PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 32 (PAGE 7): MATING AND FERTILITY AND DAYS IN COHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP 7 — 2 MG/KG PFOS + CHOLESTEROL

RAT #	DAYS IN COHABITATION	MATING STATUS	MATING DATE	PREGNANCY STATUS
10985	3	M	C	P
10986	3	M	C	P
10987	3	M	C	P
10988	3	M	C	P
10989	1	M	C	P
10990	4	M	C	P
10991	3	M	C	P
10992	4	M	C	P
10993	2	M	C	P
10994	3	M	C	P
10995	2	M	C	P
10996	3	M	C	P
10997	2	M	C	P
10998	2	M	C	NP
11586	1	M	C	P
11587	1	M	C	P
11588	5	M	C	P
11589	2	M	C	P
11590	2	M	C	P
11591	1	M	C	P
11592	13	M	C	P
11593	1	M	C	P
11594	1	M	C	P
11595	1	M	C	P
11596	1	M	C	P
11597	1	M	C	P
11598	3	M	C	P
11599	4	M	C	P

M = MATED C = CONFIRMED P = PREGNANT NP = NOT PREGNANT

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 32 (PAGE 8): MATING AND FERTILITY AND DAYS IN COHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP 8 — 0.4 MG/KG PFOS

RAT #	DAYS IN COHABITATION	MATING STATUS	MATING DATE	PREGNANCY STATUS
10999	3	M	C	P
11000	3	M	C	P
11001	2	M	C	P
11002	4	M	C	P
11003	3	M	C	P
11004	3	M	C	P
11005	3	M	C	P
11006	4	M	C	P
11007	3	M	C	P
11008	4	M	C	P
11600	3	M	C	P
11601	2	M	C	P
11602	1	M	C	P
11603	2	M	C	P
11604	2	M	C	P
11605	4	M	C	P
11606	1	M	C	P
11607	3	M	C	P
11608	3	M	C	P
11609	1	M	C	P

M = MATED C = CONFIRMED P = PREGNANT NP = NOT PREGNANT

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 32 (PAGE 9): MATING AND FERTILITY AND DAYS IN COHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP 9 — 0.8 MG/KG PFOS

RAT #	DAYS IN COHABITATION	MATING STATUS	MATING DATE	PREGNANCY STATUS
11009	3	M	C	P
11010	4	M	C	P
11011	2	M	C	P
11012	3	M	C	P
11013	4	M	C	P
11014	14	DID NOT MATE	-	-
11015	4	M	C	P
11016	1	M	C	P
11017	3	M	C	NP
11018	5	M	C	P
11610	1	M	C	NP
11611	1	M	C	P
11612	1	M	C	P
11613	2	M	C	P
11614	2	M	C	P
11615	4	M	C	P
11616	3	M	C	P
11617	1	M	C	P
11618	4	M	C	P
11619	1	M	C	P

M = MATED C = CONFIRMED P = PREGNANT NP = NOT PREGNANT

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 32 (PAGE 10): MATING AND FERTILITY AND DAYS IN COHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP 10 — 1 MG/KG PFOS

RAT #	DAYS IN COHABITATION	MATING STATUS	MATING DATE	PREGNANCY STATUS
11019	14	M	C	P
11020	3	M	C	P
11021	1	M	C	P
11022	6	M	C	NP
11023	3	M	C	P
11024	1	M	C	P
11025	5	M	C	P
11026	4	M	C	P
11027	1	M	C	P
11028	3	M	C	P
11620	2	M	C	P
11621	1	M	C	P
11622	1	M	C	P
11623	4	M	C	P
11624	2	M	C	P
11625	1	M	C	P
11626	2	M	C	P
11627	3	M	C	P
11628	1	M	C	P
11629	2	M	C	P

M = MATED C = CONFIRMED P = PREGNANT NP = NOT PREGNANT

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 32 (PAGE 11): MATING AND FERTILITY AND DAYS IN COHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP 11 — 1.2 MG/KG PFOS

RAT #	DAYS IN COHABITATION	MATING STATUS	MATING DATE	PREGNANCY STATUS
11029	4	M	C	P
11030	14	DID NOT MATE	-	-
11031	4	M	C	P
11032	2	M	C	P
11033	2	M	C	P
11034	1	M	C	P
11035	2	M	C	P
11036	3	M	C	P
11037	1	M	C	P
11038	3	M	C	P
11630	2	M	C	P
11631	2	M	C	NP
11632	1	M	C	P
11633	2	M	C	P
11634	1	M	C	P
11635	1	M	C	P
11636	1	M	C	P
11637	1	M	C	P
11638	2	M	C	P
11639	1	M	C	P

M = MATED C = CONFIRMED P = PREGNANT NP = NOT PREGNANT

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 32 (PAGE 12): MATING AND FERTILITY AND DAYS IN COHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP 12 — 1.6 MG/KG PFOS

RAT #	DAYS IN COHABITATION	MATING STATUS	MATING DATE	PREGNANCY STATUS
11039	14	DID NOT MATE	-	-
11040	1	M	C	P
11041	4	M	C	P
11042	4	M	C	P
11043	2	M	C	NP
11044	1	M	C	P
11045	1	M	C	P
11046	3	M	C	P
11047	3	M	C	P
11048	4	M	C	P
11049	5	M	C	P
11050	1	M	C	P
11051	3	M	C	P
11052	1	M	C	P
11640	3	M	C	P
11641	3	M	C	P
11642	2	M	C	P
11643	1	M	C	P
11644	2	M	C	P
11645	1	M	C	P
11646	1	M	C	P
11647	1	M	C	P
11648	4	M	C	P
11649	1	M	C	P
11650	13	M	C	P
11651	4	M	C	P
11652	3	M	C	NP
11653	1	M	C	P

M = MATED C = CONFIRMED P = PREGNANT NP = NOT PREGNANT

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 32 (PAGE 13): MATING AND FERTILITY AND DAYS IN COHABITATION - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP 13 — 2 MG/KG PFOS

RAT #	DAYS IN COHABITATION	MATING STATUS	MATING DATE	PREGNANCY STATUS
11053	4	M	C	P
11054	4	M	C	P
11055	3	M	C	P
11056	4	M	C	P
11057	1	M	C	P
11058	3	M	C	P
11059	4	M	C	P
11060	1	M	C	P
11061	3	M	C	P
11062	1	M	C	P
11063	2	M	C	P
11064	12	M	C	P
11065	1	M	C	P
11066	2	M	C	P
11654	1	M	C	P
11655	3	M	C	P
11656	2	M	C	P
11657	2	M	C	P
11658	3	M	C	P
11659	2	M	C	P
11660	3	M	C	P
11661	2	M	C	P
11662	1	M	C	P
11663	1	M	C	P
11664	2	M	C	P
11665	1	M	C	P
11666	3	M	C	P
11667	3	M	C	NP
				P

M = MATED C = CONFIRMED P = PREGNANT NP = NOT PREGNANT

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 33 (PAGE 1): CAESAREAN-SECTIONING OBSERVATIONS - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

	VIABLE FETUSES			DEAD FETUSES			EARLY RESORPTIONS			LATE RESORPTIONS			IMPLANTATION SITES			CORPORA LUTEA		
RAT #	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT OVARY	LEFT OVARY	TOTAL
DOSAGE GROUP 1								VEHICLE CONTROL										
10901	6	7	13	0	0	0	1	0	1	0	0	0	7	7	14	8	7	15
10902	5	7	12	0	0	0	0	1	1	0	0	0	5	8	13	6	8	14
10903	10	4	14	0	0	0	1	0	1	0	0	0	11	4	15	12	4	16
10904	9	5	14	0	0	0	0	1	1	0	0	0	9	6	15	9	7	16
10905	5	8	13	0	0	0	1	0	1	0	0	0	6	8	14	8	8	16
10907	9	7	16	0	0	0	0	1	1	0	0	0	9	8	17	9	10	19
10908	8	6	14	0	0	0	1	0	1	0	0	0	9	6	15	9	6	15
10910	7	5	12	0	0	0	2	2	4	0	0	0	9	7	16	10	8	18
10912	NOT PREGNANT																	
DOSAGE GROUP 2								MEVALONIC ACID CONTROL										
10915	9	5	14	0	0	0	1	1	2	0	0	0	10	6	16	12	7	19
10916	7	9	16	0	0	0	0	1	1	0	0	0	7	10	17	7	11	18
10917	7	3	10	0	0	0	4	0	4	0	0	0	11	3	14	11	5	16
10918	5	9	14	0	0	0	0	0	0	0	0	0	5	9	14	8	11	19
10919	6	9	15	0	0	0	0	0	0	0	0	0	6	9	15	11	14	25
10920	6	3	9	0	0	0	5	1	6	0	0	0	11	4	15	14	9	23
10925	8	8	16	0	0	0	0	0	0	0	0	0	8	8	16	8	9	17
10928	7	8	15	0	0	0	1	0	1	0	0	0	8	8	16	8	8	16
DOSAGE GROUP 3								1.6 MG/KG PFOS + MEVALONIC ACID										
10930	8	5	13	0	0	0	0	1	1	0	1	1	8	7	15	11	8	19
10931	8	5	13	0	0	0	1	0	1	0	0	0	9	5	14	9	5	14
10932	7	8	15	0	0	0	0	1	1	0	0	0	7	9	16	11	11	22
10933	7	9	16	0	0	0	2	0	2	0	0	0	9	9	18	9	9	18
10934	5	4	9	0	0	0	5	3	8	0	0	0	10	7	17	13	10	23
10935	6	6	12	0	0	0	0	0	0	0	0	0	6	6	12	6	6	12
10937	7	4	11	0	0	0	2	0	2	0	0	0	9	4	13	9	4	13
10940	7	12	19	0	0	0	0	0	0	0	0	0	7	12	19	7	12	19

PLACENTAE APPEARED NORMAL UNLESS NOTED OTHERWISE.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 33 (PAGE 2): CAESAREAN-SECTIONING OBSERVATIONS - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

	VIABLE FETUSES			DEAD FETUSES			EARLY RESORPTIONS			LATE RESORPTIONS			IMPLANTATION SITES			CORPORA LUTEA		
RAT #	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT OVARY	LEFT OVARY	TOTAL
DOSAGE GROUP 4								2 MG/KG PFOS + MEVALONIC ACID										
10945	10	6	16	0	0	0	0	0	0	0	0	0	10	6	16	11	6	17
10946	11	4	15	0	0	0	1	0	1	0	0	0	12	4	16	12	6	18
10947	10	5	15	0	0	0	0	0	0	0	0	0	10	5	15	11	5	16
10949	7	1	8	0	0	0	2	7	9	0	0	0	9	8	17	11	10	21
10950	9	5	14	0	0	0	1	1	2	0	0	0	10	6	16	10	7	17
10951	5	9	14	0	0	0	3	1	4	0	0	0	8	10	18	10	13	23
10953	9	5	14	0	0	0	1	0	1	0	0	0	10	5	15	10	5	15
10954	7	6	13	0	0	0	1	1	2	1	0	1	9	7	16	9	10	19
DOSAGE GROUP 5								CHOLESTEROL CONTROL										
10958	7	7	14	0	0	0	0	0	0	0	0	0	7	7	14	8	7	15
10959	9	9	18	0	0	0	0	1	1	0	0	0	9	10	19	10	10	20
10960	7	7	14	0	0	0	0	1	1	0	0	0	7	8	15	11	8	19
10961	11	5	16	0	0	0	0	0	0	0	0	0	11	5	16	11	5	16
10962	5	8	13	0	0	0	1	0	1	0	0	0	6	8	14	8	12	20
10963	11	7	18	0	0	0	0	0	0	0	0	0	11	7	18	11	8	19
10964	7	10	17	0	0	0	1	0	1	0	0	0	8	10	18	10	10	20
10965	9	3	12	0	0	0	1	0	1	0	0	0	10	3	13	10	3	13
DOSAGE GROUP 6								1.6 MG/KG PFOS + CHOLESTEROL										
10972	7	10	17	0	0	0	1	0	1	0	0	0	8	10	18	11	12	23
10974	7	11	18	0	0	0	0	0	0	0	0	0	7	11	18	7	11	18
10975	5	1	6	0	0	0	0	0	0	0	0	0	5	1	6	6	6	12
10976	6	5	11	0	0	0	2	1	3	0	0	0	8	6	14	8	8	16
10978	10	7	17	0	0	0	0	0	0	0	0	0	10	7	17	11	8	19
10980	8	8	16	0	0	0	0	0	0	0	0	0	8	8	16	11	11	22
10981	6	5	11	0	0	0	0	0	0	0	0	0	6	5	11	7	7	14
10982	7	9	16	0	0	0	1	0	1	0	0	0	8	9	17	8	9	17

PLACENTAE APPEARED NORMAL UNLESS NOTED OTHERWISE.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 33 (PAGE 3): CAESAREAN-SECTIONING OBSERVATIONS - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

	VIABLE FETUSES			DEAD FETUSES			EARLY RESORPTIONS			LATE RESORPTIONS			IMPLANTATION SITES			CORPORA LUTEA		
RAT #	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT HORN	LEFT HORN	TOTAL	RIGHT OVARY	LEFT OVARY	TOTAL
DOSAGE GROUP 7								2 MG/KG PFOS + CHOLESTEROL										
10985	9	5	14	0	0	0	0	0	0	0	0	0	9	5	14	14	6	20
10987	3	8	11	0	0	0	1	3	4	0	0	0	4	11	15	5	11	16
10988	10	4	14	0	0	0	1	1	2	0	0	0	11	5	16	11	5	16
10989	1	2	3	0	0	0	0	0	0	0	0	0	1	2	3	1	3	4
10990	6	7	13	0	0	0	1	0	1	0	0	0	7	7	14	14	12	26
10991	5	9	14	0	0	0	1	1	2	0	0	0	6	10	16	8	11	19
10992	6	3	9	0	0	0	2	1	3	0	0	0	8	4	12	12	13	25
10993	5	9	14	0	0	0	2	0	2	0	0	0	7	9	16	8	11	19
DOSAGE GROUP 12								1.6 MG/KG PFOS										
11040	3	5	8	0	0	0	0	1	1	0	0	0	3	6	9	7	6	13
11044	9	5	14	0	0	0	0	0	0	0	0	0	9	5	14	9	10	19
11045	5	9	14	0	0	0	1	0	1	0	0	0	6	9	15	6	10	16
11046	6	8	14	0	0	0	2	1	3	0	0	0	8	9	17	8	9	17
11047	0	10	10	0	0	0	0	1	1	0	0	0	0	11	11	0	11	11
11050	6	7	13	0	0	0	0	1	1	0	0	0	6	8	14	7	8	15
11051	9	4	13	0	1	1	0	0	0	0	0	0	9	5	14	9	5	14
11052	6	11	17	0	0	0	0	0	0	0	1	1	6	12	18	6	12	18
DOSAGE GROUP 13								2 MG/KG PFOS										
11053	4	11	15	0	0	0	0	0	0	0	0	0	4	11	15	5	14	19
11054	9	7	16	0	0	0	0	0	0	0	0	0	9	7	16	13	17	30
11056	7	5	12	0	0	0	0	1	1	0	0	0	7	6	13	8	9	17
11058	8	10	18	0	0	0	1	0	1	0	0	0	9	10	19	9	13	22
11060	6	8	14	0	0	0	0	0	0	0	0	0	6	8	14	6	8	14
11062	10	5	15	0	0	0	0	0	0	0	0	0	10	5	15	10	7	17
11063	7	7	14	0	0	0	0	0	0	0	0	0	7	7	14	9	7	16
11066	6	9	15	0	0	0	0	1	1	0	0	0	6	10	16	6	10	16

PLACENTAE APPEARED NORMAL UNLESS NOTED OTHERWISE.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 34 (PAGE 1): LITTER OBSERVATIONS (CAESAREAN-DELIVERED FETUSES) - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

	NUMBER OF LIVE FETUSES	POOLED FETAL BODY WEIGHT (G)	---- CONCEPTUSES ------ DEAD OR RESORBED		
RAT #	TOTAL	TOTAL	N	N	%
DOSAGE GROUP 1			VEHICLE CONTROL		
10901	13	67.36	14	1	7.1
10902	12	62.03	13	1	7.7
10903	14	74.73	15	1	6.7
10904	14	71.12	15	1	6.7
10905	13	68.98	14	1	7.1
10907	16	77.14	17	1	5.9
10908	14	72.29	15	1	6.7
10910	12	68.52	16	4	25.0
10912	NOT PREGNANT				
DOSAGE GROUP 2			MEVALONIC ACID CONTROL		
10915	14	76.48	16	2	12.5
10916	16	89.44	17	1	5.9
10917	10	53.12	14	4	28.6
10918	14	84.41	14	0	0.0
10919	15	68.96	15	0	0.0
10920	9	45.39	15	6	40.0
10925	16	77.64	16	0	0.0
10928	15	71.56	16	1	6.2
DOSAGE GROUP 3			1.6 MG/KG PFOS + MEVALONIC ACID		
10930	13	62.00	15	2	13.3
10931	13	65.26	14	1	7.1
10932	15	74.42	16	1	6.2
10933	16	82.94	18	2	11.1
10934	9	40.86	17	8	47.0
10935	12	64.44	12	0	0.0
10937	11	55.49	13	2	15.4
10940	19	86.00	19	0	0.0

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 34 (PAGE 2): LITTER OBSERVATIONS (CAESAREAN-DELIVERED FETUSES) - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

	NUMBER OF LIVE FETUSES	POOLED FETAL BODY WEIGHT (G)	---- CONCEPTUSES ------ DEAD OR RESORBED		
RAT #	TOTAL	TOTAL	N	N	%
DOSAGE GROUP 4			2 MG/KG PFOS + MEVALONIC ACID		
10945	16	72.48	16	0	0.0
10946	15	82.52	16	1	6.2
10947	15	76.37	15	0	0.0
10949	8	29.06	17	9	52.9
10950	14	74.80	16	2	12.5
10951	14	73.68	18	4	22.2
10953	14	75.62	15	1	6.7
10954	13	69.92	16	3	18.8
DOSAGE GROUP 5			CHOLESTEROL CONTROL		
10958	14	74.35	14	0	0.0
10959	18	87.28	19	1	5.3
10960	14	66.68	15	1	6.7
10961	16	82.33	16	0	0.0
10962	13	73.21	14	1	7.1
10963	18	94.52	18	0	0.0
10964	17	93.22	18	1	5.6
10965	12	63.36	13	1	7.7
DOSAGE GROUP 6			1.6 MG/KG PFOS + CHOLESTEROL		
10972	17	89.27	18	1	5.6
10974	18	89.02	18	0	0.0
10975	6	23.23	6	0	0.0
10976	11	57.91	14	3	21.4
10978	17	80.99	17	0	0.0
10980	16	74.99	16	0	0.0
10981	11	60.24	11	0	0.0
10982	16	89.48	17	1	5.9

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 34 (PAGE 3): LITTER OBSERVATIONS (CAESAREAN-DELIVERED FETUSES) - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

	NUMBER OF LIVE FETUSES	POOLED FETAL BODY WEIGHT (G)	---- CONCEPTUSES ------ DEAD OR RESORBED		
RAT #	TOTAL	TOTAL	N	N	%
DOSAGE GROUP 7			2 MG/KG PFOS + CHOLESTEROL		
10985	14	70.04	14	0	0.0
10987	11	53.47	15	4	26.7
10988	14	67.85	16	2	12.5
10989	3	17.94	3	0	0.0
10990	13	68.09	14	1	7.1
10991	14	64.65	16	2	12.5
10992	9	41.10	12	3	25.0
10993	14	66.19	16	2	12.5
DOSAGE GROUP 12			1.6 MG/KG PFOS		
11040	8	40.71	9	1	11.1
11044	14	69.56	14	0	0.0
11045	14	76.36	15	1	6.7
11046	14	72.10	17	3	17.6
11047	10	47.25	11	1	9.1
11050	13	71.08	14	1	7.1
11051	13	61.99	14	1	7.1
11052	17	88.06	18	1	5.6
DOSAGE GROUP 13			2 MG/KG PFOS		
11053	15	78.30	15	0	0.0
11054	16	71.53	16	0	0.0
11056	12	55.25	13	1	7.7
11058	18	82.23	19	1	5.3
11060	14	76.60	14	0	0.0
11062	15	75.77	15	0	0.0
11063	14	74.99	14	0	0.0
11066	15	83.80	16	1	6.2

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 35 (PAGE 1): FETAL VITAL STATUS - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
DOSAGE GROUP 1								VEHICLE CONTROL															
RAT # CLs																							
10901 8/ 7	A	A	A	E	A	A	A /	A	A	A	A	A	A	A									
10902 6/ 8	A	A	A	A	A /	A	A	A	A	E	A	A	A										
10903 12/ 4	A	A	A	A	A	A	A	A	A	A	E /	A	A	A	A								
10904 9/ 7	A	A	A	A	A	A	A	A	A /	A	A	A	A	A	E								
10905 8/ 8	E	A	A	A	A	A /	A	A	A	A	A	A	A	A									
10907 9/10	A	A	A	A	A	A	A	A	A /	E	A	A	A	A	A	A	A						
10908 9/ 6	E	A	A	A	A	A	A	A	A /	A	A	A	A	A	A								
10910 10/ 8	A	E	A	A	A	A	A	E	A /	A	E	A	E	A	A	A							
10912	NOT PREGNANT																						
DOSAGE GROUP 2								MEVALONIC ACID CONTROL															
RAT # CLs																							
10915 12/ 7	E	A	A	A	A	A	A	A	A	A /	A	A	A	A	A	E							
10916 7/11	A	A	A	A	A	A	A /	A	A	A	E	A	A	A	A	A	A						
10917 11/ 5	E	A	E	A	E	A	A	A	A	E	A /	A	A	A									
10918 8/11	A	A	A	A	A /	A	A	A	A	A	A	A	A	A									
10919 11/14	A	A	A	A	A	A /	A	A	A	A	A	A	A	A	A								
10920 14/ 9	A	E	A	A	E	E	A	E	A	E	A /	A	E	A	A								
10925 8/ 9	A	A	A	A	A	A	A	A /	A	A	A	A	A	A	A	A							
10928 8/ 8	A	A	E	A	A	A	A	A /	A	A	A	A	A	A	A	A							
DOSAGE GROUP 3								1.6 MG/KG PFOS + MEVALONIC ACID															
RAT # CLs																							
10930 11/ 8	A	A	A	A	A	A	A	A /	L	E	A	A	A	A	A								
10931 9/ 5	A	A	A	E	A	A	A	A	A /	A	A	A	A	A									
10932 11/11	A	A	A	A	A	A	A /	E	A	A	A	A	A	A	A	A							
10933 9/ 9	A	A	A	E	A	A	E	A	A /	A	A	A	A	A	A	A	A	A					
10934 13/10	E	E	E	E	A	E	A	A	A	A /	E	E	A	E	A	A	A						
10935 6/ 6	A	A	A	A	A	A /	A	A	A	A	A	A											
10937 9/ 4	A	A	A	A	A	E	A	E	A /	A	A	A	A										
10940 7/12	A	A	A	A	A	A	A /	A	A	A	A	A	A	A	A	A	A	A	A				

A = ALIVE D = DEAD E = EARLY RESORPTION L = LATE RESORPTION "/" DENOTES POSITION OF CERVIX CLs = CORPORA LUTEA/OVARY

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 35 (PAGE 2): FETAL VITAL STATUS - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
DOSAGE GROUP 4								2 MG/KG PFOS + MEVALONIC ACID															
RAT # CLs																							
10945 11/ 6	A	A	A	A	A	A	A	A	A	A /	A	A	A	A	A	A							
10946 12/ 6	A	A	E	A	A	A	A	A	A	A	A	A /	A	A	A	A							
10947 11/ 5	A	A	A	A	A	A	A	A	A	A /	A	A	A	A	A								
10949 11/10	E	E	A	A	A	A	A	A	A /	E	E	E	E	E	E	A	E						
10950 10/ 7	A	A	A	A	E	A	A	A	A	A /	A	A	A	A	A	E							
10951 10/13	A	E	A	E	A	A	A	E /	A	A	A	A	E	A	A	A	A	A					
10953 10/ 5	E	A	A	A	A	A	A	A	A	A /	A	A	A	A	A								
10954 9/10	L	A	A	E	A	A	A	A	A /	A	E	A	A	A	A	A							
DOSAGE GROUP 5								CHOLESTEROL CONTROL															
RAT # CLs																							
10958 8/ 7	A	A	A	A	A	A	A /	A	A	A	A	A	A	A									
10959 10/10	A	A	A	A	A	A	A	A	A /	E	A	A	A	A	A	A	A	A	A				
10960 11/ 8	A	A	A	A	A	A	A /	A	A	A	A	A	A	A	E								
10961 11/ 5	A	A	A	A	A	A	A	A	A	A	A /	A	A	A	A	A							
10962 8/12	A	E	A	A	A	A /	A	A	A	A	A	A	A	A									
10963 11/ 8	A	A	A	A	A	A	A	A	A	A	A /	A	A	A	A	A	A	A					
10964 10/10	A	A	A	E	A	A	A	A /	A	A	A	A	A	A	A	A	A	A					
10965 10/ 3	A	A	A	E	A	A	A	A	A	A /	A	A	A										
DOSAGE GROUP 6								1.6 MG/KG PFOS + CHOLESTEROL															
RAT # CLs																							
10972 11/12	A	E	A	A	A	A	A	A /	A	A	A	A	A	A	A	A	A	A					
10974 7/11	A	A	A	A	A	A	A /	A	A	A	A	A	A	A	A	A	A	A					
10975 6/ 6	A	A	A	A	A /	A																	
10976 8/ 8	A	A	A	E	E	A	A	A /	A	E	A	A	A	A									
10978 11/ 8	A	A	A	A	A	A	A	A	A	A /	A	A	A	A	A	A	A						
10980 11/11	A	A	A	A	A	A	A	A /	A	A	A	A	A	A	A	A							
10981 7/ 7	A	A	A	A	A	A /	A	A	A	A	A												
10982 8/ 9	A	A	A	A	E	A	A	A /	A	A	A	A	A	A	A	A	A						

A = ALIVE D = DEAD E = EARLY RESORPTION L = LATE RESORPTION "/" DENOTES POSITION OF CERVIX CLs = CORPORA LUTEA/OVARY

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 35 (PAGE 3): FETAL VITAL STATUS - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

FETUS #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
DOSAGE GROUP 7								2 MG/KG PFOS + CHOLESTEROL															
RAT # CLs																							
10985 14/ 6	A	A	A	A	A	A	A	A	A /	A	A	A	A	A									
10987 5/11	A	A	E	A /	A	A	A	A	A	A	A	A	E	E	E								
10988 11/ 5	A	A	A	A	E	A	A	A	A	A	A /	A	A	A	A	E							
10989 1/ 3	A /	A	A																				
10990 14/12	A	A	A	E	A	A	A /	A	A	A	A	A	A	A									
10991 8/11	A	A	A	E	A	A /	A	A	A	A	A	A	A	A	A	E							
10992 12/13	A	A	A	A	E	A	A	E /	E	A	A	A											
10993 8/11	E	A	A	E	A	A	A /	A	A	A	A	A	A	A	A	A							
DOSAGE GROUP 12								1.6 MG/KG PFOS															
RAT # CLs																							
11040 7/ 6	A	A	A /	E	A	A	A	A	A														
11044 9/10	A	A	A	A	A	A	A	A	A /	A	A	A	A	A									
11045 6/10	A	A	A	A	E	A /	A	A	A	A	A	A	A	A	A								
11046 8/ 9	E	A	A	A	A	A	E	A /	A	A	A	A	A	A	A	A	E						
11047 0/11 /	A	A	A	A	A	A	A	A	A	E	A												
11050 7/ 8	A	A	A	A	A	A /	A	A	A	A	A	A	A	E									
11051 9/ 5	A	A	A	A	A	A	A	A	A /	D	A	A	A	A									
11052 6/12	A	A	A	A	A	A /	A	A	A	L	A	A	A	A	A	A	A	A					
DOSAGE GROUP 13								2 MG/KG PFOS															
RAT # CLs																							
11053 5/14	A	A	A	A /	A	A	A	A	A	A	A	A	A	A	A								
11054 13/17	A	A	A	A	A	A	A	A	A /	A	A	A	A	A	A	A							
11056 8/ 9	A	A	A	A	A	A	A /	A	E	A	A	A	A										
11058 9/13	E	A	A	A	A	A	A	A	A /	A	A	A	A	A	A	A	A	A	A				
11060 6/ 8	A	A	A	A	A	A /	A	A	A	A	A	A	A	A									
11062 10/ 7	A	A	A	A	A	A	A	A	A	A /	A	A	A	A	A								
11063 9/ 7	A	A	A	A	A	A	A /	A	A	A	A	A	A	A									
11066 6/10	A	A	A	A	A	A /	A	A	E	A	A	A	A	A	A	A							

A = ALIVE D = DEAD E = EARLY RESORPTION L = LATE RESORPTION "/" DENOTES POSITION OF CERVIX CLs = CORPORA LUTEA/OVARY

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 36 (PAGE 1): NATURAL DELIVERY, IMPLANTATION SITES, AND PUP VIABILITY AND SEX - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP 1 — VEHICLE CONTROL

RAT/ LITTER NUMBER	DURATION OF GESTATION (DAYS) N	LITTER DELIVERED LIVE BORN N	STILL-BORN N	TOTAL BORN N	NUMBER OF LIVE PUPS AT COMPLETION OF DAY POSTPARTUM 1 M	1 F	2 M	2 F	3 M	3 F	4 M	4 F	5 M	5 F	TOTAL IMPLAN-TATIONS N
10906	22	16	0	16	10	6	9	6	9	6	9	6	9	6	17
10909	23	14	1	15	6	8	6	8	6	8	6	8	6	8	15
10911	23	17	0	17	8	9	8	9	8	9	8	8	8	8	19
10913	23	17	0	17	6	11	6	10	6	10	6	10	6	9	17
10914	23	10	0	10	3	7	3	7	3	7	3	7	3	7	12
11501	23	11	1	12	7	4	7	4	7	4	7	4	7	4	12
11502	23	15	1	16	9	6	9	6	9	6	9	6	9	6	16
11503	23	15	0	15	6	9	6	9	6	9	6	9	6	9	15
11504	23	15	0	15	4	11	4	11	4	10	4	10	4	10	15
11505	22	17	0	17	9	8	9	7	9	7	9	7	9	7	17
11506	23	15	0	15	9	6	9	6	9	6	9	6	9	6	16
11507	23	10	0	10	9	1	9	1	9	1	9	1	9	1	10
11508	23	11	2	13	8	3	8	3	8	3	8	3	8	3	14
11509	23	8	0	8	2	6	2	6	2	6	2	6	2	6	12
11510	23	15	0	15	9	6	9	6	9	6	9	6	9	6	15
11511	23	14	0	14	7	7	7	7	7	7	7	7	7	7	16
11512	23	14 (1)	0	14	4	9	4	9	4	9	4	9	4	9	14
11513	23	11	0	11	7	4	7	4	7	4	7	4	7	4	12
11514	23	15	0	15	6	9	6	9	6	9	6	9	6	9	15

M = MALE F = FEMALE
( ) = NUMBER OF PUPS DYING PRIOR TO WEIGHING ON DAY 1 POSTPARTUM.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 36 (PAGE 2): NATURAL DELIVERY, IMPLANTATION SITES, AND PUP VIABILITY AND SEX - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP 2 — MEVALONIC ACID CONTROL

RAT/ LITTER NUMBER	DURATION OF GESTATION (DAYS) N	LITTER DELIVERED LIVE BORN N	STILL-BORN N	TOTAL BORN N	NUMBER OF LIVE PUPS AT COMPLETION OF DAY POSTPARTUM 1 M	1 F	2 M	2 F	3 M	3 F	4 M	4 F	5 M	5 F	TOTAL IMPLAN-TATIONS N
10921	22	14	0	14	9	5	9	5	9	5	9	5	9	5	16
10922	23	13	0	13	8	5	8	5	7	5	7	5	7	5	16
10923	23	14	0	14	11	3	11	3	11	3	11	3	11	3	14
10924	23	13	0	13	8	5	8	5	8	5	8	5	8	5	14
10926	MORIBUND SACRIFICED ON DAY 12 OF GESTATION; DEATH WAS ATTRIBUTED TO AN INTUBATION ACCIDENT														
10927	22	17	0	17	6	11	6	11	6	11	6	11	6	11	18
11515	22	12	0	12	7	5	7	5	7	5	7	5	7	5	12
11516	23	14	2	16	6	8	6	8	6	8	6	8	6	8	18
11517	22	15	0	15	6	9	6	9	6	9	6	9	6	9	16
11518	23	12	0	12	9	3	9	3	9	3	9	3	9	3	15
11519	22	14(1)	0	14	6	7	6	7	6	7	6	7	6	7	14
11520	23	13	0	13	6	7	6	7	6	7	6	7	6	7	15
11521	23	7	0	7	4	3	4	3	3	3	3	3	3	3	13
11522	NOT PREGNANT														
11523	22	16	0	16	8	8	8	8	8	8	8	8	8	8	17
11524	23	11	0	11	5	6	5	6	5	6	5	6	5	6	11
11525	23	13	0	13	9	4	9	4	9	4	9	4	9	4	15
11526	23	12	1	13	8	4	8	4	8	4	8	4	8	4	13
11527	23	11	0	11	7	4	7	4	7	4	7	4	7	4	12
11528	23	13	0	13	7	6	7	6	7	6	7	6	7	6	14

M = MALE F = FEMALE
( ) = NUMBER OF PUPS DYING PRIOR TO WEIGHING ON DAY 1 POSTPARTUM.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 36 (PAGE 3): NATURAL DELIVERY, IMPLANTATION SITES, AND PUP VIABILITY AND SEX - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP 3 — 1.6 MG/KG PFOS + MEVALONIC ACID

RAT/ LITTER NUMBER	DURATION OF GESTATION (DAYS) N	LITTER DELIVERED LIVE BORN N	STILL-BORN N	TOTAL BORN N	NUMBER OF LIVE PUPS AT COMPLETION OF DAY POSTPARTUM 1 M	1 F	2 M	2 F	3 M	3 F	4 M	4 F	5 M	5 F	TOTAL IMPLAN-TATIONS N
10929	22	13	0	13	7	6	6	5	6	5	5	5	5	5	13
10936	FOUND DEAD ON DAY 2 OF STUDY														
10938	22	15(2)	0	15	7	6	4	2	4	2	4	2	4	2	15
10939	NOT PREGNANT														
10941	22	11(2)	0	11	5	4	1	3	1	2	-	-	-	-	14
10942	23	13	0	13	6	7	6	7	6	7	6	6	6	6	15
11529	22	16(1)	0	16	8	7	7	5	6	5	5	5	5	5	17
11530	23	13	2	15	6	7	5	5	5	5	5	5	5	5	15
11531	NOT PREGNANT														
11532	22	12(1)	2	14	6	5	-	-	-	-	-	-	-	-	14
11533	22	10(8)	0	10	2	-	1	-	-	-	-	-	-	-	10
11534	22	15(1)	1	16	5	9	5	3	4	3	4	3	4	3	17
11535	22	14	0	14	6	8	-	-	-	-	-	-	-	-	14
11536	23	9	0	9	4	5	3	4	3	4	3	4	3	4	11
11537	23	13	0	13	9	4	9	4	9	4	9	4	9	4	13
11538	22	12(6)	0	12	4	2	3	2	3	2	3	2	3	2	14
11539	22	9	0	9	4	5	2	1	-	-	-	-	-	-	9
11540	22	14	1	15	9	5	1	1	1	1	1	1	1	1	15
11541	22	12	0	12	7	5	-	-	-	-	-	-	-	-	13
11542	22	15	0	15	8	7	3	4	1	2	1	1	1	1	16
11543	22	11(1)	0	11	3	7	3	7	3	7	3	7	3	7	16

M = MALE F = FEMALE
( ) = NUMBER OF PUPS DYING PRIOR TO WEIGHING ON DAY 1 POSTPARTUM.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 36 (PAGE 4): NATURAL DELIVERY, IMPLANTATION SITES, AND PUP VIABILITY AND SEX - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP 4 — 2 MG/KG PFOS + MEVALONIC ACID

RAT/ LITTER NUMBER	DURATION OF GESTATION (DAYS) N	LITTER DELIVERED LIVE BORN N	STILL-BORN N	TOTAL BORN N	NUMBER OF LIVE PUPS AT COMPLETION OF DAY POSTPARTUM 1 M	1 F	2 M	2 F	3 M	3 F	4 M	4 F	5 M	5 F	TOTAL IMPLAN-TATIONS N
10943	22	13(1)	0	13	8	4	1	-	-	-	-	-	-	-	15
10944	22	13	0	13	10	3	1	2	-	1	-	1	-	-	14
10948	22	13(10)	0	13	1	2	-	2	-	1	-	-	-	-	17
10952	22	14	0	14	7	7	-	-	-	-	-	-	-	-	15
10955	22	14(7)	1	15	2	5	-	-	-	-	-	-	-	-	15
10956	22	14	1	15	7	7	-	-	-	-	-	-	-	-	15
11544	22	14	0	14	8	6	-	-	-	-	-	-	-	-	14
11545	23	12(3)	0	12	4	5	-	-	-	-	-	-	-	-	13
11546	23	14(14)	0	14	-	-	-	-	-	-	-	-	-	-	15
11547	22	15(2)	0	15	5	8	2	4	2	2	2	1	-	1	15
11548	NOT PREGNANT														
11549	22	14(5)	0	14	6	3	-	-	-	-	-	-	-	-	14
11550	21	14(2)	0	14	4	8	3	3	-	1	-	-	-	-	16
11551	22	12(9)	0	12	2	1	1	-	-	-	-	-	-	-	13
11552	22	13(7)	0	13	4	2	3	1	2	1	2	-	2	-	14
11553	22	17	0	17	6	11	-	-	-	-	-	-	-	-	17
11554	22	17(2)	0	17	5	10	-	1	-	-	-	-	-	-	17
11555	22	14	0	14	12	2	2	-	-	-	-	-	-	-	17
11556	22	16(16)	0	16	-	-	-	-	-	-	-	-	-	-	16
11557	22	15(15)	0	15	-	-	-	-	-	-	-	-	-	-	17

M = MALE F = FEMALE
( ) = NUMBER OF PUPS DYING PRIOR TO WEIGHING ON DAY 1 POSTPARTUM.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 36 (PAGE 5): NATURAL DELIVERY, IMPLANTATION SITES, AND PUP VIABILITY AND SEX - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP 5 — CHOLESTEROL CONTROL

RAT/ LITTER NUMBER	DURATION OF GESTATION (DAYS) N	LITTER DELIVERED LIVE BORN N	STILL-BORN N	TOTAL BORN N	NUMBER OF LIVE PUPS AT COMPLETION OF DAY POSTPARTUM 1 M	1 F	2 M	2 F	3 M	3 F	4 M	4 F	5 M	5 F	TOTAL IMPLAN-TATIONS N
10957	23	11	0	11	2	9	2	9	2	9	2	9	2	9	12
10966	22	15	0	15	7	8	7	8	7	8	7	8	7	8	15
10967	23	15	0	15	8	7	8	7	8	7	8	7	8	7	16
10968	22	15	0	15	8	7	8	7	8	7	8	7	8	7	15
10969	22	16	1	17	8	8	8	7	8	7	8	7	8	7	16a
10970	23	17	0	17	8	9	8	9	8	8	8	8	8	8	17
11558	23	14	0	14	10	4	10	4	10	4	10	4	10	4	14
11559	23	18	0	18	7	11	7	11	7	11	7	11	7	11	18
11560	NOT PREGNANT														
11561	23	16	0	16	12	4	12	4	12	4	12	4	12	4	16
11562	MORIBUND SACRIFICED ON DAY 16 OF STUDY														
11563	23	16	0	16	9	7	9	7	8	7	8	7	8	7	16
11564	23	15	0	15	5	10	4	10	4	10	4	10	4	10	15
11565	23	14	0	14	5	9	5	9	5	9	5	9	5	9	14
11566	NOT PREGNANT														
11567	23	10	1	11	5	5	5	5	5	5	5	5	5	5	14
11568	23	14	0	14	8	6	8	6	8	6	8	6	8	6	14
11569	23	16	0	16	8	8	8	8	8	8	8	8	8	7	16
11570	23	12	0	12	7	5	7	5	7	5	7	5	7	5	14
11571	23	11	0	11	3	8	3	8	3	8	3	8	3	8	15

M = MALE F = FEMALE

a. Value appeared incorrectly recorded and was excluded from group averages and statistical analyses.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 36 (PAGE 6): NATURAL DELIVERY, IMPLANTATION SITES, AND PUP VIABILITY AND SEX - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP 6 — 1.6 MG/KG PFOS + CHOLESTEROL

RAT/ LITTER NUMBER	DURATION OF GESTATION (DAYS) N	LITTER DELIVERED LIVE BORN N	STILL-BORN N	TOTAL BORN N	NUMBER OF LIVE PUPS AT COMPLETION OF DAY POSTPARTUM 1 M	1 F	2 M	2 F	3 M	3 F	4 M	4 F	5 M	5 F	TOTAL IMPLAN-TATIONS N
10971	22	7	1	8	3	4	2	3	-	-	-	-	-	-	15
10973	22	13	0	13	7	6	5	4	-	1	-	-	-	-	14
10977	22	15(3)	0	15	7	5	4	1	4	1	4	1	4	1	15
10979	22	14(2)	0	14	8	4	8	4	8	4	7	4	7	4	16
10983	22	15	0	15	12	3	12	3	9	3	9	3	9	3	15
10984	22	16	0	16	7	9	6	7	-	-	-	-	-	-	16
11572	22	10	0	10	6	4	1	2	-	-	-	-	-	-	10
11573	22	13	0	13	4	9	3	1	-	-	-	-	-	-	13
11574	22	13(5)	0	13	2	6	2	6	2	4	2	4	2	4	14
11575	22	13(1)	0	13	8	4	8	4	8	4	8	4	8	4	13
11576	23	12	0	12	4	8	4	8	4	8	4	8	4	8	14
11577	22	16	0	16	8	8	1	-	-	-	-	-	-	-	16
11578	22	13(1)	0	13	6	6	6	6	6	6	6	6	6	6	13
11579	21	17(1)	0	17	9	7	1	3	-	2	-	2	-	2	17
11580	23	16(1)	0	16	9	6	7	6	6	4	6	4	6	4	17
11581	22	13(1)	0	13	6	6	-	-	-	-	-	-	-	-	15
11582	22	12	0	12	3	9	2	8	2	7	2	4	2	4	12
11583	22	14	0	14	3	11	3	10	3	10	3	10	3	10	15
11584	22	15(2)	0	15	2	11	2	11	2	11	1	11	1	11	15
11585	22	12(1)	1	13	6	5	3	2	1	1	1	1	-	-	13

M = MALE F = FEMALE
( ) = NUMBER OF PUPS DYING PRIOR TO WEIGHING ON DAY 1 POSTPARTUM.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 36 (PAGE 7): NATURAL DELIVERY, IMPLANTATION SITES, AND PUP VIABILITY AND SEX - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP 7 — 2 MG/KG PFOS + CHOLESTEROL

RAT/ LITTER NUMBER	DURATION OF GESTATION (DAYS) N	LITTER DELIVERED LIVE BORN N	STILL-BORN N	TOTAL BORN N	NUMBER OF LIVE PUPS AT COMPLETION OF DAY POSTPARTUM 1 M	1 F	2 M	2 F	3 M	3 F	4 M	4 F	5 M	5 F	TOTAL IMPLAN-TATIONS N
10986	22	15	0	15	8	7	7	4	-	-	-	-	-	-	17
10994	22	15	0	15	7	8	1	-	-	-	-	-	-	-	15
10995	22	15	0	15	7	8	4	4	4	3	3	3	3	3	15
10996	22	13	0	13	5	8	-	-	-	-	-	-	-	-	13
10997	23	16	0	16	12	4	11	4	11	4	11	4	11	4	17
10998	NOT PREGNANT														
11586	23	13	1	14	7	6	1	4	-	-	-	-	-	-	14
11587	22	13	0	13	7	6	1	-	-	-	-	-	-	-	16
11588	22	13	1	14	7	6	-	-	-	-	-	-	-	-	15
11589	22	13(10)	0	13	3	-	2	-	1	-	1	-	-	-	13
11590	22	16(1)	0	16	10	5	2	3	-	-	-	-	-	-	17
11591	22	17(1)	0	17	8	8	-	-	-	-	-	-	-	-	17
11592	23	15	0	15	11	4	5	3	2	3	2	3	2	3	17
11593	22	13(1)	0	13	4	8	2	5	1	5	1	5	1	5	14
11594	22	16	0	16	9	7	-	1	-	1	-	1	-	-	16
11595	22	0	0	1[1]	-	-	-	-	-	-	-	-	-	-	9
11596	22	14	0	14	10	4	1	-	-	-	-	-	-	-	15
11597	23	10(2)	0	10	4	4	3	3	3	2	3	2	3	2	16
11598	22	15	0	15	11	4	1	1	-	-	-	-	-	-	15
11599	23	17(12)	0	17	4	1	-	-	-	-	-	-	-	-	18

M = MALE F = FEMALE
( ) = NUMBER OF PUPS DYING PRIOR TO WEIGHING ON DAY 1 POSTPARTUM.
[ ] = NUMBER OF PUPS IN WHICH CANNIBALIZATION AND/OR AUTOLYSIS PRECLUDED THE DETERMINATION OF VIABILITY.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 36 (PAGE 8): NATURAL DELIVERY, IMPLANTATION SITES, AND PUP VIABILITY AND SEX - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP 8 — 0.4 MG/KG PFOS

RAT/ LITTER NUMBER	DURATION OF GESTATION (DAYS) N	LITTER DELIVERED LIVE BORN N	STILL-BORN N	TOTAL BORN N	NUMBER OF LIVE PUPS AT COMPLETION OF DAY POSTPARTUM 1 M	1 F	2 M	2 F	3 M	3 F	4 M	4 F	5 M	5 F	TOTAL IMPLAN-TATIONS N
10999	23	14	1	15	10	4	10	4	10	4	10	4	10	4	17
11000	22	14	0	14	4	10	4	10	4	10	4	10	4	10	14
11001	23	15	0	15	10	5	10	5	10	5	10	5	10	5	15
11002	22	14	0	14	7	7	7	7	7	7	7	7	7	7	16
11003	23	14(2)	2	16	7	5	7	5	7	5	7	5	7	5	18
11004	22	16	0	16	6	10	6	10	6	9	6	9	6	9	19
11005	23	13	1	14	5	8	5	8	5	8	5	8	5	8	15
11006	23	17	1	18	5	12	5	12	5	12	5	12	5	12	18
11007	23	17	0	17	6	11	6	11	6	11	6	11	6	11	17
11008	23	13	1	14	3	10	3	10	3	10	3	10	3	10	15
11600	23	14	1	15	7	7	7	7	7	7	7	7	7	7	16
11601	22	16	0	16	6	10	6	10	6	10	6	10	6	10	16
11602	22	10	0	10	6	4	6	4	6	4	6	4	6	4	13
11603	22	15	1	16	6	9	6	8	6	8	5	7	5	7	17
11604	22	13	0	13	8	5	8	5	8	5	8	5	8	5	15
11605	23	16	0	16	7	9	7	9	7	9	7	9	7	9	16
11606	23	9	1	10	4	5	4	5	4	5	4	5	4	5	13
11607	22	14	0	14	9	5	9	5	9	5	9	5	9	5	16
11608	23	18	0	18	8	10	8	10	8	10	8	10	8	10	18
11609	22	19(1)	0	19	6	12	6	12	6	12	6	12	6	12	19

M = MALE F = FEMALE
( ) = NUMBER OF PUPS DYING PRIOR TO WEIGHING ON DAY 1 POSTPARTUM.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 36 (PAGE 9): NATURAL DELIVERY, IMPLANTATION SITES, AND PUP VIABILITY AND SEX - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP 9 — 0.8 MG/KG PFOS

