Data Requirement

EPA OPPTS 870.3650
OECD 422

STUDY NO. 03-4242

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY WITH REPRODUCTION/DEVELOPMENTAL TOXICITY AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

Amended Final Report

VOLUME III of III

[redacted]

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Amended Date: 14 May 2010

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INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 1 0 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY	PREGNANCY STATUS
1542	TERMINAL SACRIFICE	11-NOV-03	43	P
1543	TERMINAL SACRIFICE	10-NOV-03	42	P
1544	TERMINAL SACRIFICE	12-NOV-03	44	P
1545	TERMINAL SACRIFICE	9-NOV-03	41	P
1546	TERMINAL SACRIFICE	9-NOV-03	41	P
1547	TERMINAL SACRIFICE	11-NOV-03	43	P
1548	TERMINAL SACRIFICE	9-NOV-03	41	P
1549	TERMINAL SACRIFICE	9-NOV-03	41	P
1550	TERMINAL SACRIFICE	11-NOV-03	43	P
1551	TERMINAL SACRIFICE	11-NOV-03	43	P
1552	TERMINAL SACRIFICE	10-NOV-03	42	P
1553	TERMINAL SACRIFICE	12-NOV-03	44	P

NP-NOT PREGNANT, P-PREGNANT

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INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 2 900 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY	PREGNANCY STATUS
2542	TERMINAL SACRIFICE	11-NOV-03	43	P
2543	TERMINAL SACRIFICE	15-NOV-03	47	P
2544	TERMINAL SACRIFICE	14-NOV-03	46	P
2545	TERMINAL SACRIFICE	8-NOV-03	40	P
2546	TERMINAL SACRIFICE	12-NOV-03	44	P
2547	TERMINAL SACRIFICE	12-NOV-03	44	P
2548	TERMINAL SACRIFICE	12-NOV-03	44	P
2549	TERMINAL SACRIFICE	9-NOV-03	41	P
2550	TERMINAL SACRIFICE	9-NOV-03	41	P
2551	TERMINAL SACRIFICE	9-NOV-03	41	P
2552	TERMINAL SACRIFICE	9-NOV-03	41	P
2553	TERMINAL SACRIFICE	9-NOV-03	41	P

NP-NOT PREGNANT, P-PREGNANT

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INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 3 3000 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY	PREGNANCY STATUS
3542	TERMINAL SACRIFICE	11-NOV-03	43	P
3543	TERMINAL SACRIFICE	12-NOV-03	44	P
3544	TERMINAL SACRIFICE	10-NOV-03	42	P
3545	TERMINAL SACRIFICE	10-NOV-03	42	P
3546	TERMINAL SACRIFICE	8-NOV-03	40	P
3547	TERMINAL SACRIFICE	12-NOV-03	44	P
3548	TERMINAL SACRIFICE	10-NOV-03	42	P
3549	TERMINAL SACRIFICE	9-NOV-03	41	P
3550	TERMINAL SACRIFICE	9-NOV-03	41	P
3551	TERMINAL SACRIFICE	11-NOV-03	43	P
3552	TERMINAL SACRIFICE	8-NOV-03	40	P
3553	TERMINAL SACRIFICE	12-NOV-03	44	P

NP-NOT PREGNANT, P-PREGNANT

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INDIVIDUAL ANIMAL TERMINATION HISTORY

FEMALES GROUP 4 9000 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	STUDY DAY	PREGNANCY STATUS
4542	TERMINAL SACRIFICE	8-NOV-03	40	P
4543	TERMINAL SACRIFICE	10-NOV-03	42	P
4544	TERMINAL SACRIFICE	11-NOV-03	43	P
4545	TERMINAL SACRIFICE	12-NOV-03	44	P
4546	TERMINAL SACRIFICE	12-NOV-03	44	P
4547	TERMINAL SACRIFICE	11-NOV-03	43	P
4548	TERMINAL SACRIFICE	9-NOV-03	41	P
4549	TERMINAL SACRIFICE	8-NOV-03	40	P
4550	TERMINAL SACRIFICE	11-NOV-03	43	P
4551	TERMINAL SACRIFICE	12-NOV-03	44	P
4552	TERMINAL SACRIFICE	11-NOV-03	43	P
4553	TERMINAL SACRIFICE	11-NOV-03	43	P

NP-NOT PREGNANT, P-PREGNANT

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For summarization purposes, descriptive comments [i.e., location of scab(s) and sore(s), etc.] are not presented in this appendix. These data are contained in the study raw data if needed.

Note: Observations for all animals in groups 1-3 and most of group 4, for study Days 21-35, can be found in gestation observational tables.

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INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 1 0 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY	-7	0	7	14	21	28	35
1542	WITHIN NORMAL LIMITS		P	P	P				
	ALOPECIA - EXTREMITIES/SNOUT					2			
1543	WITHIN NORMAL LIMITS		P	P	P	P			
1544	WITHIN NORMAL LIMITS		P	P	P	P			
1545	WITHIN NORMAL LIMITS		P	P	P	P			
1546	WITHIN NORMAL LIMITS		P	P	P				
	ALOPECIA - EXTREMITIES/SNOUT					2			
1547	WITHIN NORMAL LIMITS		P	P	P	P			
1548	WITHIN NORMAL LIMITS		P	P	P	P			
1549	WITHIN NORMAL LIMITS		P	P	P	P			
1550	WITHIN NORMAL LIMITS		P	P	P	P			
1551	WITHIN NORMAL LIMITS		P	P	P	P			
1552	WITHIN NORMAL LIMITS		P	P	P	P			
1553	WITHIN NORMAL LIMITS		P	P	P	P			

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

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INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 2 900 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY -7	0	7	14	21	28	35
2542	WITHIN NORMAL LIMITS	P	P	P	P			
2543	WITHIN NORMAL LIMITS	P	P	P	P			
2544	WITHIN NORMAL LIMITS	P	P	P				
	ALOPECIA - EXTREMITIES/SNOUT				3			
2545	WITHIN NORMAL LIMITS	P	P	P	P			
2546	WITHIN NORMAL LIMITS	P	P	P	P			
2547	WITHIN NORMAL LIMITS	P	P	P	P			
2548	WITHIN NORMAL LIMITS	P	P	P	P			
2549	WITHIN NORMAL LIMITS	P	P	P	P			
2550	WITHIN NORMAL LIMITS	P	P	P	P			
2551	WITHIN NORMAL LIMITS	P	P	P				
	ALOPECIA - EXTREMITIES/SNOUT				2			
2552	WITHIN NORMAL LIMITS	P	P	P				
	ALOPECIA - EXTREMITIES/SNOUT				3			
2553	WITHIN NORMAL LIMITS	P	P	P	P			

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

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INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 3 3000 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY: -7	0	7	14	21	28	35
3542	WITHIN NORMAL LIMITS	P	P	P	P			
3543	WITHIN NORMAL LIMITS	P	P	P	P			
3544	WITHIN NORMAL LIMITS	P	P	P	P			
3545	WITHIN NORMAL LIMITS	P	P	P	P			
3546	WITHIN NORMAL LIMITS	P	P	P	P			
3547	WITHIN NORMAL LIMITS	P	P	P	P			
3548	WITHIN NORMAL LIMITS	P	P	P	P			
3549	WITHIN NORMAL LIMITS	P	P	P	P			
3550	WITHIN NORMAL LIMITS	P	P	P	P			
3551	WITHIN NORMAL LIMITS	P	P	P	P			
3552	WITHIN NORMAL LIMITS	P	P	P				
	ALOPECIA - EXTREMITIES/SNOUT				2			
3553	WITHIN NORMAL LIMITS	P	P	P	P			

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

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INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 4 9000 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY: -7	0	7	14	21	28	35
4542	WITHIN NORMAL LIMITS	P	P	P	P			
4543	WITHIN NORMAL LIMITS	P	P	P				
	ALOPECIA - EXTREMITIES/SNOUT				2			
4544	WITHIN NORMAL LIMITS	P	P	P	P			
4545	WITHIN NORMAL LIMITS	P	P	P	P			
4546	WITHIN NORMAL LIMITS	P	P	P				
	ALOPECIA - EXTREMITIES/SNOUT				3			
4547	WITHIN NORMAL LIMITS	P	P	P	P			
4548	WITHIN NORMAL LIMITS	P	P	P	P			
4549	WITHIN NORMAL LIMITS	P	P	P	P			
4550	WITHIN NORMAL LIMITS	P	P	P	P			
4551	WITHIN NORMAL LIMITS	P	P	P	P			
4552	WITHIN NORMAL LIMITS	P	P	P	P			
4553	WITHIN NORMAL LIMITS	P	P	P	P	P	P	P

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

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INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 1 0 PPM

FEMALE#	OBSERVATIONS	DAY OF GESTATION 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1542	ALOPECIA - EXTREMITIES/SNOUT	2							2							2						2
1543	WITHIN NORMAL LIMITS	P							P							P						P
1544	WITHIN NORMAL LIMITS	P							P							P						P
1545	WITHIN NORMAL LIMITS	P							P							P						P
1546	ALOPECIA - EXTREMITIES/SNOUT	2							2							3						3
1547	WITHIN NORMAL LIMITS	P							P							P						P
1548	WITHIN NORMAL LIMITS	P							P							P						P
1549	WITHIN NORMAL LIMITS	P							P							P						P
1550	WITHIN NORMAL LIMITS	P							P							P						P
1551	WITHIN NORMAL LIMITS	P							P							P						P
1552	WITHIN NORMAL LIMITS	P							P							P						P
1553	WITHIN NORMAL LIMITS	P							P							P						P

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

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INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 2 900 PPM

FEMALE#	OBSERVATIONS	DAY OF GESTATION 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
2542	WITHIN NORMAL LIMITS	P							P							P						P
2543	WITHIN NORMAL LIMITS	P							P							P						P
2544	ALOPECIA - EXTREMITIES/SNOUT	3							3							3						3
2545	WITHIN NORMAL LIMITS	P							P							P						P
2546	WITHIN NORMAL LIMITS	P							P							P						P
2547	WITHIN NORMAL LIMITS	P							P							P						
2548	WITHIN NORMAL LIMITS	P							P							P						P
2549	WITHIN NORMAL LIMITS	P							P							P						P
2550	WITHIN NORMAL LIMITS	P							P							P						P
2551	ALOPECIA - EXTREMITIES/SNOUT	2							2							3						3
2552	ALOPECIA - EXTREMITIES/SNOUT	3							3							3						3
2553	WITHIN NORMAL LIMITS	P							P							P						P

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

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INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 3 3000 PPM

FEMALE#	OBSERVATIONS	DAY OF GESTATION 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
3542	WITHIN NORMAL LIMITS	P							P							P						P
3543	WITHIN NORMAL LIMITS	P							P							P						P
3544	WITHIN NORMAL LIMITS	P							P							P						P
3545	WITHIN NORMAL LIMITS	P							P							P						P
3546	WITHIN NORMAL LIMITS	P							P							P						P
3547	WITHIN NORMAL LIMITS	P							P							P						P
3548	WITHIN NORMAL LIMITS	P							P							P						P
3549	WITHIN NORMAL LIMITS	P							P							P						P
3550	WITHIN NORMAL LIMITS	P							P							P						P
3551	SCABS								P							P						P
	WITHIN NORMAL LIMITS	P																				
3552	ALOPECIA - EXTREMITIES/SNOUT	2							2							2						2
3553	WITHIN NORMAL LIMITS	P							P							P						P

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

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INDIVIDUAL CLINICAL OBSERVATIONS DURING GESTATION

GROUP 4 9000 PPM

FEMALE#	OBSERVATIONS (DAY OF GESTATION)	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
4542	WITHIN NORMAL LIMITS	P							P							P						P
4543	ALOPECIA - EXTREMITIES/SNOUT	2							2							3						3
	ALOPECIA - GENERAL															2						2
4544	WITHIN NORMAL LIMITS	P							P							P						P
4545	WITHIN NORMAL LIMITS	P							P							P						P
4546	ALOPECIA - EXTREMITIES/SNOUT	3							3							3						3
	ALOPECIA - GENERAL								2							2						2
4547	WITHIN NORMAL LIMITS	P							P							P						P
4548	WITHIN NORMAL LIMITS	P							P							P						P
4549	WITHIN NORMAL LIMITS	P							P							P						P
4550	WITHIN NORMAL LIMITS	P							P							P						P
4551	WITHIN NORMAL LIMITS	P							P							P						P
4552	WITHIN NORMAL LIMITS	P							P							P						P

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

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INDIVIDUAL MATERNAL CLINICAL OBSERVATIONS DURING LACTATION

GROUP 1 0 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4
1542	TERMINAL SACRIFICE					P
	ALOPECIA - EXTREMITIES/SNOUT		2			3
1543	WITHIN NORMAL LIMITS		P			P
	TERMINAL SACRIFICE					P
1544	WITHIN NORMAL LIMITS	P	P			P
	TERMINAL SACRIFICE					P
1545	WITHIN NORMAL LIMITS	P	P			P
	TERMINAL SACRIFICE					P
1546	TERMINAL SACRIFICE					P
	ALOPECIA - EXTREMITIES/SNOUT		3			3
1547	TERMINAL SACRIFICE					P
	ALOPECIA - EXTREMITIES/SNOUT		2			2
1548	WITHIN NORMAL LIMITS	P	P			P
	TERMINAL SACRIFICE					P
1549	WITHIN NORMAL LIMITS	P	P			P
	TERMINAL SACRIFICE					P
1550	WITHIN NORMAL LIMITS		P			P
	TERMINAL SACRIFICE					P
1551	WITHIN NORMAL LIMITS		P			P
	TERMINAL SACRIFICE					P

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

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INDIVIDUAL MATERNAL CLINICAL OBSERVATIONS DURING LACTATION

GROUP 1 0 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4
1552	WITHIN NORMAL LIMITS	P				P
	TERMINAL SACRIFICE					P
	RED EXUDATE FROM ANO-GENITAL AREA		P			
1553	WITHIN NORMAL LIMITS	P	P			P
	TERMINAL SACRIFICE					P

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

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INDIVIDUAL MATERNAL CLINICAL OBSERVATIONS DURING LACTATION

GROUP 2 900 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4
2542	WITHIN NORMAL LIMITS		P			P
	TERMINAL SACRIFICE					P
2543	WITHIN NORMAL LIMITS		P			P
	TERMINAL SACRIFICE					P
	RED/BROWN STAINS AG AREA	1				
2544	TERMINAL SACRIFICE					P
	ALOPECIA - EXTREMITIES/SNOUT		3			3
2545	WITHIN NORMAL LIMITS		P			
	TERMINAL SACRIFICE					P
	ALOPECIA - EXTREMITIES/SNOUT	2				2
2546	WITHIN NORMAL LIMITS	P	P			P
	TERMINAL SACRIFICE					P
2547	WITHIN NORMAL LIMITS	P	P			P
	TERMINAL SACRIFICE					P
2548	WITHIN NORMAL LIMITS	P	P			P
	TERMINAL SACRIFICE					P
2549	WITHIN NORMAL LIMITS		P			P
	TERMINAL SACRIFICE					P
	RED/BROWN STAINS AG AREA	1				
2550	WITHIN NORMAL LIMITS	P	P			P
	TERMINAL SACRIFICE					P

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

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INDIVIDUAL MATERNAL CLINICAL OBSERVATIONS DURING LACTATION

GROUP 2 900 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4
2551	TERMINAL SACRIFICE					P
	ALOPECIA - EXTREMITIES/SNOUT		3			3
2552	TERMINAL SACRIFICE					P
	ALOPECIA - EXTREMITIES/SNOUT	3	3			3
2553	WITHIN NORMAL LIMITS		P			P
	TERMINAL SACRIFICE					P

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

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INDIVIDUAL MATERNAL CLINICAL OBSERVATIONS DURING LACTATION

GROUP 3 3000 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4
3542	WITHIN NORMAL LIMITS					P
	TERMINAL SACRIFICE					P
	SCABS		P			
3543	WITHIN NORMAL LIMITS	P	P			P
	TERMINAL SACRIFICE					P
3544	WITHIN NORMAL LIMITS	P	P			P
	TERMINAL SACRIFICE					P
3545	WITHIN NORMAL LIMITS		P			P
	TERMINAL SACRIFICE					P
3546	WITHIN NORMAL LIMITS	P	P			P
	TERMINAL SACRIFICE					P
3547	WITHIN NORMAL LIMITS	P	P			P
	TERMINAL SACRIFICE					P
3548	WITHIN NORMAL LIMITS	P	P			P
	TERMINAL SACRIFICE					P
3549	WITHIN NORMAL LIMITS		P			P
	TERMINAL SACRIFICE					P
3550	WITHIN NORMAL LIMITS		P			P
	TERMINAL SACRIFICE					P
3551	WITHIN NORMAL LIMITS					P
	TERMINAL SACRIFICE					P
	SCABS	P	P			
	RED/BROWN STAINS AG AREA	1				

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

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INDIVIDUAL MATERNAL CLINICAL OBSERVATIONS DURING LACTATION

GROUP 3 3000 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4
3552	TERMINAL SACRIFICE					P
	ALOPECIA - EXTREMITIES/SNOUT		3			3
3553	WITHIN NORMAL LIMITS	P	P			P
	TERMINAL SACRIFICE					P

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

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INDIVIDUAL MATERNAL CLINICAL OBSERVATIONS DURING LACTATION

GROUP 4 9000 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4
4542	WITHIN NORMAL LIMITS		P			P
	TERMINAL SACRIFICE					P
4543	TERMINAL SACRIFICE					P
	ALOPECIA - EXTREMITIES/SNOUT	3	3			3
	ALOPECIA - GENERAL	2	2			
	RED/BROWN STAINS AG AREA	1				
4544	WITHIN NORMAL LIMITS	P	P			P
	TERMINAL SACRIFICE					P
4545	WITHIN NORMAL LIMITS		P			
	TERMINAL SACRIFICE					P
	ALOPECIA - EXTREMITIES/SNOUT					2
	RED/BROWN STAINS AG AREA	P				
4546	TERMINAL SACRIFICE					P
	ALOPECIA - EXTREMITIES/SNOUT	2	2			
	ALOPECIA - GENERAL	2	2			2
4547	WITHIN NORMAL LIMITS		P			P
	TERMINAL SACRIFICE					P
4548	WITHIN NORMAL LIMITS					P
	TERMINAL SACRIFICE					P
	ALOPECIA - EXTREMITIES/SNOUT	2	2			
4549	TERMINAL SACRIFICE					P
	ALOPECIA - EXTREMITIES/SNOUT		2			2

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

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APPENDIX P

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL CLINICAL OBSERVATIONS DURING LACTATION

GROUP 4 9000 PPM

FEMALE#	OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4
4550	WITHIN NORMAL LIMITS	P	P			P
	TERMINAL SACRIFICE					P
4551	WITHIN NORMAL LIMITS					P
	TERMINAL SACRIFICE					P
	RED/BROWN STAINS AG AREA	P				
	INCISORS BROKEN/MISSING	P	P			
4552	TERMINAL SACRIFICE					P
	ALOPECIA - GENERAL	2	2			2
4553	WITHIN NORMAL LIMITS	P	P			P
	TERMINAL SACRIFICE					P

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

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APPENDIX Q

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

FEMALES GROUP 1 0 PPM

PREMATING INDIVIDUAL BODY WEIGHTS (GRAMS)

ANIMAL#	DAY OF STUDY -7	0	4	7	11	14	18	21	25	28	32	35	39
1542	166	202	213	219	235	231							
1543	158	204	210	218	232	239							
1544	168	214	227	235	246	250							
1545	158	187	192	191	200	208							
1546	156	185	188	203	209	213							
1547	172	217	233	237	250	253							
1548	175	207	219	222	239	244							
1549	163	183	180	187	193	200							
1550	163	198	207	209	216	210							
1551	157	189	199	213	223	216							
1552	161	185	199	213	226	236							
1553	165	206	220	227	241	237	248						
MEAN	163	198	207	214	226	228	248						
S.D.	6.0	11.9	16.2	15.5	18.3	17.9	0.0						
N	12	12	12	12	12	12	1						

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APPENDIX Q

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

FEMALES GROUP 2 900 PPM

PREMATING INDIVIDUAL BODY WEIGHTS (GRAMS)

	DAY OF STUDY												
ANIMAL#	-7	0	4	7	11	14	18	21	25	28	32	35	39
2542	170	208	226	232	250	253							
2543	165	211	225	230	243	256	262						
2544	159	198	215	221	224	236	248						
2545	153	195	204	207	218	231							
2546	167	206	209	217	225	222							
2547	162	198	212	220	238	239	249						
2548	164	207	214	230	235	244							
2549	157	191	200	200	211	223							
2550	157	188	201	197	211	216							
2551	178	225	228	232	245	256							
2552	167	205	208	211	224	236							
2553	160	190	196	200	213	217							
MEAN	163	202	211	216	228	236	253						
S.D.	6.8	10.6	10.7	13.1	13.8	14.4	7.4						
N	12	12	12	12	12	12	3						

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SATELLITE STUDY

APPENDIX Q

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

PREMATING INDIVIDUAL BODY WEIGHTS (GRAMS)

FEMALES GROUP 3 3000 PPM

ANIMAL#	DAY OF STUDY -7	0	4	7	11	14	18	21	25	28	32	35	39
3542	165	202	200	216	227	222							
3543	159	200	210	218	231	233							
3544	156	193	195	211	222	231							
3545	166	198	211	215	233	235							
3546	162	204	220	222	237	246							
3547	157	201	212	220	230	234							
3548	157	174	189	200	214	215							
3549	173	194	209	226	238	244							
3550	169	195	205	225	239	244							
3551	163	196	217	223	239	244							
3552	159	196	207	203	219	233							
3553	174	217	223	230	244	236							
MEAN	163	197	208	217	231	235							
S.D.	6.2	9.8	10.0	9.1	9.0	9.2							
N	12	12	12	12	12	12							

APPENDIX Q

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

PREMATING INDIVIDUAL BODY WEIGHTS (GRAMS)

FEMALES GROUP 4 9000 PPM

ANIMAL#	DAY OF STUDY -7	0	4	7	11	14	18	21	25	28	32	35	39
4542	168	197	208	209	220	229							
4543	175	224	237	248	267	273							
4544	158	196	204	213	222	227							
4545	160	195	203	207	216	219							
4546	164	210	213	219	234	239							
4547	158	200	211	222	237	236							
4548	172	227	239	244	251	266							
4549	166	203	215	222	234	244							
4550	165	209	214	220	230	223							
4551	157	202	208	220	234	236							
4552	162	189	199	211	218	223							
4553	152	195	199	213	222	233	235	256	270	285	316	344	386
MEAN	163	204	213	221	232	237	235	256	270	285	316	344	386
S.D.	6.5	11.7	13.0	13.0	14.8	16.9	0.0	0.0	0.0	0.0	0.0	0.0	0.0
N	12	12	12	12	12	12	1	1	1	1	1	1	1

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APPENDIX R

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

PREMATING INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

FEMALES GROUP 1 0 PPM

ANIMAL#	DAY OF STUDY -7-0	0-4	4-7	7-11	11-14	14-18	18-21	21-25	25-28	28-32	32-35	35-39	0-14
1542	36	11	6	16	-4								29
1543	46	6	8	13	8								35
1544	46	13	8	12	4								36
1545	29	5	-1	9	9								21
1546	29	3	15	6	4								28
1547	45	16	4	13	3								36
1548	31	12	3	17	5								38
1549	20	-3	6	6	8								17
1550	36	9	2	7	-7								12
1551	32	11	14	10	-7								28
1552	24	14	14	14	10								52
1553	41	15	7	13	-3	11							32
MEAN	35	9	7	11	2	11							30
S.D.	8.7	5.6	5.0	3.7	6.0	0.0							10.5
N	12	12	12	12	12	1							12

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APPENDIX R

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

PREMATING INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

FEMALES GROUP 2 900 PPM

	DAY	OF STUDY											
ANIMAL#	-7-0	0-4	4-7	7-11	11-14	14-18	18-21	21-25	25-28	28-32	32-35	35-39	0-14
2542	38	18	6	18	4								45
2543	46	14	5	13	13	6							45
2544	40	17	6	3	12	12							38
2545	42	9	3	11	12								35
2546	39	3	8	8	-3								16
2547	35	14	8	18	1	11							41
2548	43	7	16	5	9								37
2549	35	9	1	10	13								32
2550	31	13	-4	14	5								28
2551	47	3	4	13	11								31
2552	38	3	3	13	13								32
2553	30	6	5	12	5								27
MEAN	39	10	5	12	8	9							34
S.D.	5.5	5.4	4.8	4.5	5.3	3.2							8.2
N	12	12	12	12	12	3							12

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APPENDIX R

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

PREMATING INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

FEMALES GROUP 3 3000 PPM

	DAY OF STUDY												
ANIMAL#	-7-0	0-4	4-7	7-11	11-14	14-18	18-21	21-25	25-28	28-32	32-35	35-39	0-14
3542	37	-2	15	11	-4								20
3543	41	10	9	13	2								33
3544	38	2	16	11	9								37
3545	32	13	4	18	2								37
3546	42	16	2	15	9								42
3547	45	11	8	11	4								33
3548	17	15	11	15	1								41
3549	21	15	17	12	6								50
3550	26	10	20	14	5								49
3551	33	21	6	16	6								49
3552	37	11	-3	16	14								38
3553	42	7	7	14	-8								20
MEAN	34	11	9	14	4								37
S.D.	8.8	6.2	6.9	2.3	5.9								10.0
N	12	12	12	12	12								12

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APPENDIX R

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

PREMATING INDIVIDUAL BODY WEIGHT GAIN (GRAMS)

FEMALES GROUP 4 9000 PPM

	DAY	OF STUDY											
ANIMAL#	-7-0	0-4	4-7	7-11	11-14	14-18	18-21	21-25	25-28	28-32	32-35	35-39	0-14
4542	29	11	1	11	10								32
4543	49	13	12	18	6								49
4544	38	9	9	10	5								31
4545	34	9	4	8	3								24
4546	46	4	5	16	5								29
4547	42	11	11	15	-1								36
4548	55	12	5	7	16								40
4549	38	11	7	12	10								41
4550	44	5	6	10	-7								14
4551	45	6	12	13	2								34
4552	28	10	12	7	4								33
4553	42	5	14	9	11	2	20	15	15	31	28	43	38
MEAN	41	9	8	11	5	2	20	15	15	31	28	43	33
S.D.	7.9	3.2	4.0	3.6	6.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	8.8
N	12	12	12	12	12	1	1	1	1	1	1	1	12

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SATELLITE STUDY

APPENDIX S

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL GESTATION BODY WEIGHTS (GRAMS)

GROUP 1 0 PPM

	DAY OF GESTATION			
ANIMAL#	0	7	14	20
1542	243	284	330	406
1543	243	273	306	376
1544	258	293	328	396
1545	205	232	261	312
1546	217	245	287	372
1547	270	290	332	404
1548	242	290	323	386
1549	200	236	271	346
1550	223	259	292	351
1551	231	260	294	349
1552	236	276	315	371
1553	246	292	320	391
MEAN	235	269	305	372
S.D.	20.6	22.4	23.9	27.9
N	12	12	12	12

APPENDIX S

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL GESTATION BODY WEIGHTS (GRAMS)

GROUP 2 900 PPM

	DAY OF GESTATION			
ANIMAL#	0	7	14	20
2542	260	307	346	441
2543	260	292	320	376
2544	241	274	308	361
2545	226	252	282	347
2546	234	267	301	366
2547	253	291	332	419
2548	249	284	313	385
2549	221	255	298	361
2550	212	262	296	371
2551	255	289	329	405
2552	233	265	299	363
2553	217	256	294	370
MEAN	238	274	310	380
S.D.	17.1	17.8	18.7	27.6
N	12	12	12	12

APPENDIX S

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL GESTATION BODY WEIGHTS (GRAMS)

GROUP 3 3000 PPM

	DAY OF GESTATION			
ANIMAL#	0	7	14	20
3542	241	280	336	414
3543	245	288	335	396
3544	231	263	301	373
3545	232	271	309	380
3546	245	283	328	412
3547	240	271	306	384
3548	221	261	298	373
3549	242	293	336	419
3550	240	290	331	409
3551	252	282	319	388
3552	226	266	302	392
3553	265	324	386	478
MEAN	240	281	324	401
S.D.	11.8	17.4	24.6	28.9
N	12	12	12	12

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APPENDIX S

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL GESTATION BODY WEIGHTS (GRAMS)

GROUP 4 9000 PPM

ANIMAL#	DAY OF GESTATION 0	7	14	20
4542	225	265	288	360
4543	276	322	366	446
4544	239	266	309	376
4545	227	257	290	373
4546	247	273	307	370
4547	247	285	318	394
4548	265	307	347	413
4549	241	285	315	384
4550	235	265	299	381
4551	251	292	333	398
4552	224	259	289	343
MEAN	243	279	315	385
S.D.	16.4	20.9	25.1	27.5
N	11	11	11	11

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APPENDIX T

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL GESTATION BODY WEIGHT GAIN (GRAMS)

GROUP 1 0 PPM

	DAY OF GESTATION			
ANIMAL#	0 - 7	7 - 14	14 - 20	0 - 20
1542	41	46	76	163
1543	30	33	70	133
1544	35	35	68	138
1545	27	29	51	108
1546	29	42	85	155
1547	21	42	71	134
1548	48	33	63	144
1549	35	35	75	145
1550	36	33	59	128
1551	29	34	55	118
1552	40	39	57	136
1553	45	29	71	145
MEAN	35	36	67	137
S.D.	8.0	5.3	9.9	15.1
N	12	12	12	12

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APPENDIX T

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL GESTATION BODY WEIGHT GAIN (GRAMS)

GROUP 2 900 PPM

	DAY OF GESTATION			
ANIMAL#	0 - 7	7 - 14	14 - 20	0 - 20
2542	47	38	95	181
2543	32	28	56	116
2544	34	34	53	120
2545	26	30	65	121
2546	33	34	65	132
2547	37	42	87	166
2548	35	29	71	136
2549	34	43	63	139
2550	49	34	76	159
2551	34	40	76	150
2552	32	34	64	130
2553	39	38	76	153
MEAN	36	35	71	142
S.D.	6.5	4.9	12.2	20.1
N	12	12	12	12

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APPENDIX T

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL GESTATION BODY WEIGHT GAIN (GRAMS)

GROUP 3 3000 PPM

	DAY OF GESTATION			
ANIMAL#	0 - 7	7 - 14	14 - 20	0 - 20
3542	39	56	79	174
3543	43	47	62	151
3544	32	38	73	142
3545	38	38	71	147
3546	38	45	85	167
3547	31	35	78	144
3548	40	37	75	152
3549	51	43	83	176
3550	50	41	78	169
3551	30	37	69	136
3552	40	36	89	166
3553	59	62	91	213
MEAN	41	43	78	161
S.D.	8.7	8.5	8.6	20.9
N	12	12	12	12

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APPENDIX T

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL GESTATION BODY WEIGHT GAIN (GRAMS)

GROUP 4 9000 PPM

	DAY OF GESTATION			
ANIMAL#	0 - 7	7 - 14	14 - 20	0 - 20
4542	40	23	72	135
4543	46	43	80	170
4544	27	43	67	137
4545	29	34	82	145
4546	26	34	63	123
4547	38	34	76	147
4548	42	40	66	148
4549	44	30	69	143
4550	30	35	81	146
4551	41	41	65	147
4552	35	30	54	119
MEAN	36	35	71	142
S.D.	7.1	6.3	8.8	13.7
N	11	11	11	11

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APPENDIX U

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL LACTATION BODY WEIGHTS (GRAMS)

GROUP 1 0 PPM

	DAY OF LACTATION	
Animal No.	1	4
1542	282	294
1543	265	276
1544	296	288
1545	228	250
1546	248	272
1547	284	289
1548	295	325
1549	240	259
1550	252	258
1551	257	270
1552	274	300
1553	301	309
MEAN	269	283
S.D.	24.0	22.5
N	12	12

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APPENDIX U

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL LACTATION BODY WEIGHTS (GRAMS)

GROUP 2 900 PPM

	DAY OF LACTATION	
Animal No.	1	4
2542	321	327
2543	284	308
2544	249	280
2545	245	255
2546	272	280
2547	294	306
2548	267	284
2549	250	267
2550	253	283
2551	297	310
2552	281	304
2553	263	286
MEAN	273	291
S.D.	23.1	20.4
N	12	12

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APPENDIX U

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL LACTATION BODY WEIGHTS (GRAMS)

GROUP 3 3000 PPM

	DAY OF LACTATION	
Animal No.	1	4
3542	292	282
3543	278	302
3544	260	273
3545	276	284
3546	294	305
3547	286	261
3548	267	283
3549	299	306
3550	298	322
3551	282	292
3552	269	274
3553	344	355
MEAN	287	295
S.D.	21.7	25.5
N	12	12

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APPENDIX U

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL LACTATION BODY WEIGHTS (GRAMS)

GROUP 4 9000 PPM

	DAY OF LACTATION	
Animal No.	1	4
4542	268	262
4543	332	342
4544	278	287
4545	277	288
4546	274	271
4547	287	286'
4548	302	317
4549	285	294
4550	273	279
4551	298	296
4552	274	292
4553	268	275
MEAN	284	291
S.D.	18.5	21.2
N	12	12

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SATELLITE STUDY

APPENDIX V

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL LACTATION BODY WEIGHT GAIN (GRAMS)

GROUP 1 0 PPM

FEMALE#	DAY OF LACTATION 1 - 4
1542	12
1543	11
1544	-8
1545	23
1546	25
1547	5
1548	30
1549	19
1550	6
1551	14
1552	26
1553	8
MEAN	14
S.D.	10.8
N	12

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SATELLITE STUDY

APPENDIX V

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL LACTATION BODY WEIGHT GAIN (GRAMS)

GROUP 2 900 PPM

FEMALE#	DAY OF LACTATION 1 - 4
2542	6
2543	25
2544	32
2545	10
2546	9
2547	12
2548	17
2549	16
2550	30
2551	13
2552	23
2553	24
MEAN	18
S.D.	8.6
N	12

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX V

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL LACTATION BODY WEIGHT GAIN (GRAMS)

GROUP 3 3000 PPM

FEMALE#	DAY OF LACTATION 1 - 4
3542	-10
3543	24
3544	13
3545	7
3546	11
3547	-25
3548	16
3549	8
3550	24
3551	10
3552	4
3553	11
MEAN	8
S.D.	13.7
N	12

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX V

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL LACTATION BODY WEIGHT GAIN (GRAMS)

GROUP 4 9000 PPM

FEMALE#	DAY OF LACTATION 1 - 4
4542	-5
4543	10
4544	9
4545	11
4546	-3
4547	-2
4548	15
4549	9
4550	6
4551	-2
4552	18
4553	7
MEAN	6
S.D.	7.5
N	12

	Premating Individual Feed Consumption Preface	Appendix W

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SATELLITE STUDY

APPENDIX W

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

PREMATING INDIVIDUAL FEED CONSUMPTION (GRAMS/KG/DAY)

FEMALES GROUP 1 0 PPM

	DAY OF STUDY		
ANIMAL#	0	7	14
1542	107	90	83
1543	102	85	82
1544	107	91	88
1545	92	82	83
1546	100	87	79
1547	94	84	76
1548	98	89	88
1549	SF	87	97
1550	96	82	76
1551	92	89	80
1552	101	91	86
1553	100	94	83
MEAN	99	87	83
S.D.	5.2	3.8	5.7
N	11	12	12

SF=Spilled Feeder

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX W

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

PREMATING INDIVIDUAL FEED CONSUMPTION (GRAMS/KG/DAY)

FEMALES GROUP 2 900 PPM

ANIMAL#	DAY OF STUDY 0	7	14
2542	103	87	86
2543	101	89	81
2544	101	87	77
2545	106	91	90
2546	100	82	79
2547	100	87	81
2548	116	92	85
2549	107	85	91
2550	106	87	87
2551	105	82	85
2552	104	84	84
2553	99	88	84
MEAN	104	87	84
S.D.	4.7	3.2	4.1
N	12	12	12

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SATELLITE STUDY

APPENDIX W

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

PREMATING INDIVIDUAL FEED CONSUMPTION (GRAMS/KG/DAY)

FEMALES GROUP 3 3000 PPM

ANIMAL#	DAY OF STUDY 0	7	14
3542	102	84	84
3543	102	86	86
3544	102	90	83
3545	108	91	90
3546	103	89	86
3547	102	83	78
3548	90	91	84
3549	98	95	82
3550	105	100	86
3551	100	90	80
3552	103	86	91
3553	113	87	85
MEAN	102	89	85
S.D.	5.6	4.8	3.7
N	12	12	12

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX W

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

PREMATING INDIVIDUAL FEED CONSUMPTION (GRAMS/KG/DAY)

FEMALES GROUP 4 9000 PPM

ANIMAL#	DAY OF STUDY 0	7	14
4542	92	84	84
4543	101	88	81
4544	102	89	83
4545	100	83	82
4546	103	85	81
4547	111	96	89
4548	103	84	84
4549	109	91	87
4550	100	81	78
4551	SF	92	89
4552	99	CF	79
4553	110	91	90
MEAN	103	88	84
S.D.	5.6	4.7	4.0
N	11	11	12

SF=Spilled Feeder CF=Contaminated Feeder

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX X

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

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

GROUP 1 0 PPM

ANIMAL#	DAY OF GESTATION 0 - 7	7 - 14	14 - 20
1542	82	81	66
1543	78	76	64
1544	83	78	68
1545	79	76	63
1546	83	80	71
1547	72	73	63
1548	86	79	71
1549	96	84	73
1550	87	83	73
1551	82	78	67
1552	87	81	67
1553	92	80	68
MEAN	84	79	68
S.D.	6.3	3.0	3.5
N	12	12	12

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX X

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

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

GROUP 2 900 PPM

ANIMAL#	DAY OF GESTATION 0 - 7	7 - 14	14 - 20
2542	85	79	72
2543	75	74	68
2544	EF	71	57
2545	59	77	69
2546	44	80	69
2547	86	80	68
2548	120	83	73
2549	76	85	70
2550	93	85	66
2551	65	80	70
2552	84	78	75
2553	88	83	73
MEAN	79	80	69
S.D.	19.9	4.3	4.5
N	11	12	12

EF=Empty Feeder

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX X

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

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

GROUP 3 3000 PPM

	DAY OF GESTATION		
ANIMAL#	0 - 7	7 - 14	14 - 20
3542	83	85	70
3543	87	85	65
3544	83	79	69
3545	91	89	74
3546	87	85	74
3547	75	79	70
3548	85	80	67
3549	91	82	71
3550	98	88	75
3551	78	79	68
3552	86	79	73
3553	103	EF	79
MEAN	87	83	71
S.D.	7.8	3.8	3.9
N	12	11	12

EF=Empty Feeder

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX X

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

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

GROUP 4 9000 PPM

	DAY OF GESTATION		
ANIMAL#	0 - 7	7 - 14	14 - 20
4542	89	81	69
4543	86	85	72
4544	81	84	69
4545	84	78	72
4546	79	78	66
4547	92	89	74
4548	85	80	CF
4549	87	75	68
4550	81	74	66
4551	95	87	67
4552	86	78	67
MEAN	86	81	69
S.D.	4.8	4.9	3.0
N	11	11	10

CF=Contaminated Feeder

APPENDIX Y

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL LACTATION FEED CONSUMPTION -- (GRAMS/KG/DAY)

GROUP 1 0 PPM

ANIMAL#	DAY OF LACTATION 1 - 4
1542	109
1543	102
1544	83
1545	128
1546	114
1547	98
1548	131
1549	110
1550	93
1551	118
1552	118
1553	118
MEAN	110
S.D.	14.0
N	12

APPENDIX Y

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL LACTATION FEED CONSUMPTION -- (GRAMS/KG/DAY)

GROUP 2 900 PPM

ANIMAL#	DAY OF LACTATION 1 - 4
2542	86
2543	136
2544	106
2545	119
2546	128
2547	111
2548	119
2549	146
2550	112
2551	104
2552	141
2553	104
MEAN	118
S.D.	17.5
N	12

APPENDIX Y

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL LACTATION FEED CONSUMPTION -- (GRAMS/KG/DAY)

GROUP 3 3000 PPM

ANIMAL#	DAY OF LACTATION 1 - 4
3542	101
3543	119
3544	133
3545	88
3546	97
3547	85
3548	113
3549	95
3550	111
3551	105
3552	92
3553	105
MEAN	104
S.D.	13.7
N	12

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APPENDIX Y

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATERNAL LACTATION FEED CONSUMPTION -- (GRAMS/KG/DAY)

GROUP 4 9000 PPM

ANIMAL#	DAY OF LACTATION 1 - 4
4542	83
4543	79
4544	101
4545	120
4546	86
4547	88
4548	97
4549	98
4550	106
4551	111
4552	146
4553	126
MEAN	103
S.D.	19.7
N	12

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SATELLITE STUDY

APPENDIX Z

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL ESTROUS CYCLE DATA

GROUP 1 0 PPM

	DAY OF EVALUATION													
FEMALE#	15	16	17	18	19	20	21	22	23	24	25	26	27	28
1542	D	D	D	/S										
1543	D	D	/S											
1544	D	D	D	/C										
1545	/S													
1546	D	/S												
1547	D	D	D	/C										
1548	/S													
1549	D	/S												
1550	/M	D	D	/S										
1551	D	D	D	/S										
1552	D	/C												
1553	D	D	D	/E	C									

D=DIESTRUS M=METESTRUS P=PROESTRUS E=ESTRUS S=SPERM C=COPULATORY PLUG

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SATELLITE STUDY

APPENDIX Z

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL ESTROUS CYCLE DATA

GROUP 2 900 PPM

	DAY OF EVALUATION													
FEMALE#	15	16	17	18	19	20	21	22	23	24	25	26	27	28
2542	D	D	/P	S										
2543	D	D	D	D	D	D	/S							
2544	D	D	D	D	D	D	/S							
2545	/C													
2546	/M	D	D	/S										
2547	/M	D	D	/E	E	C								
2548	D	D	D	/S										
2549	/S													
2550	D	/C												
2551	D	/S												
2552	/S													
2553	D	/S												

D=DIESTRUS M=METESTRUS P=PROESTRUS E=ESTRUS S=SPERM C=COPULATORY PLUG

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX Z

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL ESTROUS CYCLE DATA

GROUP 3 3000 PPM

	DAY OF EVALUATION													
FEMALE#	15	16	17	18	19	20	21	22	23	24	25	26	27	28
3542	D	D	D	/C										
3543	D	D	D	/S										
3544	D	/S												
3545	D	/P	C											
3546	/S													
3547	D	D	D	/C										
3548	D	/S												
3549	D	/S												
3550	D	/S												
3551	D	D	/E	S										
3552	/S													
3553	/M	D	D	/S										

D=DIESTRUS M=METESTRUS P=PROESTRUS E=ESTRUS S=SPERM C=COPULATORY PLUG

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APPENDIX Z

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL ESTROUS CYCLE DATA

GROUP 4 9000 PPM

FEMALE#	DAY OF EVALUATION 15	16	17	18	19	20	21	22	23	24	25	26	27	28
4542	/S													
4543	D	D	/C											
4544	D	D	D	/S										
4545	/M	D	D	/C										
4546	/M	D	D	/S										
4547	/M	D	D	/C										
4548	/S													
4549	/S													
4550	D	D	D	/S										
4551	/M	D	D	/C										
4552	D	D	/C											
4553	D	D	/E	M	D	D	D	D	D	D	D	D	D	D

D=DIESTRUS M=METESTRUS P=PROESTRUS E=ESTRUS S=SPERM C=COPULATORY PLUG

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APPENDIX AA

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATING ASSIGNMENTS

GROUP 1 0 PPM

Female No.	Male No.	Alternate Male No.	Sperm/Plug	Outcome	Date of Cohabitation	Date of Insemination	Date of Parturition
1542	1030		+	P	13-OCT-03	17-OCT-03	7-NOV-03
1543	1031		+	P	13-OCT-03	16-OCT-03	6-NOV-03
1544	1032		+	P	13-OCT-03	17-OCT-03	8-NOV-03
1545	1033		+	P	13-OCT-03	14-OCT-03	5-NOV-03
1546	1034		+	P	13-OCT-03	15-OCT-03	5-NOV-03
1547	1035		+	P	13-OCT-03	17-OCT-03	7-NOV-03
1548	1036		+	P	13-OCT-03	14-OCT-03	5-NOV-03
1549	1037		+	P	13-OCT-03	15-OCT-03	5-NOV-03
1550	1038		+	P	13-OCT-03	17-OCT-03	7-NOV-03
1551	1039		+	P	13-OCT-03	17-OCT-03	7-NOV-03
1552	1040		+	P	13-OCT-03	15-OCT-03	6-NOV-03
1553	1041		+	P	13-OCT-03	18-OCT-03	8-NOV-03

+ = Sperm/Plug Positive - = Sperm/Plug Negative N = Not Mated

P=PREGNANT

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX AA

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATING ASSIGNMENTS

GROUP 2 900 PPM

Female No.	Male No.	Alternate Male No.	Sperm/Plug	Outcome	Date of Cohabitation	Date of Insemination	Date of Parturition
2542	2030		+	P	13-OCT-03	17-OCT-03	7-NOV-03
2543	2031		+	P	13-OCT-03	20-OCT-03	11-NOV-03
2544	2032		+	P	13-OCT-03	20-OCT-03	10-NOV-03
2545	2033		+	P	13-OCT-03	14-OCT-03	4-NOV-03
2546	2034		+	P	13-OCT-03	17-OCT-03	8-NOV-03
2547	2035		+	P	13-OCT-03	19-OCT-03	8-NOV-03
2548	2036		+	P	13-OCT-03	17-OCT-03	8-NOV-03
2549	2037		+	P	13-OCT-03	14-OCT-03	5-NOV-03
2550	2038		+	P	13-OCT-03	15-OCT-03	5-NOV-03
2551	2039		+	P	13-OCT-03	15-OCT-03	5-NOV-03
2552	2040		+	P	13-OCT-03	14-OCT-03	5-NOV-03
2553	2041		+	P	13-OCT-03	15-OCT-03	5-NOV-03

