, high-dose

Block No(s).: 99.39-19

Sex: non applicable

Photo/Negative No(s).: Z15874 - Z15878

Significant Lesions (check one): X Yes _____ No

Interpreting Pathologist (signature and date): _____

Features: Z15874. Liver. Hepatocyte surrounded by hematopoietic cell at lower left and sinusoid containing erythrocytes at upper right. Endothelial cell is poorly delineated and hepatocellular plasma membranes are indistinct. Seventeen (17) peroxisomes counted.
Z15875. Liver. Hepatocyte mixed with some hematopoietic cells. Hepatocellular boundaries are incomplete on this cell, and peroxisomes are not counted for this cell. Granular deposits are present in some mitochondria. There appears to be abundant rough endoplasmic reticulum.
Z15876. Liver. Hepatocyte with indistinct plasma membranes, but contains abundant mitochondria, endoplasmic reticulum, and peroxisomes. Thirty (30) peroxisomes counted.
Z15877. Liver. Hepatocyte, similar in overall morphology to those described above. Some granular deposits are present within some mitochondria. Endoplasmic reticulum and nuclear envelope appear dilated. Twenty-four (24) peroxisomes counted.
Z15878. Liver. Hepatocyte, similar in overall morphology to those described above. Some granular deposits are present within some mitochondria. Endoplasmic reticulum and nuclear envelope appear dilated. Sixteen (16) peroxisomes counted.

Conclusions: Tissue fixation suboptimal, but better than some previous animals. There appears to be increased numbers of peroxisomes per hepatocyte. Average 21.75 per hepatocyte (four cells counted). No other changes noted compared with control livers.

TRANSMISSION ELECTRON MICROGRAPH INTERPRETATION

Study No.: 418-013 EM-99.39

Species/Strain: Crl:CD®BR VAF/Plus® Rat

Animal No.: 19579-3

Tissue: Lung

Treatment Group: 3.2 mg/kg, high-dose

Block No(s).: 99.39-20

Sex: non applicable

Photo/Negative No(s).: Z15879 - Z15883

Significant Lesions (check one): _____ Yes ___X___ No

Interpreting Pathologist (signature and date): _____

Features: Z15879. Lung. Alveolus, lining cells and collapsed alveolar septa area. The lining cell contains several lamellar bodies and is a PN2. Some miscellaneous cellular debris appears to be in the alveolar lumen, but no lamellar material. To the right is a cell containing several cytoplasmic vacuoles and an irregular nucleus. This may be a PN2, but also may be a macrophage. Other cells appear to be compressed pneumocytes.
Z15880. Lung. Centrally is a fine granular material containing multiple lamellar bodies. This appears to be extracellular, although it appears mixed with other cellular debris and is probably a ruptured (artifactually?) PN2. Other cells lining the airway appear to be PN1s.
Z15881. Lung. Area of collapsed alveoli and septa. Centrally are several cells which contain large vacuoles containing some scant material. These may be PN2s, but also may be macrophages. At the top an elliptical vacuole appears to contain some lamellar material. Three dorsal nuclei have dilated nuclear envelopes, suggesting suboptimal fixation.
Z15882. Lung. Thickened, collapsed septal wall, lined by pneumocytes. Some free lamellar material appears in the alveolar lumen on the left mixed with some cellular debris. The central cell in the "septum" appears to be a PN1. The right margin is lined by a PN1. The dark septal cell at the lower right contains some lamellar bodies and is probably a PN2.
Z15883. Lung. Area of collapsed alveoli and septa. Similar to Z15880, this might represent a ruptured PN2. At top in the lumen is multiple lamellar bodies. The collapsed septa and capillaries appear essentially normal.

Conclusions: Essentially normal lung. Some normal type II pneumocytes identified. Some lamellar material identified within alveoli.

III. Transmission Electron Micrographs

NOTE:

The original glossy figure photographs (Figures 1 - 14) were delivered to Dr. Marvin T. Case with the draft pathology report on March 19, 1999.

Figure Legends

Magnification. Print magnification is indicated on the back of each photograph. All report figures are at a magnification of 11,200X. The measurement bar on each photomicrograph equals one micron (0.001mm).

Figure 1. Liver. Hepatocyte showing normal cytoplasmic organelles. Clumping of mitochondria and rough endoplasmic reticulum reflects suboptimal fixation. Some peroxisomes are identified. Hematopoietic cells are present ventrally. A bile canaliculus is present at the junction of three hepatocytes in the top left. Animal No. 19506-4, 0 mg/kg/day (control), 11,200X magnification.

Figure 2. Liver. Hepatocyte. Dilatation of the rough endoplasmic reticulum, an indistinct plasma membrane, and organelle clumping indicate suboptimal fixation. Mitochondria are dense and show some granular deposits and dilated cristae. Some representative peroxisomes are labeled. An endothelial cell nucleus is present lining the sinusoid in the upper left corner of the photograph. Animal No. 19509-1, 0 mg/kg/day (control), 11,200X magnification.

Figure 3. Liver. Cellular morphology is similar to Figure 2. Some peroxisomes are labeled and appear more numerous than in controls. The rough endoplasmic reticulum and nuclear envelope are dilated. A bile canaliculus is present in upper left of the photograph Animal No. 19534-1, 0.4 mg/kg/day, 11,200X magnification.

Figure 4. Liver. Mitochondria show dilatation of cristae. Some peroxisomes, increased in number, are labeled. Some hematopoietic cells are present in the adjacent sinusoid. Animal No. 19560-2, 1.6 mg/kg/day, 11,200X magnification.

Figure 5. Liver. Hepatocyte with an indistinct plasma membrane. Cristae are dilated within mitochondria. Several peroxisomes are labeled. Animal No. 19577-4, 3.2 mg/kg/day (high-dose), 11,200X magnification.

Figure 6. Liver. Hepatocyte whose plasma membrane is indistinct. Representative peroxisomes are labeled. Animal No. 19579-3, 3.2 mg/kg/day (high-dose), 11,200X magnification.

Figure 7. Lung. Alveolus and lining cells. Two type II pneumocytes containing lamellar bodies are present. The central dark cell may be a type II pneumocyte which has expressed its lamellar bodies. Type I pneumocytes can be seen lining the alveolus at the top and bottom margin of the air space. Subjacent alveoli are collapsed and the represented cells are pneumocytes and septal cells at different functions of cut. Animal No. 19505-1, 0 mg/kg/day (control), 11,200X magnification.

Figure 8. Lung. Alveoli and septum. A type II pneumocyte is present lining the right alveolus. This cell contains several lamellar bodies containing faint laminated material. The other lining cells are type I pneumocytes. An endothelial cell and capillary are present in the septum at the top of the photograph. Animal No. 18915-1, 0 mg/kg/day (control), 11,200X magnification.

Figure 9. Lung. Alveolus and septa. The central narrow alveolus is bounded by two septa containing capillaries with luminal erythrocytes. A lamellar myelin-like structure is present in the lumen of the upper capillary. Flattened type I pneumocytes line the alveolus. No type II pneumocytes or lamellar bodies are evident in this photograph. Animal No. 19504-3, 0 mg/kg/day (control), 11,200X magnification.