RAT/ LITTER NUMBER	DURATION OF GESTATION (DAYS) N	LITTER DELIVERED LIVE BORN N	STILL-BORN N	TOTAL BORN N	NUMBER OF LIVE PUPS AT COMPLETION OF DAY POSTPARTUM 1 M	1 F	2 M	2 F	3 M	3 F	4 M	4 F	5 M	5 F	TOTAL IMPLAN-TATIONS N
11009	23	13	0	13	9	4	9	4	9	4	9	4	9	4	14
11010	22	19	0	19	9	10	9	10	9	7	9	7	9	7	20
11011	23	16	0	16	8	8	8	8	8	8	8	8	8	8	16
11012	23	16	0	16	9	7	8	6	8	6	8	6	8	6	16
11013	22	16(1)	0	16	8	7	8	6	8	6	8	6	8	6	16
11014	NOT PREGNANT														
11015	22	16	0	16	6	10	5	9	5	8	4	7	4	6	18
11016	22	11	1	12	6	5	6	5	6	5	6	5	6	5	13
11017	NOT PREGNANT														
11018	23	10	0	10	6	4	6	4	6	4	6	4	6	4	12
11610	NOT PREGNANT														
11611	22	15	0	15	9	6	9	6	9	6	9	6	9	6	15
11612	23	13	0	13	3	10	3	10	3	10	3	10	3	10	13
11613	22	14	0	14	8	6	8	6	8	6	8	6	8	6	15
11614	23	17	0	17	11	6	11	6	10	6	10	6	10	6	18
11615	23	13	0	13	9	4	9	4	9	4	9	4	9	4	13
11616	22	15	0	15	8	7	8	7	8	7	8	7	8	7	15
11617	22	17	0	17	10	7	9	6	9	6	9	6	9	6	17
11618	23	11	1	12	5	6	5	6	5	6	5	5	5	5	13
11619	22	13	0	13	7	6	7	6	7	6	7	6	7	6	13

M = MALE F = FEMALE
( ) = NUMBER OF PUPS DYING PRIOR TO WEIGHING ON DAY 1 POSTPARTUM.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 36 (PAGE 10): NATURAL DELIVERY, IMPLANTATION SITES, AND PUP VIABILITY AND SEX - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP 10 — 1 MG/KG PFOS

RAT/ LITTER NUMBER	DURATION OF GESTATION (DAYS) N	LITTER DELIVERED LIVE BORN N	STILL-BORN N	TOTAL BORN N	NUMBER OF LIVE PUPS AT COMPLETION OF DAY POSTPARTUM 1 M	1 F	2 M	2 F	3 M	3 F	4 M	4 F	5 M	5 F	TOTAL IMPLAN-TATIONS N
11019	22	14	0	14	7	7	7	7	7	7	7	7	6	7	15
11020	23	15	0	15	8	7	8	7	8	7	8	7	8	7	15
11021	23	17	0	17	5	12	5	12	5	12	5	12	5	12	17
11022	NOT PREGNANT														
11023	22	16	0	16	6	10	6	7	6	7	6	7	6	7	16
11024	23	9	0	9	7	2	6	2	6	2	6	2	6	2	11
11025	24	17	0	17	5	12	5	12	5	12	5	12	5	12	18
11026	22	13	0	13	7	6	7	6	7	6	6	6	6	6	16
11027	22	16	0	16	10	6	10	6	10	6	10	6	10	6	17
11028	22	20(1)	0	20	9	10	8	9	8	9	8	9	8	9	20
11620	22	15	0	15	7	8	7	7	7	7	7	7	7	7	15
11621	22	15	0	15	5	10	5	10	5	10	5	10	5	10	16
11622	22	14	0	14	9	5	9	4	9	4	9	4	9	4	14
11623	22	15(1)	0	15	9	5	8	5	8	5	8	5	8	4	17
11624	23	14	2	16	3	11	3	11	3	11	3	11	3	11	17
11625	22	17	0	17	6	11	6	11	6	11	6	11	6	10	18
11626	23	14	0	14	4	10	4	10	4	10	4	10	4	10	15
11627	22	15(1)	0	15	10	4	5	1	-	-	-	-	-	-	16
11628	22	17	0	17	6	11	6	10	6	10	6	10	6	10	17
11629	22	12(1)	0	12	6	5	6	5	6	5	6	5	6	5	13

M = MALE F = FEMALE
( ) = NUMBER OF PUPS DYING PRIOR TO WEIGHING ON DAY 1 POSTPARTUM.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 36 (PAGE 11): NATURAL DELIVERY, IMPLANTATION SITES, AND PUP VIABILITY AND SEX - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP 11 — 1.2 MG/KG PFOS

RAT/ LITTER NUMBER	DURATION OF GESTATION (DAYS) N	LITTER DELIVERED LIVE BORN N	STILL-BORN N	TOTAL BORN N	NUMBER OF LIVE PUPS AT COMPLETION OF DAY POSTPARTUM 1 M	1 F	2 M	2 F	3 M	3 F	4 M	4 F	5 M	5 F	TOTAL IMPLAN-TATIONS N
11029	22	16(1)	0	16	6	9	6	9	6	9	6	9	6	9	16
11030	NOT PREGNANT														
11031	23	13	0	13	9	4	9	4	9	4	8	4	8	4	17
11032	22	13	0	13	9	4	9	4	6	3	5	2	5	2	16
11033	23	14	1	15	4	10	4	9	4	9	4	8	4	8	16
11034	23	13	0	13	4	9	3	9	2	8	2	7	1	7	15
11035	22	11(1)	0	11	6	4	6	4	5	4	4	4	4	4	14
11036	23	17	0	17	12	5	12	5	12	5	10	5	10	5	18
11037	22	16(3)	0	16	3	10	3	10	3	10	3	10	3	10	17
11038	22	19	0	19	9	10	8	9	6	6	5	6	4	6	19
11630	22	7	0	7	3	4	3	4	3	4	3	4	3	4	7
11631	NOT PREGNANT														
11632	23	9	0	9	5	4	3	2	3	2	3	2	3	2	13
11633	22	16	0	16	9	7	9	7	9	7	9	7	9	7	16
11634	22	13	0	13	6	7	6	7	6	7	6	7	6	7	14
11635	22	14	0	14	10	4	6	4	5	4	5	3	5	3	15
11636	22	16	0	16	9	7	9	7	9	7	9	7	9	7	16
11637	22	15(1)	0	15	7	7	7	7	7	7	7	7	7	7	16
11638	23	14	0	14	5	9	5	9	4	9	4	9	4	9	14
11639	22	16	0	16	8	8	7	7	7	7	7	7	7	7	16

M = MALE F = FEMALE

( ) = NUMBER OF PUPS DYING PRIOR TO WEIGHING ON DAY 1 POSTPARTUM.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 36 (PAGE 12): NATURAL DELIVERY, IMPLANTATION SITES, AND PUP VIABILITY AND SEX - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP 12 — 1.6 MG/KG PFOS

RAT/ LITTER NUMBER	DURATION OF GESTATION (DAYS) N	LITTER DELIVERED LIVE BORN N	STILL-BORN N	TOTAL BORN N	NUMBER OF LIVE PUPS AT COMPLETION OF DAY POSTPARTUM 1 M	1 F	2 M	2 F	3 M	3 F	4 M	4 F	5 M	5 F	TOTAL IMPLAN-TATIONS N
11039	NOT PREGNANT														
11041	22	17	0	17	6	11	6	10	-	7	-	5	-	5	17
11042	22	16(2)	0	16	7	7	-	-	-	-	-	-	-	-	16
11043	NOT PREGNANT														
11048	22	15(1)	0	15	7	7	-	-	-	-	-	-	-	-	15
11049	22	6(1)	0	6	3	2	2	1	2	1	2	1	2	1	10
11640	22	16	0	16	8	8	8	8	8	8	7	8	7	8	15
11641	22	15(2)	0	15	5	8	4	6	4	6	4	6	4	6	15
11642	22	16	0	16	8	8	8	8	8	8	8	8	8	8	17
11643	22	12	0	12	4	8	1	5	1	3	1	2	-	2	12
11644	22	14(1)	0	14	8	5	7	4	7	4	7	4	6	4	14
11645	22	10	4	14	6	4	-	-	-	-	-	-	-	-	15
11646	22	11	0	11	3	8	3	7	3	7	3	7	3	7	12
11647	22	11	0	11	4	7	-	2	-	1	-	1	-	1	13
11648	22	13(2)	0	13	5	6	4	6	4	6	4	6	4	6	15
11649	22	17(1)	0	17	8	8	3	1	2	-	2	-	-	-	18
11650	22	13	0	13	6	7	5	7	5	7	5	7	5	7	13
11651	22	11(3)	0	11	5	3	5	2	5	2	4	2	4	2	12
11652	NOT PREGNANT														
11653	22	14	0	14	9	5	8	5	8	4	8	4	8	4	14

M = MALE F = FEMALE
( ) = NUMBER OF PUPS DYING PRIOR TO WEIGHING ON DAY 1 POSTPARTUM.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 36 (PAGE 13): NATURAL DELIVERY, IMPLANTATION SITES, AND PUP VIABILITY AND SEX - INDIVIDUAL DATA - Fo GENERATION FEMALE RATS

DOSAGE GROUP 13 — 2 MG/KG PFOS

RAT/ LITTER NUMBER	DURATION OF GESTATION (DAYS) N	LITTER DELIVERED LIVE BORN N	STILL-BORN N	TOTAL BORN N	NUMBER OF LIVE PUPS AT COMPLETION OF DAY POSTPARTUM 1 M	1 F	2 M	2 F	3 M	3 F	4 M	4 F	5 M	5 F	TOTAL IMPLAN-TATIONS N
11055	22	14(1)	0	14	5	8	2	2	2	-	-	-	-	-	15
11057	22	10(1)	0	10	4	5	-	-	-	-	-	-	-	-	11
11059	23	15	0	15	11	4	11	2	11	2	11	2	11	2	18
11061	22	16	0	16	7	9	2	2	-	-	-	-	-	-	16
11064	22	10	0	10	7	3	1	-	-	-	-	-	-	-	11
11065	22	14	0	14	6	8	-	-	-	-	-	-	-	-	14
11654	22	14	0	14	5	9	5	4	4	4	4	4	4	4	14
11655	23	14	0	14	4	10	4	8	4	8	4	7	4	7	15
11656	23	12(2)	0	12	4	6	4	6	4	6	4	6	4	6	12
11657	22	13(8)	0	13	3	2	1	-	-	-	-	-	-	-	16
11658	22	14(12)	0	14	-	2	-	-	-	-	-	-	-	-	15
11659	22	6(6)	0	6	-	-	-	-	-	-	-	-	-	-	14
11660	22	14	0	14	9	5	1	2	-	-	-	-	-	-	15
11661	22	15(12)	0	15	1	2	-	-	-	-	-	-	-	-	15
11662	22	13	0	13	9	4	2	1	-	1	-	1	-	1	13
11663	22	16(2)	0	16	8	6	-	-	-	-	-	-	-	-	16
11664	22	11(2)	0	11	6	3	-	-	-	-	-	-	-	-	12
11665	22	16	0	16	6	10	2	3	1	1	1	1	-	-	17
11666	NOT PREGNANT														
11667	22	14(10)	1	15	2	2	-	-	-	-	-	-	-	-	15

M = MALE F = FEMALE

( ) = NUMBER OF PUPS DYING PRIOR TO WEIGHING ON DAY 1 POSTPARTUM.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 37 (PAGE 1): PUP BODY WEIGHTS POOLED BY LITTER FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION LITTERS

MATERNAL DOSAGE GROUP 1 — VEHICLE CONTROL

RAT/ LITTER NUMBER	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5
10906	94.8	93.2	106.5	121.1	136.0
10909	87.1	94.9	103.9	121.6	132.5
10911	108.0	111.2	117.8	123.1	131.7
10913	112.3	107.9	113.6	123.5	124.0
10914	61.4	65.4	73.2	80.5	92.7
11501	73.1	77.7	83.4	93.3	106.0
11502	96.6	107.6	121.3	133.5	148.9
11503	91.4	102.1	113.0	122.4	136.5
11504	97.7	106.8	115.0	135.6	155.9
11505	94.3	105.2	119.2	135.4	151.8
11506	103.1	113.4	127.8	148.0	166.6
11507	73.2	86.6	91.5	103.0	116.2
11508	79.7	86.8	99.5	112.4	127.1
11509	53.9	61.8	71.9	84.5	96.7
11510	92.0	97.3	107.1	119.7	134.0
11511	92.0	102.2	104.1	114.0	127.2
11512	77.6	87.1	96.4	108.5	117.5
11513	71.0	79.9	89.2	99.0	111.1
11514	92.7	106.8	118.9	135.5	146.5

DAY = DAY POSTPARTUM ALL WEIGHTS WERE RECORDED IN GRAMS (G). POOLED LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 37 (PAGE 2): PUP BODY WEIGHTS POOLED BY LITTER FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION LITTERS

MATERNAL DOSAGE GROUP 2 — MEVALONIC ACID CONTROL

RAT/ LITTER NUMBER	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5
10921	84.2	92.0	99.6	115.9	122.0
10922	80.3	88.9	92.6	107.3	119.9
10923	89.9	96.5	107.3	119.5	132.7
10924	87.0	91.0	95.4	103.1	108.0
10926	MORIBUND SACRIFICED ON DAY 12 OF GESTATION; DEATH WAS ATTRIBUTED TO AN INTUBATION ACCIDENT				
10927	95.7	103.3	116.1	131.5	144.9
11515	74.0	82.2	93.2	107.1	120.6
11516	93.0	102.8	116.6	130.0	146.7
11517	90.3	96.7	108.7	121.8	134.7
11518	79.0	90.1	97.7	106.7	117.3
11519	73.8	80.5	89.5	101.4	110.8
11520	90.1	93.2	101.5	115.1	129.9
11521	47.0	54.4	53.6	63.0	71.8
11522	NOT PREGNANT				
11523	94.4	103.5	117.1	131.5	145.3
11524	79.2	88.2	97.8	110.6	119.7
11525	85.8	91.9	103.0	112.3	126.4
11526	80.7	87.3	94.6	107.0	123.6
11527	75.9	84.3	97.5	109.8	124.1
11528	93.6	104.9	112.2	123.9	132.5

DAY = DAY POSTPARTUM ALL WEIGHTS WERE RECORDED IN GRAMS (G). POOLED LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 37 (PAGE 3): PUP BODY WEIGHTS POOLED BY LITTER FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION LITTERS

MATERNAL DOSAGE GROUP 3 — 1.6 MG/KG PFOS + MEVALONIC ACID

RAT/ LITTER NUMBER	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5
10929	72.1	62.6	65.0	67.8	75.5
10936	FOUND DEAD ON DAY 2 OF STUDY				
10938	68.0	34.5	38.5	44.8	47.9
10939	NOT PREGNANT				
10941	46.7	20.5	14.2	NO SURVIVING PUPS	
10942	83.7	84.6	89.0	95.1	104.3
11529	74.0	59.9	62.0	64.5	71.6
11530	79.3	63.9	70.0	77.9	85.4
11531	NOT PREGNANT				
11532	60.8	NO SURVIVING PUPS			
11533	11.0	5.4	NO SURVIVING PUPS		
11534	71.8	40.1	37.1	42.4	47.8
11535	72.4	NO SURVIVING PUPS			
11536	61.1	49.2	55.5	63.0	71.5
11537	84.5	86.2	93.4	135.8	109.0
11538	32.1	28.1	31.2	35.2	40.5
11539	49.4	14.8	NO SURVIVING PUPS		
11540	70.7	9.9	9.6	10.5	11.2
11541	62.9	NO SURVIVING PUPS			
11542	77.2	31.2	12.0	7.8	7.1
11543	57.5	63.7	74.3	82.1	93.2

DAY = DAY POSTPARTUM ALL WEIGHTS WERE RECORDED IN GRAMS (G). POOLED LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 37 (PAGE 4): PUP BODY WEIGHTS POOLED BY LITTER FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION LITTERS

MATERNAL DOSAGE GROUP 4 — 2 MG/KG PFOS + MEVALONIC ACID

RAT/ LITTER NUMBER	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5
10943	64.3	20.2	NO SURVIVING PUPS		
10944	67.4	13.7	4.6	3.9	NO SURVIVING PUPS
10948	14.2	8.3	4.0	NO SURVIVING PUPS	
10952	68.4	NO SURVIVING PUPS			
10955	36.8	NO SURVIVING PUPS			
10956	69.9	NO SURVIVING PUPS			
11544	77.6	NO SURVIVING PUPS			
11545	46.4	NO SURVIVING PUPS			
11546	NO SURVIVING PUPS				
11547	68.1	31.1	21.3	15.8	4.7
11548	NOT PREGNANT				
11549	49.0	NO SURVIVING PUPS			
11550	63.9	29.1	4.6	NO SURVIVING PUPS	
11551	16.1	5.2	NO SURVIVING PUPS		
11552	33.3	23.1	20.7	16.6	17.3
11553	91.0	NO SURVIVING PUPS			
11554	69.1	a	NO SURVIVING PUPS		
11555	77.6	9.6	NO SURVIVING PUPS		
11556	NO SURVIVING PUPS				
11557	NO SURVIVING PUPS				

DAY = DAY POSTPARTUM ALL WEIGHTS WERE RECORDED IN GRAMS (G). POOLED LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.
a. Value was not recorded.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 37 (PAGE 5): PUP BODY WEIGHTS POOLED BY LITTER FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION LITTERS

MATERNAL DOSAGE GROUP 5 — CHOLESTEROL CONTROL

RAT/ LITTER NUMBER	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5
10957	71.9	75.5	82.9	97.9	106.1
10966	97.0	106.9	127.2	143.1	163.6
10967	100.0	105.8	115.8	136.7	142.1
10968	83.5	88.5	93.7	109.7	120.3
10969	90.2	88.6	95.1	110.2	117.5
10970	97.8	105.3	106.4	121.1	130.3
11558	90.6	101.6	111.9	124.6	137.4
11559	110.9	120.6	135.8	152.3	173.5
11560	NOT PREGNANT				
11561	95.1	105.0	123.6	140.6	157.2
11562	MORIBUND SACRIFICED ON DAY 16 OF STUDY				
11563	106.4	117.5	122.9	140.4	152.3
11564	89.2	96.5	105.0	113.4	127.0
11565	97.2	107.6	119.0	132.9	148.1
11566	NOT PREGNANT				
11567	64.9	73.4	83.5	98.3	107.6
11568	85.1	91.0	100.0	111.9	125.0
11569	106.6	153.0	134.6	147.7	a
11570	79.6	87.8	92.7	104.3	110.9
11571	79.9	87.0	98.3	113.7	131.0

DAY = DAY POSTPARTUM ALL WEIGHTS WERE RECORDED IN GRAMS (G). POOLED LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.
a. Value was not recorded.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 37 (PAGE 6): PUP BODY WEIGHTS POOLED BY LITTER FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION LITTERS

MATERNAL DOSAGE GROUP 6 — 1.6 MG/KG PFOS + CHOLESTEROL

RAT/ LITTER NUMBER	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5
10971	35.2	22.3	NO SURVIVING PUPS		
10973	69.1	44.4	4.2	NO SURVIVING PUPS	
10977	59.9	26.8	29.7	36.4	39.8
10979	60.7	64.6	71.8	77.0	83.3
10983	82.9	75.9	68.6	78.0	85.2
10984	77.1	55.5	NO SURVIVING PUPS		
11572	55.5	14.6	NO SURVIVING PUPS		
11573	70.5	19.8	NO SURVIVING PUPS		
11574	40.1	39.9	33.1	36.5	40.0
11575	72.7	79.3	91.8	105.1	112.9
11576	72.6	74.6	81.6	94.0	102.2
11577	89.7	5.3	NO SURVIVING PUPS		
11578	69.1	72.8	81.8	92.4	99.6
11579	79.9	17.7	9.2	10.1	10.0
11580	89.1	76.1	60.2	65.6	72.2
11581	61.4	NO SURVIVING PUPS			
11582	64.9	49.4	46.0	38.4	44.5
11583	76.7	71.7	76.6	86.1	95.6
11584	69.0	72.4	79.8	83.2	91.5
11585	58.6	25.2	10.3	9.5	NO SURVIVING PUPS

DAY = DAY POSTPARTUM ALL WEIGHTS WERE RECORDED IN GRAMS (G). POOLED LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 37 (PAGE 7): PUP BODY WEIGHTS POOLED BY LITTER FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION LITTERS

MATERNAL DOSAGE GROUP 7 — 2 MG/KG PFOS + CHOLESTEROL

RAT/ LITTER NUMBER	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5
10986	79.9	52.1	NO SURVIVING PUPS		
10994	75.1	4.4	NO SURVIVING PUPS		
10995	74.8	40.4	38.6	33.6	34.1
10996	70.7	NO SURVIVING PUPS			
10997	86.0	81.2	85.9	92.5	94.6
10998	NOT PREGNANT				
11586	76.3	25.4	NO SURVIVING PUPS		
11587	69.7	4.3	NO SURVIVING PUPS		
11588	61.0	NO SURVIVING PUPS			
11589	16.6	11.0	5.8	5.2	NO SURVIVING PUPS
11590	79.6	22.7	NO SURVIVING PUPS		
11591	84.8	NO SURVIVING PUPS			
11592	87.6	41.9	27.4	30.3	34.9
11593	65.5	35.0	31.9	36.1	40.1
11594	77.5	4.8	4.7	4.5	NO SURVIVING PUPS
11595	NO SURVIVING PUPS				
11596	76.3	4.5	NO SURVIVING PUPS		
11597	47.0	36.8	33.8	35.1	35.7
11598	83.8	9.2	NO SURVIVING PUPS		
11599	23.6	NO SURVIVING PUPS			

DAY = DAY POSTPARTUM ALL WEIGHTS WERE RECORDED IN GRAMS (G). POOLED LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 37 (PAGE 8): PUP BODY WEIGHTS POOLED BY LITTER FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION LITTERS

MATERNAL DOSAGE GROUP 8 — 0.4 MG/KG PFOS

RAT/ LITTER NUMBER	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5
10999	88.0	93.2	100.9	119.5	129.8
11000	80.9	85.5	92.8	106.8	118.1
11001	59.3	96.5	96.7	112.3	119.0
11002	81.6	87.7	101.1	113.1	124.6
11003	77.4	84.0	91.8	107.5	115.5
11004	86.1	82.1	77.5	85.0	92.0
11005	84.1	89.2	96.3	109.3	118.6
11006	105.6	110.8	119.5	129.2	146.4
11007	103.0	109.5	121.0	135.3	144.9
11008	80.7	87.5	97.1	a	120.6
11600	92.5	93.9	100.7	116.1	132.0
11601	107.6	115.8	131.1	147.0	161.4
11602	57.7	61.3	66.0	74.1	81.6
11603	85.1	84.4	85.6	82.2	94.2
11604	71.9	76.6	85.9	94.6	101.5
11605	92.4	100.7	109.5	118.3	126.5
11606	59.4	66.0	72.1	80.7	90.8
11607	87.7	98.3	109.9	122.5	136.2
11608	107.3	113.6	125.8	a	147.4
11609	96.6	102.4	109.0	117.5	129.7

DAY = DAY POSTPARTUM ALL WEIGHTS WERE RECORDED IN GRAMS (G). POOLED LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.
a. Value was not recorded.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 37 (PAGE 9): PUP BODY WEIGHTS POOLED BY LITTER FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION LITTERS

MATERNAL DOSAGE GROUP 9 — 0.8 MG/KG PFOS

RAT/ LITTER NUMBER	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5
11009	85.4	88.0	93.8	101.1	101.8
11010	94.1	95.0	84.7	94.4	101.6
11011	97.5	107.1	111.3	131.0	139.2
11012	98.0	90.0	99.5	115.0	121.8
11013	76.9	73.7	78.6	89.3	95.2
11014	NOT PREGNANT				
11015	79.8	72.4	69.5	64.4	62.5
11016	64.7	68.5	76.0	86.2	96.5
11017	NOT PREGNANT				
11018	70.7	78.3	87.8	100.1	113.4
11610	NOT PREGNANT				
11611	87.9	94.9	106.2	117.2	125.7
11612	85.4	94.0	102.2	111.6	120.9
11613	83.0	96.2	108.3	123.0	135.2
11614	102.1	111.5	119.5	132.2	147.9
11615	82.2	93.9	105.4	121.2	133.5
11616	80.3	84.6	94.1	103.5	112.3
11617	93.3	89.7	93.7	100.8	109.9
11618	74.2	73.5	81.1	86.3	99.6
11619	75.2	80.7	86.6	95.0	98.1

DAY = DAY POSTPARTUM ALL WEIGHTS WERE RECORDED IN GRAMS (G). POOLED LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 37 (PAGE 10): PUP BODY WEIGHTS POOLED BY LITTER FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION LITTERS

MATERNAL DOSAGE GROUP 10 — 1 MG/KG PFOS

RAT/ LITTER NUMBER	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5
11019	79.8	82.5	91.9	104.1	107.8
11020	93.7	101.1	109.1	124.4	133.0
11021	119.4	110.7	117.2	131.2	140.5
11022	NOT PREGNANT				
11023	87.8	74.1	81.9	92.7	100.5
11024	70.8	61.3	68.8	80.5	90.1
11025	107.0	113.4	124.9	137.9	153.8
11026	76.6	81.8	91.9	90.1	96.2
11027	88.4	94.0	99.1	109.3	115.9
11028	101.1	91.2	96.1	108.4	116.3
11620	74.2	69.6	73.9	80.0	87.8
11621	86.2	92.0	103.0	114.2	122.4
11622	73.9	71.4	77.7	87.7	94.4
11623	75.9	72.2	73.9	78.5	81.0
11624	85.6	91.0	100.2	111.0	123.9
11625	101.6	107.0	113.0	121.8	125.4
11626	88.7	95.0	104.9	113.1	117.5
11627	62.4	25.6	NO SURVIVING PUPS		
11628	88.5	85.7	90.7	102.4	111.0
11629	68.9	80.4	93.1	105.0	116.3

DAY = DAY POSTPARTUM ALL WEIGHTS WERE RECORDED IN GRAMS (G). POOLED LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 37 (PAGE 11): PUP BODY WEIGHTS POOLED BY LITTER FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION LITTERS

MATERNAL DOSAGE GROUP 11 — 1.2 MG/KG PFOS

RAT/ LITTER NUMBER	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5
11029	77.7	78.9	84.3	91.3	99.8
11030	NOT PREGNANT				
11031	79.4	84.6	93.2	93.7	100.8
11032	64.0	63.0	44.9	43.7	47.3
11033	89.6	86.5	83.9	87.7	90.1
11034	79.8	70.8	60.6	55.2	49.0
11035	50.0	49.3	45.1	39.7	40.6
11036	111.6	114.2	119.1	113.2	123.7
11037	74.7	73.5	80.8	88.1	97.0
11038	87.5	75.3	55.1	50.6	49.5
11630	40.2	48.4	56.0	63.6	72.6
11631	NOT PREGNANT				
11632	59.4	32.4	34.1	37.7	41.4
11633	90.7	97.2	111.0	119.2	131.1
11634	74.9	83.7	94.6	105.9	116.9
11635	80.4	52.3	45.6	43.9	46.8
11636	91.9	99.1	111.5	120.8	133.2
11637	79.8	76.6	81.6	87.0	90.5
11638	79.1	84.7	88.4	93.0	105.0
11639	79.4	70.2	78.0	90.6	97.6

DAY = DAY POSTPARTUM ALL WEIGHTS WERE RECORDED IN GRAMS (G). POOLED LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 37 (PAGE 12): PUP BODY WEIGHTS POOLED BY LITTER FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION LITTERS

MATERNAL DOSAGE GROUP 12 — 1.6 MG/KG PFOS

RAT/ LITTER NUMBER	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5
11039	NOT PREGNANT				
11041	89.8	77.9	33.2	24.5	24.2
11042	67.5	NO SURVIVING PUPS			
11043	NOT PREGNANT				
11048	68.2	NO SURVIVING PUPS			
11049	27.6	17.3	18.7	21.1	23.4
11640	84.0	90.2	97.1	99.7	108.2
11641	67.0	54.1	60.1	64.3	69.7
11642	84.3	86.8	96.5	108.7	121.7
11643	68.2	30.2	19.5	15.5	12.9
11644	66.5	60.9	67.9	73.5	75.7
11645	52.9	NO SURVIVING PUPS			
11646	77.5	67.0	75.7	85.0	93.0
11647	57.5	8.6	4.7	5.2	5.5
11648	55.1	51.6	56.8	65.1	73.8
11649	82.6	20.3	10.1	9.7	NO SURVIVING PUPS
11650	70.4	66.8	72.0	82.6	90.1
11651	43.9	40.1	42.5	42.6	48.7
11652	NOT PREGNANT				
11653	75.6	68.0	66.5	72.6	78.7

DAY = DAY POSTPARTUM ALL WEIGHTS WERE RECORDED IN GRAMS (G). POOLED LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 37 (PAGE 13): PUP BODY WEIGHTS POOLED BY LITTER FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION LITTERS

MATERNAL DOSAGE GROUP 13 — 2 MG/KG PFOS

RAT/ LITTER NUMBER	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5
11055	65.7	19.6	9.6	NO SURVIVING PUPS	
11057	49.5	NO SURVIVING PUPS			
11059	88.4	80.4	86.0	91.9	99.0
11061	79.6	17.5	NO SURVIVING PUPS		
11064	54.9	5.0	NO SURVIVING PUPS		
11065	71.4	NO SURVIVING PUPS			
11654	78.2	46.6	45.5	53.0	57.4
11655	83.8	72.9	78.5	82.3	91.7
11656	65.2	70.2	76.9	83.1	88.3
11657	23.8	4.4	NO SURVIVING PUPS		
11658	8.6	NO SURVIVING PUPS			
11659	NO SURVIVING PUPS				
11660	75.3	14.2	NO SURVIVING PUPS		
11661	14.4	NO SURVIVING PUPS			
11662	71.2	14.9	5.1	5.1	5.0
11663	72.5	NO SURVIVING PUPS			
11664	49.1	NO SURVIVING PUPS			
11665	82.1	22.4	9.5	9.1	NO SURVIVING PUPS
11666	NOT PREGNANT				
11667	19.4	NO SURVIVING PUPS			

DAY = DAY POSTPARTUM ALL WEIGHTS WERE RECORDED IN GRAMS (G). POOLED LITTER WEIGHTS INCLUDE ONLY WEIGHTS OF LIVE PUPS.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 38 (PAGE 1): PUP VITAL STATUS AND SEX FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

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 1																						
													VEHICLE CONTROL										
10906	M A	M A	M A	M A	M A	M A	M A	M A	M A	MM 2	F A	F A	F A	F A	F A	F A							
10909	M A	M A	M A	M A	M A	M A	M S	F A	F A	F A	F A	F A	F A	F A	F A								
10911	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	FD 4						
10913	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	FM 5	FD 2						
10914	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F S												
11501	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F S								
11502	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A									
11503	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	FD 3								
11504	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	FM 2						
11505	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A									
11506	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F S	F S									
11507	M A	M A	F A	F A	F A	F A	F A	F A															
11508	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A								
11509	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A										
11510	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	FD 1									
11511	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A											
11512	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A												
11513	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A													
11514	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A									

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

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 38 (PAGE 2): PUP VITAL STATUS AND SEX FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

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 2																							
MEVALONIC ACID CONTROL																							
10921	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A									
10922	M A	M A	M A	M A	M A	M A	M A	MM 3	F A	F A	F A	F A	F A										
10923	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A									
10924	MORIBUND SACRIFICED ON DAY 12 OF GESTATION; DEATH WAS ATTRIBUTED TO AN INTUBATION ACCIDENT																						
10926	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A						
10927	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F S						
11515	M A	M A	M A	M A	M A	M A	M S	F A	F A	F A	F A	F A	F A	F A	F A								
11516	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A									
11517	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A										
11518	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	FD 1									
11519	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A												
11520	M A	M A	M A	M A	M A	M A	MM 3	F A	F A	F A													
11521	NOT PREGNANT																						
11522	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A							
11523	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A												
11524	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F S									
11525	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A												
11526	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A													
11527	M A	M A	M A	M A	M A	M A	F A	F A	F A														
11528	M A	M A	M A	M A	M A	M A	F A	F A	F A														

FIRST LETTER -- M-MALE, F-FEMALE
SECOND LETTER -- A-ALIVE, S-STILLBORN, U-UNCERTAIN, D-DIED, M-MISSING (PRESUMED CANNIBALIZED)
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PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 38 (PAGE 3): PUP VITAL STATUS AND SEX FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

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 3																						
	1.6 MG/KG PFOS + MEVALONIC ACID																						
10929	M A	M A	M A	M A	M A	MD 4	MD 2	F A	F A	F A	F A	F A	FD 2										
10936	FOUND DEAD ON DAY 2 OF STUDY																						
10938	M A	M A	M A	M A	MM 2	MM 2	MD 2	MD 1	F A	F A	FM 2	FM 2	FM 2	FM 2	FD 1								
10939	NOT PREGNANT																						
10941	MM 4	MM 2	MM 2	MM 2	MM 2	MD 1	MD 1	FM 4	FM 4	FM 3	FM 2												
10942	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	FM 4										
11529	M A	M A	M A	M A	M A	MM 4	MM 3	MD 2	F A	F A	F A	F A	F A	FD 2	FM 2	FD 1							
11530	M A	M A	M A	M A	M A	MM 2	F A	F A	F A	F A	F A	FD 2	FM 2	F S	F S								
11531	NOT PREGNANT																						
11532	MM 2	MM 2	MM 2	MM 2	MD 2	MD 2	M S	M S	FD 2	FD 2	FD 2	FD 2	FM 2	FD 1									
11533	MM 3	MM 2	MD 1	MD 1	FD 1	FD 1	FD 1	FD 1	FD 1														
11534	M A	M A	M A	M A	MM 3	M S	F A	F A	F A	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 1							
11535	MD 2	MD 2	MD 2	MD 2	MD 2	MM 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2									
11536	M A	M A	M A	MM 2	F A	F A	F A	F A	FM 2														
11537	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A										
11538	M A	M A	M A	MD 2	MD 1	MD 1	MD 1	F A	F A	FD 1	FD 1	FD 1											
11539	MD 3	MD 3	MD 2	MD 2	FM 3	FD 2	FD 2	FD 2	FD 2														
11540	M A	MD 2	MD 2	MD 2	MM 2	MM 2	MM 2	MM 2	MM 2	F A	FD 2	FD 2	FM 2	FM 2	F S								
11541	MD 2	MD 2	MD 2	MD 2	MD 2	MM 2	MM 2	FD 2	FD 2	FD 2	FD 2	FD 2											
11542	M A	MM 3	MM 3	MD 2	MD 2	MD 2	MD 2	MD 2	F A	FM 4	FD 3	FM 3	FD 2	FD 2	FD 2								
11543	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	FD 1												

FIRST LETTER -- M-MALE, F-FEMALE
SECOND LETTER -- A-ALIVE, S-STILLBORN, U-UNCERTAIN, D-DIED, M-MISSING (PRESUMED CANNIBALIZED)
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TABLE 38 (PAGE 4): PUP VITAL STATUS AND SEX FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

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 4																						
	2 MG/KG PFOS + MEVALONIC ACID																						
10943	MD 3	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	FD 2	FD 2	FD 2	FD 2	FD 1										
10944	MD 2	MD 2	MD 2	MM 2	MM 2	MM 2	MM 2	MM 2	MM 2	MM 3	FM 2	FM 5	FM 3										
10948	MM 2	MD 1	MD 1	MD 1	MD 1	MD 1	FM 4	FM 3	FD 1	FD 1	FD 1	FD 1	FD 1										
10952	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2									
10955	MD 2	MD 2	MD 1	M S	FD 2	FD 2	FD 2	FD 2	FM 2	FD 1	FD 1	FD 1	FD 1	FD 1	FD 1								
10956	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	M S	FM 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2							
11544	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2									
11545	MM 2	MM 2	MM 2	MM 2	MD 1	FM 2	FM 2	FM 2	FD 2	FD 2	FD 1	FD 1											
11546	MD 1	MD 1	MD 1	MD 1	MD 1	FD 1	FD 1	FD 1	FD 1	FD 1	FD 1	FD 1	FD 1	FD 1									
11547	MM 5	MM 5	MM 2	MM 2	MM 2	MD 1	F A	FM 4	FD 3	FM 3	FD 2	FD 2	FD 2	FM 2	FD 1								
11548	NOT PREGNANT																						
11549	MM 2	MM 2	MM 2	MM 2	MD 2	MD 2	FM 2	FD 2	FD 2	FD 1	FD 1	FD 1	FD 1	FD 1									
11550	MD 3	MD 3	MM 3	MD 2	MD 1	FM 4	FM 3	FM 3	FD 2	FD 2	FD 2	FD 2	FD 2	FD 1									
11551	MM 3	MM 2	MD 1	MD 1	MD 1	MD 1	FM 2	FD 1	FD 1	FD 1	FD 1	FD 1											
11552	M A	M A	MD 3	MM 2	MD 1	MD 1	MD 1	MD 1	FD 4	FM 2	FD 1	FD 1	FD 1										
11553	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2						
11554	MD 2	MD 2	MD 2	MD 2	MM 2	FD 3	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 1	FD 1						
11555	MD 3	MD 3	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	FD 2	FD 2									
11556	MD 1	MD 1	MD 1	MD 1	MD 1	MD 1	FD 1	FD 1	FD 1	FD 1	FD 1	FD 1	FD 1	FD 1	FD 1								
11557	MD 1	MD 1	MD 1	MD 1	MD 1	MD 1	FD 1	FD 1	FD 1	FD 1	FD 1	FD 1	FD 1	FD 1									

FIRST LETTER -- M-MALE, F-FEMALE
SECOND LETTER -- A-ALIVE, S-STILLBORN, U-UNCERTAIN, D-DIED, M-MISSING (PRESUMED CANNIBALIZED)
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TABLE 38 (PAGE 5): PUP VITAL STATUS AND SEX FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

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 5																						
10957	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A												
10966	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A								
10967	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A								
10968	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A								
10969	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A FD 2	F S							
10970	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A FM 3							
11558	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A									
11559	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A					
11560	NOT PREGNANT																						
11561	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A								
11562	MORIBUND SACRIFICED ON DAY 16 OF STUDY																						
11563	M A	M A	M A	M A	M A	M A	M A	M A MD 3	F A	F A	F A	F A	F A	F A	F A								
11564	M A	M A	M A	M A MD 2	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A									
11565	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A									
11566	NOT PREGNANT																						
11567	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F S												
11568	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A									
11569	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A FD 5								
11570	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A											
11571	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A													
													CHOLESTEROL CONTROL										

FIRST LETTER -- M-MALE, F-FEMALE
SECOND LETTER -- A-ALIVE, S-STILLBORN, U-UNCERTAIN, D-DIED, M-MISSING (PRESUMED CANNIBALIZED)
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TABLE 38 (PAGE 6): PUP VITAL STATUS AND SEX FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

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 6																						1.6 MG/KG PFOS + CHOLESTEROL
10971	MM 3	MM 3	MD 2	M S	FM 3	FM 3	FM 3	FD 2															
10973	MD 3	MM 3	MM 3	MM 3	MM 3	MD 2	MD 2	FM 4	FM 3	FM 3	FM 3	FD 2	FD 2										
10977	M A	M A	M A	M A	MM 2	MM 2	MD 2	MD 1	MD 1	F A	FM 2	FD 2	FD 2	FD 2	FD 1								
10979	M A	M A	M A	M A	M A	M A	M A	MD 4	MD 1	F A	F A	F A	F A	FD 1									
10983	M A	M A	M A	M A	M A	M A	M A	M A	M A	MD 3	MM 3	MM 3	F A	F A	F A								
10984	MD 3	MD 3	MD 3	MD 3	MD 3	MD 3	MD 2	FD 3	FD 3	FD 3	FD 3	FD 3	FD 3	FD 3	FD 2	FD 2							
11572	MM 3	MD 2	MD 2	MD 2	MD 2	MD 2	FM 3	FM 3	FD 2	FD 2													
11573	MM 3	MM 3	MM 3	MD 2	FD 3	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2										
11574	M A	M A	MD 1	MD 1	F A	F A	F A	F A	FM 3	FM 3	FD 1	FD 1	FD 1										
11575	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	FD 1										
11576	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A											
11577	MD 3	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MM 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FM 2							
11578	M A	M A	M A	M A	M A	M A	M A	MD 1	F A	F A	F A	F A	F A	F A									
11579	MM 3	MD 2	MD 2	MM 2	MM 2	MM 2	MM 2	MM 2	F A	F A	FM 3	FD 2	FD 2	FM 2	FM 2	FD 1							
11580	M A	M A	M A	M A	M A	M A	MM 3	MD 2	MM 2	F A	F A	F A	F A	FM 3	FM 3	FD 1							
11581	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MD 1	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2										
11582	M A	M A	MD 2	F A	F A	F A	F A	FD 4	FD 4	FD 4	FD 3	FD 2											
11583	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	FD 2									
11584	M A	MD 4	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	FD 1	FD 1									
11585	MD 5	MM 3	MM 3	MD 2	MM 2	MM 2	MD 1	M S	FD 5	FM 3	FD 2	FD 2	FD 2										

FIRST LETTER -- M-MALE, F-FEMALE
SECOND LETTER -- A-ALIVE, S-STILLBORN, U-UNCERTAIN, D-DIED, M-MISSING (PRESUMED CANNIBALIZED)
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TABLE 38 (PAGE 7): PUP VITAL STATUS AND SEX FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

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 7																						
	2 MG/KG PFOS + CHOLESTEROL																						
10986	MD 3	MD 3	MD 3	MD 3	MD 3	MM 3	MM 3	MD 2	FD 3	FD 3	FD 3	FM 3	FD 2	FD 2	FD 2								
10994	MM 3	MD 2	MD 2	MM 2	MM 2	MM 2	MM 2	FD 2	FD 2	FM 2	FM 2	FM 2	FM 2	FM 2	FM 2								
10995	M A	M A	M A	MD 4	MD 2	MM 2	MM 2	F A	F A	F A	FM 3	FD 2	FM 2	FM 2	FM 2								
10996	MM 2	MD 2	MD 2	MD 2	MD 2	FM 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2										
10997	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	MM 2	F A	F A	F A	F A								
10998	NOT PREGNANT																						
11586	MM 3	MD 2	MD 2	MD 2	MD 2	MM 2	MM 2	M S	FM 3	FM 3	FM 3	FD 3	FD 2	FD 2									
11587	MM 3	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2										
11588	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	F S									
11589	MD 5	MD 3	MD 2	MD 1	MD 1	MD 1	MD 1	MD 1	FD 1	FD 1	FD 1	FD 1											
11590	MM 3	MM 3	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	FM 3	FM 3	FM 3	FD 2	FD 2	FD 1								
11591	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MM 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FM 2	FD 1							
11592	M A	M A	MD 3	MM 3	MM 3	MD 2	MD 2	MD 2	MD 2	MD 2	F A	F A	F A	FD 2									
11593	M A	MD 3	MM 2	MM 2	MD 1	F A	F A	F A	F A	F A	FM 2	FM 2	FM 2										
11594	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	FD 5	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2								
11595	M U																						
11596	MD 3	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MM 2	FD 2	FD 2	FD 2	FM 2									
11597	M A	M A	M A	MM 2	MD 1	F A	F A	FM 3	FD 2	FD 1													
11598	MM 3	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	FM 3	FD 2	FD 2	FD 2									
11599	MD 2	MD 2	MM 2	MM 2	MD 1	MD 1	MD 1	MD 1	FM 2	FD 1	FD 1	FD 1	FD 1	FD 1	FD 1	FD 1	FD 1	FD 1					

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

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 38 (PAGE 8): PUP VITAL STATUS AND SEX FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

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 8																						
													0.4 MG/KG PFOS										
10999	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F S								
11000	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A									
11001	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A								
11002	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A									
11003	M A	M A	M A	M A	M A	M A	M A MD 1	MD 1	M S	F A	F A	F A	F A	F A	F A	F S							
11004	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A FD 3								
11005	M A	M A	M A	M A	M A	M S	F A	F A	F A	F A	F A	F A	F A	F A									
11006	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F S					
11007	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A							
11008	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A									
11600	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F S									
11601	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F S									
11602	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A							
11603	M A	M A	M A	M A	M A MD 4	F A	F A	F A	F A	F A	F A	F A FD 4	FD 2	F S									
11604	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A										
11605	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A									
11606	M A	M A	M A	F A	F A	F A	F A	F A	F S														
11607	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A										
11608	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A						
11609	M A	M A	M A	M A	M A	M A MD 1	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A					

FIRST LETTER -- M-MALE, F-FEMALE
SECOND LETTER -- A-ALIVE, S-STILLBORN, U-UNCERTAIN, D-DIED, M-MISSING (PRESUMED CANNIBALIZED)
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TABLE 38 (PAGE 9): PUP VITAL STATUS AND SEX FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

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 9																						
													0.8 MG/KG PFOS										
11009	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A										
11010	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	FM 3	FM 3	FM 3				
11011	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A							
11012	M A	M A	M A	M A	M A	M A	M A	MM 2	M A	F A	F A	F A	F A	F A	F A	FD 2							
11013	M A	M A	M A	M A	M A	M A	M A	M A	MD 1	F A	F A	F A	F A	F A	F A	FD 2							
11014	NOT PREGNANT																						
11015	M A	M A	M A	M A	MD 4	MM 2	F A	F A	F A	F A	F A	F A	FD 5	FD 4	FD 3	FD 2							
11016	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F S											
11017	NOT PREGNANT																						
11018	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A													
11610	NOT PREGNANT																						
11611	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A								
11612	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A										
11613	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A									
11614	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	MM 3	F A	F A	F A	F A	F A	F A						
11615	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A										
11616	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A									
11617	M A	M A	M A	M A	M A	M A	M A	M A	M A	MD 2	F A	F A	F A	F A	F A	F A	FD 2						
11618	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	FD 4	F S											
11619	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A											

FIRST LETTER -- M-MALE, F-FEMALE
SECOND LETTER -- A-ALIVE, S-STILLBORN, U-UNCERTAIN, D-DIED, M-MISSING (PRESUMED CANNIBALIZED)
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TABLE 38 (PAGE 10): PUP VITAL STATUS AND SEX FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

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 10																						
													1 MG/KG PFOS										
11019	M A	M A	M A	M A	M A	M A	MD 5	F A	F A	F A	F A	F A	F A	F A									
11020	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A								
11021	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A						
11022	NOT PREGNANT																						
11023	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	FM 2	FM 2	FM 2							
11024	M A	M A	M A	M A	M A	M A	MD 2	F A	F A														
11025	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A						
11026	M A	M A	M A	M A	M A	M A	MD 4	F A	F A	F A	F A	F A	F A										
11027	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A							
11028	M A	M A	M A	M A	M A	M A	M A	MM 2	MD 1	F A	F A	F A	F A	F A	F A	F A	F A	F A	FD 2				
11620	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	FM 2									
11621	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A								
11622	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	FD 2										
11623	M A	M A	M A	M A	M A	M A	M A	MM 2	MD 1	F A	F A	F A	F A	FM 5									
11624	M A	M A	M A	M S	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F S								
11625	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A	F A	FM 5						
11626	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A										
11627	MD 3	MD 3	MM 3	MM 3	MM 3	MD 2	MD 2	MD 2	MM 2	MM 2	FD 3	FD 2	FD 2	FM 2	FD 1								
11628	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A	FM 2							
11629	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	FD 1												

FIRST LETTER -- M-MALE, F-FEMALE
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TABLE 38 (PAGE 11): PUP VITAL STATUS AND SEX FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