+ = Sperm/Plug Positive - = Sperm/Plug Negative N = Not Mated

P=PREGNANT

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SATELLITE STUDY

APPENDIX AA

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATING ASSIGNMENTS

GROUP 3 3000 PPM

Female No.	Male No.	Alternate Male No.	Sperm/Plug	Outcome	Date of Cohabitation	Date of Insemination	Date of Parturition
3542	3030		+	P	13-OCT-03	17-OCT-03	7-NOV-03
3543	3031		+	P	13-OCT-03	17-OCT-03	8-NOV-03
3544	3032		+	P	13-OCT-03	15-OCT-03	6-NOV-03
3545	3033		+	P	13-OCT-03	16-OCT-03	6-NOV-03
3546	3034		+	P	13-OCT-03	14-OCT-03	4-NOV-03
3547	3035		+	P	13-OCT-03	17-OCT-03	8-NOV-03
3548	3036		+	P	13-OCT-03	15-OCT-03	6-NOV-03
3549	3037		+	P	13-OCT-03	15-OCT-03	5-NOV-03
3550	3038		+	P	13-OCT-03	15-OCT-03	5-NOV-03
3551	3039		+	P	13-OCT-03	17-OCT-03	7-NOV-03
3552	3040		+	P	13-OCT-03	14-OCT-03	4-NOV-03
3553	3041		+	P	13-OCT-03	17-OCT-03	8-NOV-03

+ = Sperm/Plug Positive - = Sperm/Plug Negative N = Not Mated

P=PREGNANT

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX AA

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL MATING ASSIGNMENTS

GROUP 4 9000 PPM

Female No.	Male No.	Alternate Male No.	Sperm/Plug	Outcome	Date of Cohabitation	Date of Insemination	Date of Parturition
4542	4030		+	P	13-OCT-03	14-OCT-03	4-NOV-03
4543	4031		+	P	13-OCT-03	16-OCT-03	6-NOV-03
4544	4032		+	P	13-OCT-03	17-OCT-03	7-NOV-03
4545	4033		+	P	13-OCT-03	17-OCT-03	8-NOV-03
4546	4034		+	P	13-OCT-03	17-OCT-03	8-NOV-03
4547	4035		+	P	13-OCT-03	17-OCT-03	7-NOV-03
4548	4036		+	P	13-OCT-03	14-OCT-03	5-NOV-03
4549	4037		+	P	13-OCT-03	14-OCT-03	4-NOV-03
4550	4038		+	P	13-OCT-03	17-OCT-03	7-NOV-03
4551	4039		+	P	13-OCT-03	17-OCT-03	8-NOV-03
4552	4040		+	P	13-OCT-03	16-OCT-03	7-NOV-03
4553	4041		-	P	13-OCT-03		7-NOV-03

+ = Sperm/Plug Positive - = Sperm/Plug Negative N = Not Mated

P=PREGNANT

APPENDIX BB

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL DELIVERY AND LITTER DATA

GROUP 1 0 PPM

	LITTER DELIVERED			NUMBER OF LIVE PUPS DAYS						CORPORA LUTEA	TOTAL IMPLAN-TATIONS	DURATION OF GESTATION (DAYS)
	LIVE	DEAD	TOTAL	0		1		4				
FEMALE#	N	N	N	M	F	M	F	M	F		N	N
1542	18	0	18	8	9	8	8	8	7	18	18	21
1543	16	0	16	7	9	7	9	7	9	19	17	21
1544	16	0	16	7	9	7	9	7	8	18	16	22
1545	13	0	13	7	6	7	5	7	5	20	14	22
1546	14	0	14	7	7	7	7	7	7	18	17	21
1547	15	0	15	8	7	8	7	8	7	17	17	21
1548	11	0	11	6	5	6	5	6	5	17	14	22
1549	12	0	12	7	5	7	5	7	5	12	12	21
1550	12	0	12	6	6	6	6	6	6	15	13	21
1551	14	0	14	6	8	6	8	6	8	16	14	21
1552	13	0	13	6	7	6	7	6	7	14	14	22
1553	12	0	12	7	5	7	5	7	5	15	15	21
MEAN	13.8	0.0	13.8	6.8	6.9	6.8	6.8	6.8	6.6	16.6	15.1	21.3
S.D.	2.1	0.0	2.1	0.7	1.6	0.7	1.5	0.7	1.4	2.3	1.9	0.5
N	12	12	12	12	12	12	12	12	12	12	12	12

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APPENDIX BB

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL DELIVERY AND LITTER DATA

GROUP 2 900 PPM

	LITTER DELIVERED			NUMBER OF LIVE PUPS DAYS						CORPORA LUTEA	TOTAL IMPLAN-TATIONS	DURATION OF GESTATION (DAYS)
	LIVE	DEAD	TOTAL	0		1		4				
FEMALE#	N	N	N	M	F	M	F	M	F		N	N
2542	14	1	15	6	8	6	8	6	7	19	17	21
2543	15	0	15	8	7	8	7	8	7	17	16	22
2544	18	0	18	6	12	6	12	6	12	19	18	21
2545	14	0	14	6	8	6	8	6	8	15	14	21
2546	15	0	15	10	5	10	5	10	5	15	15	22
2547	16	0	16	8	8	7	8	7	8	17	17	20
2548	17	0	17	8	9	8	9	8	9	18	18	22
2549	16	0	16	7	9	7	8	7	7	16	16	22
2550	16	0	16	8	8	7	8	7	8	21	17	21
2551	16	0	16	9	7	9	7	9	7	17	16	21
2552	15	0	15	8	7	8	7	8	7	18	15	22
2553	15	0	15	5	10	5	10	5	10	17	16	21
MEAN	15.6	0.1	15.7	7.4	8.2	7.3	8.1	7.3	7.9	17.4	16.3	21.3
S.D.	1.2	0.3	1.1	1.4	1.7	1.4	1.7	1.4	1.8	1.7	1.2	0.7
N	12	12	12	12	12	12	12	12	12	12	12	12

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX BB

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL DELIVERY AND LITTER DATA

GROUP 3 3000 PPM

	LITTER DELIVERED			NUMBER OF LIVE PUPS DAYS								
	LIVE	DEAD	TOTAL	0		1		4		CORPORA LUTEA	TOTAL IMPLAN-TATIONS	DURATION OF GESTATION (DAYS)
FEMALE#	N	N	N	M	F	M	F	M	F		N	N
3542	17	0	17	8	9	8	9	8	9	20	18	21
3543	13	0	13	6	7	6	6	6	6	15	15	22
3544	16	0	16	9	7	9	6	9	6	20	19	22
3545	13	0	13	7	6	7	6	7	5	18	17	21
3546	16	0	16	6	10	6	7	6	7	18	16	21
3547	14	0	14	6	8	6	8	6	8	15	14	22
3548	15	0	15	5	10	5	10	4	9	15	15	22
3549	16	0	16	7	9	7	9	6	9	20	16	21
3550	14	0	14	9	5	9	5	9	5	17	16	21
3551	15	1	16	9	6	9	6	9	6	17	17	21
3552	15	0	15	10	5	10	5	10	5	16	16	21
3553	18	0	18	8	10	8	10	8	10	19	18	22
MEAN	15.2	0.1	15.3	7.5	7.7	7.5	7.3	7.3	7.1	17.5	16.4	21.4
S.D.	1.5	0.3	1.5	1.6	1.9	1.6	1.9	1.8	1.8	2.0	1.4	0.5
N	12	12	12	12	12	12	12	12	12	12	12	12

Huntingdon Life Sciences 03-4242S
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APPENDIX BB

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL DELIVERY AND LITTER DATA

GROUP 4 9000 PPM

FEMALE#	LITTER DELIVERED LIVE N	DEAD N	TOTAL N	NUMBER OF LIVE PUPS DAYS 0 M	0 F	1 M	1 F	4 M	4 F	CORPORA LUTEA	TOTAL IMPLAN-TATIONS N	DURATION OF GESTATION (DAYS) N
4542	15	0	15	6	9	6	9	6	9	18	15	21
4543	16	0	16	7	9	7	8	6	7	17	16	21
4544	14	0	14	7	7	7	7	7	7	15	15	21
4545	13	1	14	8	5	7	5	7	5	14	14	22
4546	14	0	14	8	6	8	6	8	6	15	14	22
4547	15	0	15	6	9	6	9	6	9	17	17	21
4548	15	1	16	5	10	5	10	5	10	17	17	22
4549	14	0	14	6	8	6	8	6	8	14	14	21
4550	16	0	16	9	7	9	7	9	7	18	17	21
4551	14	1	15	5	9	5	9	5	9	15	15	22
4552	13	0	13	6	7	6	7	6	7	17	14	22
4553	16	0	16	6	10	6	10	6	10	17	16	no day 0
MEAN	14.6	0.3	14.8	6.6	8.0	6.5	7.9	6.4	7.8	16.2	15.3	21.5
S.D.	1.1	0.5	1.0	1.2	1.6	1.2	1.6	1.2	1.6	1.5	1.2	0.5
N	12	12	12	12	12	12	12	12	12	12	12	11

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX CC

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP SEX AND STATUS DURING LACTATION

GROUP 1 0 PPM

FEMALE#	PUP # 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
1542	UM 0	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FD 1	FK 4	FK 4	FM 2	FK 4	FK 4	FK 4	FK 4	FK 4					
1543	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4							
1544	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FD 3	FK 4	FK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4							
1545	FD 0	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4										
1546	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4									
1547	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4								
1548	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4												
1549	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4											
1550	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4											
1551	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4									
1552	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	MK 4	FK 4	MK 4										
1553	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4											

SEX CODE PRECEDES PUP STATUS CODE. NUMERICAL VALUE INDICATES DAY OF LACTATION.
SEX CODES: M-MALE F-FEMALE U-UNCERTAIN
PUP STATUS CODES: A-ALIVE D-DIED M-MISSING K-SCHEDULED SACRIFICE

Note: The uncertain sex of pup number 1542-1 not included in Summary Table 27.

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX CC

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP SEX AND STATUS DURING LACTATION

GROUP 2 900 PPM

FEMALE#	PUP # 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
2542	MS	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FM 2	FK 4								
2543	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4								
2544	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4					
2545	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4									
2546	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4								
2547	MK 4	MD 1	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4							
2548	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4						
2549	FD 0	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FM 2	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4							
2550	MK 4	MM 1	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4							
2551	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4							
2552	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4								
2553	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4								

SEX CODE PRECEDES PUP STATUS CODE. NUMERICAL VALUE INDICATES DAY OF LACTATION.
SEX CODES: M-MALE F-FEMALE U-UNCERTAIN
PUP STATUS CODES: A-ALIVE S-STILLBORN D-DIED M-MISSING K-SCHEDULED SACRIFICE

Huntingdon Life Sciences 03-4242S
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APPENDIX CC

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP SEX AND STATUS DURING LACTATION

GROUP 3 3000 PPM

FEMALE#	PUP # 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
3542	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4						
3543	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FM 1										
3544	FD 0	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4							
3545	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FM 2	FK 4	FK 4	FK 4										
3546	FD 0	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FD 1	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FM 1							
3547	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4									
3548	MK 4	MK 4	MK 4	MD 3	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FM 4	FK 4	FK 4	FK 4								
3549	MK 4	MK 4	MM 2	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4							
3550	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4									
3551	FS	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4							
3552	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4								
3553	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4					

SEX CODE PRECEDES PUP STATUS CODE. NUMERICAL VALUE INDICATES DAY OF LACTATION.
SEX CODES: M-MALE F-FEMALE U-UNCERTAIN
PUP STATUS CODES: A-ALIVE S-STILLBORN D-DIED M-MISSING K-SCHEDULED SACRIFICE

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX CC

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND
NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY
INHALATION EXPOSURES

INDIVIDUAL PUP SEX AND STATUS DURING LACTATION

GROUP 4 9000 PPM

	PUP #																						
FEMALE#	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
4542	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4								
4543	MD 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FM 2	FD 1	FK 4	FK 4	FK 4							
4544	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4									
4545	MD 0	FS	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4									
4546	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4									
4547	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4								
4548	FS	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4							
4549	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4									
4550	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4							
4551	FS	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4								
4552	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4										
4553	MK 4	MK 4	MK 4	MK 4	MK 4	MK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4	FK 4							

SEX CODE PRECEDES PUP STATUS CODE. NUMERICAL VALUE INDICATES DAY OF LACTATION.
SEX CODES: M-MALE F-FEMALE U-UNCERTAIN
PUP STATUS CODES: A-ALIVE S-STILLBORN D-DIED M-MISSING K-SCHEDULED SACRIFICE

Huntingdon Life Sciences
Princeton Research Center
East Millstone, New Jersey
Satellite Study

Raw Data Listing of Gross Observation
Study number: 034242

Printed: 17-Feb-04
Page: 1
Version 4.2.2

Animal number	Sex	Group/ Subgroup	Date data taken	Tissue / Observation(s) Locator, Color, General, Measurements, Severity levels			
1542	F	1/1	11-Nov-03	Within normal limits			
1543	F	1/1	10-Nov-03	Within normal limits			
1544	F	1/1	12-Nov-03	Within normal limits			
1545	F	1/1	09-Nov-03	Within normal limits			
1546	F	1/1	09-Nov-03	Within normal limits			
1547	F	1/1	11-Nov-03	Within normal limits			
1548	F	1/1	09-Nov-03	Within normal limits			
1549	F	1/1	09-Nov-03	Within normal limits			
1550	F	1/1	11-Nov-03	Within normal limits			
1551	F	1/1	11-Nov-03	Within normal limits			
1552	F	1/1	10-Nov-03	Within normal limits			
1553	F	1/1	12-Nov-03	Within normal limits			
2542	F	2/1		Kidneys			
			11-Nov-03	Discolored, Left, Tan, Focus, 0.2 - 0.5 cm, Slight			
				Tissues marked 'Within normal limits':			
			11-Nov-03	Adrenal Glands	Brain	Cecum	Colon
				Duodenum	Femur	Femoral Marrow	Heart
				Ileum	Jejunum	Larynx	Liver
				Lungs	Mammary-protocol	Mediastinal LN	Mesenteric LN
				Nasopharynx	Ovaries	Oviducts/Fallop	Parathyroid
				Rectum/Low Colon	Skin-protocol	Cervical SC	Thoracic SC
				Lumbar SC	Spleen	Sternum	Sternal Marrow
				Stomach	Thymus	Tibial Nerve	Trachea
				Urinary bladder	Uterus	Vagina	Thyroid
2543	F	2/1	15-Nov-03	Within normal limits			
2544	F	2/1	14-Nov-03	Within normal limits			
2545	F	2/1	08-Nov-03	Within normal limits			

Huntingdon Life Sciences
Princeton Research Center
East Millstone, New Jersey
Satellite Study

Raw Data Listing of Gross Observations
Study number: 034242

Printed: 17-Feb-04
Page: 2
Version 4.2.2

Animal number	Sex	Group/ Subgroup	Date data taken	Tissue / Observation(s) Locator, Color, General, Measurements, Severity levels
2546	F	2/1	12-Nov-03	Within normal limits
2547	F	2/1	12-Nov-03	Within normal limits
2548	F	2/1	12-Nov-03	Within normal limits
2549	F	2/1	09-Nov-03	Within normal limits
2550	F	2/1	09-Nov-03	Within normal limits
2551	F	2/1	09-Nov-03	Within normal limits
2552	F	2/1	09-Nov-03	Within normal limits
2553	F	2/1	09-Nov-03	Within normal limits
3542	F	3/1	11-Nov-03	Within normal limits
3543	F	3/1	12-Nov-03	Within normal limits
3544	F	3/1		Mesenteric LN
			10-Nov-03	Enlarged, , , , , Slight
				Tissues marked 'Within normal limits':
			10-Nov-03	Adrenal Glands, Brain, Cecum, Colon, Duodenum, Femur, Femoral Marrow, Heart, Ileum, Jejunum, Kidneys, Larynx, Liver, Lungs, Mammary-protocol, Mediastinal LN, Nasopharynx, Ovaries, Oviducts/Fallop, Parathyroid, Rectum/Low Colon, Skin-protocol, Cervical SC, Thoracic SC, Lumbar SC, Spleen, Sternum, Sternal Marrow, Stomach, Thymus, Tibial Nerve, Trachea, Urinary bladder, Uterus, Vagina, Thyroid
3545	F	3/1	10-Nov-03	Within normal limits
3546	F	3/1	08-Nov-03	Within normal limits
3547	F	3/1	12-Nov-03	Within normal limits
3548	F	3/1	10-Nov-03	Within normal limits
3549	F	3/1	09-Nov-03	Within normal limits

Huntingdon Life Sciences
Princeton Research Center
East Millstone, New Jersey
Satellite Study

Raw Data Listing of Gross Observations
Study number: 034242

Animal number	Sex	Group/ Subgroup	Date data taken	Tissue / Observation(s) Locator, Color, General, Measurements, Severity levels
3550	F	3/1	09-Nov-03	Within normal limits
3551	F	3/1	11-Nov-03	Within normal limits
3552	F	3/1	08-Nov-03	Within normal limits
3553	F	3/1	12-Nov-03	Within normal limits
4542	F	4/1	08-Nov-03	Within normal limits
4543	F	4/1	10-Nov-03	Within normal limits
4544	F	4/1	11-Nov-03	Within normal limits
4545	F	4/1	12-Nov-03	Within normal limits
4546	F	4/1	12-Nov-03	Within normal limits
4547	F	4/1	11-Nov-03	Within normal limits
4548	F	4/1	09-Nov-03	Within normal limits
4549	F	4/1	08-Nov-03	Within normal limits
4550	F	4/1	11-Nov-03	Within normal limits
4551	F	4/1	12-Nov-03	Within normal limits
4552	F	4/1	11-Nov-03	Within normal limits
4553	F	4/1	11-Nov-03	Within normal limits

	Individual Parental Organ Weights Satellite Study Preface	Appendix EE

Table of Contents

Key to Abbreviations:

g	=	Grams
wt.	=	Weight
observ.	=	Observed

Corresponding exposure levels for each group were as follows:

Group 1	-	0 ppm
Group 2	-	900 ppm
Group 3	-	3000 ppm
Group 4	-	9000 ppm

Huntingdon Life Sciences
Princeton Research Center
East Millstone, New Jersey
Individual Parental Organ Weights

Summary statistics for absolute organ weights (g)
Study number: 034242

Printed: 04-Mar-04
Page: 1
Version 4.2.2

Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
				Female Animals				
1542/F	1/1	294.0	0.1002	1.9806	1.0813	2.6487	12.4373	1.4111
1543/F	1/1	275.8	0.1231	2.0492	1.0543	2.6045	12.8532	1.5772
1544/F	1/1	288.3	0.0909	2.0320	1.0546	2.2929	12.7755	1.4550
1545/F	1/1	250.4	0.0633	2.1593	0.8067	2.5894	12.2927	1.5853
1546/F	1/1	272.3	0.0936	2.3479	0.9616	2.7693	12.6460	1.7200
1547/F	1/1	289.4	0.1223	2.0326	0.9691	2.6300	13.5365	1.4515
1548/F	1/1	325.3	0.1011	2.4205	1.1695	3.1081	16.3065	1.7137
1549/F	1/1	259.2	0.0912	2.2276	0.9357	2.8516	12.6033	1.7384
1550/F	1/1	257.7	0.0891	1.9850	0.9161	2.2772	10.6622	1.3699
1551/F	1/1	270.4	0.1043	2.0444	0.8848	2.4699	12.2748	1.5995
1552/F	1/1	300.0	0.0914	2.1063	1.0626	2.4147	13.0295	1.4658
1553/F	1/1	309.4	0.0488	2.1399	1.1177	2.7338	15.0439	1.8374
Mean:		282.7	0.0933	2.1271	1.0012	2.6158	13.0385	1.5771
Standard deviation:		22.5	0.0210	0.1411	0.1059	0.2371	1.4316	0.1498
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
2542/F	2/1	326.5	0.0941	2.1578	1.0568	2.6297	13.5656	1.5882
2543/F	2/1	308.2	0.0737	2.0292	1.0883	2.3852	13.6593	1.4953
2544/F	2/1	280.1	0.0834	2.1325	0.9354	2.2256	13.0289	1.2102
2545/F	2/1	255.1	0.0982	2.1329	0.8595	2.5633	11.5648	1.3968
2546/F	2/1	280.1	0.0866	2.0209	0.8775	2.2685	14.7749	1.4204
2547/F	2/1	306.0	0.0862	2.0399	1.1405	2.6317	13.6683	1.5216
2548/F	2/1	283.6	0.1013	2.1317	1.0820	2.3740	11.8551	1.6876
2549/F	2/1	266.7	0.0879	2.0296	0.9380	2.8491	12.1239	1.5133
2550/F	2/1	283.2	0.0960	2.2910	0.9998	2.7743	13.8120	1.7901
2551/F	2/1	309.7	0.0825	2.1938	1.0310	2.8859	12.6161	1.7278
2552/F	2/1	304.0	0.0927	2.2322	1.0361	2.8608	14.7566	1.6849
2553/F	2/1	286.1	0.0799	2.0987	0.9390	2.8573	12.1314	1.4860
Mean:		290.8	0.0885	2.1242	0.9987	2.6088	13.1297	1.5435
Standard deviation:		20.4	0.0081	0.0864	0.0885	0.2446	1.0844	0.1630
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
3542/F	3/1	281.7	0.1326	2.1849	1.1488	2.7832	13.7193	1.5662
3543/F	3/1	302.0	0.0903	2.0065	1.0225	2.8254	12.5815	1.5379
3544/F	3/1	273.1	0.1065	2.1263	0.9471	2.5988	12.5414	1.3416
3545/F	3/1	283.6	0.1132	2.0206	1.1294	2.2203	12.1526	1.4236
3546/F	3/1	305.2	0.0816	2.1614	1.0752	2.7626	13.4248	1.6333
3547/F	3/1	260.5	0.1188	2.0642	0.9847	2.4650	12.4239	1.4305
3548/F	3/1	283.4	0.0982	1.9298	0.9993	2.3290	12.0641	1.4439
3549/F	3/1	306.3	0.0983	2.2141	1.0649	2.9217	12.6375	1.7490
3550/F	3/1	321.9	0.0834	2.1467	1.0800	3.0841	13.2944	1.4336
3551/F	3/1	291.6	0.1080	2.0011	1.0282	2.6630	12.9858	1.4753
3552/F	3/1	273.5	0.1091	2.1730	0.8852	2.6439	12.1402	1.6231
3553/F	3/1	354.9	0.0988	2.1623	1.2931	3.0181	15.1312	1.8363
Mean:		294.8	0.1032	2.0992	1.0549	2.6929	12.9247	1.5412

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
Standard deviation:		25.5	0.0147	0.0910	0.1055	0.2631	0.8760	0.1469
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
4542/F	4/1	262.2	0.1023	2.0028	0.8973	2.3139	11.4637	1.6062
4543/F	4/1	341.6	0.1028	2.2928	1.1958	2.9335	15.0995	1.6108
4544/F	4/1	287.4	0.0784	1.8916	0.9623	2.2316	11.8204	1.4746
4545/F	4/1	287.6	0.1049	2.1318	1.1135	2.4349	13.3428	1.6562
4546/F	4/1	271.0	0.1066	1.9337	0.9451	2.3410	12.8819	1.7430
4547/F	4/1	285.6	0.1127	2.0569	1.2265	2.7011	13.7604	1.7340
4548/F	4/1	317.0	0.0922	2.0435	0.9080	2.7394	13.2664	1.6686
4549/F	4/1	293.7	0.1005	2.0490	1.1058	2.9960	11.6378	1.6210
4550/F	4/1	279.4	0.0838	1.9514	0.9837	2.3198	10.7240	1.4857
4551/F	4/1	296.4	0.0936	1.9318	1.1465	2.5437	14.6897	1.4607
4552/F	4/1	291.9	0.0852	2.1951	0.9682	2.8065	12.3566	1.6717
4553/F	4/1	274.8	0.0953	2.0922	1.1673	2.8288	12.3774	1.5225
M e a n:		290.7	0.0965	2.0477	1.0517	2.5992	12.7851	1.6046
Standard deviation:		21.2	0.0103	0.1180	0.1190	0.2674	1.3170	0.0981
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovary Left	Ovary Right	Spleen	Thymus	Uterus w/vagina
				Female	Animals		
1542/F	1/1	294.0	0.0784	0.0743	0.6775	0.2427	1.2206
1543/F	1/1	275.8	0.0937	0.0985	0.5620	0.3102	1.1654
1544/F	1/1	288.3	0.0660	0.0722	0.5240	0.2101	1.2201
1545/F	1/1	250.4	0.0626	0.0694	0.4845	0.2249	1.0161
1546/F	1/1	272.3	0.0639	0.0869	0.8326	0.3660	1.3020
1547/F	1/1	289.4	0.0797	0.0813	0.6179	0.1627	1.5545
1548/F	1/1	325.3	0.0779	0.0636	0.8292	0.3617	0.9904
1549/F	1/1	259.2	0.0744	0.0601	0.7126	0.2152	1.2509
1550/F	1/1	257.7	0.0673	0.0751	0.5099	0.2848	1.0320
1551/F	1/1	270.4	0.0803	0.0937	0.5117	0.1984	1.1256
1552/F	1/1	300.0	0.0869	0.0701	0.6454	0.2429	1.0853
1553/F	1/1	309.4	0.0537	0.0409	0.5964	0.2631	1.1360
	Mean:	282.7	0.0737	0.0738	0.6253	0.2569	1.1749
Standard deviation:		22.5	0.0113	0.0155	0.1193	0.0634	0.1543
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)
2542/F	2/1	326.5	0.0795	0.0909	0.7750	0.2929	1.1879
2543/F	2/1	308.2	0.0670	0.1037	0.6249	0.1817	1.1026
2544/F	2/1	280.1	0.0946	0.0831	0.6354	0.1727	1.1030
2545/F	2/1	255.1	0.0734	0.0739	0.6729	0.2794	1.0666
2546/F	2/1	280.1	0.0709	0.0772	0.7403	0.2449	0.9061
2547/F	2/1	306.0	0.0939	0.0920	0.7057	0.2899	1.1531
2548/F	2/1	283.6	0.0713	0.0736	0.7504	0.3285	1.1192
2549/F	2/1	266.7	0.0738	0.0766	0.6360	0.2625	1.2039
2550/F	2/1	283.2	0.0674	0.0972	0.7977	0.3496	1.1914
2551/F	2/1	309.7	0.0700	0.0918	0.7172	0.2866	1.4246
2552/F	2/1	304.0	0.0681	0.0581	0.7343	0.3211	1.1030
2553/F	2/1	286.1	0.0639	0.0829	0.7801	0.4120	1.4130
	Mean:	290.8	0.0745	0.0834	0.7142	0.2852	1.1645
Standard deviation:		20.4	0.0100	0.0125	0.0599	0.0668	0.1421
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)
3542/F	3/1	281.7	0.0746	0.0935	0.6358	0.2424	1.2481
3543/F	3/1	302.0	0.0821	0.0969	0.7750	0.3543	1.3563
3544/F	3/1	273.1	0.0819	0.1305	0.7523	0.2923	1.8441
3545/F	3/1	283.6	0.0890	0.0736	0.6371	0.3309	1.4467
3546/F	3/1	305.2	0.0736	0.0979	0.6706	0.3940	1.2068
3547/F	3/1	260.5	0.0831	0.0892	0.6254	0.3230	1.0670
3548/F	3/1	283.4	0.0703	0.0688	0.5901	0.2324	1.2890
3549/F	3/1	306.3	0.0945	0.0825	0.7153	0.3578	1.1951
3550/F	3/1	321.9	0.0651	0.0933	0.9294	0.4638	1.3986
3551/F	3/1	291.6	0.0745	0.0876	0.6374	0.2595	1.3613
3552/F	3/1	273.5	0.0645	0.0888	0.7554	0.3718	1.2601
3553/F	3/1	354.9	0.0964	0.0938	0.8245	0.3326	1.2976
	Mean:	294.8	0.0791	0.0914	0.7124	0.3296	1.3309

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovary Left	Ovary Right	Spleen	Thymus	Uterus w/vagina
Standard deviation:		25.5	0.0106	0.0152	0.0993	0.0666	0.1910
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)
4542/F	4/1	262.2	0.0726	0.0795	0.4830	0.3412	1.2500
4543/F	4/1	341.6	0.0965	0.0913	0.5839	0.2920	1.0645
4544/F	4/1	287.4	0.0689	0.0844	0.7227	0.3432	1.1018
4545/F	4/1	287.6	0.0686	0.0822	0.9053	0.2727	1.2379
4546/F	4/1	271.0	0.0678	0.0835	0.6847	0.3501	1.4936
4547/F	4/1	285.6	0.0870	0.0811	0.6705	0.3030	1.6158
4548/F	4/1	317.0	0.0748	0.0695	0.8115	0.3296	1.1462
4549/F	4/1	293.7	0.0758	0.0776	0.7415	0.3049	1.2978
4550/F	4/1	279.4	0.0710	0.0724	0.6668	0.2102	1.1905
4551/F	4/1	296.4	0.0724	0.0755	0.7541	0.3003	1.2246
4552/F	4/1	291.9	0.0882	0.0667	0.5838	0.2970	0.9179
4553/F	4/1	274.8	0.1515	0.0779	0.6369	0.2366	1.2299
Mean:		290.7	0.0829	0.0785	0.6871	0.2984	1.2309
Standard deviation:		21.2	0.0234	0.0068	0.1120	0.0425	0.1842
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
				Female Animals				
1542/F	1/1	294.0	0.0341	0.6737	0.3678	0.9009	4.2304	0.4800
1543/F	1/1	275.8	0.0446	0.7430	0.3823	0.9443	4.6603	0.5719
1544/F	1/1	288.3	0.0315	0.7048	0.3658	0.7953	4.4313	0.5047
1545/F	1/1	250.4	0.0253	0.8623	0.3222	1.0341	4.9092	0.6331
1546/F	1/1	272.3	0.0344	0.8622	0.3531	1.0170	4.6441	0.6317
1547/F	1/1	289.4	0.0423	0.7023	0.3349	0.9088	4.6774	0.5016
1548/F	1/1	325.3	0.0311	0.7441	0.3595	0.9555	5.0128	0.5268
1549/F	1/1	259.2	0.0352	0.8594	0.3610	1.1002	4.8624	0.6707
1550/F	1/1	257.7	0.0346	0.7703	0.3555	0.8837	4.1374	0.5316
1551/F	1/1	270.4	0.0386	0.7561	0.3272	0.9134	4.5395	0.5915
1552/F	1/1	300.0	0.0305	0.7021	0.3542	0.8049	4.3432	0.4886
1553/F	1/1	309.4	0.0158	0.6916	0.3612	0.8836	4.8623	0.5939
	Mean:	282.7	0.0332	0.7560	0.3537	0.9285	4.6092	0.5605
Standard deviation:		22.5	0.0076	0.0695	0.0175	0.0894	0.2801	0.0639
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
2542/F	2/1	326.5	0.0288	0.6609	0.3237	0.8054	4.1549	0.4864
2543/F	2/1	308.2	0.0239	0.6584	0.3531	0.7739	4.4320	0.4852
2544/F	2/1	280.1	0.0298	0.7613	0.3340	0.7946	4.6515	0.4321
2545/F	2/1	255.1	0.0385	0.8361	0.3369	1.0048	4.5334	0.5476
2546/F	2/1	280.1	0.0309	0.7215	0.3133	0.8099	5.2749	0.5071
2547/F	2/1	306.0	0.0282	0.6666	0.3727	0.8600	4.4668	0.4973
2548/F	2/1	283.6	0.0357	0.7517	0.3815	0.8371	4.1802	0.5951
2549/F	2/1	266.7	0.0330	0.7610	0.3517	1.0683	4.5459	0.5674
2550/F	2/1	283.2	0.0339	0.8090	0.3530	0.9796	4.8771	0.6321
2551/F	2/1	309.7	0.0266	0.7084	0.3329	0.9318	4.0737	0.5579
2552/F	2/1	304.0	0.0305	0.7343	0.3408	0.9411	4.8541	0.5542
2553/F	2/1	286.1	0.0279	0.7336	0.3282	0.9987	4.2403	0.5194
	Mean:	290.8	0.0306	0.7336	0.3435	0.9004	4.5237	0.5318
Standard deviation:		20.4	0.0041	0.0558	0.0199	0.0990	0.3521	0.0547
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
3542/F	3/1	281.7	0.0471	0.7756	0.4078	0.9880	4.8702	0.5560
3543/F	3/1	302.0	0.0299	0.6644	0.3386	0.9356	4.1661	0.5092
3544/F	3/1	273.1	0.0390	0.7786	0.3468	0.9516	4.5922	0.4912
3545/F	3/1	283.6	0.0399	0.7125	0.3982	0.7829	4.2851	0.5020
3546/F	3/1	305.2	0.0267	0.7082	0.3523	0.9052	4.3987	0.5352
3547/F	3/1	260.5	0.0456	0.7924	0.3780	0.9463	4.7693	0.5491
3548/F	3/1	283.4	0.0347	0.6809	0.3526	0.8218	4.2569	0.5095
3549/F	3/1	306.3	0.0321	0.7229	0.3477	0.9539	4.1259	0.5710
3550/F	3/1	321.9	0.0259	0.6669	0.3355	0.9581	4.1300	0.4454
3551/F	3/1	291.6	0.0370	0.6862	0.3526	0.9132	4.4533	0.5059
3552/F	3/1	273.5	0.0399	0.7945	0.3237	0.9667	4.4388	0.5935
3553/F	3/1	354.9	0.0278	0.6093	0.3644	0.8504	4.2635	0.5174
	Mean:	294.8	0.0355	0.7160	0.3582	0.9145	4.3958	0.5238

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
Standard deviation:		25.5	0.0071	0.0589	0.0251	0.0636	0.2438	0.0397
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
4542/F	4/1	262.2	0.0390	0.7638	0.3422	0.8825	4.3721	0.6126
4543/F	4/1	341.6	0.0301	0.6712	0.3501	0.8588	4.4202	0.4715
4544/F	4/1	287.4	0.0273	0.6582	0.3348	0.7765	4.1129	0.5131
4545/F	4/1	287.6	0.0365	0.7412	0.3872	0.8466	4.6394	0.5759
4546/F	4/1	271.0	0.0393	0.7135	0.3487	0.8638	4.7535	0.6432
4547/F	4/1	285.6	0.0395	0.7202	0.4294	0.9458	4.8181	0.6071
4548/F	4/1	317.0	0.0291	0.6446	0.2864	0.8642	4.1850	0.5264
4549/F	4/1	293.7	0.0342	0.6977	0.3765	1.0201	3.9625	0.5519
4550/F	4/1	279.4	0.0300	0.6984	0.3521	0.8303	3.8382	0.5317
4551/F	4/1	296.4	0.0316	0.6518	0.3868	0.8582	4.9560	0.4928
4552/F	4/1	291.9	0.0292	0.7520	0.3317	0.9615	4.2332	0.5727
4553/F	4/1	274.8	0.0347	0.7614	0.4248	1.0294	4.5041	0.5540
Mean:		290.7	0.0334	0.7062	0.3626	0.8948	4.3996	0.5544
Standard deviation:		21.2	0.0044	0.0430	0.0406	0.0775	0.3493	0.0509
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovary Left	Ovary Right	Spleen	Thymus	Uterus w/vagina
				F e m a l e	A n i m a l s		
1542/F	1/1	294.0	0.0267	0.0253	0.2304	0.0826	0.4152
1543/F	1/1	275.8	0.0340	0.0357	0.2038	0.1125	0.4226
1544/F	1/1	288.3	0.0229	0.0250	0.1818	0.0729	0.4232
1545/F	1/1	250.4	0.0250	0.0277	0.1935	0.0898	0.4058
1546/F	1/1	272.3	0.0235	0.0319	0.3058	0.1344	0.4781
1547/F	1/1	289.4	0.0275	0.0281	0.2135	0.0562	0.5371
1548/F	1/1	325.3	0.0239	0.0196	0.2549	0.1112	0.3045
1549/F	1/1	259.2	0.0287	0.0232	0.2749	0.0830	0.4826
1550/F	1/1	257.7	0.0261	0.0291	0.1979	0.1105	0.4005
1551/F	1/1	270.4	0.0297	0.0347	0.1892	0.0734	0.4163
1552/F	1/1	300.0	0.0290	0.0234	0.2151	0.0810	0.3618
1553/F	1/1	309.4	0.0174	0.0132	0.1928	0.0850	0.3672
M e a n:		282.7	0.0262	0.0264	0.2211	0.0910	0.4179
Standard deviation:		22.5	0.0042	0.0063	0.0386	0.0219	0.0612
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)
2542/F	2/1	326.5	0.0243	0.0278	0.2374	0.0897	0.3638
2543/F	2/1	308.2	0.0217	0.0336	0.2028	0.0590	0.3578
2544/F	2/1	280.1	0.0338	0.0297	0.2268	0.0617	0.3938
2545/F	2/1	255.1	0.0288	0.0290	0.2638	0.1095	0.4181
2546/F	2/1	280.1	0.0253	0.0276	0.2643	0.0874	0.3235
2547/F	2/1	306.0	0.0307	0.0301	0.2306	0.0947	0.3768
2548/F	2/1	283.6	0.0251	0.0260	0.2646	0.1158	0.3946
2549/F	2/1	266.7	0.0277	0.0287	0.2385	0.0984	0.4514
2550/F	2/1	283.2	0.0238	0.0343	0.2817	0.1234	0.4207
2551/F	2/1	309.7	0.0226	0.0296	0.2316	0.0925	0.4600
2552/F	2/1	304.0	0.0224	0.0191	0.2415	0.1056	0.3628
2553/F	2/1	286.1	0.0223	0.0290	0.2727	0.1440	0.4939
M e a n:		290.8	0.0257	0.0287	0.2464	0.0985	0.4014
Standard deviation:		20.4	0.0038	0.0038	0.0230	0.0240	0.0493
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)
3542/F	3/1	281.7	0.0265	0.0332	0.2257	0.0860	0.4431
3543/F	3/1	302.0	0.0272	0.0321	0.2566	0.1173	0.4491
3544/F	3/1	273.1	0.0300	0.0478	0.2755	0.1070	0.6752
3545/F	3/1	283.6	0.0314	0.0260	0.2246	0.1167	0.5101
3546/F	3/1	305.2	0.0241	0.0321	0.2197	0.1291	0.3954
3547/F	3/1	260.5	0.0319	0.0342	0.2401	0.1240	0.4096
3548/F	3/1	283.4	0.0248	0.0243	0.2082	0.0820	0.4548
3549/F	3/1	306.3	0.0309	0.0269	0.2335	0.1168	0.3902
3550/F	3/1	321.9	0.0202	0.0290	0.2887	0.1441	0.4345
3551/F	3/1	291.6	0.0255	0.0300	0.2186	0.0890	0.4668
3552/F	3/1	273.5	0.0236	0.0325	0.2762	0.1359	0.4607
3553/F	3/1	354.9	0.0272	0.0264	0.2323	0.0937	0.3656
M e a n:		294.8	0.0269	0.0312	0.2417	0.1118	0.4546

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovary Left	Ovary Right	Spleen	Thymus	Uterus w/vagina
Standard deviation:		25.5	0.0036	0.0061	0.0263	0.0204	0.0798
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)
4542/F	4/1	262.2	0.0277	0.0303	0.1842	0.1301	0.4767
4543/F	4/1	341.6	0.0282	0.0267	0.1709	0.0855	0.3116
4544/F	4/1	287.4	0.0240	0.0294	0.2515	0.1194	0.3834
4545/F	4/1	287.6	0.0239	0.0286	0.3148	0.0948	0.4304
4546/F	4/1	271.0	0.0250	0.0308	0.2527	0.1292	0.5511
4547/F	4/1	285.6	0.0305	0.0284	0.2348	0.1061	0.5658
4548/F	4/1	317.0	0.0236	0.0219	0.2560	0.1040	0.3616
4549/F	4/1	293.7	0.0258	0.0264	0.2525	0.1038	0.4419
4550/F	4/1	279.4	0.0254	0.0259	0.2387	0.0752	0.4261
4551/F	4/1	296.4	0.0244	0.0255	0.2544	0.1013	0.4132
4552/F	4/1	291.9	0.0302	0.0229	0.2000	0.1017	0.3145
4553/F	4/1	274.8	0.0551	0.0283	0.2318	0.0861	0.4476
Mean:		290.7	0.0287	0.0271	0.2368	0.1031	0.4270
Standard deviation:		21.2	0.0087	0.0028	0.0381	0.0169	0.0799
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
				Female Animals				
1542/F	1/1	294.0	5.0591	100.0000	54.5946	133.7322	627.9562	71.2461
1543/F	1/1	275.8	6.0072	100.0000	51.4493	127.0984	627.2302	76.9666
1544/F	1/1	288.3	4.4734	100.0000	51.8996	112.8396	628.7156	71.6043
1545/F	1/1	250.4	2.9315	100.0000	37.3593	119.9185	569.2910	73.4173
1546/F	1/1	272.3	3.9865	100.0000	40.9558	117.9480	538.6090	73.2570
1547/F	1/1	289.4	6.0169	100.0000	47.6779	129.3909	665.9697	71.4110
1548/F	1/1	325.3	4.1768	100.0000	48.3165	128.4074	673.6832	70.7994
1549/F	1/1	259.2	4.0941	100.0000	42.0048	128.0122	565.7794	78.0391
1550/F	1/1	257.7	4.4887	100.0000	46.1511	114.7204	537.1386	69.0126
1551/F	1/1	270.4	5.1017	100.0000	43.2792	120.8130	600.4109	78.2381
1552/F	1/1	300.0	4.3394	100.0000	50.4487	114.6418	618.5966	69.5912
1553/F	1/1	309.4	2.2805	100.0000	52.2314	127.7536	703.0189	85.8638
Mean:		282.7	4.4130	100.0000	47.1973	122.9397	613.0333	74.1206
Standard deviation:		22.5	1.0914	0.0000	5.3211	6.9491	52.9870	4.8535
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
2542/F	2/1	326.5	4.3609	100.0000	48.9758	121.8695	628.6774	73.6027
2543/F	2/1	308.2	3.6320	100.0000	53.6320	117.5439	673.1372	73.6891
2544/F	2/1	280.1	3.9109	100.0000	43.8640	104.3658	610.9684	56.7503
2545/F	2/1	255.1	4.6041	100.0000	40.2972	120.1791	542.2102	65.4883
2546/F	2/1	280.1	4.2852	100.0000	43.4212	112.2520	731.1050	70.2855
2547/F	2/1	306.0	4.2257	100.0000	55.9096	129.0112	670.0475	74.5919
2548/F	2/1	283.6	4.7521	100.0000	50.7576	111.3665	556.1336	79.1669
2549/F	2/1	266.7	4.3309	100.0000	46.2160	140.3774	597.3542	74.5615
2550/F	2/1	283.2	4.1903	100.0000	43.6403	121.0956	602.8809	78.1362
2551/F	2/1	309.7	3.7606	100.0000	46.9961	131.5480	575.0798	78.7583
2552/F	2/1	304.0	4.1529	100.0000	46.4161	128.1606	661.0789	75.4816
2553/F	2/1	286.1	3.8071	100.0000	44.7420	136.1462	578.0436	70.8057
Mean:		290.8	4.1677	100.0000	47.0723	122.8263	618.8931	72.6098
Standard deviation:		20.4	0.3388	0.0000	4.5351	10.6643	55.7727	6.3272
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
3542/F	3/1	281.7	6.0689	100.0000	52.5791	127.3834	627.9144	71.6829
3543/F	3/1	302.0	4.5004	100.0000	50.9594	140.8124	627.0372	76.6459
3544/F	3/1	273.1	5.0087	100.0000	44.5422	122.2217	589.8227	63.0955
3545/F	3/1	283.6	5.6023	100.0000	55.8943	109.8832	601.4352	70.4543
3546/F	3/1	305.2	3.7753	100.0000	49.7455	127.8153	621.1160	75.5668
3547/F	3/1	260.5	5.7553	100.0000	47.7037	119.4167	601.8749	69.3005
3548/F	3/1	283.4	5.0886	100.0000	51.7826	120.6861	625.1478	74.8212
3549/F	3/1	306.3	4.4397	100.0000	48.0963	131.9588	570.7737	78.9937
3550/F	3/1	321.9	3.8850	100.0000	50.3098	143.6670	619.2948	66.7816
3551/F	3/1	291.6	5.3970	100.0000	51.3817	133.0768	648.9331	73.7244
3552/F	3/1	273.5	5.0207	100.0000	40.7363	121.6705	558.6838	74.6940
3553/F	3/1	354.9	4.5692	100.0000	59.8021	139.5782	699.7734	84.9235
Mean:		294.8	4.9259	100.0000	50.2944	128.1809	615.9839	73.3904