Figure 10. Lung. Alveolus and lining cells. A type II pneumocyte containing multiple lamellar bodies is present centrally. Much of the lamellar material has washed-out of the lamellar bodies. A second type II pneumocyte is present near the bottom, and contains a single lamellar body. The remaining cells appear to be type I pneumocytes. Animal No. 19546-1, 0.4 mg/kg/day, 11,200X magnification.

Figure 11. Lung. Alveolus and lining cells. At the top is a cuboidal type II pneumocyte containing several lamellar bodies. The adjacent lining cells appear to be pneumocytes which have not flattened out. The lamellar myelin-like structures are extracellular within capillary spaces. Animal No. 19560-2, 1.6 mg/kg/day, 11,200X magnification.

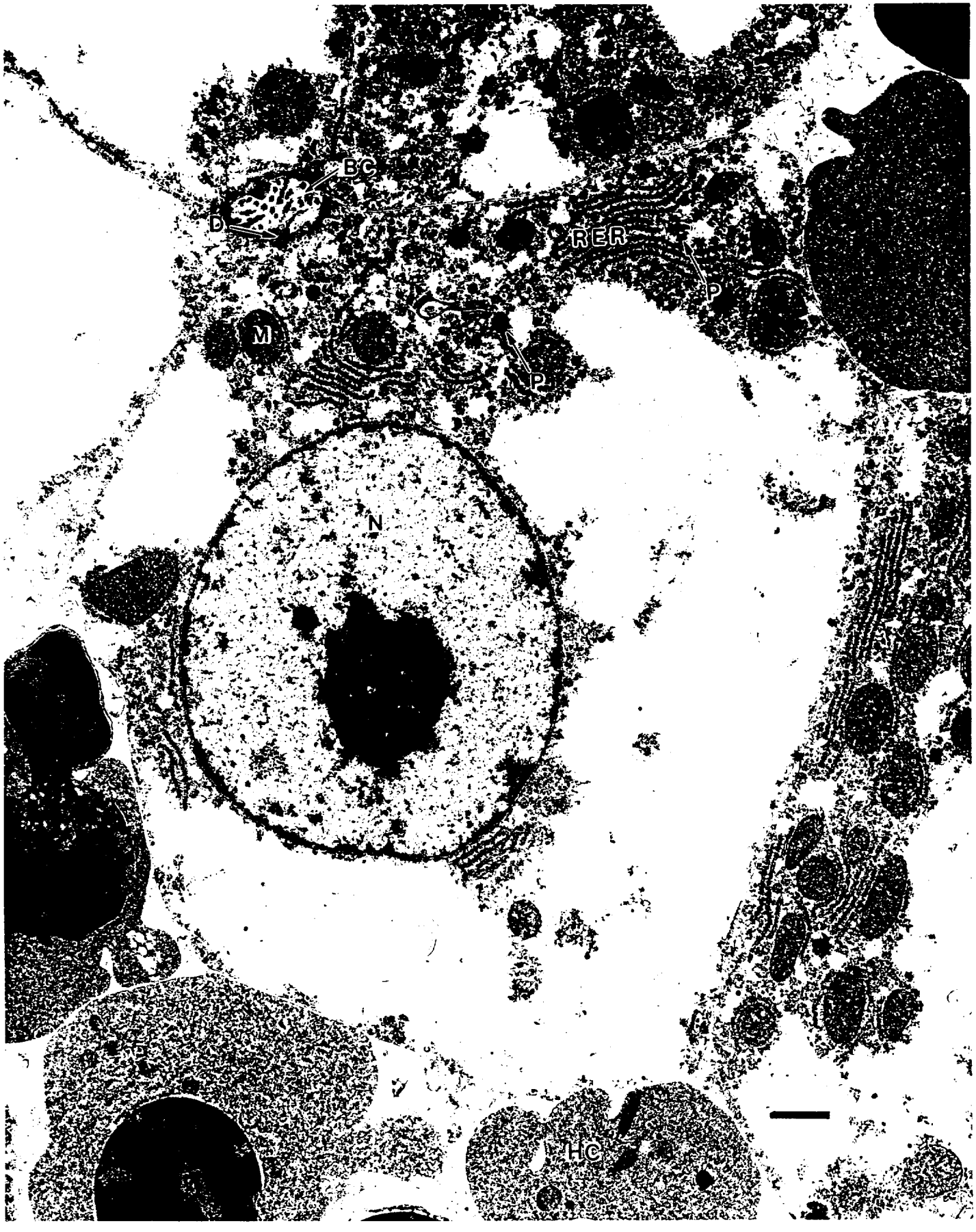
Figure 12. Lung. Alveolus and lining cells. Alveolar space contains abundant lamellar-like material, which is consistent with surfactant secreted from type II pneumocytes. The dark cellular segment near the bottom may be an extension of a type II pneumocyte. The remaining lining cells appear to be type I pneumocytes or cuboidal pneumocytes. Capillaries with lining endothelial cells are present dorsally and at the lower right. Animal No. 19560-3, 1.6 mg/kg/day (high-dose), 11,200X magnification.

Figure 13. Lung. Alveolus and lining cells. Two type II pneumocytes containing lamellar bodies are present. A type I pneumocyte is present lining the alveolus ventral to the type II pneumocytes. Within the septal wall collagen fibers and a fibroblast are evident. The material in the alveolus is nondescript cellular debris. Animal No. 19569-4, 3.2 mg/kg/day (high-dose), 11,200X magnification.

Figure 14. Lung. Alveoli and septum. Both sides of the septum are lined by flattened pneumocytes. The large central cell in the septum appears to be a type I pneumocyte. Two cells ventrally contain lamellar bodies and are type II pneumocytes. Animal No. 19579-3, 3.2 mg/kg/day (high-dose), 11,200X magnification.