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 11																						
																							1.2 MG/KG PFOS
11029	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	F A	F A								
11030	NOT PREGNANT																						
11031	M A	M A	M A	M A	M A	M A	M A	M A	MM 4	F A	F A	F A	F A	FD 1									
11032	M A	M A	M A	M A	M A	MM 4	MD 3	MM 3	MM 3	F A	F A	FM 4	FM 3										
11033	M A	M A	M A	M A	M S	F A	F A	F A	F A	F A	F A	F A	F A	FM 4	FM 2								
11034	M A	MD 5	MD 3	MD 2	F A	F A	F A	F A	F A	F A	F A	FD 4	FD 3										
11035	M A	M A	M A	M A	MM 4	MM 3	F A	F A	F A	F A	FD 1												
11036	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	MD 4	MD 4	F A	F A	F A	F A	F A						
11037	M A	M A	M A	MD 1	MD 1	F A	F A	F A	F A	F A	F A	F A	F A	F A	FD 1								
11038	M A	M A	M A	M A	MD 5	MD 4	MM 3	MD 3	MD 2	F A	F A	F A	F A	F A	F A	FM 3	FD 3	FD 3	FD 2				
11630	M A	M A	M A	F A	F A	F A	F A																
11631	NOT PREGNANT																						
11632	M A	M A	M A	MD 2	MD 2	F A	F A	FD 2	FD 2														
11633	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A							
11634	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A										
11635	M A	M A	M A	M A	M A	MD 3	MD 2	MD 2	MD 2	MD 2	F A	F A	F A	FM 4									
11636	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A							
11637	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	FD 1								
11638	M A	M A	M A	M A	MD 3	F A	F A	F A	F A	F A	F A	F A	F A										
11639	M A	M A	M A	M A	M A	M A	M A	MM 2	F A	F A	F A	F A	F A	F A	FD 2								

FIRST LETTER -- M-MALE, F-FEMALE
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TABLE 38 (PAGE 12): PUP VITAL STATUS AND SEX FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

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 12																1.6 MG/KG PFOS						
11039	NOT PREGNANT																						
11041	MD 3	MD 3	MD 3	MM 3	MM 3	MM 3	F A	F A	F A	F A	F A	FD 4	FD 4	FD 3	FD 3	FD 3	FD 2						
11042	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MM 2	FD 2	FD 2	FD 2	FD 2	FD 2	FM 2	FM 2	FD 1	FD 1							
11043	NOT PREGNANT																						
11048	MD 2	MD 2	MD 2	MM 2	MM 2	MM 2	MM 2	FD 2	FD 2	FM 2	FM 2	FM 2	FM 2	FM 2	FD 1								
11049	M A	M A	MM 2	F A	FM 2	FD 1																	
11640	M A	M A	M A	M A	M A	M A	M A	MM 4	F A	F A	F A	F A	F A	F A	F A	F A							
11641	M A	M A	M A	M A	MD 2	MD 1	F A	F A	F A	F A	F A	F A	FM 2	FM 2	FD 1								
11642	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A								
11643	MD 5	MD 2	MD 2	MD 2	F A	F A	FD 4	FM 3	FD 3	FM 2	FD 2	FD 2											
11644	M A	M A	M A	M A	M A	M A	MD 5	MM 2	F A	F A	F A	F A	FM 2	FD 1									
11645	MM 2	MM 2	MM 2	MD 2	MD 2	MD 2	M S	M S	M S	FM 2	FD 2	FD 2	FD 2	F S									
11646	M A	M A	M A	F A	F A	F A	F A	F A	F A	FM 2													
11647	MM 2	MM 2	MM 2	MM 2	F A	FM 3	FD 2	FD 2	FM 2	FM 2	FM 2												
11648	M A	M A	M A	M A	MD 2	MD 1	F A	F A	F A	F A	F A	FD 1											
11649	MM 5	MM 5	MM 3	MD 2	MD 2	MD 2	MM 2	MM 2	FM 3	FD 2	FD 2	FD 2	FD 2	FM 2	FM 2	FM 2	FD 1						
11650	M A	M A	M A	M A	M A	MD 2	F A	F A	F A	F A	F A	F A	F A										
11651	M A	M A	M A	M A	MD 4	F A	F A	FD 2	FD 1	FD 1	FD 1												
11652	NOT PREGNANT																						
11653	M A	M A	M A	M A	M A	M A	M A	MD 2	M A	F A	F A	F A	F A	FD 3									

FIRST LETTER -- M-MALE, F-FEMALE
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TABLE 38 (PAGE 13): PUP VITAL STATUS AND SEX FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

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 13																						2 MG/KG PFOS
11055	MM 4	MM 4	MM 2	MD 2	MD 2	FM 3	FM 3	FM 2	FM 2	FM 2	FD 2	FD 2	FD 2	FD 1									
11057	MM 2	MM 2	MD 2	MD 2	FM 2	FM 2	FM 2	FD 2	FD 2	FD 2	FD 1												
11059	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	M A	F A	F A	FM 2	FM 2								
11061	MM 3	MM 3	MD 2	MD 2	MD 2	MD 2	MD 2	FM 3	FM 3	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2							
11064	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MM 3	FD 2	FD 2	FD 2													
11065	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FD 2	FM 2								
11654	M A	M A	M A	M A	MD 3	F A	F A	F A	F A	FD 2	FM 2	FM 2	FM 2	FM 2									
11655	M A	M A	M A	M A	F A	F A	F A	F A	F A	F A	F A	FD 4	FM 2	FM 2									
11656	M A	M A	M A	M A	MD 1	MD 1	F A	F A	F A	F A	F A	F A	F A										
11657	MD 3	MM 2	MD 2	MD 1	MD 1	MD 1	MD 1	MD 1	FM 2	FD 2	FD 1	FD 1	FD 1										
11658	MD 1	MD 1	MD 1	MD 1	MD 1	MD 1	MD 1	MD 1	FM 2	FM 2	FD 1	FD 1	FD 1	FD 1									
11659	MD 1	MD 1	FD 1	FD 1	FD 1	FD 1																	
11660	MD 3	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	FM 3	FM 3	FD 2	FD 2	FD 2										
11661	MD 2	MD 1	MD 1	MD 1	MD 1	MD 1	FD 2	FD 2	FD 1	FD 1	FD 1	FD 1	FD 1	FD 1	FD 1								
11662	MD 3	MD 3	MD 2	MD 2	MD 2	MM 2	MM 2	MM 2	MM 2	F A	FM 2	FM 2	FM 2										
11663	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MD 2	MD 1	FD 2	FD 2	FD 2	FD 2	FD 2	FM 2	FD 1							
11664	MD 2	MD 2	MD 2	MD 2	MD 2	MM 2	MD 1	FD 2	FD 2	FD 2	FD 1												
11665	MM 5	MM 3	MD 2	MM 2	MM 2	MM 2	FM 5	FD 3	FM 3	FD 2	FD 2	FD 2	FD 2	FD 2	FM 2	FM 2							
11666	NOT PREGNANT																						
11667	MM 2	MM 2	MD 1	MD 1	MD 1	MD 1	MD 1	M S	FM 2	FM 2	FD 1	FD 1	FD 1	FD 1	FD 1	FD 1							

FIRST LETTER -- M-MALE, F-FEMALE
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NUMBER FOLLOWING "SECOND LETTER" INDICATES THE DAY POSTPARTUM THE EVENT OCCURRED.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 39 (PAGE 1): CLINICAL OBSERVATIONS FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY (S) POSTPARTUM	OBSERVATIONS a
1 VEHICLE CONTROL	10906	4- 5	1/15 PUPS: TIP OF TAIL BLACK.b
	11504	2	1/15 PUPS: COLD TO TOUCH.
2 MEVALONIC ACID CONTROL	-	-	-
3 1.6 MG/KG PFOS + MEVALONIC ACID	10929	3	1/11 PUPS: NOT NURSING.
	10941	3	3/ 4 PUPS: COLD TO TOUCH. NOT NURSING.
	11530	3	1/10 PUPS: DECREASED MOTOR ACTIVITY.
	11532	2	1/11 PUPS: NO MILK IN STOMACH.
	11542	1	15/15 PUPS: NOT NURSING.
4 2 MG/KG PFOS + MEVALONIC ACID	10944	4	1/ 1 PUP: NOT NURSING.
	11547	5	1/ 3 PUPS: NOT NURSING.
	11549	1	1/14 PUPS: DISTAL PORTION OF TAIL MISSING.
	11550	2	6/12 PUPS: COLD TO TOUCH.
	11552	5	2/ 2 PUPS: COLD TO TOUCH.
	11553	1	17/17 PUPS: NOT NURSING.
		2	2/17 PUPS: COLD TO TOUCH.
	11554	1	15/17 PUPS: NOT NURSING.
	11555	1	1/14 PUPS: NOT NURSING.
		2	2/14 PUPS: COLD TO TOUCH.

a. Tabulation restricted to adverse observations; all other pups appeared normal.
b. Observation confirmed at necropsy.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 39 (PAGE 2): CLINICAL OBSERVATIONS FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY (S) POSTPARTUM	OBSERVATIONS a
5 CHOLESTEROL CONTROL	10957	3- 5	1/11 PUPS: TIP OF TAIL BLACK.b
	10967	4- 5	1/15 PUPS: RIGHT EYE, EXOPHTHALMOS.b
	11559	4- 5	1/18 PUPS: RIGHT EYE, EXOPHTHALMOS.
	11563	4	1/15 PUPS: SWOLLEN 56,57. COLD TO TOUCH.
	11567	4- 5	1/10 PUPS: TIP OF TAIL MISSING.b
6 1.6 MG/KG PFOS + CHOLESTEROL	10984	1	1/16 PUPS: COLD TO TOUCH. NOT NURSING.
		2	13/16 PUPS: COLD TO TOUCH.
	11572	2	3/10 PUPS: COLD TO TOUCH.
	11573	2	4/13 PUPS: NOT NURSING.
	11574	2	8/ 8 PUPS: COLD TO TOUCH.
	11577	1	2/16 PUPS: DECREASED MOTOR ACTIVITY.
		2	1/16 PUPS: COLD TO TOUCH. NOT NURSING.
	11578	1	1/13 PUPS: DISTAL PORTION OF TAIL MISSING.
		2- 5	1/12 PUPS: DISTAL PORTION OF TAIL MISSING.b
	11580	2	13/15 PUPS: COLD TO TOUCH.
		3	10/13 PUPS: COLD TO TOUCH.

a. Tabulation restricted to adverse observations; all other pups appeared normal.
b. Observation confirmed at necropsy.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 39 (PAGE 3): CLINICAL OBSERVATIONS FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY (S) POSTPARTUM	OBSERVATIONS a
7 2 MG/KG PFOS + CHOLESTEROL			
	10986	2	11/15 PUPS: COLD TO TOUCH. DECREASED MOTOR ACTIVITY.
	10994	1	2/15 PUPS: NOT NESTING. NOT NURSING. DECREASED MOTOR ACTIVITY.
	10995	5	6/ 6 PUPS: COLD TO TOUCH.
	10997	1	1/16 PUPS: COLD TO TOUCH. NOT NESTING.
		5	1/15 PUPS: COLD TO TOUCH. NOT NESTING. NOT NURSING.
	11587	2	1/13 PUPS: NOT NURSING.
	11588	1	13/14 PUPS: NOT NURSING.
	11589	4	1/ 1 PUP: NOT NURSING.
	11590	1	15/16 PUPS: NOT NURSING.
		2	5/15 PUPS: COLD TO TOUCH.
	11592	1	15/15 PUPS: NOT NURSING.
	11593	2	1/12 PUPS: TAIL MISSING.
		3	1/ 7 PUPS: TAIL MISSING.
		4- 5	1/ 6 PUPS: TAIL MISSING.b
	11596	2	1/14 PUPS: COLD TO TOUCH. NOT NURSING.
	11598	2	2/15 PUPS: COLD TO TOUCH.
8 0.4 MG/KG PFOS	11000	1	1/14 PUPS: DECREASED MOTOR ACTIVITY. GASPING. NOT NURSING. NOT NESTING.
	11603	3	1/14 PUPS: DECREASED MOTOR ACTIVITY. LABORED BREATHING. COLD TO TOUCH.

a. Tabulation restricted to adverse observations; all other pups appeared normal.
b. Observation confirmed at necropsy.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 39 (PAGE 4): CLINICAL OBSERVATIONS FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY (S) POSTPARTUM	OBSERVATIONS a
9 0.8 MG/KG PFOS	11009	4- 5	1/13 PUPS: TIP OF TAIL BLACK.b
	11015	1	16/16 PUPS: COLD TO TOUCH.
	11617	1	1/17 PUPS: NOT NURSING.
10 1 MG/KG PFOS	11620	2	1/15 PUPS: TIP OF TAIL MISSING.
		3- 5	1/14 PUPS: TIP OF TAIL MISSING.b
	11624	1	14/16 PUPS: COLD TO TOUCH.
	11628	1	1/17 PUPS: DECREASED MOTOR ACTIVITY.
11 1.2 MG/KG PFOS	11035	1	10/11 PUPS: COLD TO TOUCH.
		2	10/10 PUPS: COLD TO TOUCH.
	11038	3	12/17 PUPS: COLD TO TOUCH.
	11630	1- 5	1/ 7 PUPS: TAIL MISSING FROM BASE.b
	11633	2	16/16 PUPS: COLD TO TOUCH.
	11635	3	1/10 PUPS: NOT NURSING.
12 1.6 MG/KG PFOS	11041	5	1/ 5 PUPS: DECREASED MOTOR ACTIVITY. COLD TO TOUCH.
	11643	4	1/ 4 PUPS: COLD TO TOUCH. NOT NURSING.
	11647	5	1/ 1 PUP: COLD TO TOUCH. NOT NURSING.

a. Tabulation restricted to adverse observations; all other pups appeared normal.
b. Observation confirmed at necropsy.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 39 (PAGE 5): CLINICAL OBSERVATIONS FROM BIRTH TO DAY 5 POSTPARTUM - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY (S) POSTPARTUM	OBSERVATIONS a
13 2 MG/KG PFOS	11055	3	1/ 4 PUPS: COLD TO TOUCH. NOT NURSING. 1/ 4 PUPS: NOT NURSING.
	11065	2	2/14 PUPS: COLD TO TOUCH.
	11662	5	1/ 1 PUP: COLD TO TOUCH. NOT NURSING.
	11665	4	2/ 2 PUPS: NOT NURSING.

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

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 40 (PAGE 1): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
1 VEHICLE CONTROL	10906	5	ALL PUPS APPEARED NORMAL.
	10909	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	10911	4	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	10913	2	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	ALL PUPS APPEARED NORMAL.
	10914	5	ALL PUPS APPEARED NORMAL.
	11501	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11502	1	1 PUP: STILLBORN. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	ALL PUPS APPEARED NORMAL.
	11503	5	ALL PUPS APPEARED NORMAL.
	11504	3	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	ALL PUPS APPEARED NORMAL.
	11505	5	ALL PUPS APPEARED NORMAL.
	11506	5	ALL PUPS APPEARED NORMAL.
	11507	5	ALL PUPS APPEARED NORMAL.
	11508	1	2 PUPS: STILLBORN. TONGUE PROTRUDED. ALL OTHER TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11509	5	ALL PUPS APPEARED NORMAL.
	11510	5	ALL PUPS APPEARED NORMAL.
	11511	5	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 39) for external clinical observations confirmed at necropsy.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 40 (PAGE 2): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
1 VEHICLE CONTROL (CONT.)	11512	1	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	ALL PUPS APPEARED NORMAL.
	11513	5	ALL PUPS APPEARED NORMAL.
	11514	5	ALL PUPS APPEARED NORMAL.
2 MEVALONIC ACID CONTROL	10921	5	ALL PUPS APPEARED NORMAL.
	10922	5	ALL PUPS APPEARED NORMAL.
	10923	5	ALL PUPS APPEARED NORMAL.
	10924	5	ALL PUPS APPEARED NORMAL.
	10927	5	ALL PUPS APPEARED NORMAL.
	11515	5	ALL PUPS APPEARED NORMAL.
	11516	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL. 1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11517	5	ALL PUPS APPEARED NORMAL.
	11518	5	ALL PUPS APPEARED NORMAL.
	11519	1	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11520	5	ALL PUPS APPEARED NORMAL.
	11521	5	ALL PUPS APPEARED NORMAL.
	11523	5	ALL PUPS APPEARED NORMAL.
	11524	5	ALL PUPS APPEARED NORMAL.
	11525	5	ALL PUPS APPEARED NORMAL.
	11526	1	1 PUP: STILLBORN. NO ORAL OPENING, NO EYES, EARS DISPLACED. ALL OTHER TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11527	5	ALL PUPS APPEARED NORMAL.
	11528	5	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 39) for external clinical observations confirmed at necropsy.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 40 (PAGE 3): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
3 1.6 MG/KG PFOS + MEVALONIC ACID	10929	2	2 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		4	1 PUP: FOUND DEAD. NO MILK IN STOMACH. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	ALL PUPS APPEARED NORMAL.
	10938	1	2 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	1 PUP: FOUND DEAD. NO MILK IN STOMACH. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	ALL PUPS APPEARED NORMAL.
	10941	1	2 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
	10942	5	ALL PUPS APPEARED NORMAL.
	11529	1	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL. 1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	ALL PUPS APPEARED NORMAL.
	11530	1	2 PUPS: STILLBORN. ALL TISSUES APPEARED NORMAL.
		2	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	ALL PUPS APPEARED NORMAL.
	11532	1	2 PUPS: STILLBORN. ALL TISSUES APPEARED NORMAL. 1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	6 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 39) for external clinical observations confirmed at necropsy.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 40 (PAGE 4): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
3 1.6 MG/KG PFOS + MEVALONIC ACID (CONT.)	11533	1	8 PUPS: FOUND DEAD. NO MILK IN STOMACH. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
	11534	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL. 1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	6 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11535	2	13 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
	11536	5	ALL PUPS APPEARED NORMAL.
	11537	5	ALL PUPS APPEARED NORMAL.
	11538	1	4 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL. 2 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		2	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	ALL PUPS APPEARED NORMAL.
	11539	2	6 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		3	2 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
	11540	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL.
		2	5 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	ALL PUPS APPEARED NORMAL.
	11541	2	10 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.

a. Complete necropsies were not performed on pups in which autolysis or cannibalization precluded evaluation. Refer to the individual pup clinical observations table (Table 39) for external clinical observations confirmed at necropsy.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 40 (PAGE 5): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
3 1.6 MG/KG PFOS + MEVALONIC ACID (CONT.)	11542	2	7 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		3	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL. 1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	ALL PUPS APPEARED NORMAL.
	11543	1	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
4 2 MG/KG PFOS + MEVALONIC ACID	10943	1	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	8 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL. 3 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		3	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
	10944	2	3 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
	10948	1	10 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
	10952	2	14 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
	10955	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL. 7 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	6 PUPS: FOUND DEAD. NO MILK IN STOMACH. AUTOLYSIS PRECLUDED FURTHER EVALUATION.

a. Complete necropsies were not performed on pups in which autolysis or cannibalization precluded evaluation. Refer to the individual pup clinical observations table (Table 39) for external clinical observations confirmed at necropsy.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 40 (PAGE 6): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
4 2 MG/KG PFOS + MEVALONIC ACID (CONT.)	10956	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL.
		2	13 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
	11544	2	14 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
	11545	1	3 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	2 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
	11546	1	11 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
			3 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
	11547	1	2 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		2	3 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		3	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	PUP APPEARED NORMAL.
	11549	1	5 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	4 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
	11550	1	2 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	2 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
			4 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		3	2 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.

a. Complete necropsies were not performed on pups in which autolysis or cannibalization precluded evaluation. Refer to the individual pup clinical observations table (Table 39) for external clinical observations confirmed at necropsy.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 40 (PAGE 7): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
4 2 MG/KG PFOS + MEVALONIC ACID (CONT.)	11551	1	2 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL. 7 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
	11552	1	7 PUPS: FOUND DEAD. NO MILK IN STOMACH. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		3	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		4	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11553	2	15 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL. 2 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
	11554	1	2 PUPS: FOUND DEAD. NO MILK IN STOMACH. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		2	3 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION. 10 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		3	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
	11555	2	12 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		3	2 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
	11556	1	16 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
	11557	1	10 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION. 3 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL. 2 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 39) for external clinical observations confirmed at necropsy.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 40 (PAGE 8): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
5 CHOLESTEROL CONTROL	10957	5	ALL PUPS APPEARED NORMAL.
	10966	5	ALL PUPS APPEARED NORMAL.
	10967	5	ALL PUPS APPEARED NORMAL.
	10968	5	ALL PUPS APPEARED NORMAL.
	10969	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL.
		2	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	10970	5	ALL PUPS APPEARED NORMAL.
	11558	5	ALL PUPS APPEARED NORMAL.
	11559	5	ALL PUPS APPEARED NORMAL.
	11561	5	ALL PUPS APPEARED NORMAL.
	11563	3	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11564	2	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11565	5	ALL PUPS APPEARED NORMAL.
	11567	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11568	5	ALL PUPS APPEARED NORMAL.
	11569	5	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL. ALL OTHER PUPS APPEARED NORMAL.
	11570	5	ALL PUPS APPEARED NORMAL.
	11571	5	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 39) for external clinical observations confirmed at necropsy.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 40 (PAGE 9): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
6 1.6 MG/KG PFOS + CHOLESTEROL			
	10971	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL.
		2	2 PUPS: FOUND DEAD. NO MILK IN STOMACH. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
	10973	2	4 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		3	1 PUP: FOUND DEAD. CANNIBALIZATION PRECLUDED FURTHER EVALUATION.
	10977	1	3 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	4 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	10979	1	2 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		4	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	10983	3	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	ALL PUPS APPEARED NORMAL.
	10984	2	3 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		3	12 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
			1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
	11572	2	6 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
			1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.

a. Complete necropsies were not performed on pups in which autolysis or cannibalization precluded evaluation. Refer to the individual pup clinical observations table (Table 39) for external clinical observations confirmed at necropsy.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 40 (PAGE 10): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
6 1.6 MG/KG PFOS + CHOLESTEROL (CONT.)	11573	2	9 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		3	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
	11574	1	5 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11575	1	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11576	5	ALL PUPS APPEARED NORMAL.
	11577	2	13 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		3	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
	11578	1	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	ALL PUPS APPEARED NORMAL.
	11579	1	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	4 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	ALL PUPS APPEARED NORMAL.
	11580	1	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	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 39) for external clinical observations confirmed at necropsy.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 40 (PAGE 11): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
6 1.6 MG/KG PFOS + CHOLESTEROL (CONT.)	11581	1	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	12 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
	11582	2	2 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		4	3 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11583	2	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	ALL PUPS APPEARED NORMAL.
	11584	1	2 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		4	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11585	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL. 1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	4 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	2 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 39) for external clinical observations confirmed at necropsy.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 40 (PAGE 12): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
7 2 MG/KG PFOS + CHOLESTEROL	10986	2	4 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		3	8 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
	10994	2	4 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
	10995	2	2 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		4	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	10996	2	11 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
	10997	5	ALL PUPS APPEARED NORMAL.
	11586	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL.
		2	6 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		3	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
	11587	2	12 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
	11588	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL.
		2	13 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
	11589	1	9 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL. 1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		2	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		3	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.

a. Complete necropsies were not performed on pups in which autolysis or cannibalization precluded evaluation. Refer to the individual pup clinical observations table (Table 39) for external clinical observations confirmed at necropsy.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 40 (PAGE 13): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
7 2 MG/KG PFOS + CHOLESTEROL (CONT.)	11590	1	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	8 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL. 2 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
	11591	1	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	14 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
	11592	2	7 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		3	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	ALL PUPS APPEARED NORMAL.
	11593	1	1 PUP: 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.
		5	ALL PUPS APPEARED NORMAL.
	11594	2	15 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
	11596	2	11 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		3	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
	11597	1	2 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		2	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	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 39) for external clinical observations confirmed at necropsy.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 40 (PAGE 14): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
7 2 MG/KG PFOS + CHOLESTEROL (CONT.)	11598	2	13 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
	11599	1	11 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL. 1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		2	2 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
8 0.4 MG/KG PFOS	10999	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11000	5	ALL PUPS APPEARED NORMAL.
	11001	5	ALL PUPS APPEARED NORMAL.
	11002	5	ALL PUPS APPEARED NORMAL.
	11003	1	2 PUPS: STILLBORN. ALL TISSUES APPEARED NORMAL. 1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL. 1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11004	3	1 PUP: FOUND DEAD. NO MILK IN STOMACH. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	ALL PUPS APPEARED NORMAL.
	11005	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11006	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11007	5	ALL PUPS APPEARED NORMAL.
	11008	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL.
		5	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 39) for external clinical observations confirmed at necropsy.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 40 (PAGE 15): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
8 0.4 MG/KG PFOS (CONT.)	11600	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11601	5	ALL PUPS APPEARED NORMAL.
	11602	5	ALL PUPS APPEARED NORMAL.
	11603	1	1 PUP: STILLBORN. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		2	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		4	2 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	ALL PUPS APPEARED NORMAL.
	11604	5	ALL PUPS APPEARED NORMAL.
	11605	5	1 PUP: LIVER, MEDIAN LOBE, TAN AREA (4.0 CM IN DIAMETER). ALL OTHER PUPS APPEARED NORMAL.b
	11606	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11607	5	ALL PUPS APPEARED NORMAL.
	11608	5	ALL PUPS APPEARED NORMAL.
	11609	1	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
9 0.8 MG/KG PFOS	11009	5	ALL PUPS APPEARED NORMAL.
	11010	5	ALL PUPS APPEARED NORMAL.
	11011	5	ALL PUPS APPEARED NORMAL.
	11012	2	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		5	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 39) for external clinical observations confirmed at necropsy.
b. Necropsy observations were not recorded for ten of the sixteen pups.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 40 (PAGE 16): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
9			
0.8 MG/KG PFOS (CONT.)	11013	1	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11015	2	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		3	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		4	1 PUP: FOUND DEAD. NO MILK IN STOMACH. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
			1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL. ALL OTHER PUPS APPEARED NORMAL.
	11016	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11018	5	ALL PUPS APPEARED NORMAL.
	11611	5	ALL PUPS APPEARED NORMAL.
	11612	5	ALL PUPS APPEARED NORMAL.
	11613	5	ALL PUPS APPEARED NORMAL.
	11614	5	ALL PUPS APPEARED NORMAL.
	11615	5	ALL PUPS APPEARED NORMAL.
	11616	5	ALL PUPS APPEARED NORMAL.
	11617	2	2 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	ALL PUPS APPEARED NORMAL.
	11618	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL.
		4	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	ALL PUPS APPEARED NORMAL.
	11619	5	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 39) for external clinical observations confirmed at necropsy.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 40 (PAGE 17): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
10 1 MG/KG PFOS	11019	5	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL. ALL OTHER PUPS APPEARED NORMAL.
	11020	5	ALL PUPS APPEARED NORMAL.
	11021	5	ALL PUPS APPEARED NORMAL.
	11023	5	ALL PUPS APPEARED NORMAL.
	11024	2	1 PUP: FOUND DEAD. NO MILK IN STOMACH. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	ALL PUPS APPEARED NORMAL.
	11025	5	ALL PUPS APPEARED NORMAL.
	11026	4	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11027	5	ALL PUPS APPEARED NORMAL.
	11028	1	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	1 PUP: FOUND DEAD. NO MILK IN STOMACH. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	ALL PUPS APPEARED NORMAL.
	11620	5	ALL PUPS APPEARED NORMAL.
	11621	5	ALL PUPS APPEARED NORMAL.
	11622	2	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11623	1	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11624	1	2 PUPS: STILLBORN. ALL TISSUES APPEARED NORMAL.
		5	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 39) for external clinical observations confirmed at necropsy.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 40 (PAGE 18): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
10 1 MG/KG PFOS (CONT.)	11625	5	ALL PUPS APPEARED NORMAL.
	11626	5	ALL PUPS APPEARED NORMAL.
	11627	1	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
			4 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		3	3 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
	11628	5	ALL PUPS APPEARED NORMAL.
	11629	1	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
11 1.2 MG/KG PFOS	11029	1	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11031	5	ALL PUPS APPEARED NORMAL.
	11032	3	1 PUP: FOUND DEAD. NO MILK IN STOMACH. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	ALL PUPS APPEARED NORMAL.
	11033	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11034	2	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		3	2 PUPS: FOUND DEAD. NO MILK IN STOMACH. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		4	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL. ALL OTHER 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 39) for external clinical observations confirmed at necropsy.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 40 (PAGE 19): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
11 1.2 MG/KG PFOS (CONT.)	11035	1	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11036	4	2 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11037	1	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
			1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
			1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11038	2	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
			1 PUP: FOUND DEAD. NO MILK IN STOMACH. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		3	2 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
			1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		4	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		5	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
			ALL OTHER PUPS APPEARED NORMAL.
	11630	5	ALL PUPS APPEARED NORMAL.
	11632	2	4 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	ALL PUPS APPEARED NORMAL.
	11633	5	ALL PUPS APPEARED NORMAL.
	11634	5	ALL PUPS APPEARED NORMAL.
	11635	2	4 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		3	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	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 39) for external clinical observations confirmed at necropsy.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 40 (PAGE 20): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
11 1.2 MG/KG PFOS (CONT.)	11636	5	ALL PUPS APPEARED NORMAL.
	11637	1	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11638	3	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11639	2	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
12 1.6 MG/KG PFOS	11041	2	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		3	3 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
			3 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		4	2 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	ALL PUPS APPEARED NORMAL.
	11042	1	2 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	11 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
	11048	1	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	3 PUPS: FOUND DEAD. CANNIBALIZATION PRECLUDED FURTHER EVALUATION.
			2 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
	11049	1	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		5	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 39) for external clinical observations confirmed at necropsy.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 40 (PAGE 21): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
12 1.6 MG/KG PFOS (CONT.)	11640	5	ALL PUPS APPEARED NORMAL.
	11641	1	2 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11642	5	ALL PUPS APPEARED NORMAL.
	11643	2	5 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		3	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		4	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION. ALL OTHER PUPS APPEARED NORMAL.
	11644	1	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		5	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION. ALL OTHER PUPS APPEARED NORMAL.
	11645	1	4 PUPS: STILLBORN. ALL TISSUES APPEARED NORMAL.
		2	1 PUP: FOUND DEAD. CANNIBALIZATION PRECLUDED FURTHER EVALUATION. 2 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL. 1 PUP: FOUND DEAD. NO MILK IN STOMACH. AUTOLYSIS PRECLUDED FURTHER EVALUATION. 3 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
	11646	5	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 39) for external clinical observations confirmed at necropsy.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 40 (PAGE 22): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
12 1.6 MG/KG PFOS (CONT.)	11647	2	2 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	PUP APPEARED NORMAL.
	11648	1	2 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		2	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11649	1	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	7 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
	11650	2	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11651	1	3 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		2	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		4	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	ALL PUPS APPEARED NORMAL.
	11653	2	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		3	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		5	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 39) for external clinical observations confirmed at necropsy.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 40 (PAGE 23): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
13 2 MG/KG PFOS	11055	1	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	5 PUPS: FOUND DEAD. NO MILK IN STOMACH. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
	11057	1	1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	4 PUPS: FOUND DEAD. NO MILK IN STOMACH. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
	11059	5	ALL PUPS APPEARED NORMAL.
	11061	2	12 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
	11064	2	7 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
			2 PUPS: FOUND DEAD. NO MILK IN STOMACH. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
	11065	2	11 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
			2 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
	11654	2	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		3	1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		5	ALL PUPS APPEARED NORMAL.
	11655	4	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	ALL PUPS APPEARED NORMAL.
	11656	1	2 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	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 39) for external clinical observations confirmed at necropsy.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 40 (PAGE 24): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
13 2 MG/KG PFOS (CONT.)	11657	1	3 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL. 5 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	2 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
	11658	1	7 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL. 5 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
	11659	1	6 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
	11660	2	10 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION. 1 PUP: FOUND DEAD. ALL TISSUES APPEARED NORMAL.
		3	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
	11661	1	11 PUPS: FOUND DEAD. ALL TISSUES APPEARED NORMAL. 1 PUP: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	3 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
	11662	2	3 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		3	2 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		5	PUP APPEARED NORMAL.
	11663	1	2 PUPS: FOUND DEAD. NO MILK IN STOMACH. ALL OTHER TISSUES APPEARED NORMAL.
		2	13 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
	11664	1	2 PUPS: STILLBORN. ALL TISSUES APPEARED NORMAL.
		2	8 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 39) for external clinical observations confirmed at necropsy.

PROTOCOL 418-018: ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS (SPONSOR'S STUDY NUMBER: T-6295.25)

TABLE 40 (PAGE 25): NECROPSY OBSERVATIONS - INDIVIDUAL DATA - F1 GENERATION PUPS

MATERNAL DOSAGE GROUP TEST SUBSTANCE	LITTER NUMBER	DAY POSTPARTUM	OBSERVATIONS a
13 2 MG/KG PFOS (CONT.)	11665	2	6 PUPS: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
		3	1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION.
	11667	1	1 PUP: STILLBORN. ALL TISSUES APPEARED NORMAL. 1 PUP: FOUND DEAD. AUTOLYSIS PRECLUDED FURTHER EVALUATION. 9 PUPS: FOUND DEAD. ALL 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 39) for external clinical observations confirmed at necropsy.

APPENDIX C

PROTOCOL AND AMENDMENTS

PRIMEDICA

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

PROTOCOL 418-018

SPONSOR'S STUDY NUMBER: T-6295.25

STUDY TITLE: One Generation Reproduction Study of PFOS - Mevalonic Acid/Cholesterol Challenge and NOEL Investigation in Rats

PURPOSE: The purposes of this study are to determine whether or not co-administration of mevalonic acid or cholesterol can prevent or antagonize the adverse maternal and fetal effects (reduced maternal body weight gain, increased percent stillborn, decreased birth weight and decreased pup survival) observed in a previous study (Argus Research Protocol 418-008, 3M study number T-6295.9) and to better define the no observed effect level (NOEL).

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

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

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

STUDY MONITOR:
Deanna J. Luebker, M.S.
3M Corporate Toxicology
3M Medical Department
Telephone: (651) 737-1374
Telefax: (651) 733-1773

ALTERNATE STUDY MONITOR:
John Butenhoff, Ph.D., DABT, CIH
3M Corporate Toxicology
3M Medical Department
Telephone: (651) 737-1962
Telefax: (651) 733-1773

REGULATORY CITATIONS:

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

Should any portion of the study be conducted by a subcontractor or by the Sponsor, the QAU for that facility will conduct critical phase inspections and audit respective results and reports for that study portion according to the SOPs of that facility. Such critical phase inspection reports and report audits will be submitted by that facility to the Study Director. The dates of the inspections and report submissions will be incorporated into a QAU Statement generated by that facility and provided to the Testing Facility for inclusion in the final report.

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

STUDY SCHEDULE:

See ATTACHMENT 1 to the protocol.

TEST ARTICLE AND VEHICLE:

Identification:

Test Article:

Name:	Perfluorooctane Sulfonic Acid Potassium Salt (PFOS).
Physical Description:	Light-colored powder.
Lot/Batch Number:	217
Specific Gravity:	0.6
Purity:	98.9%
Expiration Date:	NA

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

Control Articles:

Name:	Mevalonic Acid.
Physical Description:	White with dark yellow cast, semisolid.
Lot Number:	070K2603
Specific Gravity:	NA
Purity:	Approximately 97%
Expiration Date:	August 2004

Name:	Cholesterol.
Physical Description:	White powder
Lot Number:	119HO218
Specific Gravity:	NA
Purity:	95%
Expiration Date:	July 2004

Information on the identity, composition, strength and purity of the control articles will be maintained in the raw data.

Vehicles:

0.5% Tween® 80 in reverse osmosis membrane processed deionized water (RODI H_2O). Supplier and lot identification of Tween® 80 to be documented in the raw data.

Reverse Osmosis Membrane Processed Deionized Water (RODI H_2O).

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

Safety Precautions:

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

Storage:

Bulk Test Article:	Room temperature.
Control Article Components:	Room temperature.
Vehicle Components:	Room temperature.
Prepared Vehicle (0.5% Tween® 80):	Room temperature.
Prepared Test Article Formulations:	Frozen (-20°C).

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

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

FORMULATION:

Frequency of Preparation:

Formulations of PFOS (suspensions) will be prepared weekly at the Testing Facility.

The vehicle (0.5% Tween® 80) will be prepared weekly.

Mevalonic acid will be prepared twice daily in reverse osmosis membrane processed deionized water.

Cholesterol will be prepared as a suspension once daily in 0.5% Tween® 80.

Detailed preparation procedures are attached to this protocol (ATTACHMENT 3) and documentation of formulation preparation will be maintained in the raw data.

Adjustment for Purity:

The test and control articles 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 (1 g or 5 mL) of each lot of the control article and 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. The Certificate of Analysis is on file with the Sponsor and a copy will be included in the final report.

Analyses of Prepared Formulations:

Stability:

Stability data for prepared test article formulations bracketing the range of concentrations and conditions of this study are on file with the Sponsor and will not be determined during the conduct of this study. Test article suspensions will be prepared weekly at the Testing Facility.

Homogeneity Analyses:

Homogeneity of the test article in prepared suspensions will be verified during the course of this study. A syringe will be used to withdraw samples (5 mL each) from the top, middle and bottom of the highest concentration on the first day of preparation. Each sample (5 mL) will be divided into two aliquots and placed into glass containers, one of 2 mL and one of 3 mL. One aliquot (2 mL) will be shipped for analysis; the other aliquot (3 mL) will be retained at the Testing Facility as a backup sample. Backup samples will be stored under the previously cited conditions and discarded at the Testing Facility upon the request of the Sponsor.

Concentration Analyses:

Concentration of the prepared test article suspensions will be verified during the course of this study. A syringe will be used to withdraw samples (5 mL each) from each concentration once during each of the following periods of the study: premating, gestation and postnatal. Each sample (5 mL each) will be divided into two aliquots and placed into glass containers, one of 2 mL and one of 3 mL. One aliquot (2 mL) will be shipped for analysis; the other aliquot (3 mL) will be retained at the Testing Facility as a backup sample. Backup samples will be stored under the previously cited conditions and discarded at the Testing Facility upon the request of the Sponsor.

Shipping Instructions:

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

Dave Ehresman
3M Corporate Toxicology
3M Center Building 236-0C-48
St. Paul, Minnesota 55144
Telephone: (651) 733-5070
Telefax: (651) 733-1773

Both the recipient and the Study Monitor will be notified in advance of sample shipment.

DISPOSITION:

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

TEST SYSTEM:

Species/Strain and Reason for Selection:

The Crl:CD®(SD) IGS BR VAF/Plus® rat was selected as the Test System because: 1) this strain of rat has been demonstrated to be sensitive to reproductive and developmental toxins and has been widely used throughout industry for reproductive and developmental toxicity evaluations; 2) historical data and experience exist at the Testing Facility[1-3]; 3) the test article is pharmacologically active in the species and strain; and 4) this strain has been used in previous reproduction studies of PFOS.

Number:

Initial population acclimated:	360 virgin female rats (two shipments of 180 female rats each designated as Replicates 1 and 2).
Population selected for study:	332 female rats (28 in each of Groups 1 to 7, 12 and 13, and 20 in each of Groups 8 to 11).

Eight mated female rats in each of Groups 1 to 7, 12 and 13 (Replicate 1) will be assigned to Caesarean-sectioning on day 21 of presumed gestation; the remaining female rats will be permitted to deliver litters.

Body Weight and Age:

Female rats will be ordered to weigh from 175 g to 225 g each at receipt, at which time they will be expected to be at least 56 days of age. Actual body weights will be recorded the day after receipt and will be documented in the raw data. The weight ranges 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 on the basis of physical appearance and body weights recorded during acclimation.

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 assigned to natural delivery will be individually housed in nesting boxes. Each dam and delivered litter will be housed in a common nesting box during the postpartum period.

Nesting Material:

Bedding material (bed-o'cobs®) will be supplied to female rats assigned to natural delivery.

Bedding will be changed as often as necessary to keep the animals dry and clean. Analyses for possible contamination are conducted semi-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. 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 drinking water or the nesting material at levels that would interfere with the results of this study. The Sponsor is aware of a potential contaminant present at extremely low levels in the certified diet. This low-level contamination will not interfere with the results of this study. Therefore, no analyses other than those routinely performed by the feed supplier or those mentioned in this protocol will be conducted.

RANDOMIZATION AND COHABITATION:

Fo Generation:

In order to facilitate scheduling, female rats will be received in two shipments (180 rats each) separated by two weeks. The first shipment will be designated as Replicate 1 and the second shipment will be designated as Replicate 2. Upon arrival, rats will be assigned to individual housing on the basis of computer-generated random units. After acclimation, female rats will be selected for study on the basis of physical appearance and body weights recorded during acclimation. The rats will be assigned to dosage groups based on computer-generated (weight-ordered) randomization procedures.

Within each dosage group, consecutive order will be used to assign rats to cohabitation, one male rat per female rat. The cohabitation period will consist of a maximum of 14 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. Female rats not mated within the first 7 days of cohabitation will be assigned alternate male rats that have mated and will remain in cohabitation for a maximum of seven additional days.

The first eight female rats per dosage group (groups 1 to 7, 12 and 13, Replicate 1) with a confirmed date of mating will be assigned to Caesarean-sectioning on day 21 of presumed gestation. The remaining female rats (including those with no confirmed mating date) will be permitted to naturally deliver litters.

F1 Generation Pups:

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).

ADMINISTRATION:

Route and Reason for Choice:

The oral (gavage) route was selected for use because: 1) in comparison with the dietary route, the exact dosage can be accurately administered; 2) it is one of the possible routes of human exposure; and 3) it is the route used in previous reproduction studies on PFOS.

Method and Frequency:

Dosages will be adjusted for the most recently recorded body weight and given at approximately the same times each day. Dosages will be administered according to the table in the Dosage Levels, Concentrations and Volumes section of the protocol. The mevalonic acid dosing needle will be wiped clean before administration for each animal.

Fo Generation Female Rats:

Female rats will be given the test article daily beginning 42 days before cohabitation (maximum of 14 days) and continuing through day 20 of presumed gestation (rats assigned to Caesarean-sectioning), day 24 of presumed gestation (rats assigned to natural delivery that do not deliver a litter) or day 4 postpartum (rats that deliver a litter). Rats in the process of delivering will not be given test/control article; such animals may not receive any or all of their daily dosage(s) on the day of parturition.

F1 Generation:

F1 generation pups will not be directly given the test article, but will 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 by the Sponsor on the basis of previous studies conducted with the test article.

Dosage Levels, Concentrations and Volumes:

Dosage Groups and Dosing Schedule					
Dosage Groups			Dosing Schedule		
Number	Identification	Number of Animals	1st dosage	2nd dosage ½ hour ± 10 minutes after 1st	3rd dosage 5 hr ± 30 minutes after 2nd
1	Vehicle Control	28	RODI H_2O	0.5% Tween 80	RODI H_2O
2	Mevalonic Acid Control	28	500 mg/kg Mevalonic Acid	0.5% Tween 80	500 mg/kg Mevalonic Acid
3	1.6 mg/kg PFOS + Mevalonic Acid	28	500 mg/kg Mevalonic Acid	1.6 mg/kg PFOS	500 mg/kg Mevalonic Acid
4	2 mg/kg PFOS + Mevalonic Acid	28	500 mg/kg Mevalonic Acid	2 mg/kg PFOS	500 mg/kg Mevalonic Acid
5	Cholesterol Control	28	500 mg/kg Cholesterol	0.5% Tween 80	NA
6	1.6 mg/kg PFOS + Cholesterol	28	500 mg/kg Cholesterol	1.6 mg/kg PFOS	NA
7	2 mg/kg PFOS + Cholesterol	28	500 mg/kg Cholesterol	2 mg/kg PFOS	NA
8	0.4 mg/kg PFOS	20	NA	0.4 mg/kg PFOS	NA
9	0.8 mg/kg PFOS	20	NA	0.8 mg/kg PFOS	NA
10	1 mg/kg PFOS	20	NA	1 mg/kg PFOS	NA
11	1.2 mg/kg PFOS	20	NA	1.2 mg/kg PFOS	NA
12	1.6 mg/kg PFOS	28	NA	1.6 mg/kg PFOS	NA
13	2 mg/kg PFOS	28	NA	2 mg/kg PFOS	NA

Compound Identification	Dosage (mg/kg/day)	Concentration (mg/mL)	Dosage Volume (mL/kg)	Argus Batch Number
RODI H_2O	0	0	5	B-418-018-A(Day.Month.Year)
0.5% Tween® 80	0	0	5	B-418-018-B(Day.Month.Year)
Mevalonic Acid	1000	100	5*	B-418-018-C(Day.Month.Year)
Cholesterol	500	100	5	B-418-018-D(Day.Month.Year)
PFOS	0.4	0.08	5	B-418-018-E(Day.Month.Year)
PFOS	0.8	0.16	5	B-418-018-F(Day.Month.Year)
PFOS	1	0.20	5	B-418-018-G(Day.Month.Year)
PFOS	1.2	0.24	5	B-418-018-H(Day.Month.Year)
PFOS	1.6	0.32	5	B-418-018-I(Day.Month.Year)
PFOS	2	0.40	5	B-418-018-J(Day.Month.Year)

The test and control articles will be considered 100% pure for the purpose of dosage calculations.
* Mevalonic acid will be dosed twice daily.

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:	Prior to dosage administration, approximately one hour after the second dosage and at the end of the working day (approximately one hour after the third dosage).
Day of Sacrifice:	Once.
Maternal Behavior:	Days 1 and 5 postpartum. Any 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:	Weekly to cohabitation. Daily during presumed gestation and on Day 1 postpartum (rats assigned to natural delivery).
Sacrifice:	Terminal weight.

Feed Consumption Values (recorded and tabulated):

Dosage Period:	Weekly to cohabitation. On days 0, 7, 14, 21 and 25 (if necessary) of presumed gestation and on days 1 and 5 postpartum (rats assigned to natural delivery).

Feed consumption values may be recorded more frequently than cited above if it is necessary to replenish the feed. During cohabitation, when two rats occupy the same cage with one feed jar, replenishment of the feed jars will be documented. Individual values will not be recorded or 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*.

Fertility Parameters:

Fertility Index (percentage of matings that result in pregnancies).

Gestation Index (percentage of pregnancies that result in birth of live litters).

Number of offspring per litter (live and dead pups).

Number of implantation sites.

General condition of dam and litter during the postpartum period.

Viability Indices (percentage of pups born that survive 5 days).

Caesarean-Sectioning Observations:

Eight rats from dosage groups 1 to 7, 12 and 13 (Replicate 1) will be Caesarean-sectioned on day 21 of presumed gestation. The fetuses will be removed from the uterus and pooled by litter for body weights. The rats will be examined for number and distribution of:

Corpora Lutea.

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

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

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

Fetal Observations:

Body Weights:

Fetuses will be pooled by litter and litter body weights will be recorded. (Only body weights of live fetuses will be recorded.)

Blood and Tissue Samples (See ATTACHMENT 4 for tissue collection and processing):

Caps and labeled tubes will be weighed (combined weight, to the nearest .001 gram) before (empty) and after retention of pooled fetus 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. Sample tubes will be labeled with the study number, litter identification, date of collection, study day, sample identification and collection timepoint.

Blood samples will be collected from each fetus via decapitation. Blood from approximately one-half of the fetuses in each litter will be placed into EDTA-coated tubes and the remaining fetal blood will be transferred into serum separator tubes. The samples will be spun in a centrifuge and the resulting serum (divided into two aliquots)/plasma (one aliquot) will be transferred into labeled polypropylene tubes. All samples will be immediately frozen on dry ice and maintained frozen (≤-20°C) until shipment for analysis.

The liver from each fetus will be collected. One fetal liver from each litter will be removed and fixed in gluteraldehyde for possible future analysis by electron microscopy. The remaining fetal livers in each litter will be divided into three samples of equal number (when possible). Two of the samples will be frozen and stored (≤-20°C) until shipment for analysis. The remaining sample will be flash frozen in liquid nitrogen and maintained frozen (≤-70°C) until shipment for possible analysis. Carcasses will be discarded without further evaluation.

Sample Analysis and Shipping Instructions:

Appropriate samples will be maintained frozen until shipment for analysis. Samples will be shipped frozen on dry ice via overnight mail.

One of each pair of serum samples, frozen liver samples, and liver samples fixed in gluteraldehyde will be sent to Dave Ehresman, at the previously cited address. The sample tube and liver weights and a packing list will be included with the samples sent to Dave Ehresman.

The remaining serum and liver samples will be analyzed for LDL, HDL, total cholesterol and triglycerides. These samples will be shipped to:

Dr. Saroj R. Das
Ani Lytics, Inc.
200 Gerard Street, Suite 200
Gaithersburg, Maryland 20877
Telephone: (301) 921-0168
Telefax: (301) 977-0433

Plasma mevalonic acid levels will be measured. These samples will be shipped to:

Jim Jersey
Primedica Worcester Laboratories
57 Union Street
Worcester, Massachusetts 01608
Telephone: (508) 890-0151
Telefax: (508) 753-1834

Both the recipients and the Study Monitor will be notified in advance of sample shipment.