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
Standard deviation:		25.5	0.7178	0.0000	4.9277	10.0633	36.8221	5.7329
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)
4542/F	4/1	262.2	5.1078	100.0000	44.8023	115.5333	572.3837	80.1977
4543/F	4/1	341.6	4.4836	100.0000	52.1546	127.9440	658.5616	70.2547
4544/F	4/1	287.4	4.1446	100.0000	50.8723	117.9742	624.8890	77.9552
4545/F	4/1	287.6	4.9207	100.0000	52.2329	114.2180	625.8937	77.6902
4546/F	4/1	271.0	5.5127	100.0000	48.8752	121.0633	666.1789	90.1381
4547/F	4/1	285.6	5.4791	100.0000	59.6286	131.3190	668.9873	84.3016
4548/F	4/1	317.0	4.5119	100.0000	44.4336	134.0543	649.2000	81.6540
4549/F	4/1	293.7	4.9048	100.0000	53.9678	146.2177	567.9747	79.1118
4550/F	4/1	279.4	4.2944	100.0000	50.4100	118.8788	549.5542	76.1351
4551/F	4/1	296.4	4.8452	100.0000	59.3488	131.6751	760.4152	75.6134
4552/F	4/1	291.9	3.8814	100.0000	44.1073	127.8529	562.9174	76.1560
4553/F	4/1	274.8	4.5550	100.0000	55.7929	135.2070	591.5974	72.7703
M e a n:		290.7	4.7201	100.0000	51.3855	126.8281	624.8795	78.4982
Standard deviation:		21.2	0.5034	0.0000	5.3165	9.5620	60.5752	5.2527
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)	(12)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovary Left	Ovary Right	Spleen	Thymus	Uterus w/vagina
				Female	Animals		
1542/F	1/1	294.0	3.9584	3.7514	34.2068	12.2539	61.6278
1543/F	1/1	275.8	4.5725	4.8068	27.4253	15.1376	56.8710
1544/F	1/1	288.3	3.2480	3.5531	25.7874	10.3396	60.0443
1545/F	1/1	250.4	2.8991	3.2140	22.4378	10.4154	47.0569
1546/F	1/1	272.3	2.7216	3.7012	35.4615	15.5884	55.4538
1547/F	1/1	289.4	3.9211	3.9998	30.3995	8.0045	76.4784
1548/F	1/1	325.3	3.2183	2.6276	34.2574	14.9432	40.9172
1549/F	1/1	259.2	3.3399	2.6980	31.9896	9.6606	56.1546
1550/F	1/1	257.7	3.3904	3.7834	25.6877	14.3476	51.9899
1551/F	1/1	270.4	3.9278	4.5833	25.0294	9.7046	55.0577
1552/F	1/1	300.0	4.1257	3.3281	30.6414	11.5321	51.5264
1553/F	1/1	309.4	2.5095	1.9113	27.8705	12.2950	53.0866
Mean:		282.7	3.4860	3.4965	29.2662	12.0185	55.5220
Standard deviation:		22.5	0.6207	0.8178	4.1900	2.5088	8.6270
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)
2542/F	2/1	326.5	3.6843	4.2126	35.9162	13.5740	55.0514
2543/F	2/1	308.2	3.3018	5.1104	30.7954	8.9543	54.3367
2544/F	2/1	280.1	4.4361	3.8968	29.7960	8.0985	51.7233
2545/F	2/1	255.1	3.4413	3.4648	31.5486	13.0995	50.0070
2546/F	2/1	280.1	3.5083	3.8201	36.6322	12.1184	44.8365
2547/F	2/1	306.0	4.6032	4.5100	34.5948	14.2115	56.5273
2548/F	2/1	283.6	3.3447	3.4526	35.2020	15.4102	52.5027
2549/F	2/1	266.7	3.6362	3.7741	31.3362	12.9336	59.3171
2550/F	2/1	283.2	2.9419	4.2427	34.8189	15.2597	52.0035
2551/F	2/1	309.7	3.1908	4.1845	32.6921	13.0641	64.9376
2552/F	2/1	304.0	3.0508	2.6028	32.8958	14.3849	49.4131
2553/F	2/1	286.1	3.0447	3.9501	37.1706	19.6312	67.3274
Mean:		290.8	3.5154	3.9351	33.6166	13.3950	54.8320
Standard deviation:		20.4	0.5245	0.6191	2.4371	2.9836	6.4469
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)
3542/F	3/1	281.7	3.4143	4.2794	29.0997	11.0943	57.1239
3543/F	3/1	302.0	4.0917	4.8293	38.6245	17.6576	67.5953
3544/F	3/1	273.1	3.8518	6.1374	35.3807	13.7469	86.7281
3545/F	3/1	283.6	4.4046	3.6425	31.5302	16.3763	71.5975
3546/F	3/1	305.2	3.4052	4.5295	31.0262	18.2289	55.8342
3547/F	3/1	260.5	4.0258	4.3213	30.2975	15.6477	51.6907
3548/F	3/1	283.4	3.6429	3.5651	30.5783	12.0427	66.7945
3549/F	3/1	306.3	4.2681	3.7261	32.3066	16.1601	53.9768
3550/F	3/1	321.9	3.0326	4.3462	43.2944	21.6053	65.1512
3551/F	3/1	291.6	3.7230	4.3776	31.8525	12.9679	68.0276
3552/F	3/1	273.5	2.9682	4.0865	34.7630	17.1100	57.9890
3553/F	3/1	354.9	4.4582	4.3380	38.1307	15.3818	60.0102
Mean:		294.8	3.7739	4.3482	33.9070	15.6683	63.5432

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovary Left	Ovary Right	Spleen	Thymus	Uterus w/vagina
Standard deviation:		25.5	0.5013	0.6768	4.2541	2.9188	9.6675
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)
4542/F	4/1	262.2	3.6249	3.9694	24.1162	17.0361	62.4126
4543/F	4/1	341.6	4.2088	3.9820	25.4667	12.7355	46.4280
4544/F	4/1	287.4	3.6424	4.4618	38.2058	18.1434	58.2470
4545/F	4/1	287.6	3.2179	3.8559	42.4665	12.7920	58.0683
4546/F	4/1	271.0	3.5062	4.3181	35.4088	18.1052	77.2405
4547/F	4/1	285.6	4.2297	3.9428	32.5976	14.7309	78.5551
4548/F	4/1	317.0	3.6604	3.4010	39.7113	16.1292	56.0900
4549/F	4/1	293.7	3.6994	3.7872	36.1884	14.8804	63.3382
4550/F	4/1	279.4	3.6384	3.7102	34.1703	10.7718	61.0075
4551/F	4/1	296.4	3.7478	3.9083	39.0361	15.5451	63.3917
4552/F	4/1	291.9	4.0180	3.0386	26.5956	13.5301	41.8159
4553/F	4/1	274.8	7.2412	3.7234	30.4416	11.3087	58.7850
Mean:		290.7	4.0363	3.8416	33.7004	14.6424	60.4483
Standard deviation:		21.2	1.0493	0.3737	5.9775	2.4764	10.4752
Number of observ. :		(12)	(12)	(12)	(12)	(12)	(12)

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SATELLITE STUDY

APPENDIX FF

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 1 0 PPM

FEMALE#		OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
1542	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P																					
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P																					
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
	PUP# 15	WITHIN NORMAL LIMITS	P				P																	
	PUP# 16	WITHIN NORMAL LIMITS	P				P																	
	PUP# 17	WITHIN NORMAL LIMITS	P				P																	
	PUP# 18	WITHIN NORMAL LIMITS	P				P																	
1543	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	

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

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APPENDIX FF

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 1 0 PPM

FEMALE#		OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
1543	PUP# 15	WITHIN NORMAL LIMITS	P				P																	
	PUP# 16	WITHIN NORMAL LIMITS	P				P																	
1544	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P																					
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
	PUP# 15	WITHIN NORMAL LIMITS	P				P																	
	PUP# 16	WITHIN NORMAL LIMITS	P				P																	
1545	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	

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

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Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX FF

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND
NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY
INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 1 0 PPM

FEMALE#		OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
1546	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
1547	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
	PUP# 15	WITHIN NORMAL LIMITS	P				P																	

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

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX FF

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INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 1 0 PPM

FEMALE#		OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
1548	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
1549	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
1550	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	

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

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Huntingdon Life Sciences 03-4242S
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APPENDIX FF

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 1 0 PPM

DAY OF LACTATION

FEMALE#		OBSERVATIONS	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
1550	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
1551	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
1552	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	

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

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX FF

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 1 0 PPM

FEMALE#		OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
1552	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
1553	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	

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

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NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY
INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 2 900 PPM

FEMALE#		OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
2542	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P																					
	PUP# 15	WITHIN NORMAL LIMITS	P				P																	
2543	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
	PUP# 15	WITHIN NORMAL LIMITS	P				P																	

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

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SATELLITE STUDY

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NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY
INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 2 900 PPM

FEMALE#		OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
2544	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
	PUP# 15	WITHIN NORMAL LIMITS	P				P																	
	PUP# 16	WITHIN NORMAL LIMITS	P				P																	
	PUP# 17	WITHIN NORMAL LIMITS	P				P																	
	PUP# 18	WITHIN NORMAL LIMITS	P				P																	
2545	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	

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

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NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY
INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 2 900 PPM

FEMALE#		OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
2545	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
2546	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
	PUP# 15	WITHIN NORMAL LIMITS	P				P																	
2547	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P																					
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	

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

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INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 2 900 PPM

FEMALE#		OBSERVATIONS	DAY OF LACTATION	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
2547	PUP# 15	WITHIN NORMAL LIMITS		P				P																	
	PUP# 16	WITHIN NORMAL LIMITS		P				P																	
2548	PUP# 1	WITHIN NORMAL LIMITS		P				P																	
	PUP# 2	WITHIN NORMAL LIMITS		P				P																	
	PUP# 3	WITHIN NORMAL LIMITS		P				P																	
	PUP# 4	WITHIN NORMAL LIMITS		P				P																	
	PUP# 5	WITHIN NORMAL LIMITS		P				P																	
	PUP# 6	WITHIN NORMAL LIMITS		P				P																	
	PUP# 7	WITHIN NORMAL LIMITS		P				P																	
	PUP# 8	WITHIN NORMAL LIMITS		P				P																	
	PUP# 9	WITHIN NORMAL LIMITS		P				P																	
	PUP# 10	WITHIN NORMAL LIMITS		P				P																	
	PUP# 11	WITHIN NORMAL LIMITS		P				P																	
	PUP# 12	WITHIN NORMAL LIMITS		P				P																	
	PUP# 13	WITHIN NORMAL LIMITS		P				P																	
	PUP# 14	WITHIN NORMAL LIMITS		P				P																	
	PUP# 15	WITHIN NORMAL LIMITS		P				P																	
	PUP# 16	WITHIN NORMAL LIMITS		P				P																	
	PUP# 17	WITHIN NORMAL LIMITS		P				P																	
2549	PUP# 2	WITHIN NORMAL LIMITS		P				P																	
	PUP# 3	WITHIN NORMAL LIMITS		P				P																	
	PUP# 4	WITHIN NORMAL LIMITS		P				P																	
	PUP# 5	WITHIN NORMAL LIMITS		P				P																	
	PUP# 6	WITHIN NORMAL LIMITS		P				P																	
	PUP# 7	WITHIN NORMAL LIMITS		P				P																	
	PUP# 8	WITHIN NORMAL LIMITS		P				P																	
	PUP# 9	WITHIN NORMAL LIMITS		P																					
	PUP# 10	WITHIN NORMAL LIMITS		P				P																	
	PUP# 11	WITHIN NORMAL LIMITS		P				P																	
	PUP# 12	WITHIN NORMAL LIMITS		P				P																	

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

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INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 2 900 PPM

FEMALE#	PUP#	OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
2549	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
	PUP# 15	WITHIN NORMAL LIMITS	P				P																	
	PUP# 16	WITHIN NORMAL LIMITS	P				P																	
2550	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P																					
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
	PUP# 15	WITHIN NORMAL LIMITS	P				P																	
	PUP# 16	WITHIN NORMAL LIMITS	P				P																	
2551	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	

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

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INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 2 900 PPM

FEMALE#		OBSERVATIONS	DAY OF LACTATION	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
2551	PUP# 11	WITHIN NORMAL LIMITS		P				P																	
	PUP# 12	WITHIN NORMAL LIMITS		P				P																	
	PUP# 13	WITHIN NORMAL LIMITS		P				P																	
	PUP# 14	WITHIN NORMAL LIMITS		P				P																	
	PUP# 15	WITHIN NORMAL LIMITS		P				P																	
	PUP# 16	WITHIN NORMAL LIMITS		P				P																	
2552	PUP# 1	WITHIN NORMAL LIMITS		P				P																	
	PUP# 2	WITHIN NORMAL LIMITS		P				P																	
	PUP# 3	WITHIN NORMAL LIMITS		P				P																	
	PUP# 4	WITHIN NORMAL LIMITS		P				P																	
	PUP# 5	WITHIN NORMAL LIMITS		P				P																	
	PUP# 6	WITHIN NORMAL LIMITS		P				P																	
	PUP# 7	WITHIN NORMAL LIMITS		P				P																	
	PUP# 8	WITHIN NORMAL LIMITS		P				P																	
	PUP# 9	WITHIN NORMAL LIMITS		P				P																	
	PUP# 10	WITHIN NORMAL LIMITS		P				P																	
	PUP# 11	WITHIN NORMAL LIMITS		P				P																	
	PUP# 12	WITHIN NORMAL LIMITS		P				P																	
	PUP# 13	WITHIN NORMAL LIMITS		P				P																	
	PUP# 14	WITHIN NORMAL LIMITS		P				P																	
	PUP# 15	WITHIN NORMAL LIMITS		P				P																	
2553	PUP# 1	WITHIN NORMAL LIMITS		P				P																	
	PUP# 2	WITHIN NORMAL LIMITS		P				P																	
	PUP# 3	WITHIN NORMAL LIMITS		P				P																	
	PUP# 4	WITHIN NORMAL LIMITS		P				P																	
	PUP# 5	WITHIN NORMAL LIMITS		P				P																	
	PUP# 6	WITHIN NORMAL LIMITS		P				P																	
	PUP# 7	WITHIN NORMAL LIMITS		P				P																	
	PUP# 8	WITHIN NORMAL LIMITS		P				P																	
	PUP# 9	WITHIN NORMAL LIMITS		P				P																	

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

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX FF

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 2 900 PPM

FEMALE#		OBSERVATIONS	DAY OF LACTATION	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
2553	PUP# 10	WITHIN NORMAL LIMITS		P				P																	
	PUP# 11	WITHIN NORMAL LIMITS		P				P																	
	PUP# 12	WITHIN NORMAL LIMITS		P				P																	
	PUP# 13	WITHIN NORMAL LIMITS		P				P																	
	PUP# 14	WITHIN NORMAL LIMITS		P				P																	
	PUP# 15	WITHIN NORMAL LIMITS		P				P																	

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

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX FF

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 3 3000 PPM

FEMALE#		OBSERVATIONS DAY OF LACTATION	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
3542	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
	PUP# 15	WITHIN NORMAL LIMITS	P				P																	
	PUP# 16	WITHIN NORMAL LIMITS	P				P																	
	PUP# 17	WITHIN NORMAL LIMITS	P				P																	
3543	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P																					

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

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX FF

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 3 3000 PPM

FEMALE#		OBSERVATIONS DAY OF LACTATION	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
3544	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
	PUP# 15	WITHIN NORMAL LIMITS	P				P																	
	PUP# 16	WITHIN NORMAL LIMITS	P				P																	
3545	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P																					
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	

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

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BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 3 3000 PPM

FEMALE#		OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
3546	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P																					
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
	PUP# 15	WITHIN NORMAL LIMITS	P				P																	
	PUP# 16	WITHIN NORMAL LIMITS	P																					
3547	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	

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

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SATELLITE STUDY

APPENDIX FF

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 3 3000 PPM

FEMALE#	PUP#	OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
3548	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P																					
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P																					
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
	PUP# 15	WITHIN NORMAL LIMITS	P				P																	
3549	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P																					
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
	PUP# 15	WITHIN NORMAL LIMITS	P				P																	
	PUP# 16	WITHIN NORMAL LIMITS	P				P																	

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

11-FEB-2004 16:32

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX FF

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 3 3000 PPM

FEMALE#		OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
3550	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
3551	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
	PUP# 15	WITHIN NORMAL LIMITS	P				P																	
	PUP# 16	WITHIN NORMAL LIMITS	P				P																	

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

11-FEB-2004 16:32

Huntingdon Life Sciences 03-4242S
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APPENDIX FF

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 3 3000 PPM

FEMALE#		OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
3552	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
	PUP# 15	WITHIN NORMAL LIMITS	P				P																	
3553	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
	PUP# 15	WITHIN NORMAL LIMITS	P				P																	
	PUP# 16	WITHIN NORMAL LIMITS	P				P																	

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

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APPENDIX FF

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 3 3000 PPM

FEMALE#		OBSERVATIONS	DAY OF LACTATION	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
3553	PUP# 17	WITHIN NORMAL LIMITS		P				P																	
	PUP# 18	WITHIN NORMAL LIMITS		P				P																	

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

Huntingdon Life Sciences 03-4242S
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APPENDIX FF

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND
NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY
INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 4 9000 PPM

FEMALE#		OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
4542	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
	PUP# 15	WITHIN NORMAL LIMITS	P				P																	
4543	PUP# 1	WITHIN NORMAL LIMITS	P																					
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P																					
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P																					
	PUP# 13	WITHIN NORMAL LIMITS	P																					
	PUP# 14	WITHIN NORMAL LIMITS	P																					
	PUP# 15	WITHIN NORMAL LIMITS	P																					
	PUP# 16	WITHIN NORMAL LIMITS	P				P																	

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

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INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 4 9000 PPM

FEMALE#	PUP#	OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
4543	PUP# 6	SCABS					P																	
	PUP# 15	SCABS					P																	
	PUP# 14	SCABS					P																	
4544	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
4545	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	

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

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Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX FF

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 4 9000 PPM

FEMALE#		OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
4546	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
4547	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
	PUP# 15	WITHIN NORMAL LIMITS	P				P																	

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

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX FF

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND
NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY
INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 4 9000 PPM

FEMALE#		OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
4548	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
	PUP# 15	WITHIN NORMAL LIMITS	P				P																	
	PUP# 16	WITHIN NORMAL LIMITS	P				P																	
4549	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	

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

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX FF

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND
NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY
INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 4 9000 PPM

FEMALE#	PUP#	OBSERVATIONS (DAY OF LACTATION)	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
4550	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
	PUP# 15	WITHIN NORMAL LIMITS	P				P																	
	PUP# 16	WITHIN NORMAL LIMITS	P				P																	
4551	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
	PUP# 15	WITHIN NORMAL LIMITS	P				P																	

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

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Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX FF

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP CLINICAL OBSERVATIONS DURING LACTATION

GROUP 4 9000 PPM

FEMALE#		OBSERVATIONS	DAY OF LACTATION 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
4552	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
4553	PUP# 1	WITHIN NORMAL LIMITS	P				P																	
	PUP# 2	WITHIN NORMAL LIMITS	P				P																	
	PUP# 3	WITHIN NORMAL LIMITS	P				P																	
	PUP# 4	WITHIN NORMAL LIMITS	P				P																	
	PUP# 5	WITHIN NORMAL LIMITS	P				P																	
	PUP# 6	WITHIN NORMAL LIMITS	P				P																	
	PUP# 7	WITHIN NORMAL LIMITS	P				P																	
	PUP# 8	WITHIN NORMAL LIMITS	P				P																	
	PUP# 9	WITHIN NORMAL LIMITS	P				P																	
	PUP# 10	WITHIN NORMAL LIMITS	P				P																	
	PUP# 11	WITHIN NORMAL LIMITS	P				P																	
	PUP# 12	WITHIN NORMAL LIMITS	P				P																	
	PUP# 13	WITHIN NORMAL LIMITS	P				P																	
	PUP# 14	WITHIN NORMAL LIMITS	P				P																	
	PUP# 15	WITHIN NORMAL LIMITS	P				P																	
	PUP# 16	WITHIN NORMAL LIMITS	P				P																	

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

APPENDIX GG

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP BODY WEIGHTS (GRAMS)

GROUP 1 0 PPM

LACTATION DAY 1

FEMALE#	MEAN	PUP# 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
1542	6.1	M	6.1	5.8	6.6	6.7	5.9	6.6	6.4	6.6	5.5	6.0	5.8	5.7	5.8	6.2	6.2	5.6	6.2	
1543	6.1	6.3	6.6	6.4	5.8	5.9	5.9	6.4	6.0	6.1	6.0	5.9	6.1	6.0	5.7	6.0	6.3			
1544	6.8	6.5	7.3	7.0	7.3	6.9	6.8	7.2	6.4	7.0	7.2	6.5	6.9	6.7	6.4	7.0	6.0			
1545	6.7	D	7.0	6.6	6.5	7.0	7.1	7.1	6.9	6.4	6.6	7.0	5.7	6.9						
1546	6.5	6.8	7.2	7.0	6.9	6.5	6.6	6.9	6.6	6.5	6.2	6.1	6.2	6.5	5.6					
1547	6.8	7.2	7.7	6.4	6.9	6.9	6.9	7.1	6.8	6.3	6.3	7.1	6.2	6.7	6.6	6.3				
1548	7.7	8.3	8.5	8.0	8.2	8.2	8.0	6.7	7.5	6.4	7.1	7.6								
1549	6.7	7.0	6.6	6.9	7.0	6.9	6.9	7.0	6.4	6.9	6.8	5.7	6.4							
1550	6.8	6.9	7.2	7.0	7.1	7.2	7.4	6.3	6.6	6.7	6.9	6.1	6.3							
1551	6.1	6.3	6.2	6.3	6.1	6.1	6.3	5.8	6.2	6.1	5.5	6.1	6.2	6.0	5.9					
1552	7.6	7.7	8.1	8.4	8.2	7.4	7.2	7.6	7.4	7.5	7.6	7.5	6.8	7.8						
1553	7.7	7.9	8.0	7.8	7.8	7.1	7.7	8.0	7.3	7.6	7.3	8.0	7.7							

MEAN	6.8
S.D.	0.59
N	12

PUP STATUS CODES: D-DIED M-MISSING

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX GG

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP BODY WEIGHTS (GRAMS)

GROUP 2 900 PPM

LACTATION DAY 1

FEMALE#	MEAN	PUP# 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
2542	5.8	S	6.3	6.1	6.4	5.7	6.3	6.0	5.3	5.2	6.6	4.9	5.5	5.9	6.0	5.6				
2543	7.2	7.2	7.3	7.6	7.3	8.1	7.5	6.7	7.4	7.2	6.6	6.7	6.6	7.9	7.2	6.9				
2544	5.3	4.7	4.7	5.4	5.7	5.9	5.4	4.7	4.8	5.5	5.4	5.0	5.9	5.8	5.3	5.4	6.0	5.2	5.3	
2545	6.4	6.9	6.6	6.8	6.0	6.7	6.1	6.6	6.5	6.6	6.2	6.0	6.5	6.1	6.6					
2546	7.0	7.1	7.0	7.3	7.6	7.0	7.2	8.0	7.3	6.9	6.3	6.8	6.1	6.8	6.3	7.4				
2547	6.3	5.2	D	6.6	6.6	6.7	6.5	6.6	6.4	5.9	6.3	6.4	5.5	6.6	5.9	7.2	6.0			
2548	6.7	6.5	6.6	7.3	7.0	7.3	7.0	6.5	6.8	7.2	6.5	6.6	6.2	6.8	6.8	6.7	6.0	6.8		
2549	7.1	D	7.5	8.2	7.5	6.6	7.9	6.9	7.0	6.8	7.1	6.2	7.0	7.2	6.9	7.0	6.9			
2550	6.3	5.9	M	6.4	6.8	6.6	7.5	6.6	5.2	6.3	6.8	5.9	5.8	6.3	6.4	6.4	5.3			
2551	6.4	6.4	6.4	6.3	6.9	6.6	6.8	6.0	6.4	6.5	5.9	6.0	6.3	6.1	6.7	6.5	6.9			
2552	7.1	6.8	7.1	7.4	6.9	6.8	7.2	7.0	7.1	7.1	7.1	7.1	7.1	6.7	7.6	6.8				
2553	6.2	6.7	7.1	6.1	6.4	6.9	5.3	6.3	6.3	6.0	6.1	6.1	6.1	5.7	6.0	6.1				

MEAN	6.5
S.D.	0.56
N	12

PUP STATUS CODES: S-STILLBORN D-DIED M-MISSING

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX GG

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP BODY WEIGHTS (GRAMS)

GROUP 3 3000 PPM

LACTATION DAY 1

FEMALE#	MEAN	PUP# 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
3542	6.6	7.1	6.3	6.6	6.7	6.7	7.2	7.3	6.8	5.7	6.5	6.7	6.7	6.3	6.3	6.6	6.2	5.8		
3543	7.9	8.3	8.2	7.9	8.3	7.5	8.0	8.0	7.6	7.5	8.0	7.4	7.8	M						
3544	7.1	D	7.6	7.0	8.1	6.9	7.0	7.6	7.0	6.7	7.1	6.7	6.7	7.2	7.1	6.5	6.9			
3545	6.6	6.9	6.8	7.5	7.1	6.9	7.0	7.5	6.5	6.5	4.0	6.2	6.7	6.3						
3546	6.2	D	6.2	6.8	6.9	6.8	6.6	6.0	5.5	D	5.0	5.4	5.0	6.9	6.9	6.7	M			
3547	7.7	7.7	8.2	8.3	7.7	8.0	8.4	7.5	7.1	7.1	7.4	8.4	7.3	7.5	7.2					
3548	6.8	7.5	7.5	6.3	7.1	6.8	6.5	6.8	7.0	5.8	7.4	6.4	6.9	6.6	6.9	6.5				
3549	6.3	7.0	6.5	6.5	6.3	6.5	6.3	6.5	6.5	6.6	6.2	6.9	6.3	6.3	5.6	6.1	5.4			
3550	6.9	6.9	6.5	7.7	6.5	6.6	7.4	7.3	7.5	7.6	6.5	6.7	6.6	6.2	6.6					
3551	6.3	S	5.9	6.7	6.2	6.5	6.1	7.3	5.9	5.7	5.7	6.4	6.6	6.2	5.9	6.5	6.5			
3552	6.4	6.7	6.3	5.7	6.9	6.8	6.6	6.3	6.6	7.2	6.6	6.4	6.2	5.7	6.0	6.5				
3553	7.2	7.4	7.2	7.4	8.1	7.8	7.6	7.7	7.5	7.2	7.1	7.4	6.8	6.7	7.2	7.0	6.8	6.5	6.7	

MEAN	6.8
S.D.	0.55
N	12

PUP STATUS CODES: S-STILLBORN D-DIED M-MISSING

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX GG

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP BODY WEIGHTS (GRAMS)

GROUP 4 9000 PPM

LACTATION DAY 1

FEMALE#	MEAN	PUP# 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
4542	6.2	6.7	6.7	6.4	6.8	6.0	6.3	6.1	6.4	6.5	5.6	6.4	6.4	6.1	5.1	6.0				
4543	5.8	4.6	6.3	6.4	6.7	5.5	5.7	6.4	5.9	6.4	5.6	5.3	4.3	D	6.0	5.8	6.1			
4544	6.4	6.4	6.4	5.9	6.6	6.7	6.5	6.4	6.2	6.6	6.4	6.1	6.6	6.5	5.8					
4545	7.4	D	S	7.8	7.4	7.8	8.0	7.2	7.7	7.0	6.8	7.0	7.4	7.4	7.5					
4546	7.3	7.9	7.5	7.4	7.1	7.5	7.4	7.8	7.1	6.4	7.3	7.3	7.5	6.4	7.0					
4547	6.2	6.7	6.1	7.2	5.3	5.7	6.7	6.1	6.2	6.4	5.9	6.6	6.1	5.9	6.2	6.3				
4548	7.1	S	7.6	7.2	6.9	8.3	7.4	7.0	7.4	7.3	7.0	7.1	7.0	6.6	6.9	6.4	7.1			
4549	6.0	6.8	6.5	6.4	6.3	6.3	6.1	5.6	5.8	5.8	5.6	5.8	5.9	5.8	5.4					
4550	6.1	5.9	6.1	6.2	6.3	6.7	6.0	6.3	6.1	6.4	5.7	5.9	5.7	6.3	6.0	5.3	6.1			
4551	7.7	S	8.4	6.3	8.3	7.9	8.2	7.9	7.7	7.6	7.9	7.9	7.8	7.9	7.1	7.5				
4552	7.3	7.0	6.5	7.9	7.6	7.1	7.8	7.3	7.3	7.1	7.1	7.3	7.5	7.3						
4553	7.3	7.4	8.2	7.3	7.5	7.5	7.3	7.2	7.1	7.0	7.3	6.6	7.9	7.1	7.1	7.3	6.3			

MEAN	6.7
S.D.	0.67
N	12

PUP STATUS CODES: S-STILLBORN D-DIED

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Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX GG

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP BODY WEIGHTS (GRAMS)

GROUP 1 0 PPM

LACTATION DAY 4

FEMALE#	MEAN	PUP# 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
1542	8.7	M	8.6	8.6	9.7	8.8	8.7	8.9	8.5	9.1	D	8.4	8.1	M	8.1	8.8	8.9	7.9	8.8	
1543	7.8	8.1	8.1	8.1	7.4	8.1	7.6	7.7	7.9	7.6	7.8	7.3	7.7	7.4	7.6	7.7	8.3			
1544	9.4	8.9	10.0	9.3	10.0	10.1	9.7	D	8.9	9.8	10.1	8.9	9.8	9.1	8.9	9.4	7.9			
1545	9.9	D	10.5	9.9	9.9	10.3	10.1	10.0	9.7	9.3	9.8	10.5	8.8	9.8						
1546	8.9	8.8	9.5	9.2	9.1	9.2	9.1	9.2	9.2	8.7	8.5	8.7	8.6	8.5	7.9					
1547	9.3	9.6	10.5	8.4	9.6	9.0	9.4	9.7	9.3	8.9	9.0	9.7	8.6	9.4	8.9	9.0				
1548	12.2	12.5	13.6	13.6	13.2	13.0	12.9	11.9	11.2	10.2	10.9	11.7								
1549	9.3	9.8	9.4	9.6	9.6	9.3	9.3	9.5	9.0	8.9	8.0	9.4	9.3							
1550	10.0	10.1	10.4	10.1	10.1	10.6	10.6	9.3	9.8	10.0	10.3	9.3	9.4							
1551	9.1	9.5	8.9	9.3	8.8	9.4	9.1	8.7	9.3	9.4	9.6	8.3	9.0	9.3	8.7					
1552	10.7	11.4	11.3	11.2	11.3	10.3	10.4	10.4	10.2	10.4	11.4	10.5	9.5	11.1						
1553	11.4	11.6	11.0	11.7	11.8	11.1	11.6	11.9	11.1	11.3	10.9	11.8	11.5							

MEAN	9.7
S.D.	1.24
N	12

PUP STATUS CODES: D-DIED M-MISSING

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX GG

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP BODY WEIGHTS (GRAMS)

GROUP 2 900 PPM

LACTATION DAY 4

FEMALE#	MEAN	PUP# 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
2542	8.6	S	9.2	9.3	9.5	8.0	8.8	9.0	7.3	7.3	9.5	7.2	9.0	9.3	M	8.6				
2543	9.4	8.9	9.9	9.9	9.2	11.0	9.6	8.9	9.4	9.7	8.6	8.5	8.8	10.6	9.7	8.8				
2544	6.9	6.7	5.8	7.2	7.7	7.5	7.1	5.9	6.5	7.0	6.9	6.9	6.9	7.4	7.5	6.7	7.6	7.0	6.7	
2545	8.6	9.3	8.6	8.9	8.1	9.5	8.3	8.3	8.6	9.0	8.5	8.4	7.9	8.6	8.6					
2546	9.8	10.0	9.8	9.8	10.2	10.0	9.9	10.9	10.2	9.8	8.8	9.7	8.8	9.3	9.5	10.3				
2547	9.3	8.4	D	9.9	9.5	9.7	10.0	9.7	10.0	8.6	8.9	9.5	8.0	9.6	9.0	9.9	9.4			
2548	9.4	8.9	9.1	9.6	10.1	10.1	10.7	9.0	9.4	9.8	9.2	8.8	8.5	9.6	9.7	9.7	8.5	9.8		
2549	9.8	D	10.4	10.8	10.4	9.4	9.9	10.1	9.6	M	9.5	7.5	10.3	9.8	9.7	9.8	9.4			
2550	9.2	8.8	M	10.0	9.9	9.3	11.1	10.0	7.9	9.4	10.0	8.4	9.2	9.1	8.4	9.4	7.8			
2551	8.8	9.0	9.1	7.9	9.3	9.5	9.0	7.8	9.2	9.2	8.2	7.8	9.1	8.5	9.1	9.1	9.5			
2552	10.4	10.2	10.7	10.2	9.5	10.3	10.9	10.6	10.8	11.0	10.7	10.2	10.6	9.7	10.7	9.6				
2553	9.1	10.0	9.5	9.0	9.2	9.7	8.1	9.6	8.8	9.3	9.4	8.6	8.7	8.8	9.0	8.9				

MEAN	9.1
S.D.	0.86
N	12

PUP STATUS CODES: S-STILLBORN D-DIED M-MISSING

11-FEB-2004 16:35

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX GG

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP BODY WEIGHTS (GRAMS)

GROUP 3 3000 PPM

LACTATION DAY 4

FEMALE#	MEAN	PUP# 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
3542	8.2	8.8	8.2	8.0	8.6	7.9	9.0	8.9	8.5	7.5	8.9	8.7	8.1	7.6	7.7	8.4	7.4	7.3		
3543	11.5	11.9	11.9	11.8	11.7	10.8	10.9	11.2	11.3	11.0	12.0	10.9	12.0	M						
3544	9.7	D	10.6	9.7	10.9	9.3	9.5	9.9	9.8	9.1	9.7	9.2	9.5	9.2	9.5	9.6	9.9			
3545	9.8	10.1	9.6	10.4	10.1	10.1	10.0	10.9	9.5	9.4	M	9.2	9.3	8.8						
3546	8.7	D	8.2	9.1	9.6	9.8	9.6	8.1	7.3	D	7.0	7.4	7.3	9.9	9.7	9.6	M			
3547	9.8	9.7	10.6	10.6	10.0	10.0	10.1	9.5	9.1	9.4	9.1	10.3	9.5	9.5	9.1					
3548	9.4	10.5	10.6	9.5	D	9.4	9.1	9.3	9.6	8.3	8.7	8.8	M	9.1	9.6	9.2				
3549	9.1	10.2	9.3	M	9.2	9.2	8.8	9.1	9.7	9.5	9.1	9.9	9.3	9.2	8.0	8.5	8.1			
3550	9.7	10.1	9.4	10.3	9.3	9.8	9.0	9.7	10.5	10.9	9.5	10.0	9.2	9.2	9.2					
3551	8.8	S	7.6	8.7	8.8	8.7	9.1	9.4	9.0	8.3	8.5	8.7	9.0	9.1	8.7	9.3	8.9			
3552	8.8	9.5	8.6	8.1	9.0	8.8	8.8	8.8	9.0	9.4	9.0	8.8	8.5	7.7	8.4	9.2				
3553	10.4	11.2	11.0	11.1	12.1	10.4	10.8	10.6	10.1	11.1	9.5	10.9	9.1	9.0	11.2	10.4	9.7	8.8	9.5	

MEAN	9.5
S.D.	0.87
N	12

PUP STATUS CODES: S-STILLBORN D-DIED M-MISSING

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX GG

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP BODY WEIGHTS (GRAMS)

GROUP 4 9000 PPM LACTATION DAY 4

FEMALE#	MEAN	PUP# 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
4542	8.2	8.2	9.1	8.2	9.0	8.0	8.4	8.2	8.1	8.3	7.4	8.5	8.5	8.0	7.3	8.3				
4543	9.0	D	9.2	9.1	9.9	8.5	8.4	9.6	9.0	9.2	8.3	8.5	M	D	9.3	8.5	9.3			
4544	9.6	9.8	9.7	9.1	10.2	9.4	9.5	9.5	10.1	9.6	9.4	9.3	10.0	9.7	8.5					
4545	10.1	D	S	10.4	10.1	10.7	10.8	9.8	10.1	9.1	9.7	10.0	10.2	10.2	10.0					
4546	9.6	10.4	9.8	9.3	9.0	9.9	9.9	9.9	9.3	9.0	9.6	9.3	10.3	9.1	9.6					
4547	8.9	9.5	9.2	10.0	7.8	8.2	9.3	8.4	9.1	9.3	8.9	9.3	8.9	8.3	8.7	9.0				
4548	9.6	S	9.7	9.4	9.4	9.3	10.2	9.8	9.7	10.1	10.1	9.4	9.2	8.9	9.5	9.3	9.9			
4549	9.1	9.8	9.4	9.5	9.5	10.0	9.2	8.5	9.2	8.3	8.6	8.6	9.0	8.9	9.0					
4550	8.5	8.0	8.8	9.2	8.4	9.2	8.3	8.8	8.9	9.0	8.1	8.1	7.9	8.0	8.6	7.8	8.6			
4551	10.7	S	11.1	9.7	11.5	11.2	10.0	11.2	10.7	11.1	10.5	10.9	10.8	10.8	10.8	9.7				
4552	11.1	10.1	10.2	11.8	11.5	11.0	11.7	11.5	11.2	10.5	10.7	11.3	11.6	11.3						
4553	10.0	10.3	10.8	10.4	10.3	10.8	10.1	10.1	9.4	9.1	10.5	9.7	10.5	9.9	9.7	9.8	8.9			

MEAN	9.5
S.D.	0.86
N	12

PUP STATUS CODES: S-STILLBORN D-DIED M-MISSING

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX HH

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
1542	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9M	K	4		NO REMARKABLE OBSERVATIONS
	10F	D	1	STOMACH	MILK IN STOMACH
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
	16F	K	4		NO REMARKABLE OBSERVATIONS
	17F	K	4		NO REMARKABLE OBSERVATIONS
	18F	K	4		NO REMARKABLE OBSERVATIONS
1543	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
	16F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: D-DIED K-SCHEDULED SACRIFICE

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX HH

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
1544	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7F	D	3	GROSS EXAM	AUTOLYSIS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10M	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
	16F	K	4		NO REMARKABLE OBSERVATIONS
1545	1F	D	0	LUNGS	LUNG FLOATATION TEST - FOUND DEAD
				STOMACH	NO MILK IN STOMACH
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: D-DIED K-SCHEDULED SACRIFICE

APPENDIX HH

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
1546	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
1547	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: K-SCHEDULED SACRIFICE

APPENDIX HH

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
1548	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
1549	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
1550	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: K-SCHEDULED SACRIFICE

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX HH

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
1550 (CONTINUED)					
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
1551	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
1552	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5F	K	4		NO REMARKABLE OBSERVATIONS
	6F	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11M	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13M	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: K-SCHEDULED SACRIFICE

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX HH

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 1 0 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
1553	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: K-SCHEDULED SACRIFICE

Huntingdon Life Sciences 03-4242S
SATELLITE STUDY

APPENDIX HH

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 2 900 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
2542	1M	S		STOMACH	NO MILK IN STOMACH
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
2543	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: S-STILLBORN K-SCHEDULED SACRIFICE

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BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 2 900 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
2544	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
	16F	K	4		NO REMARKABLE OBSERVATIONS
	17F	K	4		NO REMARKABLE OBSERVATIONS
	18F	K	4		NO REMARKABLE OBSERVATIONS
2545	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: K-SCHEDULED SACRIFICE

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BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 2 900 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
2546	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9M	K	4		NO REMARKABLE OBSERVATIONS
	10M	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4	LIMBS	EDEMA
					LEFT FORELIMB WITH TAN SCAB
	15F	K	4		NO REMARKABLE OBSERVATIONS
2547	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	D	1	STOMACH	NO MILK IN STOMACH
				LUNGS	LUNG FLOATATION TEST - FOUND DEAD
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: D-DIED K-SCHEDULED SACRIFICE

APPENDIX HH

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 2 900 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
2547 (CONTINUED)					
	16F	K	4		NO REMARKABLE OBSERVATIONS
2548	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
	16F	K	4		NO REMARKABLE OBSERVATIONS
	17F	K	4		NO REMARKABLE OBSERVATIONS
2549	1F	D	0	LUNGS	LUNG FLOATATION TEST - FOUND DEAD
				STOMACH	NO MILK IN STOMACH
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: D-DIED K-SCHEDULED SACRIFICE

APPENDIX HH

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 2 900 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
2549 (CONTINUED)					
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
	16F	K	4		NO REMARKABLE OBSERVATIONS
2550	1M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
	16F	K	4		NO REMARKABLE OBSERVATIONS
2551	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9M	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: K-SCHEDULED SACRIFICE

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BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 2 900 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
2551 (CONTINUED)					
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
	16F	K	4		NO REMARKABLE OBSERVATIONS
2552	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
2553	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6F	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: K-SCHEDULED SACRIFICE

APPENDIX HH

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 2 900 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
2553 (CONTINUED)					
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: K-SCHEDULED SACRIFICE

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BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 3 3000 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
3542	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
	16F	K	4		NO REMARKABLE OBSERVATIONS
	17F	K	4		NO REMARKABLE OBSERVATIONS
3543	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: K-SCHEDULED SACRIFICE

APPENDIX HH

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 3 3000 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
3544	1F	D	0	LUNGS	LUNG FLOATATION TEST - FOUND DEAD
				STOMACH	NO MILK IN STOMACH
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9M	K	4		NO REMARKABLE OBSERVATIONS
	10M	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
	16F	K	4		NO REMARKABLE OBSERVATIONS
3545	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: D-DIED K-SCHEDULED SACRIFICE

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BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 3 3000 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
3546	1F	D	0	LUNGS	LUNG FLOATATION TEST - FOUND DEAD
				STOMACH	NO MILK IN STOMACH
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	D	1	STOMACH	NO MILK IN STOMACH
				LUNGS	LUNG FLOATATION TEST - FOUND DEAD
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
3547	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: D-DIED K-SCHEDULED SACRIFICE

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BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 3 3000 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
3548	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	D	3		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6F	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
3549	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
	16F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: D-DIED K-SCHEDULED SACRIFICE

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BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 3 3000 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
3550	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9M	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
3551	1F	S		LUNGS	LUNG FLOATATION TEST - STILLBORN
				STOMACH	NO MILK IN STOMACH
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9M	K	4		NO REMARKABLE OBSERVATIONS
	10M	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
	16F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: S-STILLBORN K-SCHEDULED SACRIFICE

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BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 3 3000 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
3552	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9M	K	4		NO REMARKABLE OBSERVATIONS
	10M	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
3553	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
	16F	K	4		NO REMARKABLE OBSERVATIONS
	17F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: K-SCHEDULED SACRIFICE

APPENDIX HH

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 3 3000 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
3553 (CONTINUED)					
	18F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: K-SCHEDULED SACRIFICE

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BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 4 9000 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
4542	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
4543	1M	D	4	GROSS EXAM	AUTOLYSIS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4	EXTERNAL EXAM	TIP OF TAIL MISSING
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4	EXTERNAL EXAM	SCAB TOP OF HEAD EXTERNAL FINDING CONFIRMED 0.6 CM IN DIAMETER, RED
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	M	2	STOMACH	MILK IN STOMACH
	13F	D	1	STOMACH	MILK IN STOMACH
	14F	K	4	EXTERNAL EXAM	SCAB RIGHT SHOULDER EXTERNAL FINDING CONFIRMED RED, 0.5 X 0.2 CM

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: D-DIED M-MISSING K-SCHEDULED SACRIFICE

APPENDIX HH

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 4 9000 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
4543 (CONTINUED)					
	15F	K	4	EXTERNAL EXAM	SCAB
					DORSAL CERVICAL
					EXTERNAL FINDING CONFIRMED
					RED, 0.5 X 0.2 CM
	16F	K	4		NO REMARKABLE OBSERVATIONS
4544	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
4545	1M	D	0	LUNGS	LUNG FLOATATION TEST - FOUND DEAD
				STOMACH	NO MILK IN STOMACH
	2F	S		LUNGS	LUNG FLOATATION TEST - STILLBORN
				STOMACH	NO MILK IN STOMACH
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9M	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: S-STILLBORN D-DIED K-SCHEDULED SACRIFICE

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BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 4 9000 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
4545 (CONTINUED)					
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
4546	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
4547	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: K-SCHEDULED SACRIFICE

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BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 4 9000 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
4547 (CONTINUED)					
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
4548	1F	S		LUNGS	LUNG FLOATATION TEST - STILLBORN
				STOMACH	NO MILK IN STOMACH
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
	16F	K	4		NO REMARKABLE OBSERVATIONS
4549	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: S-STILLBORN K-SCHEDULED SACRIFICE

APPENDIX HH

BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 4 9000 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
4549 (CONTINUED)					
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
4550	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7M	K	4		NO REMARKABLE OBSERVATIONS
	8M	K	4		NO REMARKABLE OBSERVATIONS
	9M	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
	16F	K	4		NO REMARKABLE OBSERVATIONS
4551	1F	S		LUNGS	LUNG FLOATATION TEST - STILLBORN
				STOMACH	NO MILK IN STOMACH
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: S-STILLBORN K-SCHEDULED SACRIFICE

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BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 4 9000 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
4551 (CONTINUED)					
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS
4552	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
4553	1M	K	4		NO REMARKABLE OBSERVATIONS
	2M	K	4		NO REMARKABLE OBSERVATIONS
	3M	K	4		NO REMARKABLE OBSERVATIONS
	4M	K	4		NO REMARKABLE OBSERVATIONS
	5M	K	4		NO REMARKABLE OBSERVATIONS
	6M	K	4		NO REMARKABLE OBSERVATIONS
	7F	K	4		NO REMARKABLE OBSERVATIONS
	8F	K	4		NO REMARKABLE OBSERVATIONS
	9F	K	4		NO REMARKABLE OBSERVATIONS
	10F	K	4		NO REMARKABLE OBSERVATIONS
	11F	K	4		NO REMARKABLE OBSERVATIONS
	12F	K	4		NO REMARKABLE OBSERVATIONS
	13F	K	4		NO REMARKABLE OBSERVATIONS
	14F	K	4		NO REMARKABLE OBSERVATIONS
	15F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: K-SCHEDULED SACRIFICE

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BUTANE: COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

INDIVIDUAL PUP NECROPSY OBSERVATIONS

GROUP 4 9000 PPM

FEMALE#	PUP#	STATUS	DAY	ORGAN	OBSERVATION
4553 (CONTINUED)					
	16F	K	4		NO REMARKABLE OBSERVATIONS

SEX CODES: M-Male, F=Female, U=Undetermined
PUP STATUS CODES: K-SCHEDULED SACRIFICE

	Inhalation Report	Appendix II

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1. INTRODUCTION

This appendix presents the methodology for exposure atmosphere generation monitoring and results.

2. MATERIALS AND METHODS

2.1. HUSBANDRY DURING EXPOSURE PERIODS

2.1.1. HOUSING

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

2.1.2. FEED

None was provided during exposure.

2.1.3. WATER

None was provided during exposure.

2.1.4. ENVIRONMENTAL CONDITIONS

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

Temperature

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

Relative Humidity

Desired:	40 to 60%
Actual:	42 to 65%

2.2. TEST SUBSTANCE ADMINISTRATION AND CHAMBER OPERATIONS

2.2.1. ROUTE OF ADMINISTRATION

Inhalation as a gas, via whole-body exposures

2.2.2. TEST SUBSTANCE ADMINISTRATION

The test substance was administered as a gas in the breathing air of the animals. The test atmosphere was generated by an appropriate procedure determined during the pre-study trials. The trials were performed (at least two 6-hour periods) to evaluate the optimal set of conditions and equipment to generate a stable atmosphere at the target exposure levels and maintain uniform conditions throughout the exposure chambers.