Index of Labels for Ultrastructural Structures

Abbreviation	Structure
A	Alveolar space
BC	Bile canaliculus
BE	Bronchiolar epithelium
CL	Capillary lumen
Cap	Capillary
CN	Centrioles
CO	Collagen
CP	Cuboidal pneumocyte
D	Desmosome
DD	Dense deposits
DC	Dilated cristae
DN	Dilated nuclear envelope
DR	Dilated RER
EC	Endothelial cell
ER	Erythrocyte
FB	Fibroblast
G	Glycogen
HC	Hematopoietic cells
L	Lipid droplet
LB	Lamellar body
M	Mitochondria
N	Nucleus
P	Peroxisome
PN1	Type I pneumocyte
PN2	Type II pneumocyte
PM	Plasma membrane
RER	Rough endoplasmic reticulum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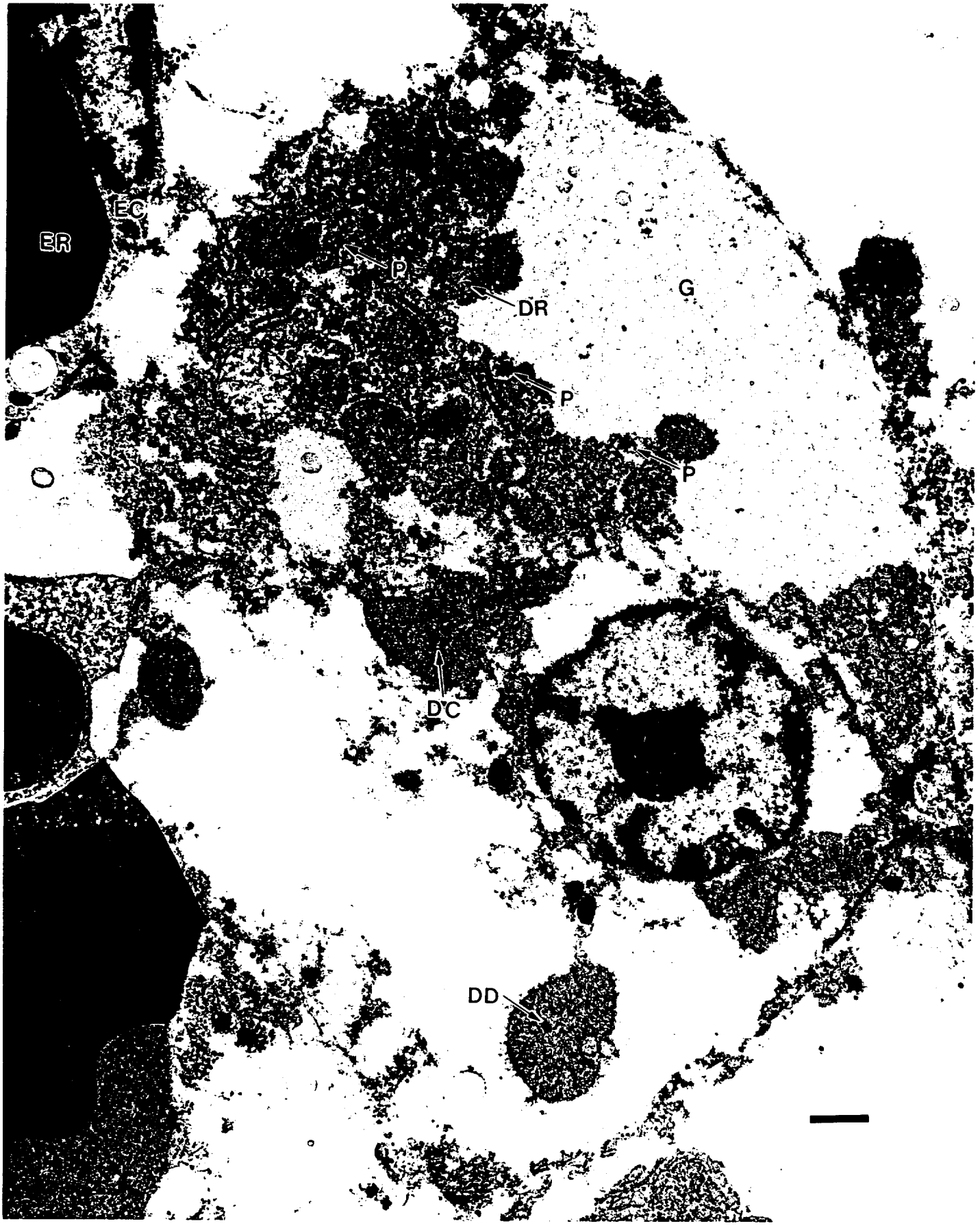
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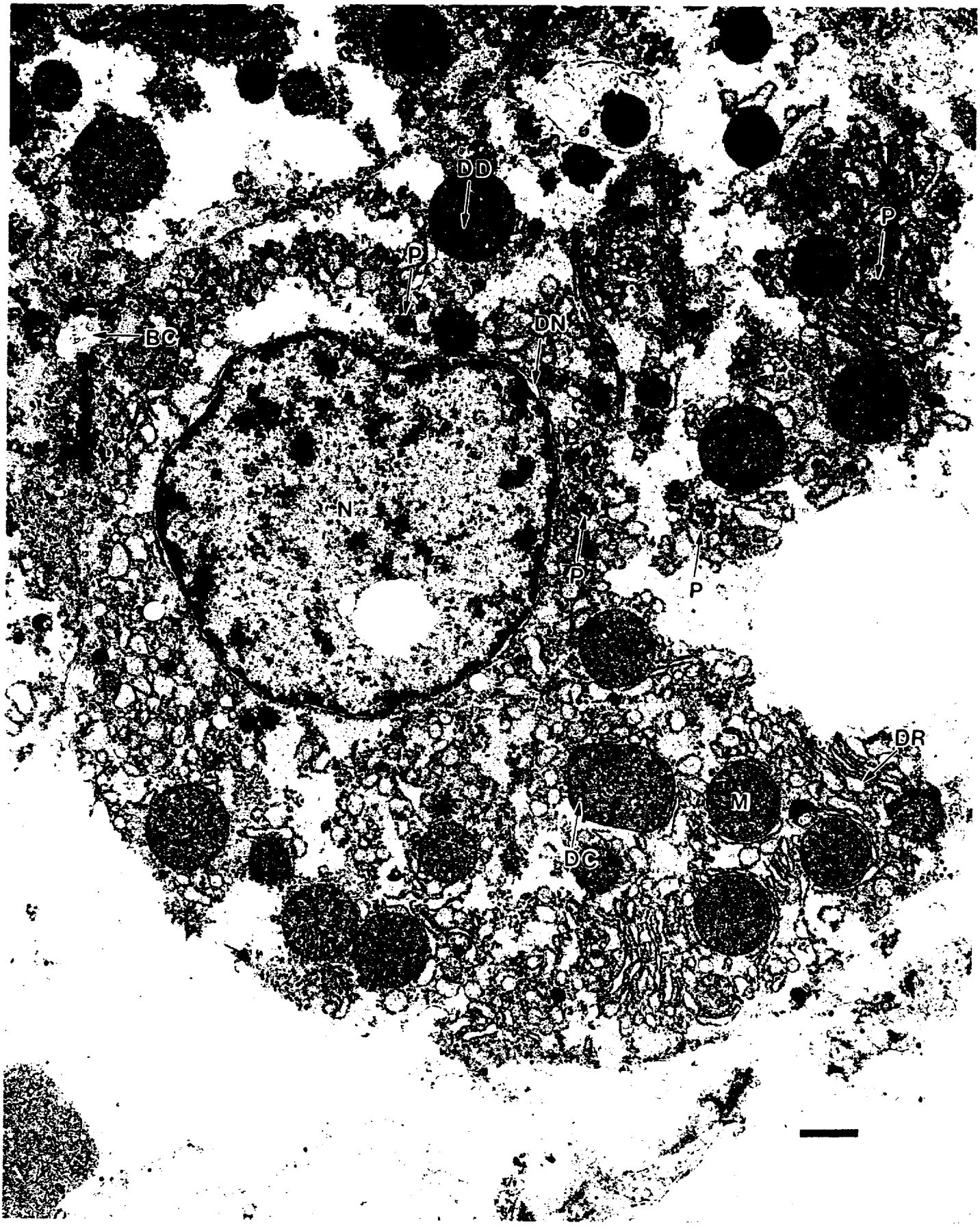
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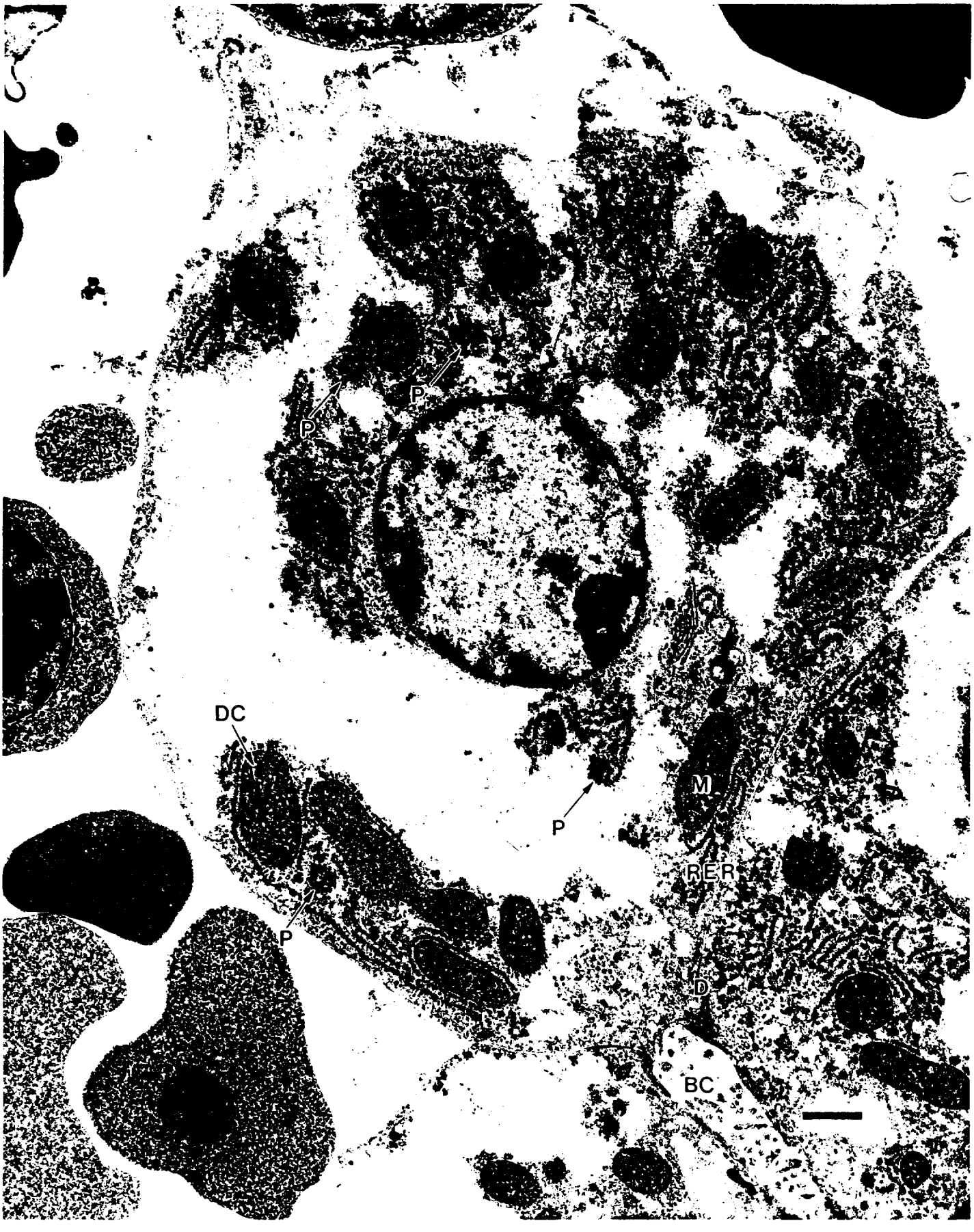