Natural Delivery:

Female rats will be evaluated for:

Adverse Clinical Signs Observed During Parturition.

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

Litter Size (defined as all pups delivered).

Pup Viability at Birth.

METHOD OF SACRIFICE - Fo GENERATION:

Rats will be sacrificed by carbon dioxide asphyxiation. Fetuses will be sacrificed via decapitation. When possible, rats, pups and fetuses will be sacrificed and tissues collected at approximately the same time each day.

NECROPSY - Fo GENERATION:

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 assigned to Caesarean-section 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.

Blood and Tissue Sample Collection (See ATTACHMENT 4 for tissue collection and processing):

Caps and labeled tubes will be weighed (combined weight, to the nearest .001 gram) before (empty) and after retention of 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. Sample tubes will be labeled with the study number, animal identification, date of collection, study day, sample identification and collection timepoint.

Female Rats Assigned to Caesarean-Sectioning:

On day 21 of presumed gestation, blood and liver samples will be collected from the eight rats designated for Caesarean-section in dosage groups 1 to 7, 12 and 13. The time of sample collections will be recorded in the raw data.

Blood samples (at least 4 mL each) will be collected from the rats via the inferior vena cava and separated into two approximately equal aliquots. The first aliquot will be placed into EDTA-coated tubes and the second aliquot will be transferred into serum separator tubes. The samples will be spun in a centrifuge and the resulting serum (divided into two aliquots)/plasma (one aliquot) will be transferred into labeled polypropylene tubes. All samples will be immediately frozen on dry ice and maintained frozen (≤-20°C) until shipment for analysis.

Following collection of blood samples, the liver of each rat will be excised and the liver weight will be recorded. A portion of each liver sample (right lateral lobe) will be flash frozen in liquid nitrogen and maintained frozen (≤-70°C) until shipment for possible analysis. The median liver lobe will be frozen and stored (≤-20°C) until shipment for analysis. A section (approximately 0.3 to 0.5 cm wide) from the remaining portion of the liver will be fixed in gluteraldehyde for possible future analysis by electron microscopy. The remaining portion of the liver will be frozen and stored (≤-20°C) until shipment for analysis.

Female Rats Assigned to Natural Delivery:

Blood, milk, heart and liver samples will be collected from maternal rats on day 5 postpartum. Time of sample collections (blood and milk) will be recorded in the raw data.

On day 5 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 (≤-20°C) until shipment for analysis.

Following milk sample collection, blood samples (at least 4 mL each) will be collected from the rats via the inferior vena cava and separated into two approximately equal aliquots. The first aliquot will be placed into EDTA-coated tubes and the second aliquot will be transferred into serum separator tubes. The samples will be spun in a centrifuge and the resulting serum (divided into two aliquots)/plasma (one aliquot) will be transferred into labeled polypropylene tubes. All samples will be immediately frozen on dry ice and maintained frozen (≤-20°C) until shipment for analysis.

Following collection of milk and blood samples, the heart and liver of each dam will be collected. The liver weight will be recorded. A portion of each liver sample (right lateral lobe) will be flash frozen in liquid nitrogen and maintained frozen (≤-70°C) until shipment for possible analysis. The median liver lobe will be frozen and stored (≤-20°C) until shipment for analysis. The heart will be excised and two cuts will be made to allow proper fixation. The first cut will start to the right of the ventral midline surface at the apex and extend anteriorly and ventrally to the pulmonary artery. The second cut will be made starting to the left of the ventral midline surface at the apex and extend through the left ventricle to the ascending aorta. The cut heart and a section (approximately 0.3 to 0.5 cm wide) from the remaining portion of the liver will be fixed in gluteraldehyde for possible future analysis by electron microscopy and/or light microscopy. The remaining portion of the liver will be frozen and stored (≤-20°C) until shipment for analysis.

Sample Analysis and Shipping Instructions:

Appropriate samples will be maintained frozen until shipment for analysis. Samples will be shipped frozen on dry ice via overnight mail.

One of each pair of serum samples, frozen maternal liver samples (right lateral and median lobes), and liver and heart samples fixed in gluteraldehyde will be sent to Dave Ehresman, at the previously cited address. The sample tube and liver weights and a packing list will be included with the samples sent to Dave Ehresman.

The remaining serum and liver samples will be analyzed for LDL, HDL, total cholesterol and triglycerides. Milk samples will be analyzed for total cholesterol. These samples will be shipped to:

Dr. Saroj R. Das
Ani Lytics, Inc.
200 Gerard Street, Suite 200
Gaithersburg, Maryland 20877
Telephone: (301) 921-0168
Telefax: (301) 977-0433

Plasma mevalonic acid levels will be measured. These samples will be shipped to:

Jim Jersey
Primedica Worcester Laboratories
57 Union Street
Worcester, Massachusetts 01608
Telephone: (508) 890-0151
Telefax: (508) 753-1834

Both the recipients and the Study Monitor will be notified in advance of sample shipment.

Scheduled Sacrifice - Female Rats Assigned to Caesarean-Sectioning:

On day 21 of presumed gestation, female rats will be sacrificed, Caesarean-sectioned, and a gross necropsy of the thoracic, abdominal and pelvic viscera will be performed. Blood and tissue samples (blood serum/plasma and liver) will be collected as previously described. Uteri of apparently nonpregnant rats will be stained with 10% ammonium sulfide to confirm the absence of implantation sites[5] and retained in neutral buffered 10% formalin for possible future evaluation.

Scheduled Sacrifice - Female Rats Assigned to Natural Delivery:

On day 5 of lactation, female rats will be sacrificed and a gross necropsy of the thoracic, abdominal and pelvic viscera will be performed. Blood and tissue samples (blood serum/plasma, heart and liver) will be collected as previously described.

Rats that do not deliver a litter will be sacrificed on day 25 of presumed gestation and examined for gross lesions. Blood and tissue samples will not be collected. Uteri will be stained with 10% ammonium sulfide to confirm the absence of implantation sites[5] and retained in neutral buffered 10% formalin for possible future evaluation.

Dams with No Surviving Pups:

Dams with no surviving pups will be sacrificed after the last pup is found dead, missing or presumed cannibalized. Blood and tissue samples (blood serum/plasma, heart and liver) will be collected as previously described. A gross necropsy of the thoracic, abdominal and pelvic viscera will be performed. 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 or abortion 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. When possible (not precluded by autolysis), blood serum/plasma, heart and liver samples will be retained as previously described for rats assigned to natural delivery. 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] and retained in neutral buffered 10% formalin for possible future evaluation.

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:	Clinical observations and sex will be recorded 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), 2, 3, 4 and 5 postpartum. Pooled litter weights will be recorded.

METHOD OF SACRIFICE - F1 GENERATION PUPS:

As previously cited for Fo generation rats. When possible, pups will be sacrificed and tissues collected at approximately the same time each day. The time of sample collection will be recorded.

F1 Generation 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 livebom, and to have died shortly after birth. Pups with gross lesions will be preserved in Bouin's solution for possible future evaluation. Should postmortem autolysis preclude these evaluations, it will be noted in the necropsy data.

F1 Generation Pups Found Dead or Moribund on Days 2 to 5 Postpartum:

Pups found dead or sacrificed due to moribund condition will be examined for gross lesions and for the cause of the moribund condition or death. 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 day 5 postpartum will be preserved in neutral buffered 10% formalin. Should postmortem autolysis preclude these evaluations it will be noted in the necropsy data.

Scheduled Sacrifice - F1 Generation Pups (See ATTACHMENT 4 for tissue collection and processing):

On day 5 postpartum, pups will be sacrificed and examined for gross lesions. Gross lesions will be preserved in neutral buffered 10% formalin. Necropsy will include a single cross-section of the head at the level of the frontal-parietal suture and examination of the cross-sectioned brain for apparent hydrocephaly.

Caps and labeled tubes will be weighed (combined weight, to the nearest .001 gram) before (empty) and after retention of 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. Sample tubes will be labeled with the study number, animal identification, date of collection, study day, sample identification and collection timepoint.

Blood samples will be collected via cardiac puncture from each pup, pooled (by sex per litter) and separated into four (two per sex) approximately equal aliquots. The first aliquot per sex will be placed into EDTA-coated tubes and the second aliquot per sex will be transferred into serum separator tubes. The samples will be spun in a centrifuge and the resulting serum (divided into two aliquots)/plasma (one aliquot) will be transferred into labeled polypropylene tubes. All samples will be immediately frozen on dry ice and maintained frozen (≤-20°C) until shipment for analysis.

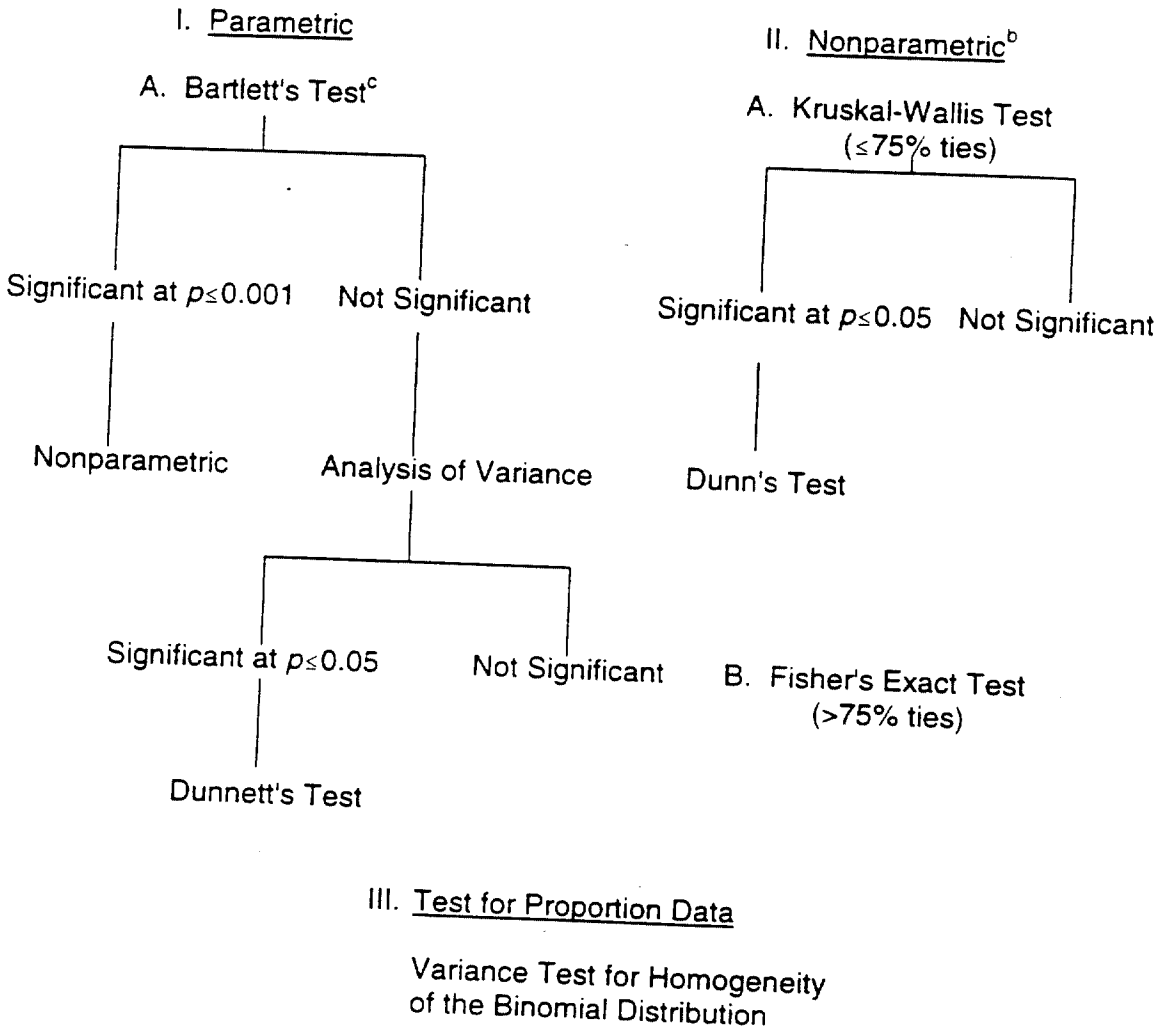
The liver from each pup will be collected, pooled (by sex per litter) and the pooled weight recorded. One liver from each litter pool will be removed and fixed in gluteraldehyde for possible future analysis by electron microscopy. The remaining livers in each litter pool will be divided into three samples of equal number (when possible). Two of the samples will be frozen and stored (≤-20°C) until shipment for analysis. The remaining sample will be flash frozen in liquid nitrogen and maintained frozen (≤-70°C) until shipment for possible analysis. The hearts will be collected from the first two male and two female pups from each litter (pooled by sex per litter) and will be fixed in gluteraldehyde for possible future analysis by electron microscopy and/or light microscopy. The remaining carcasses will be discarded without further evaluation

Samples will be shipped for analysis as previously described for dams and fetuses.

PROPOSED STATISTICAL METHODS[6-12]:

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

Type of Test[a]



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

DATA ACQUISITION, VERIFICATION AND STORAGE:

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

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

RECORDS TO BE MAINTAINED:

Protocol and Amendments.
Test and Control 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.
Pharmacokinetic Sample Collection, Processing and Shipment.
Body Weights.
Feed Consumption Values.
Caesarean-Sectioning Observations.
Natural Delivery Observations.
Litter Observations.
Gross Necropsy Observations.
Organ Weights.
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 Operations and Compliance: Barbara J. Patterson, B.A.
Director of Laboratory Operations: John F. Barnett, B.S.
Director of Study Management: Valerie A. Sharper, M.S.
Manager of Animal Operations and Chairperson, Institutional Animal Care and Use Committee: Dena C. Lebo, V.M.D.
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.

The Sponsor will receive one copy of the draft report and two copies of the final report.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE STATEMENT:

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

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

REFERENCES:

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

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

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

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

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

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

7. Sokal, R.R. and Rohlf, F.J. (1969). Bartlett's test of homogeneity of variances. *Biometry*, W.H. Freeman and Co., San Francisco, pp. 370-371.

8. Snedecor, G.W. and Cochran, W.G. (1967). Analysis of Variance. *Statistical Methods*, 6th Edition, Iowa State University Press, Ames, pp. 258-275.

9. Dunnett, C.W. (1955). A multiple comparison procedure for comparing several treatments with a control. J. Amer. Stat. Assoc. 50:1096-1121.

10. Sokal, R.R. and Rohlf, F.J. (1969). Kruskal-Wallis Test. *Biometry*, W.H. Freeman and Co., San Francisco, pp. 388-389.

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

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

PROTOCOL APPROVAL:

FOR THE TESTING FACILITY

George E. Dearlove, Ph.D., DABT
Associate Director of Research

21-AUG 00
Date

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

21-AUG-00
Date

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

21 Aug 00
Date

FOR THE SPONSOR

Deanna J. Luebker, M.S.
Study Monitor

8/22/2000
Date

John Butenhoff, Ph.D., DABT, CIH
Alternate Study Monitor

23-AUG-2000
Date

ATTACHMENT 1

STUDY SCHEDULE

ATTACHMENT 1

SCHEDULE[a]

REPLICATE 1[b]

22 AUG 00	Animal Receipt - Acclimation Begins (Female Rats).
29 AUG 00 - 12 NOV 00	Dosage Period - Female Rats Assigned to Caesarean-Sectioning (42 days before cohabitation and continuing through day 20 of presumed gestation).
29 AUG 00 - 20 NOV 00	Dosage Period - Female Rats Assigned to Natural Delivery [42 days before cohabitation through day 24 of presumed gestation (rats that do not deliver a litter) or day 4 postpartum (rats that deliver a litter)].
09 OCT 00 PM - 16 OCT 00 AM 16 OCT 00 PM - 23 OCT 00 AM	Cohabitation Period (Maximum of 14 days). Male 1 (07 days) Male 2 (07 days)
10 OCT 00 23 OCT 00	First Possible Day 0 of Presumed Gestation. Last Possible Day 0 of Presumed Gestation.
31 OCT 00 13 NOV 00	First Possible Day 21 of Presumed Gestation Caesarean-sectioning. Last Possible Day 21 of Presumed Gestation Caesarean-sectioning.
31 OCT 00 17 NOV 00	First Possible Delivery (Day 21 of presumed gestation). Last Possible Delivery (Day 25 of presumed gestation).
04 NOV 00 17 NOV 00	First Possible Day 25 of Presumed Gestation Female Sacrifice. Last Possible Day 25 of Presumed Gestation Female Sacrifice.

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a. The study initiation date is the day the Study Director signs the protocol.
b. Replicate 2 will be initiated two weeks after the start of Replicate 1 (see Page 2 of ATTACHMENT 1).

04 NOV 00	First Possible Day 5 Sacrifice (Dams and F1 generation pups).
21 NOV 00	Last Possible Day 5 Sacrifice.

REPLICATE 2

05 SEP 00	Animal Receipt - Acclimation Begins (Female Rats).
14 SEP 00 – 06 DEC 00	Dosage Period - Female Rats Assigned to Natural Delivery [42 days before cohabitation through day 24 of presumed gestation (rats that do not deliver a litter) or day 4 postpartum (rats that deliver a litter)].
25 OCT 00 PM – 01 NOV 00 AM 01 NOV 00 PM - 08 NOV 00 AM	Cohabitation Period (Maximum of 14 days). Male 1 (07 days) Male 2 (07 days)
26 OCT 00	First Possible Day 0 of Presumed Gestation.
08 NOV 00	Last Possible Day 0 of Presumed Gestation.
16 NOV 00	First Possible Delivery (Day 21 of presumed gestation).
03 DEC 00	Last Possible Delivery (Day 25 of presumed gestation).
20 NOV 00	First Possible Day 25 of Presumed Gestation Female Sacrifice.
03 DEC 00	Last Possible Day 25 of Presumed Gestation Female Sacrifice.
20 NOV 00	First Possible Day 5 Sacrifice (Dams and F1 generation pups).
07 DEC 00	Last Possible Day 5 Sacrifice.
01 MAR 01	Draft Final Report.

ATTACHMENT 2

MATERIAL SAFETY DATA SHEET

DATA SHEET

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

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1) the information is copied in full with no changes unless prior agreement is obtained from 3M, and
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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

	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

5. ENVIRONMENTAL INFORMATION (continued)

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

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.

7. PRECAUTIONARY INFORMATION

EYE PROTECTION:
Avoid eye contact. Wear vented goggles.

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.

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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AMH JWF MC JG DLN JFB BJP

PRODUCT #: C8503 NAME: CHOLESTEROL

MATERIAL SAFETY DATA SHEET, Valid 8/2000 - Printed 07/25/2000 15:03

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ARZEN MARK POKER

SECTION 1. - - - - - - - - - - CHEMICAL IDENTIFICATION- - - - - - - - - -

CATALOG #: C8503
NAME: CHOLESTEROL

SECTION 2. - - - - - COMPOSITION/INFORMATION ON INGREDIENTS - - - - - -

CAS #: 57-88-5
MF: C27H46O
EC NO: 200-353-2

SYNONYMS

CHOLEST-5-EN-3-OL (3-BETA)- (9CI) * CHOLEST-5-EN-3-BETA-OL * DELTA(SUP 5)-CHOLESTEN-3-BETA-OL * 5-CHOLESTEN-3-BETA-OL * 5:6-CHOLESTEN-3-OL * 5:6-CHOLESTEN-3-BETA-OL * CHOLESTERIN * CHOLESTERINE * CHOLESTRIN * (-)-CHOLESTEROL * CHOLESTERYL ALCOHOL * DYTHOL * 3-BETA-HYDROXYCHOLEST-5-ENE * PROVITAMIN D *

SECTION 3. - - - - - - - - - - HAZARDS IDENTIFICATION - - - - - - - - -

DATA NOT AVAILABLE

SECTION 4. - - - - - - - - - - FIRST-AID MEASURES- - - - - - - - - - -

IN CASE OF CONTACT, IMMEDIATELY FLUSH EYES WITH COPIOUS AMOUNTS OF WATER FOR AT LEAST 15 MINUTES.
IN CASE OF CONTACT, IMMEDIATELY WASH SKIN WITH SOAP AND COPIOUS AMOUNTS OF WATER.
IF INHALED, REMOVE TO FRESH AIR. IF NOT BREATHING GIVE ARTIFICIAL RESPIRATION. IF BREATHING IS DIFFICULT, GIVE OXYGEN.
IF SWALLOWED, WASH OUT MOUTH WITH WATER PROVIDED PERSON IS CONSCIOUS. CALL A PHYSICIAN.
WASH CONTAMINATED CLOTHING BEFORE REUSE.

SECTION 5. - - - - - - - - - - FIRE FIGHTING MEASURES - - - - - - - - - -

EXTINGUISHING MEDIA

WATER SPRAY.
CARBON DIOXIDE, DRY CHEMICAL POWDER OR APPROPRIATE FOAM.

SPECIAL FIREFIGHTING PROCEDURES

WEAR SELF-CONTAINED BREATHING APPARATUS AND PROTECTIVE CLOTHING TO PREVENT CONTACT WITH SKIN AND EYES.

UNUSUAL FIRE AND EXPLOSIONS HAZARDS

EMITS TOXIC FUMES UNDER FIRE CONDITIONS.

SECTION 6. - - - - - - - - - ACCIDENTAL RELEASE MEASURES- - - - - - - - -

CHEMICAL SAFETY GOGGLES.
USE PROTECTIVE CLOTHING, GLOVES AND MASK.
SWEEP UP, PLACE IN A BAG AND HOLD FOR WASTE DISPOSAL.
AVOID RAISING DUST.
VENTILATE AREA AND WASH SPILL SITE AFTER MATERIAL PICKUP IS COMPLETE.

SECTION 7. - - - - - - - - - - HANDLING AND STORAGE- - - - - - - - - - -

REFER TO SECTION 8.

SECTION 8. - - - - - - EXPOSURE CONTROLS/PERSONAL PROTECTION- - - - - -

CHEMICAL SAFETY GOGGLES.
COMPATIBLE CHEMICAL-RESISTANT GLOVES.
NIOSH/MSHA-APPROVED RESPIRATOR.

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SAFETY SHOWER AND EYE BATH.
MECHANICAL EXHAUST REQUIRED.
AVOID INHALATION.
AVOID CONTACT WITH EYES, SKIN AND CLOTHING.
AVOID PROLONGED OR REPEATED EXPOSURE.
WASH THOROUGHLY AFTER HANDLING.
KEEP TIGHTLY CLOSED.
STORE IN A COOL DRY PLACE.

SECTION 9. - - - - - - - PHYSICAL AND CHEMICAL PROPERTIES - - - - - - -

APPEARANCE AND ODOR
WHITE POWDER

PHYSICAL PROPERTIES
BOILING POINT: 360 C
MELTING POINT: 147 C TO 149 C
SPECIFIC GRAVITY: 1.067

SECTION 10. - - - - - - - - - -STABILITY AND REACTIVITY - - - - - - - - - -

STABILITY
STABLE.

INCOMPATIBILITIES
STRONG OXIDIZING AGENTS

HAZARDOUS COMBUSTION OR DECOMPOSITION PRODUCTS
TOXIC FUMES OF:
CARBON MONOXIDE, CARBON DIOXIDE

HAZARDOUS POLYMERIZATION
WILL NOT OCCUR.

SECTION 11. - - - - - - - - - - TOXICOLOGICAL INFORMATION - - - - - - - -

ACUTE EFFECTS
MAY BE HARMFUL BY INHALATION, INGESTION, OR SKIN ABSORPTION.
MAY CAUSE IRRITATION.
TOXICOLOGICAL DATA INDICATE A LOW ORDER OF TOXICITY. GENERAL GOOD-HOUSEKEEPING PRACTICES SHOULD BE FOLLOWED.

RTECS #: FZ8400000
CHOLESTEROL

TARGET ORGAN DATA
KIDNEY, URETER, BLADDER (BLADDER TUMORS)
EFFECTS ON FERTILITY (POST-IMPLANTATION MORTALITY)
EFFECTS ON FERTILITY (LITTER SIZE)
SPECIFIC DEVELOPMENTAL ABNORMALITIES (CRANIOFACIAL)
TUMORIGENIC (EQUIVOCAL TUMORIGENIC AGENT BY RTECS CRITERIA)
TUMORIGENIC (TUMORS AT SITE OF APPLICATION)
ONLY SELECTED REGISTRY OF TOXIC EFFECTS OF CHEMICAL SUBSTANCES (RTECS) DATA IS PRESENTED HERE. SEE ACTUAL ENTRY IN RTECS FOR COMPLETE INFORMATION.

SECTION 12. - - - - - - - - - - ECOLOGICAL INFORMATION - - - - - - - - - -
DATA NOT YET AVAILABLE.

SECTION 13. - - - - - - - - - - DISPOSAL CONSIDERATIONS - - - - - - - - -
DISSOLVE OR MIX THE MATERIAL WITH A COMBUSTIBLE SOLVENT AND BURN IN A CHEMICAL INCINERATOR EQUIPPED WITH AN AFTERBURNER AND SCRUBBER.
OBSERVE ALL FEDERAL, STATE AND LOCAL ENVIRONMENTAL REGULATIONS.

SECTION 14. - - - - - - - - - - TRANSPORT INFORMATION - - - - - - - - -
CONTACT SIGMA CHEMICAL COMPANY FOR TRANSPORTATION INFORMATION.

SECTION 15. - - - - - - - - - - REGULATORY INFORMATION - - - - - - - - - -

REVIEWS, STANDARDS, AND REGULATIONS
OEL=MAK
IARC CANCER REVIEW:ANIMAL INADEQUATE EVIDENCE IMEMDT 10,99,1976

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IARC CANCER REVIEW:HUMAN INADEQUATE EVIDENCE IMEMDT 31,95,1983
IARC CANCER REVIEW:GROUP 3 IMSUDL 7,161,1987
NOHS 1974: HZD 80865; NIS 8; TNF 1321; NOS 10; TNE 13980
NOES 1983: HZD 80865; NIS 5; TNF 4091; NOS 11; TNE 41411; TFE 30220
EPA GENETOX PROGRAM 1988, NEGATIVE: SHE-CLONAL ASSAY
EPA TSCA SECTION 8(B) CHEMICAL INVENTORY
EPA TSCA SECTION 8(D) UNPUBLISHED HEALTH/SAFETY STUDIES
EPA TSCA TEST SUBMISSION (TSCATS) DATA BASE, DECEMBER 1999

SECTION 16. - - - - - - - - - - - OTHER INFORMATION- - - - - - - - - - - -

THE ABOVE INFORMATION IS BELIEVED TO BE CORRECT BUT DOES NOT PURPORT TO BE ALL INCLUSIVE AND SHALL BE USED ONLY AS A GUIDE. SIGMA, ALDRICH, FLUKA SHALL NOT BE HELD LIABLE FOR ANY DAMAGE RESULTING FROM HANDLING OR FROM CONTACT WITH THE ABOVE PRODUCT. SEE REVERSE SIDE OF INVOICE OR PACKING SLIP FOR ADDITIONAL TERMS AND CONDITIONS OF SALE.

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SIGMA-ALDRICH

Material Safety Data Sheet

Date Printed: 07/25/2000
Date Updated: 11/01/1999
Version: 1.0

Section 1 - Product and Company Information

Product Name DL-MEVALONIC ACID LACTONE
Product Number M4667
Brand Sigma Chemical

Company Sigma-Aldrich
Street Address 3050 Spruce Street
City, State, Zip, Country St. Louis, MO, 63103, US
Technical Phone: 314 771 5765
Fax: 800 325 5052
Emergency Phone: 414 273 3850 Ext.5996

Section 2 - Composition/Information on Ingredient

Substance Name	CAS #	SARA 313
DL-MEVALONIC ACID LACTONE	674-26-0	No

Formula C6H10O3
Synonyms

Section 3 - Hazards Identification

For additional information on toxicity, please refer to Section 11.

Section 4 - First Aid Measures

Oral Exposure
If swallowed, wash out mouth with water provided person is conscious. Call a physician.

Inhalation Exposure
If inhaled, remove to fresh air. If not breathing give artificial respiration. If breathing is difficult, give oxygen.

Dermal Exposure
In case of contact, immediately wash skin with soap and copious amounts of water.

Eye Exposure
In case of contact, immediately flush eyes with copious amounts of water for at least 15 minutes.

Section 5 - Fire Fighting Measures

Flash Point: 235 °F 113 °C

Autoignition Temp: N/A **Flammability:** N/A

Extinguishing Media
Suitable
Water spray. Carbon dioxide, dry chemical powder, or appropriate foam.

Firefighting

Protective Equipment

Wear self-contained breathing apparatus and protective clothing to prevent contact with skin and eyes.

Section 6 - Accidental Release Measures

Procedure(s) of Personal Precaution(s)

Wear respirator, chemical safety goggles, rubber boots, and heavy rubber gloves.

Methods for Cleaning Up

Absorb on sand or vermiculite and place in closed containers for disposal. Ventilate area and wash spill site after material pickup is complete.

Section 7 - Handling and Storage

Handling

User Exposure

Avoid inhalation. Avoid contact with eyes, skin, and clothing. Avoid prolonged or repeated exposure.

Storage

Suitable

Keep tightly closed.

Section 8 - Exposure Controls / PPE

Engineering Controls

Safety shower and eye bath. Mechanical exhaust required.

Personal Protective Equipment

Respiratory

NIOSH/MSHA-approved respirator.

Hand

Compatible chemical-resistant gloves.

Eye

Chemical safety goggles.

General Hygiene Measures

Wash contaminated clothing before reuse. Wash thoroughly after handling

Section 9 - Physical/Chemical Properties

Appearance

Color	Form
Faintly beige	Solidified mass or fragments

Molecular Weight: 130.15 AMU

Property	Value	At Temperature or Pressure
pH	N/A	
BP/BP Range	145 - 150 °C	5 mmHg
MP/MP Range	24 °C	
Freezing Point	N/A	
Vapor Pressure	N/A	
Vapor Density	N/A	
Saturated Vapor Conc.	N/A	
SG/Density	N/A	
Bulk Density	N/A	
Odor Threshold	N/A	

Volatile%	N/A
VOC Content	N/A
Water Content	N/A
Solvent Content	N/A
Evaporation Rate	N/A
Viscosity	N/A
Partition Coefficient	N/A
Decomposition Temp.	N/A
Flash Point °F	235 °F
Flash Point °C	113 °C
Explosion Limits	N/A
Autoignition Temp	N/A
Refractive Index	1.473
Solubility	N/A

Section 10 - Stability and Reactivity

Stability

Conditions of Instability

Protect from moisture.

Conditions to Avoid

Protect from moisture.

Materials to Avoid

Strong oxidizing agents.

Hazardous Decomposition Products

Hazardous Decomposition Products

Carbon monoxide, Carbon dioxide.

Section 11 - Toxicological Information

Route of Exposure

Skin Contact

May cause skin irritation.

Eye Contact

May cause eye irritation.

Inhalation

Material may be irritating to mucous membranes and upper respiratory tract.

Multiple Routes

May be harmful by inhalation, ingestion, or skin absorption.

Signs and Symptoms of Exposure

To the best of our knowledge, the chemical, physical, and toxicological properties have not been thoroughly investigated.

RTECS Number:

Section 12 - Ecological Information

Section 13 - Disposal Considerations

Appropriate Method of Disposal of Substance or Preparation

Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber. Observe all federal, state, and local environmental regulations.

Section 14 - Transport Information

DOT

Proper Shipping Name: None

Non-Hazardous for Transport: This substance is considered to be non-hazardous for transport.

IATA

Proper Shipping Name: None

Non-Hazardous for Air Transport: Non-hazardous for air transport.

Section 15 - Regulatory Information

United States Regulatory Information

SARA 313 Listed: No

Section 16 - Other Information

Warranty

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ATTACHMENT 3

TEST ARTICLE, CONTROL ARTICLE AND VEHICLE PREPARATION PROCEDURE

ATTACHMENT 3

TEST ARTICLE, CONTROL ARTICLE AND VEHICLE PREPARATION PROCEDURE

Test Article:	PFOS
Control Articles:	Cholesterol Mevalonic acid
Vehicle:	0.5% Tween® 80 in R.O. Deionized Water for PFOS and Cholesterol R.O. deionized water for Mevalonic Acid

A. Purpose: The purpose of this procedure is to provide a method for the preparation of dosage formulations of PFOS, mevalonic acid, cholesterol and the 0.5% Tween® 80 vehicle for oral administration to rats on Primedica Argus Research Laboratories, Inc. Study 418-018.

B. General Information:

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

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

2b. Formulations of the control articles will be prepared:
_X_ Once Daily (cholesterol) _X_ Twice daily (Mevalonic acid)

2c. The 0.5% Tween® 80 Vehicle will be prepared:
___ Daily _X_ Weekly __ For____ days of use

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

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

5. Dosage formulations of the test article and control articles adjusted for Free base and % Purity.
__ Yes _X_ No (Calculations based on 100%)
___ Free Base ___ Purity

TEST ARTICLE, CONTROL ARTICLE AND VEHICLE PREPARATION PROCEDURE

6. Sampling requirements: Cited in protocol.

7. Storage: Cited in protocol.

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

C. Preparation of the 0.5% Tween® 80 Vehicle:

1. Add 2985 mL of R.O. deionized water to an appropriately labeled container. Heat the water to 50°C ± 5°C, then add 15 mL of Tween® 80 and mix until uniform.

D. Test Article Suspension Preparation:

NOTE: Prior to preparation of the 0.40 mg/mL suspension, precalibrate an appropriately sized container to the desired volume with R.O. deionized water.

1. To prepare the 0.40 mg/mL suspension, weigh the required amount of test article (See TEST ARTICLE PREPARATION CALCULATIONS) into an appropriately sized, labeled, pre-calibrated container. QS ad to the required amount with 0.5% Tween® 80 and heat the mixture to 80°C ±5°C for approximately 30 minutes or until the TA/S dissolves.

2. Once the test article has dissolved, remove the suspension from the water bath, add a magnetic stir bar to the container, place on a magnetic stir plate and mix until the suspension equilibrates to room temperature. (Be sure there is a visible vortex, this will achieve the desired emulsion.) Be sure that the suspension is mixed prior to and during preparation of other dosage groups, aliquotting, dosage and/or sampling.

3. To prepare the 0.32 mg/mL suspension, remove the required amount of 0.40 mg/mL suspension (See TEST ARTICLE PREPARATION CALCULATIONS) and add it to an appropriately sized graduated cylinder. QS ad to the final required volume with 0.5% Tween® 80 (See TEST ARTICLE PREPARATION CALCULATIONS). Stopper the graduated cylinder and invert several times to ensure proper mixing. Transfer the suspension to an appropriately sized, labeled container. Add a magnetic

TEST ARTICLE, CONTROL ARTICLE AND VEHICLE PREPARATION PROCEDURE

stir bar to the container, place on a magnetic stir plate and mix prior to and during preparation of other dosage groups, aliquotting, dosage and/or sampling.

4. To prepare the 0.24 mg/mL suspension, remove the required amount of 0.32 mg/mL suspension (See TEST ARTICLE PREPARATION CALCULATIONS) and add it to an appropriately sized graduated cylinder. QS ad to the final required volume with 0.5% Tween® 80 (See TEST ARTICLE PREPARATION CALCULATIONS). Stopper the graduated cylinder and invert several times to ensure proper mixing. Transfer the suspension to an appropriately sized, labeled container. Add a magnetic stir bar to the container, place on a magnetic stir plate and mix prior to and during preparation of other dosage groups, aliquotting, dosage and/or sampling.

5. To prepare the 0.20 mg/mL suspension, remove the required amount of 0.24 mg/mL suspension (See TEST ARTICLE PREPARATION CALCULATIONS) and add it to an appropriately sized graduated cylinder. QS ad to the final required volume with 0.5% Tween® 80 (See TEST ARTICLE PREPARATION CALCULATIONS). Stopper the graduated cylinder and invert several times to ensure proper mixing. Transfer the suspension to an appropriately sized, labeled container. Add a magnetic stir bar to the container, place on a magnetic stir plate and mix prior to and during preparation of other dosage groups, aliquotting, dosage and/or sampling.

6. To prepare the 0.16 mg/mL suspension, remove the required amount of 0.20 mg/mL suspension (See TEST ARTICLE PREPARATION CALCULATIONS) and add it to an appropriately sized graduated cylinder. QS ad to the final required volume with 0.5% Tween® 80 (See TEST ARTICLE PREPARATION CALCULATIONS). Stopper the graduated cylinder and invert several times to ensure proper mixing. Transfer the suspension to an appropriately sized, labeled container. Add a magnetic stir bar to the container, place on a magnetic stir plate and mix prior to and during preparation of other dosage groups, aliquotting, dosage and/or sampling.

7. To prepare the 0.08 mg/mL suspension, remove the required amount of 0.16 mg/mL suspension (See TEST ARTICLE PREPARATION CALCULATIONS) and add it to an appropriately sized graduated cylinder. QS ad to the final required volume with 0.5% Tween® 80 (See TEST ARTICLE PREPARATION CALCULATIONS). Stopper the graduated

cylinder and invert several times to ensure proper mixing. Transfer the suspension to an appropriately sized, labeled container. Add a magnetic stir bar to the container, place on a magnetic stir plate and mix prior to and during aliquotting, dosage and/or sampling.

8. To prepare the 0 mg/mL suspension, add the required amount of the appropriate vehicle (R.O. deionized water or 0.5% Tween® 80) to an appropriately sized, labeled container (See TEST ARTICLE PREPARATION CALCULATIONS). Add a magnetic stir bar to the container, place on a magnetic stir plate and mix prior to and during aliquotting, dosage and/or sampling.

E. Preparation of Mevalonic Acid Solution:

1. Weigh the required amount of mevalonic acid into an appropriately labeled container (See TEST ARTICLE/VEHICLE PREPARATION CALCULATIONS).

2. Add approximately 80% of R.O. deionized water to the container. Add a stir bar to the container, place on a magnetic stir plate and agitate until the control article has dissolved completely.

3. Transfer solution to an appropriately sized graduated cylinder and Q.S. to the final desired volume with R.O. deionized water (See TEST ARTICLE/VEHICLE PREPARATION CALCULATIONS).

4. Cover the graduated cylinder with a glass stopper and mix by inversion. Return the solution to the original container. Add a magnetic stir bar to the container, place on a magnetic stir plate and mix prior to and during dosage.

F. Preparation of Cholesterol Suspension:

NOTE: Prior to preparation of the cholesterol suspension, precalibrate an appropriately sized container to the desired volume with R.O. deionized water.

1. Weigh the required amount of cholesterol into an appropriately sized, labeled container (see TEST ARTICLE/VEHICLE PREPARATION CALCULATIONS).

ATTACHMENT 3

TEST ARTICLE, CONTROL ARTICLE AND VEHICLE PREPARATION PROCEDURE

2. Add a small amount of 0.5% Tween® 80 to the container and wet the cholesterol by using a glass rod. QS ad with the 0.5% Tween® 80 to the final required volume (see TEST ARTICLE/VEHICLE PREPARATION CALCULATIONS).

3. Add a magnetic stir bar to the vessel, place on a magnetic stir plate and mix until uniform prior to and during dosage administration.

Written by: Patricia A. Kelly

Approved by: [illegible] Date: 21-AUG-00

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

Initials/Date : [illegible] 12/12/00

ATTACHMENT 4

TISSUE COLLECTION AND PROCESSING

ATTACHMENT 4

Tissue Collection and Processing

Sample Type	Units	Aliquots	Storage/Shipping Conditions	Shipped to	Analysis
Day 21 Gestation Fetuses					
Blood	Pooled/litter	1/2 plasma	≤-20	PWL	Mevalonic acid
		1/4 serum	≤-20	3M	PFOS
		1/4 serum	≤-20	AniLytics	LDL, HDL, tot chol, trigl
Liver	Pooled/litter	1 liver	Gluteraldehyde, RT	3M	Possible EM
		1/3 all livers	≤-20	3M	PFOS
		1/3 all livers	≤-20	AniLytics	LDL, HDL, tot chol, trigl
		1/3 all livers	Liquid nitrogen, ≤-70	3M	Possible Biochemical
Day 21 Gestation Dams					
Blood	4 mL/dam	1/2 plasma	≤-20	PWL	Mevalonic acid
		1/4 serum	≤-20	3M	PFOS
		1/4 serum	≤-20	AniLytics	LDL, HDL, tot chol, trigly
Liver	each dam	right lateral lobe	Liquid nitrogen, ≤-70	3M	Possible Biochemical
		median lobe	≤-20	3M	PFOS
		0.3-0.5 cm section	Gluteraldehyde, RT	3M	Possible EM
		remainder	≤-20	Ani Lytics	LDL, HDL, tot chol, trigly
Day 5 Lactation Dams					
Milk	100 µL/dam		≤-20	AniLytics	Total cholesterol
Blood	4 mL/dam	1/2 plasma	≤-20	PWL	Mevalonic acid
		1/4 serum	≤-20	3M	PFOS
		1/4 serum	≤-20	Ani Lytics	LDL, HDL, tot chol, trigl
Liver	each dam	right lateral lobe	Liquid nitrogen, ≤-70	3M	Possible Biochemical
		median lobe	≤-20	3M	PFOS
		0.3-0.5 cm section	Gluteraldehyde, RT	3M	Possible EM
		Remainder	≤-20	Ani Lytics	LDL, HDL, tot chol, trigly
Heart	each dam		Gluteraldehyde, RT	3M	Possible EM & light microscopy
Day 5 Postpartum Pups					
Blood	Pooled/sex/litter	1/2 plasma	≤-20	PWL	Mevalonic acid
		1/4 serum	≤-20	3M	PFOS
		1/4 serum	≤-20	AniLytics	LDL, HDL, tot chol, trigl
Liver	Pooled/sex/litter	1/3 all livers	≤-20	3M	PFOS
		1/3 all livers	≤-20	AniLytics	LDL, HDL, tot chol, trigl
		1/3 all livers	Liquid nitrogen, ≤-70	3M	Possible Biochemical
Hearts	2 male, 2 female, per sex per litter		Gluteraldehyde, RT	3M	Possible EM & light microscopy

PWL = Primedica Worcester Laboratories
RT = Room Temperature
Tot chol = Total cholesterol
EM = Electron Microscopy
trigl = Triglyceride

PRIMEDICA

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905 Sheehy Drive, Building A
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Telefax: (215) 443-8587

PROTOCOL 418-018

ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/ CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS

SPONSOR'S STUDY NUMBER: T-6295.25

Amendment 1 - 13 September 2000

1. Storage (page 4 of the protocol):

The storage conditions for the Mevalonic Acid should be frozen, rather than room temperature.

Reason for Change:

This change was made at the request of the Sponsor.

2. Shipping Instructions (page 6 of the protocol):

The correct address for Dave Ehresman is the following:

Dave Ehresman
3M Corporate Toxicology
3M Center Building 236-0C-148
St. Paul, Minnesota 55144
Telephone: (651) 733-5070
Telefax: (651) 737-4754

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

Reason for Change:

This change corrects the protocol.

George E. Dearlove 13 Sep 00
George E. Dearlove, Ph.D., DABT Date
Associate Director of Research

Raymond G. York 13-SEP-00
Raymond G. York, Ph.D., DABT Date
Associate Director of Research
Study Director

for Therese H. Woodard 13 SEP 00
Dena C. Lebo, V.M.D. Date
Chairperson, Institutional Animal Care
and Use Committee

Deanna J. Luebker 9/14/00
Deanna J. Luebker, M.S. Date
Study Monitor

John V. Butenhoff 9/14/2000
John Butenhoff, Ph.D., DABT, CIH Date
Alternate Study Monitor

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

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PROTOCOL 418-018

ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/ CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS

SPONSOR'S STUDY NUMBER: T-6295.25

Amendment 2 - 22 November 2000

1. Alternate Study Monitor (page 1 of the protocol):

The telephone number for John Butenhoff, Ph.D., DABT, CIH is (651) 733-1962, rather than (651) 737-1962.

Reason for Change:

This change corrects the protocol.

2. Sample Analysis and Shipping Instructions (page 14 of the protocol):

The following paragraphs will replace the paragraph which states that serum and liver samples will be analyzed for LDL, HDL, total cholesterol and triglycerides:

The remaining liver samples will be analyzed for LDL, HDL, total cholesterol and triglycerides.

Serum samples collected from all dams and pups will be analyzed for total cholesterol, glucose, total and free T_3, T_4 and TSH levels, LDL, HDL and triglycerides. The first priority will be analysis for total cholesterol and glucose. The second priority will be analysis for total and free T_3, T_4 and TSH levels. The third priority will be analysis for LDL, HDL and triglycerides.

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

The liver and serum samples will be shipped to:

Dr. Saroj R. Das
Ani Lytics, Inc.
200 Gerard Street, Suite 2000
Gaithersburg, Maryland 20877
Telephone: (301) 921-0168
Telefax: (301) 977-0433

Reason for Change:

This change was made at the request of the Sponsor in order to include additional tissue samples and to prioritize the use of samples for analyses.

3. Scheduled Sacrifice - F1 Generation Pups (page 20 of the protocol):

[Effective Date: 3 November 2000] For Replicate 1, blood samples will be pooled per litter, samples from male and female pups combined, rather than pooled per sex. Samples will be aliquoted as follows, rather than as described in paragraph 3. Approximately 1 mL of blood will be transferred into serum separator tubes; any remaining blood will be transferred into EDTA-coated tubes. The samples will be spun in a centrifuge and the resulting serum will be divided into two aliquots. The first aliquot (approximately 200 µL) will be used for PFOS analysis. The second aliquot (approximately 300 µL of serum) will be used for analysis of total cholesterol, glucose, total and free T_3, T_4 and TSH levels and LDL, HDL and triglyceride levels, according to the priorities described in item 1, above. Any resulting plasma will be transferred into one aliquot. Resulting serum will be prioritized as follows: clinical chemistries first (according to the priorities described in item 2, above) and then PFOS samples. All samples will be immediately frozen on dry ice and maintained frozen (≤-70°C) until shipment for analysis.

Reason for Change:

This change was made at the request of the Sponsor in order to prioritize the use of samples for analyses.

4. Scheduled Sacrifice - F1 Generation Pups (page 20 of the protocol):

[Effective Date: 17 November 2000] For Replicate 2, blood samples will be pooled (two litters per sample within each dosage group). Samples will be aliquoted as follows, rather than as described in paragraph 3. Approximately 0.3 mL of blood will be transferred into EDTA-coated tubes. The remaining blood will be transferred into serum separator tubes. The samples will be spun in a centrifuge and the resulting serum will be divided into two aliquots. Resulting plasma will be transferred into one aliquot. The serum will be prioritized as follows: clinical chemistries first (according

to the priorities described in item 2, above) and then PFOS samples. All samples will be frozen on dry ice and maintained frozen (≤-70°C) until shipment for analysis.

Reason for Change:

This change was made at the request of the Sponsor in order to prioritize the use of samples for analyses.

5. Scheduled Sacrifice - F1 Generation Pups (page 21 of the protocol):

[Effective Date: 3 November 2000] Thyroids will be excised from each pup, pooled (by sex per litter). Thyroids will be retained in neutral buffered 10% formalin for possible future evaluation.

Reason for Change:

This change was made at the request of the Sponsor.

George E. Dearlove 22 Nov 00
George E. Dearlove, Ph.D., DABT Date
Associate Director of Research

Raymond G. York 22-Nov-00
Raymond G. York, Ph.D., DABT Date
Associate Director of Research
Study Director

Theresa H. Woodard 22 Nov 00
per
Dena C. Lebo, V.M.D. Date
Chairperson, Institutional Animal Care and Use Committee

Deanna J. Luebker 11/30/00
Deanna J. Luebker, M.S. Date
Study Monitor

John E. Butenhoff 11/30/2000
John Butenhoff, Ph.D., DABT, CIH Date
Alternate Study Monitor

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

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PROTOCOL 418-018

ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/ CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS

SPONSOR'S STUDY NUMBER: T-6295.25

Amendment 3 - 11 January 2001

1. Control Articles (page 3 of the protocol):

   The lot number for mevalonic acid is lot number 070K26603, rather than 070K2603.