2.2.3. TARGET EXPOSURE LEVELS

Group 1 - 0 ppm
Group 2 - 900 ppm
Group 3 - 3000 ppm
Group 4 - 9000 ppm

2.2.4. DURATION AND FREQUENCY OF ADMINISTRATION

Main Study male rats were exposed once daily, seven days/week for 2 weeks prior to mating initiation. Exposure of Main Study male rats (12/group) continued during the mating and post-mating periods until euthanized for a minimum exposure of 28 days. Main Study female rats (12/group) were exposed once daily, seven days/week for a minimum exposure of 28 days. Satellite female rats (12/group) for the reproduction study were exposed once daily, seven days/week for at least two weeks prior to mating initiation. Satellite female rats continued to be exposed once daily during mating. Once mated, Satellite female rats were exposed once daily during gestation (Days 0-19). One Group 4 female continued for 7 days post-mating until it appeared to be at a presumed Gestation Day 19.

2.2.5. CHAMBER OPERATIONS

The whole-body exposure chambers each had a volume of approximately 1000 liters. The chambers were operated at a minimum flow rate of 200 liters per minute. The final airflow was set to provide at least one air change (calculated by dividing the chamber volume by the airflow rate) in 5.0 minutes (12 air changes/hour) and a T_{99} equilibrium time (calculated by multiplying the air change by the exponential factor 4.6) of at most 23 minutes. Initial settings for each group are as follows:

Group	Airflow Rate (Lpm)	Air Change (min)	T_{99} (min)
1	221	4.5	21
2	201	5.0	24
3	204	4.9	23
4	212	4.7	22

This chamber size and airflow rates were considered adequate to maintain the animal loading factor below 5% and the oxygen level at 19% or higher. At the end of the exposure, all animals remained in chamber for a minimum of 30 minutes. During this time, the chamber was operated at the same flow rate as used during the exposure using clean air only. Recordings of airflow rate and static pressure were made every half-hour during the exposure.

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

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

2.2.6. EXPOSURE PROCEDURE

Group 1

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

Groups 2 - 4

The test substance was delivered from a single cylinder, through a regulator and two backpressure gauges, and branched, via ¼" tubing, to the three exposure chambers. For each chamber, ¼" tubing directed the test substance to a flowmeter, regulated by a metering valve, and into the inlet of a 1000 Liter stainless steel and glass whole-body exposure chamber.

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

2.3. EXPOSURE CONCENTRATION DETERMINATION

2.3.1. NOMINAL CONCENTRATION

A nominal exposure concentration (ppm) was calculated by dividing the average test substance flow (ccm) during each exposure by the average chamber airflow (Lpm).

$$\text{Nominal (ppm)} = \frac{\text{Test Substance Flow (ccm)}}{\text{Chamber Airflow (Lpm)}} \times 1000$$

An overall nominal exposure concentration (ppm) was also calculated (for Groups 2, 3 and 4 combined) by weighing the cylinder before and after each day of exposure and dividing the weight differential (grams) by the total chamber airflow (L).

$$\text{Nominal (ppm)} = \frac{\Delta\text{Wt (g)} \times 10^6\ \mu\text{g/g} \times 22.4\ \mu\text{L}/\mu\text{mole} \times 295°\text{K}/273°\text{K}}{\text{Chamber Airflow (Lpm)} \times \text{Exposure Duration (min)} \times 58.12\ \mu\text{g}/\mu\text{mole}}$$

See Table III for equipment list.

2.3.2. CHAMBER SAMPLING

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

See Table III for equipment list.

2.3.3. PARTICLE SIZE DISTRIBUTION

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

See Table III for equipment list.

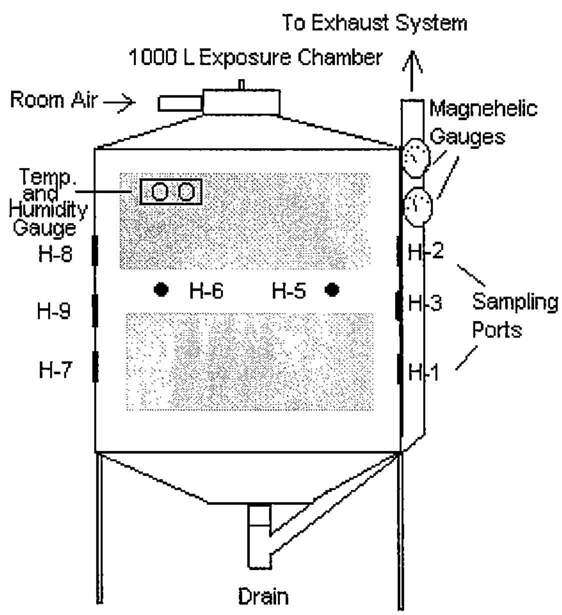
2.3.4. CHAMBER AND EXPOSURE ROOM ENVIRONMENT

Chamber oxygen levels (maintained at least 19%) were measured pretest and at the beginning, middle and end of the study. Air samples were taken in the vapor generation area pretest and at the beginning, middle and end of the study. Light (maintained approximately 30-40 foot-candles at 1.0 meter above the floor) and noise levels (maintained below 85 decibels) in the exposure room were measured pretest and at the beginning, middle and end of the study.

See Table III for equipment list.

Group 1	Inhalation Report	Appendix II

Figure I
Chamber Generation System
and Whole-Body Exposure Chamber



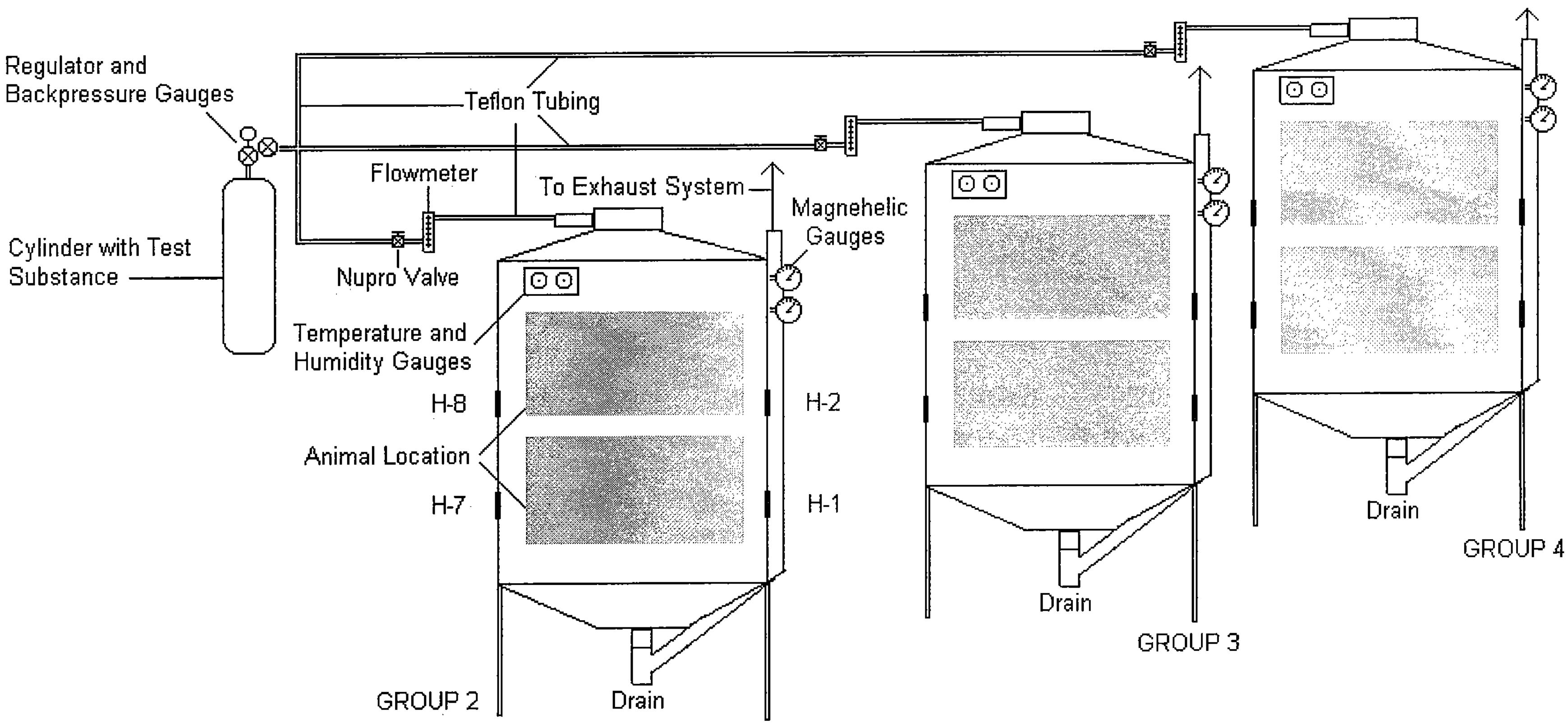
Notes:

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

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

Groups 2 - 4	Inhalation Report	Appendix II

Figure 2
Chamber Generation System
and Whole-Body Exposure Chamber



	Inhalation Report	Appendix II

Table I
Summary of In-Chamber Observations

Exposure Day	0	1	2	3	4	5	6	7	8	9	10	11	12	13
Group 1 – 0 ppm														
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All	All
Group 2 – 900 ppm														
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All	All
Group 3 – 3000 ppm														
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All	All
Group 4 – 9000 ppm														
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All	All

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

	Inhalation Report	Appendix II

Table I
Summary of In-Chamber Observations

Exposure Day	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**	**25**	**26**
Group 1 – 0 ppm													
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All
Group 2 – 900 ppm													
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All
Group 3 – 3000 ppm													
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All
Group 4 – 9000 ppm													
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All

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

	Inhalation Report	Appendix II

Table I
Summary of In-Chamber Observations

Exposure Day	**27**	**28**	**29**	**30**	**31**	**32**	**33**	**34**	**35**	**36**	**37**	**38**	**39**	**40**
Group 1 – 0 ppm														
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All		
Group 2 – 900 ppm														
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All	All
Group 3 – 3000 ppm														
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All			
Group 4 – 9000 ppm														
Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All			

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

	Inhalation Report	Appendix II

Table II
Chamber Monitoring Results
Preface

Key to Abbreviations

MMAD	=	Mass Median Aerodynamic Diameter
GSD	=	Geometric Standard Deviation
TMC	=	Total Mass Concentration
N (gf)	=	Nominal (by gas flow)
N (wt)	=	Nominal (by weight)

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

Day	Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration Mean (ppm)	Individual (ppm)				Particle Size Determinations MMAD (μm)	GSD	TMC (mg/m^3)	Chamber Environment Mean Temperature (°C)	Humidity (%)
0	29-Sep-03	1	0	0.00	0.00	0.00	0.00	0.00				25	55
1	30-Sep-03	2	0	0.00	0.00	0.00	0.00	0.00				25	57
2	1-Oct-03	3	0	0.00	0.00	0.00	0.00	0.00	3.195	2.386	2.39E-03	24	56
3	2-Oct-03	4	0	0.00	0.00	0.00	0.00	0.00				25	55
4	3-Oct-03	5	0	0.00	0.00	0.00	0.00	0.00				25	54
5	4-Oct-03	6	0	0.00	0.00	0.00	0.00	0.00				24	56
6	5-Oct-03	7	0	0.00	0.00	0.00	0.00	0.00				24	56
7	6-Oct-03	8	0	0.00	0.00	0.00	0.00	0.00				24	55
8	7-Oct-03	9	0	0.00	0.00	0.00	0.00	0.00				24	59
9	8-Oct-03	10	0	0.00	0.00	0.00	0.00	0.00	1.108	2.273	8.08E-03	24	57
10	9-Oct-03	11	0	0.00	0.00	0.00	0.00	0.00				25	58
11	10-Oct-03	12	0	0.00	0.00	0.00	0.00	0.00				24	59
12	11-Oct-03	13	0	0.00	0.00	0.00	0.00	0.00				24	57
13	12-Oct-03	14	0	0.00	0.00	0.00	0.00	0.00				25	47
14	13-Oct-03	15	0	0.00	0.00	0.00	0.00	0.00				25	43
15	14-Oct-03	16	0	0.00	0.00	0.00	0.00	0.00				25	50
16	15-Oct-03	17	0	0.00	0.00	0.00	0.00	0.00	3.390	1.930	1.30E-03	25	47
17	16-Oct-03	18	0	0.00	0.00	0.00	0.00	0.00				25	55
18	17-Oct-03	19	0	0.00	0.00	0.00	0.00	0.00				25	59
19	18-Oct-03	20	0	0.00	0.00	0.00	0.00	0.00				24	60
20	19-Oct-03	21	0	0.00	0.00	0.00	0.00	0.00				24	58
21	20-Oct-03	22	0	0.00	0.00	0.00	0.00	0.00				24	57
22	21-Oct-03	23	0	0.00	0.00	0.00	0.00	0.00				24	58
23	22-Oct-03	24	0	0.00	0.00	0.00	0.00	0.00	4.260	2.450	2.61E-03	24	57
24	23-Oct-03	25	0	0.00	0.00	0.00	0.00	0.00				24	57
25	24-Oct-03	26	0	0.00	0.00	0.00	0.00	0.00				24	57
26	25-Oct-03	27	0	0.00	0.00	0.00	0.00	0.00				25	53

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

Day	Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration Mean (ppm)	Individual (ppm)				Particle Size Determinations MMAD (µm)	GSD	TMC (mg/m^3)	Chamber Environment Mean Temperature (°C)	Humidity (%)
27	26-Oct-03	28	0	0.00	0.00	0.00	0.00	0.00				25	58
28	27-Oct-03	29	0	0.00	0.00	0.00	0.00	0.00				25	58
29	28-Oct-03	30	0	0.00	0.00	0.00	0.00	0.00				25	57
30	29-Oct-03	31	0	0.00	0.00	0.00	0.00	0.00	13.27	2.130	5.08E-03	23	58
31	30-Oct-03	32	0	0.00	0.00	0.00	0.00	0.00				22	58
32	31-Oct-03	33	0	0.00	0.00	0.00	0.00	0.00				22	58
33	1-Nov-03	34	0	0.00	0.00	0.00	0.00	0.00				22	57
34	2-Nov-03	35	0	0.00	0.00	0.00	0.00	0.00				23	57
35	3-Nov-03	36	0	0.00	0.00	0.00	0.00	0.00				22	59
36	4-Nov-03	37	0	0.00	0.00	0.00	0.00	0.00				22	58
37	5-Nov-03	38	0	0.00	0.00	0.00	0.00	0.00	0.7893	1.573	2.23E-03	22	58
38	6-Nov-03	39	0	0.00	0.00	0.00	0.00	0.00				21	58
		Mean	**0**		**0.00**				**4.335**	**2.124**	**3.62E-03**	**23.9**	**56.1**
		S.D.	**0**		**0.00**				**4.583**	**0.328**	**2.52E-03**	**1.1**	**3.6**

Chamber Monitoring Results
Cumulative Exposure Record
Group 2 - 900 ppm

Day	Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration Mean (ppm)	Individual (ppm)				Particle Size Determinations MMAD (µm)	GSD	TMC (mg/m^3)	Chamber Environment Mean Temperature (°C)	Humidity (%)
0	29-Sep-03	1	958	969.5	982	993	933	970				24	56
1	30-Sep-03	2	940	943.5	932	924	956	962				24	57
2	1-Oct-03	3	940	940.5	947	953	932	930	4.254	2.202	3.67E-03	24	56
3	2-Oct-03	4	940	931.0	925	939	937	923				24	56
4	3-Oct-03	5	940	931.0	911	933	940	940				24	55
5	4-Oct-03	6	940	929.0	896	949	938	933				24	55
6	5-Oct-03	7	940	928.8	909	945	916	945				24	57
7	6-Oct-03	8	940	955.8	954	954	947	968				24	54
8	7-Oct-03	9	940	950.8	962	950	941	950				24	59
9	8-Oct-03	10	935	907.8	769	936	970	956	1.073	1.978	6.82E-03	24	57
10	9-Oct-03	11	940	943.0	941	933	956	942				24	60
11	10-Oct-03	12	940	942.8	941	950	948	932				24	59
12	11-Oct-03	13	940	917.8	897	916	920	938				a	a
13	12-Oct-03	14	940	903.8	886	911	909	909				24	47
14	13-Oct-03	15	940	945.8	950	945	950	938				24	43
15	14-Oct-03	16	940	965.8	948	971	968	976				24	50
16	15-Oct-03	17	940	952.8	956	950	947	958	4.569	1.915	1.33E-03	24	45
17	16-Oct-03	18	940	960.8	953	963	965	962				24	57
18	17-Oct-03	19	940	949.3	955	958	940	944				24	57
19	18-Oct-03	20	940	933.0	963	949	925	895				24	61
20	19-Oct-03	21	940	934.8	903	937	954	945				24	57
21	20-Oct-03	22	940	936.8	930	927	940	950				24	56
22	21-Oct-03	23	917	939.3	924	940	945	948				24	59
23	22-Oct-03	24	917	924.5	945	895	923	935	10.50	2.596	4.53E-03	24	56
24	23-Oct-03	25	917	931.5	954	927	922	923				24	57
25	24-Oct-03	26	917	940.3	945	947	962	907				24	58
26	25-Oct-03	27	917	947.5	933	945	949	963				24	53

Chamber Monitoring Results
Cumulative Exposure Record
Group 2 - 900 ppm

Day	Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration Mean (ppm)	Individual (ppm)				Particle Size Determinations MMAD (µm)	GSD	TMC (mg/m^3)	Chamber Environment Mean Temperature (°C)	Humidity (%)
27	26-Oct-03	28	917	936.0	956	937	947	904				24	56
28	27-Oct-03	29	917	922.0	939	907	924	918				24	58
29	28-Oct-03	30	917	919.0	909	913	915	939				24	57
30	29-Oct-03	31	917	920.5	930	914	919	919	7.219	2.125	2.02E-03	23	58
31	30-Oct-03	32	917	877.3	881	883	874	871				22	58
32	31-Oct-03	33	917	911.3	881	930	919	915				22	57
33	1-Nov-03	34	917	903.8	902	897	911	905				22	58
34	2-Nov-03	35	917	910.0	883	909	928	920				22	57
35	3-Nov-03	36	917	928.5	973	888	912	941				22	59
36	4-Nov-03	37	917	904.0	886	899	922	909				21	58
37	5-Nov-03	38	917	904.3	899	887	932	899	0.8063	1.786	2.34E-03	21	58
38	6-Nov-03	39	917	910.3	850	937	931	923				21	58
39	7-Nov-03	40	917	934.8	955	902	920	962				21	57
40	8-Nov-03	41	917	918.0	890	901	974	907				21	59
		Mean	**930**		**930.6**				**4.737**	**2.100**	**3.45E-03**	**23.4**	**56.1**
		S.D.	**12**		**28.1**				**3.702**	**0.285**	**2.02E-03**	**1.1**	**3.8**

[a]Due to euipment malfunction, temperature and humidity could not be recorded for 2.5 to 6.0 hours on Day 12 exposure.

Chamber Monitoring Results
Cumulative Exposure Record
Group 3 - 3000 ppm

Day	Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration Mean (ppm)	Individual (ppm)				Particle Size Determinations MMAD (µm)	GSD	TMC (mg/m^3)	Chamber Environment Mean Temperature (°C)	Humidity (%)
0	29-Sep-03	1	2950	3058	3030	3120	3090	2990				24	56
1	30-Sep-03	2	2950	3055	3060	3040	3090	3030				25	60
2	1-Oct-03	3	2950	3035	2950	3040	3080	3070	2.864	2.098	2.97E-03	24	57
3	2-Oct-03	4	2950	3043	3060	3000	3050	3060				24	58
4	3-Oct-03	5	2950	3008	3010	3040	3030	2950				24	58
5	4-Oct-03	6	2950	3043	2970	3110	3010	3080				24	58
6	5-Oct-03	7	2950	2995	3000	2970	2960	3050				24	59
7	6-Oct-03	8	2950	3070	3050	3050	3090	3090				24	57
8	7-Oct-03	9	2950	3035	3050	3030	3020	3040				24	62
9	8-Oct-03	10	2950	3000	2990	2950	3030	3030	1.092	2.224	8.12E-03	24	59
10	9-Oct-03	11	2950	3058	3040	3060	3050	3080				24	61
11	10-Oct-03	12	2950	3005	2990	3000	3030	3000				24	60
12	11-Oct-03	13	2950	2960	2940	2940	2960	3000				24	59
13	12-Oct-03	14	2950	2943	3000	2860	2980	2930				24	49
14	13-Oct-03	15	2950	3053	3050	3030	3070	3060				24	44
15	14-Oct-03	16	2950	3008	2950	3020	3060	3000				24	51
16	15-Oct-03	17	2950	2935	3000	2930	2910	2900	5.160	2.075	1.69E-03	24	45
17	16-Oct-03	18	2950	2973	2990	2990	2960	2950				24	59
18	17-Oct-03	19	2950	2955	2940	2950	2970	2960				24	59
19	18-Oct-03	20	2950	2998	3000	3020	2940	3030				24	65
20	19-Oct-03	21	2950	3028	2960	3050	2990	3110				24	60
21	20-Oct-03	22	2950	3098	3090	3110	3090	3100				24	59
22	21-Oct-03	23	2950	2995	3020	2900	3000	3060				24	61
23	22-Oct-03	24	2950	3030	3060	2990	3020	3050	1.733	2.047	1.55E-03	24	61
24	23-Oct-03	25	2950	3118	3200	3060	3090	3120				24	62
25	24-Oct-03	26	2950	3053	3020	3040	3100	3050				24	61
26	25-Oct-03	27	2950	3033	2970	3010	3100	3050				24	56

Chamber Monitoring Results
Cumulative Exposure Record
Group 3 - 3000 ppm

Day	Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration: Mean (ppm)	Individual (ppm)				Particle Size Determinations: MMAD (µm)	GSD	TMC (mg/m^3)	Chamber Environment Mean: Temperature (°C)	Humidity (%)
27	26-Oct-03	28	2950	3030	3020	3030	3040	3030				24	59
28	27-Oct-03	29	2950	3045	3140	3070	2980	2990				24	59
29	28-Oct-03	30	2950	3025	3000	3070	3050	2980				24	59
30	29-Oct-03	31	2950	2928	2930	2890	2930	2960	3.084	1.897	8.38E-04	23	59
31	30-Oct-03	32	2950	3023	3000	3090	2970	3030				22	61
32	31-Oct-03	33	2950	3095	3050	3070	3130	3130				22	60
33	1-Nov-03	34	2950	3003	2980	2970	3020	3040				22	59
34	2-Nov-03	35	2950	3010	3010	3000	2980	3050				22	58
35	3-Nov-03	36	2950	3065	3130	2980	3090	3060				22	60
36	4-Nov-03	37	2950	3038	3050	2980	3070	3050				21	59
37	5-Nov-03	38	2950	3000	3030	2910	2980	3080	0.7985	1.595	2.46E-03	21	59
		Mean	**2950**		**3022**				**2.455**	**1.989**	**2.94E-03**	**23.6**	**58.1**
		S.D.	**0**		**58**				**1.613**	**0.220**	**2.64E-03**	**0.9**	**4.2**

Chamber Monitoring Results
Cumulative Exposure Record
Group 4 - 9000 ppm

Day	Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration: Mean (ppm)	Individual (ppm)				Particle Size Determinations: MMAD (µm)	GSD	TMC (mg/m^3)	Chamber Environment Mean: Temperature (°C)	Humidity (%)
0	29-Sep-03	1	9480	8518	8520	8420	8510	8620				24	53
1	30-Sep-03	2	9830	8623	8290	8340	8880	8980				24	54
2	1-Oct-03	3	9510	9048	9130	9070	9070	8920	4.299	2.444	3.80E-03	24	54
3	2-Oct-03	4	10500	9415	9350	9570	9400	9340				24	55
4	3-Oct-03	5	10100	9723	10100	9650	9540	9600				24	54
5	4-Oct-03	6	9860	9198	9430	9060	9140	9160				24	56
6	5-Oct-03	7	9820	9105	9170	9020	9020	9210				24	56
7	6-Oct-03	8	9820	9243	9290	9310	9310	9060				24	55
8	7-Oct-03	9	9820	8880	8800	9000	8740	8980				24	59
9	8-Oct-03	10	9820	9123	8950	9200	9000	9340	1.002	1.790	6.54E-03	24	57
10	9-Oct-03	11	9820	9083	9050	8820	9230	9230				24	58
11	10-Oct-03	12	9820	9283	9270	9250	9320	9290				24	57
12	11-Oct-03	13	9820	9103	9170	9070	9000	9170				24	56
13	12-Oct-03	14	9820	8940	8960	8770	9070	8960				24	47
14	13-Oct-03	15	9820	9250	9380	9180	9240	9200				24	42
15	14-Oct-03	16	9820	9210	9290	9140	9200	9210				24	48
16	15-Oct-03	17	9820	8920	9100	8890	8850	8840	4.736	1.876	1.94E-03	24	43
17	16-Oct-03	18	9820	9303	9790	9320	9100	9000				24	56
18	17-Oct-03	19	9820	9148	9320	9160	8980	9130				24	55
19	18-Oct-03	20	9820	9420	9780	9180	9360	9360				24	63
20	19-Oct-03	21	9820	9480	9650	9460	9310	9500				24	57
21	20-Oct-03	22	9820	9430	9430	9310	9490	9490				24	57
22	21-Oct-03	23	9820	9195	9230	9020	9320	9210				24	58
23	22-Oct-03	24	9820	9158	9310	9050	9180	9090	8.134	2.590	3.48E-03	24	57
24	23-Oct-03	25	9820	9293	9470	9030	9320	9350				24	58
25	24-Oct-03	26	9820	9190	9390	9100	9170	9100				24	56
26	25-Oct-03	27	9820	9055	9100	8990	9100	9030				24	53

Chamber Monitoring Results
Cumulative Exposure Record
Group 4 - 9000 ppm

Day	Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration Mean (ppm)	Individual (ppm)				Particle Size Determinations MMAD (µm)	GSD	TMC (mg/m^3)	Chamber Environment Mean Temperature (°C)	Humidity (%)
27	26-Oct-03	28	9820	9085	9320	9000	9070	8950				24	56
28	27-Oct-03	29	9820	9175	9360	8960	9290	9090				24	56
29	28-Oct-03	30	9820	9253	9360	9170	9200	9280				24	55
30	29-Oct-03	31	9820	9345	9390	9470	9280	9240	2.032	1.725	6.22E-04	23	57
31	30-Oct-03	32	9820	8828	8920	8920	8450	9020				22	57
32	31-Oct-03	33	9820	9120	8810	9250	9130	9290				22	56
33	1-Nov-03	34	9820	8930	8930	8840	9020	8930				22	57
34	2-Nov-03	35	9820	9118	9100	8920	9400	9050				22	56
35	3-Nov-03	36	9820	9393	9340	9030	9500	9700				22	58
36	4-Nov-03	37	9820	9095	9380	9000	9050	8950				22	57
37	5-Nov-03	38	9820	9280	9350	9350	9210	9210	0.8159	1.745	2.67E-03	22	58
		Mean	**9829**		**9157**				**3.503**	**2.028**	**3.18E-03**	**23.6**	**55.2**
		S.D.	**142**		**269**				**2.801**	**0.385**	**2.01E-03**	**0.8**	**4.0**

Exposures Summary						
	Nominal by gas flow (ppm)					
Date	Group 2	Group 3	Group 4	Total Nominal by gas flow (ppm)	Total Nominal by weight (ppm)	N(gf):N(wt)
29-Sep-03	958	2950	9480	13388	12400	1.08
30-Sep-03	940	2950	9830	13720	13500	1.02
1-Oct-03	940	2950	9510	13400	12200	1.10
2-Oct-03	940	2950	10500	14390	12600	1.14
3-Oct-03	940	2950	10100	13990	14900	0.94
4-Oct-03	940	2950	9860	13750	13700	1.00
5-Oct-03	940	2950	9820	13710	13700	1.00
6-Oct-03	940	2950	9820	13710	13700	1.00
7-Oct-03	940	2950	9820	13710	14900	0.92
8-Oct-03	935	2950	9820	13705	12600	1.09
9-Oct-03	940	2950	9820	13710	14900	0.92
10-Oct-03	940	2950	9820	13710	13700	1.00
11-Oct-03	940	2950	9820	13710	13700	1.00
12-Oct-03	940	2950	9820	13710	14900	0.92
13-Oct-03	940	2950	9820	13710	14900	0.92
14-Oct-03	940	2950	9820	13710	12600	1.09
15-Oct-03	940	2950	9820	13710	12600	1.09
16-Oct-03	940	2950	9820	13710	12600	1.09
17-Oct-03	940	2950	9820	13710	12600	1.09
18-Oct-03	940	2950	9820	13710	13700	1.00
19-Oct-03	940	2950	9820	13710	13700	1.00
20-Oct-03	940	2950	9820	13710	13700	1.00
21-Oct-03	917	2950	9820	13687	12600	1.09
22-Oct-03	917	2950	9820	13687	13700	1.00
23-Oct-03	917	2950	9820	13687	13700	1.00
24-Oct-03	917	2950	9820	13687	12600	1.09
25-Oct-03	917	2950	9820	13687	12600	1.09
26-Oct-03	917	2950	9820	13687	12600	1.09
27-Oct-03	917	2950	9820	13687	13700	1.00
28-Oct-03	917	2950	9820	13687	14900	0.92

Exposures Summary						
	Nominal by gas flow (ppm)					
Date	Group 2	Group 3	Group 4	Total Nominal by gas flow (ppm)	Total Nominal by weight (ppm)	N(gf):N(wt)
29-Oct-03	917	2950	9820	13687	13700	1.00
30-Oct-03	917	2950	9820	13687	13700	1.00
31-Oct-03	917	2950	9820	13687	13700	1.00
1-Nov-03	917	2950	9820	13687	12600	1.09
2-Nov-03	917	2950	9820	13687	12600	1.09
3-Nov-03	917	2950	9820	13687	13700	1.00
4-Nov-03	917	2950	9820	13687	13700	1.00
5-Nov-03	917	2950	9820	13687	13700	1.00
6-Nov-03	917	-	-	917	1150	0.80
7-Nov-03	917	-	-	917	1150	0.80
8-Nov-03	917	-	-	917	1150	0.80
					Mean:	1.02

	Inhalation Report	Appendix II

Table III
Equipment List

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

Compound Reservoir
Butane Cylinder (MG Industries).

Flowmeter
Dwyer®, size 0-20 Lpm (Dwyer® Instruments).
Top Trak™ Mass Flow Meter, sizes 0 - 1 and 0 -10 Lpm, Model 821-1 (Sierra Instruments).

Pressure/Vacuum Gauges
Backpressure gauge (MG Industries), P/N 10206 and 10201.
GAST® vacuum gauge.

Chamber Air Flow
Dwyer® Magnehelic® gauge (Dwyer® Instruments Inc.), calibrated prestudy with a Side Trak™ III, equipped with a Digital Meter, Model 831-N2 (Sierra Instruments, Inc.).

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

Regulators
MG Industries Series 300

Metering Valve
Metering Valve, Model SS-4L Series (Nupro® Co.).

Vacuum Pumps
Thomas Industries Inc., Model 707CM50.
Closed-loop pump.

	Inhalation Report	Appendix II

Table III
Equipment List

Tubing
Clear plastic, sizes ¼", ½" (Norton, Baxter).
Plastic, size 1/8" (Tygon).
½" stainless steel.
Teflon®, size ¼ ".
Plastic "T".

Air Analyzer
MIRAN® 1A-CVF Ambient Air Analyzer (Wilks) with a Cole Parmer Strip Chart Recorder, Model 201, and a Micronta® LCD Benchtop Digital Multimeter, Model No. 22-195
Gas-tight syringe, size 1500 mL, plastic, Model S-1500 (Hamilton).
Balston® Microfibre™ Disposable Filter Unit was attached in-line.
Syringe, size 0 - 10 mL, plastic (Precision).
Syringe, size 0 - 100 mL, plastic, No. 1100 (Hamilton).

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

Environmental Monitoring
VWR Temperature and Humidity Gauge, tested prestudy with a Big Digit Traceable Hygrometer/Thermometer.
Digital Sound Meter 840029 (SPER Scientific & Quantum Instruments Photo Meter 1).

Balance
Pelouze, No. 4040

	Inhalation Report	Appendix II

Table IV
Chamber Distribution Records

Group (target)	Date	Port	IR Conc (ppm)	Ratio to H-1
2 (900 ppm)	23 September 2003	H-1	909	1.00
		H-2	894	0.98
		H-7	968	1.06
		H-8	976	1.07
		H-1	916	1.00
		H-11	956	1.04
		H-12	962	1.05
		H-13	949	1.04
		H-14	962	1.05
3 (3000 ppm)	22 September 2003	H-1	3090	1.00
		H-2	3080	1.00
		H-7	2800	0.91
		H-1	3040	1.00
		H-8	2750	0.90
		H-11	3020	0.99
		H-1	2920	1.00
		H-12	2960	1.01
		H-13	2930	1.00
		H-14	3040	1.04
4 (9000 ppm)	22 September 2003	H-1	9130	1.00
		H-2	7400	0.81
		H-7	9350	1.02
		H-8	8920	0.98
		H-1	9030	1.00
		H-11	9420	1.04
		H-12	9250	1.02
		H-13	8920	0.99
		H-1	9130	1.00
		H-14	7740	0.85
	23 September 2003	H-1	9090	1.00
		H-2	8410	0.93
		H-14	8960	0.99

	Inhalation Report	Appendix II

Table V
Miran Calibration

Methodology for Butane

Settings: The instrument settings for the Miran 07 unit are summarized below:

wavelength, microns	10.3
pathlength, dial setting	3.29
slit width, mm	1
range, absorbance	1
response, seconds	40
gain	High
chart speed, cm/min	1
chart volts	1

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

Injection Volume (µL)	Calculated Concentration[1] (ppm)	Absorbance Operator 1 (volts)	Absorbance Operator 2 (volts)	Absorbance Average (volts)
4000	709	0.0683	0.0611	0.0647
5000	887	0.0840	0.0777	0.0809
17000	3014	0.2573	0.2622	0.2598
51000	9043	0.711	0.717	0.714
61000	10816	0.830	0.850	0.840

[1]Calculated Conc. (ppm) $= \dfrac{\text{Injection volume (µL)}}{\text{5.64 L (Volume of Miran cell)}}$

	Inhalation Report	Appendix II

Table V
Miran Calibration

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

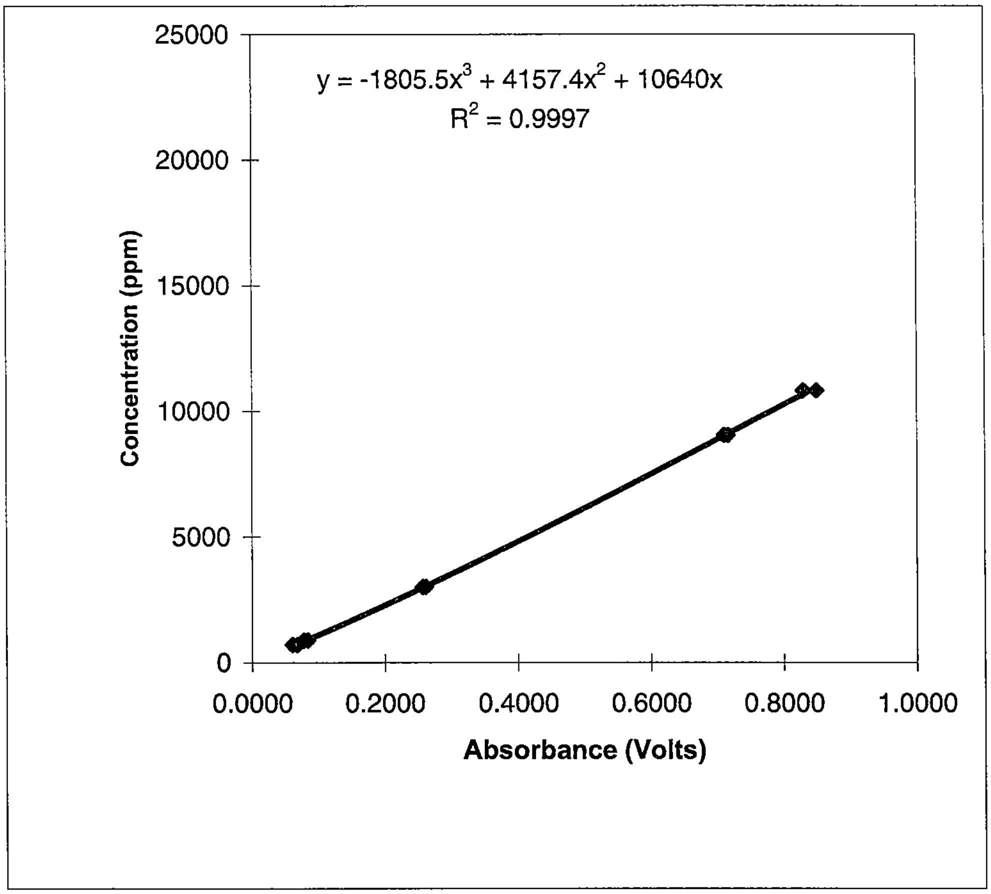
Injection Volume (µL)	Calculated Concentration (ppm)	Expected Absorbance Reading (volts)	Acceptable Absorbance Range (volts)
5000	887	0.0809	0.0688 – 0.0930
17000	3014	0.2598	0.2208 – 0.2988
51000	9043	0.714	0.607 – 0.821

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

	Inhalation Report	Appendix II

Table V
Miran Calibration

Calibration Curve for Butane



		Appendix II

Table VI
Testing Room and Chambers EnviroNMental Monitoring

Interval	Location	Test Substance (ppm)	Light (Ft Candles)	Noise (dB)	Oxygen (%)	Particle Sizing (mg/m^3)[a]
Pretest	Room 813A	0	35.0	61.5	NM	
	Group 1	0	NM	NM	21	1.77×10^{-3}
	Group 2	0	NM	NM	21	1.91×10^{-3}
	Group 3	0	NM	NM	21	2.19×10^{-3}
	Group 4	0	NM	NM	21	2.54×10^{-3}
Day 1	Room 813A	0	36.0	62.0	NM	
	Group 1	0	NM	NM	21	
	Group 2	944	NM	NM	21	
	Group 3	3055	NM	NM	21	
	Group 4	8623	NM	NM	21	
Day 28	Room 813A	0	33.6	61.8	NM	
	Group 1	0	NM	NM	21	
	Group 2	922	NM	NM	21	
	Group 3	3045	NM	NM	21	
	Group 4	9175	NM	NM	21	
Day 37	Room 813A	0	36.0	65.7	NM	
	Group 1	0	NM	NM	21	
	Group 2	904	NM	NM	21	
	Group 3	3000	NM	NM	21	
	Group 4	9280	NM	NM	21	

NM = Not measured.
[a]Pretest results presented. For on-test results, see CMR (Table II in Appendix II).

STUDY TITLE

Analytical Report For:

Butane:
Combined Repeated-Exposure Toxicity, Reproduction and Neurotoxicity Screening in Rats via Whole-Body Inhalation Exposures

AUTHOR

Yonggang Wang

REPORT DATE

14 August 2008

STUDY NUMBER

03-4242

	Analytical Report	Appendix JJ

SIGNATURES

Written by: ______________________ 14 Aug 08
Yonggang Wang, M.S. Date
Laboratory Manager
Formulation Chemistry Services

Reviewed by: K. A. Saladdin 14 Aug 08
Kay Saladdin, B.S. Date
Associate Director
Formulation Chemistry Services

Approved by: B. L. 14 Aug 08
Barbara A. Litzenberger, B.S. MT (ASCP) Date
Director Analytical Services

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1. Summary

The test substance and the analytical standard (Butane) were analyzed ("pre-study" and "post-study") to determine the purity and stability of the test substance by comparison to the analytical standard. The analytical method was validated at Huntingdon Life Sciences (HLS). The analytical method involved gas bag sampling of the test substance and the analytical standard and quantification using Gas Chromatography with Flame Ionization Detection (FID).

2. Experimental Procedures

The analytical method (HLS-012-03) was validated by Formulation Chemistry at HLS. Details of the analytical method and the validation are maintained in this study file.

Gas bag sampling of the test substance and the analytical standard was performed in the Inhalation Department at HLS. The test substance and the analytical standard were analyzed using a Gas Chromatograph equipped with a HP Plot Q (30 m x 0.32 mm, 20 µm) column and Flame Ionization Detector (FID) to determine the purity of Butane test substance. HP 3396A integrator was used for data collection and Excel was used for processing the data.

Date of sample analysis is listed as follows:

Interval	Date Analyzed
"Pre-Study" Characterization	30 May 03
"Post-Study" Characterization	11 Nov 03

3. Results and Discussion

The test substance and analytical standard (Butane) were analyzed prior to the initiation of the study and after completion of the study to determine the purity and stability of the test substance. The results of the characterization are presented in Tables I and II. A typical chromatogram of Butane standard is presented in Figure I. A typical chromatogram of Butane test substance is presented in Figure II.

Table I: Characterization ("Pre-Study")

Sample ID	Area % of Ethane	Area % of Propane	Area % of Isobutane	Area % of Other Impurities	Area % of Butane Standard	Mean Area % of Butane Standard
Butane Standard	0.00	0.00	0.00	0.01	99.99	99.96
Butane Standard	0.00	0.00	0.00	0.06	99.94	
Butane Standard	0.00	0.00	0.00	0.05	99.95	

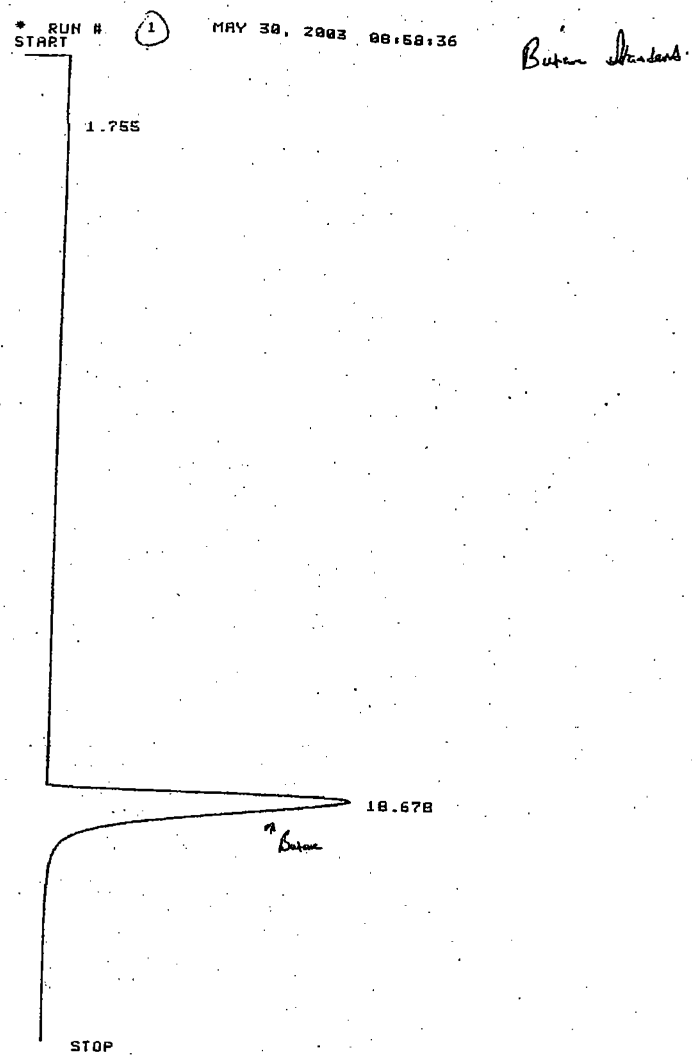
Sample ID	Area % of Ethane	Area % of Propane	Area % of Isobutane	Area % Other Impurities	Area % of Butane Substance	Mean Area % of Butane Test Substance
Butane Test Substance	0.02	0.12	0.69	0.01	99.16	99.23
Butane Test Substance	0.02	0.12	0.54	0.02	99.30	
Butane Test Substance	0.02	0.12	0.60	0.02	99.24	

Table II: Characterization ("Post-Study")

Sample ID	Area % of Ethane	Area % of Propane	Area % of Isobutane	Area % of Other Impurities	Area % of Butane Standard	Mean Area % of Butane Standard
Butane Standard	0.00	0.00	0.00	0.02	99.98	99.98
Butane Standard	0.00	0.00	0.00	0.03	99.97	
Butane Standard	0.00	0.00	0.00	0.02	99.98	

Sample ID	Area % of Ethane	Area % of Propane	Area % of Isobutane	Area % Other Impurities	Area % of Butane Substance	Mean Area % of Butane Test Substance
Butane Test Substance	0.00	0.00	0.00	0.02	99.98	99.98
Butane Test Substance	0.00	0.00	0.00	0.02	99.98	
Butane Test Substance	0.00	0.00	0.00	0.02	99.98	

Figure I. A Typical Gas Chromatogram of Butane Analytical Standard



RUN# 1 MAY 30, 2003 08:58:36

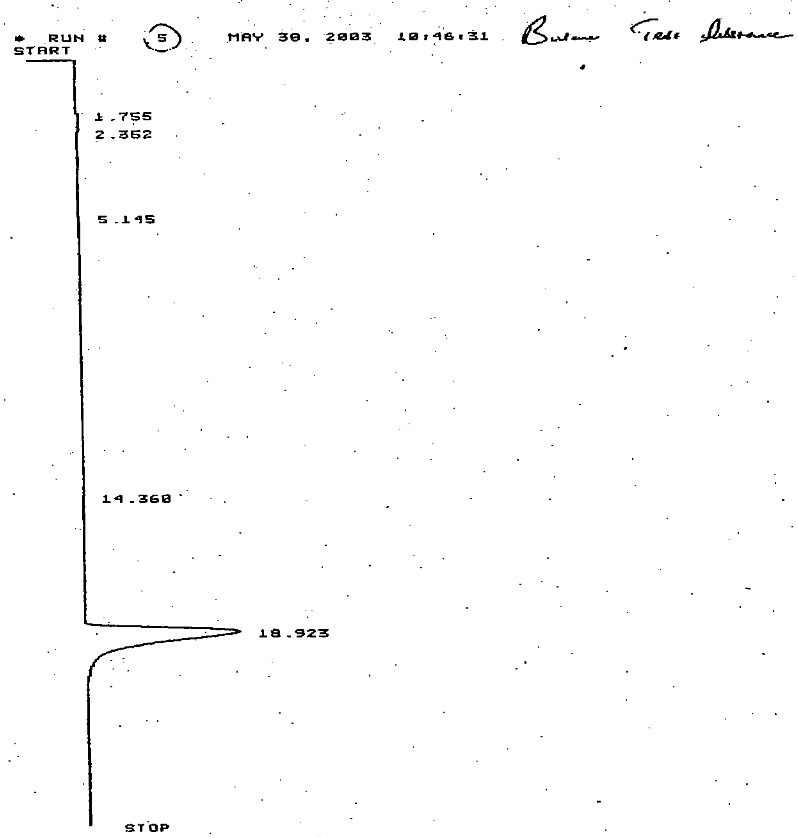
AREA%

RT	AREA	TYPE	WIDTH	AREA%
1.755	330	VB	.018	.01466
18.678	2250757	PV	.674	99.98534

TOTAL AREA=2251086
MUL FACTOR=1.0000E+00

Response (mV) vs Time (minutes)

Figure II. A Typical Gas Chromatogram of Butane Test Substance



RUN# 5 MAY 30, 2003 10:46:31

AREA%

RT	AREA	TYPE	WIDTH	AREA%
1.755	195	VB	.018	.02188
2.352	176	BB	.019	.01976
5.145	1098	BP	.085	.12321
14.360	4779	PV	.664	.53625
18.923	884943	BB	.566	99.29891

TOTAL AREA= 891191
MUL FACTOR=1.0000E+00

Response (mV) vs Time (minutes)

	Neurobehavioral Positive Control Data	Appendix KK

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	Neurobehavioral Positive Control Data: Functional Observational Battery Preface	Appendix KK

This is an abridged version of text and tables from Study No. H-34, 00-14500 as amended on 24 November 2008.