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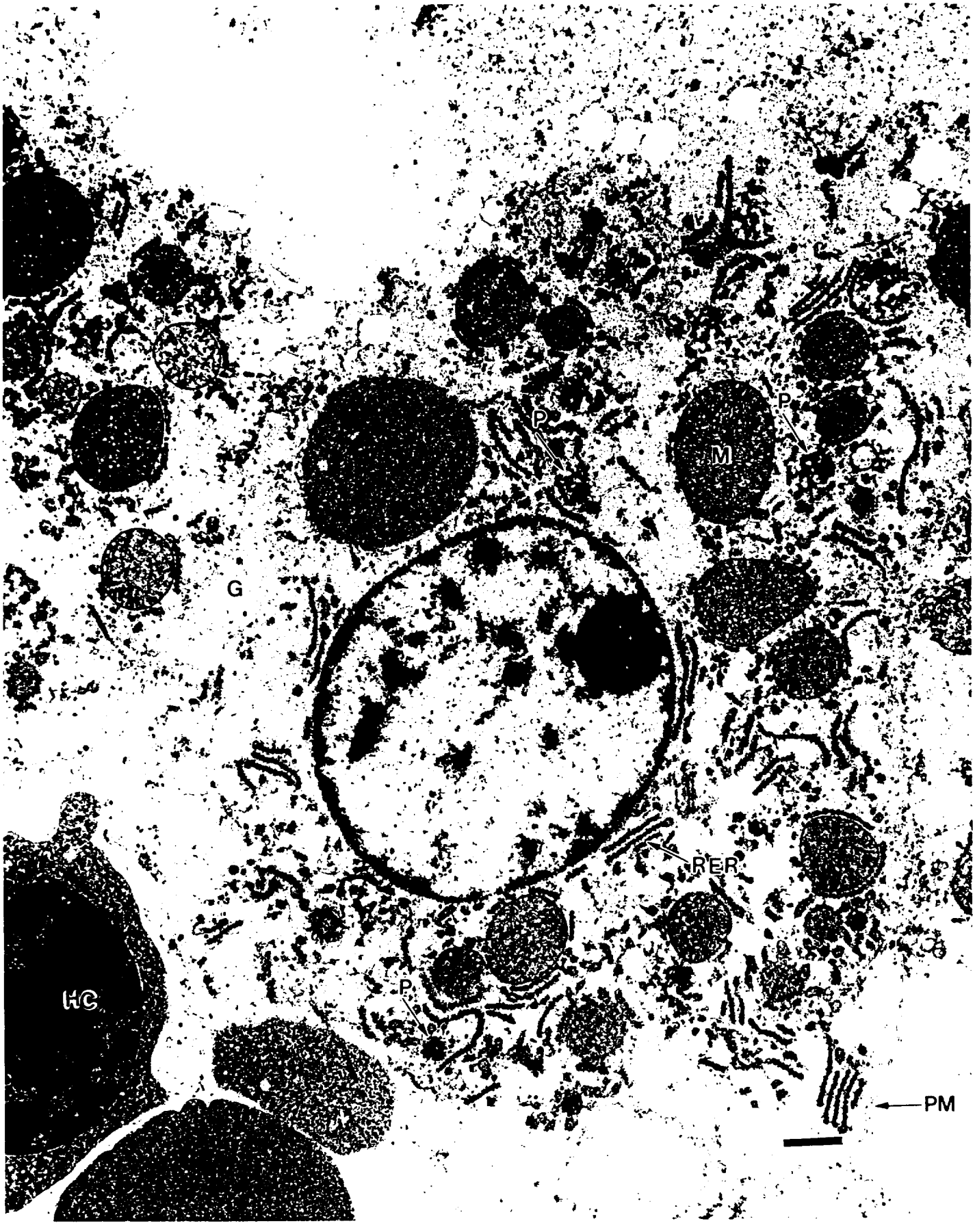
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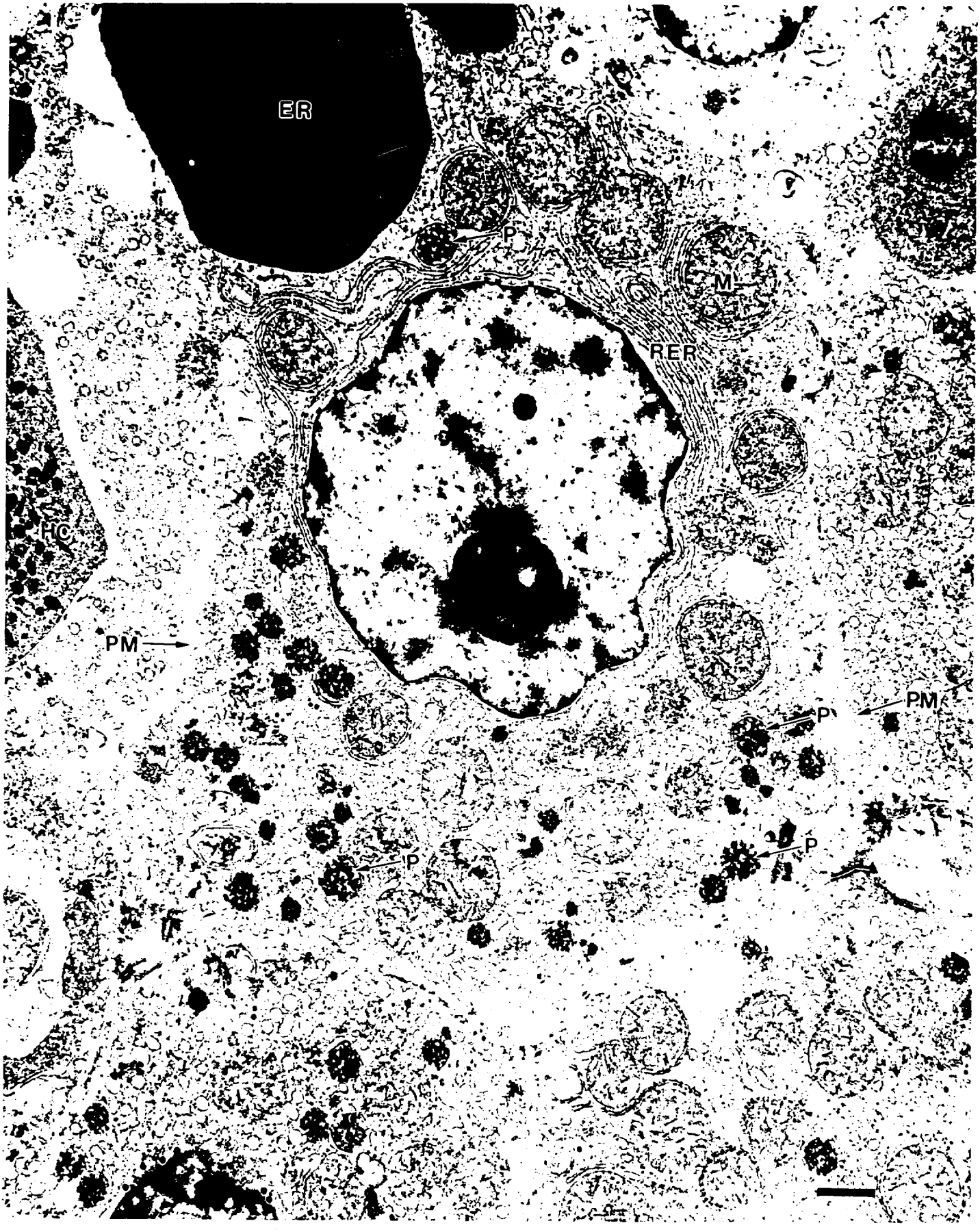
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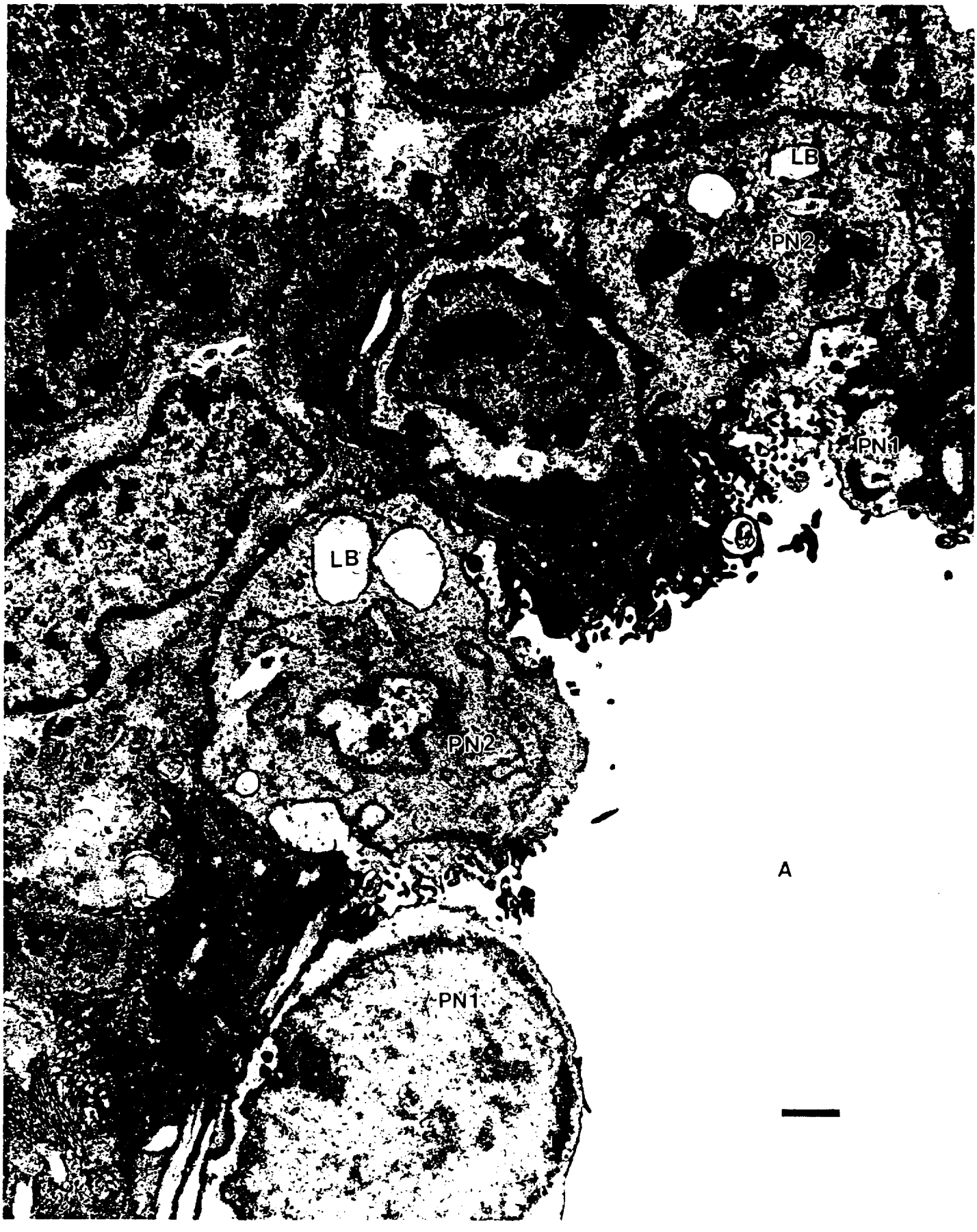
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PN1
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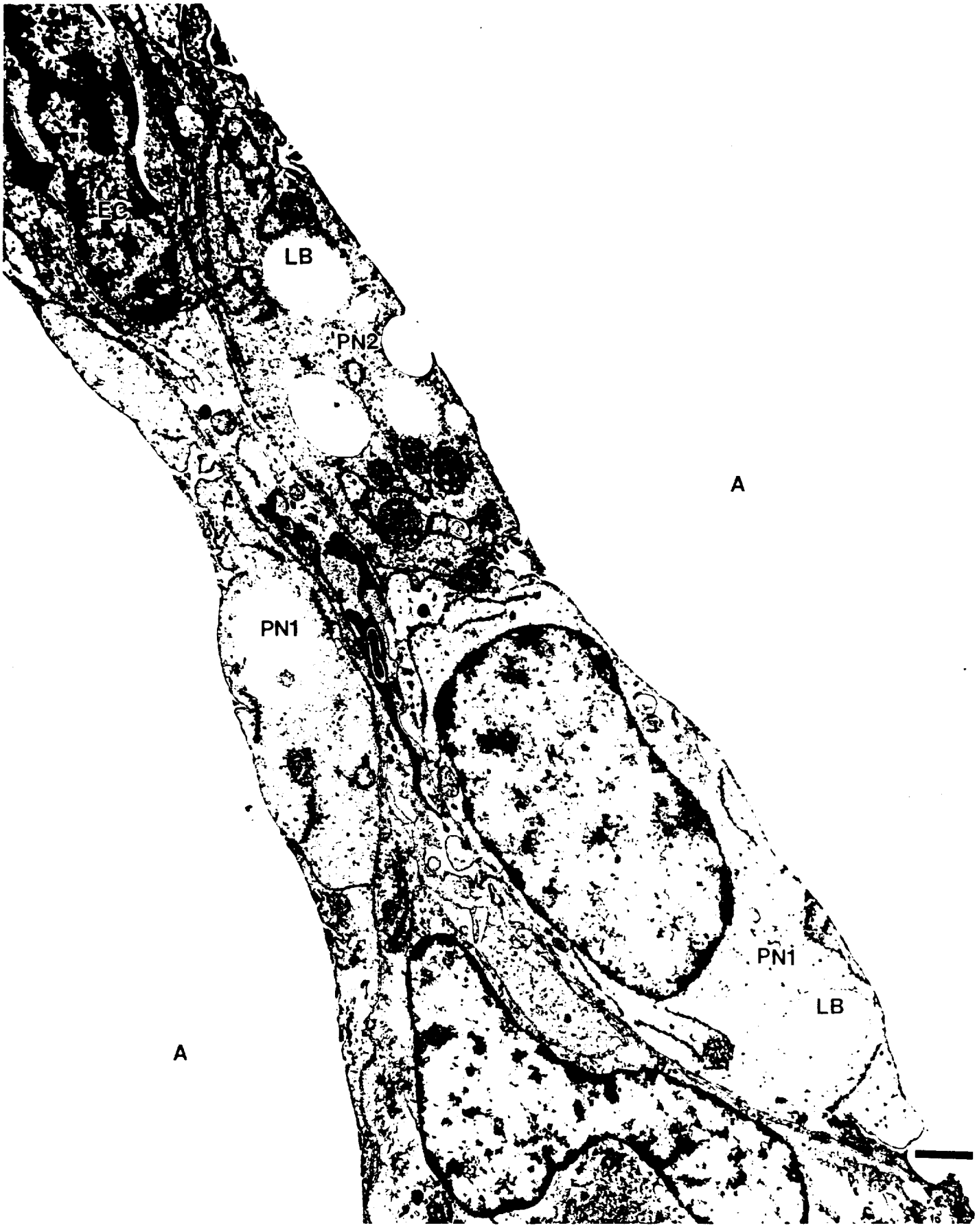
PN1