   Reason for Change:

   This change corrects a typographical error.

2. Control Articles (page 3 of the protocol):

   For mevalonic acid, lot number 080K2618, expiration date September 2004, was used in addition to lot number 070K26603.

   Reason for Change:

   Additional mevalonic acid was required for the preparation of the mevalonic acid control and PFOS plus mevalonic acid formulations.

3. Sample Analysis and Shipping Instructions (page 14 of the protocol):

   Plasma mevalonic acid levels will be measured for the following dosage groups: Vehicle Control (Group 1), Mevalonic Acid Control (Group 2), 1.6 mg/kg PFOS + Mevalonic Acid (Group 3), 2 mg/kg PFOS + Mevalonic Acid (Group 4), 1.2 mg/kg PFOS (Group 11), 1.6 mg/kg PFOS (Group 12) and 2 mg/kg PFOS (Group 13), rather than all dosage groups. Mevalonic acid levels may be measured in the lower PFOS dosage groups after evaluation of the results of the above analyses. Remaining samples will be retained at Primedica Worcester Laboratories or the Testing Facility until notification from the Sponsor for disposition.

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

Reason for Change:

This change was made at the request of the Sponsor.

4. Sample Analysis and Shipping Instructions (page 1 of Amendment 2 to the protocol):

Total and free T_3, T_4 and TSH levels will be measured for the following dosage groups: Vehicle Control (Group 1), 1.2 mg/kg PFOS (Group 11), 1.6 mg/kg PFOS (Group 12) and 2 mg/kg PFOS (Group 13), rather than all dosage groups. Total and free T_3, T_4 and TSH levels may be measured in the lower PFOS dosage groups after evaluation of the results of the above analyses.

Reason for Change:

This change was made at the request of the Sponsor.

George E. Dearlove 11-JAN-01
George E. Dearlove, Ph.D., DABT Date
Associate Director of Research

Raymond G. York 11-JAN-01
Raymond G. York, Ph.D., DABT Date
Associate Director of Research and
Study Director

Per Dena H. Woodland 11 JAN 01
Dena C. Lebo, V.M.D. Date
Chairperson, Institutional Animal Care
and Use Committee

Deanna J. Luebker 1/15/01
Deanna J. Luebker, M.S. Date
Study Monitor

John T. Butenhoff 15 JAN 01
John Butenhoff, Ph.D., DABT, CIH Date
Alternate Study Monitor

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

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PROTOCOL 418-018

ONE GENERATION REPRODUCTION STUDY OF PFOS - MEVALONIC ACID/ CHOLESTEROL CHALLENGE AND NOEL INVESTIGATION IN RATS

SPONSOR'S STUDY NUMBER: T-6295.25

Amendment 4 - 18 April 2001

1. F1 Generation Pups (page 10 of the protocol):

[Effective Date: 21 August 2000] Day 1 of lactation (postpartum) is defined as the day of birth and is also the first day on which all of the pups in a litter are weighed. The pups will not be individually weighed; pooled litter weights will be recorded.

Reason for Change:

This change was made to be consistent with Tests, Analyses and Measurements - F1 Generation, Body Weights.

2. Scheduled Sacrifice - F1 Generation Pups (page 20, 21, page 1 of ATTACHMENT 4 and item 5 of Amendment 2 to the protocol):

Histopathology will be performed on the heart and thyroid of one male and one female F1 generation pup from each of four litters from the Vehicle Control group (Group 1) and 2 mg/kg PFOS group (Group 13). If any difference is found, histopathology will be performed on the heart and thyroid of one male and one female F1 generation pup from each of four litters, when possible, from the 0.4 and 1.6 mg/kg PFOS dosage groups (Groups 8 and 12, respectively). Tissues will be shipped (ambient conditions) for evaluation to:

W. Ray Brown, D.V.M., Ph.D., ACVP
Veterinary Pathologist
Research Pathology Services, Inc.
438 E. Butler Avenue
New Britain, Pennsylvania 18901
Telephone: (215) 345-7070
Telefax: (215) 345-4326

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

Reason for Change:

This change was made at the request of the Sponsor.

George E. Dearlove 18 APR 01
George E. Dearlove, Ph.D., DABT Date
Associate Director of Research

Raymond G. York 18 APR 01
Raymond G. York, Ph.D., DABT Date
Associate Director of Research
and Study Director

for Theresa H. Woodard 18 APR 01
Theresa H. Woodard, D.V.M. Date
Chairperson, Institutional Animal Care
and Use Committee

Deanna J. Luebker 4/19/01
Deanna J. Luebker, M.S. Date
Study Monitor

John T. Butenhoff April 23, 2001
John Butenhoff, Ph.D., DABT, CIH Date
Alternate Study Monitor

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

APPENDIX D

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

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

1. Rats were ordered to weigh 175 g to 200 g at receipt, rather than 175 g to 225 g at receipt. This deviation did not adversely affect the outcome or interpretation of the study because the rats were a sufficient weight to go on study.

2. The following dosage administrations were performed from two minutes early to 60 minutes late.

Dosage Group	Identification	Date	Day of Study[a]	Dosage Number Administered Early or Late	Rat Number
1	Vehicle Control	15 SEP 00	DS 2	2	11501 - 11514
		22 SEP 00	DS 9	3	11501 - 11514
		10 OCT 00	DS 43, DG 0	3	10901 - 10914
		14 OCT 00	DS 47, DGs 1 - 4	3	10901 - 10914
		14 OCT 00	DS 31	3	11501 - 11514
		20 OCT 00	DS 9	2	10901
		24 OCT 00	DGs 2, 11 - 14	2	10901 - 10914
		10 NOV 00	DG 19	2	10913
2	Mevalonic Acid Control	15 SEP 00	DS 2	2	11515, 11517
		22 SEP 00	DS 9	3	11515 - 11528
		28 SEP 00	DS 15	2	11526 - 11528
		10 OCT 00	DS 43, DG 0	3	10915 - 10928
		14 OCT 00	DS 47, DGs 1 - 4	3	10915 - 10928
		14 OCT 00	DS 31	3	11515 - 11528
		24 OCT 00	DGs 3, 9, 11 - 14	2	10915 - 10928
		10 NOV 00	DG 20	2	10927
3	1.6 mg/kg PFOS + Mevalonic Acid	16 SEP 00	DS 19	2	10930
		22 SEP 00	DS 9	3	11529 - 11543
		28 SEP 00	DS 15	2	11529 - 11543
		10 OCT 00	DS 43, DG 0	3	10929 - 10942
		14 OCT 00	DGs 2 - 4	3	10929 - 10942
		14 OCT 00	DS 31	3	11529 - 11543
		24 OCT 00	DGs 12, 14	2	10929 - 10932, 10934
4	2 mg/kg PFOS + Mevalonic Acid	16 SEP 00	DS 19	2	10943 - 10945
		22 SEP 00	DS 9	3	11544 - 11557
		28 SEP 00	DS 15	2	11544 - 11557
		10 OCT 00	DS 43, DG 0	3	10943 - 10956
		14 OCT 00	DS 47, DGs 0 - 4	3	10943 - 10956
		14 OCT 00	DS 31	3	11544 - 11557
		10 NOV 00	DG 20	2	10952
5	Cholesterol Control	28 SEP 00	DS 15	2	11558 - 11571
		10 NOV 00	DG 18	2	10967

a. DS is used as an abbreviation for day of study. DG is used as an abbreviation for day of (presumed) gestation. DL is used as an abbreviation for day of lactation.

Dosage Group	Identification	Date	Day of Study	Dosage Number Administered Early or Late	Rat Number
6	1.6 mg/kg PFOS + Cholesterol	21 SEP 00	DS 8	2	11583 - 11585
		28 SEP 00	DS 15	2	11572 - 11585
		07 OCT 00	DS 24	2	11572
		11 OCT 00	DS 44	2	10984
		21 OCT 00	DG 8	2	10983
		01 NOV 00	DG 20, DL 2	2	10972, 10973
		17 NOV 00	DG 21, DL 2	2	11584, 11585
7	2 mg/kg PFOS + Cholesterol	02 SEP 00	DS 5	2	10985
		28 SEP 00	DS 15	2	11586 - 11595
		11 OCT 00	DS 44, DG 0	2	10994 - 10998
		12 OCT 00	DS 45, DG 0	2	10990, 10992, 10994
		21 OCT 00	DGs 9, 11	2	10985 - 10989, 10991
		01 NOV 00	DG 21	2	10997, 10998
		01 NOV 00	DG 6	2	11591
		02 NOV 00	DS 50, DGs 4, 5, 7	2	11591 - 11599
		17 NOV 00	DL 1	2	11586

These deviations did not adversely affect the outcome or interpretation of the study because the time deviated was small and the deviation occurred on no more than four days of the approximately 60 to 80 day dosage period for any rat.

3. At least one event of dosage administration and/or postdosage observation was not recorded for the following rats.

Dosage Group	Identification	Date	Day of Study	Rat Number
1	Vehicle Control	28 SEP 00	DS 15	11502 - 11512
2	Mevalonic Acid Control	28 SEP 00	DS 15	11513 - 11524

These deviations did not adversely affect the outcome or interpretation of the study because sufficient data were available to evaluate this parameter.

4. Dosage administration was not performed for the following rats.

Dosage Group	Identification	Dosage Not Administered	Date	Day of Study	Rat Number
7	2 mg/kg PFOS + Cholesterol	Cholesterol	28 SEP 00	DS 15	11596
10	1 mg/kg PFOS	PFOS	01 OCT 00	DS 18	11623

These deviations did not adversely affect the outcome or interpretation of the study because it was a single occurrence for each rat.

5. On 1 October 2000, DS 18, the following rats in Group 3, 1.6 mg/kg PFOS + Mevalonic Acid, were administered the incorrect volume of test article.

Rat Number	Target Volume (mL)	Actual Volume (mL)
11532	1.2	1.3
11537	1.2	1.4
11539	1.0	1.3
11541	1.1	1.3

These deviations did not adversely affect the outcome or interpretation of the study because only four rats were affected and the additional volume was small (0.1 to 0.3 mL).

6. On 10 October 2000, DS 43 or DG 0, rats 10943 through 10956 in Group 4, 2 mg/kg PFOS + Mevalonic Acid, were administered the 0.32 mg/mL concentration of PFOS, rather than the 0.40 mg/mL at 5 mL/kg. Approximately 20 minutes later the rats were administered the 0.08 mg/mL concentration of PFOS at 5 mL/kg. These deviations did not adversely affect the outcome or interpretation of the study because the total correct dosage was administered to all of the rats.

7. On 20 November 2000, DL 3, rat 11589 in the 2 mg/kg PFOS + Cholesterol dosage group (Group 7) received 1.9 mL of test article rather than 1.5 mL. This deviation did not adversely affect the outcome or interpretation of the study because the amount of extra volume received was small and this was a single event.

8. Clinical observations, body weights and dosage administration were not recorded for the following rats.

Dosage Group	Identification	Date	Day of Study	Rat Number
12	1.6 mg/kg PFOS	01 NOV 00	DS 65	11039
			DG 19	11041
			DG 19	11042
			DG 21	11043
		07 NOV 00	DG 12	11647
			DG 9	11648
			DG 12	11649
			DG 0	11650
			DG 9	11651
			DG 10	11652
			DG 12	11653
13	2 mg/kg PFOS	07 NOV 00	DG 12	11654
			DG 10	11655
			DG 11	11656
			DG 11	11657
			DG 10	11658
			DG 11	11659
			DG 10	11660

These deviations did not adversely affect the outcome or interpretation of the study because sufficient data were available to evaluate these parameters.

9. Data for the following rats were not collected due to a computer filing error.

Dosage Group	Identification	Date	Day of Study	Rat Number
1	Vehicle Control	20 SEP 00	DS 7	11501 - 11512
3	1.6 mg/kg PFOS + Mevalonic Acid	20 SEP 00	DS 7	11538 - 11543
4	2 mg/kg PFOS + Mevalonic Acid	20 SEP 00	DS 7	11544 - 11548
5	Cholesterol Control	20 OCT 00	DG 10, 7	10965, 10966

These deviations did not adversely affect the outcome or interpretation of the study because sufficient data were available for evaluation of this parameter.

10. The feed left and/or feed fed values were not recorded for the following rats.

Dosage Group	Identification	Date	Day of Study	Rat Number
3	1.6 mg/kg PFOS + Mevalonic Acid	02 NOV 00	DG 21	10939
4	2 mg/kg PFOS + Mevalonic Acid	21 SEP 00	DS 8	11553

These deviations did not adversely affect the outcome or interpretation of the study because sufficient data were available to evaluate this parameter.

11. Maternal behavior was not recorded for the following rats.

Dosage Group	Identification	Date	Day of Study	Rat Number
1	Vehicle Control	04 NOV 00	DL 1	10914
2	Mevalonic Acid Control	04 NOV 00	DL 1	10923, 10924
5	Cholesterol Control	19 NOV 00 22 NOV 00	DL 5 DL 5	10967 11567
6	1.6 mg/kg PFOS + Mevalonic Acid	03 NOV 00	DL 1	10977

These deviations did not adversely affect the outcome or interpretation of the study because sufficient data were available to evaluate this parameter.

12. The terminal blood collection data (time collected, volume collected, performed by and date) was not recorded for the following rats.

Dosage Group	Identification	Date	Day of Study	Rat Number
3	1.6 mg/kg PFOS + Mevalonic Acid	02 NOV 00	DG 21	10931
4	2 mg/kg PFOS + Mevalonic Acid	02 NOV 00	DG 21	10949
6	1.6 mg/kg PFOS + Cholesterol	03 NOV 00	DG 21	10980
8	0.4 mg/kg PFOS	22 NOV 00	DL 5	11601
10	1 mg/kg PFOS	22 NOV 00	DL 5	11629

These deviations did not adversely affect the outcome or interpretation of the study because the blood was collected and available for evaluation.

13. On 31 October 2000, DG 21, the maternal liver weight for rat 10932 in the 1.6 mg/kg PFOS + Mevalonic Acid dosage group (Group 3) was not recorded. This deviation did not adversely affect the outcome or interpretation of the study because sufficient data were available to evaluate this parameter.

14. The pooled litter weights were not recorded for the pups of the following dams.

Dosage Group	Identification	Date	Day of Study	Rat Number
5	Cholesterol Control	22 NOV 00	DL 4	11608
8	0.4 mg/kg PFOS	22 NOV 00	DL 5	11569

These deviations did not adversely affect the outcome or interpretation of the study because sufficient data were available to evaluate this parameter.

15. On 19 November 2000, DL 3, the necropsy observations for rat 11554 in the 2 mg/kg/day PFOS + Mevalonic Acid dosage group (Group 4) were not recorded. This deviation did not adversely affect the outcome or interpretation of the study because sufficient data were available to evaluate this parameter.

16. The weight of the pooled liver samples was not recorded for the male pups of the following dams.

Dosage Group	Identification	Date	Day of Study	Rat Number
1	Vehicle Control	25 NOV 00	DL 5	11504
4	2 mg/kg PFOS + Mevalonic Acid	25 NOV 00	DL 5	11547

These deviations did not adversely affect the outcome or interpretation of the study because sufficient data were available to evaluate this parameter.

All deviations are documented in the raw data.

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

Date

APPENDIX E

CERTIFICATE OF ANALYSIS

Certificate Of Analysis

FC-95, Lot 217

March 9, 2000

Richard M. Payfer

This sample was analyzed using LC/MS, ^{1}H-NMR, ^{19}F-NMR, and elemental analyses techniques. The results of these tests show the sample to contain the following weight percent composition:

$C_2F_5SO_3^-K^+$	0.04 %
$C_3F_7SO_3^-K^+$	0.83 %
$C_4F_9SO_3^-K^+$	1.38 %
$C_5F_{11}SO_3^-K^+$	1.30 %
$C_6F_{13}SO_3^-K^+$	3.71 %
$C_7F_{15}SO_3^-K^+$	1.19 %
$C_8F_{17}SO_3^-K^+$	90.49 %
$C_9F_{19}SO_3^-K^+$	0.49 %
$C_{10}F_{21}SO_3^-K^+$	0.13 %
$C_{11}F_{23}SO_3^-K^+$	0.04 %
$CF_3\text{-}CO_2^-K^+$	0.05 %
$SF_5C_8F_{16}SO_3^-K^+$	0.35 %

Additionally, the isomer distribution of the sample was determined using ^{19}F-NMR techniques and found to contain the following mole percent composition:

$CF_3(CF_2)_x\text{-}SO_3^-K^+$ (Normal chain, where x is mainly 7)	70.5%
$CF_3(CF_2)_x\text{-}CF(CF_3)\text{-}(CF_2)_y\text{-}SO_3^-K^+$ (Internal monomethyl branch, where x+y is mainly 5, and $x \neq 0$, $y \neq 0$)	17.1%
$(CF_3)_2CF\text{-}(CF_2)_x\text{-}SO_3^-K^+$ (Isopropyl branch, where x is mainly 5)	10.3%
$C_xF_{2x+1}\text{-}CF(CF_3)\text{-}SO_3^-K^+$ (Alpha branch, where x is mainly 6)	1.6%
$(CF_3)_3C\text{-}(CF_2)_x\text{-}SO_3^-K^+$ (t-butyl branch, where x is mainly 4)	0.2%
$CF_3\text{-}(CF_2)_x\text{-}C(CF_3)_2\text{-}(CF_2)_y\text{-}SO_3^-K^+$ (Internal gem-dimethyl branch, where x+y is mainly 4, and $x \neq 0$)	0.2%

SIGMA

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www.sigma-aldrich.com

CERTIFICATE OF ANALYSIS

DL-MEVALONIC ACID LACTONE
PRODUCT NO: M4667
LOT NO: 070K2603
FORMULA WEIGHT: 130.1

FORMULA: $C_6H_{10}O_3$

CAS NO: 674-26-0

STORE IN A FREEZER

TEST	SPECIFICATION	RESULTS
APPEARANCE	WHITE WITH A DARK YELLOW CAST SEMISOLID	CONFORMS
SOLUBILITY	CLEAR TO VERY SLIGHTLY HAZY FAINT YELLOW SOLUTION AT 400 MG PLUS 4 ML OF ETHANOL	CLEAR FAINT YELLOW
IDENTITY	CONSISTENT WITH STRUCTURE BY IR OR NMR	CONFORMS BY NMR
PURITY BY TITRATION	APPROX. 97%	99.2%

QC ACCEPTANCE DATE JULY 2000

DAVID FELDKER
MANAGER, ANALYTICAL SERVICES
191/200007#1/YXB1
DOCUMENT DATE: 07/26/00

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EXP. 8/04

We are committed to the Success of our Customers, Employees and Shareholders through Life Science, Technology and Service.

APPENDIX F

HOMOGENEITY AND CONCENTRATION ANALYSIS REPORT

To be added at a later date.

APPENDIX G

TEMEPRATURE AND RELATIVE HUMIDITY REPORTS

ARGUS

Temperature and Relative Humidity Report
Location: Room 17

Protocol Number: 418018

Range of Dates: 22-Aug-2000 14:44 to 12-Nov-2000 08:59

	Temperature		Relative Humidity	
Target Range:	64°F to 79°F		30% to 70%	
Species: rat				
Total Number of Days:	83		83	
Total Number of Hours:	1962.0		1962.0	
Total Number of Data Points:	1956		1956	
Mean (± SD):	70.6	(± 1.3)	56.6	(± 4.8)
Maximum:	73.9		70.6	
Median:	71.0		57.0	
Minimum:	63.8		40.7	
Number of Points in Range (%):	1954	(99.9)	1955	(99.9)
Number of Points High (%):	0	(0.0)	1	(0.1)
Number of Points Low (%):	2	(0.1)	0	(0.0)

Report Generated: 30-Nov-2000 at 14:02

COMMENTS: _____

REVIEWED BY: _____ **DATE:** 3-28-01

ARGUS

Temperature Deviations Report
Location: Room 17

Protocol Number: 418018

Range of Dates: 22-Aug-2000 14:44 to 12-Nov-2000 08:59

Temperature Target Range: 64°F to 79°F
Species: rat

Date	Time	Temp.	Date	Time	Temp.
07-Sep-2000	06:00	63.8 L			
07-Sep-2000	07:00	63.8 L			

H = Value out of range - High L = Value out of range - Low
Temp. = Temperature °F

Report Generated: 30-Nov-2000 at 14:10

✓ 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: 30-MAR-01

ARGUS

Relative Humidity Deviations Report
Location: Room 17

Protocol Number: 418018

Range of Dates: 22-Aug-2000 14:44 to 12-Nov-2000 08:59

Humidity Target Range: 30% to 70%
Species: rat

Date	Time	R.H.	Date	Time	R.H.
04-Oct-2000	22:00	70.6 H			

H = Value out of range - High L = Value out of range - Low
R.H. = Relative Humidity (%)

Report Generated: 30-Nov-2000 at 14:18

✓ 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: 30-MAR-01

ARGUS

Temperature and Relative Humidity Report
Location: Room 18

Protocol Number: 418-018

Range of Dates: 05-Sep-2000 14:00 to 03-Dec-2000 13:59

	Temperature 64°F to 79°F		Relative Humidity 30% to 70%	
Target Range:				
Species: rat				
Total Number of Days:	90		90	
Total Number of Hours:	2135.75		2135.75	
Total Number of Data Points:	2129		2129	
Mean (± SD):	69.2	(± 0.5)	53.6	(± 4.1)
Maximum:	70.8		70.2	
Median:	69.2		53.3	
Minimum:	67.6		42.3	
Number of Points in Range (%):	2129	(100.0)	2128	(100.0)
Number of Points High (%):	0	(0.0)	1	(0.0)
Number of Points Low (%):	0	(0.0)	0	(0.0)

Report Generated: 27-Mar-2001 at 18:18

COMMENTS: _____

REVIEWED BY: _____ **DATE:** 3·28·01

APPENDIX H

BIOANALYTICAL REPORTS (ANILYTICS)

ANILYTICS INCORPORATED
200 Girard Street, Suite 200, Gaithersburg, MD 20877
301-921-0168 Fax: 301-977-0433

Client: ARGUS RESEARCH LABORATORIES, INC.
905 SHEEHY DRIVE
BUILDING A
HORSHAM, PA 19044-
(215) 443-8710

Date Collected:
Date Received: 12/08/2000
Date Reported: 01/16/2001

Client No. 1028 Study: 418018 DAMS GD21 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0030145	10901	1	F		95	117	12	44	322
B 0030146	10902	1	F		79	116	10	61	151
B 0030147	10903	1	F		82	89	7	65	116
B 0030148	10904	1	F		77	87	7	51	176
B 0030149	10905	1	F		79	99	15	54	156
B 0030150	10907	1	F		97	90	1	13	771
B 0030151	10908	1	F		103	94	2	18	559
B 0030152	10910	1	F		62	99	3	40	257
	Mean				84.3	98.9	7.1	43.3	313.5
	S.D.				13.3	11.7	5	19	233.6
Group 1									
B 0030201	11040	12	F		88	103	3	58	240
B 0030202	11044	12	F		76	93	12	42	132
B 0030203	11045	12	F		84	111	14	50	171
B 0030204	11046	12	F		77	98	17	27	313
B 0030205	11047	12	F		75	119	13	53	127
B 0030206	11050	12	F		84	106	9	51	174
B 0030207	11051	12	F		55	104	7	33	153
B 0030208	11052	12	F		86	105	11	34	244
	Mean				78.1	104.9	10.8	43.5	194.3
	S.D.				10.5	7.8	4.4	11.2	65.2
Group 12									
Reference Range					48 - 96	74 - 319	0 - 0	0 - 0	3 - 104

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BUILDING A
HORSHAM, PA 19044-
(215) 443-8710

Date Collected:
Date Received: 12/08/2000
Date Reported: 01/16/2001

Client No. 1028 Study: 418018 DAMS GD21 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0030209	11053	13	F		64	78	9	43	158
B 0030210	11054	13	F		73	76	7	26	318
B 0030211	11056	13	F		83	79	15	44	152
B 0030212	11058	13	F		69	129	8	34	270
B 0030213	11060	13	F		70	103	9	59	79
B 0030214	11062	13	F		66	98	15	26	296
B 0030215	11063	13	F		75	103	11	45	216
B 0030216	11066	13	F		78	104	16	51	119
	Mean				72.3	96.3	11.3	41	201
	S.D.				6.3	18	3.6	11.7	87.5
Group 13									
B 0030153	10915	2	F		79	121	4	46	249
B 0030154	10916	2	F		76	108	6	62	85
B 0030155	10917	2	F		90	110	2	19	459
B 0030156	10918	2	F		88	111	10	55	203
B 0030157	10919	2	F		99	112	0	16	719
B 0030158	10920	2	F		83	121	1	35	337
B 0030159	10925	2	F		119	101	0	17	552
B 0030160	10928	2	F		106	84	0	9	1027
	Mean				92.5	108.5	2.9	32.4	453.9
	S.D.				14.6	11.9	3.6	20	307.8
Group 2									
Reference Range					48 - 96	74 - 319	0 - 0	0 - 0	3 - 104

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(215) 443-8710

Date Collected:
Date Received: 12/08/2000
Date Reported: 01/16/2001

Client No. 1028 Study: 418018 DAMS GD21 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0030161	10930	3	F		76	118	10	49	228
B 0030162	10931	3	F		75	102	11	47	221
B 0030163	10932	3	F		131	113	31	26	439
B 0030164	10933	3	F		85	107	15	33	226
B 0030165	10934	3	F		90	93	1	23	407
B 0030166	10935	3	F		117	137	14	49	279
B 0030167	10937	3	F		74	87	6	35	294
B 0030168	10940	3	F		80	108	6	19	353
	Mean				91	108.1	11.8	35.1	305.9
	S.D.				21.4	15.4	9	12.1	85.1
Group 3									
B 0030169	10945	4	F		134	86	0	11	887
B 0030170	10946	4	F		74	88	9	56	115
B 0030171	10947	4	F		94	125	10	48	197
B 0030172	10949	4	F		53	110	6	50	42
B 0030173	10950	4	F		84	108	17	56	113
B 0030174	10951	4	F		87	102	13	61	93
B 0030175	10953	4	F		100	107	12	59	259
B 0030176	10954	4	F		85	122	10	41	243
	Mean				88.9	106	9.6	47.8	243.6
	S.D.				23.1	14	5	16.2	270.8
Group 4									
Reference Range					48 - 96	74 - 319	0 - 0	0 - 0	3 - 104

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Date Received: 12/08/2000
Date Reported: 01/16/2001

Client No. 1028 Study: 418018 DAMS GD21 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0030177	10958	5	F		113	115	2	16	531
B 0030178	10959	5	F		114	91	9	16	583
B 0030179	10960	5	F		72	125	8	31	133
B 0030180	10961	5	F		68	99	11	33	213
B 0030181	10962	5	F		75	110	13	47	140
B 0030182	10963	5	F		75	58	10	36	220
B 0030183	10964	5	F		108	108	15	30	280
B 0030184	10965	5	F		92	97	0	15	690
	Mean				89.6	100.4	8.5	28	348.8
	S.D.				19.6	20.2	5.2	11.5	218.6
Group 5									
B 0030185	10972	6	F		82	90	14	33	122
B 0030186	10974	6	F		78	79	13	25	265
B 0030187	10975	6	F		77	140	4	54	161
B 0030188	10976	6	F		71	97	11	43	143
B 0030189	10978	6	F		76	103	9	44	175
B 0030190	10980	6	F		72	85	5	27	344
B 0030191	10981	6	F		77	96	9	37	214
B 0030192	10982	6	F		101	98	14	65	111
	Mean				79.3	98.5	9.9	41	191.9
	S.D.				9.4	18.5	3.9	13.6	79.3
Group 6									
Reference Range					48 - 96	74 - 319	0 - 0	0 - 0	3 - 104

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BUILDING A
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(215) 443-8710

Date Collected:
Date Received: 12/08/2000
Date Reported: 01/16/2001

Client No. 1028 Study: 418018 DAMS GD21 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0030193	10985	7	F		89	95	16	61	111
B 0030194	10987	7	F		79	109	7	61	95
B 0030195	10988	7	F		83	99	30	37	196
B 0030196	10989	7	F		81	145	12	69	48
B 0030197	10990	7	F		63	100	7	49	140
B 0030198	10991	7	F		72	109	10	34	294
B 0030199	10992	7	F		94	84	1	12	632
B 0030200	10993	7	F		62	110	13	50	91
	Mean				77.9	106.4	12	46.6	200.9
	S.D.				11.5	17.9	8.6	18.4	190.1

Group 7

Reference Range	48 - 96	74 - 319	0 - 0	0 - 0	3 - 104

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(215) 443-8710

Date Collected:
Date Received: 12/08/2000
Date Reported: 01/16/2001

Client No. 1028 Study: 418018 DAMS GD21 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	T4,TOTAL UG/DL	T3,TOTAL NG/DL	FREE T3 PG/ML	TSH NG/ML	FREE T4 NG/DL
B 0030145	10901	1	F		1.45	86.51	0.74	3.22	0.39
B 0030146	10902	1	F		0.54	76.54	0.76	2.09	0.39
B 0030147	10903	1	F		0.12	62.42	0.41	1.63	0.28
B 0030148	10904	1	F		0.76	66.55	0.51	1.32	0.35
B 0030149	10905	1	F		0.95	62.61	0.73	1.87	0.38
B 0030150	10907	1	F		0.65	116.76	0.77	2.14	0.22
B 0030151	10908	1	F		0.20	75.48	0.52	1.84	0.23
B 0030152	10910	1	F		0.00	44.96	0.19	0.41	0.15
	Mean				.584	73.979	.579	1.815	.299
	S.D.				.482	21.234	.209	.794	.092
Group 1									
B 0030201	11040	12	F		0.00	65.52	0.19	3.79	0.15
B 0030202	11044	12	F		0.00	43.96			0.06
B 0030203	11045	12	F		0.00	42.05	0.06	1.11	0.06
B 0030204	11046	12	F		0.00	44.97	0.24	2.43	0.04
B 0030205	11047	12	F		0.00	39.63	0.06	1.47	0.05
B 0030206	11050	12	F		0.00	51.85	0.10	1.20	0.05
B 0030207	11051	12	F		0.00	34.20	0.00	2.12	0.03
B 0030208	11052	12	F		0.00	57.84	0.33	4.30	0.09
	Mean				0	47.503	.14	2.346	.066
	S.D.				0	10.268	.117	1.263	.038
Group 12									
Reference Range					3 - 7	50 - 100	0 - 0	.57 - 3.41	1.9 - 2.5

ANALYTICS INCORPORATED
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Client: ARGUS RESEARCH LABORATORIES, INC.
905 SHEEHY DRIVE
BUILDING A
HORSHAM, PA 19044-
(215) 443-8710

Date Collected:
Date Received: 12/08/2000
Date Reported: 01/16/2001

Client No. 1028 Study: 418018 DAMS GD21 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	T4,TOTAL UG/DL	T3,TOTAL NG/DL	FREE T3 PG/ML	TSH NG/ML	FREE T4 NG/DL
B 0030209	11053	13	F		0.00	33.47	0.02	1.52	0.04
B 0030210	11054	13	F		0.00	54.87	0.32	2.07	0.05
B 0030211	11056	13	F		0.00	42.95	0.16	1.37	0.04
B 0030212	11058	13	F		0.00	52.33	0.40	3.21	0.08
B 0030213	11060	13	F		0.00	35.61	0.00	1.22	0.10
B 0030214	11062	13	F		0.00	36.45			0.03
B 0030215	11063	13	F		0.00	47.52	0.20	1.21	0.05
B 0030216	11066	13	F		0.00	36.32	0.00	0.00	0.05
	Mean				0	42.44	.157	1.514	.055
	S.D.				0	8.271	.161	.973	.023
Group 13									
B 0030153	10915	2	F		0.69	73.81	0.34	1.78	0.42
B 0030154	10916	2	F		0.22	56.28	0.26	2.75	0.28
B 0030155	10917	2	F		1.58	104.24			0.45
B 0030156	10918	2	F		0.14	66.85	0.42	2.03	0.29
B 0030157	10919	2	F		0.23	70.56	0.78	3.88	0.26
B 0030158	10920	2	F		0.27	80.36	0.76	4.12	0.26
B 0030159	10925	2	F		0.16	72.56	0.60	1.20	0.27
B 0030160	10928	2	F		0.02	63.91	0.44		0.14
	Mean				.414	73.571	.514	2.627	.296
	S.D.				.51	14.314	.203	1.177	.098
Group 2									
Reference Range					3 - 7	50 - 100	0 - 0	.57 - 3.41	1.9 - 2.5

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HORSHAM, PA 19044-
(215) 443-8710

Date Collected:
Date Received: 12/08/2000
Date Reported: 01/16/2001

Client No. 1028 Study: 418018 DAMS GD21 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	T4,TOTAL UG/DL	T3,TOTAL NG/DL	FREE T3 PG/ML	TSH NG/ML	FREE T4 NG/DL
B 0030161	10930	3	F		0.00	48.86	0.06		0.03
B 0030162	10931	3	F		0.00	44.68	0.38	1.96	0.05
B 0030163	10932	3	F		0.00	55.32	0.12	2.40	0.04
B 0030164	10933	3	F		0.02	59.16	0.43	2.12	0.14
B 0030165	10934	3	F		0.00	62.09	0.43	2.05	0.09
B 0030166	10935	3	F		0.00	62.03	0.44	1.58	0.12
B 0030167	10937	3	F		0.00	52.27	0.31	1.91	0.06
B 0030168	10940	3	F		0.00	47.93	0.33	1.20	0.02
	Mean				.003	54.043	.313	1.889	.069
	S.D.				.007	6.67	.146	.391	.044
Group 3									
B 0030169	10945	4	F		0.00	65.48	0.55	4.56	0.04
B 0030170	10946	4	F		0.00	41.50	0.07	2.05	0.03
B 0030171	10947	4	F		0.00	46.55	0.25	1.79	0.08
B 0030172	10949	4	F		0.00	38.85	0.12	1.78	0.10
B 0030173	10950	4	F		0.00	36.70	0.00	0.94	0.07
B 0030174	10951	4	F		0.00	50.05	0.15	3.16	0.14
B 0030175	10953	4	F		0.00	45.31	0.09	2.42	0.06
B 0030176	10954	4	F		0.00	46.82	0.24	2.30	0.06
	Mean				0	46.408	.184	2.375	.073
	S.D.				0	8.895	.17	1.086	.035
Group 4									
Reference Range					3 - 7	50 - 100	0 - 0	.57 - 3.41	1.9 - 2.5

ANILYTICS INCORPORATED
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Date Received: 12/08/2000
Date Reported: 01/16/2001

Client No. 1028 Study: 418018 DAMS GD21 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	T4,TOTAL UG/DL	T3,TOTAL NG/DL	FREE T3 PG/ML	TSH NG/ML	FREE T4 NG/DL
B 0030177	10958	5	F		1.29	91.13	0.85	3.72	0.30
B 0030178	10959	5	F		0.44	80.57	0.77	2.54	0.21
B 0030179	10960	5	F		0.00	27.60			
B 0030180	10961	5	F		1.27	81.69	0.86	2.64	0.36
B 0030181	10962	5	F		0.81	98.93	0.68	2.14	0.52
B 0030182	10963	5	F		0.12	86.18	0.63		0.16
B 0030183	10964	5	F		0.00	67.30	0.16	1.68	0.21
B 0030184	10965	5	F		0.39	81.80	0.91		0.21
	Mean				.54	76.9	.694	2.544	.281
	S.D.				.529	21.899	.256	.759	.125
Group 5									
B 0030185	10972	6	F		0.10	64.17	0.15	2.72	0.21
B 0030186	10974	6	F		0.00	49.59	0.26		0.04
B 0030187	10975	6	F		0.00	62.37	0.36		0.27
B 0030188	10976	6	F		0.00	61.84	0.27	0.94	0.17
B 0030189	10978	6	F		0.00	45.53	0.17	0.76	0.13
B 0030190	10980	6	F		0.00	41.40	0.30	1.28	0.02
B 0030191	10981	6	F		0.00	48.59	0.37	1.53	0.16
B 0030192	10982	6	F		0.00	42.76	0.00	1.48	0.07
	Mean				.013	52.031	.235	1.452	.134
	S.D.				.035	9.331	.123	.691	.086
Group 6									
Reference Range					3 - 7	50 - 100	0 - 0	.57 - 3.41	1.9 - 2.5

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Client: ARGUS RESEARCH LABORATORIES, INC.
905 SHEEHY DRIVE
BUILDING A
HORSHAM, PA 19044-
(215) 443-8710

Date Collected:
Date Received: 12/08/2000
Date Reported: 01/16/2001

Client No. 1028 Study: 418018 DAMS GD21 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	T4,TOTAL UG/DL	T3,TOTAL NG/DL	FREE T3 PG/ML	TSH NG/ML	FREE T4 NG/DL
B 0030193	10985	7	F		0.00	51.27	0.08	2.61	0.10
B 0030194	10987	7	F		0.00	51.82	0.16	1.74	0.14
B 0030195	10988	7	F		0.00	32.73	0.13	1.12	0.04
B 0030196	10989	7	F		0.00	59.37	0.29	1.02	0.29
B 0030197	10990	7	F		0.00	43.11	0.27	2.47	0.09
B 0030198	10991	7	F		0.00	44.67	0.08		0.04
B 0030199	10992	7	F		0.00	56.54	0.62		0.05
B 0030200	10993	7	F		0.00	52.65	0.34	3.12	0.13
	Mean				0	49.02	.246	2.013	.11
	S.D.				0	8.527	.18	.854	.082

Group 7

Reference Range	3 - 7	50 - 100	0 - 0	.57 - 3.41	1.9 - 2.5

Approved ---------- Date ---1/16/01

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Date Collected:
Date Received: 12/12/2000
Date Reported: 01/16/2001

Client No. 1028 Study: 418018 DAMS LD5 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0030547	10906	1	F		63	152	0	28	246
B 0030548	10909	1	F		84	155	2	54	141
B 0030549	10911	1	F		82	110	0	21	512
B 0030550	10913	1	F		57	146	4	45	88
B 0030551	10914	1	F		80	148	0	27	177
B 0030630	10912	1	F		81	192	1	66	147
	Mean				74.5	150.5	1.2	40.2	218.5
	S.D.				11.5	26.1	1.6	17.7	152.8
Group 1									
B 0030589	11019	10	F		72	159	5	57	96
B 0030590	11021	10	F		56	187	5	44	67
B 0030591	11020	10	F		74	154	1	32	259
B 0030592	11023	10	F		41	183	3	33	98
B 0030593	11024	10	F		51	170	4	46	45
B 0030594	11025	10	F		58	230	4	49	70
B 0030595	11026	10	F		56	181	5	46	60
B 0030596	11027	10	F		49	153	6	39	60
B 0030597	11028	10	F		52	165	0	36	178
	Mean				56.6	175.8	3.7	42.4	103.7
	S.D.				10.6	23.9	2	8.2	70.2
Group 10									
Reference Range					48 - 96	74 - 319	0 - 0	0 - 0	3 - 104

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Client No. 1028 Study: 418018 DAMS LD5 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0030598	11029	11	F		50	168	1	31	243
B 0030599	11031	11	F		58	172	4	46	115
B 0030600	11032	11	F		61	156	2	43	70
B 0030601	11033	11	F		53	174	4	40	87
B 0030602	11034	11	F		44	179	0	37	132
B 0030603	11035	11	F		44	183	0	31	186
B 0030604	11036	11	F		50	150	0	17	370
B 0030605	11037	11	F		58	150	0	36	195
B 0030606	11038	11	F		69	193	3	55	60
	Mean				54.1	169.4	1.6	37.3	162
	S.D.				8.2	15	1.7	10.7	99.4
Group 11									
B 0030607	11041	12	F		53	172	5	42	58
B 0030608	11049	12	F		38	195	6	37	39
B 0030622	11042	12	F		70	212	1	41	234
B 0030623	11048	12	F		80	175	8	61	87
	Mean				60.3	188.5	5	45.3	104.5
	S.D.				18.6	18.7	2.9	10.7	88.6
Group 12									
B 0030609	11059	13	F		49	158	2	42	104
	Mean				49	158	2	42	104
	S.D.				0	0	0	0	0
Group 13									
Reference Range					48 - 96	74 - 319	0 - 0	0 - 0	3 - 104

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Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0030552	10921	2	F		68	132	0	38	188
B 0030553	10922	2	F		49	171	0	30	202
B 0030554	10923	2	F		78	134	1	36	131
B 0030555	10924	2	F		70	144	11	47	52
B 0030556	10927	2	F		105	151	2	65	151
	Mean				74	146.4	2.8	43.2	144.8
	S.D.				20.3	15.8	4.7	13.6	59.1
Group 2									
B 0030557	10929	3	F		53	141	2	45	82
B 0030558	10938	3	F		51	149	2	37	96
B 0030559	10942	3	F		53	143	0	40	165
B 0030610	10941	3	F		44	161	3	34	90
	Mean				50.3	148.5	1.8	39	108.3
	S.D.				4.3	9	1.3	4.7	38.3
Group 3									
B 0030611	10943	4	F		69	184	3	48	93
B 0030612	10948	4	F		56	179	0	46	192
B 0030613	10952	4	F		77	194	4	54	107
B 0030614	10955	4	F		66	138	3	50	141
B 0030615	10956	4	F		76	235	6	65	87
Reference Range					48 - 96	74 - 319	0 - 0	0 - 0	3 - 104

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Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0030629	10944	4	F		65	158	13	48	43
	Mean				68.2	181.3	4.8	51.8	110.5
	S.D.				7.8	33.1	4.4	7	51
Group 4									
B 0030560	10957	5	F		59	152	1	27	230
B 0030561	10966	5	F		74	123	0	51	159
B 0030562	10967	5	F		66	163	6	45	49
B 0030563	10968	5	F		72	144	0	32	252
B 0030564	10969	5	F		72	161	2	45	143
B 0030565	10970	5	F		54	136	0	19	288
	Mean				66.2	146.5	1.5	36.5	186.8
	S.D.				8.1	15.4	2.3	12.4	87.2
Group 5									
B 0030566	10977	6	F		44	135	0	33	135
B 0030567	10979	6	F		45	142	3	34	102
B 0030568	10983	6	F		57	152	3	45	62
B 0030616	10971	6	F		81	176	12	53	96
B 0030617	10973	6	F		45	163	6	38	42
B 0030618	10984	6	F		69	209	3	57	84
	Mean				56.8	162.8	4.5	43.3	86.8
	S.D.				15.3	26.9	4.1	10.1	32.5
Group 6									
Reference Range					48 - 96	74 - 319	0 - 0	0 - 0	3 - 104

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Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0030569	10995	7	F		41	192	4	33	78
B 0030570	10997	7	F		40	196	3	35	75
B 0030619	10986	7	F		77	176	9	59	72
B 0030620	10994	7	F		47	158	6	41	50
B 0030621	10996	7	F		68	147	3	54	116
	Mean				54.6	173.8	5	44.4	78.2
	S.D.				16.9	21.2	2.5	11.6	23.8
Group 7									
B 0030571	10999	8	F		77	127	1	52	240
B 0030572	11000	8	F		57	164	6	46	64
B 0030573	11001	8	F		51	216	2	35	119
B 0030574	11002	8	F		56	146	3	32	147
B 0030575	11003	8	F		69	153	1	32	286
B 0030576	11004	8	F		53	168	2	45	79
B 0030577	11005	8	F		64	150	0	32	260
B 0030578	11006	8	F		70	185	1	38	154
B 0030579	11007	8	F		56	133	0	37	243
B 0030580	11008	8	F		61	147	2	38	153
B 0030624	11055	8	F		58	188	7	48	48
B 0030625	11057	8	F		63	156	7	46	67
B 0030626	11061	8	F		74	277	5	70	89
B 0030627	11064	8	F		72	193	6	64	72
B 0030628	11065	8	F		61	157	3	52	90
	Mean				62.8	170.7	3.1	44.5	140.7
	S.D.				8	37.8	2.5	11.5	80.3
Group 8									
Reference Range					48 - 96	74 - 319	0 - 0	0 - 0	3 - 104

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Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0030581	11009	9	F		50	158	4	32	116
B 0030582	11010	9	F		56	135	0	43	167
B 0030583	11011	9	F		51	144	1	33	164
B 0030584	11012	9	F		74	144	6	42	100
B 0030585	11013	9	F		58	148	0	24	324
B 0030586	11015	9	F		47	179	1	35	195
B 0030587	11016	9	F		45	150	4	35	89
B 0030588	11018	9	F		63	183	4	52	85
	Mean				55.5	155.1	2.5	37	155
	S.D.				9.5	17.3	2.3	8.5	79.5

Group 9

Reference Range	48 - 96	74 - 319	0 - 0	0 - 0	3 - 104

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Accession No.	Spec. ID	Gp	Sex	Age	T4,TOTAL UG/DL	T3,TOTAL NG/DL	FREE T3 PG/ML	TSH NG/ML	FREE T4 NG/DL
B 0030547	10906	1	F		1.66	100.60	1.14	1.18	0.88
B 0030548	10909	1	F		2.25	99.04	0.97	3.92	0.84
B 0030549	10911	1	F		2.63	102.40	0.75	1.26	1.08
B 0030550	10913	1	F		1.71	80.08	0.90		0.57
B 0030551	10914	1	F		0.87	94.35	0.72	0.00	0.65
B 0030630	10912	1	F		2.44	91.84	0.97	1.66	0.82
	Mean				1.927	94.718	.908	1.604	.807
	S.D.				.648	8.185	.156	1.435	.18
Group 1									
B 0030589	11019	10	F		0.88	79.66	0.86		0.31
B 0030590	11021	10	F		1.15	77.77	0.85	1.22	0.47
B 0030591	11020	10	F		1.02	77.15	0.44	0.92	0.32
B 0030592	11023	10	F		0.71	50.76	0.27	2.22	0.21
B 0030593	11024	10	F		0.57	59.72	0.71	0.96	0.25
B 0030594	11025	10	F		0.45	65.05	0.31	0.80	0.35
B 0030595	11026	10	F		0.60	45.51	0.35	0.94	0.19
B 0030596	11027	10	F		0.70	49.83	0.49	0.46	0.19
B 0030597	11028	10	F		0.47	55.68	0.69	1.36	0.20
	Mean				.728	62.348	.552	1.11	.277
	S.D.				.243	13.181	.23	.523	.095
Group 10									
Reference Range					3 - 7	50 - 100	0 - 0	.57 - 3.41	1.9 - 2.5

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Accession No.	Spec. ID	Gp	Sex	Age	T4,TOTAL UG/DL	T3,TOTAL NG/DL	FREE T3 PG/ML	TSH NG/ML	FREE T4 NG/DL
B 0030598	11029	11	F		0.87	61.61	0.62	1.46	0.36
B 0030599	11031	11	F		0.00	44.85	0.00	1.56	0.08
B 0030600	11032	11	F		0.52	73.96	0.86	0.60	0.26
B 0030601	11033	11	F		0.42	58.43	0.61	1.76	0.18
B 0030602	11034	11	F		0.89	73.76	0.87	2.53	0.67
B 0030603	11035	11	F		0.35	53.37	0.55	0.50	0.23
B 0030604	11036	11	F		0.00	57.45	0.52		0.23
B 0030605	11037	11	F		0.26	61.84	0.45	0.82	0.18
B 0030606	11038	11	F		0.90	85.82	0.69	0.00	0.33
	Mean				.468	63.454	.574	1.154	.28
	S.D.				.358	12.409	.259	.819	.168
Group 11									
B 0030607	11041	12	F		0.14	67.01	0.49	1.49	0.22
B 0030608	11049	12	F		0.60	53.37	0.33	1.96	0.29
B 0030622	11042	12	F		0.46	100.62	0.72	1.16	0.32
B 0030623	11048	12	F		0.27	73.23	0.43	1.31	0.26
	Mean				.368	73.558	.493	1.48	.273
	S.D.				.203	19.857	.165	.347	.043
Group 12									
B 0030609	11059	13	F		0.24	48.45	0.16	0.97	0.15
	Mean				.24	48.45	.16	.97	.15
	S.D.				0	0	0	0	0
Group 13									
Reference Range					3 - 7	50 - 100	0 - 0	.57 - 3.41	1.9 - 2.5