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	Neurobehavioral Positive Control Data: Functional Observational Battery	Appendix KK

1. **INTRODUCTION**

This study was designed to train technicians to perform the functional observational battery evaluations for rats and to provide evidence, by use of test materials with known neurological effects, that the observational methods used at Huntingdon Life Sciences, Princeton Research Center, are capable of detecting major neurotoxic endpoints. In addition, these studies were used to demonstrate interobserver reliability for neurobehavioral assessments by evaluating consistency of observations performed by different technicians.

2. **MATERIALS AND METHODS**

2.1. REGULATORY REFERENCES

2.1.1. TEST GUIDELINES

This study was designed to provide positive control data for neurotoxicity screening studies in accord with the US EPA Health Effects Test Guidelines, OPPTS 870.6200 Neurotoxicity Screening Battery, August 1998.

2.1.2. GOOD LABORATORY PRACTICES

This study was conducted in compliance with Part 160 of 40 CFR (EPA/FIFRA Good Laboratory Practice Standards) with the exception that assays to verify concentration, stability and homogeneity of the test articles in carriers were not performed.

2.1.3. ANIMAL WELFARE ACT COMPLIANCE

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

2.1.4. FACILITIES MANAGEMENT/ANIMAL HUSBANDRY

Currently acceptable practices of good animal husbandry were followed e.g., *Guide for the Care and Use of Laboratory Animals*;

National Academy Press, 1996. Huntingdon Life Sciences, East Millstone, New Jersey is fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC).

2.2. STUDY MANAGEMENT

2.2.1. SPONSOR

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

2.2.2. TESTING FACILITY

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

2.2.3. STUDY DIRECTOR

Rosemary C. Mandella, Ph.D., D.A.B.T.

	Neurobehavioral Positive Control Data: Functional Observational Battery	Appendix KK

2.3. EXPERIMENTAL DESIGN

2.3.1. TRAINING SESSIONS

Training consisted of two parts. In the first part, the technicians were required to view a training video for a functional observational battery (United States Environmental Protection Agency/American Industrial Health Council Training Video and Reference Manual for an FOB, 1996). The second part consisted of observations of animals treated with chemicals known to produce neurological effects as indicated below:

						Number of Animals			
			Daily Doses[a]			Initial		Functional Observational Battery	
Group	Route of Admin.	Test Article	Dose (mg/kg)	Volume (mL/kg)	Conc. (mg/mL)	M	F	M	F
1[b]	i.p.	Control	-	5	-	3	-	3	-
2	i.p.	Chlorpromazine	4	5	0.8	3	-	3	-
3	i.p.	Amphetamine	2	5	0.4	3	-	3	-
4	i.p.	Amphetamine	8	5	1.6	-	3	-	3
5	i.p.	Physostigmine	1	5	0.2	-	3	-	3
6	Oral	Ethanol	3000	10	300	-	3	-	3

[a]Represent doses of test article as supplied; i.e., no correction for percent active ingredient was made.
[b]Control animals received 0.9% saline.
M = Male; F = Female; i.p. = intraperitoneal; Oral, via gastric intubation;
mg/kg = milligrams of test article per kilogram of body weight

2.3.2. FOB PERFORMANCE EVALUATIONS

After completion of the training session, each technician was required to perform a functional observational battery evaluation in which the technician was blinded as to the treatment group. Each technician evaluated 20 males or 20 females (5 animals/group).

			Daily Doses[a]			Number of Animals			
						Initial		Functional Observational Battery	
Group	Route of Admin.	Test Article	Dose (mg/kg)	Volume (mL/kg)	Conc. (mg/mL)	M	F	M	F
1[b]	i.p.	Control	-	5	-	5	5	5	5
2	i.p.	Chlorpromazine	4	5	0.8	5	5	5	5
3	i.p.	Amphetamine	2	5	0.4	5	5	5	5
4	s.c.[c]	Physostigmine	1	5	0.2	5	5	5	5

[a]Represent doses of test article as supplied; i.e., no correction for percent active ingredient was made.
[b]Control animals received 0.9% saline.
[c]Intraperitoneal injections were administered for the Training Sessions and for the Performance Evaluations conducted by Observer 8; subcutaneous injections were administered for the Performance Evaluations conducted by all other observers.

M = Male; F = Female; i.p. = intraperitoneal; s.c. = subcutaneous injection
mg/kg = milligrams of test article per kilogram of body weight

2.4. STUDY DATES

2.4.1. STUDY INITIATION

15 February 2000 (Date Study Director signed the Protocol)

2.4.2. DATE OF ANIMAL RECEIPT

3 March 2000

2.4.3. DOSING INITIATION

Training Session: 23 March 2000 (Experimental Start Date)
Performance Evaluations: 26 April 2000

	Neurobehavioral Positive Control Data: Functional Observational Battery	Appendix KK

2.4.4. DOSING TERMINATION

6 July 2000

2.4.5. EXPERIMENTAL TERMINATION

1 August 2001

2.4.6. STUDY COMPLETION

1 August 2003 (Date Study Director signed the Final Report)

2.5. TEST ARTICLES

2.5.1. CHLORPROMAZINE

Manufacturer

Sigma Chemical Company
St. Louis, Missouri 63178

Lot Number

48H1403

Purity

98%

Description

White/white with a yellow cast powder

Date Received

1 December 1999

Expiration Date

April 2001

Storage

Room temperature, protected from light

2.5.2. D-AMPHETAMINE SULFATE

Manufacturer

Sigma Chemical Company
St. Louis, Missouri 63178

Lot Number

69H1239

Purity

Assume 100%

Description

Powder

Date Received

7 January 2000

Expiration Date

June 2001

Storage

Room temperature

	Neurobehavioral Positive Control Data: Functional Observational Battery	Appendix KK

2.5.3. PHYSOSTIGMINE

Manufacturer

Sigma Chemical Company
St. Louis, Missouri 63178

Lot Number

48H1126

Purity

Assume 100%

Description

Powder

Date Received

1 December 1999

Expiration Date

1 December 2004

Storage

Room temperature, protected from light

2.5.4. ETHANOL

Manufacturer

Spectrum Chemical Manufacturing Corporation
Gardena, California 90248

Lot Number

MI0504

Purity

100%

Description

Clear liquid

Date Received

16 March 1998

Expiration Date

March 2003

Storage

Room temperature

2.5.5. ANALYSIS

Documentation of the identity, strength, purity, composition and stability; and synthesis, fabrication, and/or derivation of the test articles was the responsibility of the Manufacturers.

2.5.6. ARCHIVAL SAMPLE

Samples from the lots of Chlorpromazine, D-Amphetamine Sulfate, Physostigmine and Ethanol are stored in the Archives of the Testing Facility under conditions specified for test article storage.

2.5.7. DISPOSITION

The unused portions of Chlorpromazine, D-Amphetamine Sulfate and Physostigmine were submitted to the Archives of the Testing Facility as archival samples. The remaining portions of Ethanol were retained by the Testing Facility for possible future use.

2.6. CONTROL ARTICLE

0.9% Saline

2.6.1. MANUFACTURER

Baxter Healthcare Corporation
Deerfield, Illinois 60015

2.6.2. LOT NUMBER

G949941

2.6.3. PURITY

100%

2.6.4. DESCRIPTION

Clear, colorless liquid

2.6.5. DATE RECEIVED

5 November 1999

2.6.6. EXPIRATION DATE

October 2000

2.6.7. STORAGE

Room Temperature

2.6.8. ANALYSIS

Documentation of the identity, strength, purity, composition and stability; and synthesis, fabrication, and/or derivation of the control article was the responsibility of the Manufacturer.

2.6.9. ARCHIVAL SAMPLE

A sample from each lot of control article is stored in the Archives of the Testing Facility under conditions specified for control article storage.

2.6.10. DISPOSITION

The unused portion of the control article will be retained for use in future studies. Any empty control article containers will be discarded by the Testing Facility following completion of the study.

2.7. TEST ANIMALS

2.7.1. SPECIES

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

2.7.2. SUPPLIER

Charles River Laboratories
Kingston, New York 12484

2.7.3. JUSTIFICATION FOR ANIMAL SELECTION

The rat is the animal model recommended by the testing guidelines for use in neurotoxicity screening studies. In addition, a historical database is available for comparative evaluation.

2.7.4. NUMBER OF ANIMALS

Transferred from the In-house Colony:
60 total (30 males, 30 females)

Placed on test:
40 total (20 males, 20 females)

Females were nulliparous and non-pregnant.

2.7.5. JUSTIFICATION FOR NUMBER OF ANIMALS

The neurotoxicants used in this study were chosen because they produce transient neurological effects and do not cause permanent damage to the nervous system at the doses used in this study. Therefore, the animals were used more than once during the training program. During the training portion of the study, a total of 18 animals (3 males or 3 females/chemical) were used. This was considered the minimum number necessary to demonstrate the range of effects of the chemical based on individual animal variability. During the performance part of the study, a total of 20 males and 20 females were used (including animals used in the training portion of the study). This allowed each technician undergoing training to perform the FOB evaluation for 20 animals (5 males or 5 females/group) and allowed two separate evaluations per week. Five animals per group were considered the minimum number necessary to produce scientific and statistically valid data.

2.7.6. AGE AT RECEIPT

23 days

2.7.7. AGE AT INITIATION OF TRAINING SESSION

43 days

2.7.8. AGE AT INITIATION OF PERFORMANCE EVALUATIONS

77 days

2.7.9. WEIGHT AT INITIATION OF TRAINING SESSION (GRAMS)

	Mean	Range
Male:	205	178 to 225
Female:	172	161 to 180

2.7.10. WEIGHT AT INITIATION OF PERFORMANCE EVALUATIONS (GRAMS)

	Mean	Range
Male:	440	379 to 498
Female:	270	235 to 339

2.7.11. ACCLIMATION PERIOD

Animals were acclimated for approximately 3 weeks. All animals were examined during the acclimation period to confirm suitability for study.

2.8. SELECTION AND GROUP ASSIGNMENT

More animals than required for the study were transferred from the in-house colony. Twenty males and twenty females were randomly selected for use on study and randomly assigned to control or treatment groups. Individual weights of animals used on study at initiation of the training session were within ±20% of the mean weight for each sex. Disposition of all animals not utilized in the study is maintained in the study file.

2.9. ANIMAL IDENTIFICATION

Each rat was identified with a metal ear tag bearing its assigned animal number. The assigned animal number plus the study number comprised the unique animal number for each animal. In addition, each cage was provided with a cage card which was color-coded for dose level identification and contained study number and animal number information.

2.10. VETERINARY CARE

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

2.11. HUSBANDRY

2.11.1. HOUSING

Animals were doubly housed in elevated, stainless steel, wire mesh cages during the first week of the acclimation period and individually housed thereafter.

2.11.2. FEED

Certified Rodent Diet, No. 5002; (Meal) (PMI Nutrition International, St. Louis, Missouri) was available without restriction. Fresh feed was presented weekly.

2.11.3. FEED ANALYSIS

Analysis of each feed lot used during this study was performed by the manufacturer. Results are maintained on file.

2.11.4. WATER

Water was available without restriction via an automated watering system (Elizabethtown Water Company, Westfield, New Jersey).

2.11.5. WATER ANALYSIS

Water analyses are conducted by Elizabethtown Water Company, Westfield, New Jersey (Raritan-East Millstone Plant) to ensure that water meets standards specified under the EPA Federal Safe Drinking Water Act Regulations (40 CFR Part 141). In addition, water samples are collected biannually from representative rooms in the Testing Facility; chemical and microbiological water analyses are conducted on these samples by a subcontract laboratory. Results of all water analyses are maintained on file at the Testing Facility.

2.11.6. CONTAMINANTS

There were no known contaminants in the feed or water which were expected to interfere with the results of this study.

2.11.7. ENVIRONMENTAL CONDITIONS

Light/Dark Cycle

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

Temperature

Temperature was monitored and recorded twice daily and maintained within the specified range to the maximum extent possible. Excursions outside the specified range were not considered to have affected the integrity of the study.

Desired: 18 to 26°C
Actual: 15 to 24°C

Relative Humidity

Relative humidity was monitored and recorded once daily and maintained within the specified range to the maximum extent possible. Excursions outside the specified range were not considered to have affected the integrity of the study.

Desired: 30 to 70%
Actual: 28 to 68%

2.12. TEST ARTICLE PREPARATION

Appropriate amounts of the test articles were mixed with 0.9% saline to achieve the desired concentrations. Dosing solutions were prepared either the day prior to or the day of dose administration and were stored refrigerated when not in use.

2.13. ANALYSIS OF DOSE SOLUTIONS

Analysis of the dosing solutions was not performed for this study.

2.14. TEST ARTICLE ADMINISTRATION

2.14.1. ROUTE OF ADMINISTRATION

Chlorpromazine, D-Amphetamine Sulfate and saline were administered by intraperitoneal injection into the abdominal cavity near the inguinal region using a sterile needle and syringe of appropriate size. Doses were calculated using the most recent body weights available. A volume of 5 mL/kg of body weight was administered.

Physostigmine was administered by intraperitoneal injection into the abdominal cavity near the inguinal region or by subcutaneous injection into an area on the back, using a sterile needle and syringe of appropriate size. Intraperitoneal injections were administered for the Training Sessions and for the Performance Evaluations conducted by Observer 8; subcutaneous injections were administered for the Performance Evaluations conducted by all other observers. Doses were calculated using the most recent body weights available. A volume of 5 mL/kg of body weight was administered.

Ethanol was administered by oral intubation using a stainless steel dosing needle and syringe of appropriate size. Doses were calculated using the most recent body weights available. A volume of 10 mL/kg of body weight was administered.

2.14.2. ROUTE JUSTIFICATION

The intraperitoneal, subcutaneous and oral routes provide rapid test article absorption and have been used in previous studies with the test articles.

2.14.3. DOSE LEVELS

Training Sessions

4 mg Chlorpromazine/kg body weight (males)
2 mg D-Amphetamine Sulfate/kg body weight (males)
8 mg D-Amphetamine Sulfate/kg body weight (females)
1 mg Physostigmine/kg body weight (females)
3000 mg Ethanol/kg body weight (females)

Performance Evaluations

4 mg Chlorpromazine/kg body weight
2 mg D-Amphetamine Sulfate/kg body weight
1 mg Physostigmine/kg body weight

2.14.4. DOSE VOLUME

0.9% Saline, Chlorpromazine, D-Amphetamine Sulfate, and Physostigmine were administered at a volume of 5 mL/kg of body weight. Ethanol was administered at a volume of 10 mL/kg of body weight.

2.14.5. FREQUENCY OF DOSING

Each animal was dosed no more than once per week. There was a washout period of approximately one to five weeks between doses.

2.15. EXPERIMENTAL EVALUATIONS

2.15.1. VIABILITY CHECKS

Animals were observed in their cages once daily for mortality and signs of severe toxic or pharmacologic effects.

2.15.2. PHYSICAL/NEUROBEHAVIORAL EXAMINATIONS

Animals were removed from their cages and examined once pretest to determine suitability for study. Examinations included observations of general condition, skin and fur, eyes, nose, oral cavity, abdomen and external genitalia, occurrence of secretions and excretions, autonomic activity (e.g., lacrimation, piloerection, pupil size, unusual respiratory pattern), changes in gait or posture, response to handling, presence of clonic or tonic movements, stereotypy (e.g., excessive grooming, repetitive circling) and bizarre behavior (e.g., self-mutilation, walking backward).

2.15.3. BODY WEIGHT

Animals were removed from their cages and weighed once pretest and once prior to each dose to determine dose volumes. Body weights were also recorded during the study as part of the functional observational battery.

2.15.4. FUNCTIONAL OBSERVATIONAL BATTERY EVALUATIONS

Training Session

Training consisted of two parts. In the first part, all technicians were required to view a training video for a functional observational battery (United States Environmental Protection Agency/American Industrial Health Council Training Video and Reference Manual for an FOB, 1996). The second part consisted of observations of animals treated with chemicals known to produce neurological effects. Two experienced technicians performed the FOB evaluations and instructed the novice technicians, under the direction of the Study Director or other senior staff member. These evaluations were not performed "blind".

FOB Performance Evaluation

After training, the experienced and novice technicians were each required to evaluate 20 animals (5 males or females/group) using the Functional Observational Battery. Observations by each technician were performed blind, i.e., the observer was unaware of the treatment of each animal. Animals were randomized and blinded according to the standard operating procedures of the Testing Facility.

The results of each FOB evaluation were tabulated and the Study Director determined whether the observations performed by each technician comprised a treatment profile consistent with known neurological effects of each test article. Interobserver reliability was considered established for technicians that accurately identified the treatment profile for each test article. The expected neurological effects were based on published reports in the literature, a previous validation study conducted at the Testing Facility (Study No. 96-4516), and observations by the experienced technicians.

Technicians not accurately identifying the treatment profile for each test article were given additional training and/or conducted additional performance evaluations before being allowed to conduct FOB evaluations on a study.

In addition to being able to identify the treatment profile for each test article, each technician was required to demonstrate consistency in performing the quantitative measures of hindlimb and forelimb grip strength and landing foot splay. This was done by determining the mean and standard deviation for the control animals during the performance evaluation for each technician and calculating the coefficient of variance [(standard deviation/mean) x 100%]. The coefficient of variance was required to be approximately 25% or lower to be considered consistent. If a technician did not achieve this level of consistency, further training and evaluations were performed.

Parameters Evaluated

Temperature, humidity, noise level and illumination were measured and recorded to ensure that variations in environmental conditions were minimal during all evaluations.

Evaluations were performed according to the Testing Facility's standard operating procedures that include defined scales for each function listed below:

1. Assessment of signs of autonomic function:
   Ranking of the degree of lacrimation and salivation
   Presence or absence of piloerection and exophthalmus
   Count of urination and defecation
   Pupillary function (constriction of pupil in response to light)
   Degree of palpebral closure

2. Description, incidence, and severity of any convulsions, tremors, or abnormal motor movements

3. Ranking of general level of activity in the open field

4. Description and incidence of posture and gait abnormalities and ranking of gait abnormalities

5. Quantitative measures of forelimb and hindlimb grip strength

6. Quantitative measure of landing foot splay

7. Ranking of reactivity to general stimuli; sensorimotor responses to visual and auditory stimuli; and the response to a tail pinch.

2.16. POSTMORTEM

At the conclusion of all evaluations, all animals were sacrificed and discarded. No necropsy was performed and no tissues were collected. Animals were euthanized by carbon dioxide inhalation.

2.17. STATISTICAL ANALYSIS

The following parameters were analyzed statistically:

body weight (from the functional observational battery)
forelimb and hindlimb grip strength measurements
landing foot splay measurements

2.17.1. METHOD OF ANALYSIS

Mean values of all dose groups were compared to the mean value for the control group at each time interval.

Evaluation of equality of group means was made by the appropriate statistical method, followed by a multiple comparison test if needed. Bartlett's test (Bartlett, 1937) was performed to determine if groups had equal variances. If the variances were equal, parametric procedures were used; if not, nonparametric procedures were used. The parametric method was the standard one-way analysis of variance (ANOVA) using the F ratio to assess significance (Armitage, 1971). If significant differences among the means were indicated, Dunnett's test (Dunnett, 1955, 1964) or Williams test (Williams, 1971, 1972) were used to determine which means were significantly different from the control. The nonparametric method was the Kruskal-Wallis test (Kruskal and Wallis, 1952, 1953) and if differences were indicated, Shirley's test (Shirley, 1977) or Dunn's test (Dunn, 1964) were used to determine which means differed from control. Bartlett's test for equality of variance was conducted at the 1% significance level; all other statistical tests were conducted at the 5% and 1% significance levels.

2.18. DATA STORAGE

All raw data and retained samples, as well as the original study protocol and the original final report will be maintained in the Archives of the Testing Facility upon completion of the study.

2.19. PROTOCOL DEVIATIONS

The following protocol deviations occurred during the study but were not considered to have compromised the validity or integrity of the study.

1. Viability checks were performed once per day instead of twice per day as specified in the Protocol.

2. Animals were approximately 3 weeks old at receipt instead of approximately 4 weeks old as specified in the protocol. In addition, the animals were approximately 11 weeks old at initiation of performance evaluations rather than 8 weeks or less as specified by the protocol.

3. Animals were not randomly assigned to study groups to try to equalize mean body weights as specified in the Protocol. Animals were arbitrarily assigned animal numbers and placed into groups by animal number (i.e. Nos. 5001 to 5005 were assigned to Group 1; Nos. 5006 to 5010 were assigned to Group 2; etc.).

4. Body weights of some animals exceeded the Protocol specified range of 150 to 250 grams at first dose.

5. Initial FOB performance evaluations by Observers 1 and 6 conducted on 26 April 2000 were performed on 10 animals/sex/observer instead of 20 males or 20 females/observer as specified in the Protocol. Evaluations were re-conducted by these observers using the correct number of animals. The initial evaluations are not presented in this report, but are maintained with the study data.

6. The washout period between doses was approximately one to five weeks instead of approximately one week as specified in the Protocol.

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7. Body weights for the calculation of dose volumes were not recorded weekly as specified in the Protocol, but were recorded prior to each dose.

8. Fresh dosing solutions were prepared on the day prior to or on day of dose rather than once weekly as required by protocol.

9. The acceptable variability established in the report of 25-30% differed from the range specified in the protocol of 25% or less.

3. RESULTS AND DISCUSSION

3.1. FUNCTIONAL OBSERVATIONAL BATTERY (FOB) EVALUATIONS

Nine technicians were trained or retrained in the performance of the FOB evaluations and subsequently tested for their ability to identify the behavioral pattern produced by three test articles that are known to produce neurological effects. Three of the technicians (Observers 1, 5, and 6) had been previously trained and helped to set the standard for the expected pattern of observations for each compound. Results of a previous training study conducted at the Testing Facility (Study No. 96-4516), as well as published data, were also used to set the performance standards. Results of the FOB evaluations for each test article are presented in Table 2 for all nine observers. The standard pattern of effects for each of the test articles and the comparative evaluations for each observer are presented in the following sections for all observers, with the exception of Observer 3 who is no longer employed at the Testing Facility.

3.2. FOB EVALUATIONS FOR RATS TREATED WITH CHLORPROMAZINE

The pattern of effects observed after administration of chlorpromazine (Text Table 1) are consistent with the actions of the drug which is a central nervous system depressant. The pattern of effects is also similar to that observed in previous training studies. All observers noted postural effects in the home cage, with the animal lying on its side or flattened; effects on gait and posture in the open field, mainly body drags or limbs splayed or dragging; decreased or no locomotion; low or very low arousal level; and no response to the approach of a blunt object. Seven of the eight observers that were compared also noted effects on palpebral closure in the home cage, with eyelids slightly drooping or half-closed and moderate or extreme lacrimation. Six of the eight observers also noted no response to an auditory stimulus and some in coordination in the air righting reflex. In the functional evaluations, there was an increase in landing foot splay of

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17% to 46% for the Chlorpromazine-treated animals, as compared to the saline controls, for 7/7 observers.

Text Table 1 - FOB Evaluations for Rats Treated with Chlorpromazine

	No. of Observations							
	Males (n = 5))				Females (n = 5)			
Evaluations	**Obs. 1**	**Obs. 2**	**Obs. 4**	**Obs. 5**	**Obs. 6**	**Obs. 7**	**Obs. 8**	**Obs. 9**
Home Cage								
• Posture								
lying on Side	2	0	2	0	1	0	0	0
flattened	1	1	0	1	2	2	1	4
• Palpebral Closure								
sl. drooping	4	1	0	1	1	2	4	4
half-closed	1	0	0	1	0	0	0	0
Handling								
• Lacrimation								
moderate	4	1	2	0	1	1	2	2
extreme	0	0	0	0	3	2	1	2
Open Field								
• Gait and Posture								
body drags	1	0	2	2	1	2	3	2
limbs splayed	5	5	1	1	3	2	2	3
• Locomotion								
decreased	0	0	0	1	0	1	4	1
none	5	5	3	4	4	4	1	4
• Arousal								
low	0	0	0	0	0	2	1	1
very low	5	5	3	5	4	3	4	4
Reflex								
• Approach								
no response	3	3	2	4	3	5	2	5
• Audition								
no response	0	2	2	0	2	2	2	4
• Air Righting								
sl. uncoordinated	3	2	0	3	2	0	0	1
lands on side	1	0	1	0	0	0	0	1
Landing Foot Splay								
• % increase	35%	34%	17%	21%	46%	17%	[a]	25%

[a]Some measurements were performed incorrectly and not considered valid. The number of valid measurements was considered to be too small to provide a valid comparison.

3.3. FOB EVALUATIONS FOR RATS TREATED WITH AMPHETAMINE

D-amphetamine, a catecholamine analog, is a central nervous system stimulant that induces increased locomotor activity, mainly through noradrenergic receptors, and/or produces stereotypic behavior via dopaminergic mechanisms. The predominant effects that are produced are dependent on both the dose of amphetamine and individual variability. The effects observed in the FOB after administration of D-amphetamine to rats are consistent with both actions of the drug. Stereotypic behavior, consisting of excessive repetitive actions such as sniffing, was noted by all eight observers and was seen in most of the animals. Increased locomotor activity and high or very high arousal state was noted by seven of eight observers, although the incidence was lower than that for stereotypic behavior. Decreased locomotor activity and low or very low arousal was also noted by some observers. This paradoxical effect was attributed to the predominance of the stereotypic effects compared to the stimulation of motor activity, which resulted in less movement and arousal in the animals.

Text Table 2 – FOB Evaluations for Rats Treated with Amphetamine

	No. of Observations							
	Males (n = 5))				Females (n = 5)			
Evaluations	Obs. 1	Obs. 2	Obs. 4	Obs. 5	Obs. 6	Obs. 7	Obs. 8	Obs. 9
Open Field								
• Locomotion								
increased	1	2	2	0	3	5	4	4
decreased	3	1	0	0	2	0	0	0
• Arousal								
high, sl. excitement	1	0	2	4	4	5	4	5
very high, hyperalert	1	1	0	0	0	0	0	0
low	1	1	0	1	1	0	0	0
very low	1	1	0	0	0	0	0	0
Stereotypic Behavior								
present	4	5	2	4	5	5	4	5
Reflex								
• Approach								
no response	1	0	3	1	4	1	0	0

3.4. FOB EVALUATIONS FOR RATS TREATED WITH PHYSOSTIGMINE

Physostigmine is a cholinesterase inhibitor whose administration results in an excess of the neurotransmitter acetylcholine at cholinergic nerve endings. This results in stimulation of cholinergic nerves in both the peripheral and central nervous system. The effects observed in the FOB are consistent with the wide range of effects produced by cholinergic stimulation (Text Table 3). Findings associated with stimulation of the parasympathetic nervous system, including increased salivation and miosis, were noted by all observers in most of the animals. Effects on muscles, as indicated by abnormal posture in the home cage, abnormal posture and gait in the open field, decreased or absent locomotion, muscle fasciculations, and incoordination in the air righting reflex, were also noted by all observers in most animals. In addition, 5/7 observers noted increases of 19% to 30% in mean landing foot splay measurements. Findings indicative of depression of the central nervous system included a low or very low arousal state, as noted by all observers, and no reaction to the approach of a blunt object (6/8 observers) and no reaction to a pain stimulus (7/8 observers). The incidence scores for Observer No. 8 were lower than those recorded by the other observers. Since the scores were low for all measures of cholinergic activity, this suggests that the animals were not evaluated at the time of peak effect or that the animals did not receive a full dose of physostigmine and this was not considered an indication of inability to recognize these effects.

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Text Table 3 – FOB Evaluations for Rats Treated with Physostigmine

	No. of Observations							
	Males (n = 5))				Females (n = 5)			
Evaluations	**Obs. 1**	**Obs. 2**	**Obs. 4**	**Obs. 5**	**Obs. 6**	**Obs. 7**	**Obs. 8**	**Obs. 9**
Home Cage								
• Posture								
lying on side	0	3	0	0	0	0	0	0
flattened	5	2	4	5	5	1	1	5
Handling								
• Salivation								
slight	3	2	2	2	2	3	1	2
moderate	2	1	3	3	1	1	0	0
extreme	0	2	0	0	0	0	0	0
Open Field								
• Gait and Posture								
ataxia	0	0	0	0	0	2	0	2
body drags	3	5	5	5	3	1	1	3
limbs splayed	5	3	0	3	3	1	0	1
hunched posture	0	0	0	0	0	1	0	0
• Locomotion								
decreased	0	0	3	0	2	5	1	3
none	5	5	2	5	3	0	0	2
• Arousal								
low	2	0	1	0	1	3	1	0
very low	3	5	4	5	4	2	0	5
Motor Movements								
• Fasciculations								
slight	4	4	5	4	1	5	1	3
severe	1	1	0	1	4	0	0	2
Reflex								
• Approach								
no response	2	0	3	4	2	2	0	2
• Pain								
no reaction	4	4	5	5	1	1	0	4
• Pupil Response								
miosis	5	5	5	5	5	5	2	5
• Air Righting								
sl. uncoordinated	3	5	1	2	2	2	0	2
lands on side	2	0	3	0	3	2	1	1
lands on back	0	0	1	1	0	0	0	0
Landing Foot Splay								
• % increase	29%	22%	[a]	23%	30%	[a]	[b]	19%

[a]No change in landing foot splay, as compared to saline-treated animals.

[b]Some measurements were performed incorrectly and not considered valid. The number of valid measurements was considered to be too small to provide a valid comparison.

3.5. CONSISTENCY OF GRIP STRENGTH AND LANDING FOOT SPLAY MEASUREMENTS

Acceptable variability (25-30%) in the measurement of forelimb and hindlimb grip strength and landing foot splay was achieved by all observers.

Text Table 4 - Consistency of Grip Strength and Landing Foot Splay Measurements

Evaluations	Coefficient of Variability (%)							
	Obs. 1	Obs. 2	Obs. 4	Obs. 5	Obs. 6	Obs. 7	Obs. 8	Obs. 9
Forelimb grip strength	11.1	21.1	21.3	22.0	16.0[b]	8.7	8.8	21.1[b]
Hindlimb grip strength	15.3	25.3	32.8[a] 27.2[a]	13.6	18.4	20.5	16.0	20.6
Landing foot splay	23.5	19.1	25.4	22.4	15.4	23.4	9.8[c]	29.1

[a]Original value was unacceptable. Evaluations were repeated using untreated animals (5 males and 5 females).

[b]Original value was unacceptable. Evaluations were repeated using untreated animals (10 females).

[c]Measurements of landing foot splay were performed incorrectly and were repeated with ten untreated animals.

4. CONCLUSION

Treatment of Sprague-Dawley rats with Chlorpromazine, D-Amphetamine Sulfate, or Physostigmine produced patterns of behavior consistent with their expected neurological effects. These data provide evidence that the procedures used for the Functional Observational Battery evaluations in the Testing Facility are capable of detecting major neurotoxic endpoints. In addition, the neurobehavioral profiles for each compound were correctly identified by Observers 1-2 and 4-9, who were blinded with respect to treatment. This demonstrates that there is interobserver reliability among the trained technicians at the Testing Facility in the conduct of the Functional Observational Battery evaluations. Acceptable variability in the performance of forelimb and hindlimb grip strength measurements and landing foot splay measurements were achieved by all observers. In conclusion, Observers 1, 2, 4, 5, 6, 7, 8, and 9 were considered to be fully qualified to perform Functional Observational Battery evaluations.

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Mean Body Weights, Grip Strength and Landing Foot Splay Values	Appendix KK

Observer 1 Test Article:		Group 1 Saline	Group 2 Chlorpromazine	Group 3 D-Amphetamine Sulfate	Group 4 Physostigmine
Body Weight	Mean	567.0	569.7	604.1	544.0
	S.D.	27.9	25.0	39.8	45.7
	N	5	5	5	5
Forelimb Grip Strength	Mean	926.0	* 680.5	1070.0	851.5
	S.D.	102.5	142.5	137.5	167.6
	N	5	5	5	5
	%CV	11.1			
Hindlimb Grip Strength	Mean	781.5	635.5	831.0	* 622.5
	S.D.	119.8	85.6	69.9	80.4
	N	5	5	5	5
	%CV	15.3			
Landing Foot Splay	Mean	4.8	6.5	5.4	6.2
	S.D.	1.1	1.6	1.7	1.6
	N	5	5	5	5
	%CV	23.5			

*Significantly different from control mean; p≤0.05.

**Significantly different from control mean; p≤0.01.

If no asterisks, no statistically significant differences from control mean.

%CV = (Control Group S.D./Control Group Mean) x 100.

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Mean Body Weights, Grip Strength and Landing Foot Splay Values	Appendix KK

Observer 2 **Test Article:**		**Group 1** **Saline**	**Group 2** **Chlorpromazine**	**Group 3** **D-Amphetamine Sulfate**	**Group 4** **Physostigmine**
Body Weight	Mean	572.4	572.0	608.2	547.6
	S.D.	20.9	26.6	36.4	45.9
	N	5	5	5	5
Forelimb Grip Strength	Mean	858.0	1210.0	797.0	941.5
	S.D.	181.2	369.8	266.0	244.6
	N	5	5	5	5
	%CV	21.1			
Hindlimb Grip Strength	Mean	908.5	876.5	773.0	807.5
	S.D.	230.1	216.4	103.4	127.5
	N	5	5	5	5
	%CV	25.3			
			*		
Landing Foot Splay	Mean	6.7	9.0	5.7	8.2
	S.D.	1.3	1.8	0.9	1.0
	N	5	5	5	5
	%CV	19.1			

*Significantly different from control mean; p≤0.05.

**Significantly different from control mean; p≤0.01.

If no asterisks, no statistically significant differences from control mean.

%CV = (Control Group S.D./Control Group Mean) x 100.

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Mean Body Weights, Grip Strength and Landing Foot Splay Values	Appendix KK

Observer 3 Test Article:		Group 1 Saline	Group 2 Chlorpromazine	Group 3 D-Amphetamine Sulfate	Group 4 Physostigmine
Body Weight	Mean	475.4	490.0	506.3	462.3
	S.D.	24.2	30.2	28.9	37.5
	N	5	5	5	5
Forelimb Grip Strength	Mean	1499.5	1323.5	1909.0	1278.0
	S.D.	470.4	715.3	344.9	351.5
	N	5	5	5	5
	%CV	31.4			
Hindlimb Grip Strength	Mean	955.5	837.5	1102.0	906.5
	S.D.	270.5	255.7	230.2	251.5
	N	5	5	5	5
	%CV	28.3			
Landing Foot Splay	Mean	6.8	8.3	6.1	6.3
	S.D.	0.9	2.5	0.8	1.4
	N	5	5	5	5
	%CV	13.4			

*Significantly different from control mean; p≤0.05.

**Significantly different from control mean; p≤0.01.

If no asterisks, no statistically significant differences from control mean.

%CV = (Control Group S.D./Control Group Mean) x 100.

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Mean Body Weights, Grip Strength and Landing Foot Splay Values	Appendix KK

Observer 4 **Test Article:**		**Group 1** **Saline**	**Group 2** **Chlorpromazine**	**Group 3** **D-Amphetamine Sulfate**	**Group 4** **Physostigmine**
Body Weight	Mean	456.9	468.7	494.6	448.3
	S.D.	21.3	30.1	26.5	37.0
	N	5	5	5	5
Forelimb Grip Strength	Mean	1224.0	1161.0	1311.0	* 901.5
	S.D.	261.3	149.0	179.6	276.0
	N	5	5	5	5
	%CV	21.3			
Hindlimb Grip Strength	Mean	622.5	577.5	601.0	572.0
	S.D.	238.7	202.9	122.3	206.0
	N	5	5	5	5
	%CV	38.3			
Landing Foot Splay	Mean	7.2	8.4	7.1	6.9
	S.D.	1.8	1.8	1.1	1.5
	N	5	5	5	5
	%CV	25.4			

*Significantly different from control mean; p≤0.05.

**Significantly different from control mean; p≤0.01.

If no asterisks, no statistically significant differences from control mean.

%CV = (Control Group S.D./Control Group Mean) x 100.

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Mean Body Weights, Grip Strength and Landing Foot Splay Values	Appendix KK

Observer 5 Test Article:		Group 1 Saline	Group 2 Chlorpromazine	Group 3 D-Amphetamine Sulfate	Group 4 Physostigmine
Body Weight	Mean	558.9	564.5	591.7	530.9
	S.D.	27.4	30.3	37.8	41.4
	N	5	5	5	5
Forelimb Grip Strength	Mean	1352.5	1179.0	1458.5	* 980.5
	S.D.	296.9	327.7	170.8	186.7
	N	5	5	5	5
	%CV	22.0			
Hindlimb Grip Strength	Mean	1428.0	1105.0	1266.0	** 941.0
	S.D.	193.8	312.4	162.7	300.3
	N	5	5	5	5
	%CV	13.6			
Landing Foot Splay	Mean	8.7	10.5	8.9	10.7
	S.D.	1.9	1.7	1.3	1.5
	N	5	5	5	5
	%CV	22.4			

*Significantly different from control mean; $p \leq 0.05$.

**Significantly different from control mean; $p \leq 0.01$.

If no asterisks, no statistically significant differences from control mean.

%CV = (Control Group S.D./Control Group Mean) x 100.

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Mean Body Weights, Grip Strength and Landing Foot Splay Values	Appendix KK

Observer 6 **Test Article:**		**Group 1** **Saline**	**Group 2** **Chlorpromazine**	**Group 3** **D-Amphetamine Sulfate**	**Group 4** **Physostigmine**
Body Weight	Mean	313.0	314.5	311.5	311.0
	S.D.	18.4	26.3	46.9	10.5
	N	5	5	5	5
Forelimb Grip Strength	Mean	667.0	847.5	1005.5	708.0
	S.D.	294.4	143.6	159.5	203.3
	N	5	5	5	5
	%CV	44.1			
Hindlimb Grip Strength	Mean	827.5	835.5	947.0	820.0
	S.D.	152.2	161.6	50.1	136.6
	N	5	5	5	5
	%CV	18.4			
Landing Foot Splay	Mean	5.0	* 7.3	4.0	6.5
	S.D.	0.8	0.6	0.8	1.8
	N	5	5	5	5
	%CV	15.4			

*Significantly different from control mean; p≤0.05.

**Significantly different from control mean; p≤0.01.

If no asterisks, no statistically significant differences from control mean.

%CV = (Control Group S.D./Control Group Mean) x 100.

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Mean Body Weights, Grip Strength and Landing Foot Splay Values	Appendix KK

Observer 7 Test Article:		Group 1 Saline	Group 2 Chlorpromazine	Group 3 D-Amphetamine Sulfate	Group 4 Physostigmine
Body Weight	Mean	313.0	312.3	305.5	310.1
	S.D.	17.5	26.1	33.0	13.2
	N	5	5	5	5
Forelimb Grip Strength	Mean	815.0	869.5	975.5	766.5
	S.D.	71.2	124.3	147.4	161.4
	N	5	5	5	5
	%CV	8.7			
Hindlimb Grip Strength	Mean	620.0	560.5	673.0	642.5
	S.D.	127.2	116.7	105.2	174.5
	N	5	5	5	5
	%CV	20.5			
Landing Foot Splay	Mean	6.6	7.7	5.7	6.4
	S.D.	1.5	0.8	0.8	1.8
	N	5	5	5	5
	%CV	23.4			

*Significantly different from control mean; p≤0.05.

**Significantly different from control mean; p≤0.01.

If no asterisks, no statistically significant differences from control mean.

%CV = (Control Group S.D./Control Group Mean) x 100.

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Mean Body Weights, Grip Strength and Landing Foot Splay Values	Appendix KK

Observer 8 **Test Article:**		**Group 1** **Saline**	**Group 2** **Chlorpromazine**	**Group 3** **D-Amphetamine Sulfate**	**Group 4** **Physostigmine**
Body Weight	Mean	268.7	298.0	276.1	280.3
	S.D.	19.5	55.7	27.3	12.4
	N	5	5	5	5
Forelimb Grip Strength	Mean	1006.5	799.5	912.5	829.5
	S.D.	88.6	148.1	108.9	180.2
	N	5	5	5	5
	%CV	8.8			
Hindlimb Grip Strength	Mean	735.0	605.5	571.0	695.5
	S.D.	117.9	158.6	101.9	238.0
	N	5	5	5	5
	%CV	16.0			
Landing Foot Splay	Mean	6.4	6.2	6.0	5.1
	S.D.	1.6	0.3	-	0.6
	N	3	3	1	2
	%CV	25.0			

*Significantly different from control mean; $p \leq 0.05$.

**Significantly different from control mean; $p \leq 0.01$.

If no asterisks, no statistically significant differences from control mean.

%CV = (Control Group S.D./Control Group Mean) x 100.

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Mean Body Weights, Grip Strength and Landing Foot Splay Values	Appendix KK

Observer 9 **Test Article:**		**Group 1** **Saline**	**Group 2** **Chlorpromazine**	**Group 3** **D-Amphetamine Sulfate**	**Group 4** **Physostigmine**
Body Weight	Mean	315.9	313.5	310.8	311.1
	S.D.	18.3	25.5	48.3	11.1
	N	5	5	5	5
Forelimb Grip Strength	Mean	539.5	963.0	823.0	606.5
	S.D.	292.8	456.9	330.6	327.3
	N	5	5	5	5
	%CV	54.3			
Hindlimb Grip Strength	Mean	632.0	588.0	637.0	647.5
	S.D.	130.3	67.2	128.0	161.7
	N	5	5	5	5
	%CV	20.6			
Landing Foot Splay	Mean	6.3	7.9	4.4	7.5
	S.D.	1.8	1.4	1.3	1.8
	N	5	5	5	5
	%CV	29.1			

*Significantly different from control mean; p≤0.05.

**Significantly different from control mean; p≤0.01.

If no asterisks, no statistically significant differences from control mean.

%CV = (Control Group S.D./Control Group Mean) x 100.

Repeats	Neurobehavioral Positive Control Data: Functional Observational Battery Mean Body Weights, Grip Strength and Landing Foot Splay Values	Appendix KK

Observer 4 Repeat

Test Article:		**Untreated Males**	**Untreated Females**
Forelimb Grip Strength	Mean	1373.0	1167.0
	S.D.	168.3	293.8
	N	5	5
	%CV	12.3	25.2
Hindlimb Grip Strength	Mean	864.5	645.5
	S.D.	235.0	211.9
	N	5	5
	%CV	27.2	32.8

Observer 6 Repeat

Test Article:		**Untreated Females**
Forelimb Grip Strength	Mean	970.5
	S.D.	154.9
	N	10
	%CV	16.0
Hindlimb Grip Strength	Mean	743.3
	S.D.	147.0
	N	10
	%CV	19.8

Observer 8 Repeat

Test Article:		**Saline Males**
Landing Foot Splay	Mean	9.5
	S.D.	0.9
	N	10
	%CV	9.8

%CV = (Control Group S.D./Control Group Mean) x 100.

Repeats	Neurobehavioral Positive Control Data: Functional Observational Battery Mean Body Weights, Grip Strength and Landing Foot Splay Values	Appendix KK

Observer 9 Repeat

Test Article:		**Untreated Females**
Forelimb Grip Strength	Mean	882.0
	S.D.	186.0
	N	10
	%CV	21.1
Hindlimb Grip Strength	Mean	555.8
	S.D.	178.3
	N	10
	%CV	32.1

%CV = (Control Group S.D./Control Group Mean) x 100.

	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations Preface	Appendix KK

Corresponding test articles for each group were as follows:

Group 1	-	Saline
Group 2	-	Chlorpromazine
Group 3	-	D-Amphetamine Sulfate
Group 4	-	Physostigmine

For summarization purposes, comments describing location [i.e., forelimb, hindlimb, right, unilateral, etc.] are not presented in this appendix. These data are contained in the study raw data if needed.

When an animal received two scores during Open Field Evaluations of Gait and Posture (i.e. the animal was noted to be dragging it's body and it's limbs were splayed or dragging), the two scores were summarized individually. Therefore, the total incidence of scores may be greater than the number of animals examined.