A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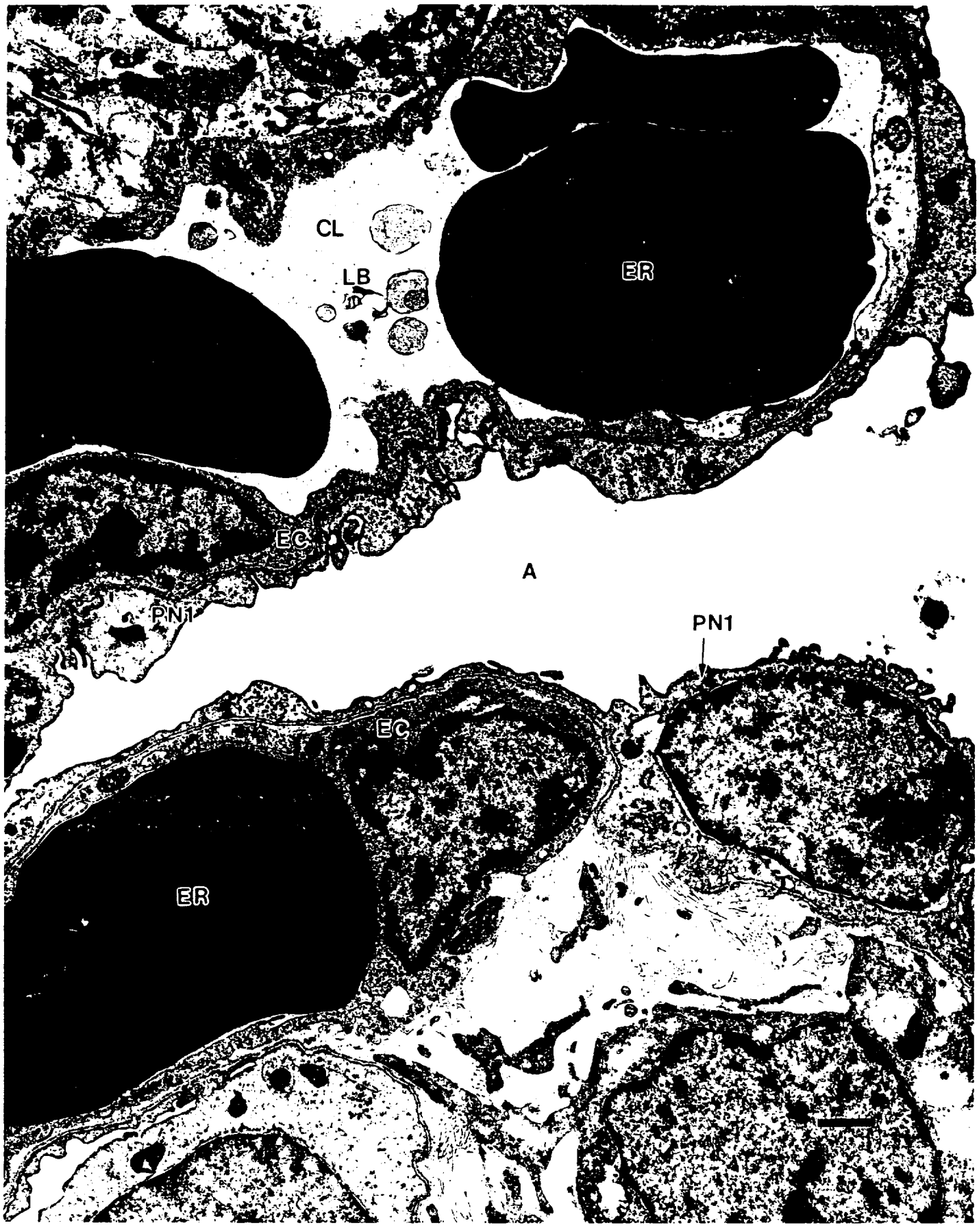
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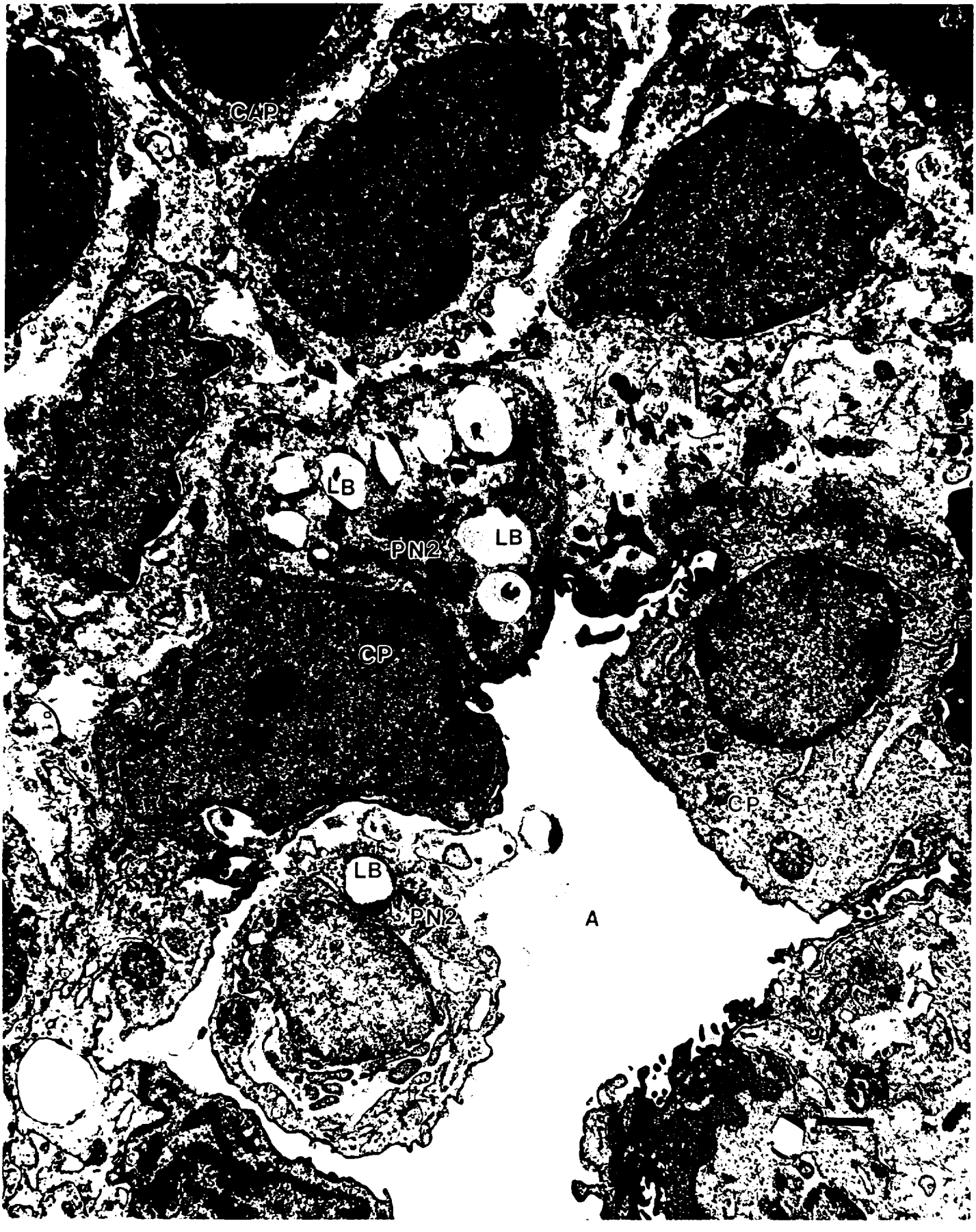
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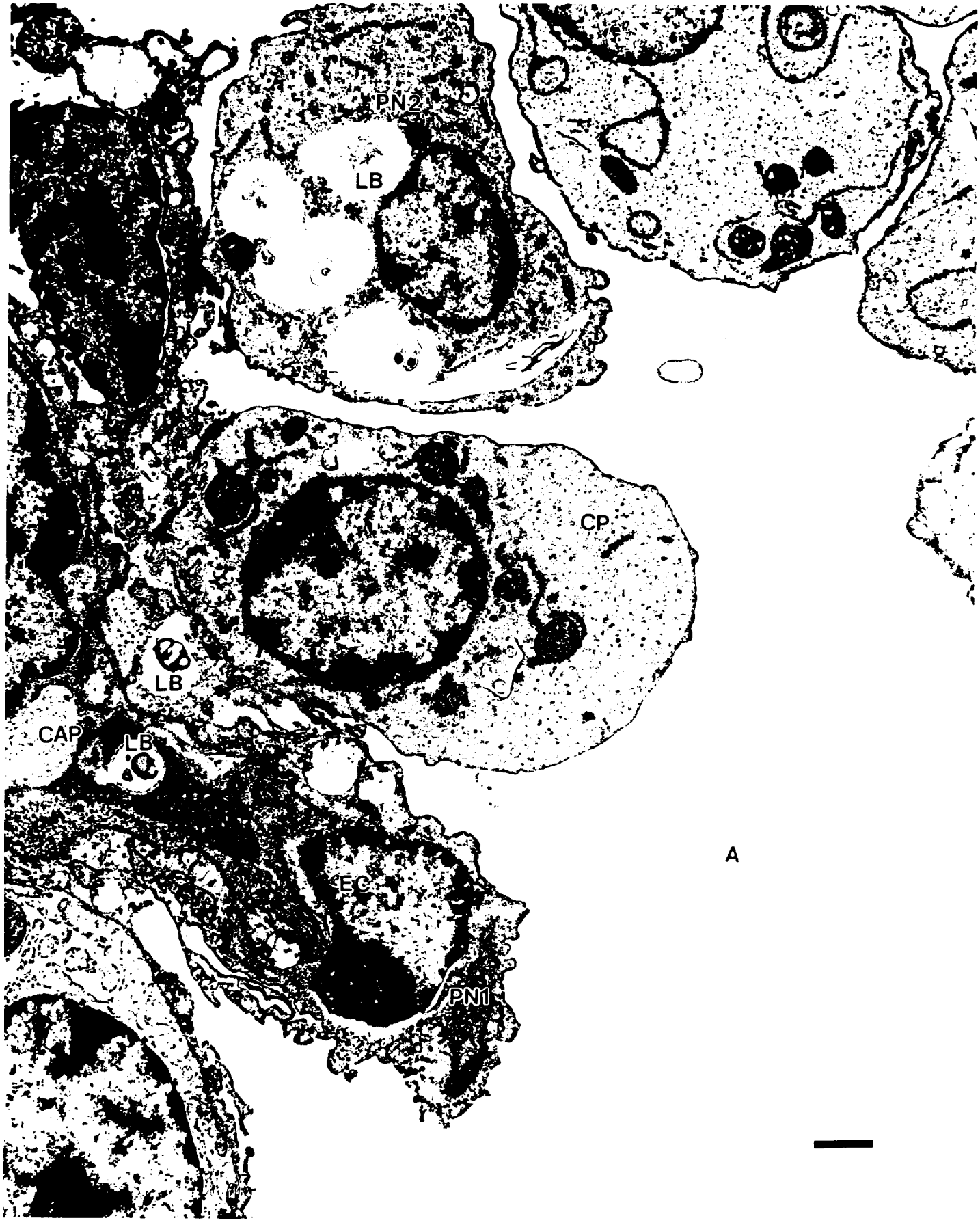
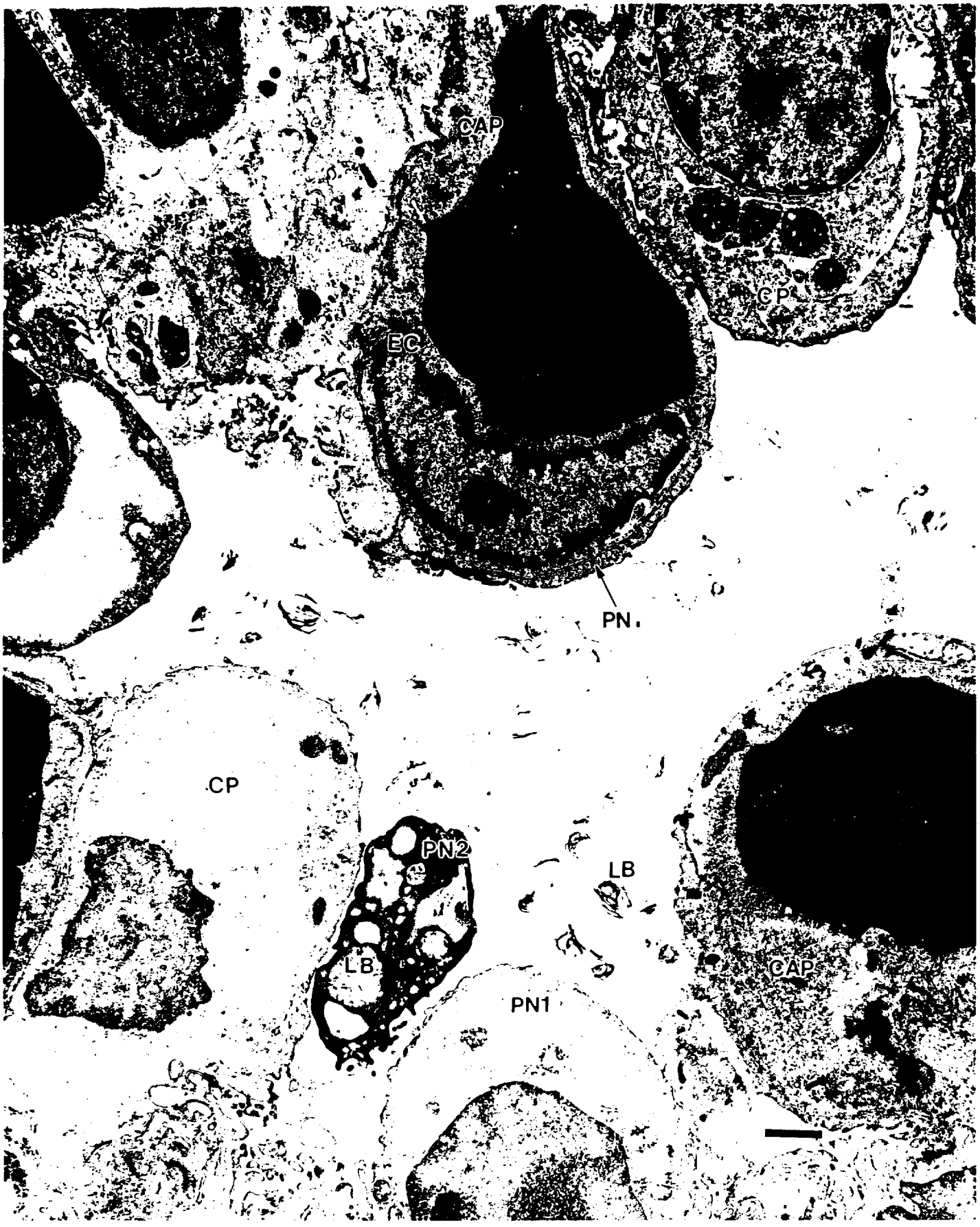
LB
PN2
LB
CP
CP
LB
PN2
A


PN2
LB
CP
LB
CAP
LB
EC
PN1
A


CAP
CP
EC
PN
CP
PN2
LB
LB
CAP
PN1


PN2
LB
FB
CO
LB
PN2
CO
PN1


LB
PN1
PN1
PN1
A
A
LB
PN2
LB
PN2

IV. Quality Assurance Statement

QUALITY ASSURANCE STATEMENT

This electron microscopy study has been inspected and audited by the Quality Assurance Unit as required by the Good Laboratory Practices Regulations promulgated by the U.S. Food and Drug Administration. PAI has a functioning and responsive Quality Assurance Unit which reports directly to management. The following is a record of inspections/audits and their resulting reports:

Date of Inspection	Phase Inspected	Date Findings Reported to Management and Study Director
2/22/99	Processing and Embedding	2/22/99
3/22, 23, 24, 25/99	Data Audit	3/25/99
3/25/99	Draft Report Audit	3/25/99
4/5/99	Final Report Audit	4/5/99

Jeanne deWard, B.S., RQAP-GLP
Quality Assurance Specialist

4/5/99
Date

Sponsor: 3M Corporate Toxicology

Test Article: PFOS

Study Number: 418-013, PAI Study EM-99.39