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Accession No.	Spec. ID	Gp	Sex	Age	T4,TOTAL UG/DL	T3,TOTAL NG/DL	FREE T3 PG/ML	TSH NG/ML	FREE T4 NG/DL
B 0030552	10921	2	F		4.22	81.28	0.83	1.04	1.21
B 0030553	10922	2	F		2.31	88.13	0.72	4.41	0.74
B 0030554	10923	2	F		2.89	95.06	0.79	0.96	1.02
B 0030555	10924	2	F		1.24	63.21	0.48	0.48	0.57
B 0030556	10927	2	F		2.38	116.64	1.29	2.92	0.93
	Mean				2.608	88.864	.822	1.962	.894
	S.D.				1.083	19.533	.295	1.655	.248
Group 2									
B 0030557	10929	3	F		0.08	68.57	0.65	1.12	0.30
B 0030558	10938	3	F		0.00	56.59	0.53	0.43	0.17
B 0030559	10942	3	F		0.11	70.90	0.81	2.78	0.30
B 0030610	10941	3	F		0.54	66.95	0.79	0.58	0.31
	Mean				.183	65.753	.695	1.228	.27
	S.D.				.243	6.32	.131	1.077	.067
Group 3									
B 0030611	10943	4	F		0.24	67.82			
B 0030612	10948	4	F		0.32	74.34	0.82	0.84	0.35
B 0030613	10952	4	F		0.77	94.97	0.75	1.42	0.21
B 0030614	10955	4	F		0.23	81.22	0.58	2.02	0.16
B 0030615	10956	4	F		0.39	73.68	0.74	2.15	0.22
Reference Range					3 - 7	50 - 100	0 - 0	.57 - 3.41	1.9 - 2.5

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B 0030629	10944	4	F		0.04	64.92	0.30	0.40	0.17
	Mean				.332	76.158	.638	1.366	.222
	S.D.				.245	10.815	.208	.751	.076
Group 4									
B 0030560	10957	5	F		2.80	108.48	1.00	0.52	0.87
B 0030561	10966	5	F		3.23	87.83	0.79	1.50	1.51
B 0030562	10967	5	F		1.51	94.97	1.04	1.15	0.78
B 0030563	10968	5	F		1.69	104.99	1.02	0.55	0.70
B 0030564	10969	5	F		1.35	84.75	0.69	0.44	0.89
B 0030565	10970	5	F		1.94	69.56	0.78	0.70	0.81
	Mean				2.087	91.763	.887	.81	.927
	S.D.				.758	14.299	.151	.422	.294
Group 5									
B 0030566	10977	6	F		0.00	50.71	0.36	0.62	0.21
B 0030567	10979	6	F		0.00	55.20	0.48	1.16	0.27
B 0030568	10983	6	F		0.00	75.66			0.25
B 0030616	10971	6	F		0.53	65.47	0.39	0.68	0.30
B 0030617	10973	6	F		0.45	64.98	0.60	2.02	0.32
B 0030618	10984	6	F		0.65	79.39	0.72	1.92	0.28
	Mean				.272	65.235	.51	1.28	.272
	S.D.				.304	11.143	.15	.665	.039
Group 6									
Reference Range					3 - 7	50 - 100	0 - 0	.57 - 3.41	1.9 - 2.5

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Client: ARGUS RESEARCH LABORATORIES, INC.
905 SHEEHY DRIVE
BUILDING A
HORSHAM, PA 19044-
(215) 443-8710

Date Collected:
Date Received: 12/12/2000
Date Reported: 01/16/2001

Client No. 1028 Study: 418018 DAMS LD5 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	T4,TOTAL UG/DL	T3,TOTAL NG/DL	FREE T3 PG/ML	TSH NG/ML	FREE T4 NG/DL
B 0030569	10995	7	F		0.00	54.80	0.33	1.32	0.19
B 0030570	10997	7	F		0.00	40.79	0.25	0.74	0.14
B 0030619	10986	7	F		0.43	78.34	0.94	3.12	0.31
B 0030620	10994	7	F		0.24	67.17	0.85	3.12	0.30
B 0030621	10996	7	F		0.00	87.47	0.64	1.12	0.27
	Mean				.134	65.714	.602	1.884	.242
	S.D.				.195	18.542	.306	1.147	.074
Group 7									
B 0030571	10999	8	F		1.05	81.63	0.79		0.47
B 0030572	11000	8	F		1.14	76.76	0.78	1.54	0.50
B 0030573	11001	8	F		0.61	51.06	0.40	1.00	0.41
B 0030574	11002	8	F		0.65	64.38	0.86	1.35	0.64
B 0030575	11003	8	F		0.43	80.94	1.15	0.92	0.30
B 0030576	11004	8	F		1.48	88.66	0.84	1.36	0.60
B 0030577	11005	8	F		1.12	81.56	0.56	1.02	0.55
B 0030578	11006	8	F		1.03	86.75	0.78	1.06	0.44
B 0030579	11007	8	F		0.38	56.62	0.39	1.15	0.40
B 0030580	11008	8	F		0.19	60.76	0.43	0.88	0.31
B 0030624	11055	8	F		0.23	61.96	0.76	3.48	0.25
B 0030625	11057	8	F		0.00	72.68			
B 0030626	11061	8	F		0.33	76.74	0.64	0.82	0.17
B 0030627	11064	8	F		0.26	66.25	0.50	1.79	0.26
B 0030628	11065	8	F		0.60	83.98	0.41	2.14	0.16
	Mean				.633	72.715	.664	1.424	.39
	S.D.				.434	11.753	.225	.728	.153
Group 8									
Reference Range					3 - 7	50 - 100	0 - 0	.57 - 3.41	1.9 - 2.5

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BUILDING A
HORSHAM, PA 19044-
(215) 443-8710

Date Collected:
Date Received: 12/12/2000
Date Reported: 01/16/2001

Client No. 1028 Study: 418018 DAMS LD5 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	T4,TOTAL UG/DL	T3,TOTAL NG/DL	FREE T3 PG/ML	TSH NG/ML	FREE T4 NG/DL
3 0030581	11009	9	F		0.00	57.68	0.44	2.23	0.22
3 0030582	11010	9	F		0.34	60.23	0.55		0.28
3 0030583	11011	9	F		1.21	59.71	0.70	1.30	0.26
3 0030584	11012	9	F		0.14	55.40	0.40	0.04	0.21
3 0030585	11013	9	F		0.71	73.47	0.85	0.63	0.26
3 0030586	11015	9	F		1.00	71.68	0.70	2.18	0.34
3 0030587	11016	9	F		0.98	68.23	0.49	1.16	0.39
3 0030588	11018	9	F		0.39	63.84	0.57	2.52	0.27
	Mean				.596	63.78	.588	1.437	.279
	S.D.				.443	6.684	.152	.918	.06

Group 9

Reference Range					
	3 - 7	50 - 100	0 - 0	.57 - 3.41	1.9 - 2.5

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Date Collected:
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Client No. 1028 Study: 418018 LD5 MILK Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL
B 0031037	10906	1	F		26
B 0031038	10909	1	F		10
B 0031039	10911	1	F		27
B 0031040	10913	1	F		10
B 0031041	10914	1	F		11
	Mean				16.8
	S.D.				8.9

Group 1

B 0031079	11019	10	F		17
B 0031080	11021	10	F		0
B 0031081	11020	10	F		2
B 0031082	11023	10	F		38
B 0031083	11024	10	F		0
B 0031084	11025	10	F		0
B 0031085	11026	10	F		41
B 0031086	11027	10	F		17
B 0031087	11028	10	F		23
	Mean				15.3
	S.D.				16.3

Group 10

Reference Range 48 - 96

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Client No. 1028 Study: 418018 LD5 MILK Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL
B 0031088	11029	11	F		18
B 0031089	11031	11	F		0
B 0031090	11032	11	F		0
B 0031091	11033	11	F		10
B 0031092	11034	11	F		15
B 0031093	11035	11	F		19
B 0031094	11036	11	F		14
B 0031095	11037	11	F		0
B 0031096	11038	11	F		3
	Mean				8.8
	S.D.				8.1
Group 11					
B 0031097	11041	12	F		34
B 0031098	11049	12	F		0
	Mean				17
	S.D.				24
Group 12					
B 0031099	11059	13	F		0
	Mean				0
	S.D.				0
Group 13					
Reference Range					48 - 96

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Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL
B 0031042	10921	2	F		0
B 0031043	10922	2	F		4
B 0031044	10923	2	F		5
B 0031045	10924	2	F		31
B 0031046	10927	2	F		0
	Mean				8
	S.D.				13.1
Group 2					
B 0031047	10929	3	F		9
B 0031048	10938	3	F		10
B 0031049	10942	3	F		0
	Mean				6.3
	S.D.				5.5
Group 3					
B 0031050	10957	5	F		7
B 0031051	10966	5	F		0
B 0031052	10967	5	F		9
B 0031053	10968	5	F		20
B 0031054	10969	5	F		10
B 0031055	10970	5	F		23
	Mean				11.5
	S.D.				8.5
Group 5					
Reference Range					48 - 96

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Client No. 1028 Study: 418018 LD5 MILK Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL
B 0031056	10977	6	F		0
B 0031057	10979	6	F		6
B 0031058	10983	6	F		7
	Mean				4.3
	S.D.				3.8
Group 6					
B 0031059	10995	7	F		47
B 0031060	10997	7	F		61
	Mean				54
	S.D.				9.9
Group 7					
B 0031061	10999	8	F		12
B 0031062	11000	8	F		18
B 0031063	11001	8	F		41
B 0031064	11002	8	F		18
B 0031065	11003	8	F		22
B 0031066	11004	8	F		25
B 0031067	11005	8	F		9
B 0031068	11006	8	F		19
B 0031069	11007	8	F		3
Reference Range					48 - 96

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Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL
B 0031070	11008	8	F		17
	Mean				18.4
	S.D.				10.2
Group 8					
B 0031071	11009	9	F		110
B 0031072	11010	9	F		22
B 0031073	11011	9	F		4
B 0031074	11012	9	F		2
B 0031075	11013	9	F		12
B 0031076	11015	9	F		19
B 0031077	11016	9	F		15
B 0031078	11018	9	F		1
	Mean				23.1
	S.D.				36
Group 9					
Reference Range					48 - 96

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Page 5 of 5
Date ----4/25/01

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Date Collected:
Date Received: 12/08/2000
Date Reported: 01/16/2001

Client No. 1028 Study: 418018 PUPS GD21 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0030217	10901	1			40	69	15	12	28
B 0030218	10902	1			55	55	34	14	31
B 0030219	10903	1			58	70	35	15	34
B 0030220	10904	1			60	56	35	13	41
B 0030221	10905	1			49	69	25	12	39
B 0030222	10907	1			43	61	17	11	39
B 0030223	10908	1			58	64	32	16	36
B 0030224	10910	1			43	66	25	11	27
	Mean				50.8	63.8	27.3	13	34.4
	S.D.				8	5.9	8	1.9	5.3
Group 1									
B 0030273	11040	12			57	61	41	16	19
B 0030274	11044	12			51	74	38	12	26
B 0030275	11045	12			65	82	44	14	38
B 0030276	11046	12			60	78	37	13	36
B 0030277	11047	12			73	59	52	15	38
B 0030278	11050	12			63	79	51	16	21
B 0030279	11051	12			50	96	39	14	25
B 0030280	11052	12			71	80	57	16	20
	Mean				61.3	76.1	44.9	14.5	27.9
	S.D.				8.5	11.8	7.5	1.5	8.2
Group 12									
Reference Range					48 - 96	74 - 319	0 - 0	0 - 0	3 - 125

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Date Collected:
Date Received: 12/08/2000
Date Reported: 01/16/2001

Client No. 1028 Study: 418018 PUPS GD21 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0030281	11053	13			58	70	39	14	37
B 0030282	11054	13			62	51	37	12	44
B 0030283	11056	13			66	51	54	14	21
B 0030284	11058	13			49	84	38	14	21
B 0030285	11060	13			60	75	45	15	19
B 0030286	11062	13			56	82	36	13	33
B 0030287	11063	13			65	88	51	16	17
B 0030288	11066	13			76	90	63	14	24
	Mean				61.5	73.9	45.4	14	27
	S.D.				8	15.5	9.8	1.2	9.8

Group 13

B 0030225	10915	2			49	91	28	15	22
B 0030226	10916	2			57	71	35	14	33
B 0030227	10917	2			54	71	25	14	42
B 0030228	10918	2			53	62	30	14	38
B 0030229	10919	2			42	63	21	12	27
B 0030230	10920	2			59	51	36	13	48
B 0030231	10925	2			58	57	34	16	37
B 0030232	10928	2			53	41	26	13	44
	Mean				53.1	63.4	29.4	13.9	36.4
	S.D.				5.5	15	5.3	1.2	8.7

Group 2

Reference Range					48 - 96	74 - 319	0 - 0	0 - 0	3 - 125

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HORSHAM, PA 19044-
(215) 443-8710

Date Collected:
Date Received: 12/08/2000
Date Reported: 01/16/2001

Client No. 1028 Study: 418018 PUPS GD21 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0030233	10930	3			71	69	48	17	31
B 0030234	10931	3			66	66	49	16	27
B 0030235	10932	3			64	76	48	16	26
B 0030236	10933	3			58	79	44	14	25
B 0030237	10934	3			100	62	67	23	47
B 0030238	10935	3			63	70	46	15	32
B 0030239	10937	3			63	62	41	13	36
B 0030240	10940	3			61	73	43	15	30
	Mean				68.3	69.6	48.3	16.1	31.8
	S.D.				13.4	6.2	8.1	3	7.1
Group 3									
B 0030241	10945	4			65	61	45	13	31
B 0030242	10946	4			72	74	55	17	29
B 0030243	10947	4			65	80	50	16	14
B 0030244	10949	4			42	56	32	12	25
B 0030245	10950	4			49	80	35	16	12
B 0030246	10951	4			71	70	48	16	35
B 0030247	10953	4			76	95	60	17	27
B 0030248	10954	4			65	80	50	17	28
	Mean				63.1	74.5	46.9	15.5	25.1
	S.D.				11.7	12.3	9.4	1.9	8.1
Group 4									
Reference Range					48 - 96	74 - 319	0 - 0	0 - 0	3 - 125

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Client No. 1028 Study: 418018 PUPS GD21 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0030249	10958	5			54	62	30	13	34
B 0030250	10959	5			40	65	18	13	39
B 0030251	10960	5			44	81	20	11	35
B 0030252	10961	5			41	68	21	12	27
B 0030253	10962	5			45	78	29	12	21
B 0030254	10963	5			47	71	29	14	25
B 0030255	10964	5			44	78	27	12	29
B 0030256	10965	5			46	60	19	12	44
	Mean				45.1	70.4	24.1	12.4	31.8
	S.D.				4.3	7.9	5.1	.9	7.6
Group 5									
B 0030257	10972	6			45	99	39	14	10
B 0030258	10974	6			64	57	46	16	26
B 0030259	10975	6			82	50	49	14	55
B 0030260	10976	6			59	99	44	16	26
B 0030261	10978	6			47	81	36	14	16
B 0030262	10980	6			54	58	39	11	29
B 0030263	10981	6			66	92	51	15	25
B 0030264	10982	6			56	83	47	15	16
	Mean				59.1	77.4	43.9	14.4	25.4
	S.D.				11.8	19.8	5.4	1.6	13.6
Group 6									
Reference Range					48 - 96	74 - 319	0 - 0	0 - 0	3 - 125

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Client No. 1028 Study: 418018 PUPS GD21 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0030265	10985	7			64	90	47	16	28
B 0030266	10987	7			85	77	62	17	32
B 0030267	10988	7			67	74	49	12	37
B 0030268	10989	7			59	69	45	15	25
B 0030269	10990	7			65	65	45	15	29
B 0030270	10991	7			49	69	35	13	20
B 0030271	10992	7			65	58	43	14	36
B 0030272	10993	7			58	60	39	13	33
	Mean				64	70.3	45.6	14.4	30
	S.D.				10.3	10.3	8	1.7	5.7

Group 7

Reference Range	48 - 96	74 - 319	0 - 0	0 - 0	3 - 125

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Accession No.	Spec. ID	Gp	Sex	Age	T4,TOTAL UG/DL	T3,TOTAL NG/DL	FREE T3 PG/ML	TSH NG/ML	FREE T4 NG/DL
B 0030217	10901	1			0.00	0.00			
B 0030218	10902	1			0.00				
B 0030219	10903	1			0.00	0.00			
B 0030220	10904	1							
B 0030221	10905	1			0.00				
B 0030222	10907	1			0.00				
B 0030223	10908	1			0.00	0.00			
B 0030224	10910	1			0.00	1.69			0.05
	Mean				0	.423			.05
	S.D.				0	.845			0
Group 1									
B 0030273	11040	12			0.00	0.00			
B 0030274	11044	12			0.00	0.00			
B 0030275	11045	12			0.00	0.00	0.00		0.00
B 0030276	11046	12			0.00	0.00			0.00
B 0030277	11047	12			0.00	0.00			
B 0030278	11050	12			0.00	0.00			
B 0030279	11051	12			0.00	0.00			
B 0030280	11052	12			0.00	0.00			0.00
	Mean				0	0	0		0
	S.D.				0	0	0		0
Group 12									
Reference Range					3 - 7	50 - 100	0 - 0	.57 - 3.41	1.9 - 2.5

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Client: ARGUS RESEARCH LABORATORIES, INC.
905 SHEEHY DRIVE
BUILDING A
HORSHAM, PA 19044-
(215) 443-8710

Date Collected:
Date Received: 12/08/2000
Date Reported: 01/16/2001

Client No. 1028 Study: 418018 PUPS GD21 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	T4,TOTAL UG/DL	T3,TOTAL NG/DL	FREE T3 PG/ML	TSH NG/ML	FREE T4 NG/DL
B 0030281	11053	13			0.00	1.16			0.00
B 0030282	11054	13			0.00				0.00
B 0030283	11056	13			0.00			1.16	
B 0030284	11058	13			0.00	1.59			0.00
B 0030285	11060	13			0.00	0.00			0.00
B 0030286	11062	13			0.00	2.80			0.00
B 0030287	11063	13			0.00	0.00			
B 0030288	11066	13			0.00	0.00			
	Mean				0	.925		1.16	0
	S.D.				0	1.147		0	0
Group 13									
B 0030225	10915	2			0.00	8.43			0.07
B 0030226	10916	2			0.00	0.00			
B 0030227	10917	2			0.00	0.00			
B 0030228	10918	2			0.00				
B 0030229	10919	2			0.00				
B 0030230	10920	2							
B 0030231	10925	2			0.00				
B 0030232	10928	2			0.00				
	Mean				0	2.81			.07
	S.D.				0	4.867			0
Group 2									
Reference Range					3 - 7	50 - 100	0 - 0	.57 - 3.41	1.9 - 2.5

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BUILDING A
HORSHAM, PA 19044-
(215) 443-8710

Date Collected:
Date Received: 12/08/2000
Date Reported: 01/16/2001

Client No. 1028 Study: 418018 PUPS GD21 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	T4,TOTAL UG/DL	T3,TOTAL NG/DL	FREE T3 PG/ML	TSH NG/ML	FREE T4 NG/DL
B 0030233	10930	3			0.00	0.00			
B 0030234	10931	3			0.00	0.00			
B 0030235	10932	3			0.00	2.19	0.00		
B 0030236	10933	3			0.00	0.00			
B 0030237	10934	3			0.00				
B 0030238	10935	3			0.00	2.70			0.00
B 0030239	10937	3			0.00	0.00			0.00
B 0030240	10940	3			0.00	2.78			
	Mean				0	1.096	0		0
	S.D.				0	1.379	0		0
Group 3									
B 0030241	10945	4			0.00	0.00	0.00		0.00
B 0030242	10946	4			0.00	5.10	0.00		0.00
B 0030243	10947	4			0.00				
B 0030244	10949	4			0.00				
B 0030245	10950	4			0.00	1.33			
B 0030246	10951	4			0.00	6.68			
B 0030247	10953	4			0.00	0.38			0.00
B 0030248	10954	4			0.00	4.08			0.00
	Mean				0	2.928	0		0
	S.D.				0	2.747	0		0
Group 4									
Reference Range					3 - 7	50 - 100	0 - 0	.57 - 3.41	1.9 - 2.5

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BUILDING A
HORSHAM, PA 19044-
(215) 443-8710

Date Collected:
Date Received: 12/08/2000
Date Reported: 01/16/2001

Client No. 1028 Study: 418018 PUPS GD21 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	T4,TOTAL UG/DL	T3,TOTAL NG/DL	FREE T3 PG/ML	TSH NG/ML	FREE T4 NG/DL
B 0030249	10958	5			0.00	0.00			
B 0030250	10959	5			0.00				
B 0030251	10960	5			0.00				
B 0030252	10961	5			0.00	2.96	0.00		0.05
B 0030253	10962	5			0.00	0.00			
B 0030254	10963	5			0.00	1.89			0.04
B 0030255	10964	5			0.00	0.00	0.00		0.02
B 0030256	10965	5			0.00	2.01			
	Mean				0	1.143	0		.037
	S.D.				0	1.306	0		.015
Group 5									
B 0030257	10972	6			0.00	0.00			
B 0030258	10974	6			0.00	3.20	0.00		0.00
B 0030259	10975	6						0.04	
B 0030260	10976	6			0.00				
B 0030261	10978	6			0.00	0.00			
B 0030262	10980	6			0.00				0.00
B 0030263	10981	6			0.00	0.60			0.00
B 0030264	10982	6			0.00	0.00	0.00		0.00
	Mean				0	.76	0	.04	0
	S.D.				0	1.389	0	0	0
Group 6									
Reference Range					3 - 7	50 - 100	0 - 0	.57 - 3.41	1.9 - 2.5

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Date Reported: 01/16/2001

Client No. 1028 Study: 418018 PUPS GD21 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	T4,TOTAL UG/DL	T3,TOTAL NG/DL	FREE T3 PG/ML	TSH NG/ML	FREE T4 NG/DL
B 0030265	10985	7			0.00	1.96			
B 0030266	10987	7			0.00				
B 0030267	10988	7			0.00	0.00	0.00		0.00
B 0030268	10989	7							
B 0030269	10990	7			0.00				
B 0030270	10991	7			0.00	0.00			0.00
B 0030271	10992	7							
B 0030272	10993	7			0.00				
	Mean				0	.653	0		0
	S.D.				0	1.132	0		0
Group 7									
Reference Range					3 - 7	50 - 100	0 - 0	.57 - 3.41	1.9 - 2.5

Approved ---------- Date ----1/16/01

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Date Reported: 01/16/2001

Client No. 1028 Study: 418018 PUPS LD5 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0030631	10906	1			92	292	25	26	203
B 0030632	10909	1			117	229	35	38	243
B 0030633	10911	1			108	188	22	25	213
B 0030634	10913	1			104	276	22	28	153
B 0030635	10914	1			120	250	29	18	235
	Mean				108.2	247	26.6	27	209.4
	S.D.				11.1	40.9	5.5	7.2	35.4
Group 1									
B 0030673	11019	10			118	217	26	35	229
B 0030674	11021	10			99	154	26	32	173
B 0030675	11020	10			107	206	25	33	218
B 0030676	11023	10			133	222	29	28	265
B 0030677	11024	10			145	282	39	36	216
B 0030678	11025	10			102	154	26	39	184
B 0030679	11026	10			137	197	27	31	270
B 0030680	11027	10			79	170	22	40	84
B 0030681	11028	10			110	176	24	38	100
	Mean				114.4	197.6	27.1	34.7	193.2
	S.D.				21	40.6	4.9	4	65.7
Group 10									
Reference Range					48 - 96	74 - 319	0 - 0	0 - 0	3 - 125

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Date Reported: 01/16/2001

Client No. 1028 Study: 418018 PUPS LD5 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0030682	11029	11			131	348	32	26	359
B 0030683	11031	11			108	259	32	39	133
B 0030684	11032	11			126	202	33	24	254
B 0030685	11033	11			120	175	21	26	417
B 0030686	11034	11			131	153	26	26	211
B 0030687	11035	11			198	301	80	39	222
B 0030688	11036	11			100	179	30	39	136
B 0030689	11037	11			135	166	17	28	188
B 0030690	11038	11			107	261	32	31	158
	Mean				128.4	227.1	33.7	30.9	230.9
	S.D.				28.8	68.1	18.3	6.4	98.6
Group 11									
B 0030691	11049	12			192	245	77	40	212
	Mean				192	245	77	40	212
	S.D.				0	0	0	0	0
Group 12									
B 0030692	11059	13			110	249	23	32	149
	Mean				110	249	23	32	149
	S.D.				0	0	0	0	0
Group 13									
Reference Range					48 - 96	74 - 319	0 - 0	0 - 0	3 - 125

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Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0030636	10921	2			128	237	31	33	246
B 0030637	10922	2			128	153	28	30	311
B 0030638	10923	2			118	179	47	35	106
B 0030639	10924	2			119	99	38	50	71
B 0030640	10927	2			107	323	27	21	193
	Mean				120	198.2	34.2	33.8	185.4
	S.D.				8.7	85.6	8.3	10.5	98.6
Group 2									
B 0030641	10929	3			148	203	47	42	232
B 0030642	10938	3			202	267	80	30	371
B 0030643	10942	3			151	394	29	30	333
	Mean				167	288	52	34	312
	S.D.				30.3	97.2	25.9	6.9	71.8
Group 3									
B 0030644	10957	5			125	277	23	28	215
B 0030645	10966	5			130	382	20	20	789
B 0030646	10967	5			112	155	22	21	149
B 0030647	10968	5			117	289	28	30	285
B 0030648	10969	5			124	262	20	30	139
B 0030649	10970	5			104	244	1	19	681
	Mean				118.7	268.2	19	24.7	376.3
	S.D.				9.6	73.3	9.3	5.2	284.8
Group 5									
Reference Range					48 - 96	74 - 319	0 - 0	0 - 0	3 - 125

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HORSHAM, PA 19044-
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Date Collected:
Date Received: 12/12/2000
Date Reported: 01/16/2001

Client No. 1028 Study: 418018 PUPS LD5 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0030650	10977	6			173	275	66	41	354
B 0030651	10979	6			118	181	36	44	134
B 0030652	10983	6			128	311	30	34	281
	Mean				139.7	255.7	44	39.7	256.3
	S.D.				29.3	67.1	19.3	5.1	112.1
Group 6									
B 0030653	10995	7			181	204	93	63	99
B 0030654	10997	7			121	216	37	50	85
	Mean				151	210	65	56.5	92
	S.D.				42.4	8.5	39.6	9.2	9.9
Group 7									
B 0030655	10999	8			114	319	17	25	366
B 0030656	11000	8			109	290	21	26	342
B 0030657	11001	8			101	177	30	50	100
B 0030658	11002	8			123	375	20	21	444
B 0030659	11003	8			139	190	37	31	269
B 0030660	11004	8			121	240	26	28	230
B 0030661	11005	8			118	228	30	34	235
B 0030662	11006	8			104	190	31	39	127
B 0030663	11007	8			98	174	28	40	124
Reference Range					48 - 96	74 - 319	0 - 0	0 - 0	3 - 125

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Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0030664	11008	8			122	227	37	35	142
	Mean				114.9	241	27.7	32.9	237.9
	S.D.				12.4	67.2	6.8	8.6	117.5
Group 8									
B 0030665	11009	9			131	229	50	65	42
B 0030666	11010	9			125	272	25	25	272
B 0030667	11011	9			106	168	24	36	155
B 0030668	11012	9			113	117	33	44	160
B 0030669	11013	9			102	225	19	29	188
B 0030670	11015	9			132	239	32	27	195
B 0030671	11016	9			125	186	35	37	146
B 0030672	11018	9			119	334	34	34	243
	Mean				119.1	221.3	31.5	37.1	175.1
	S.D.				11.2	66.1	9.4	12.8	69.4
Group 9									
Reference Range					48 - 96	74 - 319	0 - 0	0 - 0	3 - 125

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Client No. 1028 Study: 418018 PUPS LD5 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	T4,TOTAL UG/DL	T3,TOTAL NG/DL	FREE T3 PG/ML	TSH NG/ML	FREE T4 NG/DL
B 0030631	10906	1			0.45	39.28			
B 0030632	10909	1			0.43	70.81	0.25		0.06
B 0030633	10911	1			0.79	70.59			0.08
B 0030634	10913	1			0.13	70.66		0.76	0.07
B 0030635	10914	1			0.40	94.97	0.10		0.06
	Mean				.44	69.262	.175	.76	.068
	S.D.				.235	19.786	.106	0	.01
Group 1									
B 0030673	11019	10			0.00	51.23			
B 0030674	11021	10			0.00	40.88	0.00	2.36	0.01
B 0030675	11020	10			0.00	56.43	0.00		0.01
B 0030676	11023	10			0.00				0.01
B 0030677	11024	10			0.00	50.60			
B 0030678	11025	10			0.15	41.97	0.00		0.01
B 0030679	11026	10			0.00	57.95			0.03
B 0030680	11027	10			0.00	34.91	0.00		0.03
B 0030681	11028	10			0.00				0.01
	Mean				.017	47.71	0	2.36	.016
	S.D.				.05	8.613	0	0	.01
Group 10									
Reference Range					3 - 7	50 - 100	0 - 0	.57 - 3.41	1.9 - 2.5

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Accession No.	Spec. ID	Gp	Sex	Age	T4,TOTAL UG/DL	T3,TOTAL NG/DL	FREE T3 PG/ML	TSH NG/ML	FREE T4 NG/DL
B 0030682	11029	11			0.00	103.98	0.00		0.01
B 0030683	11031	11			0.00	47.45	0.03		0.01
B 0030684	11032	11			0.00	31.37	0.00		0.00
B 0030685	11033	11							
B 0030686	11034	11			0.00				
B 0030687	11035	11			0.00				
B 0030688	11036	11			0.00	39.69	0.00		0.00
B 0030689	11037	11			0.00	59.42	0.00		0.03
B 0030690	11038	11			0.00	33.50			0.00
	Mean				0	52.568	.006		.008
	S.D.				0	27.185	.013		.012
Group 11									
B 0030691	11049	12			0.00	42.35			0.02
	Mean				0	42.35			.02
	S.D.				0	0			0
Group 12									
B 0030692	11059	13			0.00	40.17	0.15		0.01
	Mean				0	40.17	.15		.01
	S.D.				0	0	0		0
Group 13									
Reference Range					3 - 7	50 - 100	0 - 0	.57 - 3.41	1.9 - 2.5

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Accession No.	Spec. ID	Gp	Sex	Age	T4,TOTAL UG/DL	T3,TOTAL NG/DL	FREE T3 PG/ML	TSH NG/ML	FREE T4 NG/DL
B 0030636	10921	2			0.80	92.83			0.08
B 0030637	10922	2			0.21	67.70	0.51	0.58	0.05
B 0030638	10923	2			0.61	134.10	0.98		0.18
B 0030639	10924	2			0.37	52.98	0.00	0.28	0.10
B 0030640	10927	2			0.44	69.49			0.04
	Mean				.486	83.42	.497	.43	.09
	S.D.				.227	31.721	.49	.212	.056
Group 2									
B 0030641	10929	3			0.00	58.69			0.01
B 0030642	10938	3			0.00	54.04		0.68	0.00
B 0030643	10942	3			0.00	99.17			
	Mean				0	70.633		.68	.005
	S.D.				0	24.823		0	.007
Group 3									
B 0030644	10957	5			0.20	90.58			0.06
B 0030645	10966	5			0.40	102.31	0.10		0.04
B 0030646	10967	5			0.81	87.31	0.44	1.38	0.11
B 0030647	10968	5			0.00	62.28			0.05
B 0030648	10969	5			0.31	63.95			0.06
B 0030649	10970	5			0.22	64.00			
	Mean				.323	78.405	.27	1.38	.064
	S.D.				.273	17.178	.24	0	.027
Group 5									
Reference Range					3 - 7	50 - 100	0 - 0	.57 - 3.41	1.9 - 2.5

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Accession No.	Spec. ID	Gp	Sex	Age	T4,TOTAL UG/DL	T3,TOTAL NG/DL	FREE T3 PG/ML	TSH NG/ML	FREE T4 NG/DL
B 0030650	10977	6			0.00	40.98		0.00	
B 0030651	10979	6			0.00	36.70	0.00		0.00
B 0030652	10983	6			0.00	44.84			0.00
	Mean				0	40.84	0	0	0
	S.D.				0	4.072	0	0	0
Group 6									
B 0030653	10995	7			0.00	25.90			
B 0030654	10997	7							
	Mean				0	25.9			
	S.D.				0	0			
Group 7									
B 0030655	10999	8			0.00	80.67			
B 0030656	11000	8			0.00	39.92			0.01
B 0030657	11001	8			0.00	47.53	0.00		
B 0030658	11002	8			0.00	85.19	0.08		0.03
B 0030659	11003	8			0.00	74.96			0.01
B 0030660	11004	8			0.00				0.01
B 0030661	11005	8			0.00	49.96	0.00		
B 0030662	11006	8			0.00	37.35	0.00		0.02
B 0030663	11007	8			0.00	41.44			0.02
									0.01
Reference Range					3 - 7	50 - 100	0 - 0	.57 - 3.41	1.9 - 2.5

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Client: ARGUS RESEARCH LABORATORIES, INC.
905 SHEEHY DRIVE
BUILDING A
HORSHAM, PA 19044-
(215) 443-8710

Date Collected:
Date Received: 12/12/2000
Date Reported: 01/16/2001

Client No. 1028 Study: 418018 PUPS LD5 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	T4,TOTAL UG/DL	T3,TOTAL NG/DL	FREE T3 PG/ML	TSH NG/ML	FREE T4 NG/DL
B 0030664	11008	8			0.00	44.97	0.00		0.03
	Mean				0	55.777	.016		.018
	S.D.				0	18.934	.036		.009
Group 8									
B 0030665	11009	9			0.00	31.44	0.00		0.05
B 0030666	11010	9			0.00	89.23	0.00		0.00
B 0030667	11011	9			0.00	51.55	0.00		0.02
B 0030668	11012	9			0.00	46.42			
B 0030669	11013	9			0.00	44.09			0.00
B 0030670	11015	9			0.00	51.27	0.00		0.00
B 0030671	11016	9			0.00	38.39			0.01
B 0030672	11018	9			0.00	38.21	0.00		0.02
	Mean				0	48.825	0		.014
	S.D.				0	17.72	0		.018
Group 9									
Reference Range					3 - 7	50 - 100	0 - 0	.57 - 3.41	1.9 - 2.5

Approved ----------[signature]---------- Date ---1/16/01

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301-921-0168 800-237-2815

QA AUDIT REPORT

The report listed below was reviewed for compliance with the FDA Good Laboratory Practices and with EPA Good Laboratory Practices. The final report and all associated raw data were reviewed for accuracy and consistency and the findings were reported to management.

The methods used were the methods described and the report accurately reflects the data. Therefore, these studies were done in compliance with the FDA and EPA Good Laboratory Practices.

Franklin B. Newman
QA Auditor

SPONSOR: ARGUS RESEARCH LABS STUDY: 418018

REPORT TYPE:	AUDIT DATE:	REPORT TO MANAGEMENT:	AUDIT #:
CHEM, T3, TH, TSH FT3, FTH, CHOL	1-22-01	1-22-01	01-063

3/5/01
DATE SUBMITTED TO CLIENT

TO Dr Raymond York

MANAGEMENT 1/22/01

ANALYTICS INCORPORATED
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Client: ARGUS RESEARCH LABORATORIES, INC.
905 SHEEHY DRIVE
BUILDING A
HORSHAM, PA 19044-
(215) 443-8710

Date Collected:
Date Received: 02/01/2001
Date Reported: 02/05/2001

Client No. 1028 Study: 418018 LD5 MILK Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL
B 0035529	11501	1	F		165
B 0035530	11502	1	F		158
B 0035531	11503	1	F		169
B 0035532	11504	1	F		99
B 0035533	11505	1	F		135
B 0035534	11506	1	F		126
B 0035535	11507	1	F		104
B 0035536	11508	1	F		130
B 0035537	11509	1	F		97
B 0035538	11510	1	F		116
B 0035539	11511	1	F		129
B 0035540	11512	1	F		98
B 0035541	11513	1	F		92
B 0035542	11514	1	F		135
	Mean				125.2
	S.D.				25.8

Group 1

B 0035609	11620	10	F		78
B 0035610	11621	10	F		112
B 0035611	11622	10	F		130
B 0035612	11623	10	F		103
B 0035613	11624	10	F		78
B 0035614	11625	10	F		78
B 0035615	11626	10	F		164
Reference Range					48 - 96

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905 SHEEHY DRIVE
BUILDING A
HORSHAM, PA 19044-
(215) 443-8710

Date Collected:
Date Received: 02/01/2001
Date Reported: 02/05/2001

Client No. 1028 Study: 418018 LD5 MILK Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL
B 0035616	11628	10	F		84
B 0035617	11629	10	F		111
	Mean				104.2
	S.D.				29.2
Group 10					
B 0035618	11630	11	F		86
B 0035619	11632	11	F		82
B 0035620	11633	11	F		70
B 0035621	11634	11	F		77
B 0035622	11635	11	F		87
B 0035623	11636	11	F		129
B 0035624	11637	11	F		67
B 0035625	11638	11	F		75
B 0035626	11639	11	F		91
	Mean				84.9
	S.D.				18.4
Group 11					
B 0035627	11640	12	F		93
B 0035628	11641	12	F		57
B 0035629	11642	12	F		80
Reference Range					48 - 96

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BUILDING A
HORSHAM, PA 19044-
(215) 443-8710

Date Collected:
Date Received: 02/01/2001
Date Reported: 02/05/2001

Client No. 1028 Study: 418018 LD5 MILK Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL
B 0035630	11643	12	F		106
B 0035631	11644	12	F		76
B 0035632	11646	12	F		89
B 0035633	11647	12	F		25
B 0035634	11648	12	F		93
B 0035635	11650	12	F		59
B 0035636	11651	12	F		69
B 0035637	11653	12	F		59
	Mean				73.3
	S.D.				22.7
Group 12					
B 0035638	11654	13	F		92
B 0035639	11655	13	F		98
B 0035640	11656	13	F		84
B 0035641	11662	13	F		96
	Mean				92.5
	S.D.				6.2
Group 13					
B 0035543	11515	2	F		89
B 0035544	11516	2	F		
Reference Range					48 - 96

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(215) 443-8710

Date Collected:
Date Received: 02/01/2001
Date Reported: 02/05/2001

Client No. 1028 Study: 418018 LD5 MILK Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL
B 0035545	11517	2	F		118
B 0035546	11518	2	F		97
B 0035547	11519	2	F		97
B 0035548	11520	2	F		87
B 0035549	11521	2	F		103
B 0035550	11523	2	F		109
B 0035551	11524	2	F		130
B 0035552	11525	2	F		116
B 0035553	11526	2	F		120
B 0035554	11527	2	F		111
B 0035555	11528	2	F		167
	Mean				112
	S.D.				21.7

Group 2

B 0035556	11529	3	F		77
B 0035557	11530	3	F		96
B 0035558	11534	3	F		62
B 0035559	11536	3	F		81
B 0035560	11537	3	F		109
B 0035561	11538	3	F		42
B 0035562	11540	3	F		121
B 0035563	11542	3	F		136
B 0035564	11543	3	F		103
	Mean				91.9
	S.D.				29.5

Group 3

Reference Range 48 - 96

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905 SHEEHY DRIVE
BUILDING A
HORSHAM, PA 19044-
(215) 443-8710

Date Collected:
Date Received: 02/01/2001
Date Reported: 02/05/2001

Client No. 1028 Study: 418018 LD5 MILK Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL
B 0035565	11547	4	F		269
B 0035566	11552	4	F		107
	Mean				188
	S.D.				114.6

Group 4

B 0035567	11558	5	F		109
B 0035568	11559	5	F		94
B 0035569	11561	5	F		136
B 0035570	11563	5	F		137
B 0035571	11564	5	F		104
B 0035572	11565	5	F		149
B 0035573	11567	5	F		100
B 0035574	11568	5	F		99
B 0035575	11569	5	F		92
B 0035576	11570	5	F		187
B 0035577	11571	5	F		88
B 0035578	11574	5	F		72
B 0035579	11575	5	F		127
B 0035580	11576	5	F		138
B 0035581	11578	5	F		68
B 0035582	11579	5	F		116
B 0035583	11580	5	F		105
B 0035584	11582	5	F		149
B 0035585	11583	5	F		93
	Mean				113.8
	S.D.				29.9

Group 5

Reference Range 48 - 96

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Client: ARGUS RESEARCH LABORATORIES, INC.
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BUILDING A
HORSHAM, PA 19044-
(215) 443-8710

Date Collected:
Date Received: 02/01/2001
Date Reported: 02/05/2001

Client No. 1028 Study: 418018 LD5 MILK Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL
B 0035586	11584	6	F		102
	Mean				102
	S.D.				0
Group 6					
B 0035587	11592	7	F		
B 0035588	11593	7	F		47
B 0035589	11597	7	F		76
	Mean				61.5
	S.D.				20.5
Group 7					
B 0035590	11600	8	F		134
B 0035591	11601	8	F		79
B 0035592	11602	8	F		74
B 0035593	11603	8	F		89
B 0035594	11604	8	F		146
B 0035595	11605	8	F		106
B 0035596	11606	8	F		226
B 0035597	11607	8	F		126
B 0035598	11608	8	F		155
B 0035599	11609	8	F		103
	Mean				123.8
	S.D.				45.3
Group 8					

Reference Range 48 - 96

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HORSHAM, PA 19044-
(215) 443-8710

Date Collected:
Date Received: 02/01/2001
Date Reported: 02/05/2001

Client No. 1028 Study: 418018 LD5 MILK Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL
B 0035600	11611	9	F		97
B 0035601	11612	9	F		98
B 0035602	11613	9	F		139
B 0035603	11614	9	F		141
B 0035604	11615	9	F		77
B 0035605	11616	9	F		92
B 0035606	11617	9	F		96
B 0035607	11618	9	F		100
B 0035608	11619	9	F		135
	Mean				108.3
	S.D.				23.5

Group 9

Reference Range 48 - 96

Approved ---------- Date --02/5/01

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Client: ARGUS RESEARCH LABORATORIES, INC.
905 SHEEHY DRIVE
BUILDING A
HORSHAM, PA 19044-
(215) 443-8710

Date Collected:
Date Received: 02/02/2001
Date Reported: 02/13/2001

Client No. 1028 Study: 418018 DAMS LD5 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0035787	11501	1	F		96	207	7	81	133
B 0035788	11502	1	F		86	132	10	73	82
B 0035789	11503	1	F		67	162	7	53	125
B 0035790	11504	1	F		100	206	7	83	83
B 0035791	11505	1	F		64	204	5	60	71
B 0035792	11506	1	F		85	145	6	70	107
B 0035793	11507	1	F		91	174	4	73	183
B 0035794	11508	1	F		97	154	7	85	92
B 0035795	11509	1	F		95	168	5	85	112
B 0035796	11510	1	F		59	155	1	51	137
B 0035797	11511	1	F		53	149	1	45	149
B 0035798	11512	1	F		84	209	6	74	112
B 0035799	11513	1	F		69	177	3	50	173
B 0035800	11514	1	F		62	203	2	48	173
	Mean				79.1	174.6	5.1	66.5	123.7
	S.D.				16.2	26.7	2.6	14.8	36.2
Group 1									
B 0035801	11630	11	F		44	200	5	39	102
B 0035802	11632	11	F		78	145	1	67	170
B 0035803	11633	11	F		66	208	4	62	129
B 0035804	11634	11	F		79	161	6	74	107
B 0035805	11635	11	F		49	166	1	42	157
B 0035806	11636	11	F		74	156	6	70	93
B 0035807	11637	11	F		63	180	3	61	136
Reference Range					48 - 96	74 - 319	0 - 0	20 - 80	3 - 104

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BUILDING A
HORSHAM, PA 19044-
(215) 443-8710

Date Collected:
Date Received: 02/02/2001
Date Reported: 02/13/2001

Client No. 1028 Study: 418018 DAMS LD5 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0035808	11638	11	F		69	179	6	62	98
B 0035809	11639	11	F		69	185	4	67	90
	Mean				65.7	175.6	4	60.4	120.2
	S.D.				12.1	20.6	2	12.1	29.2
Group 11									
B 0035810	11640	12	F		61	179	2	54	183
B 0035811	11641	12	F		43	186	1	43	77
B 0035812	11642	12	F		57	165	7	51	63
B 0035813	11643	12	F		39	190	3	37	68
B 0035814	11644	12	F		46	180	3	38	153
B 0035815	11645	12	F		77	175	2	59	190
B 0035816	11646	12	F		52	157	2	51	62
B 0035817	11647	12	F		41	207	2	40	44
B 0035818	11648	12	F		68	145	2	66	77
B 0035819	11649	12	F		78	206	8	69	62
B 0035820	11650	12	F		50	159	2	48	54
B 0035821	11651	12	F		47	176	1	46	56
B 0035822	11653	12	F		63	159	7	58	60
	Mean				55.5	175.7	3.2	50.8	88.4
	S.D.				13.1	18.7	2.4	10.2	51
Group 12									
Reference Range					48 - 96	74 - 319	0 - 0	20 - 80	3 - 104

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BUILDING A
HORSHAM, PA 19044-
(215) 443-8710

Date Collected:
Date Received: 02/02/2001
Date Reported: 02/13/2001

Client No. 1028 Study: 418018 DAMS LD5 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0035823	11654	13	F		44	208	4	39	125
B 0035824	11655	13	F		59	168	4	56	48
B 0035825	11656	13	F		50	175	3	45	122
B 0035826	11657	13	F		64	222	6	60	74
B 0035827	11658	13	F		52	206	7	46	50
B 0035828	11659	13	F		61	158	2	60	99
B 0035829	11660	13	F		57	196	5	54	66
B 0035830	11661	13	F		69	197	5	65	93
B 0035831	11662	13	F		37	202	2	36	20
B 0035832	11663	13	F		58	153	3	51	118
B 0035833	11664	13	F		77	152	5	61	159
B 0035834	11665	13	F		60	227	7	53	54
B 0035835	11667	13	F		67	202	5	61	126
	Mean				58.1	189.7	4.5	52.8	88.8
	S.D.				10.6	25.6	1.7	9	40.4

Group 13

Reference Range	48 - 96	74 - 319	0 - 0	20 - 80	3 - 104

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(215) 443-8710

Date Collected:
Date Received: 02/02/2001
Date Reported: 02/13/2001

Client No. 1028 Study: 418018 DAMS LD5 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	T3,TOTAL NG/DL	T4,TOTAL UG/DL	TSH NG/ML	FREE T3 PG/ML	FREE T4 NG/DL
B 0035787	11501	1	F		65.64	1.30	1.68	0.43	0.62
B 0035788	11502	1	F		104.47	2.97	1.55	1.19	1.42
B 0035789	11503	1	F		37.77	0.85	0.91	0.04	0.55
B 0035790	11504	1	F		73.00	1.11	2.95	0.58	0.78
B 0035791	11505	1	F		55.01	1.35	1.67	0.50	0.77
B 0035792	11506	1	F		63.16	1.28	1.19	0.47	0.70
B 0035793	11507	1	F		57.61	1.08	3.24	0.15	0.64
B 0035794	11508	1	F		76.31	2.39	2.62	0.59	1.03
B 0035795	11509	1	F		79.83	1.49	1.42	0.89	0.68
B 0035796	11510	1	F		71.86	0.88	0.77	0.56	0.79
B 0035797	11511	1	F		58.43	0.68	1.43	0.54	0.48
B 0035798	11512	1	F		80.84	1.25	2.03	0.69	0.92
B 0035799	11513	1	F		53.33	0.95	0.91	0.39	0.80
B 0035800	11514	1	F		65.08	0.92	0.66	0.62	0.77
	Mean				67.31	1.321	1.645	.546	.782
	S.D.				15.865	.628	.808	.28	.232
Group 1									
B 0035801	11630	11	F		26.82	0.37	2.54	0.18	0.28
B 0035802	11632	11	F		47.75	0.06	0.50	0.55	0.20
B 0035803	11633	11	F		37.99	0.00	1.66	0.11	0.17
B 0035804	11634	11	F		46.74	0.01	0.98	0.15	0.29
B 0035805	11635	11	F		46.41	0.06	1.52	0.18	0.28
B 0035806	11636	11	F		43.09	0.05	1.58	0.26	0.26
B 0035807	11637	11	F		48.31	0.11	4.35	0.35	0.21
Reference Range					50 - 100	3 - 7	.57 - 3.41	0 - 0	1.9 - 2.5