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 1		**Group:** **1**	**2**	**3**	**4**
Number of Animals Examined		5	5	5	5
Home Cage Evaluations					
Posture	Sitting or Standing Normally	1	2	1	0
	Alert, Oriented Toward Observer	4	0	4	0
	Asleep	0	0	0	0
	Lying on Side	0	2	0	0
	Flattened	0	1	0	5
	Crouched	0	0	0	0
Vocalizations	Not Present	5	5	5	5
	Present	0	0	0	0
Palpebral Closure	Eyelids Open	5	0	5	5
	Eyelids Completely Closed	0	0	0	0
	Eyelids Slightly Drooping	0	4	0	0
	Eyelids Half Closed	0	1	0	0
Handling Evaluations					
Ease of Removal	Very Easy	3	4	2	5
	Easy	1	1	2	0
	Moderately Difficult	1	0	1	0
	Freezes	0	0	0	0
	Difficult	0	0	0	0
Ease of Handling	Normal (easy, alert)	4	5	4	5
	Moderately Difficult	1	0	1	0
	Freezes	0	0	0	0
	Difficult	0	0	0	0
	Totally limp	0	0	0	0
Chromodacryorrhea	Not Present	5	5	5	5
	Present	0	0	0	0
Lacrimation	Not Present	5	1	5	5
	Moderate	0	4	0	0
	Extreme	0	0	0	0
Coat	Normal	5	5	5	5
	Slightly Soiled	0	0	0	0
	Moderately Soiled	0	0	0	0
	Extremely Soiled	0	0	0	0
Salivation	Not Present	5	5	4	0
	Slight	0	0	1	3
	Moderate	0	0	0	2
	Extreme	0	0	0	0

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 1		**Group:** 1	2	3	4
Number of Animals Examined		5	5	5	5
Open Field Evaluations					
Gait and Posture	Normal	5	0	4	0
	Ataxia	0	0	1	0
	Body Drags	0	1	0	3
	Limbs Splayed or Dragging	0	5	0	5
	Hunched Posture	0	0	0	0
Locomotion	Normal	5	0	1	0
	Increased Movement	0	0	1	0
	Decreased Movement	0	0	3	0
	None	0	5	0	5
Arousal	Normal	4	0	1	0
	Low, Slight Stupor	1	0	1	2
	Very Low, Stupor	0	5	1	3
	High, Slight Excitement, Tense	0	0	1	0
	Very High, Hyper-Alert	0	0	1	0
Piloerection	Not Present	5	5	5	5
	Present	0	0	0	0
Exophthalmia	Not Present	5	5	5	5
	Present	0	0	0	0
Feces	Number of Boluses	6	11	0	3
	Unformed Stool	0	0	0	0
Urine	Number of Pools	4	3	0	5
	Polyuria	0	0	0	0
Stereotypic Behavior					
Stereotypic Behavior	Not Present	5	5	1	5
	Present	0	0	4	0
Motor Movements					
Fasciculations	Not Present	5	5	5	0
	Slight	0	0	0	4
	Severe	0	0	0	1
Convulsions	Not Present	5	5	5	5
	Slight	0	0	0	0
	Severe	0	0	0	0
Tremors	Not Present	5	5	5	5
	Slight	0	0	0	0
	Severe	0	0	0	0

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 1	**Group:**	**1**	**2**	**3**	**4**
Number of Animals Examined		5	5	5	5
Reflex Assessments					
Approach Response	Normal: Slowly Approaches, Sniffs and/or Turns Away	5	2	4	3
	No Reaction	0	3	1	2
	Freezes or Pulls Away Slightly	0	0	0	0
	Jumps or Turns Abruptly to Avoid, or attacks and/or bites	0	0	0	0
Audition	Normal: Flinches or Flicks Ears	5	5	5	5
	No Reaction	0	0	0	0
	Exaggerated; Jumps, Flips, Bites	0	0	0	0
Pain	Normal: Turns/Bites or Walks Forward/Away	5	4	3	1
	No Reaction	0	1	2	4
	Apparent Increased Pain	0	0	0	0
Pupil Response	Pupil Constricts	5	4	5	0
	No Constriction	0	0	0	0
	Miosis	0	1	0	5
	Mydriasis	0	0	0	0
Pinna	Ear Flattens Against Head	0	0	0	0
	Animal Shakes Head	5	5	5	5
	No Response	0	0	0	0
Proprioception	Normal: Returns Leg to Original Position	5	5	5	5
	Returns Leg Only Partially to Original Position	0	0	0	0
	No Response	0	0	0	0
Air Righting Reflex	Normal: Lands on All Four Feet	5	1	5	0
	Slightly Uncoordinated	0	3	0	3
	Lands on Side	0	1	0	2
	Lands on Back	0	0	0	0

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 2		**Group: 1**	**2**	**3**	**4**
Number of Animals Examined		5	5	5	5
Home Cage Evaluations					
Posture	Sitting or Standing Normally	4	3	1	0
	Alert, Oriented Toward Observer	1	1	4	0
	Asleep	0	0	0	0
	Lying on Side	0	0	0	3
	Flattened	0	1	0	2
	Crouched	0	0	0	0
Vocalizations	Not Present	5	5	5	5
	Present	0	0	0	0
Palpebral Closure	Eyelids Open	5	4	5	5
	Eyelids Completely Closed	0	0	0	0
	Eyelids Slightly Drooping	0	1	0	0
	Eyelids Half Closed	0	0	0	0
Handling Evaluations					
Ease of Removal	Very Easy	0	1	4	4
	Easy	5	4	1	1
	Moderately Difficult	0	0	0	0
	Freezes	0	0	0	0
	Difficult	0	0	0	0
Ease of Handling	Normal (easy, alert)	5	5	5	5
	Moderately Difficult	0	0	0	0
	Freezes	0	0	0	0
	Difficult	0	0	0	0
	Totally limp	0	0	0	0
Chromodacryorrhea	Not Present	5	4	5	5
	Present	0	1	0	0
Lacrimation	Not Present	5	4	5	5
	Moderate	0	1	0	0
	Extreme	0	0	0	0
Coat	Normal	5	5	5	5
	Slightly Soiled	0	0	0	0
	Moderately Soiled	0	0	0	0
	Extremely Soiled	0	0	0	0
Salivation	Not Present	5	5	4	0
	Slight	0	0	1	2
	Moderate	0	0	0	1
	Extreme	0	0	0	2

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 2		**Group:** 1	2	3	4
Number of Animals Examined		5	5	5	5
Open Field Evaluations					
Gait and Posture	Normal	5	0	4	0
	Ataxia	0	0	1	0
	Body Drags	0	0	0	5
	Limbs Splayed or Dragging	0	5	0	3
	Hunched Posture	0	0	0	0
Locomotion	Normal	4	0	2	0
	Increased Movement	0	0	2	0
	Decreased Movement	1	0	1	0
	None	0	5	0	5
Arousal	Normal	4	0	2	0
	Low, Slight Stupor	1	0	1	0
	Very Low, Stupor	0	5	1	5
	High, Slight Excitement, Tense	0	0	0	0
	Very High, Hyper-Alert	0	0	1	0
Piloerection	Not Present	5	5	5	5
	Present	0	0	0	0
Exophthalmia	Not Present	5	5	5	5
	Present	0	0	0	0
Feces	Number of Boluses	6	1	1	1
	Unformed Stool	0	0	0	0
Urine	Number of Pools	12	7	6	12
	Polyuria	0	0	0	0
Stereotypic Behavior					
Stereotypic Behavior	Not Present	5	5	0	4
	Present	0	0	5	1
Motor Movements					
Fasciculations	Not Present	5	5	5	0
	Slight	0	0	0	4
	Severe	0	0	0	1
Convulsions	Not Present	5	5	5	5
	Slight	0	0	0	0
	Severe	0	0	0	0
Tremors	Not Present	5	5	5	5
	Slight	0	0	0	0
	Severe	0	0	0	0

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 2	**Group:**	**1**	**2**	**3**	**4**
Number of Animals Examined		5	5	5	5
Reflex Assessments					
Approach Response	Normal: Slowly Approaches, Sniffs and/or Turns Away	5	2	5	5
	No Reaction	0	3	0	0
	Freezes or Pulls Away Slightly	0	0	0	0
	Jumps or Turns Abruptly to Avoid, or attacks and/or bites	0	0	0	0
Audition	Normal: Flinches or Flicks Ears	4	3	5	3
	No Reaction	1	2	0	0
	Exaggerated; Jumps, Flips, Bites	0	0	0	2
Pain	Normal: Turns/Bites or Walks Forward/Away	5	5	5	1
	No Reaction	0	0	0	4
	Apparent Increased Pain	0	0	0	0
Pupil Response	Pupil Constricts	5	3	4	0
	No Constriction	0	0	0	0
	Miosis	0	2	1	5
	Mydriasis	0	0	0	0
Pinna	Ear Flattens Against Head	0	0	1	0
	Animal Shakes Head	5	5	4	5
	No Response	0	0	0	0
Proprioception	Normal: Returns Leg to Original Position	5	5	5	5
	Returns Leg Only Partially to Original Position	0	0	0	0
	No Response	0	0	0	0
Air Righting Reflex	Normal: Lands on All Four Feet	5	3	5	0
	Slightly Uncoordinated	0	2	0	5
	Lands on Side	0	0	0	0
	Lands on Back	0	0	0	0

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 3		**Group:** 1	2	3	4
Number of Animals Examined		5	5	5	5
Home Cage Evaluations					
Posture	Sitting or Standing Normally	2	3	0	1
	Alert, Oriented Toward Observer	3	0	5	0
	Asleep	0	0	0	0
	Lying on Side	0	0	0	1
	Flattened	0	2	0	3
	Crouched	0	0	0	0
Vocalizations	Not Present	5	5	5	5
	Present	0	0	0	0
Palpebral Closure	Eyelids Open	5	3	5	5
	Eyelids Completely Closed	0	0	0	0
	Eyelids Slightly Drooping	0	2	0	0
	Eyelids Half Closed	0	0	0	0
Handling Evaluations					
Ease of Removal	Very Easy	3	3	5	5
	Easy	1	2	0	0
	Moderately Difficult	1	0	0	0
	Freezes	0	0	0	0
	Difficult	0	0	0	0
Ease of Handling	Normal (easy, alert)	3	4	5	5
	Moderately Difficult	2	1	0	0
	Freezes	0	0	0	0
	Difficult	0	0	0	0
	Totally limp	0	0	0	0
Chromodacryorrhea	Not Present	5	5	5	4
	Present	0	0	0	1
Lacrimation	Not Present	5	3	5	5
	Moderate	0	2	0	0
	Extreme	0	0	0	0
Coat	Normal	5	5	5	4
	Slightly Soiled	0	0	0	1
	Moderately Soiled	0	0	0	0
	Extremely Soiled	0	0	0	0
Salivation	Not Present	5	5	5	2
	Slight	0	0	0	1
	Moderate	0	0	0	2
	Extreme	0	0	0	0

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 3		**Group:** 1	2	3	4
Number of Animals Examined		5	5	5	5
Open Field Evaluations					
Gait and Posture	Normal	5	0	5	0
	Ataxia	0	1	0	1
	Body Drags	0	3	0	4
	Limbs Splayed or Dragging	0	3	0	3
	Hunched Posture	0	0	0	0
Locomotion	Normal	5	0	4	0
	Increased Movement	0	0	1	1
	Decreased Movement	0	2	0	1
	None	0	3	0	3
Arousal	Normal	5	0	1	0
	Low, Slight Stupor	0	2	0	2
	Very Low, Stupor	0	3	0	3
	High, Slight Excitement, Tense	0	0	4	0
	Very High, Hyper-Alert	0	0	0	0
Piloerection	Not Present	5	5	5	5
	Present	0	0	0	0
Exophthalmia	Not Present	5	5	5	5
	Present	0	0	0	0
Feces	Number of Boluses	1	1	0	2
	Unformed Stool	0	0	0	0
Urine	Number of Pools	3	5	0	3
	Polyuria	0	0	0	0
Stereotypic Behavior					
Stereotypic Behavior	Not Present	5	5	2	5
	Present	0	0	3	0
Motor Movements					
Fasciculations	Not Present	5	5	5	2
	Slight	0	0	0	2
	Severe	0	0	0	1
Convulsions	Not Present	5	5	5	5
	Slight	0	0	0	0
	Severe	0	0	0	0
Tremors	Not Present	5	5	5	4
	Slight	0	0	0	0
	Severe	0	0	0	1

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 3	**Group:**	**1**	**2**	**3**	**4**
Number of Animals Examined		5	5	5	5
Reflex Assessments					
Approach Response	Normal: Slowly Approaches, Sniffs and/or Turns Away	5	1	2	3
	No Reaction	0	4	3	2
	Freezes or Pulls Away Slightly	0	0	0	0
	Jumps or Turns Abruptly to Avoid, or attacks and/or bites	0	0	0	0
Audition	Normal: Flinches or Flicks Ears	5	4	5	4
	No Reaction	0	1	0	1
	Exaggerated; Jumps, Flips, Bites	0	0	0	0
Pain	Normal: Turns/Bites or Walks Forward/Away	5	5	5	3
	No Reaction	0	0	0	2
	Apparent Increased Pain	0	0	0	0
Pupil Response	Pupil Constricts	5	5	5	2
	No Constriction	0	0	0	1
	Miosis	0	0	0	2
	Mydriasis	0	0	0	0
Pinna	Ear Flattens Against Head	0	0	1	0
	Animal Shakes Head	5	5	4	5
	No Response	0	0	0	0
Proprioception	Normal: Returns Leg to Original Position	5	5	5	4
	Returns Leg Only Partially to Original Position	0	0	0	0
	No Response	0	0	0	1
Air Righting Reflex	Normal: Lands on All Four Feet	5	5	5	1
	Slightly Uncoordinated	0	0	0	2
	Lands on Side	0	0	0	2
	Lands on Back	0	0	0	0

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 4		Group: 1	2	3	4
Number of Animals Examined		5	5	5	5
Home Cage Evaluations					
Posture	Sitting or Standing Normally	5	3	3	1
	Alert, Oriented Toward Observer	0	0	2	0
	Asleep	0	0	0	0
	Lying on Side	0	0	0	0
	Flattened	0	2	0	4
	Crouched	0	0	0	0
Vocalizations	Not Present	5	5	5	5
	Present	0	0	0	0
Palpebral Closure	Eyelids Open	5	5	5	5
	Eyelids Completely Closed	0	0	0	0
	Eyelids Slightly Drooping	0	0	0	0
	Eyelids Half Closed	0	0	0	0
Handling Evaluations					
Ease of Removal	Very Easy	4	4	4	5
	Easy	1	1	0	0
	Moderately Difficult	0	0	1	0
	Freezes	0	0	0	0
	Difficult	0	0	0	0
Ease of Handling	Normal (easy, alert)	5	5	5	5
	Moderately Difficult	0	0	0	0
	Freezes	0	0	0	0
	Difficult	0	0	0	0
	Totally limp	0	0	0	0
Chromodacryorrhea	Not Present	5	5	5	5
	Present	0	0	0	0
Lacrimation	Not Present	5	3	5	3
	Moderate	0	2	0	0
	Extreme	0	0	0	2
Coat	Normal	5	5	5	5
	Slightly Soiled	0	0	0	0
	Moderately Soiled	0	0	0	0
	Extremely Soiled	0	0	0	0
Salivation	Not Present	5	5	5	0
	Slight	0	0	0	2
	Moderate	0	0	0	3
	Extreme	0	0	0	0

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 4		Group: 1	2	3	4
Number of Animals Examined		5	5	5	5
Open Field Evaluations					
Gait and Posture	Normal	5	2	5	0
	Ataxia	0	0	0	0
	Body Drags	0	2	0	5
	Limbs Splayed or Dragging	0	1	0	0
	Hunched Posture	0	0	0	0
Locomotion	Normal	5	2	3	0
	Increased Movement	0	0	2	0
	Decreased Movement	0	0	0	3
	None	0	3	0	2
Arousal	Normal	4	2	3	0
	Low, Slight Stupor	0	0	0	1
	Very Low, Stupor	0	3	0	4
	High, Slight Excitement, Tense	1	0	2	0
	Very High, Hyper-Alert	0	0	0	0
Piloerection	Not Present	5	5	4	5
	Present	0	0	1	0
Exophthalmia	Not Present	5	5	5	5
	Present	0	0	0	0
Feces	Number of Boluses	5	8	0	1
	Unformed Stool	0	0	0	0
Urine	Number of Pools	4	5	2	6
	Polyuria	0	0	0	0
Stereotypic Behavior					
Stereotypic Behavior	Not Present	5	5	3	4
	Present	0	0	2	1
Motor Movements					
Fasciculations	Not Present	5	5	5	0
	Slight	0	0	0	5
	Severe	0	0	0	0
Convulsions	Not Present	5	5	5	5
	Slight	0	0	0	0
	Severe	0	0	0	0
Tremors	Not Present	5	5	5	3
	Slight	0	0	0	1
	Severe	0	0	0	1

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 4	**Group:**	**1**	**2**	**3**	**4**
Number of Animals Examined		5	5	5	5
Reflex Assessments					
Approach Response	Normal: Slowly Approaches, Sniffs and/or Turns Away	5	3	2	2
	No Reaction	0	2	3	3
	Freezes or Pulls Away Slightly	0	0	0	0
	Jumps or Turns Abruptly to Avoid, or attacks and/or bites	0	0	0	0
Audition	Normal: Flinches or Flicks Ears	5	3	5	4
	No Reaction	0	2	0	0
	Exaggerated; Jumps, Flips, Bites	0	0	0	1
Pain	Normal: Turns/Bites or Walks Forward/Away	5	5	4	0
	No Reaction	0	0	1	5
	Apparent Increased Pain	0	0	0	0
Pupil Response	Pupil Constricts	5	5	5	0
	No Constriction	0	0	0	0
	Miosis	0	0	0	5
	Mydriasis	0	0	0	0
Pinna	Ear Flattens Against Head	0	1	1	0
	Animal Shakes Head	5	4	4	5
	No Response	0	0	0	0
Proprioception	Normal: Returns Leg to Original Position	5	5	5	5
	Returns Leg Only Partially to Original Position	0	0	0	0
	No Response	0	0	0	0
Air Righting Reflex	Normal: Lands on All Four Feet	5	4	5	0
	Slightly Uncoordinated	0	0	0	1
	Lands on Side	0	1	0	3
	Lands on Back	0	0	0	1

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 5		**Group:** 1	2	3	4
Number of Animals Examined		5	5	5	5
Home Cage Evaluations					
Posture	Sitting or Standing Normally	3	3	0	0
	Alert, Oriented Toward Observer	2	1	5	0
	Asleep	0	0	0	0
	Lying on Side	0	0	0	0
	Flattened	0	1	0	5
	Crouched	0	0	0	0
Vocalizations	Not Present	5	5	5	5
	Present	0	0	0	0
Palpebral Closure	Eyelids Open	5	3	5	5
	Eyelids Completely Closed	0	0	0	0
	Eyelids Slightly Drooping	0	1	0	0
	Eyelids Half Closed	0	1	0	0
Handling Evaluations					
Ease of Removal	Very Easy	5	4	5	5
	Easy	0	1	0	0
	Moderately Difficult	0	0	0	0
	Freezes	0	0	0	0
	Difficult	0	0	0	0
Ease of Handling	Normal (easy, alert)	5	4	5	5
	Moderately Difficult	0	1	0	0
	Freezes	0	0	0	0
	Difficult	0	0	0	0
	Totally limp	0	0	0	0
Chromodacryorrhea	Not Present	5	5	5	5
	Present	0	0	0	0
Lacrimation	Not Present	5	5	5	5
	Moderate	0	0	0	0
	Extreme	0	0	0	0
Coat	Normal	5	5	5	4
	Slightly Soiled	0	0	0	1
	Moderately Soiled	0	0	0	0
	Extremely Soiled	0	0	0	0
Salivation	Not Present	5	5	4	0
	Slight	0	0	1	2
	Moderate	0	0	0	3
	Extreme	0	0	0	0

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 5		**Group:**	**1**	**2**	**3**	**4**
Number of Animals Examined			5	5	5	5
Open Field Evaluations						
Gait and Posture[a]	Normal		5	1	5	0
	Ataxia		0	0	0	0
	Body Drags		0	2	0	5
	Limbs Splayed or Dragging		0	1	0	3
	Hunched Posture		0	0	0	0
Locomotion	Normal		5	0	5	0
	Increased Movement		0	0	0	0
	Decreased Movement		0	1	0	0
	None		0	4	0	5
Arousal	Normal		4	0	0	0
	Low, Slight Stupor		1	0	1	0
	Very Low, Stupor		0	5	0	5
	High, Slight Excitement, Tense		0	0	4	0
	Very High, Hyper-Alert		0	0	0	0
Piloerection	Not Present		5	5	5	5
	Present		0	0	0	0
Exophthalmia	Not Present		5	5	5	5
	Present		0	0	0	0
Feces	Number of Boluses		6	4	0	1
	Unformed Stool		0	0	0	0
Urine	Number of Pools		2	6	0	6
	Polyuria		0	0	0	0
Stereotypic Behavior						
Stereotypic Behavior	Not Present		5	5	1	5
	Present		0	0	4	0
Motor Movements						
Fasciculations	Not Present		5	5	5	0
	Slight		0	0	0	4
	Severe		0	0	0	1
Convulsions	Not Present		5	5	5	5
	Slight		0	0	0	0
	Severe		0	0	0	0
Tremors	Not Present		5	5	5	5
	Slight		0	0	0	0
	Severe		0	0	0	0

[a]Gait for two Group 2 animals could not be determined because the animals did not move during the observation period.

Males	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 5	Group:	1	2	3	4
Number of Animals Examined		5	5	5	5
Reflex Assessments					
Approach Response	Normal: Slowly Approaches, Sniffs and/or Turns Away	5	1	4	1
	No Reaction	0	4	1	4
	Freezes or Pulls Away Slightly	0	0	0	0
	Jumps or Turns Abruptly to Avoid, or attacks and/or bites	0	0	0	0
Audition	Normal: Flinches or Flicks Ears	5	5	4	4
	No Reaction	0	0	0	0
	Exaggerated; Jumps, Flips, Bites	0	0	1	1
Pain	Normal: Turns/Bites or Walks Forward/Away	5	5	4	0
	No Reaction	0	0	0	5
	Apparent Increased Pain	0	0	1	0
Pupil Response	Pupil Constricts	5	5	5	0
	No Constriction	0	0	0	0
	Miosis	0	0	0	5
	Mydriasis	0	0	0	0
Pinna	Ear Flattens Against Head	2	1	1	0
	Animal Shakes Head	3	4	4	5
	No Response	0	0	0	0
Proprioception	Normal: Returns Leg to Original Position	5	4	5	1
	Returns Leg Only Partially to Original Position	0	0	0	1
	No Response	0	1	0	3
Air Righting Reflex	Normal: Lands on All Four Feet	5	2	5	2
	Slightly Uncoordinated	0	3	0	2
	Lands on Side	0	0	0	0
	Lands on Back	0	0	0	1

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 6		**Group:** 1	2	3	4
Number of Animals Examined		5	5	5	5
Home Cage Evaluations					
Posture	Sitting or Standing Normally	4	1	0	0
	Alert, Oriented Toward Observer	1	1	5	0
	Asleep	0	0	0	0
	Lying on Side	0	1	0	0
	Flattened	0	2	0	5
	Crouched	0	0	0	0
Vocalizations	Not Present	5	5	5	5
	Present	0	0	0	0
Palpebral Closure	Eyelids Open	5	4	5	5
	Eyelids Completely Closed	0	0	0	0
	Eyelids Slightly Drooping	0	1	0	0
	Eyelids Half Closed	0	0	0	0
Handling Evaluations					
Ease of Removal	Very Easy	3	5	4	5
	Easy	1	0	1	0
	Moderately Difficult	0	0	0	0
	Freezes	0	0	0	0
	Difficult	0	0	0	0
Ease of Handling	Normal (easy, alert)	5	5	5	5
	Moderately Difficult	0	0	0	0
	Freezes	0	0	0	0
	Difficult	0	0	0	0
	Totally limp	0	0	0	0
Chromodacryorrhea	Not Present	5	5	5	5
	Present	0	0	0	0
Lacrimation	Not Present	5	1	5	3
	Moderate	0	1	0	1
	Extreme	0	3	0	1
Coat	Normal	5	5	5	5
	Slightly Soiled	0	0	0	0
	Moderately Soiled	0	0	0	0
	Extremely Soiled	0	0	0	0
Salivation	Not Present	5	5	5	2
	Slight	0	0	0	2
	Moderate	0	0	0	1
	Extreme	0	0	0	0

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 6		**Group:** 1	2	3	4
Number of Animals Examined		5	5	5	5
Open Field Evaluations					
Gait and Posture	Normal	5	1	5	0
	Ataxia	0	0	0	0
	Body Drags	0	1	0	3
	Limbs Splayed or Dragging	0	3	0	3
	Hunched Posture	0	1	0	0
Locomotion	Normal	5	1	0	0
	Increased Movement	0	0	3	0
	Decreased Movement	0	0	2	2
	None	0	4	0	3
Arousal	Normal	5	1	0	0
	Low, Slight Stupor	0	0	1	1
	Very Low, Stupor	0	4	0	4
	High, Slight Excitement, Tense	0	0	4	0
	Very High, Hyper-Alert	0	0	0	0
Piloerection	Not Present	5	5	5	5
	Present	0	0	0	0
Exophthalmia	Not Present	5	5	5	5
	Present	0	0	0	0
Feces	Number of Boluses	0	3	0	0
	Unformed Stool	0	0	0	0
Urine	Number of Pools	0	5	0	4
	Polyuria	0	0	0	0
Stereotypic Behavior					
Stereotypic Behavior	Not Present	5	5	0	3
	Present	0	0	5	2
Motor Movements					
Fasciculations	Not Present	5	5	5	0
	Slight	0	0	0	1
	Severe	0	0	0	4
Convulsions	Not Present	5	5	5	5
	Slight	0	0	0	0
	Severe	0	0	0	0
Tremors	Not Present	5	5	5	5
	Slight	0	0	0	0
	Severe	0	0	0	0

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 6	**Group:**	**1**	**2**	**3**	**4**
Number of Animals Examined		5	5	5	5
Reflex Assessments					
Approach Response	Normal: Slowly Approaches, Sniffs and/or Turns Away	5	2	1	3
	No Reaction	0	3	4	2
	Freezes or Pulls Away Slightly	0	0	0	0
	Jumps or Turns Abruptly to Avoid, or attacks and/or bites	0	0	0	0
Audition	Normal: Flinches or Flicks Ears	5	3	5	5
	No Reaction	0	2	0	0
	Exaggerated; Jumps, Flips, Bites	0	0	0	0
Pain	Normal: Turns/Bites or Walks Forward/Away	5	5	5	4
	No Reaction	0	0	0	1
	Apparent Increased Pain	0	0	0	0
Pupil Response	Pupil Constricts	5	5	5	0
	No Constriction	0	0	0	0
	Miosis	0	0	0	5
	Mydriasis	0	0	0	0
Pinna	Ear Flattens Against Head	0	0	2	0
	Animal Shakes Head	5	5	3	5
	No Response	0	0	0	0
Proprioception	Normal: Returns Leg to Original Position	5	3	5	3
	Returns Leg Only Partially to Original Position	0	1	0	1
	No Response	0	1	0	1
Air Righting Reflex	Normal: Lands on All Four Feet	5	3	5	0
	Slightly Uncoordinated	0	2	0	2
	Lands on Side	0	0	0	3
	Lands on Back	0	0	0	0

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 7		**Group:** 1	2	3	4
Number of Animals Examined		5	5	5	5
Home Cage Evaluations					
Posture	Sitting or Standing Normally	2	3	1	3
	Alert, Oriented Toward Observer	3	0	4	1
	Asleep	0	0	0	0
	Lying on Side	0	0	0	0
	Flattened	0	2	0	1
	Crouched	0	0	0	0
Vocalizations	Not Present	5	5	5	5
	Present	0	0	0	0
Palpebral Closure	Eyelids Open	5	3	5	5
	Eyelids Completely Closed	0	0	0	0
	Eyelids Slightly Drooping	0	2	0	0
	Eyelids Half Closed	0	0	0	0
Handling Evaluations					
Ease of Removal	Very Easy	5	5	4	5
	Easy	0	0	1	0
	Moderately Difficult	0	0	0	0
	Freezes	0	0	0	0
	Difficult	0	0	0	0
Ease of Handling	Normal (easy, alert)	5	5	4	5
	Moderately Difficult	0	0	1	0
	Freezes	0	0	0	0
	Difficult	0	0	0	0
	Totally limp	0	0	0	0
Chromodacryorrhea	Not Present	5	4	5	5
	Present	0	1	0	0
Lacrimation	Not Present	5	2	5	5
	Moderate	0	1	0	0
	Extreme	0	2	0	0
Coat	Normal	5	5	5	5
	Slightly Soiled	0	0	0	0
	Moderately Soiled	0	0	0	0
	Extremely Soiled	0	0	0	0
Salivation	Not Present	4	5	5	1
	Slight	1	0	0	3
	Moderate	0	0	0	1
	Extreme	0	0	0	0

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 7		**Group:** 1	2	3	4
Number of Animals Examined		5	5	5	5
Open Field Evaluations					
Gait and Posture	Normal	5	1	5	0
	Ataxia	0	0	0	2
	Body Drags	0	2	0	1
	Limbs Splayed or Dragging	0	2	0	1
	Hunched Posture	0	0	0	1
Locomotion	Normal	2	0	0	0
	Increased Movement	1	0	5	0
	Decreased Movement	2	1	0	5
	None	0	4	0	0
Arousal	Normal	3	0	0	0
	Low, Slight Stupor	2	2	0	3
	Very Low, Stupor	0	3	0	2
	High, Slight Excitement, Tense	0	0	5	0
	Very High, Hyper-Alert	0	0	0	0
Piloerection	Not Present	5	5	5	5
	Present	0	0	0	0
Exophthalmia	Not Present	5	5	5	5
	Present	0	0	0	0
Feces	Number of Boluses	0	8	0	0
	Unformed Stool	0	0	0	0
Urine	Number of Pools	0	4	1	4
	Polyuria	0	0	0	0
Stereotypic Behavior					
Stereotypic Behavior	Not Present	5	5	0	1
	Present	0	0	5	4
Motor Movements					
Fasciculations	Not Present	5	5	5	0
	Slight	0	0	0	5
	Severe	0	0	0	0
Convulsions	Not Present	5	5	5	5
	Slight	0	0	0	0
	Severe	0	0	0	0
Tremors	Not Present	5	5	5	5
	Slight	0	0	0	0
	Severe	0	0	0	0

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 7

		Group: 1	2	3	4
Number of Animals Examined		5	5	5	5
Reflex Assessments					
Approach Response	Normal: Slowly Approaches, Sniffs and/or Turns Away	3	0	4	3
	No Reaction	2	5	1	2
	Freezes or Pulls Away Slightly	0	0	0	0
	Jumps or Turns Abruptly to Avoid, or attacks and/or bites	0	0	0	0
Audition	Normal: Flinches or Flicks Ears	5	3	5	5
	No Reaction	0	2	0	0
	Exaggerated; Jumps, Flips, Bites	0	0	0	0
Pain	Normal: Turns/Bites or Walks Forward/Away	5	5	5	4
	No Reaction	0	0	0	1
	Apparent Increased Pain	0	0	0	0
Pupil Response	Pupil Constricts	5	4	5	0
	No Constriction	0	1	0	0
	Miosis	0	0	0	5
	Mydriasis	0	0	0	0
Pinna	Ear Flattens Against Head	3	0	4	0
	Animal Shakes Head	2	5	1	5
	No Response	0	0	0	0
Proprioception	Normal: Returns Leg to Original Position	5	4	5	5
	Returns Leg Only Partially to Original Position	0	1	0	0
	No Response	0	0	0	0
Air Righting Reflex	Normal: Lands on All Four Feet	4	5	4	1
	Slightly Uncoordinated	1	0	1	2
	Lands on Side	0	0	0	2
	Lands on Back	0	0	0	0

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 8	**Group:**	**1**	**2**	**3**	**4**
Number of Animals Examined		5	5	5	5
Home Cage Evaluations					
Posture	Sitting or Standing Normally	0	4	0	3
	Alert, Oriented Toward Observer	4	0	4	1
	Asleep	1	0	0	0
	Lying on Side	0	0	0	0
	Flattened	0	1	0	1
	Crouched	0	0	0	0
Vocalizations	Not Present	5	5	5	5
	Present	0	0	0	0
Palpebral Closure	Eyelids Open	4	1	5	5
	Eyelids Completely Closed	1	0	0	0
	Eyelids Slightly Drooping	0	4	0	0
	Eyelids Half Closed	0	0	0	0
Handling Evaluations					
Ease of Removal	Very Easy	3	4	4	3
	Easy	2	1	1	2
	Moderately Difficult	0	0	0	0
	Freezes	0	0	0	0
	Difficult	0	0	0	0
Ease of Handling	Normal (easy, alert)	4	5	5	5
	Moderately Difficult	1	0	0	0
	Freezes	0	0	0	0
	Difficult	0	0	0	0
	Totally limp	0	0	0	0
Chromodacryorrhea	Not Present	5	4	5	5
	Present	0	1	0	0
Lacrimation	Not Present	5	2	5	5
	Moderate	0	2	0	0
	Extreme	0	1	0	0
Coat	Normal	5	5	5	5
	Slightly Soiled	0	0	0	0
	Moderately Soiled	0	0	0	0
	Extremely Soiled	0	0	0	0
Salivation	Not Present	5	5	5	4
	Slight	0	0	0	1
	Moderate	0	0	0	0
	Extreme	0	0	0	0

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 8	**Group:**	**1**	**2**	**3**	**4**
Number of Animals Examined		5	5	5	5
Open Field Evaluations					
Gait and Posture	Normal	5	1	5	4
	Ataxia	0	0	0	0
	Body Drags	0	3	0	1
	Limbs Splayed or Dragging	0	2	0	0
	Hunched Posture	0	0	0	0
Locomotion	Normal	5	0	1	4
	Increased Movement	0	0	4	0
	Decreased Movement	0	4	0	1
	None	0	1	0	0
Arousal	Normal	5	0	1	4
	Low, Slight Stupor	0	1	0	1
	Very Low, Stupor	0	4	0	0
	High, Slight Excitement, Tense	0	0	4	0
	Very High, Hyper-Alert	0	0	0	0
Piloerection	Not Present	5	5	5	5
	Present	0	0	0	0
Exophthalmia	Not Present	5	5	5	5
	Present	0	0	0	0
Feces	Number of Boluses	0	4	0	0
	Unformed Stool	0	0	0	0
Urine	Number of Pools	0	0	0	1
	Polyuria	0	0	0	0
Stereotypic Behavior					
Stereotypic Behavior	Not Present	5	5	1	4
	Present	0	0	4	1
Motor Movements					
Fasciculations	Not Present	5	5	5	4
	Slight	0	0	0	1
	Severe	0	0	0	0
Convulsions	Not Present	5	5	5	5
	Slight	0	0	0	0
	Severe	0	0	0	0
Tremors	Not Present	5	5	5	5
	Slight	0	0	0	0
	Severe	0	0	0	0

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 8	Group:	1	2	3	4
Number of Animals Examined		5	5	5	5
Reflex Assessments					
Approach Response	Normal: Slowly Approaches, Sniffs and/or Turns Away	5	3	5	5
	No Reaction	0	2	0	0
	Freezes or Pulls Away Slightly	0	0	0	0
	Jumps or Turns Abruptly to Avoid, or attacks and/or bites	0	0	0	0
Audition	Normal: Flinches or Flicks Ears	5	3	5	5
	No Reaction	0	2	0	0
	Exaggerated; Jumps, Flips, Bites	0	0	0	0
Pain	Normal: Turns/Bites or Walks Forward/Away	5	4	5	5
	No Reaction	0	1	0	0
	Apparent Increased Pain	0	0	0	0
Pupil Response	Pupil Constricts	5	3	4	2
	No Constriction	0	2	0	1
	Miosis	0	0	0	2
	Mydriasis	0	0	1	0
Pinna	Ear Flattens Against Head	0	1	1	0
	Animal Shakes Head	5	4	4	5
	No Response	0	0	0	0
Proprioception	Normal: Returns Leg to Original Position	5	5	5	5
	Returns Leg Only Partially to Original Position	0	0	0	0
	No Response	0	0	0	0
Air Righting Reflex	Normal: Lands on All Four Feet	5	5	5	4
	Slightly Uncoordinated	0	0	0	0
	Lands on Side	0	0	0	1
	Lands on Back	0	0	0	0

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 9	**Group:**	**1**	**2**	**3**	**4**
Number of Animals Examined		5	5	5	5
Home Cage Evaluations					
Posture	Sitting or Standing Normally	4	1	4	0
	Alert, Oriented Toward Observer	1	0	1	0
	Asleep	0	0	0	0
	Lying on Side	0	0	0	0
	Flattened	0	4	0	5
	Crouched	0	0	0	0
Vocalizations	Not Present	5	5	5	5
	Present	0	0	0	0
Palpebral Closure	Eyelids Open	5	1	5	5
	Eyelids Completely Closed	0	0	0	0
	Eyelids Slightly Drooping	0	4	0	0
	Eyelids Half Closed	0	0	0	0
Handling Evaluations					
Ease of Removal	Very Easy	3	4	4	4
	Easy	2	1	1	1
	Moderately Difficult	0	0	0	0
	Freezes	0	0	0	0
	Difficult	0	0	0	0
Ease of Handling	Normal (easy, alert)	5	5	5	5
	Moderately Difficult	0	0	0	0
	Freezes	0	0	0	0
	Difficult	0	0	0	0
	Totally limp	0	0	0	0
Chromodacryorrhea	Not Present	5	4	5	5
	Present	0	1	0	0
Lacrimation	Not Present	5	1	5	3
	Moderate	0	2	0	2
	Extreme	0	2	0	0
Coat	Normal	5	5	4	2
	Slightly Soiled	0	0	1	3
	Moderately Soiled	0	0	0	0
	Extremely Soiled	0	0	0	0
Salivation	Not Present	5	5	5	3
	Slight	0	0	0	2
	Moderate	0	0	0	0
	Extreme	0	0	0	0

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 9		**Group:** 1	2	3	4
Number of Animals Examined		5	5	5	5
Open Field Evaluations					
Gait and Posture	Normal	5	1	5	0
	Ataxia	0	0	0	2
	Body Drags	0	2	0	3
	Limbs Splayed or Dragging	0	3	0	1
	Hunched Posture	0	0	0	0
Locomotion	Normal	3	0	1	0
	Increased Movement	0	0	4	0
	Decreased Movement	2	1	0	3
	None	0	4	0	2
Arousal	Normal	3	0	0	0
	Low, Slight Stupor	2	1	0	0
	Very Low, Stupor	0	4	0	5
	High, Slight Excitement, Tense	0	0	5	0
	Very High, Hyper-Alert	0	0	0	0
Piloerection	Not Present	5	5	5	5
	Present	0	0	0	0
Exophthalmia	Not Present	5	5	5	5
	Present	0	0	0	0
Feces	Number of Boluses	0	3	0	0
	Unformed Stool	0	0	0	0
Urine	Number of Pools	0	2	0	0
	Polyuria	0	0	0	0
Stereotypic Behavior					
Stereotypic Behavior	Not Present	5	5	0	0
	Present	0	0	5	5
Motor Movements					
Fasciculations	Not Present	5	5	5	0
	Slight	0	0	0	3
	Severe	0	0	0	2
Convulsions	Not Present	5	5	5	5
	Slight	0	0	0	0
	Severe	0	0	0	0
Tremors	Not Present	5	5	5	5
	Slight	0	0	0	0
	Severe	0	0	0	0

Females	Neurobehavioral Positive Control Data: Functional Observational Battery Incidence Summary of Functional Observational Battery Evaluations	Appendix KK

Observer 9	**Group:**	**1**	**2**	**3**	**4**
Number of Animals Examined		5	5	5	5
Reflex Assessments					
Approach Response	Normal: Slowly Approaches, Sniffs and/or Turns Away	3	0	5	3
	No Reaction	2	5	0	2
	Freezes or Pulls Away Slightly	0	0	0	0
	Jumps or Turns Abruptly to Avoid, or attacks and/or bites	0	0	0	0
Audition	Normal: Flinches or Flicks Ears	5	1	5	3
	No Reaction	0	4	0	2
	Exaggerated; Jumps, Flips, Bites	0	0	0	0
Pain	Normal: Flinches or Flicks Ears	5	5	5	1
	No Reaction	0	0	0	4
	Exaggerated; Jumps, Flips, Bites	0	0	0	0
Pupil Response	Pupil Constricts	4	3	5	0
	No Constriction	1	1	0	0
	Miosis	0	1	0	5
	Mydriasis	0	0	0	0
Pinna	Ear Flattens Against Head	0	0	0	0
	Animal Shakes Head	5	5	5	5
	No Response	0	0	0	0
Proprioception	Normal: Returns Leg to Original Position	5	5	5	5
	Returns Leg Only Partially to Original Position	0	0	0	0
	No Response	0	0	0	0
Air Righting Reflex	Normal: Lands on All Four Feet	5	3	5	2
	Slightly Uncoordinated	0	1	0	2
	Lands on Side	0	1	0	1
	Lands on Back	0	0	0	0

	Neurobehavioral Positive Control Data: Motor Activity Preface	Appendix KK

This is an abridged version of text and tables from Study No. H-34, 00-14501 as amended on 23 December 2008.

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1. INTRODUCTION

This study was designed to assess the effect of Amphetamine and Chlorpromazine on the locomotor activity in young rats 13, 17, 21, and 62 days of age. This work was performed in order to provide Positive Control data and was conducted according to test guidelines of the U.S. Environmental Protection Agency (Office of Prevention, Pesticides and Toxic Substances, Health Effects Guidelines, OPPTS 870.6300, Developmental Neurotoxicity, August 1998).

2. MATERIALS AND METHODS

2.1. REGULATORY REFERENCES

2.1.1. TEST GUIDELINES

This study was designed to provide positive control data for neurotoxicity screening studies in accord with the US EPA Health Effects Test Guidelines, OPPTS 870.6200 Neurotoxicity Screening Battery, August 1998.

2.1.2. GOOD LABORATORY PRACTICES

This study was conducted in compliance with Part 160 of 40 CFR (EPA/FIFRA Good Laboratory Practice Regulations) with the exception that assays to verify concentration, stability and homogeneity of the test articles in carriers were not performed.

2.1.3. ANIMAL WELFARE ACT COMPLIANCE

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

2.2. FACILITIES MANAGEMENT/ANIMAL HUSBANDRY

Currently acceptable practices of good animal husbandry were followed, e.g., *Guide for the Care and Use of Laboratory Animals*; National Academy Press, 1996. Huntingdon Life Sciences is fully accredited by the

Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC).

2.3. STUDY MANAGEMENT

2.3.1. SPONSOR AND TESTING FACILITY

Huntingdon Life Sciences
Mettlers Road
PO Box 2360
East Millstone, NJ 08875-2360

2.3.2. STUDY DIRECTOR[1]

Suzanne R. Thornton, Ph.D.
P.J. Shem Patyna, Ph.D.
George L. Brown, M.S.
Edward R. Frizell, M.D., Ph.D.

2.4. EXPERIMENTAL DESIGN

Group	Treatment	Dosage (mg/kg)	Dose Volume (mL/kg)	Treatment Schedule	Locomotor Activity Assessment	Number of Animals
I[a]	Control	0	5	Postnatal Day 13, 17, 21, 62	Approximately 30 minutes after injection	10/sex
II	Amphetamine	2.0	5	Postnatal Day 13, 17, 21, 62	Approximately 30 minutes after injection	10/sex
III	Chlorpromazine	10.0	5	Postnatal Day 13, 17, 21, 62	Approximately 30 minutes after injection	10/sex

[a]Control animals were administered 0.9% saline at the same dose volume as the test articles.

[1]Suzanne R. Thornton, Ph.D. served as Study Director during the testing portion of Study No. 00-14501. Effective 19 May 2000, P.J. Shem Patyna assumed the responsibilities of Study Director. George Brown, M.S. assumed all Study Director responsibilities following Dr. Patyna's departure from Huntingdon Life Sciences, effective 22 December 2000. Effective 10 Nov 2008, Edward R. Frizell, M.D., Ph.D. assumed Study Director responsibilities for Study No. 00-14501 for the purpose of amending the Final Report only.

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2.5. STUDY DATES

2.5.1. STUDY INITIATION

10 February 2000

2.5.2. DATE OF ANIMAL RECEIPT

11 February 2000

2.5.3. DOSE INITIATION DATES FOR LOCOMOTOR ACTIVITY ASSESSMENTS

Postnatal Day 13: 14 February 2000
Postnatal Day 17: 18 February 2000
Postnatal Day 21: 22 February 2000
Postnatal Day 62: 03 April 2000

2.5.4. TRANSFER OF ANIMALS TO EXTRA RAT COLONY

04 April 2000

2.5.5. STUDY COMPLETION

13 March 2001 (Date Study Director signed the Final Report)

2.6. TEST ARTICLES

2.6.1. AMPHETAMINE

Supplier

Sigma
3050 Spruce Street
St. Louis, MO 63103

Lot Number

69H1239

Purity

Assume 100%

Date Received

07 January 2000

Expiration Date

June 2001

Description

Powder

Storage

Room temperature

Archival Sample

A sample of amphetamine is stored in the Archives of the Testing Facility under conditions specified for test article storage.

Disposition of Unused Test Article

Unused test article was used as the archival sample for this test article.

2.6.2. CHLORPROMAZINE

Supplier

Sigma
3050 Spruce Street
St. Louis, MO 63103

Lot Number

48H1403

Purity

98%

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Date Received

01 December 1999

Expiration Date

April 2001

Description

White/White with a yellow cast, powder

Characteristics

Light sensitive

Storage

Room temperature, protected from light

Archival Sample

A sample of chlorpromazine is stored in the Archives of the Testing Facility under conditions specified for test article storage.

Disposition of Unused Test Article

Unused test article was used as the archival sample for this test article.

2.7. CONTROL ARTICLE

0.9 % Saline

2.7.1. SUPPLIER

VWR Scientific Products
200 Center Square Rd.
Bridgeport, NJ 08014

2.7.2. LOT/BATCH NUMBER

G-949941 / 173-191

2.7.3. DATE RECEIVED

04 June 1999

2.7.4. EXPIRATION DATE

October 2000

2.7.5. DESCRIPTION

Clear liquid

2.7.6. STORAGE

Room temperature

2.7.7. ARCHIVAL SAMPLE

A sample of the control article is stored in the Archives of the Testing Facility under conditions specified for test article storage.

2.8. TEST ARTICLE AND CONTROL ARTICLE PREPARATION

2.8.1. CONTROL ARTICLE PREPARATION

Control article was used neat; as received.

2.8.2. TEST ARTICLE PREPARATION

Appropriate amounts of test article were mixed with 0.9% saline to achieve the desired concentrations in a graduated cylinder, capped, inverted and shaken well prior to use. Fresh dosing solutions were prepared either 1 or 3 days prior to or the day of dose administration and were refrigerated (2-8°C) when not in use.

2.9. ANALYSIS OF DOSING SUSPENSIONS

Analyses were not performed in this study.