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905 SHEEHY DRIVE
BUILDING A
HORSHAM, PA 19044-
(215) 443-8710

Date Collected:
Date Received: 02/02/2001
Date Reported: 02/13/2001

Client No. 1028 Study: 418018 DAMS LD5 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	T3,TOTAL NG/DL	T4,TOTAL UG/DL	TSH NG/ML	FREE T3 PG/ML	FREE T4 NG/DL
B 0035808	11638	11	F		31.70	0.10	0.60	0.09	0.18
B 0035809	11639	11	F		51.74	0.13	1.64	0.36	0.29
	Mean				42.283	.099	1.708	.248	.24
	S.D.				8.387	.111	1.17	.149	.049
Group 11									
B 0035810	11640	12	F		36.31	0.00	1.13	0.03	0.19
B 0035811	11641	12	F		32.93	0.20	2.25	0.12	0.23
B 0035812	11642	12	F		32.46	0.08	3.11	0.00	0.14
B 0035813	11643	12	F		41.21	0.24	1.25	0.34	0.29
B 0035814	11644	12	F		26.20	0.08	1.68	0.02	0.19
B 0035815	11645	12	F		54.83	0.29	1.30	0.31	0.21
B 0035816	11646	12	F		28.42	0.38	1.46	0.29	0.20
B 0035817	11647	12	F		55.92	0.63	1.48	0.50	0.41
B 0035818	11648	12	F		33.95	0.16	1.79	0.00	0.21
B 0035819	11649	12	F		59.37	0.26	2.38	0.57	0.31
B 0035820	11650	12	F		31.35	0.29	3.38	0.14	0.21
B 0035821	11651	12	F		29.13	0.31	0.46	0.06	0.30
B 0035822	11653	12	F		43.24	0.23	0.71	0.00	0.32
	Mean				38.871	.242	1.722	.183	.247
	S.D.				11.249	.158	.861	.199	.074
Group 12									
Reference Range					50 - 100	3 - 7	.57 - 3.41	0 - 0	1.9 - 2.5

ANILYTICS INCORPORATED
200 Girard Street, Suite 200, Gaithersburg, MD 20877
301-921-0168 Fax: 301-977-0433

Client: ARGUS RESEARCH LABORATORIES, INC.
905 SHEEHY DRIVE
BUILDING A
HORSHAM, PA 19044-
(215) 443-8710

Date Collected:
Date Received: 02/02/2001
Date Reported: 02/13/2001

Client No. 1028 Study: 418018 DAMS LD5 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	T3,TOTAL NG/DL	T4,TOTAL UG/DL	TSH NG/ML	FREE T3 PG/ML	FREE T4 NG/DL
B 0035823	11654	13	F		35.84	0.25	1.70	0.14	0.24
B 0035824	11655	13	F		39.95	0.49	1.45	0.24	0.33
B 0035825	11656	13	F		28.99	0.10	1.27	0.00	0.17
B 0035826	11657	13	F		46.76	0.18	1.51	0.41	0.36
B 0035827	11658	13	F		46.50	0.11	1.18	0.24	0.23
B 0035828	11659	13	F		33.35	0.22	2.23	0.01	0.30
B 0035829	11660	13	F		48.66	0.23	1.03	0.75	0.26
B 0035830	11661	13	F		59.68	0.38	2.19	0.47	0.37
B 0035831	11662	13	F		21.45	0.32	0.93	0.01	0.20
B 0035832	11663	13	F		56.44	0.06	0.91	0.38	0.21
B 0035833	11664	13	F		77.52	0.18	1.76	0.53	0.25
B 0035834	11665	13	F		52.57	0.20	0.74	0.36	0.35
B 0035835	11667	13	F		54.46	0.08	1.49	0.35	0.40
	Mean				46.321	.215	1.415	.299	.282
	S.D.				14.728	.124	.47	.224	.074

Group 13

Reference Range	50 - 100	3 - 7	.57 - 3.41	0 - 0	1.9 - 2.5

Approved ---------- Date 2/13/01

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Date Collected:
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Date Reported: 02/13/2001

Client No. 1028 Study: 418018 DAMS LD5 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0035934	11620	10	F		44	197	2	43	115
B 0035935	11621	10	F		73	172	8	66	90
B 0035936	11622	10	F		67	155	5	59	122
B 0035937	11623	10	F		46	151	3	44	47
B 0035938	11624	10	F		80	175	3	67	123
B 0035939	11625	10	F		67	149	4	62	47
B 0035940	11626	10	F		48	156	4	45	91
B 0035941	11627	10	F		55	188	4	50	84
B 0035942	11628	10	F		72	170	3	66	116
B 0035943	11629	10	F		50	171	1	48	154
	Mean				60.2	168.4	3.7	55	98.9
	S.D.				13	15.9	1.9	9.9	34.1

Group 10

B 0035836	11515	2	F		86	196	3	69	148
B 0035837	11516	2	F		101	168	5	96	48
B 0035838	11517	2	F		66	157	1	62	113
B 0035839	11518	2	F		83	168	4	78	127
B 0035840	11519	2	F		94	210	9	82	94
B 0035841	11520	2	F		88	162	4	61	179
B 0035842	11521	2	F		65	279	6	60	90
B 0035843	11523	2	F		105	157	4	81	149
B 0035844	11524	2	F		64	203	3	61	114
B 0035845	11525	2	F		89	243	4	82	133
B 0035846	11526	2	F		89	178	5	71	157
Reference Range					48 - 96	74 - 319	0 - 0	20 - 80	3 - 104

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Date Collected:
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Client No. 1028 Study: 418018 DAMS LD5 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0035847	11527	2	F		69	137	1	50	293
B 0035848	11528	2	F		80	148	3	78	72
	Mean				83	185.1	4	71.6	132.1
	S.D.				13.6	40.5	2.1	12.6	60.5
Group 2									
B 0035849	11529	3	F		67	225	5	63	103
B 0035850	11530	3	F		67	166	5	60	113
B 0035851	11532	3	F		79	194	2	63	184
B 0035852	11533	3	F		74	184	4	67	88
B 0035853	11534	3	F		55	188	4	52	48
B 0035854	11535	3	F		68	163	1	56	201
B 0035855	11536	3	F		59	185	2	58	67
B 0035856	11537	3	F		60	144	5	55	109
B 0035857	11538	3	F		51	198	1	52	80
B 0035858	11539	3	F		56	210	5	44	89
B 0035859	11540	3	F		106	155	8	79	46
B 0035860	11541	3	F		77	172	6	60	110
B 0035861	11542	3	F		53	182	3	42	130
B 0035862	11543	3	F		72	189	3	69	58
	Mean				67.4	182.5	3.9	58.6	101.9
	S.D.				14.3	21.5	2	9.7	46.1
Group 3									
Reference Range					48 - 96	74 - 319	0 - 0	20 - 80	3 - 104

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(215) 443-8710

Date Collected:
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Date Reported: 02/13/2001

Client No. 1028 Study: 418018 DAMS LD5 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0035863	11544	4	F		69	163	2	44	211
B 0035864	11545	4	F		62	178	1	55	158
B 0035865	11546	4	F		79	186	2	59	139
B 0035866	11547	4	F		50	254	2	48	41
B 0035867	11549	4	F		73	191	1	72	84
B 0035868	11550	4	F		55	247	6	51	65
B 0035869	11551	4	F		82	180	8	75	71
B 0035870	11552	4	F		44	148	1	39	135
B 0035871	11553	4	F		89	211	5	68	169
B 0035872	11554	4	F		62	193	4	55	113
B 0035873	11555	4	F		68	184	5	62	78
B 0035874	11556	4	F		72	170	2	62	138
B 0035875	11557	4	F		64	171	2	44	190
	Mean				66.8	190.5	3.2	56.5	122.5
	S.D.				12.7	30.7	2.2	11.2	52.1
Group 4									
B 0035876	11558	5	F		91	154	1	66	189
B 0035877	11559	5	F		91	136	3	70	139
B 0035878	11561	5	F		88	159	7	79	84
B 0035879	11563	5	F		62	178	6	54	100
B 0035880	11564	5	F		59	189	7	49	101
B 0035881	11565	5	F		71	186	5	65	96
B 0035882	11567	5	F		75	220	4	55	147
B 0035883	11568	5	F		84	172	2	69	136
Reference Range					48 - 96	74 - 319	0 - 0	20 - 80	3 - 104

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Date Collected:
Date Received: 02/02/2001
Date Reported: 02/13/2001

Client No. 1028 Study: 418018 DAMS LD5 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0035884	11569	5	F		108	189	9	90	133
B 0035885	11570	5	F		53	234	3	51	69
B 0035886	11571	5	F		112	174	8	78	169
	Mean				81.3	181	5	66	123.9
	S.D.				19.3	28	2.6	13	37.1
Group 5									
B 0035887	11572	6	F		56	194	6	52	53
B 0035888	11573	6	F		82	192	5	78	92
B 0035889	11574	6	F		49	175	6	45	60
B 0035890	11575	6	F		57	188	5	53	92
B 0035891	11576	6	F		57	137	6	50	89
B 0035892	11577	6	F		63	170	2	51	148
B 0035893	11578	6	F		52	177	3	44	110
B 0035894	11579	6	F		47	192	8	40	57
B 0035895	11580	6	F		46	157	1	43	103
B 0035896	11581	6	F		71	181	2	68	153
B 0035897	11582	6	F		37	164	2	37	46
B 0035898	11583	6	F		62	172	6	56	89
B 0035899	11584	6	F		54	143	2	53	63
B 0035900	11585	6	F		49	185	6	43	69
	Mean				55.9	173.4	4.3	50.9	87.4
	S.D.				11.3	17.9	2.2	11	33.1
Group 6									
Reference Range					48 - 96	74 - 319	0 - 0	20 - 80	3 - 104

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Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0035901	11586	7	F		88	194	11	79	86
B 0035902	11587	7	F		69	188	5	66	67
B 0035903	11588	7	F		68	182	4	60	135
B 0035904	11589	7	F		41	206	1	39	31
B 0035905	11590	7	F		57	173	7	47	104
B 0035906	11591	7	F		74	152	7	57	105
B 0035907	11592	7	F		52	192	2	51	75
B 0035908	11593	7	F		38	256	4	31	130
B 0035909	11594	7	F		63	248	6	58	54
B 0035910	11595	7	F		44	163	3	41	51
B 0035911	11596	7	F		67	181	4	65	43
B 0035912	11597	7	F		38	198	5	35	79
B 0035913	11598	7	F		69	203	6	63	87
B 0035914	11599	7	F		62	217	4	54	177
	Mean				59.3	196.6	4.9	53.3	87.4
	S.D.				15	29	2.5	13.5	40.1
Group 7									
B 0035915	11600	8	F		100	167	5	96	58
B 0035916	11601	8	F		81	180	3	71	220
B 0035917	11602	8	F		44	144	4	40	67
B 0035918	11603	8	F		67	216	5	64	104
B 0035919	11604	8	F		64	190	5	60	60
B 0035920	11605	8	F		61	200	3	57	81
B 0035921	11606	8	F		48	157	3	46	58
Reference Range					48 - 96	74 - 319	0 - 0	20 - 80	3 - 104

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Client No. 1028 Study: 418018 DAMS LD5 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0035922	11607	8	F		79	212	9	70	56
B 0035923	11608	8	F		68	165	5	62	63
B 0035924	11609	8	F		74	172	5	70	90
	Mean				68.6	180.3	4.7	63.6	85.7
	S.D.				16.3	23.8	1.8	15.3	49.8
Group 8									
B 0035925	11611	9	F		59	182	6	55	118
B 0035926	11612	9	F		44	162	2	44	99
B 0035927	11613	9	F		72	182	4	69	48
B 0035928	11614	9	F		87	145	4	71	147
B 0035929	11615	9	F		77	187	7	62	167
B 0035930	11616	9	F		43	162	2	37	148
B 0035931	11617	9	F		61	154	4	58	83
B 0035932	11618	9	F		72	181	3	70	55
B 0035933	11619	9	F		46	176	2	46	66
	Mean				62.3	170.1	3.8	56.9	103.4
	S.D.				15.8	14.8	1.8	12.4	43.9
Group 9									
Reference Range					48 - 96	74 - 319	0 - 0	20 - 80	3 - 104

Approved ---------- Date 2/13/01

ANI LYTICS, INC.
200 GIRARD STREET
SUITE 200
GAITHERSBURG, MD 20877
(301) 921-0168 or (FAX) 977-0433

CLIENT:	ARGUS RESEARCH LABORATORIES, INC	DATE SPEC. COLLECTED:	
SPECIMEN ID:	11654	DATE SPEC. RECEIVED:	02/02/2001
SPECIES:	RAT	DATE REPORTED:	02/13/2001
STUDY:	418018 PUPS LD5	AGE:	
GROUP:	13	SEX:	
ACCESSION:	B 0035745		

PROFILE/TEST	RESULTS	UNITS	REFERENCE RANGE
ARGUS CHEM PROFILE			
CHOLESTEROL	172	MG/DL	48 - 96
GLUCOSE	217	MG/DL	74 - 319
LDL-DIRECT	81	MG/DL	
HDL-DIRECT	39	MG/DL	20 - 80
TRIGLYCERIDE	255	MG/DL	3 - 125
TRIIODOTHYRONINE	18.74	NG/DL	50 - 100
THYROXINE	0.00	UG/DL	3.0 - 7.0
TSH, RAT	QNS	NG/ML	0.57 - 3.41
T3, FREE	0.00	PG/ML	
FREE T4	0.00	NG/DL	1.9 - 2.5

Laboratory Director: Saroj R. Das, Ph.D.

FINAL REPORT

SRD/13/01

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200 Girard Street, Suite 200, Gaithersburg, MD 20877
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BUILDING A
HORSHAM, PA 19044-
(215) 443-8710

Date Collected:
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Client No. 1028 Study: 418018 PUPS LD5 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0035782	11620/626	10			115	173	37	48	135
B 0035783	11621/622	10			108	255	34	43	169
B 0035784	11623	10			106	290	28	27	258
B 0035785	11624/629	10			108	177	32	31	298
B 0035786	11625/628	10			117	267	36	47	170
	Mean				110.8	232.4	33.4	39.2	206
	S.D.				4.9	53.9	3.6	9.6	68.7
Group 10									
B 0035747	11515/524	2			111	213	42	41	158
B 0035748	11517/520	2			111	357	31	31	225
B 0035749	11519/518	2			110	238	30	44	173
B 0035750	11521/516	2			121	327	37	30	294
B 0035751	11523/527	2			117	152	49	50	152
B 0035752	11525/528	2			109	244	28	31	188
B 0035753	11526	2			106	375	36	29	202
	Mean				112.1	272.3	36.1	36.6	198.9
	S.D.				5.1	82.3	7.4	8.3	49
Group 2									
B 0035754	11536/537	3			149	217	53	32	247
B 0035755	11538/534	3			174	310	75	37	329
Reference Range					48 - 96	74 - 319	0 - 0	20 - 80	3 - 125

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Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0035756	11540/530	3			145	284	40	32	234
B 0035757	11543/529	3			130	238	32	28	370
	Mean				149.5	262.3	50	32.3	295
	S.D.				18.3	42.4	18.8	3.7	65.3
Group 3									
B 0035758	11558/569	5			122	325	24	24	289
B 0035759	11559/570	5			102	288	41	39	145
B 0035760	11561/568	5			111	253	37	32	295
B 0035761	11563/564	5			119	237	21	22	370
B 0035762	11565/567	5			118	223	41	39	178
B 0035763	11571	5			129	230	44	40	321
	Mean				116.8	259.3	34.7	32.7	266.3
	S.D.				9.3	39.6	9.7	8	86.7
Group 5									
B 0035764	11574/575	6			131	227	47	40	193
B 0035765	11576/578	6			117	257	40	44	147
B 0035766	11582	6			125	303	37	37	286
B 0035767	11583/580	6			132	243	40	38	243
B 0035768	11584/579	6			116	185	32	36	225
	Mean				124.2	243	39.2	39	218.8
	S.D.				7.5	43.1	5.4	3.2	52.3
Group 6									
Reference Range					48 - 96	74 - 319	0 - 0	20 - 80	3 - 125

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B 0035769	11592	7			130	255	42	28	160
B 0035770	11593	7			121	211	46	44	160
B 0035771	11597	7			121	230	58	51	98
	Mean				124	232	48.7	41	139.3
	S.D.				5.2	22.1	8.3	11.8	35.8
Group 7									
B 0035772	11600/608	8			106	307	35	33	249
B 0035773	11602/609	8			97	244	18	33	228
B 0035774	11603/604	8			114	286	31	31	195
B 0035775	11606/601	8			104	179	34	31	248
B 0035776	11607/605	8			109	242	41	34	225
	Mean				106	251.6	31.8	32.4	229
	S.D.				6.3	49.2	8.5	1.3	22
Group 8									
B 0035777	11611	9			100	194	28	46	121
B 0035778	11612/613	9			120	173	37	46	120
B 0035779	11614/616	9			108	284	33	30	233
B 0035780	11617/619	9			106	233	26	45	178
B 0035781	11618/615	9			106	210	33	31	276
	Mean				108	218.8	31.4	39.6	185.6
	S.D.				7.3	42.6	4.4	8.3	68.8
Group 9									
Reference Range					48 - 96	74 - 319	0 - 0	20 - 80	3 - 125

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Date Reported: 02/13/2001

Client No. 1028 Study: 418018 PUPS LD5 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	T3,TOTAL NG/DL	T4,TOTAL UG/DL	TSH NG/ML	FREE T3 PG/ML	FREE T4 NG/DL
B 0035728	11501/506	1			38.73	0.60	0.88	0.00	0.11
B 0035729	11502/507	1			48.84	0.65	1.17	0.00	0.12
B 0035730	11504	1			45.82	0.97	1.27	0.00	0.12
B 0035731	11508/503	1			44.65	0.54	0.99	0.00	0.11
B 0035732	11509/510	1			46.29	0.67	1.10	0.00	0.11
B 0035733	11512/511	1			43.06	0.57	1.06	0.00	0.08
B 0035734	11513/514	1			38.90	0.32	0.91	0.00	0.07
	Mean				43.756	.617	1.054	0	.103
	S.D.				3.8	.194	.14	0	.02
Group 1									
B 0035735	11630/633	11			35.45	0.00	1.09	0.00	0.01
B 0035736	11632/636	11			33.85	0.05	1.07	0.00	0.02
B 0035737	11635/637	11			32.59	0.00	1.35	0.00	0.01
B 0035738	11638	11			47.34	0.00	0.79	0.00	0.01
B 0035739	11639/634	11			27.23	0.02	0.75	0.00	0.02
	Mean				35.292	.014	1.01	0	.014
	S.D.				7.409	.022	.246	0	.005
Group 11									
B 0035740	11640/641	12			35.15	0.00	1.91	0.02	0.01
B 0035741	11646/644	12			36.35	0.03	1.15	0.00	0.01
Reference Range					50 - 100	3 - 7	.57 - 3.41	0 - 0	1.9 - 2.5

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Date Collected:
Date Received: 02/02/2001
Date Reported: 02/13/2001

Client No. 1028 Study: 418018 PUPS LD5 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	T3,TOTAL NG/DL	T4,TOTAL UG/DL	TSH NG/ML	FREE T3 PG/ML	FREE T4 NG/DL
B 0035742	11648/651	12			33.69	0.00	1.62	0.00	0.01
B 0035743	11650	12			18.76	0.00	1.48	0.00	0.00
B 0035744	11653/642	12			29.95	0.00	1.09	0.00	0.01
	Mean				30.78	.006	1.45	.004	.008
	S.D.				7.137	.013	.339	.009	.004
Group 12									
B 0035745	11654	13			18.74	0.00		0.00	0.00
B 0035746	11656/655	13			39.42	0.00	1.50	0.00	0.02
	Mean				29.08	0	1.5	0	.01
	S.D.				14.623	0	0	0	.014
Group 13									
Reference Range					50 - 100	3 - 7	.57 - 3.41	0 - 0	1.9 - 2.5

Approved ---------- Date 2/13/01

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Date Collected:
Date Received: 02/02/2001
Date Reported: 02/13/2001

Client No. 1028 Study: 418018 PUPS LD5 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0035728	11501/506	1			110	327	32	24	235
B 0035729	11502/507	1			111	312	35	29	212
B 0035730	11504	1			107	320	36	28	298
B 0035731	11508/503	1			111	314	30	25	241
B 0035732	11509/510	1			136	245	41	29	271
B 0035733	11512/511	1			115	148	47	42	134
B 0035734	11513/514	1			119	169	48	45	133
	Mean				115.6	262.1	38.4	31.7	217.7
	S.D.				9.8	76.1	7.1	8.3	63.7
Group 1									
B 0035735	11630/633	11			114	141	28	28	242
B 0035736	11632/636	11			115	267	37	38	207
B 0035737	11635/637	11			120	201	48	38	218
B 0035738	11638	11			125	201	32	30	266
B 0035739	11639/634	11			116	187	39	35	213
	Mean				118	199.4	36.8	33.8	229.2
	S.D.				4.5	45.1	7.6	4.6	24.5
Group 11									
B 0035740	11640/641	12			132	217	29	26	263
B 0035741	11646/644	12			118	184	30	37	276
Reference Range					48 - 96	74 - 319	0 - 0	20 - 80	3 - 125

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Date Collected:
Date Received: 02/02/2001
Date Reported: 02/13/2001

Client No. 1028 Study: 418018 PUPS LD5 Species: RAT

Accession No.	Spec. ID	Gp	Sex	Age	CHOLEST MG/DL	GLUCOSE MG/DL	LDL-DIR MG/DL	HDL-DIR MG/DL	TRIG MG/DL
B 0035742	11648/651	12			145	227	50	36	292
B 0035743	11650	12			95	233	23	31	163
B 0035744	11653/642	12			112	226	33	46	185
	Mean				120.4	217.4	33	35.2	235.8
	S.D.				19.1	19.5	10.2	7.5	57.9
Group 12									
B 0035745	11654	13			172	217	81	39	255
B 0035746	11656/655	13			102	222	30	32	235
	Mean				137	219.5	55.5	35.5	245
	S.D.				49.5	3.5	36.1	4.9	14.1
Group 13									
Reference Range					48 - 96	74 - 319	0 - 0	20 - 80	3 - 125

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QA AUDIT REPORT

The report listed below was reviewed for compliance with the FDA Good Laboratory Practices and with EPA Good Laboratory Practices. The final report and all associated raw data were reviewed for accuracy and consistency and the findings were reported to management.

The methods used were the methods described and the report accurately reflects the data. Therefore, these studies were done in compliance with the FDA and EPA Good Laboratory Practices.

Franklin B. Newman
QA Auditor

SPONSOR: ARGUS RESEARCH LABS STUDY: H18018

REPORT TYPE:	AUDIT DATE:	REPORT TO MANAGEMENT:	AUDIT #:
CHEM, T3, T4, TSH FREE T3, FREE T4	2-15-01	2-15-01	01-098

3/8/01
DATE SUBMITTED TO CLIENT
To UK Regulatory Affairs

MANAGEMENT 2/15/01

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QA AUDIT REPORT

The report listed below was reviewed for compliance with the FDA Good Laboratory Practices and with EPA Good Laboratory Practices. The final report and all associated raw data were reviewed for accuracy and consistency and the findings were reported to management.

The methods used were the methods described and the report accurately reflects the data. Therefore, these studies were done in compliance with the FDA and EPA Good Laboratory Practices.

Franklin B. Newman
QA Auditor

SPONSOR: ARGUS RESEARCH LABS STUDY: 418018

REPORT TYPE:	AUDIT DATE:	REPORT TO MANAGEMENT:	AUDIT #:
CHOL	2-15-01	2-15-01	01-121

3/8/01
DATE SUBMITTED TO CLIENT

MANAGEMENT 2/15/01

TO Dr Raymond York

APPENDIX I

BIOANALYTICAL REPORTS (PRIMEDICA WORCESTER)

PRIMEDICA

DRAFT FINAL REPORT

VALIDATION OF A GAS CHROMATOGRAPHIC-MASS SPECTROMETRIC METHOD FOR THE ANALYSIS OF MEVALONIC ACID IN EDTA RAT PLASMA FOR PRIMEDICA ARGUS STUDY 418-018

Primedica-Worcester Project Number: PABX-BVA

Submitted to:

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905 Sheehy Drive, Building A
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Submitted by:

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Worcester, MA 01608

Primedica-Worcester Report # PABX-BVA-01-62

Issue Date: April 6, 2001

Mark A. Netsch / Date
Project Scientist
Department of Analytical Chemistry
Primedica-Worcester

COMPLIANCE STATEMENT

This study was conducted in compliance with the Food and Drug Administration Good Laboratory Practice Regulations (GLP) as set forth in Title 21 of the U.S. Code of Federal Regulations (CFR) Part 58, issued December 22, 1978 (and all applicable revisions). There were no deviations from the aforementioned standards, which affected the quality or integrity of the study or the interpretation of the results in this report.

Mark A. Netsch / Date
Project Scientist

PRIMEDICA

QUALITY ASSURANCE STATEMENT

The following are the inspection dates and report dates of QAU audit/inspections for Validation Of A Gas Chromatographic-Mass Spectrometric Method For The Analysis Of Mevalonic Acid In EDTA Rat Plasma For Primedica Argus Study 418-018, Project Number PABX-BVA.

Critical Phases	Date Inspected	Date Report Submitted to Project Scientist	Date Report Submitted to Management
1. Laboratory Procedures	10/19/2000	10/20/2000	10/23/2000
1. Raw Data	11/07/2000	04/06/2001	04/06/2001
2. Draft Final Report	03/26/2001	03/26/2001	04/04/2001

The Draft Final Report for Validation Of A Gas Chromatographic-Mass Spectrometric Method For The Analysis Of Mevalonic Acid In EDTA Rat Plasma For Primedica Argus Study 418-018, report number PABX-BVA-01-62, was reviewed for compliance with the Good Laboratory Practice Regulations, 21CFR, Part 58, on XX/XX/XXXX. The results as presented accurately reflect the raw data.

Quality Assurance Auditor / Date

TABLE OF CONTENTS

Page No.

COMPLIANCE STATEMENT 2

QUALITY ASSURANCE STATEMENT 3

CONTRIBUTING PERSONNEL 7

ANALYTICAL REFERENCE STANDARD CHARACTERIZATION/STABILITY 8

ARCHIVAL STORAGE 9

ABSTRACT 10

INTRODUCTION 11

EXPERIMENTAL DESIGN 11
- Overview 11
- Materials and Methods 11
- General Comments 11
- Validation Design 11
  - Validation Description 11
  - Parameters Evaluated 12

RESULTS AND DISCUSSION 14
- Validation Results 14
  - Water/Plasma Extraction Comparison 14
  - Accuracy 15
  - Precision 15
  - Dilution QC 16
  - Recovery 16
  - Linearity 16
  - Specificity 16
  - Specificity 17
  - Stability 17

CONCLUSIONS 18

LIST OF TABLES, FIGURES AND APPENDICES

Page No.

TEXT TABLE 1
Validation Course 12

FIGURE 1
Day 3 Validation Calibration Curve 20

TABLE 1
Summary of Interpolated Mevalonic Acid Lactone QC Standard Concentrations with Inter and Intra-Day Summary Statistics 22

TABLE 2
Summary of Back-Calculated Mevalonic Acid Lactone Calibration Standard Concentrations 24

TABLE 3
Mevalonic Acid Lactone Extraction Data & Recovery Calculations 25

TABLE 4
Internal Standard Extraction Data & Recovery Calculations 26

TABLE 5
Summary of Least-Squares Linear Regression Constants and Analysis Dates 27

TABLE 6
Summary of QC Standard 72-Hour Room Temperature Stability in Matrix 28

TABLE 7
Summary of QC Standard Freeze/Thaw (3 Cycles) Stability in Matrix 29

TABLE 8
Summary of Interpolated Mevalonic Acid Lactone Dilution QC Concentrations for Dilution Validation 30

LIST OF TABLES, FIGURES AND APPENDICES - CONCLUDED

Page No.

TABLE 9
6-Day Room Temperature Final Extract Stability Back-Calculated Calibration Standard Concentrations 31

TABLE 10
6-Day Room Temperature Final Extract Stability Quality Control Standard Concentrations 32

TABLE 11
Summary of Control Blank EDTA Rat Plasma Concentrations 33

TABLE 12
Summary of Unique Lots of EDTA Plasma Concentrations 34

TABLE 13
Summary of Internal Standard Peak Areas 35

TABLE 14
Summary of Plasma QC Standard Concentrations with Inter- and Intra-Day Summary Statistics 37

APPENDIX A
Materials and Methods 39

APPENDIX B
Representative Chromatograms from Validation Day 50

CONTRIBUTING PERSONNEL

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Research Associate ..... Heidi Gagnon, B.S.

Director, Analytical Chemistry ..... James A. Jersey, Ph.D.

Report Coordinator ..... Brenda L. Brooks

ANALYTICAL REFERENCE STANDARD CHARACTERIZATION/STABILITY

Analytical Reference Standard:	DL-Mevalonic Acid Lactone
Common Name:	Mevalonic Acid Lactone or Mevalonolacetone or MVL
Physical Description:	White crystals
Lot Number:	47300/1 50498
Storage Conditions:	5±3 °C, desiccate, store under nitrogen
Expiration Date:	September 13, 2002 (Assigned by Primedica)
Date Received:	September 13, 2000
Amount Received:	5 grams
Supplier:	Aldrich Chemical Co.
Internal Standard:	DL-Mevalonolacetone-4,4,5,5-d_4
Common Name:	MVL-d_4
Physical Description:	Clear liquid
Lot Number:	U-295
Storage Conditions:	22±5 °C
Expiration Date:	September 11, 2002 (Assigned by Primedica)
Date Received:	September 11, 2000
Amount Received:	0.1 gram
Supplier:	Cambridge Isotope Laboratories

Characterization and Stability: The characterization of the analytical standard and internal standard is the responsibility of the Supplier, as is the method of synthesis, fabrication or derivation and stability determination.

ARCHIVAL STORAGE

Archival Storage: The original Final Report and raw data will be maintained for a minimum period of five years following submission of the final report in the Primedica-Worcester Archives in Worcester, MA. After five years the Sponsor will be contacted for disposition instructions. Archival material will be indexed by Primedica-Worcester Report #PABX-BVA-01-62.

ABSTRACT:

A procedure has been developed and validated for the determination of mevalonic acid in EDTA rat plasma. The procedure involves the conversion of mevalonic acid (MVA) to mevalonic acid lactone (MVL) and the analysis of a liquid/liquid extract by gas chromatography coupled with mass spectrometry (GC/MS) using positive chemical ionization (PCI). A mathematical factor to convert sample concentrations of MVL to MVA is included in the Laboratory Method in Appendix A. Calibration and quality control standards are prepared in water since mevalonic acid is a naturally occurring compound in plasma and concentrations vary with diet. The internal standard, MVL-d_4, was used for quantification.

The results for the validation indicate that the method is sufficiently linear, specific, reproducible and accurate to support the analysis of mevalonic acid in EDTA rat plasma samples.

INTRODUCTION:

The objective of this study was to develop and validate an analytical method for determining levels of mevalonic acid (MVA) in EDTA rat plasma.

EXPERIMENTAL DESIGN:

Overview:
The assay described in this report employed the conversion of mevalonic acid (MVA) to mevalonic acid lactone (MVL) and the analysis of liquid/liquid EDTA rat plasma samples by GC/MS using positive chemical ionization. The internal standard, MVL-d_4, was used for quantitation. The validated assay covered the concentration range of 10.0 ng/mL to 250 ng/mL of MVL in EDTA rat plasma using 100 µL sample volumes.

Materials and Methods:
Refer to Appendix A for a detailed description of materials and methods employed during the course of this validation study. In addition, quality control (QC) standards were prepared in water at the lower limit of quantiation (LLOQ QC, 10.0 mg/mL) using the same stock solutions used for the water QC standards. A set of QC standards (Low, Mid and High) was prepared in rat plasma using the same stock standards and dilution procedure used for the water QC standards. One set of solution calibration standards was prepared to mimic final extract concentration assuming 100% recovery using the same stock standards used for the calibration standards.

General Comments:
Representative raw chromatographic data from validation day 1 are provided in Appendix B.

Validation Design:

Validation Description:
The assay was comprised of five analytical runs. Three of the five analytical runs were comprised of bracketing seven-point water matrix calibration curves with six replicates of water matrix quality control (QC) samples at four concentrations, six replicates of EDTA rat plasma matrix QC samples at three concentrations and six replicates of rat matrix control samples (EDTA rat plasma with internal standard). Multiple water matrix blanks and water matrix control samples (matrix with internal standard) were analyzed in each

run. An analysis of the method recovery was included in the third analytical run, which consisted of an extracted calibration curve and a solvent calibration curve. The analysis of freeze/thaw (F/T) stability and room temperature (RT) stability, both in water and matrix, was included in the fourth analytical run. The fifth analytical run was a re-injection of the extracts from the first run to evaluate the final extract stability when stored at room temperature. Text Table 1 lists each validation analytical run and the assay performance parameters that were evaluated for the study.

TEXT TABLE 1

Validation Course

Validation Run Identification	Parameters Evaluated
Day 1	Precision, accuracy, linearity, and water/plasma equivalency
Day 2	Precision, accuracy, linearity, specificity, and water/plasma equivalency
Day 3	Precision, accuracy, linearity, recovery, dilution accuracy, precision, and water/plasma equivalency
Day 4	Freeze/thaw and room temperature stability
Day 5	6-day room temperature final extract stability

Parameters Evaluated:

Mevalonic acid is a naturally occurring compound in plasma. The concentration levels found in blank plasma were anticipated to be above the validated lower limit of quantitation (LLOQ) of 10 ng/mL. This level of background concentration would significantly skew the results of plasma QC's at the lower concentration levels. Therefore, calibration and QC standards were prepared in water matrix to evaluate precision, accuracy and linearity of the method. The second set of QC's was prepared at three concentration levels in EDTA rat plasma to evaluate the ability of the method to extract and quanitate MVL equally from water or plasma matrices. The plasma QC's were also used to evaluate matrix stability.

Water/plasma extraction equivalency was evaluated by the analysis of six replicates of each QC standard concentration levels in both water and plasma. Mean peak area counts of the isotopically labeled mevalonic acid lactone internal standard were calculated. The difference between the water and plasma mean peak areas were expressed as percent difference. The acceptable limits were ±10% difference. The isotopically labeled internal standard was used to evaluate extraction equivalency because it is chemically identical to mevalonic acid lactone and is not present in blank plasma. Therefore, the internal standard mimics the extraction behavior of mevalonic acid lactone but has no naturally occurring background concentration to interfere with the results.

Water/plasma extraction equivalency was also evaluated by the six replicates of High QC standards in both water and plasma. The endogenous concentration of mevalonic acid was low compared to the high QC concentration and did not make a significant contribution to the concentration results. Mean concentrations of mevalonic acid lactone were calculated and expressed as percent bias compared to the nominal concentration. The present bias values from the high QC in plasma were compared with the water QC and expressed as percent difference. The acceptable limits were ±10% difference.

Inter- and intra-day accuracy and precision of the method were evaluated at four concentrations by analyzing six replicates of the QC standards prepared in water over the course of three validation batches. Accuracy results are reported as % bias. Method precision for QC standards is expressed as % variance. Inter-day method precision and accuracy were also evaluated for calibration standards.

Dilution accuracy and precision was measured by analyzing six replicate dilutions of a QC standard diluted 1:5 water. Intra-day precision and accuracy was evaluated and reported as % RSD and % bias, respectively.
Recovery of the assay was evaluated by comparing the absolute peak areas in extracted standards to those obtained from solvent standards prepared to mimic final extract concentrations assuming 100% recovery.

Linearity of the method was evaluated by visual inspection of the calibration curve and examination of the correlation coefficient (r) for each standard curve.

Freeze-Thaw (F/T) stability in both water and plasma matrices were evaluated by analyzing six replicates of quality control samples prepared at two levels, which were subjected to three F/T cycles, prior to their extraction and analysis.

Room temperature stability in both water and plasma matrices were demonstrated by analyzing six replicates of QC standards prepared at two levels which were left standing at room temperature for seventy-two hours prior to their extraction and analysis.

Six-day room temperature stability of final extracts was evaluated by re-analyzing the day-one validation extracts consisting of duplicate calibration curves, six replicates of QC standards in both water and plasma matrices.
Assay specificity with respect to endogenous compounds was evaluated by assaying six unique plasma lots from untreated rats.

RESULTS AND DISCUSSION:

Validation Results:

Water/Plasma Extraction Equivalency:
The ability of the method to extract and quantitate mevalonic acid equivalently from water or plasma matrices was evaluated.

The equivalence was evaluated by the analysis of six replicates of each of three QC standard levels in water and plasma during the first three validation runs. Mean peak area counts of the internal standard (isotopically labeled mevalonic acid lactone) found for the plasma matrix QC's during each run were compared to the results for water matrix QC's. The difference was expressed as % difference. Percent difference values for the first three validation runs were 0.5%, 0.5% and 4.4%, respectively. Refer to Table 13 for a complete summary of results.

The comparison was also evaluated by the analysis of six replicates of high-QC standards in water and plasma during the first three validation runs. At this concentration level (200 ng/mL) the endogenous level of mevalonic acid was not a significant interference. Mean concentrations of found for the plasma matrix High-QC's during each run was compared to the results for water matrix High-QC's. The results were expressed as % difference. Percent difference values for the first three validation runs were –2.0%, 0.5% and 0.5%, respectively. Refer to Table 14 for a complete summary of results.

The percent difference results were all within the acceptable limits of ±10%. The extraction of mevalonic acid lactone from water and plasma are equivalent. Therefore,

the calibration curve and quality control sample prepared in water can be used to quantitate mevalonic acid lactone concentration levels in plasma.

Accuracy:
Inter-day and intra-day accuracy were acceptable for the assay of Mevalonic acid lactone in water over the concentration range of 10.0 ng/mL to 250 ng/mL.

Intra-day accuracy was evaluated by the analysis of six replicates of each of four QC standard levels in water during the first three validation runs. Mean concentrations found during each run were compared to theoretical nominal concentrations and the difference relative to theoretical nominal concentrations was expressed as % bias. Percent bias values for the lower limit of quantitation (LLOQ-QC, 10 ng/mL), low-QC (25 ng/mL), middle-QC (70 ng/mL), and high-QC (200 ng/mL) standards ranged from –4.8% to 0.1% over the three analytical runs. Refer to Table 1 for a complete summary of results.

Inter-day accuracy was evaluated by the analysis of six replicates of each of four QC standard levels in water during the first three validation runs. Mean concentrations across these runs were compared to theoretical nominal concentrations and the difference was expressed as % bias. Percent bias values ranged from –3.6% to –1.4% across concentrations. Refer to Table 1 for a complete summary of results.

The inter-day accuracy statistics for the back-calculated calibration standard concentrations are also represented by % bias. The % bias values for the calibration standards ranged from –1.6% to 1.7%. See Table 2 for a complete summary of results.

Precision:
Inter-day and intra-day precision was acceptable for the assay of mevalonic acid lactone in water over the concentration range of 10.0 ng/mL to 250 ng/mL.

Intra-day precision was evaluated by the analysis of six replicates of each of four QC standard levels in water during the first three validation runs. The intra-assay variance estimate of the interpolated concentrations for the replicate QC standards ranged from 1.3% to 4.5% across concentrations. Refer to Table 1 for a complete summary of results.
Inter-day precision was evaluated by the analysis of six replicates of each of four QC standard levels in water during the first three validation runs. The inter-assay variance estimate of the interpolated concentrations for the replicate QC standards ranged from 0.4% to 1.2% across concentrations. Refer to Table 1 for a complete summary of results.

The inter-day precision statistics for the back-calculated calibration standards ranged from 1.6% to 3.0% relative standard deviation (RSD) across concentrations and analytical runs. See Table 2 for a complete summary of results.

Dilution QC:
The dilution QC results were acceptable. Six replicates of the dilution QC with a pre-dilution concentration of 200 ng/mL, were diluted with water by a factor of 5 prior to extraction and analysis. The mean concentration found was compared to the theoretical nominal concentration (40 ng/mL) and the difference relative to the theoretical nominal concentration was expressed as % bias. The result was –1.8% bias with an RSD of 3.0%. See Table 8 for a complete summary of results.

Recovery:
Recovery values were calculated by comparison of mean duplicate spiked and extracted calibration standard peak areas in water to the peak areas obtained for solution standards prepared to mimic final extract concentrations assuming 100% recovery. Recovery ranged from 32.9% to 39.6% for mevalonic acid lactone and from 33.6% to 42.0% for the internal standard across concentrations. Refer to Tables 3 and 4 for a complete summary of results.

Linearity:
The assay was linear for mevalonic acid lactone within the calibration range of 10.0 ng/mL to 250 ng/mL.

Figure 1 shows the $1/X^2$ weighted least-squares linear regression plot with the actual spiked calibration standard data points for one of the validation runs. Linearity was also indicated by the correlation coefficients (r) obtained, which were greater than or equal to 0.998 for each of the first three validation runs. Refer to Table 5 for a summary of regression constants.

Specificity:
Mevalonic acid is a naturally occurring compound in plasma. The background concentration level in the plasma QC's was evaluated by the analysis of six replicates of control blank EDTA rat plasma matrix during the first three validation runs. The inter-assay mean concentration found was 16.6 ng/mL. Refer to Table 11 for complete results for the control blanks of plasma.

The variation of background concentration levels in EDTA rat plasma was evaluated by the analysis of six unique lots of plasma during validation Day 2. The result was a mean concentration of 15.8 ng/mL.

See Tables 12 for complete results of the six unique lots of plasma.

Stability:
The acceptable criteria for stability evaluations were a mean bias of ≤±15% from the theoretical values except for the lowest calibration, Low-QC and LLOQ QC standards, where the criteria were ≤±20%. Due to the presence of background concentrating of mevalonic acid lactone the theoretical values used for the Plasma QC standards were the mean concentrations obtain during the same analytical run from the analysis of six control Plasma QC standards.

Room temperature matrix stability was evaluated by analyzing six replicates of quality control samples prepared at two levels, in both water and EDTA rat plasma matrices, which were exposed to room temperature for 72-hours prior to their extraction and analysis. The values for % bias were within the acceptance criteria for both concentrations for the 72-hour room temperature stability assessment. Refer to Table 6 for a complete summary of the results.

Freeze/thaw matrix stability was evaluated by analyzing six replicates of QC standards prepared at two levels, in both water and EDTA rat plasma matrices that were subjected to four freeze/thaw cycles. The values for % bias were within the acceptance criteria. Refer to Table 7 for a complete summary of the results.

Six-day room temperature stability of final extracts was evaluated by re-analyzing the duplicate calibration curves and the six replicates of QC standards, in both water and EDTA rat plasma matrices, from the first day of the validation. The solvent in the extracts evaporated from the vials during the storage period. More solvent was added to each vial to reconstitute the extracts. Results from the re-analyses demonstrated that the extracts were stable for a minimum period of six days when stored at room temperature. See Tables 9 and 10 for the final extract stability results.

Studies of long-term storage stability of mevalonic acid in matrix at -20°C are ongoing.

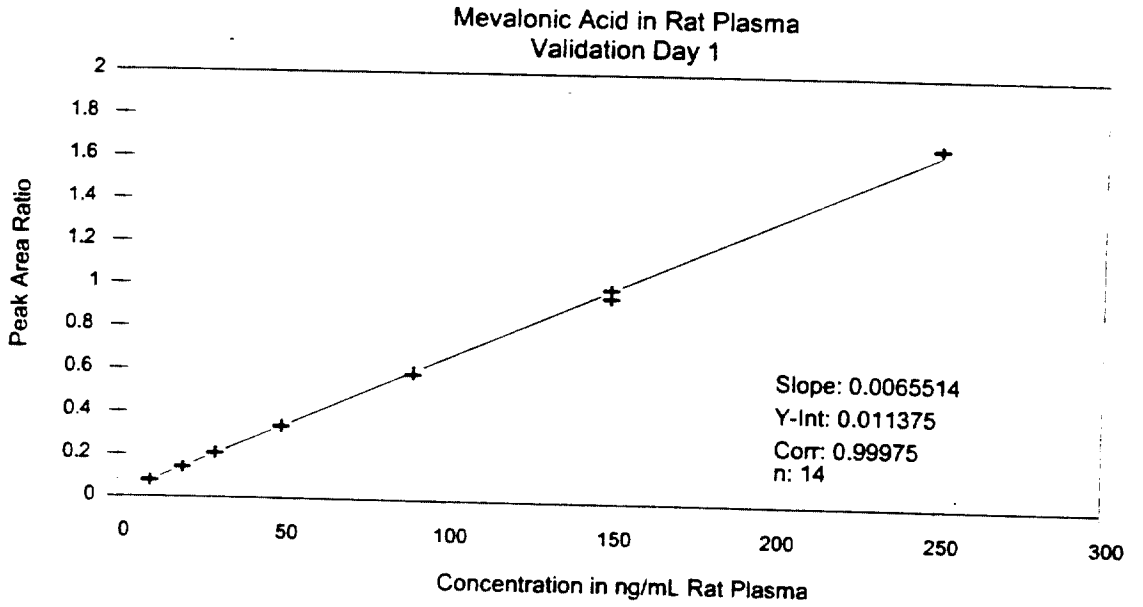
CONCLUSIONS:

Overall, the results for the validation indicated that the method was sufficiently linear, specific, reproducible and accurate to support EDTA rat plasma sample analyses for mevalonic acid content.

FIGURE

FIGURE 1

Day 1 Validation Calibration Curve



TABLES

TABLE 1

SUMMARY OF INTERPOLATED MEVALONIC ACID LACTONE QC STANDARD CONCENTRATIONS WITH INTER- AND INTRA-DAY SUMMARY STATISTICS

	Theoretical Nominal Concentrations (ng/mL)			
Day 1	10.0	25.0	70.0	200
Rep 1	9.63	23.6	70.1	202
Rep 2	8.91	25.0	68.7	200
Rep 3	9.51	25.0	67.8	196
Rep 4	9.38	23.9	68.3	196
Rep 5	9.75	24.0	67.4	195
Rep 6	9.92	23.9	69.8	199
Mean	9.52	24.2	68.7	198
n	6	6	6	6
% Bias	-4.8%	-3.2%	-1.9%	-1.0%

	Theoretical Nominal Concentrations (ng/mL)			
Day 2	10.0	25.0	70.0	200
Rep 1	9.87	24.4	69.9	202
Rep 2	9.29	24.8	68.1	195
Rep 3	10.3	24.1	68.4	195
Rep 4	9.07	23.8	68.2	193
Rep 5	9.10	24.8	68.0	194
Rep 6	10.2	24.5	67.3	195
Mean	9.64	24.4	68.3	196
n	6	6	6	6
% Bias	-3.6%	-2.4%	-2.4%	-2.0%

TABLE 1 (Concluded)

SUMMARY OF INTERPOLATED MEVALONIC LACTONE ACID QC STANDARD CONCENTRATIONS WITH INTER- AND INTRA-DAY SUMMARY STATISTICS

	Theoretical Nominal Concentrations (ng/mL)			
Day 3	10.0	25.0	70.0	200
Rep 1	9.49	23.9	70.6	198
Rep 2	10.1	25.2	70.1	197
Rep 3	9.49	25.4	70.6	200
Rep 4	9.96	24.6	70.0	198
Rep 5	9.84	24.8	70.0	199
Rep 6	NA	23.5	69.0	188
Mean	9.78	24.6	70.1	197
n	5	6	6	6
% Bias	-2.2%	-1.6%	0.1%	-1.5%
Intra-assay variance estimate	4.5%	2.5%	1.3%	1.8%
Inter-assay variance estimate	1.2%	0.7%	1.2%	0.4%
Inter-day Mean	9.64	24.4	69.0	197
n	17	18	18	18
% Bias	-3.6%	-2.4%	-1.4%	-1.5%

NA = Not Available. This sample was accidentally spilled during preparation

TABLE 2

SUMMARY OF BACK-CALCULATED MEVALONIC ACID LACTONE CALIBRATION STANDARD CONCENTRATIONS

	Theoretical Nominal Concentrations (ng/mL)						
	10.0	20.0	30.0	50.0	90.0	150	250
Day 1	9.90	20.0	30.7	50.6	89.5	151	254
	10.1	20.0	30.0	49.7	88.1	144	254
Day 2	9.84	19.5	29.6	50.4	90.8	152	250
	10.3	19.3	31.6	49.2	91.7	146	250
Day 3	10.3	19.7	30.5	51.7	91.7	147	261
	9.54	20.9	30.6	47.8	84.8	146	251
Mean	10.0	19.9	30.5	49.9	89.4	148	253
Std. Dev.	0.296	0.562	0.681	1.34	2.66	3.14	4.18
n	6	6	6	6	6	6	6
%RSD	3.0%	2.8%	2.2%	2.7%	3.0%	2.1%	1.6%
% Bias	0.0%	-0.5%	1.7%	-0.2%	-0.6%	-1.6%	1.3%

TABLE 3

MEVALONIC ACID LACTONE EXTRACTION DATA & RECOVERY CALCULATIONS

	Extracted Standards Mean Response Areas	Solution Standards Response Areas	% Recovery
Std 1	417.5	1066	39.2%
Std 2	785	1981	39.6%
Std 3	1057.5	2963	35.7%
Std 4	1896	4975	38.1%
Std 5	3144	8678	36.2%
Std 6	4693.5	14279	32.9%
Std 7	8433	25380	33.2%
		Mean	36.4%
		Std. Dev.	0.0327
		% RSD	7.4%

TABLE 4

INTERNAL STANDARD EXTRACTION DATA & RECOVERY CALCULATIONS

	Extracted Standards Mean Response Area	Solution Standards Response Area	% Recovery
Std 1	6142	15019	40.9%
Std 2	5876	14959	39.3%
Std 3	5365	15158	35.4%
Std 4	6004	14283	42.0%
Std 5	5657	14739	38.4%
Std 6	5117.5	15226	33.6%
Std 7	5274.5	15286	34.5%
		Mean	37.7%
		Std. Dev.	0.0327
		% RSD	8.7%

TABLE 5

SUMMARY OF LEAST-SQUARES LINEAR REGRESSION CONSTANTS AND ANALYSIS DATES

	Slope	Intercept	Correlation Coefficient (r)	Analysis Date
Day 1	0.0065514	0.0113750	0.99975	10/17/00
Day 2	0.0063508	0.0082756	0.99939	10/18/00
Day 3	0.0062253	0.0067910	0.99884	10/19/00
Day 4	0.0062800	0.0060925	0.99891	10/20/00
Day 5	0.0065156	0.0112850	0.99981	10/23/00

TABLE 6

SUMMARY OF QC STANDARD 72-HOUR ROOM TEMPERATURE STABILITY IN MATRIX

WATER QC's

	Theoretical Nominal Concentrations (ng/mL)	
	25.0	200
Rep 1	23.8	189
Rep 2	23.1	191
Rep 3	23.8	193
Rep 4	22.9	193
Rep 5	23.0	194
Rep 6	22.9	194
Mean	23.3	192
Std. Dev.	0.432	1.97
n	6	6
%RSD	1.9%	1.0%
% Bias	-6.8%	-4.0%

EDTA RAT PLASMA QC's

	Theoretical Nominal Concentrations (ng/mL)	
	34.2*	192*
Rep 1	35.1	199
Rep 2	34.2	200
Rep 3	34.0	197
Rep 4	33.2	195
Rep 5	33.6	194
Rep 6	33.5	188
Mean	33.9	196
Std. Dev.	0.674	4.32
n	6	6
%RSD	2.0%	2.2%
% Bias	-0.9%	2.1%

* = Mean concentration of six control Plasma QC's analyzed in the same analytical batch.

TABLE 7

SUMMARY OF QC STANDARD FREEZE/THAW (3 CYCLES) STABILITY IN MATRIX

WATER QC's

	Theoretical Nominal Concentrations (ng/mL)	
	25.0	200
Rep 1	24.3	194
Rep 2	23.6	194
Rep 3	23.2	194
Rep 4	23.8	194
Rep 5	23.0	196
Rep 6	23.3	192
Mean	23.5	194
Std. Dev	0.472	1.26
n	6	6
%RSD	2.0%	0.6%
% Bias	-6.0%	-3.0%

EDTA RAT PLASMA QC's

	Theoretical Nominal Concentrations (ng/mL)	
	34.2*	192*
Rep 1	33.5	194
Rep 2	34.4	200
Rep 3	32.9	197
Rep 4	33.6	193
Rep 5	32.3	190
Rep 6	32.4	184
Mean	33.2	193
Std. Dev	0.804	5.59
n	6	6
%RSD	2.4%	2.9%
% Bias	-2.9%	0.5%

* = Mean concentration of six control Plasma QC's analyzed in the same analytical batch.

TABLE 8

SUMMARY OF INTERPOLATED MEVALONIC ACID LACTONE DILUTION QC CONCENTRATIONS FOR DILUTION VALIDATION

	Theoretical Nominal Concentration (ng/mL)
	200 *
Rep 1	40.4
Rep 2	39.5
Rep 3	40.7
Rep 4	38.1
Rep 5	38.9
Rep 6	37.9
Mean	39.3
Std. Dev	1.16
n	6
%RSD	3.0%
% Bias	-1.8%

* = Dilution QC's undiluted concentration was 200 ng/mL (1:5 dilution performed prior to extraction and analysis)

TABLE 9

6-DAY ROOM TEMPERATURE FINAL EXTRACT STABILITY BACK-CALCULATED CALIBRATION STANDARD CONCENTRATIONS

	Theoretical Nominal Concentrations (ng/mL)						
	10.0	20.0	30.0	50.0	90.0	150	250
	9.87	19.8	30.2	50.2	89.9	150	254
	10.2	19.7	30.5	49.4	90.6	146	253
Mean	10.0	19.8	30.4	49.8	90.3	148	254
n	2	2	2	2	2	2	2
% Bias	0.4%	-1.3%	1.2%	-0.4%	0.3%	-1.3%	1.4%

TABLE 10

6-DAY ROOM TEMPERATURE FINAL EXTRACT STABILITY QUALITY CONTROL STANDARD CONCENTRATIONS

WATER QC'S

	Theoretical Nominal Concentrations (ng/mL)			
	10.0	25.0	70.0	200
Rep 1	9.89	24.3	68.8	198
Rep 2	9.17	25.1	67.7	198
Rep 3	10.5	25.5	68.7	197
Rep 4	9.75	24.4	68.3	200
Rep 5	10.7	24.7	67.7	198
Rep 6	10.1	24.3	69.9	199
Mean	10.0	24.7	68.5	198
Std. Dev.	0.550	0.492	0.826	1.03
n	6	6	6	6
%RSD	5.5%	2.0%	1.2%	0.5%
% Bias	0.0%	-1.2%	-2.1%	-1.0%

EDTA RAT PLASMA QC'S

	Theoretical Nominal Concentrations (ng/mL)		
	33.1	73.9	194*
Rep 1	35.0	73.5	195
Rep 2	34.4	75.6	189
Rep 3	32.8	76.2	192
Rep 4	32.2	71.4	191
Rep 5	31.6	70.7	186
Rep 6	33.7	74.9	185
Mean	33.3	73.7	190
Std. Dev.	1.31	2.26	3.78
n	6	6	6
%RSD	3.9%	3.1%	2.0%
% Bias	0.6%	-0.3%	-2.1%

* = Mean concentration obtained on the first day of validation

TABLE 11

SUMMARY OF CONTROL BLANK EDTA RAT PLASMA CONCENTRATIONS

	Concentrations (ng/mL)		
	Day 1	Day 2	Day 3
Rep 1	16.4	16.5	17.0
Rep 2	16.2	15.9	16.8
Rep 3	16.6	16.3	16.8
Rep 4	17.4	17.4	17.3
Rep 5	16.3	16.1	17.1
Rep 6	15.8	16.2	17.0
Mean	16.5	16.4	17.0
Std. Dev.	0.536	0.529	0.190
n	6	6	6
%RSD	3.2%	3.2%	1.1%
Inter-Assay Mean	16.6		
n	18		
Std. Dev.	0.506		
%RSD	3.0%		

TABLE 12

SUMMARY OF UNIQUE LOTS OF EDTA RAT PLASMA CONCENTRATIONS

	Concentrations (ng/mL)
Lot 1	11.0
Lot 2	16.2
Lot 3	16.8
Lot 4	16.1
Lot 5	17.6
Lot 6	17.0
Mean	15.8
Std. Dev.	2.41
n	6
%RSD	15.3%

TABLE 13

SUMMARY OF INTERNAL STANDARD PEAK AREAS

Water QC's

		Day 1	Day 2	Day 3
Low-QC	Rep 1	4096	4303	5191
	Rep 2	4380	4861	5911
	Rep 3	5310	5511	6016
	Rep 4	4968	6253	5585
	Rep 5	4124	5620	6203
	Rep 6	6187	6437	3846
Mid-QC	Rep 1	4323	4827	4928
	Rep 2	4390	5502	5230
	Rep 3	4522	5757	5681
	Rep 4	4777	5771	5479
	Rep 5	5024	5881	5960
	Rep 6	6314	6632	5452
High-QC	Rep 1	4021	4124	5197
	Rep 2	5545	5015	5314
	Rep 3	4246	5029	6189
	Rep 4	3568	3950	5978
	Rep 5	5531	5027	7684
	Rep 6	5458	6200	6335
	Mean Area	4821	5372	5677

TABLE 13 (Concluded)

SUMMARY OF INTERNAL STANDARD PEAK AREAS

Plasma QC's

		Day 1	Day 2	Day 3
Low-QC	Rep 1	4700	4503	6100
	Rep 2	4321	5363	6151
	Rep 3	3850	6736	6067
	Rep 4	5084	5184	5909
	Rep 5	3350	6350	5159
	Rep 6	5138	5493	6755
Mid-QC	Rep 1	3988	4091	5413
	Rep 2	4580	5157	6040
	Rep 3	4925	6063	6238
	Rep 4	4477	3722	6216
	Rep 5	5132	5601	6049
	Rep 6	4988	6044	5746
High-QC	Rep 1	6540	4445	5985
	Rep 2	5208	5474	5811
	Rep 3	5002	6088	5615
	Rep 4	6790	4231	6084
	Rep 5	5671	7133	5879
	Rep 6	3508	5471	5467
	Mean Area	4847	5397	5927

Comparison of Plasma QC vs Water QC Mean Areas

% Difference	0.5%	0.5%	4.4%

TABLE 14

SUMMARY OF PLASMA QC STANDARD CONCENTRATIONS WITH INTER- AND INTRA-DAY SUMMARY STATISTICS

	Theoretical Nominal Concentrations (ng/mL)		
Day 1	25.0	70.0	200
Rep 1	34.5	75.7	198
Rep 2	33.4	74.3	191
Rep 3	32.4	75.3	192
Rep 4	33.0	71.8	199
Rep 5	32.2	72.7	193
Rep 6	33.2	73.3	190
Mean	33.1	73.9	194
n	6	6	6
% Bias	32.4%	5.6%	-3.0%
% Difference vs Water QC (Table 1)			-2.0%

	Theoretical Nominal Concentrations (ng/mL)		
Day 2	25.0	70.0	200
Rep 1	34.3	76.4	198
Rep 2	33.2	75.9	194
Rep 3	33.0	76.9	202
Rep 4	33.4	75.3	194
Rep 5	34.8	78.3	194
Rep 6	35.1	78.4	199
Mean	34.0	76.9	197
n	6	6	6
% Bias	36.0%	9.9%	-1.5%
% Difference vs Water QC (Table 1)			0.5%

TABLE 14 (Concluded)

SUMMARY OF PLASMA QC STANDARD CONCENTRATIONS WITH INTER- AND INTRA-DAY SUMMARY STATISTICS

	Theoretical Nominal Concentrations (ng/mL)		
Day 3	25.0	70.0	200
Rep 1	34.9	75.5	198
Rep 2	34.5	76.8	197
Rep 3	35.1	77.1	199
Rep 4	34.2	77.9	195
Rep 5	34.7	76.0	202
Rep 6	35.7	74.7	195
Mean	34.9	76.3	198
n	6	6	6
% Bias	39.6%	9.0%	-1.0%
% Difference vs Water QC (Table 1)			0.5%
Intra-assay variance estimate	2.3%	1.8%	1.7%
Inter-assay variance estimate	2.4%	2.0%	0.8%
Inter-Assay Mean	34.0	75.7	196
n	18	18	18
% Bias	36.0%	8.1%	-2.0%

APPENDIX A
LABORATORY METHOD

PRIMEDICA CORPORATION

Worcester, Massachusetts

Laboratory Method For
Analysis of Mevalonic Acid in Rat Plasma By GC/MSD

LM Number MVAL00

Revision Number 00

Effective Date November 1, 2000

Page 1 of 12

Prepared By: Mark Netzel Date: 11/8/00

Reviewed By: Brian S Ille Date: 11/08/00

Authorized By: James Jersey, Ph.D. Date: 11/8/00
Director of Bioanalytical Chemistry

1 Purpose

The purpose of this Laboratory Method (LM) is to describe procedures to accurately determine the concentrations of mevalonic acid in rat plasma samples by GC/MSD.

2 Scope

The procedures provided in this LM are applicable for the quantification of mevalonic acid in rat plasma EDTA. During the extraction mevalonic acid (MVA) is converted to mevalonic acid lactone (MVL). The validated calibration range is 10.0 ng/mL to 250 ng/mL of mevalonic acid lactone in rat plasma EDTA. The results can be converted to the units of pmol/mL of mevalonic acid in rat plasma EDTA using the conversion described in the calculation section below.

3 Definitions/Abbreviations

GC:	Gas Chromatography
MSD:	Mass Selective Detector
IS:	Internal Standard
MVA:	Mevalonic Acid
MVL:	Mevalonic Acid Lactone or DL-Mevalonic Acid Lactone or Mevalonolactone
MVL-d_4:	DL-Mevalonolactone-4,4,5,5-d_4
QC:	Quality Control
G:	Gravitational Constant

4 Materials

4.1 Chemicals

DL-Mevalonic acid lactone, Sigma Chemical Co., approximately 97% grade, or equivalent
DL-Mevalonolactone-4,4,5,5-d_4, Cambridge Isotope Laboratories, Inc., 98% grade, or equivalent
Ethyl acetate, J.T. Baker, HPLC grade or equivalent
Methylene chloride, J.T. Baker, HPLC grade or equivalent
2-Propanol (isopropyl alcohol), EM Science, HPLC grade or equivalent
Formic acid, J.T. Baker, reagent grade or equivalent
Chloroform, J.T. Baker, HPLC grade or equivalent
Sodium sulfate, Aldrich, reagent grade, or equivalent
Deionized water, Millipore Milli-Q water, or equivalent
Helium, Northeast Airgas, Inc., ultra high purity or equivalent

Isobutane, Matheson Gas Products, research grade or equivalent
Hexanes, J.T. Baker, HPLC grade or equivalent
Pooled rat blank plasma EDTA

4.2 Consumables

Disposable 15 mL conical bottom polypropylene test tubes
Pipetman and tips
Eppendorf repeater and tips
Disposable polyethylene transfer pipettes or equivalent
Glass crimp top autosampler vials with flat bottom inserts or equivalent
Polypropylene vials with o-ring sealed caps or equivalent

4.3 Equipment

VWR Multi-Tube Vortexer or equivalent
Lab Industries Pipet Dispenser or equivalent
Beckman GS-6KR centrifuge or equivalent
Zymark Turbovap LV Evaporator or equivalent
AND ER-182A analytical balance or equivalent
J&W GC column, DB-210, 30 m, 0.25 mm ID, 0.25 µm film thickness or equivalent
Hewlett Packard 7683 injector or equivalent
Hewlett Packard 6890 gas chromatograph or equivalent
Hewlett Packard 5973 mass selective detector or equivalent
Hewlett Packard ChemStation (G1701BA, Revision B.01.00) or equivalent
Microsoft Excel 97 version SR-2 or equivalent

Note: Equipment, reagents, or consumables can be substituted provided that equivalent assay performance is demonstrated.

5 Procedure

This method has been validated for the analysis of mevalonic acid (as mevalonic acid lactone) in rat plasma EDTA by GC/MSD using 100 µL sample volumes. The validated concentration range is 10.0 ng/mL to 250 ng/mL of mevalonic acid lactone in rat plasma EDTA. The conversion of the results to pmol/mL of mevalonic acid in rat plasma EDTA is described in the calculations section below. Note that the calibration curve and quality control standards are all prepared in water, not plasma. Mevalonic acid is a naturally occurring compound in plasma and concentrations will vary with diet. Concentrations found in pooled lots of blank rat plasma EDTA during the method validation were approximately 17 ng/mL. This background concentration level would interfere with the quantitation, especially at the lower calibration level. This method has been validated to use water matrix calibration curves and quality control samples. The validation demonstrated that the mevalonic acid lactone calculated results for the water matrix is equivalent to rat plasma EDTA.

5.1 Preparation of Reagents

Note: Other volumes than those specified may be prepared using the same proportions.

5.1.1 Methylene Chloride:2-Propanol, (90:10, v:v) Solution

Combine 900 mL of methylene chloride with 100 mL of 2-propanol and mix. Store at room temperature. The expiration date for this solution is one week after preparation.

5.2 Preparation of Internal Standard Solutions

Concentration calculations are based on assuming that the standard reference materials are 100% pure unless noted otherwise. The following standard preparation scheme is a suggested approach. Appropriate modifications to reach the targeted nominal concentrations are acceptable and will be documented in the study notebook. All standard solutions will be stored at ≤-20°C unless noted otherwise. The expiration dates for these solutions are six months after preparation unless noted otherwise. Ongoing stability studies may change the expiration dates.

5.2.1 Internal Standard Stock (ISA)

MVL-d_4 is a liquid at room temperature and is purchased in vials containing approximately 100 mg. Weigh the vial and MVL-d_4. Transfer the MVL-d_4 to a 50 mL volumetric flask. Weigh the empty vial. Subtract the weights to obtain the amount of MVL-d_4 in the volumetric flask. Bring to volume with Milli-Q water and mix. The nominal MVL-d_4 IS concentration of this solution is 2000 µg/mL.

5.2.2 Internal Standard Spiking Solution

Transfer 20.0 µL of internal standard stock (ISA) into a 100 mL volumetric flask. Dilute to volume with Milli-Q water and mix. The nominal MVL-d_4 concentration of this solution is 400 ng/mL.

5.3 Preparation of Calibration Standard Stock Solutions

The following standard preparation scheme is a suggested approach. Appropriate modifications to reach the targeted nominal concentrations are acceptable and will be documented in the project notebook. For example, if the targeted nominal concentration is not achieved when preparing the analytical calibration stocks, the volume of the stock solutions used in subsequent dilutions can be modified so that the nominal calibration standard spiking solution concentrations are achieved. Standard reference materials are assumed to be 100% pure. Standard weights listed are not corrected for purity. All standard solutions will be stored at ≤-20°C unless noted otherwise. Ongoing stability studies are establishing the expiration dates of these solutions.

5.3.1 MVL Primary Stock (A)

Note that MVL is hydroscopic. A large amount of MVL is used and it is weighed out quickly to minimize the effects of absorbing moisture out of the air. Store the analytical reference standard under an inert gas such as nitrogen.

Weigh out approximately 100 mg of MVL and transfer it into a 100 mL volumetric flask. Bring to volume with ethyl acetate and mix. The nominal MVL concentration of this solution is 1000 µg/mL.

5.3.2 Secondary Stock (B)

Transfer 3.75 mL of the Primary Stock (A) into a 25.0 mL volumetric flask. Bring to volume with ethyl acetate and mix. The nominal MVL concentration of this solution is 150 µg/mL.

5.3.3 Preparation of Calibration Standard Spiking (CSS) Solutions

The following standard preparation scheme is a suggested approach. Appropriate modifications to reach the targeted nominal concentrations are acceptable and will be documented in the study notebook. All standard solutions will be stored at ≤-20°C unless noted otherwise. Ongoing stability studies are establishing the expiration dates of these solutions.

5.3.4 Prepare CSS solutions in 25.0 mL volumetric flasks as shown in the table below. All solutions are brought to volume with ethyl acetate. Final volumes of these calibration standard spiking solutions can be adjusted as long as proportionality is maintained and their preparation is properly documented in the study notebook.

Calibration Standard Spiking Solution Preparation					
Spiking Solution ID	Stock Solution ID	Stock Solution Volume (µL)	Stock Solution Concentration (µg/mL)	Spiking Solution Final Volume (mL)	Spiking Solution Concentration (ng/mL)
CSS-1	Secondary Stock B	168	150	25.0	1010
CSS-2	Secondary Stock B	337	150	25.0	2020
CSS-3	Secondary Stock B	505	150	25.0	3030
CSS-4	Secondary Stock B	842	150	25.0	5050
CSS-5	Primary Stock A	227	1000	25.0	9090
CSS-6	Primary Stock A	379	1000	25.0	15150
CSS-7	Primary Stock A	631	1000	25.0	25250

5.3.5 Once prepared, aliquot the Calibration Spiking Solutions (suggested approximately 0.6 mL volumes) into plastic vials with o-ring sealed caps and store them at ≤-20°C until the time of analysis.

5.4 Preparation of Calibration Standards (STD) in Water

Prepare calibration standards on the day of analysis by combining 2.50 mL of Milli-Q water, individually, with 0.0250 mL of the respective Calibration Spiking Solution (CSS) followed by mixing. The final concentration in water is listed in the table below.

Calibration Standard Preparation					
Calibration Standard ID	Water Volume (mL)	Spiking Solution Volume Added (mL)	Spiking Solution ID	Spiking Solution Concentration (ng/mL)	Final Nominal Plasma Conc. (ng/mL)
STD 1	2.50	0.0250	CSS-1	1010	10.0
STD 2	2.50	0.0250	CSS-2	2020	20.0
STD 3	2.50	0.0250	CSS-3	3030	30.0
STD 4	2.50	0.0250	CSS-4	5050	50.0
STD 5	2.50	0.0250	CSS-5	9090	90.0
STD 6	2.50	0.0250	CSS-6	15150	150
STD 7	2.50	0.0250	CSS-7	25250	250

5.5 Preparation of Quality Control (QC) Stock Solutions

The following standard preparation scheme is a suggested approach. Appropriate modifications to reach the targeted nominal concentrations are acceptable and will be documented in the project notebook. Standard reference materials are assumed to be 100% pure. Standard weights listed are not corrected for purity. All standard solutions will be stored at ≤-20°C unless noted otherwise. Ongoing stability studies are establishing the expiration dates of these solutions.

5.5.1 Primary QC Stock (AA)

Note that MVL is hydroscopic. A large amount of MVL is used and it is weighed out quickly to minimize the effects of absorbing moisture out of the air. Store the analytical reference standard under an inert gas such as nitrogen.

Weigh out approximately 100 mg of MVL and transfer it into a 100 mL volumetric flask. Bring to volume with ethyl acetate and mix. The nominal MVL concentration of this solution is 1000 µg/mL.

5.5.2 Secondary QC Stock (BB)

Transfer 5.00 mL of the Primary QC Stock (AA) into a 25.0 mL volumetric flask. Bring to volume with ethyl acetate and mix. The nominal MVL concentration of this solution is 200 µg/mL.

5.6 Preparation of Quality Control Spiking Solutions (QCSS)

The following standard preparation scheme is a suggested approach. Appropriate modifications to reach the targeted nominal concentrations are acceptable and will be documented in the study notebook. All standard solutions will be stored at ≤-20°C unless noted otherwise. Ongoing stability studies are establishing the expiration dates of these solutions.

Prepare QCSS solutions in 25.0 mL volumetric flasks as shown in the table below. All solutions are brought to volume with ethyl acetate. Final volumes of these quality control spiking solutions can be adjusted as long as proportionality is maintained and their preparation is properly documented in the study notebook.

QC Standard Spiking Solution Preparation					
Spiking Solution ID	Stock Solution ID Used	Stock Solution Volume (µL)	Stock Solution Conc. (µg/mL)	Spiking Solution Final Volume (mL)	Spiking Solution Conc. (ng/mL)
QCSS-LOW	Secondary QC Stock BB	316	200	25.0	2525
QCSS-MED	Secondary QC Stock BB	884	200	25.0	7070
QCSS-HIGH	Primary QC Stock AA	505	1000	25.0	20200

5.7 Preparation of Quality Control (QC) Standards in Water

Combine 100 mL of Milli-Q water, individually, with 1.00 mL of each Quality Control Spiking Solution (QCSS) as shown on the table below.

Quality Control Standard Preparation					
Quality Control Standard ID	Stock Solution ID	Stock Solution Concentration (ng/mL)	Stock Solution Spiking Volume (mL)	Final Volume. (mL)	QC Standard Concentration (ng/mL)
Low QC	QCSS-LOW	2525	1.00	100	25.0
Mid QC	QCSS-MED	7070	1.00	100	70.0
High QC	QCSS-HIGH	20200	1.00	100	200

5.7.1 Once prepared, aliquot the QC standards (suggested approximately 1.2 mL volumes) into plastic vials with o-ring sealed caps and store them at ≤-20°C until the time of analysis.

5.8 Sample Extraction

5.8.1 Transfer 100 µL of each standard (total of 14), method blanks (in duplicate), control blanks (in duplicate), Quality Control Standards (duplicates at three concentration levels), and study samples into individual 15 mL conical bottom polypropylene test tubes.

5.8.2 Add 50.0 µL of Milli-Q water to each method blank.

5.8.3 Add 50.0 µL of the Internal Standard Spiking Solution to each tube except for the method blanks.

5.8.4 Vortex the tubes for a minimum of 5 seconds.

5.8.5 Add 0.100 mL of formic acid to each tube and vortex for a minimum of 5 seconds.

5.8.6 Allow tubes to sit on the bench for approximately 30 minutes to allow time for the conversion of MVA to MVL.

5.8.7 Add 0.800 mL of Milli-Q water to each tube and vortex for a minimum of 5 seconds.

5.8.8 Add 0.500 mL of chloroform to each tube and vortex for a minimum of 5 seconds. Note: a pipet dispenser may be used to add this reagent.

5.8.9 Centrifuge the tubes approximately 5 minutes at approximately 3500 rpm (approximately 2500 G). Distinct layers should form in each sample tube. Centrifuge again any sample which does not have distinct layers.

5.8.10 Transfer the top (aqueous) layer into new individual 15 mL conical bottom polypropylene test tubes and discard the choroform layer.

5.8.11 Saturate the aqueous layer with sodium sulfate. (Note: approximately 0.15 grams of sodium sulfate is plenty to saturate the aqueous layer. A measuring spoon may be used to add the sodium sulfate because the exact weight is not critical.)

5.8.12 Add 1.0 mL of methylene chloride:2-propanol solution to each tube containing the aqueous layer and vortex for a minimum of 5 seconds. Note: a pipet dispenser may be used to add this reagent.

5.8.13 Centrifuge the tubes approximately 5 minutes at approximately 3500 rpm (approximately 2500 G).

5.8.14 Transfer the bottom (organic) layer into new 15 mL conical bottom polypropylene test tubes.

5.8.15 Repeat the previous three steps.

5.8.16 Evaporate the organic layer to dryness in a Turbovap at 40 ±5°C at approximately 10 psi.

5.8.17 Add 50 uL of the ethyl acetate to each tube and vortex for a minimum of 5 seconds.

5.8.18 Transfer into crimp top autosampler vials with flat bottom inserts. Extracts are stable in autosampler vials stored at room temperature for up to 6 days. Note: If the extracts evaporate to dryness while waiting for analysis they may be reconstituted with more ethyl acetate before injecting.

5.9 Analytical Conditions

GC/MSD analysis is performed as follows:

5.9.1 Oven

Column:	J&W, DB-210, 30 m, 0.25 mm ID, 0.25 µm film thickness		
Initial Temperature:	50°C		
Initial Time:	1.50 minutes		
Oven Ramp:	Rate (°C/min.)	Final Temp. (°C)	Final Time (min.)
	30.0	160	3.50
	50.0	230	3.50
Run Time:	approximately 14 minutes		

5.9.2 Inlet

Injection Volume:	1 µL
Rinse Solvent:	Hexanes
Mode:	Splitless
Temperature:	240 °C
Purge Flow:	50.0 mL/minute
Purge Time:	0.75 minutes
Gas Type:	Helium
Initial Flow:	3.5 mL/minute
Flow Ramp:	Constant Flow Mode

5.9.3 Mass Selective Detector

Source:	Chemical Ionization (CI)
Source Mode:	Positive
CI Gas:	Isobutane
Flow Control Setting:	20
Acquisition Mode:	Selective Ion Monitoring (SIM)
Solvent Delay:	6.0 minutes (may be adjusted to be as long as possible without eliminating the first peak of interest)
MS Quad:	106°C
MS Source:	250°C
MSD Transfer Line:	250°C

5.9.4 Ions Monitored:

5.9.4.1 Group 1: Start time approximately 6.00[3]

Compound Name	Nominal Ion (m/z)	Dwell Time[1] (msec.)	Retention Time[2] (min.)
MVL	131	100	7.2
MVL-d_4	135	100	7.2

[1] = Dwell times may be modified to optimize performance.
[2] = Approximate retention time (RT) for a new column. Actual RT may vary as the column is shortened during maintenance. The RT is confirmed using the isotopically labeled internal standard.
[3] = Start time may be adjusted.

5.10 Analytical Run Sequence and Composition

Each analytical run will be comprised of bracketing water calibration curves (7 points) each with a water method blank sample (water with neither analyte nor internal standard spiked) and a water control blank (water with only internal standard included). Duplicate water QC standards at each of the three concentrations will be interspersed between the calibration curves.
Plasma Dilution QC's will be analyzed within analytical batches in which plasma samples are analyzed at a dilution. The dilution of plasma samples and plasma QC's will be performed using water as the diluent.

5.11 Calculations

5.11.1 Chromatograms will be automatically integrated and visually inspected for an acceptable integration using HP ChemStation (or equivalent). Manual integrations will be performed when necessary.

5.11.2 Compute the $1/X^2$-weighted least-squares linear regression relating the peak area ratios (relative to internal standard) of the calibration standards to their respective nominal concentration (ng/mL of MVL in water) using validated Excel spreadsheets (or equivalent).

5.11.3 Using the peak area ratios of the analyte (relative to the internal standards) in the samples and the appropriate regression equation constants, determine the concentration in ng/mL of MVL in water or plasma for all standards and samples using validated Excel spreadsheets (or equivalent). Correct for dilutions if appropriate.

5.11.4 If requested, the units of ng/mL of MVL in water or plasma may be converted to pmol/mL of MVA in water or plasma by multiplying by a unit conversion value (1000 pmol g/mol ng) and dividing by the molecular weight of MVL (130.14 g/mol). Below is an example showing the conversion of a sample concentration of 25 ng/mL of MVL in plasma.

$$\frac{25.0\ \cancel{ng}}{mL} \times \frac{1000\ pmol\ \cancel{g}}{\cancel{mol}\ \cancel{ng}} \times \frac{1\ \cancel{mol}}{130.14\ \cancel{g}} = \frac{192\ pmol}{mL}$$

5.12 Acceptance Criteria

5.12.1 Calibration Standards

5.12.1.1 The lower limit of quantitation (LLOQ) standard's back-calculated concentration must be within ±20% of theoretical nominal concentration.

5.12.1.2 All other standards' back-calculated concentration must be within ±15% of their nominal theoretical concentrations.

5.12.1.3 A minimum of 75% of the calibration standards must meet the back-calculated concentration criteria. (Note: this limit will be rounded down when using 14 calibration standards. Thus, a maximum of 4 standards may be rejected when analyzing a total of 14 calibration standards in a batch.)

5.12.1.4 At least one standard at the LLOQ and at the upper limit of quantitation (ULOQ) must meet the back-calculated concentration criteria.

5.12.2 Quality Control (QC) Standards

5.12.2.1 The lowest level QC's calculated concentration must be within ±20% of the nominal theoretical concentration.

5.12.2.2 All other QC's calculated concentration must be within ±15% of their nominal theoretical concentration

5.12.2.3 A minimum of 66% of all QC's must meet the calculated concentration criteria.

5.12.2.4 At least one QC at each concentration level must meet the calculated concentration criteria.

5.12.3 Blanks and Controls

A control blank should have a response (peak area ratio) less than or equal to 33% of the lowest accepted LLOQ calibration standard

The control blanks (in water) should have a response (peak area ratio) ≤33% of the lowest accepted LLOQ calibration standard.

5.13 Data Reporting

5.13.1 Sample concentrations less than the lowest calibration standard will be flagged as Below the Quantitation Limit (BQL).

5.13.2 Sample concentrations greater than the highest calibration standard will be appropriately diluted with Milli-Q water, re-extracted, and re-analyzed, provided that enough sample volume remains. If there is insufficient sample available, the original result will be reported as Above the Quantitation Limit (AQL).

6 Revision History

Initial laboratory method.

APPENDIX B

REPRESENTATIVE CHROMATOGRAMS FROM VALIDATION DAY 1

Sequence Name: D:\MSD_DATA\PAB\PABX-BVA\1-062-1\1-062-1.S
Comment: PABX-BVA-1-62
Operator: MAN
Data Path: D:\MSD_DATA\PAB\PABX-BVA\1-062-1\
Pre-Seq Cmd:
Post-Seq Cmd:

Method Sections To Run
(X) Full Method
( ) Reprocessing Only

On A Barcode Mismatch
(X) Inject Anyway
( ) Don't Inject

Line	Type	Vial	DataFile	Method	Sample Name
1	Sample	1	0621001	PABX_BVA	1x Blank Water
2	Sample	2	0621002	PABX_BVA	1x Std-1 Water
3	Sample	3	0621003	PABX_BVA	1x Std-2 Water
4	Sample	4	0621004	PABX_BVA	1x Std-3 Water
5	Sample	5	0621005	PABX_BVA	1x Std-4 Water
6	Sample	6	0621006	PABX_BVA	1x Std-5 Water
7	Sample	7	0621007	PABX_BVA	1x Std-6 Water
8	Sample	8	0621008	PABX_BVA	1x Std-7 Water
9	Sample	9	0621009	PABX_BVA	1x Control Water
10	Sample	10	0621010	PABX_BVA	1x QC HIGH Water
11	Sample	11	0621011	PABX_BVA	1x QC MID Water
12	Sample	12	0621012	PABX_BVA	1x QC LOW Water
13	Sample	13	0621013	PABX_BVA	1x QC LLOQ Water
14	Sample	14	0621014	PABX_BVA	1x QC HIGH Plasma
15	Sample	15	0621015	PABX_BVA	1x QC MID Plasma
16	Sample	16	0621016	PABX_BVA	1x QC LOW Plasma
17	Sample	17	0621017	PABX_BVA	1x Control Plasma
18	Sample	18	0621018	PABX_BVA	2 x QC HIGH Water
19	Sample	19	0621019	PABX_BVA	2 x QC MID Water
20	Sample	20	0621020	PABX_BVA	2 x QC LOW Water
21	Sample	21	0621021	PABX_BVA	2 x QC LLOQ Water
22	Sample	22	0621022	PABX_BVA	2 x QC HIGH Plasma
23	Sample	23	0621023	PABX_BVA	2 x QC MID Plasma
24	Sample	24	0621024	PABX_BVA	2 x QC LOW Plasma
25	Sample	25	0621025	PABX_BVA	2 x Control Plasma
26	Sample	26	0621026	PABX_BVA	3 x QC HIGH Water
27	Sample	27	0621027	PABX_BVA	3 x QC MID Water
28	Sample	28	0621028	PABX_BVA	3 x QC LOW Water
29	Sample	29	0621029	PABX_BVA	3 x QC LLOQ Water
30	Sample	30	0621030	PABX_BVA	3 x QC HIGH Plasma
31	Sample	31	0621031	PABX_BVA	3 x QC MID Plasma
32	Sample	32	0621032	PABX_BVA	3 x QC LOW Plasma
33	Sample	33	0621033	PABX_BVA	3 x Control Plasma
34	Sample	34	0621034	PABX_BVA	4 x QC HIGH Water
35	Sample	35	0621035	PABX_BVA	4 x QC MID Water
36	Sample	36	0621036	PABX_BVA	4 x QC LOW Water
37	Sample	37	0621037	PABX_BVA	4 x QC LLOQ Water
38	Sample	38	0621038	PABX_BVA	4 x QC HIGH Plasma
39	Sample	39	0621039	PABX_BVA	4 x QC MID Plasma
40	Sample	40	0621040	PABX_BVA	4 x QC LOW Plasma
41	Sample	41	0621041	PABX_BVA	4 x Control Plasma
42	Sample	42	0621042	PABX_BVA	5 x QC HIGH Water
43	Sample	43	0621043	PABX_BVA	5 x QC MID Water

Last Modified: Tue Oct 17 13:49:48 2000

Page: 1

Sequence Name: D:\MSD_DATA\PAB\PABX-BVA\1-062-1\1-062-1.S

Line	Type	Vial	DataFile	Method	Sample Name
44	Sample	44	0621044	PABX_BVA 5 x	QC LOW Water
45	Sample	45	0621045	PABX_BVA 5 x	QC LLOQ Water
46	Sample	46	0621046	PABX_BVA 5 x	QC HIGH Plasma
47	Sample	47	0621047	PABX_BVA 5 x	QC MID Plasma
48	Sample	48	0621048	PABX_BVA 5 x	QC LOW Plasma
49	Sample	49	0621049	PABX_BVA 5 x	Control Plasma
50	Sample	50	0621050	PABX_BVA 6 x	QC HIGH Water
51	Sample	51	0621051	PABX_BVA 6 x	QC MID Water
52	Sample	52	0621052	PABX_BVA 6 x	QC LOW Water
53	Sample	53	0621053	PABX_BVA 6 x	QC LLOQ Water
54	Sample	54	0621054	PABX_BVA 6 x	QC HIGH Plasma
55	Sample	55	0621055	PABX_BVA 6 x	QC MID Plasma
56	Sample	56	0621056	PABX_BVA 6 x	QC LOW Plasma
57	Sample	57	0621057	PABX_BVA 6 x	Control Plasma
58	Sample	58	0621058	PABX_BVA 2 x	Blank Water
59	Sample	59	0621059	PABX_BVA 2 x	Control Water
60	Sample	60	0621060	PABX_BVA 2 x	STD-1 Water
61	Sample	61	0621061	PABX_BVA 2 x	STD-2 Water
62	Sample	62	0621062	PABX_BVA 2 x	STD-3 Water
63	Sample	63	0621063	PABX_BVA 2 x	STD-4 Water
64	Sample	64	0621064	PABX_BVA 2 x	STD-5 Water
65	Sample	65	0621065	PABX_BVA 2 x	STD-6 Water
66	Sample	66	0621066	PABX_BVA 2 x	STD-7 Water

Last Modified: Tue Oct 17 13:49:48 2000

Page: 2

[illegible] 10/18/00

Peak Area Report

Sample Name: 1x Blank Water
Notebook Reference: PABX-BVA-1-062

Date Acquired: 10/17/2000 13:52
Operator: MAN

Data File Name: 0621001.D
Data File Path: D:\MSD_DATA\PAB\PABX-BVA\1-062-1\
Instrument Method Name: PABX_BVA

Instrument Name: MS7
Instrument Vial Number: 1

Compound #	Compound Name	Retention Time (Min.)	Ion	Peak Area	M*	Peak Area Ratio
1)	MVL	0.00	131	0		#DIV/0!
2)	MVL-d4	0.00	135	0		

M* = The letter "m" in this column indicates that manual integration was performed on that compound.

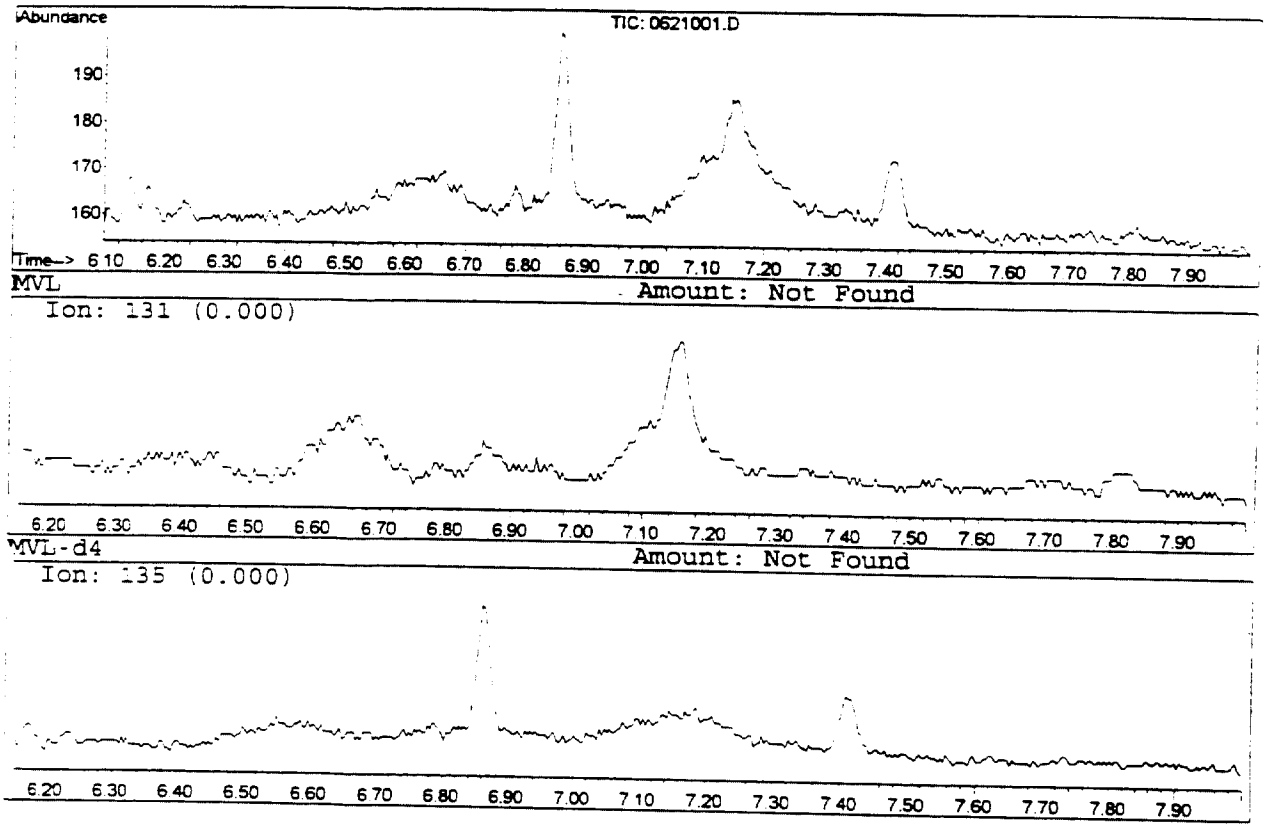
Print Date and Time: 10/18/2000 12:39

Page 1

Quantitation Report (QT Reviewed)

Data File : D:\MSD_DATA\PAB\PABX-BVA\1-062-1\0621001.D Vial: 1
Acq On : 17 Oct 2000 13:52 Operator: MAN
Sample : 1x Blank Water Inst : MS7
Misc :

MS Integration Params: rteint.p
Quant Method : D:\HPCHEM\1\METHODS\PABX_BVA.M (RTE Integrator)



Peak Area Report

Sample Name: 1x Std-1 Water
Notebook Reference: PABX-BVA-1-062

Date Acquired: 10/17/2000 14:11
Operator: MAN

Data File Name: 0621002.D
Data File Path: D:\MSD_DATA\PAB\PABX-BVA\1-062-1\
Instrument Method Name: PABX_BVA

Instrument Name: MS7
Instrument Vial Number: 2

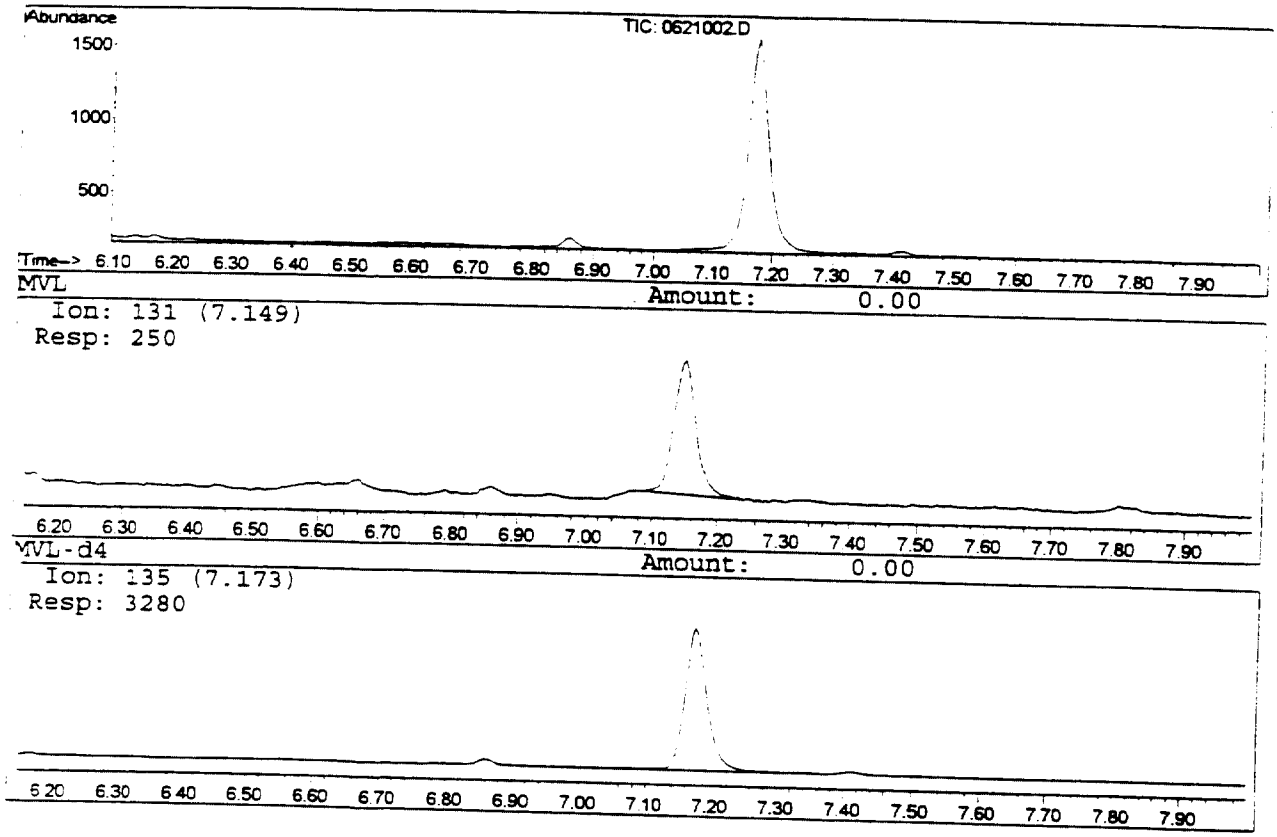
Compound #	Compound Name	Retention Time (Min.)	Ion	Peak Area	M*	Peak Area Ratio
1)	MVL	7.15	131	250		762.2E-4
2)	MVL-d4	7.17	135	3280		

M* = The letter "m" in this column indicates that manual integration was performed on that compound.

Print Date and Time: 10/18/2000 12:40

Page 1

Quantitation Report (QT Reviewed)

Data File : D:\MSD_DATA\PAB\PABX-BVA\1-062-1\0621002.D Vial: 2
Acq On : 17 Oct 2000 14:11 Operator: MAN
Sample : 1x Std-1 Water Inst : MS7
Misc :

MS Integration Params: rteint.p
Quant Method : D:\HPCHEM\1\METHODS\PABX_BVA.M (RTE Integrator)