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2.10. TEST ANIMALS

2.10.1. SPECIES

Albino Rats
[Crl: CD® (SD) IGS BR]

2.10.2. SUPPLIER

Charles River Laboratories
Kingston, NY facility

2.10.3. JUSTIFICATION FOR TEST SYSTEM SELECTION

The rat is a rodent animal model commonly utilized in reproduction studies as recommended in the referenced guidelines.

2.10.4. ANIMAL RECEIPT INFORMATION

Purchased	8 litters (dam and 5 pups/sex/litter)
Placed on study	6 litters (dam and 5/sex/litter)

2.10.5. AGE OF PUPS AT RECEIPT

Pups were received on Postnatal Day 10.

2.10.6. ACCLIMATION PERIOD

All female rats and their litters were acclimated from the time they were received until locomotor activity assessment began on the pups.

2.11. SELECTION/GROUP ASSIGNMENT

More animals than required for the study were purchased and acclimated. Animals considered suitable for the study on the basis of pretest physical examinations were randomized into groups at receipt using a method which ranked the Postnatal Day 10 body weights and randomly assigned each within the block of three into groups. Animals were replaced as required based on physical examinations and/or body weight change up to Postnatal Day 13 to achieve the desired number of animals (10/sex/group).

Disposition of all animals not utilized in this study is maintained in the study file.

2.12. ANIMAL IDENTIFICATION

Each female was ear tagged (metal ear tag) with a unique identification number by the supplier. Each Postnatal Day 10 pup was uniquely identified by tattoo upon receipt. At weaning (Postnatal Day 21), each pup was ear-tagged with a number assigned by the Testing Facility upon receipt. These numbers plus the study number served as each animal's unique and permanent identification for the duration of the study. Each cage was also provided with a cage card which contained the study number and animal number.

2.13. VETERINARY CARE

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

2.14. ANIMAL HUSBANDRY

2.14.1. HOUSING

Each female rat and litter, from the time of receipt through Postnatal Day 20 were individually housed in a covered, clear plastic "shoebox" with bedding. From Postnatal Day 21 until Postnatal Day 28, the weanling pups (two or three of the same sex) were housed in stainless steel suspended cages with wire mesh floors and fronts. After Postnatal Day 28, and for the remainder of the study, animals were individually housed in stainless steel suspended cages with wire mesh floors. A glass food jar with a stainless steel lid, and food saver, was secured in each cage. Clean food jars and fresh feed were provided at least weekly.

2.14.2. FEED

Certified Rodent Diet, No. 5002; (Meal) (PMI Nutrition International, St. Louis, MO) was provided *ad libitum*.

Analytical certification of batches of feed, provided by the manufacturer, were maintained on file at the Testing Facility. Feed was analyzed for nutritional content (protein, fat, fiber), inorganic constituents (arsenic, cadmium, calcium, lead, mercury, phosphorus, selenium), organophosphates (diazinon, ethion, methyl parathion, thimet, trithion, disulfoton, malathion, parathion, thiodan), and pesticides (aldrin, beta-BHC, DDE, delta-BHC, endrin, heptachlor, lindane, mirex, alpha-BHC, chlordane, total DDT, dieldrin, HCB, heptachlor epoxide, methoxychlor), plus PCB, and aflatoxin.

There were no known contaminants in the feed which were considered capable of interfering with the results of this study.

2.14.3. WATER

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

Monthly water analyses were conducted by Elizabethtown Water Company, Westfield, New Jersey (Raritan-East Millstone Plant) to ensure that water meets standards specified under the EPA Federal Safe Drinking Water Act Regulations (40 CFR part 141). Water analyses, provided by the supplier, were maintained on file at the Testing Facility. In addition, water samples were collected biannually from representative rooms in the Testing Facility; chemical and microbiological water analyses were conducted on these samples by a subcontract laboratory. Results were maintained on file at the Testing Facility. There are no known contaminants in the water which are expected to interfere with this study.

2.14.4. BEDDING ARTICLE

Ground corncob bedding (Bed-O'-Cobs® 1/4 inch Irradiated, The Andersons, Maumee, Ohio) was provided for each female rat and litter from time of receipt through Postnatal Day 20. Fresh bedding was provided weekly and as needed.

Bedding was analyzed for inorganic constituents (arsenic, bismuth, cadmium, lead, magnesium, manganese, mercury, nickel, zinc), organophosphates (diazinon, ethion, methyl parathion, trithion, malthion, ethyl parathion), and pestcides (aldrin, beta-BHC, DDE, delta-BHC, endrin, heptchlor, lindane, mirex, alpha-BHC, chlordane, total DDT, dieldrin, HCB, heptachlor epoxide, methoxychlor), plus PCB, and aflatoxin. There were no known contaminants in the bedding which were expected to interfere with the results of this study. Contaminant analyses were performed periodically. Results of the bedding analysis were maintained on file at the Testing Facility.

2.14.5. ENVIRONMENTAL CONDITIONS

Light/Dark Cycle

Twelve-hour light/dark cycle provided via automatic timer.

Temperature

Temperature was monitored and recorded twice daily and maintained within the desired ranges to the maximum extent possible.

Desired:	18 - 26°C
Actual:	21 - 24°C

Relative Humidity

Relative humidity was monitored and recorded once daily and maintained within the desired ranges to the maximum extent possible.

Desired:	30 - 70%
Actual:	20 – 68%

Relative humidity was not within the specified range on eight occasions during this study (20-28%). This was not considered to have affected the integrity of the study.

2.15. TEST ARTICLE ADMINISTRATION

2.15.1. ROUTE OF ADMINISTRATION

Intraperitoneal injection

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2.15.2. JUSTIFICATION FOR ROUTE OF ADMINISTRATION

The intraperitoneal route provides rapid test article absorption and has been used in previous studies with the test articles.

2.15.3. FREQUENCY AND DURATION OF ADMINISTRATION

The test articles (Amphetamine, Chlorpromazine) and control article were administered to pups on Postnatal Days 13, 17, 21, and 62. Each animal was dosed more than once per week with a washout period of 4 to 41 days between doses.

2.15.4. ADMINISTRATION OF TEST AND/OR CONTROL ARTICLE

The test articles (Amphetamine, Chlorpromazine) and the control article (saline) were administered by intraperitoneal injection into the abdominal cavity near the inguinal region using a sterile needle and syringe of appropriate size. Doses were calculated using the most recent body weights available. A volume of 5 mL/kg of body weight was administered.

2.16. EXPERIMENTAL EVALUATION

2.16.1. VIABILITY OBSERVATIONS (CAGESIDE)

Observations for mortality, morbidity and signs of severe toxic or pharmacological effects were made at least twice daily (morning and afternoon) for the female rats and pups.

2.16.2. CLINICAL OBSERVATIONS

A detailed physical examination was given to all female rats and pups upon receipt. The rat pups had a detailed physical examination on the day of locomotor activity behavioral assessment and weekly during the postweaning period until they were placed in a colony.

2.16.3. BODY WEIGHTS

Body weights were recorded for pups on Postnatal Days 10, 13, 17, 21, 62, and weekly during the postweaning period.

2.17. LITTER EVALUATIONS

2.17.1. OBSERVATIONS

Litters were observed and each pup was sexed at the time of receipt. Pups in the litter were counted on Postnatal Days 10,13,17, and 21.

2.17.2. WEANING

Pups were weaned on Postnatal Day 21 and housed two or three of the same sex per cage.

2.17.3. LOCOMOTOR ACTIVITY BEHAVIORAL ASSESSMENT

The locomotor activity assessment was measured in 10 pups/sex/group on Postnatal Days 13, 17, 21 and 62. On each day of testing, 10 rat pups/sex/group were adminstered either vehicle, amphetamine, or chlorpromazine. Approximately thirty minutes after the injection they were placed in a clear plastic shoebox cage equipped with a 5-beam automated Photobeam Activity System (PAS; San Diego Instruments, Inc.). Activity was monitored during a 60-minute session composed of 12, five-minute intervals. A record was made of the total number of photobeam breaks which occurred during each of the 12, five-minute intervals. The locomotor activity was assessed using a repeated measures analysis of variance to determine if there was a test article effect. Rat pups were randomized so that there was an equal representation of the treatment groups during each locomotor activity session.

Temperature

Temperature was monitored and recorded twice daily, just prior to the first evaluation and just after the last evaluation.

Desired:	18 to 26°C
Actual:	22 to 24°C

Relative Humidity

Relative humidity was monitored and recorded twice daily, just prior to the first evaluation and just after the last evaluation.

Desired: 30 to 70%
Actual: 29 to 56%

Noise Level

Noise level was monitored using a Digital Sound Level Meter, Model 840029 (Sper Scientific, Ltd., Scottsdale, Arizona) and recorded twice daily, just prior to the first evaluation and just after the last evaluation.

Desired: 55 to 65 dB
Actual: 60.1 to 61.4 dB

Illumination

Illumination was monitored using a Photometer 1 (Quantum Instruments, Inc., Garden City, New York) and recorded twice daily, just prior to the first evaluation and just after the last evaluation.

Desired: <80 footcandles
Actual: 36.5 to 55.3 footcandles

2.18. POSTMORTEM

No postmortem examinations were performed as all animals were transferred to the in-house rat colony.

2.19. DISPOSITION OF ANIMALS

After the pups were weaned, the female rats were euthanized via an overdose of carbon dioxide and discarded. After the locomotor activity behavioral assessment on 62, the rats were transferred to the in-house rat colony.

2.20. PRESERVATION OF RECORDS AND SPECIMENS

All data documenting experimental details and study procedures and observations were recorded and maintained as raw data.

At the completion of the study, all reports, raw data, protocol and amendments, and retained samples will be maintained in the Testing Facility's Archives.

2.21. PROTOCOL DEVIATIONS

The following protocol deviations occurred during the study, but were not considered to have compromised the validity or integrity of the study.

1. Litter counts were not recorded on Postnatal Days 10, 13, 17, and 21 due to technician error. However, individual body weights recorded for those days (Postnatal Days 10, 13, 17, and 21) are considered documentation for the count.

2. Documentation of pups not selected for this study was omitted from the data due to technician error.

3. As there is no documentation in the study data indicating the age of the dams at time of receipt at the Testing Facility, it can not be determined that the protocol requirement that the dams be 75-90 days old was met.

4. Protocol specified that the washout period between doses would be approximately 2 days even though it also specified dosing would occur on Postnatal Days 13, 17, 21 and 60 (±2) days. The washout periods in this study ranged from 4 to 41 days.

5. Fresh dosing solutions were prepared either 1 or 3 days prior to or the day of dose administration rather than once weekly as specified in the protocol.

2.22. COMPUTER SYSTEM

The Toxicology Analysis System Customized - Reproduction Module (TASC-R), version 1.1.13, from Pathologist Associates International (PAI), Frederick, Maryland, was the computer software system utilized during the conduct of this study for randomizations, data collection, reporting, and statistical analysis.

2.23. STATISTICAL EVALUATIONS

The locomotor activity behavioral assessments were analyzed for each period using split-plot repeated measures analysis of variance with model terms for group, animal within group, interval and group by interval interaction. If the group by treatment interaction was statistically significant, indicating non-parallelism in the behavioral profile between groups, a separate one-way ANOVA for group effects was performed at each interval. If the response data passed on the parallel hypothesis, an ANOVA (using summed responses over intervals for each animal) was used to test for the overall treatment effect with respect to the level hypothesis. If any significant overall treatment group effect was found by any of the above ANOVAs, Dunnett's t-test was used to find groups that differed from control. No investigation of model fit was requested or performed. Analyses were performed for sexes separately and combined. Treatment group effects were deemed significant at the α=0.05 level. Plots, tables, listings, and analyses were generated using SAS® version 6.12 for WINDOWS. Analyses were conducted by CATO Research, 200 Westpark Corporate Center, 4364 South Alston Avenue, Durham, NC 27713-2280.

3. RESULTS

Results from pups treated with 2 mg/kg Amphetamine (Group II) indicate a statistically significant increase in locomotor activity for male and female rats combined, on Postnatal Days 13, 17, 21, and 62, when compared to the control group. Statistically significant increases in locomotor activity were observed for Group II male and female rats individually, on Postnatal Day 21 and 62 only.

Results from pups treated with 10 mg/kg Chlorpromazine (Group III) indicated a statistically significant decrease in locomotor activity for male and female rats combined, on Postnatal Days 17, 21, and 62, when compared to the control group. Statistically significant decreases in locomotor activity were observed for Group III male and female rats individually, on Postnatal Days 17, 21, and 62 only.

	Neurobehavioral Positive Control Data: Motor Activity	Appendix KK

4. DISCUSSION

This study evaluated the behavioral effects of Amphetamine and Chlorpromazine on locomotor activity of young male and female rats, in order to generate positive control data for future developmental neurotoxicity studies.

Rats dosed and tested on Postnatal Day 17, 21, and 62 responded to test article treatment, with increased activity for Group II (2 mg/kg amphetamine) and decreased activity for Group III (10 mg/kg chlorpromazine). Amphetamine or Chlorpromazine behavioral effects were observed equally in both male and female rats in the treatment groups.

Rats treated with Amphetamine exhibited locomotor activity similar to control levels at the beginning of the testing period. Unlike the control animals, the Amphetamine treated animals did not habituate, and remained in a more active state for the duration of the 60-minute testing period.

Rats treated with Chlorpromazine exhibited decreased locomotor activity compared to control levels at the beginning of the testing period. Unlike the control animals, the Chlorpromazine treated animals did not habituate, and remained in a less active state for the duration of the 60-minute testing period.

The pups dosed and tested on Postnatal Day 13 did not respond to treatment as dramatically as in latter dosing/testing days. The lack of statistically significant locomotor activity differences in the Postnatal Day 13 treatment groups may stem from the low basal level of activity in pups of such a young age. The presence of age-related differences in locomotor activity in this study suggests the importance of evaluating behavioral endpoints at several different time-points, when testing for developmental neurotoxicity.

5. CONCLUSION

Under the conditions of this study, 2 mg/kg of Amphetamine or 10 mg/kg of Chlorpromazine, administered to young male and female rats on Postnatal Days 13, 17, 21, and 62, via intraperitoneal injection produced statistically significant behavioral effects on locomotor activity. Based on these results, it was shown that both amphetamine and chlorpromazine are excellent model compounds for the generation of locomotor activity alterations in young Sprague Dawley rats.

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Summary of Statistical Results for Motor Activity Data

Post Natal Day	Sex	Parallel Hypothesis (p-value)	Level Hypothesis (p-value)	Significant Pairwise Results*
13	Male	0.1824	0.3593	NA
	Female	0.1097	0.0723	NA
	Combined	0.0074	NA	**1**:NS; **2**:NS;**10**:II>I; **11**:II>I; **12**:II>I
17	Male	0.0203	NA	**1**:I>III; **2**:I>III; **4**:I>III
	Female	0.0001	NA	**1**:I>III; **2**:I>III; **3**:I>III; **4**:NS; **5**:I>III
	Combined	0.0001	NA	**1**:I>III; **2**:I>III; **3**:I>III; **4**:I>III; **5**:I>III; **8**:NS; **10**:NS; **11**:NS; **12**:II>I
21	Male	0.0001	NA	**1**:II>I, I>III; **2**:II>I, I>III; **3**:II>I, I>III; **4**:II>I; **5**:II>I; **6**:II>I; **7**:II>I; **8**:II>I; **9**:II>I; **10**:II>I; **11**:II>I; **12**:II>I
	Female	0.0001	NA	**1**:II>I, I>III; **2**:II>I, I>III; **3**:II>I, I>III; **4**:II>I; **5**:II>I; **6**:II>I; **7**:II>I; **8**:II>I; **9**:II>I; **10**:II>I; **11**:II>I; **12**:II>I
	Combined	0.0001	NA	**1**:II>I, I>III; **2**:II>I, I>III; **3**:II>I, I>III; **4**:II>I; **5**:II>I; **6**:II>I, I>III; **7**:II>I; **8**:II>I; **9**:II>I; **10**:II>I; **11**:II>I; **12**:II>I
62	Male	0.0001	NA	**1**:I>III; **2**:I>III; **3**:I>III; **4**:I>III; **5**:I>III; **6**:II>I, I>III; **7**:II>I, I>III; **8**:II>I, I>III; **9**:II>I, I>III; **10**:II>I, I>III; **11**:II>I; **12**:II>I
	Female	0.0001	NA	**1**:I>III; **2**:I>III; **3**:I>III; **4**:I>III; **5**:II>I, I>III; **6**:II>I, I>III; **7**:I>III; **8**:II>I, I>III; **9**:II>I, I>III; **10**:II>I, I>III; **11**:II>I; **12**:II>I, I>III
	Combined	0.0001	NA	**1**:I>III; **2**:I>III; **3**:I>III; **4**:I>III; **5**:II>I, I>III; **6**:II>I, I>III; **7**:II>I, I>III; **8**:II>I, I>III; **9**:II>I, I>III; **10**:II>I, I>III; **11**:II>I, I>III; **12**:II>I, I>III

*Only intervals with significant differences between treatments are reported.

NA = Not applicable; NS = No significant differences from control

x: a>b indicates mean for group a significantly greater than mean for group b in interval x.

I = control, II = amphetamine, III = chlorpromazine

Males	Neurobehavioral Positive Control Data: Motor Activity Mean Motor Activity Values Postnatal Day 13	Appendix KK

	Interval											
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Group I – Control												
Mean	27.70	12.30	18.40	23.60	10.60	14.10	12.90	7.40	7.10	9.40	8.80	9.90
S.D.	21.88	15.32	30.96	40.81	12.43	20.80	12.81	10.24	11.32	10.15	7.18	11.90
N	10	10	10	10	10	10	10	10	10	10	10	10
Group II – 2.0 mg/kg Amphetamine												
Mean	37.70	21.10	18.40	17.20	10.20	9.20	6.10	8.10	19.60	36.70	28.80	41.60
S.D.	39.38	25.14	29.86	25.17	14.29	11.15	8.48	9.05	20.01	43.02	39.89	58.17
N	10	10	10	10	10	10	10	10	10	10	10	10
Group III – 10.0 mg/kg Chlorpromazine												
Mean	14.80	8.10	8.80	12.30	7.40	5.70	8.20	25.70	12.80	12.00	8.60	17.70
S.D.	26.95	15.17	13.21	21.67	11.84	13.05	11.38	55.13	22.52	27.05	27.20	54.93
N	10	10	10	10	10	10	10	10	10	10	10	10

Females	Neurobehavioral Positive Control Data: Motor Activity Mean Motor Activity Values Postnatal Day 13	Appendix KK

	Interval											
	1	2	3	4	5	6	7	8	9	10	11	12
Group I – Control												
Mean	25.00	14.70	17.10	20.90	16.60	14.30	9.70	6.20	12.50	10.00	7.60	5.70
S.D.	32.00	17.81	24.47	19.77	19.29	14.19	11.61	8.98	13.82	10.72	11.35	4.27
N	10	10	10	10	10	10	10	10	10	10	10	10
Group II – 2.0 mg/kg Amphetamine												
Mean	36.30	19.40	29.10	24.00	30.40	26.40	41.30	33.20	38.90	52.00	49.90	31.90
S.D.	45.41	26.53	40.16	34.50	51.56	49.40	65.11	55.36	74.84	87.22	55.36	38.23
N	10	10	10	10	10	10	10	10	10	10	10	10
Group III – 10.0 mg/kg Chlorpromazine												
Mean	4.00	1.50	11.40	24.30	0.80	2.50	3.50	4.90	3.10	5.10	6.20	1.90
S.D.	8.07	3.75	19.41	50.71	1.62	4.06	5.76	9.34	5.51	10.79	10.25	2.88
N	10	10	10	10	10	10	10	10	10	10	10	10

Males	Neurobehavioral Positive Control Data: Motor Activity Mean Motor Activity Values Postnatal Day 17	Appendix KK

	Interval											
	1	2	3	4	5	6	7	8	9	0	11	12
Group I – Control												
Mean	75.00	55.80	49.40	50.90	36.30	36.00	39.10	35.20	32.00	31.00	33.20	14.50
S.D.	42.95	49.40	33.92	40.33	35.24	38.39	43.53	32.15	39.34	39.73	39.81	18.33
N	10	10	10	10	10	10	10	10	10	10	10	10
Group II – 2.0 mg/kg Amphetamine												
Mean	52.00	30.80	42.70	41.20	29.90	26.50	32.40	52.40	64.10	62.00	51.60	28.80
S.D.	45.11	34.37	45.49	30.49	26.91	30.95	34.10	46.85	69.09	59.57	55.35	29.13
N	10	10	10	10	10	10	10	10	10	10	10	10
Group III – 10.0 mg/kg Chlorpromazine												
Mean	13.10	10.80	12.30	8.20	13.40	9.20	10.30	18.30	10.70	17.30	10.60	11.60
S.D.	29.41	24.51	22.45	18.00	25.18	16.30	15.91	18.29	19.24	27.38	13.85	14.45
N	10	10	10	10	10	10	10	10	10	10	10	10

Females	Neurobehavioral Positive Control Data: Motor Activity Mean Motor Activity Values Postnatal Day 17	Appendix KK

	Interval											
	1	2	3	4	5	6	7	8	9	10	11	12
Group I – Control												
Mean	99.10	39.90	34.00	22.70	30.20	16.30	24.60	32.10	30.70	25.60	27.70	14.50
S.D.	37.91	43.36	30.81	43.34	36.66	25.23	29.95	42.49	36.06	39.64	39.21	22.14
N	10	10	10	10	10	10	10	10	10	10	10	10
Group II – 2.0 mg/kg Amphetamine												
Mean	85.20	47.40	30.20	47.40	34.00	15.80	17.50	18.40	26.50	33.60	19.10	34.40
S.D.	35.75	31.80	26.19	26.08	24.68	13.77	19.73	23.20	21.84	31.32	22.29	26.34
N	10	10	10	10	10	10	10	10	10	10	10	10
Group III – 10.0 mg/kg Chlorpromazine												
Mean	2.20	4.80	1.00	0.90	2.70	17.70	14.20	3.70	23.60	4.80	6.10	12.60
S.D.	3.16	6.09	2.31	2.51	6.96	52.49	37.67	5.85	46.08	9.17	18.94	28.88
N	10	10	10	10	10	10	10	10	10	10	10	10

Males	Neurobehavioral Positive Control Data: Motor Activity Mean Motor Activity Values Postnatal Day 21	Appendix KK

	Interval											
	1	2	3	4	5	6	7	8	9	10	11	12
Group I – Control												
Mean	73.60	50.10	25.30	17.10	16.50	28.50	25.70	14.60	27.00	16.10	7.90	8.80
S.D.	46.33	35.63	29.06	26.53	20.99	28.32	23.84	21.48	25.73	18.54	10.16	10.77
N	10	10	10	10	10	10	10	10	10	10	10	10
Group II – 2.0 mg/kg Amphetamine												
Mean	157.30	154.00	144.00	152.60	141.50	141.20	127.50	136.70	133.80	127.10	125.00	113.20
S.D.	30.36	22.58	9.13	36.00	25.08	28.27	27.20	26.42	28.39	23.50	31.85	25.57
N	10	10	10	10	10	10	10	10	10	10	10	10
Group III – 10.0 mg/kg Chlorpromazine												
Mean	14.20	6.90	0.70	2.60	5.10	4.50	4.20	11.50	8.60	10.50	5.20	5.20
S.D.	18.40	12.31	1.49	8.22	7.69	7.68	7.28	17.28	10.48	14.39	10.81	7.13
N	10	10	10	10	10	10	10	10	10	10	10	10

Females	Neurobehavioral Positive Control Data: Motor Activity Mean Motor Activity Values Postnatal Day 21	Appendix KK

	Interval											
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Group I – Control												
Mean	93.30	29.80	27.50	17.50	17.80	27.10	15.10	14.50	8.70	7.80	8.80	10.40
S.D.	51.26	23.93	20.88	25.10	29.56	30.45	23.90	20.60	14.43	12.41	17.87	21.70
N	10	10	10	10	10	10	10	10	10	10	10	10
Group II – 2.0 mg/kg Amphetamine												
Mean	149.10	133.50	114.30	118.80	118.40	116.60	108.60	104.90	113.20	111.30	108.00	95.00
S.D.	27.65	29.30	18.88	27.45	32.05	33.02	36.06	30.71	20.07	22.88	27.81	22.40
N	10	10	10	10	10	10	10	10	10	10	10	10
Group III – 10.0 mg/kg Chlorpromazine												
Mean	8.00	3.40	3.20	4.70	4.40	5.60	5.00	10.80	4.60	5.20	5.90	8.00
S.D.	11.19	6.92	4.78	5.72	7.79	7.73	12.27	12.46	7.44	12.89	12.75	9.43
N	10	10	10	10	10	10	10	10	10	10	10	10

Males	Neurobehavioral Positive Control Data: Motor Activity Mean Motor Activity Values Postnatal Day 62	Appendix KK

	Interval											
	1	2	3	4	5	6	7	8	9	10	11	12
Group I – Control												
Mean	233.1	211.1	182.2	156.5	157.3	120.3	82.4	80.1	65.4	51.3	44.2	18.3
S.D.	49.84	31.37	18.05	28.60	35.20	50.12	53.69	57.66	63.58	56.90	52.93	23.21
N	10	10	10	10	10	10	10	10	10	10	10	10
Group II – 2.0 mg/kg Amphetamine												
Mean	242.5	228.8	190.8	190.5	185.6	163.8	165	169.4	160.5	155.7	142.5	133.2
S.D.	61.10	44.69	47.22	55.66	32.24	41.13	48.15	53.80	49.25	35.92	38.54	42.49
N	10	10	10	10	10	10	10	10	10	10	10	10
Group III – 10.0 mg/kg Chlorpromazine												
Mean	28.8	31.3	26.4	20.3	16.8	19.7	10.6	9.1	5.9	7.4	6.3	4.2
S.D.	69.09	63.0	54.62	60.03	34.86	29.18	31.09	8.57	11.08	18.65	12.41	9.07
N	10	10	10	10	10	10	10	10	10	10	10	10

Females	Neurobehavioral Positive Control Data: Motor Activity Mean Motor Activity Values Postnatal Day 62	Appendix KK

	Interval 1	2	3	4	5	6	7	8	9	10	11	12
Group I – Control												
Mean	171.10	153.40	143.90	124.00	103.60	95.50	91.00	55.80	57.60	37.90	32.30	32.20
S.D.	24.85	23.08	37.22	35.57	29.28	37.63	28.77	30.97	42.84	39.45	42.60	30.80
N	10	10	10	10	10	10	10	10	10	10	10	10
Group II – 2.0 mg/kg Amphetamine												
Mean	150.10	144.90	133.60	132.00	137.80	150.50	120.30	130.40	124.00	134.10	143.30	105.30
S.D.	45.19	29.05	31.40	33.97	31.90	46.83	39.06	43.90	39.58	35.23	31.92	40.12
N	10	10	10	10	10	10	10	10	10	10	10	10
Group III – 10.0 mg/kg Chlorpromazine												
Mean	33.30	18.20	12.40	10.20	8.70	0.90	4.10	2.30	6.90	5.50	2.50	0.00
S.D.	43.27	30.08	33.27	13.49	23.79	2.51	8.57	2.63	9.69	8.45	5.04	0.00
N	10	10	10	10	10	10	10	10	10	10	10	10

PROTOCOL

BUTANE

COMBINED REPEATED-EXPOSURE TOXICITY, REPRODUCTION AND NEUROTOXICITY SCREENING IN RATS VIA WHOLE-BODY INHALATION EXPOSURES

CONFIDENTIAL

HLS Study No.:	**03-4242**
Protocol No.:	**Final**
Date:	**17 September 2003**

PROTOCOL PREFACE

(Confidential Information - to be distributed on a need-to-know basis)

Study Title: Butane: Combined Repeated-Exposure Toxicity, Reproduction and Neurotoxicity Screening in Rats via Whole-Body Inhalation Exposures

HLS Study No.: 03-4242

This is the Final Protocol. It has been reviewed and approved by:

22 Sep 03
Date

Gary M. Hoffman, B.A., DABT
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9/19/03
Date

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TABLE OF CONTENTS

1. INTRODUCTION

HLS Study No.	03-4242
Title	Butane: Combined Repeated-Exposure Toxicity, Reproduction and Neurotoxicity Screening in Rats via Whole-Body Inhalation Exposures
Testing Facility	Huntingdon Life Sciences 100 Mettlers Road East Millstone, NJ 08875-2360
Purpose	This study is designed to assess the potential toxicity, including neurotoxicity, and reproductive performance in male and female rats when the test substance is administered by whole-body inhalation exposure. For male and female rats, it should permit detection of effects on gonadal function which may not be detected by histological examination of the reproductive organs and on mating behavior. In addition, for female rats this study should detect effects on conception, development of the conceptus and parturition and pup survival to Lactation Day 4.

2. STUDY PERSONNEL

Study Director	Gary M. Hoffman, BA, DABT
Alternate Contact	Edward R. Frizell, MD, PhD Toxicologist, Reproductive & Developmental Toxicology Tel.: 732-873-2550 x2598
Director of Reproductive Toxicology	Keith P. Hazelden, BSc, CBiol, MIBiol Tel.: 732-873-2550 x2590

Additional personnel will be documented in the project file and presented in the final report.

3. PROPOSED STUDY DATES

Study Initiation Date	Date Study Director Signs Protocol
Receipt of Test Animals	15 September 2003 (Experimental Start)
Initiation of Exposures	29 September 2003
Initiation of Mating	13 October 2003
Termination of Mating	27 October 2003
Termination of Exposures	Main Study Rats: 28 October 2003 Satellite Female Rats: 21 November 2003
Necropsy:	Main Study Rats: 28-29 October 2003 Satellite Female Rats: 8-22 November 2003
Submission of Draft Final Report:	19 March 2004
Experimental Termination:	Date of last data collection
Study Completion Date:	Date final report is signed by Study Director

4. EXPERIMENTAL DESIGN

Group	Group Designation	Exposure Levels (ppm)	Treatment Schedule Pre-mating Period		Number of Animals	
			Main Study Male Rats[b]	Main Study and Satellite Female Rats[b,c]	Main Study Male Rats	Main Study and Satellite Female Rats*
1	Air Control[a]	0	2 weeks	2 weeks	12	24
2	Low	900	2 weeks	2 weeks	12	24
3	Mid	3000	2 weeks	2 weeks	12	24
4	High	9000	2 weeks	2 weeks	12	24

*12/group = main study animals for subchronic evaluations only
*12/group = satellite animals for reproductive evaluations only
[a] Control animals will be treated with air only with the same treatment regimen as the treated groups.
[b] Main Study male rats (12/group) will be exposed once daily (6 hours/day), seven days/week for 2 weeks prior to mating initiation. Exposure of Main Study male rats will continue during the mating and post-mating periods until euthanized for a minimum exposure of 28 days. Main Study female rats (12/group) will be exposed once daily (6 hours/day), seven days/week for 4 weeks (28 days).
[c] Satellite female rats (12/group) for the reproduction study will be exposed once daily (6 hours/day), seven days/week for at least two weeks prior to mating initiation. Satellite female rats will continue to be treated once daily (6 hours/day) during mating. Once mated, Satellite female rats will be treated once daily (6 hours/day) during gestation (days 0-19). Satellite female rats without evidence of mating will continue to be treated for 25 days (6 hours/day) following completion of the mating period. In the event that Satellite female rats without evidence of mating appear pregnant, exposure will be terminated on the estimated Gestation Day 19.

The first day of exposures will be defined as Day 0 of the study.

4.1. JUSTIFICATION FOR ROUTE, DURATION AND FREQUENCY

The inhalation route is one of the potential routes of human exposure to this test substance and is the route specified in the referenced guidelines. The duration of the study and frequency of exposures are as recommended in the referenced guidelines.

4.2. JUSTIFICATION FOR TEST SYSTEM SELECTION

The rat is a rodent animal model acceptable under OECD and EPA testing guidelines for reproductive toxicity and neurotoxicity studies. In addition, a historical database is available in the Testing Facility for comparative evaluation with this strain of rat.

4.3. JUSTIFICATION FOR NUMBER OF ANIMALS

The number of animals in this study is considered the minimum necessary to allow for meaningful interpretation of the data, as required by OECD and EPA guidelines. Ten pregnancies per group are considered an adequate number for screening for developmental toxicities. The reference guideline indicates 8-10 litters per group provide the necessary degree of consistency between studies. With the group size of 12 used in this study, and with recent pregnancy rates of 80-90%, this should provide between 8-10 litters/group for evaluation. On this basis, group sizes of 12 paired Main Study male and Satellite female rats are considered appropriate for this study and will provide a sufficient number of litters in each group to meet guideline requirements. Group sizes of 12 Main Study female rats are considered appropriate for providing comparable data to the Main Study male rats.

4.4. JUSTIFICATION FOR EXPOSURE LEVEL SELECTION

The exposure levels are based on results of a 2-week range-finding Study 03-6143 which showed no toxicity at exposure levels of 90, 900 and 9000 ppm. Therefore, the high exposure level was established (for safety reasons) at 9000 ppm since it is 50% of the lower explosion limit (1.8% = 18000 ppm) for the test substance.

5. TEST SUBSTANCE

5.1. TEST SUBSTANCE BUTANE

Test Substance Category: industrial gas

Description, lot number, storage, expiration date (if available) and handling procedures, as well as other pertinent information will be documented in the study data. The Testing Facility will purchase the test substance from a Sponsor approved vendor (MG Industries, Malvern PA). The test substance will be stored (ambient conditions) in an outside solvent shed except when in use in the inhalation laboratory. The test substance will be handled as a flammable gas.

5.1.1. Purity — To be determined by the Testing Facility by assaying by GC before the study.

5.1.2. Stability — To be determined by the Testing Facility by assaying by GC before and after the study.

5.2. IDENTIFICATION OF TEST SUBSTANCE

Unless otherwise noted, the identity, strength, purity, composition, stability, and method of synthesis, fabrication and/or derivation of each batch of the test substance will be documented by the Supplier. This documentation will be maintained by the Supplier. The Testing Facility will ensure that the location of the documentation of fabrication is provided in the report.

5.3. ARCHIVAL SAMPLES

An archival sample from each lot of test substance will be taken and stored in the Archives of the Sponsor (EPL Archives, Inc., 45610 Terminal Drive, Sterling, VA 20166). If multiple studies are conducted with the same test substance, a common archival sample may be taken and appropriately labeled.

5.4. UNUSED TEST SUBSTANCE

The unused portion of the test substance as well as any empty test substance containers will be returned to the Supplier following submission of the final report of the final study with this test substance.

6. TEST ANIMALS

6.1. SPECIES

Albino Rats (Outbred) Vaf/Plus®
Sprague-Dawley - derived (CD®)
Crl: CD (SD) IGS BR

6.2. SUPPLIER

Charles River Laboratories
Raleigh, North Carolina

6.3. ANIMAL REQUIREMENTS/SPECIFICATIONS

6.3.1. Number

Male Rats	Female Rats	Total
48	96	144

6.3.2. Age and Weight

Animals will be ordered with body weight stipulations to allow all rats of the same sex to be within ± 20% of the mean weight at the time of randomization.

Male rats will be approximately six weeks at receipt and approximately 8 weeks (200-300 grams) at initiation of treatment. Animals outside this weight range will be used at the discretion of the Study Director.

Female rats will be approximately six weeks at receipt and approximately 8 weeks (150-250 grams) at initiation of treatment. Female rats will be nulliparous and non-pregnant. Animals outside this weight range will be used at the discretion of the Study Director.

6.4. ANIMAL HUSBANDRY

6.4.1. Facilities Management/Animal Husbandry

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

6.4.2. Veterinary Care

Animals are monitored by the technical staff for any conditions requiring possible veterinary care. If any such conditions are identified, a staff veterinarian will be notified for an examination and evaluation. Animals will be treated as outlined in the Animal Welfare Act Compliance section of this protocol.

6.4.3. Housing

All animals will be housed individually in stainless steel suspended cages with wire mesh floors and fronts except for the mating period when one Main Study male and one Satellite female rat will be housed together. During cohabitation (when Satellite female rats will be brought to the Main Study male rat's cages), male and female rats will then be housed in stainless steel cages of appropriate size for group housing animals. Each cage will be fitted to secure a glass feeder jar with a stainless steel lid. Clean feeder jars and fresh feed will be provided at least weekly. From Day 18 of gestation and during lactation, the dam will be housed with her litter in plastic "shoebox" cages with bedding. Clean feed jars and fresh feed will be provided at least weekly for periods when feed consumption is not being recorded and at each interval when feed consumption will be recorded.

6.4.4. Feed and Feed Analysis

Certified Rodent Diet, No. 5002; (Meal) supplied by PMI Nutrition International (St. Louis, MO) and provided *ad libitum.*

Analytical certification of batches of feed provided by the manufacturer will be maintained on file at the Testing Facility. There are no known contaminants in the feed which are expected to interfere with the objectives of this study.

6.4.5. Water and Water Analysis

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

Water analyses are conducted by Elizabethtown Water Company to assure that water meets standards specified under the EPA Federal Safe Drinking Water Act Regulations (40 CFR Part 141). Water analysis, provided by the supplier, will be maintained on file at the Testing Facility. In addition, chemical and microbiological analyses are conducted biannually on water samples collected from representative rooms in this facility. Results are maintained on file at the Testing Facility. There are no known contaminants which are expected to interfere with the objectives of this study.

6.4.6. Bedding and Bedding Analysis

Ground corncob bedding (Bed-O'-Cobs® 1/4 inch Irradiated, The Andersons, Maumee, Ohio) will be provided for each mated female rat on Gestation Day 18. Fresh bedding will be provided weekly or as needed throughout lactation.

Analyses for each batch of bedding used on study provided by the supplier, will be maintained on file at the Testing Facility. There are no known contaminants in the bedding that are expected to interfere with the results of this study.

6.4.7. Environmental Conditions

Light/Dark Cycle

Twelve hour light/dark cycle provided via automatic timer.

Temperature

Temperature will be monitored in accordance with Testing Facility SOPs to ensure that the desired range of 18 to 26°C is maintained to the maximum extent possible.

Humidity

Humidity will be monitored in accordance with Testing Facility SOPs to ensure that the desired range of 30 to 70% is maintained to the maximum extent possible.

6.5. ACCLIMATION PERIOD

Approximately 2 weeks; all animals will be checked for viability twice daily. Prior to assignment to study, all animals will be examined to ascertain suitability for study.

6.6. ANIMAL ASSIGNMENT

More animals than required for the study will be purchased and acclimated. Animals considered suitable for study on the basis of pretest physical examinations, body weight data and any other pretest evaluations, will be randomly assigned to control or treated groups in an attempt to equalize mean group body weights. Female animals will be randomly assigned to Main Study or Satellite groups. Individual weights of animals placed on test shall be within ±20% of the mean weight for each sex. Disposition of all animals not utilized in the study will be maintained in the study file.

6.7. ANIMAL IDENTIFICATION

Each animal will be assigned a temporary identification number upon receipt. After selection for study, each animal will be ear-tagged with a number assigned by the Testing Facility. This number plus the study number will comprise the unique animal number for each animal. If the tag is lost, it will be replaced or the animal will be tattooed for identification. Each cage will be provided with a cage card which will be color coded for exposure level identification and will contain the study number and animal number.

6.8. MATING PROCEDURE

Within each treatment group, the Main Study male and Satellite female rats will be co-housed (1:1) until evidence of mating is seen or for 2 consecutive weeks. Satellite female rats will be observed at approximately the same time each morning for the presence of a vaginal plug or sperm in the vaginal smear. The day on which evidence of mating is observed will be defined as day 0 of gestation. Once mated, the Satellite female rat will be removed from the mating unit and housed individually for the remainder of the study. After the mating period is over, Satellite female rats without evidence of copulation will be removed from the mating unit and housed individually for the remainder of the study (26 days) and monitored for visible signs of pregnancy with corresponding body weight gain.

6.9. ANIMAL HUSBANDRY DURING EXPOSURE

Housing - individually in suspended stainless steel cages
Feed – none
Water - none

7. TEST SUBSTANCE ADMINISTRATION

7.1. ROUTE OF ADMINISTRATION

Inhalation via whole-body exposure.

7.2. JUSTIFICATION FOR ROUTE OF ADMINISTRATION

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

7.3. DURATION AND FREQUENCY OF ADMINISTRATION

Main Study male rats will be exposed once daily, seven days/week for 2 weeks prior to mating initiation. Exposure of Main Study male rats (12/group) will continue during the mating and post-mating periods until euthanized for a minimum exposure of 28 days. Main Study female rats (12/group) will be exposed once daily, seven days/week for 4 weeks (28 days). Satellite female rats (12/group) for the reproduction study will be exposed once daily, seven days/week for at least two weeks prior to mating initiation. Satellite female rats will continue to be treated once daily during mating. Once mated, Satellite female rats will be treated once daily during gestation (days 0-19). Satellite female rats without evidence of mating will continue to be treated for 19 days following completion of the mating period and then held for an additional 7 days. In the event that

Satellite female rats without evidence of mating appear pregnant, exposure will be terminated on the estimated Gestation Day 19.

7.4. ADMINISTRATION OF TEST SUBSTANCE

The test substance will be administered as a gas in the breathing air of the animals. The test atmosphere will be generated by an appropriate procedure determined during pre-study trials. The trials will be performed (at least two 6-hour periods) to evaluate the optimal set of conditions and equipment to generate a stable and uniform atmosphere at the target exposure level(s). The method will be described in the raw data of the study and in the report.

The whole-body exposure chambers will each have a volume of approximately 1000 liters. The chambers will be operated at a minimum flow rate of 200 liters per minute. The final airflow will be set to provide at least one air change in 5.0 minutes (12 air changes/hour) and a T_{99} equilibrium time of at most 23 minutes. This chamber size and air flowrate is considered adequate to maintain the animal loading factor below 5% and the oxygen level at 19% or higher. At the end of the 6-hour exposure, all animals will remain in the chambers for a minimum of 30 minutes. During this time, the chambers will be operated at approximately the same flow rate using clean air only.

7.5. EXPOSURE CONCENTRATION ADMINISTRATION

A nominal exposure concentration will be calculated daily, if possible. The flow of test substance into the chamber and the flow of air through the chamber will be monitored using appropriate calibrated equipment. The average test substance flow during each exposure will be divided by the average chamber airflow to give the nominal concentration. Also, the additive nominal concentration for all 3 test substance chambers for each exposure day will be measured by weighing the test substance cylinder before and after the exposure and dividing the difference by the average chamber airflow.

During each exposure, measurements of airborne concentrations of test substance in the animal's breathing zone will be performed at least four times using an appropriate sampling procedure and infrared spectrophotometric analytical procedure. If more than the normal amount of trials is required because of test substance generation or monitoring problems (50 technician hours), the Sponsor will be consulted prior to additional trials (additional cost).

7.6. PARTICLE SIZE DISTRIBUTION ANALYSIS

During each week of exposure, particle size determinations will be performed using a TSI Aerodynamic Particle Sizer to characterize the aerodynamic particle size distribution of any aerosol present.

7.7. CHAMBER AND EXPOSURE ROOM ENVIRONMENT

Chamber temperature, humidity, airflow rate and static pressure will be monitored continuously and recorded every 30 minutes during exposure. Chamber temperature and relative humidity will be maintained, to the maximum extent possible, between 20 to 24°C and 40 to 60%, respectively. Chamber oxygen levels (maintained at least 19%) will be measured pretest and at the beginning, middle and end of the study.

Air samples will be taken in the vapor generation area pretest and at the beginning, middle and end of the study. Light (maintained approximately 30-40 foot-candles at 1.0 meter above the floor) and noise levels (maintained below 85 decibels) in the exposure room will be measured pretest and at the beginning, middle and end of the study.

7.8. SUMMARY OF CHAMBER ACTIVITY

The minimum frequency of chamber activity is summarized below:

Activity	Frequency/chamber
Measured Test Substance Concentration	4X/day
Particle Size	1X/week
Temperature	13X/day
Relative Humidity	13X/day
Airflow Rate	13X/day
Nominal Test Substance Concentration (excluding the air control chamber)	1X/day
Rotation Pattern of Exposure Cages	1X/day
Loading/Unloading Verification	1X/day

8. EXPERIMENTAL EVALUATION

8.1. OBSERVATIONS

8.1.1. Viability Checks (Cageside)

Observations for mortality and general condition will be made at least twice daily (once in the morning and once in the afternoon). Animals in poor health or in a possible moribund condition will be identified for further monitoring and possible euthanasia.

8.1.2. Detailed Physical Observations

All animals will be observed as a group at least once during each exposure. This will routinely be performed near the middle of each exposure and may be performed more frequently if significant signs of toxicity are noted.

Each animal will be removed from its cage and a detailed physical observation performed prior to randomization. Main Study male rats will have a detailed physical observation performed once weekly beginning during the premating period and continuing through euthanasia. Main Study female rats will have a detailed physical observation performed once weekly beginning after randomization and continuing through euthanasia. Satellite female rats will have a detailed physical observation performed weekly during the premating period and on Gestation Days 0, 7, 14, 20 and Lactation Days 0, 1 and 4. Satellite female rats without evidence of mating will continue to be observed weekly during the mating and post-mating period until euthanized.

Examinations during non-exposure periods will include observations of general condition, skin and fur, eyes, nose, oral cavity, abdomen and external genitalia, occurrence of secretions and excretions, and autonomic activity (e.g., lacrimation, piloerection, pupil size, unusual respiratory pattern). Changes in gait, posture and response to handling as well as the presence of clonic or tonic movements, stereotypy (e.g., excessive grooming, repetitive circling) or bizarre behavior (e.g., self-mutilation, walking backward) will be recorded.

8.2. BODY WEIGHTS

Body weights of the Main Study male rats and the Main Study female rats will be recorded at the time of randomization into test groups, on the day treatment is initiated and weekly thereafter throughout the study until euthanized. Satellite female rats for the reproduction study will be weighed at the time of randomization into test groups, on the day treatment is initiated and twice weekly until evidence of copulation is observed. Mated Satellite female rats will be weighed on Gestation Days 0, 7, 14 and 20 and Satellite female rats that deliver litters will be weighed on Lactation Days 1 and 4. Satellite female rats without evidence of mating will continue to be weighed weekly during the mating and post-mating period until euthanized. A terminal body weight will also be recorded for each animal.

8.3. FEED CONSUMPTION

Feed consumption for the Main Study male rats will be recorded weekly during the pre-mating treatment period and post-mating period until euthanized. Feed consumption for the Main Study female rats will be recorded weekly during the treatment period until euthanized. Feed consumption for Satellite female rats will be recorded weekly during the premating period. Feed consumption will not be recorded during the mating period when Main Study male rats are being co-housed with Satellite female rats. For pregnant or confirmed mated Satellite female rats, feed consumption will be recorded on Gestation Days 0-7, 7-14, and 14-20 and on Lactation Days 1-4.

8.4. PARTURITION AND LACTATION

On Day 18 of Gestation, several days prior to expected parturition, Satellite female rats will be transferred to solid, plastic cages with bedding article provided. Thereafter, examination for signs of parturition will be made twice daily (morning and afternoon). The duration of gestation will be documented. Evidence of difficult or prolonged parturition or bizarre behavior (including but not limited to self-mutilation, walking backwards), if observed, will be recorded. The day on which parturition initiates will be defined as Lactation Day 0. Litters will be observed as soon as possible after parturition completion for the number of live and dead pups, pup abnormalities and each pup will be sexed. Thereafter, litters will be observed twice daily (morning and afternoon). All pups in the litter will be uniquely identified by toe tattoo after parturition completion. The presence of dead pups will be recorded, and these will be removed from the litter as found. Unusual observations and the presence or absence of milk in the stomach will be noted.

8.5. F_1 PUP EVALUATIONS

8.5.1. Pup Physical Examinations

Each pup will be given a gross physical examination on Lactation Days 0 and 4. Pups will also be observed for any abnormal behavior.

8.5.2. Body Weights and Sexing Data

Individual pup body weights data will be recorded on Lactation Days 1 and 4. Pups will be sexed on Lactation Day 0 and sex verified on Lactation Day 4.

8.6. NEUROBEHAVIORAL EXAMINATIONS

Observations, as outlined below, on all Main Study male rats and all Main Study female rats from all exposure groups will be recorded. Observations will be assessed during the last week of exposure to the test substance. The functional observational battery and motor activity assessments will be performed for all animals on a non-exposure day. Testing will be staggered over several sessions. Each session will consist of approximately equal numbers of animals per sex per exposure level. Noise level will be maintained within a level of 55 to 65 decibels by a white noise generator. Temperature, humidity, and illumination will be measured and recorded to ensure that variations in environmental conditions are minimal during all evaluations. The functional observational battery will be performed for all animals before evaluation of motor activity.

FUNCTIONAL OBSERVATIONAL BATTERY

The time of testing will be balanced across treatment groups. All observations during the treatment period will be performed blind, i.e., the observer will be unaware of the animals' treatment.

Sensory Observations
- startle response to auditory stimuli
- tail pinch response

Neuromuscular Observations
- grip strength – hindlimb and forelimb

Physiological Observations
- rectal temperature

MOTOR ACTIVITY

Activity will be monitored using an automated Photobeam Activity System (San Diego Instruments, Inc.) Sessions will be 60 minutes in length; each session will be divided into 12 five-minute intervals. The time of testing will be balanced across treatment groups. Positive historical control data demonstrating the sensitivity of the procedure will be documented in the final report.

8.7. CLINICAL PATHOLOGY

Clinical pathology procedures and parameters are based on those recommended in guidelines published by the Joint Scientific Committee for International Harmonization of Clinical Pathology Testing in "Harmonization of Animal Clinical Pathology Testing in Toxicity and Safety Studies", *Fund. Appl. Tox.*: 29, 198-201 (1996).

Blood samples for hematology, coagulation and clinical chemistry studies will be obtained from lightly anesthetized (CO_2/O_2) Main Study animals via puncture of the orbital sinus (retrobulbar). Animals will be fasted overnight prior to clinical chemistry blood collection. Blood will be collected and studies performed as follows:

8.7.1. HEMATOLOGY

Blood for hematology studies (~ 0.25 mL) will be collected into tubes containing EDTA anticoagulant.

Number of Animals/Intervals 12/sex/group at termination

Parameters Evaluated

erythrocyte count
hematocrit
hemoglobin
mean corpuscular volume
mean corpuscular hemoglobin
mean corpuscular hemoglobin concentration
leukocyte count (total and differential)
platelet count
reticulocyte count
erythrocyte morphology (from peripheral blood smear)
platelet morphology (from peripheral blood smear)

To be evaluated only if deemed necessary by the Study Director, based on results of other hematology and/or pathology results (additional cost):

bone marrow differential count

8.7.2. COAGULATION

Blood for coagulation studies (~ 1.0 mL) will be collected into tubes containing sodium citrate anticoagulant.

Number of Animals/Intervals 12/sex/group at termination

Parameters Evaluated

prothrombin time
activated partial thromboplastin time

8.7.3. CLINICAL CHEMISTRY

Blood for clinical chemistry studies (~ 1.0 mL) will be collected into tubes with no anticoagulant, allowed to clot, and centrifuged to obtain serum. If an adequate volume of serum is not available for all assays, they will be performed in the order listed.

Number of Animals/Intervals 12/sex/group at termination

Parameters Evaluated

alanine aminotransferase
aspartate aminotransferase
alkaline phosphatase
gamma glutamyl transpeptidase
urea nitrogen
creatinine
glucose
total cholesterol
triglycerides
total protein
albumin
globulin (calculated as total protein - albumin = globulin)
albumin/globulin ratio (calculated)
bilirubin (total)
sodium
potassium
chloride
calcium
phosphorus

8.7.4. RETENTION/STORAGE OF SPECIMENS

Any remaining (frozen) serum, which may have limited storage stability, will be stored for up to 6 months after completion of assays and will then be discarded. Peripheral blood smears will be retained and archived with the study.

9. POSTMORTEM

9.1. METHOD OF EUTHANASIA

All animals (except Lactation day 4 pups) will be euthanized using an overexposure of inhaled carbon dioxide. Lactation day 4 pups will be euthanized using an intraperitoneal injection of sodium pentobarbital.

9.2. POSTMORTEM EXAMINATION - ANIMALS DYING DURING THE STUDY

Animals that die during the study will be given a macroscopic postmortem examination and gross lesions will be saved and preserved in 10% neutral buffered formalin. Reproductive tissues as indicated below will also be saved but no organ weights recorded. Satellite female rats dying during the study will have the number of implantation sites and corpora lutea recorded.

9.3. EUTHANASIA SCHEDULE

9.3.1. Main Study Male and Female Rats

Main Study male rats and female rats will be euthanized after at least 28 days of exposure.

9.3.2. Satellite Female Rats in the Reproduction Study

Mated Satellite female rats will be euthanized on post-partum day 4. Satellite female rats in which evidence of mating was detected but failed to deliver will be sacrificed 26 days after evidence of mating. Satellite female rats where no evidence of mating was detected and who failed to deliver will be euthanized 26 days after the completion of the mating period. Satellite female rats with total litter loss will be euthanized on post-partum day 4.

9.4. MACROSCOPIC EXAMINATION – MAIN STUDY MALE RATS

Macroscopic postmortem examinations will be performed on all Main Study male rats, including those dying spontaneously or euthanized in a moribund condition. Postmortem examinations will include examination of external surface, all orifices, cranial cavity, nasal cavity (external examination), neck and its associated tissues and organs, thoracic, abdominal and pelvic cavities and their associated tissues and organs, and external surfaces of the brain. Gross lesions or tissues with significant findings will be preserved in 10% neutral buffered formalin. If lesions are saved, corresponding tissues from several control animals may be saved for comparative purposes.

9.5. MACROSCOPIC EXAMINATIONS – FEMALE RATS

Macroscopic postmortem examinations will be performed on all Main

Study and Satellite female rats, including those dying spontaneously or euthanized in a moribund condition and on Satellite female rats sacrificed after aborting or premature delivery of a litter. Postmortem examinations will include examination of external surface, all orifices, cranial cavity, nasal cavity (external examination), neck and its associated tissues and organs, thoracic, abdominal and pelvic cavities and their associated tissues and organs, and external surfaces of the brain. The number of implantation sites and corpora lutea will be recorded for each Satellite female rat. Gross lesions or tissues with significant findings will be saved in 10% neutral buffered formalin. If lesions are saved, corresponding tissues from several control animals may be saved for comparative purposes.

9.6. ORGAN WEIGHTS

Organs indicated below will be taken at the scheduled necropsy, weighed wet, recorded and organ/body and organ/brain weight ratios calculated. Organs will not be weighed for animals found dead or euthanized in a moribund condition and for those Satellite female rats not delivering pups. Prior to weighing, all organs will be carefully dissected and properly trimmed to remove fat and other contiguous tissue in a uniform manner. Organs will be weighed as soon as possible after dissection to avoid drying. Paired reproductive organs will be weighed separately. All other paired organs will be weighed together.

Main Study Male Rats	Main Study and Satellite Female Rats	All Rats	
Testes	Ovaries with Oviducts	Adrenal Glands	
Epididymides	Uterus with Vagina	Brain with Brainstem	
		Heart	Lungs
		Kidneys	Spleen
		Liver	Thymus

9.7. TISSUES PRESERVED

Tissues listed in Appendix A will be obtained at necropsy for all Main Study male and all Main Study and Satellite female rats from each exposure group and preserved in 10% neutral buffered formalin with the exception of testes and epididymides which will be preserved in a modified Davidson's fixative for at least 24 hours and then stored in 10% neutral buffered formalin. Lungs and urinary bladder will be infused with 10% neutral buffered formalin for optimal preservation.

9.8. MICROSCOPIC PATHOLOGY EVALUATIONS

Microscopic examinations for control and high exposure group Main Study male and Main Study female animals will be performed on tissues and organs as designated in Appendix A. During the microscopic examination of the testes, special emphasis will be placed on the stages of spermatogenesis and the histopathology of interstitial testicular cell structure. Note: Any abnormalities not noted during macroscopic postmortem examinations which are seen during histological processing will be recorded. If treatment-related changes are observed in the high exposure group, microscopic examinations will be performed on the animals of the low and mid exposure groups upon Sponsor approval (additional cost).

Stains: Standard stains (hematoxylin and eosin) will be used. Special stains may be employed on selected tissues to aid in making a diagnosis at the discretion of the Study Pathologist. Special stains may also be employed at the request of the Sponsor (additional cost).

9.9. MACROSCOPIC POSTMORTEM EXAMINATION - F_1 PUPS

Macroscopic postmortem examinations (internal and external) will be performed on all F1 pups found dead during lactation. Unusual observations, including gross abnormalities and the presence or absence of milk in the stomach, will be noted and then the carcasses will be discarded. F1 pups found dead at birth will be identified (lung floatation test) as stillborn or alive but found dead. Macroscopic postmortem examinations (external only) will be performed on all F1 pups on Lactation Day 4 for pups surviving to that interval. Unusual observations, including gross abnormalities, will be noted and then the carcasses will be discarded.

10. PRESERVATION OF RECORDS AND SPECIMENS

All data documenting experimental details and study procedures and observations will be recorded and maintained as raw data. At the completion of the study, all reports, raw data, preserved archival specimens and retained samples will be maintained in the Testing Facility's Archives for a period of 10 years after submission of the signed final report. Biological samples collected for clinical pathology will be discarded as described elsewhere in this protocol.

The Sponsor will be contacted in order to determine the final disposition of these materials. The Sponsor is responsible for all cost associated with the storage of these materials beyond 10 years from the issuance of the final report and for any costs associated with the shipment of these materials to the Sponsor or to any other facility designated by the Sponsor.

11. STATISTICAL EVALUATIONS

11.1. CONTINUOUS DATA - to include but not be limited to:

- Body weights
- Body weight changes
- Feed consumption values
- Rectal temperature
- Hematology and Coagulation values
- Clinical Chemistry values
- Gestation length
- Corpora lutea
- F_1 pup weights (each weighing interval during lactation)
- Number of pups (F_1 litters) per pregnant female rats
- Number of male and female pups
- Pup weight distinguished by sex and as a composite for both sexes (litter as experimental unit)
- Organ weights and organ weight to body weight and brain weight ratios
- Grip strength measurements

Evaluation of equality of group means will be made by the appropriate statistical method. For all parameters except for organ weights, the standard one-way analysis of variance (ANOVA) using the F ratio to assess significance will be used (Dunlap and Duffy, 1975). If significant differences among the means are indicated, additional testing will be performed using Dunnet's t-test to determine which means are significantly different from the control (Dunlap et al., 1981). Organ weight data will be analyzed only by parametric methods. Bartlett's test (Bartlett, 1937; Sokal and Rohlf, 1995) will be performed to determine if groups have equal variances. The standard one-way analysis of variance (ANOVA) using the F ratio to assess significance will be used (Dunlap and Duffy, 1975). If significant differences among the means are indicated, additional tests will be used to determine which means are significantly different from the control: Dunnett's t-test (Dunlap et al., 1981; Dunnett, 1955, 1964) for homogeneous data, or Cochran and Cox's modified t-test (Cochran and Cox, 1959) for non-homogeneous data.

All t-tests will be conducted at the 5% and 1% significance levels.

References for these procedures are:

Bartlett, M.S. 1937. Properties of sufficiency and statistical tests. *Proceedings of the Royal Society, Series A,* 160: 268-282; Cochran, W.G. and Cox, G.M. 1959. *Experimental Designs*, New York: John Wiley, pp. 100-102; Dunlap, W.P. and Duffy, J.A. 1975. Fortran IV Functions for

Calculating Exact Probabilities Associated with Z, Chi-Square, T and F Values. *Behav. Res. Methods and Instrumentations* 7:59-60; Dunlap, W.P., Marx, M.S. and Agamy, G.G. 1981. Fortran IV functions for calculating probabilities associated with Dunnett's test. *Behav. Res. Methods and Instrumentation* 13: 363-366; Dunnett, C.W. 1955. A multiple comparison procedure for comparing several treatments with a control. *Journal of the American Statistical Association* 50: 1096-1121; Dunnett, C.W. 1964. New tables for multiple comparisons with a control. *Biometrics* 20-3: 482-491; Sokal, R.R. and Rohlf, F.J. 1995. Biometry. 3rd Edition. San Francisco: W.H. Freeman pp. 369-371; Steel, R.G.D. 1959. A multiple comparison rank sum test: treatment versus control. *Biometrics* 15: 560-572.

11.2. INCIDENCE DATA - to include but not be limited to:

- Mortality rate
- Mating indices, pregnancy rates, male rat fertility indices
- Litter survival indices
- Gestation indices
- Incidence of dams with no viable pups
- Mean pup survival indices (Days 0 and 4)

A Fisher Exact Test with Bonferonni correction will be performed to identify differences between the control and treatment groups. All statistical tests will be conducted at the 5% and 1%, two-sided risk levels.

11.3. MOTOR ACTIVITY DATA

The data will be analyzed using split-plot repeated measures ANOVA with model terms for group, animal within group, interval and group by interval interaction. If the group x interval interaction is statistically significant (p=0.05), indicating non-parallelism in the behavioral profile between groups, a separate one-way ANOVA for group effects will be performed at each interval. If the response data passes on the parallel hypothesis, an ANOVA (using summed responses over intervals) will be used to test for the overall treatment effect which constitutes the level hypothesis. If any significant overall treatment group effect is found by any of the above ANOVAs, Dunnett's t-test will be used to find groups that differed from control. Analyses will be performed for sexes separately and combined. Treatment group effects will be deemed significant at the p=0.05 level. Plots, tables, listings, and analyses will be generated using SAS® version 6.12 for WINDOWS. Analyses will be conducted by CATO Research, 200 Westpark Corporate Center, 4364 South Alston Avenue, Durham, NC 27713-2280. The Testing Facility will be responsible for the GLP compliance of this subcontractor.

12. REPORTING

12.1. STATUS REPORTS

Periodic verbal and written updates on study progress will be provided by the Study Director. In general, written status reports will be submitted weekly and at termination of the study.

12.2. FINAL REPORT

One unbound hard copy and one electronic copy of an audited draft report will be submitted following termination of the study. After receipt and review of the Sponsor's comments, appropriate changes will be made and two hard copies and one electronic copy of a signed, final report will be issued. (Additional copies will be provided at additional cost). The report will minimally include:

12.2.1. Body of Report

- Compliance Statement (including Sponsor signature line)
- Quality Assurance Statement
- Abstract
- Introduction
- Experimental Design
- Materials and Methods
- Results and Discussion
- Conclusion concerning a No-Observed-Adverse Effect Level (NOAEL)
- Statistical Procedures
- Protocol deviations and study impact statements

12.2.2. Summary Tables

- Exposures
- Mortality
- Mating indices, pregnancy rates and male rat fertility indices
- Physical in-life observations
- Mean body weight data
- Mean animal weight gain data
- Mean feed consumption data
- Mean Hematology and Coagulation
- Mean Clinical Chemistry
- Mean Functional Observation Battery
- Mean gestation length
- Mean number of corpora lutea

- Mean female rat litter data to include the number of pups (live, dead and total) at birth and number of live pups on Lactation Days 0 and 4
- Litter survival indices
- Mean litter pup survival indices (Lactation Days 0 and 4)
- Mean pup weights (Lactation Days 0 and 4)
- Mean pup sex ratio (Days 0 and 4)
- Macroscopic postmortem examination (Male Rats, Female Rats, F_1 pups)
- Mean organ weights and organ weight to body weight and brain weight ratios
- Microscopic Pathology

12.2.3. Miscellaneous

- Mating performance data
- Recent historical control data for the Testing Facility
- Quality Assurance Statement

12.2.4. Appendix Tables (Individual data)

- Mortality
- Mating indices, pregnancy rates and male rat fertility indices
- Physical in-life observations
- Mean and individual body weight data
- Mean and individual animal weight gain data
- Individual feed consumption data
- Individual Hematology and Coagulation
- Individual Clinical Chemistry
- Individual Functional Observation Battery
- Individual gestation length
- Individual number of corpora lutea
- Individual female rat litter data to include the number of pups (live, dead and total) at birth and number of live pups on Lactation Days 0 and 4
- Individual litter survival indices
- Individual litter pup survival indices (Days 0 and 4)
- Individual pup weights (Days 0 and 4)
- Individual macroscopic postmortem examination (Male Rats, Female Rats, F_1 pups)
- Individual organ weights and organ weight to body weight and brain weight ratios
- Individual Microscopic Pathology

12.2.5. Appendices

- Motor activity evaluation by CATO
- Personnel involved in the study
- Protocol and Amendments

A Robust Summary in IUCLID electronic format will also be separately provided by the Testing Facility's UK office.

13. REGULATORY REFERENCES

13.1. TEST GUIDELINE

This study complies with the Organization for Economic Cooperation and Development (March 22, 1996). OECD Guidelines for Testing of Chemicals; OECD Guideline 422: Combined Repeated Exposure Toxicity Study with the Reproduction/Development Toxicity Screening Test, pp. 1-14 and US EPA OPPTS Health Effects Test Guidelines 870.3650, Combined Repeated Exposure Toxicity Study with the Reproduction/Development Toxicity Screening Test, July 2000.

13.2. GOOD LABORATORY PRACTICES

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

13.3. ANIMAL WELFARE ACT COMPLIANCE

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

1. The Sponsor's signature on this protocol documents for the study described, that there are no generally accepted non-animal alternatives and the study does not unnecessarily duplicate previous experiments.

2. All procedures used in this study have been designed to avoid discomfort, distress and pain to the animals. All methods are described in this study protocol or in written laboratory standard operating procedures.

3. Any procedures outlined in this study protocol which are expected to

cause more than momentary or slight pain or distress to the animals will be performed with appropriate sedatives, analgesics or anesthetics unless the withholding of these agents is justified for scientific reasons, in writing, by the Sponsor and the Study Director and approved by the IACUC; in which case the procedure will continue for the minimum time necessary. Documentation of the justification for withholding treatment for pain or distress and IACUC approval of the procedures will be made prior to study initiation on the IACUC Protocol Review form.

4. Animals experiencing more than momentary or slight pain or distress due to test substance or emergency situations such as injury or illness will be treated by the Testing Facility's veterinarian staff with approved analgesics or agents to relieve pain. If possible, the Study Director will be consulted prior to treatment; however, the veterinary staff is authorized to administer emergency treatment as necessary. Any subsequent treatment or euthanasia will be administered after consultation with the Study Director. The Sponsor will be advised by the Study Director of all emergency situations in as timely a manner as possible.

5. Methods of euthanasia used during this study are in conformance with the above referenced regulations.

13.4. INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC)

The IACUC Protocol Review Subcommittee has reviewed this protocol and found it to be in compliance with appropriate animal welfare regulations.

14. QUALITY ASSURANCE MONITORING

The Quality Assurance Unit of Huntingdon Life Sciences (East Millstone, NJ) will monitor the facilities, equipment, personnel, methods, practices, records, raw data, draft and final reports and controls used in this study to assure that they are in conformance with this protocol, company Standard Operating Procedures and the referenced Good Laboratory Practice regulations.

15. ALTERATION OF DESIGN

Alterations of this protocol may be made as the study progresses. No changes in the protocol will be made without the consent of the Sponsor. In the event that the Sponsor authorizes a protocol change verbally, such changes will be honored by the Testing Facility and will be followed by a written verification. All protocol modifications will be signed by the Study Director and a Sponsor representative. Any modifications potentially affecting animal welfare will also be signed by two members of the Institutional Animal Care and Use Committee prior to the modification's implementation.

APPENDIX A
TISSUES PRESERVED/EXAMINED

Tissue	Tissues Preserved	Microscopic[a] Examination
Adrenal Glands	X	X
Bone (sternum/femur)[b]	X	X
Bone Marrow (rib)[c]	X	
Brain (medulla/pons, cerebrum and cerebellum)	X	X
Epididymides	X	X
Heart	X	X
Kidneys	X	X
Large Intestine (cecum, colon, and rectum)	X	X
Larynx	X	
Liver	X	X
Lungs (with mainstem bronchi)	X	X
Lymph Node (mesenteric)	X	X
Lymph Node (mediastinal)	X	X
Mammary Gland (with adjacent skin)	X	X
Nasopharynx	X	
Ovary with oviducts	X	X
Prostate	X	X
Seminal Vesicles	X	X
Small Intestine (duodenum, ileum and jejunum)	X	X
Spinal Cord (cervical, thoracic, lumbar)	X	X
Spleen	X	X
Stomach	X	X
Testes	X	X
Thymus	X	X
Thyroid with Parathyroids	X	X
Tibial Nerve	X	X
Trachea	X	X
Urinary Bladder	X	X
Uterus with Vagina	X	X
All Macroscopic Lesions and Tissue Masses	X	X

[a] Control and high exposure Main Study male and female animals. If a treatment-related change is observed in the high exposure group, microscopic examinations will be performed on the low and mid exposure groups upon Sponsor approval (additional cost).
[b] Qualitative examination (no differential count).
[c] Bone marrow smears will be prepared. They will only be evaluated (Sponsor approval, additional cost) if needed.

Protocol Amendment No. 1

Study Title: Butane: Combined Repeated-Exposure Toxicity, Reproduction and Neurotoxicity Screening in Rats via Whole-Body Inhalation Exposures

Changes

1. Proposed Study Dates, page 2:

Revise:

Receipt of Test Animals	**16** ~~15~~ September 2003 (Experimental Start)
Termination of Exposures	Main Study Rats: 28 October 2003 Satellite Female Rats: **15** ~~24~~ November 2003

2. Experimental Design, page 3:

Revise: [c] Satellite female rats (12/group) for the reproduction study will be exposed once daily (6 hours/day), seven days/week for at least two weeks prior to mating initiation. Satellite female rats will continue to be treated once daily (6 hours/day) during mating. Once mated, Satellite female rats will be treated once daily (6 hours/day) during gestation (days 0-19). Satellite female rats without evidence of mating will continue to be treated for **19** ~~25~~ days (6 hours/day) following completion of the mating period **and then held for an additional 7 days**. In the event that Satellite female rats without evidence of mating appear pregnant, exposure will be terminated on the estimated Gestation Day 19.

Reasons for Changes

1. Correction of scheduled dates.
2. Clarification that unsuccessfully mated Satellite female rats will be exposed until their last possible Gestation Day 19 and then held without exposure until the scheduled sacrifice.

Additional Cost Required: NO

Amendment approved by:

Gary M. Hoffman, B.A., DABT
Study Director

2 oct 03
Date

Thomas M. Gray, M.S., DABT
Sponsor Representative

02 October 2003
Date

Protocol Amendment No. 2

Study Title: Butane: Combined Repeated-Exposure Toxicity, Reproduction and Neurotoxicity Screening in Rats via Whole-Body Inhalation Exposures

Changes

1. Experimental Design, page 3:

Revise: Main Study female rats (12/group) will be exposed once daily (6 hours/day), seven days/week for 4 weeks **for a minimum exposure of** 28 days.

2. Mating Procedure, page 9:

Add: ….**During mating, cohabitation of male and female littermates will be prohibited.** Satellite female rats will be observed at approximately the same time each morning for the presence of a vaginal plug or sperm in the vaginal smear. **If not mated, the stage of estrous will instead be recorded.** The day on which evidence of mating is observed will be defined as day 0 of gestation….

3. Duration and Frequency of Administration, page 9:

Revise: Main Study female rats (12/group) will be exposed once daily, seven days/week for 4 weeks **for a minimum exposure of** 28 days.

4. Body Weights, page 12:

Revise: …. Satellite female rats without evidence of mating will continue to be weighed **twice** weekly during the mating and post-mating period until euthanized….

5. Feed Consumption, page 13:

Revise: Feed consumption for the Main Study male rats will be recorded **pretest and** weekly during the pre-mating treatment period ~~and post-mating period until euthanized~~. Feed consumption for the Main Study female rats will be recorded **pretest and** weekly during the treatment period until euthanized. Feed consumption for Satellite female rats will be recorded **pretest and** weekly during the premating period **and, if not mated, during the post-mating period**….

6. Parturition and Lactation, page 13:

Revise: …. Unusual observations and the ~~presence or~~ absence of milk in the stomach will be noted.

7. Coagulation, page 15:

Revise: Blood for coagulation studies (~ **0.75** ~~1.0~~ mL) will be collected into tubes containing sodium citrate anticoagulant.

8. Method of Euthanasia, page 16:

Protocol Amendment No. 2

Revise: All animals (except Lactation day 4 pups) will be euthanized **by exsanguination following** ~~using~~ an overexposure of inhaled carbon dioxide....

9. Macroscopic Postmortem Examinations – F_1 Pups, page 19:

Revise: .... Unusual observations, including gross abnormalities and the ~~presence or~~ absence of milk in the stomach, will be noted and then the carcasses will be discarded....

10. Preservation of Records and Specimens, page 19:

Revise: ....At the completion of the study, all reports, raw data, preserved specimens and retained samples will be maintained in the Testing Facility's Archives for a period of **1** ~~10~~ year~~s~~ after submission of the signed final report. Biological samples collected for clinical pathology will be discarded as described elsewhere in this protocol. The Sponsor will be contacted in order to determine the final disposition of these materials. The Sponsor is responsible for all cost associated with the storage of these materials beyond **1** ~~10~~ year~~s~~ from the issuance of the final report and for any costs associated with the shipment of these materials to the Sponsor or to any other facility designated by the Sponsor.

11. Incidence Data, page 21:

Revise: A Fisher Exact Test with Bonferonni correction **(Seigel, S. 1956. Nonparametric Statistics for the Behavioral Sciences. New York: McGraw-Hill.)** will be performed to identify differences between the control and treatment groups....

12. Motor Activity Data, page 21:

Revise: .... Plots, tables, listings, and analyses will be generated using SAS® version **8.2** ~~6.12~~ for WINDOWS....

13. Summary Tables, page 23:

Revise: Mean pup weights (Lactation Days **1** ~~0~~ and 4)

14. Miscellaneous, page 23:

Delete: ~~Quality Assurance Statement~~

15. Appendix Tables, page 23:

Revise: ~~Mean and~~ individual body weight data
~~Mean and~~ individual animal weight gain data

16. Appendix Tables, page 23:

Revise: Individual pup weights (Days **1** ~~0~~ and 4)

Reasons for Changes

1. Clarification that the exposure period for these animals will be at least 28 days not exactly 28 days.

Protocol Amendment No. 2

2. Clarification that littermates will not be mated (by acquiring males and females from separate colony rooms) and that the estrous stages will be documented until such time that the animal is mated or the mating period is completed.
3. Clarification that the exposure period for these animals will be at least 28 days not exactly 28 days.
4. Correction of oversight in original protocol.
5. Clarification that feed consumption will also be measured pretest for all animals and will not be measured post-mating for the males since they are sacrificed immediately after the mating period but will be measured post-mating for the unmated Satellite females.
6. Clarification that the 'presence of milk in the stomach' is considered a normal observation for pups of this age and need not be separately recorded.
7. Reduction in the overall collected volume of blood because some of the females may be too small to tolerate the originally intended volume of blood.
8. Clarification that the adult test animals will be exsanguinated following anesthesia.
9. Clarification that the 'presence of milk in the stomach' is considered a normal observation for pups of this age and need not be separately recorded.
10. Correction of the archival storage period.
11. Addition of the reference for this statistical procedure.
12. Update of the SAS version currently adopted by CATO Research.
13. Correction of the weighing days to be reported for the pups.
14. Deletion of a duplicate entry already listed on page 22 in the Body of Report.
15. Correction that these appendix tables will only be individual and not summary data.
16. Correction of the weighing days to be reported for the pups.

Additional Cost Required: NO
Amendment approved by:

IACUC	12 Nov 03 Date
IACUC	12 Nov 03 Date
Gary M. Hoffman, B.A., DABT Study Director	12 Nov 03 Date
Thomas M. Gray, M.S., DABT Sponsor Representative	10 November, 2003 Date

Protocol Amendment No. 3

Study Title: Butane: Combined Repeated-Exposure Toxicity, Reproduction and Neurotoxicity Screening in Rats via Whole-Body Inhalation Exposures

Changes

1. Proposed Study Dates, page 2:
Revise and Add:

Receipt of Test Animals	16 September 2003 (Experimental Start)*
Initiation of Exposures	29 September 2003 (**Experimental Start)****

***as per OECD GLP's**
****as per EPA GLP's**

2. Detailed Physical Observations, page 12:

Revise: ………Satellite female rats will have a detailed physical observation performed weekly during the premating period and on Gestation Days 0, 7, 14, 20 and Lactation Days 0 **(except if parturition doesn't complete on the same day as it initiates)**, 1 and 4……

3. Statistical Evaluations, page 20:

Replace existing description for Continuous Data:

Evaluation of equality of group means will be made by the appropriate statistical method, followed by a multiple comparison test if needed. Bartlett's test (Bartlett, 1937; Sokal and Rohlf, 1995) will be performed to determine if groups have equal variances. For all FOB and clinical pathology parameters, if the variances are equal, parametric procedures will be used; if not, nonparametric procedures will be used. All other data will be analyzed only by parametric methods. The parametric method will be the standard one-way analysis of variance (ANOVA) using the F ratio to assess significance (Armitage, 1971; Dunlap and Duffy, 1975). If significant differences among the means are indicated, additional tests will be used to determine which means are significantly different from the control: Dunnett's (Dunlap et al., 1981; Dunnett, 1955, 1964), Williams (Williams, 1971, 1972), or Cochran and Cox's modified t-test (Cochran and Cox, 1959). The nonparametric method will be the Kruskal-Wallis test (Kruskal and Wallis, 1952, 1953) and if differences are indicated, Shirley's test (Shirley, 1977) or Steel's test (Steel, 1959) will be used to determine which means differ from control. Bartlett's test for equality of variance will be conducted at the 1% significance level; all other statistical tests will be conducted at the 5% and 1% significance levels.

Replace existing references for Continuous Data:

Armitage, P. 1971. Statistical Methods in Medical Research. Oxford, UK: Blackwell Scientific Publications; Bartlett, M.S. 1937. Properties of sufficiency and statistical tests. Proceedings of the Royal Society, Series A, 160: 268-282; Cochran, W.G. and Cox, G.M. 1959. Experimental Designs, New York: John Wiley, pp. 100-102; Dunlap, W.P. and Duffy, J.A. 1975. Fortran IV Functions for Calculating Exact Probabilities Associated with Z, Chi-Square, T and F Values. Behav. Res. Methods and Instrumentations 7:59-60; Dunlap, W.P., Marx, M.S. and Agamy, G.G. 1981. Fortran IV functions for calculating probabilities associated with Dunnett's test. Behav. Res. Methods and Instrumentation 13: 363-366;

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Dunnett, C.W. 1955. A multiple comparison procedure for comparing several treatments with a control. Journal of the American Statistical Association 50: 1096-1121; Dunnett, C.W. 1964. New tables for multiple comparisons with a control. Biometrics 20-3: 482-491; Kruskal, W.H. and Wallis, W.A. 1952. Use of Ranks in one-criterion variance analysis. Journal of the American Statistical Association 47: 583-621; Kruskal, W.H. and Wallis, W.A. 1953. Errata for Kruskal-Wallis (1952) Journal of the American Statistical Association 48: 907-911; Shirley, E.A.C. 1977. A non-parametric equivalent of Williams' test for contrasting increasing dose levels of a treatment. Biometrics 33: 386-389; Sokal, R.R. and Rohlf, F.J. 1995. Biometry. 3rd Edition. San Francisco: W.H. Freeman pp. 369-371; Steel, R.G.D. 1959. A multiple comparison rank sum test: treatment versus control. Biometrics 15: 560-572.; Williams, D.A. 1971. A test for differences between treatment means when several dose levels are compared with a zero dose control. Biometrics 27: 103-117; Williams, D.A. 1972. The comparison of several dose levels with a zero dose control. Biometrics 28: 519-531.

Add reference for Incidence Data:

A Fisher Exact Test with Bonferonni correction **(Seigel, S. 1956. Nonparametric Statistics for the Behavioral Sciences. New York: McGraw-Hill.)** will be performed to identify differences between the control and treatment groups. All statistical tests will be conducted at the 5% and 1%, two-sided risk levels.

Reasons for Changes

1. Clarification of the Experimental Start dates as per the relevant GLPs.
2. Clarification of the observation intervals during lactation if a dam doesn't complete its delivery of pups until the morning after delivery is initiated.
3. Clarification of the appropriate statistical routines and/or their references for the data capture systems that were actually used.

Additional Cost Required: NO

Amendment approved by:

Gary M. Hoffman, B.A., DABT
Study Director

5Apr04
Date

Thomas M. Gray
Thomas M. Gray, M.S., DABT
Sponsor Representative

05 April, 2004
Date

Protocol Amendment No. 4

Study Title: Butane: Combined Repeated-Exposure Toxicity with Reproduction/Developmental Toxicity and Neurotoxicity Screening in Rats via Whole-Body Inhalation Exposures

Changes

Revise Study Title from:

Combined Repeated-Exposure Toxicity, Reproduction and Neurotoxicity Screening in Rats via Whole-Body Inhalation Exposures

to

Combined Repeated-Exposure Toxicity with Reproduction/Developmental Toxicity and Neurotoxicity Screening in Rats via Whole-Body Inhalation Exposures

Reasons for Changes

Clarification of the study title to accurately reflect the relevant OECD and EPA test guidelines as per protocol.

Note that in the final report that the study title will only be revised on the Cover Page and the Summary Page since all other pages were computer generated based on the original study title.

Amendment approved by:

Gary M. Hoffman, B.A., DABT
Study Director

16NOV09
Date

Thomas M. Gray
Thomas M. Gray, M.S., DABT
Sponsor Representative

11/11/2009
Date

	Testing Facility Personnel	Appendix MM

TITLE/DEPARTMENT	NAME/DEGREE
SENIOR VICE PRESIDENT, SAFETY ASSESSMENT	Sylvie J. Gosselin, D.V.M., Ph.D., Diplomate A.C.V.P.
SENIOR DIRECTOR, SAFETY ASSESSMENT	Carol S. Auletta, M.B.A., D.A.B.T., R.A.C.
DIRECTOR, ANALYTICAL SERVICES	Barbara A. Litzenberger, B.S., M.T. (ASCP)
DIRECTOR, TOXICOLOGY OPERATIONS	Ian Vanterpool, F.I.A.T.
DIRECTOR, QUALITY ASSURANCE	Nicki S. Iacono, B.S.
STUDY DIRECTOR	Gary M. Hoffman, B.A., D.A.B.T.
DIRECTOR, REPRODUCTIVE AND DEVELOPMENTAL TOXICOLOGY	Keith P. Hazelden, B.Sc., C.Biol., M.I.Biol.
PATHOLOGIST	Wanda B. High, D.V.M., Ph.D.
STUDY MONITOR	Georgia Burnett, A.A.S.
VETERINARIAN	Teresa S. Kusznir, V.M.D.
MANAGER/SUPERVISOR	
Reproductive Toxicology	Sally Wilcox, B.Sc.
Inhalation	Stuart Cracknell, CBiol, MIBiol.
Pharmacy	Michael S. McCarthy
Analytical Services	Kay Saladdin, B.S.
Necropsy and Fetal Pathology	G. Elizabeth Baxter, B.S.
Histology	Janet Kusisto, B.S., H.T. (ASCP)

	2-Week Range-Finding Study Report	Appendix NN

STUDY NO. 03-6143

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

Final Report

Submitted to: American Petroleum Institute (API)
1220 L Street, Northwest
Washington, D.C. 20005-4070

Attn: Thomas M. Gray, M.S., D.A.B.T.

Date: 15 August 2008

STATEMENT OF COMPLIANCE

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

1) The supplier was responsible for the identity and stability of the test substance and those tests were not performed in compliance with GLP regulations.
2) A lot number for the test substance was not available.

Gary M. Hoffman, B.A., D.A.B.T.	15Aug08
Study Director	Date

Thomas M. Gray, M.S., D.A.B.T.	Date
Sponsor Representative	

SIGNATURE PAGE

SCIENTIST

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

15Aug08

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

SCIENTIFIC REVIEW

The following Scientist has reviewed and approved this report:

Robert M Parker for

14AUG08

Keith P. Hazelden, B.Sc., M.I.Biol. — Date
Director of Reproductive Toxicology

QUALITY ASSURANCE STATEMENT

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

Type of Inspection	Date(s) of Inspection	Reported to Study Director and Management
GLP Protocol Review	28 & 30 Jun 03	30 Jun 03
Exposure, Monitoring & Equipment Records	8 Jul 03	8 Jul 03
Body Weight, Feeder Weight & Physical Observations Data Collection	15 Jul 03	16 Jul 03
Necropsy & Training Records	22 Jul 03	23 Jul 03
Purity Analysis Report & Study Data	7 Oct 03	8 Oct 03
Final Report, Study Data & Protocol Amendment No. 1	3 – 10 Oct 03	10 Oct 03
Protocol Amendment No. 2	21 Jan 08	21 Jan 08

Sonya Gray
Quality Assurance Senior Auditor

30 Jan 08
Date

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

SUMMARY

This study was designed to provide a preliminary assessment of the toxicity of butane, an industrial gas, when administered via whole-body inhalation to rats for 2 weeks in order to determine exposure levels for a subsequent OECD 422 inhalation study.

Male and female Sprague-Dawley CD® rats (10/sex/group) were exposed for six hours per day to 0, 90, 900 or 9000 ppm butane for 14 or 15 consecutive days. At the end of the treatment period, all animals were euthanized and necropsied. The following parameters were evaluated: viability, clinical observations, body weights, feed consumption, organ weights and macroscopic observations.

Exposure levels were determined using an infrared spectrophotometer 4 times per chamber per day. Particle size distribution measurements were also made once per chamber per day using a TSI Aerodynamic Particle Sizer.

The mean (± standard deviation) analytical exposure concentrations of butane were determined to be 0.0 ± 0.0, 91.26 ± 4.74, 910.5 ± 32.9 and 9197 ± 328 ppm for the air control and the exposure groups, respectively. Particle sizing results indicated that the atmospheres were essentially gas only, as expected, since there was no substantial difference between the test substance chambers and the air control chamber.

All animals survived to termination. The test animals were unremarkable during the daily exposure periods and the non-exposure periods. There were no statistically significant or exposure-related differences in body weights or in feed consumption in the test substance exposed animals compared to the air control animals.

No gross abnormalities related to test substance exposure were evident at necropsy examination and there were no exposure-related differences in organ weights (absolute and relative to body weight or brain weight) in the test substance exposed animals compared to the air control animals.

In conclusion, two weeks of exposure of rats to butane gas at exposure levels of 90, 900 and 9000 ppm resulted in no effects of exposure. Therefore, the 9000 ppm exposure level was a no observable effect level (NOEL) and was considered an acceptable high exposure level (limited by safety considerations for a flammable gas) for a subsequent OECD 422 study.

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1. INTRODUCTION

This study was designed to provide a preliminary assessment of the toxicity of butane when administered via whole-body inhalation to rats for 2 weeks in order to determine exposure levels for a subsequent OECD 422 inhalation study (03-4242).

2. MATERIALS AND METHODS

2.1. STUDY MANAGEMENT

2.1.1. SPONSOR

American Petroleum Institute (API)
1220 L Street, Northwest
Washington, D.C. 20005-4070

2.1.2. SPONSOR REPRESENTATIVE

Thomas M. Gray, M.S., D.A.B.T.

2.1.3. TESTING FACILITY

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

2.1.4. STUDY DIRECTOR

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

2.2. STUDY DATES

2.2.1. STUDY INITIATION

1 July 2003 (Date Study Director signed the Protocol)

2.2.2. DATE OF ANIMAL RECEIPT

24 June 2003 (experimental start date, per OECD GLP's)

2.2.3. EXPOSURE INITIATION

8 July 2003 (experimental start date, per EPA GLP's)

2.2.4. EXPOSURE TERMINATION

22 July 2003

2.2.5. TERMINAL SACRIFICE

22 and 23 July 2003

2.2.6. EXPERIMENTAL TERMINATION DATE

23 July 2003 (Date of last data collection)

2.2.7. STUDY COMPLETION

15 August 2008 (Date Final Report is signed by the Study Director)

2.3. EXPERIMENTAL OUTLINE

Group	Test Substance	Exposure Level[a]	Number of Animals[b]	
		ppm	Males	Females
1	Air Control	0	10	10
2	Butane	90	10	10
3	Butane	900	10	10
4	Butane	9000	10	10

[a]Exposures were 6 hours per day for 7 consecutive days per week for 2 weeks. Exposure levels are expressed as ppm of test substance. The exposures were conducted via whole-body exposure.

[b]Complete postmortem evaluations were performed on all animals at termination of the study.

The first day of exposures was defined as Day 0 of the study.

2.4. JUSTIFICATIONS

2.4.1. ROUTE, DURATION AND FREQUENCY

The inhalation route is one of the potential routes of human exposure to this test substance. The duration of the study and frequency of exposures are considered to be the minimum necessary for determining exposure levels for a subsequent OECD 422 study.

2.4.2. TEST ANIMAL SELECTION

The rat is a rodent animal model commonly utilized in toxicity testing, as recommended in OECD and EPA guidelines, and will be the species used in the subsequent OECD 422 study. In addition, a historical database is available for comparative evaluation.

2.4.3. NUMBER OF ANIMALS

The number of animals in the study was considered to have been the minimum necessary for scientific and statistical reasons in order to evaluate the data with sufficient confidence levels.

2.4.4. EXPOSURE LEVEL SELECTION

The exposure levels were selected based on prior results (see MSDS attached to protocol in Appendix M) of minimal toxicity up to 1% (10000 ppm). Therefore, the high exposure level was established (for safety reasons) as 50% of the lower explosion limit (1.8% = 18000 ppm) for the test substance.

2.5. TEST SUBSTANCE

Butane

2.5.1. TEST SUBSTANCE CATEGORY

Industrial gas

2.5.2. CAS NUMBER

106-97-8

2.5.3. SUPPLIER

MG Industries
3 Great Valley Parkway
Malvern, Pennsylvania, 19355

2.5.4. LOT NUMBER

Not available

2.5.5. PURITY

99.5% per supplier. The testing facility also determined the purity by gas chromatography (GC) before the study (see Appendix N).

2.5.6. DESCRIPTION

Colorless gas

2.5.7. DATE RECEIVED

6 May 2003

2.5.8. EXPIRATION DATE

Not available, stable per MSDS.

2.5.9. ANALYSIS

The identity, strength, purity, composition, stability and method of synthesis, fabrication and/or derivation of the test substance were documented by the supplier before its use in the study. The maintenance of these records (at the above address) was the responsibility of the supplier. The identity, strength, purity, composition and stability were also confirmed by the testing facility.

2.5.10. STORAGE

Ambient

2.5.11. ARCHIVAL SAMPLE

An archival sample from the lot of test substance was taken and stored in the archives of the sponsor (EPL Archives, Inc., 45610

Terminal Drive, Sterling, Virginia 20166). A common archival sample was taken for this range-finding study and the subsequent OECD 422 study.

2.5.12. DISPOSITION

The unused portion of the test substance as well as any empty test substance containers will be returned to the supplier following submission of the final report of the final study with this test substance.

2.6. TEST ANIMALS

2.6.1. SPECIES

Albino Rats (Outbred) VAF/Plus®
Sprague-Dawley – Derived (CD®)
Crl:CD® (SD) IGS BR

2.6.2. SUPPLIER

Charles River Laboratories
Raleigh, North Carolina 27610

2.6.3. NUMBER OF ANIMALS

Received:
86 total (43 males, 43 females)

Placed on test:
80 total (40 males, 40 females)

Females were nulliparous and non-pregnant.

2.6.4. AGE AT RECEIPT

Approximately 6 weeks

2.6.5. AGE AT INITIATION OF EXPOSURES

Approximately 8 weeks

2.6.6. WEIGHT AT INITIATION OF EXPOSURES (GRAMS)

	Mean	Range
Male:	276	254 - 301
Female:	200	183 - 221

Individual weights of animals placed on test were within ±20% of the mean weight for each sex.

2.6.7. ACCLIMATION PERIOD

Animals were acclimated for 2 weeks. All animals were checked for viability twice daily. Prior to assignment to study, all animals were examined to ascertain suitability for study.

2.7. ANIMAL ASSIGNMENT

More animals than required for the study were purchased and acclimated. Animals considered unsuitable for the study on the basis of pretest physical examinations and body weight data were eliminated prior to random selection for group assignment. Animals considered suitable for study were distributed into 4 groups of 10 animals per sex by a computerized random sort program so that body weight means for each group were comparable. Disposition of all animals not utilized in the study is maintained in the study file.

2.8. ANIMAL IDENTIFICATION

Each animal was assigned a temporary identification number upon receipt. After selection for study, each animal was ear-tagged with a number assigned by the testing facility. The assigned animal number plus the study number comprised the unique animal number for each animal. If the tag was lost, it was replaced. In addition, each cage was provided with a cage card, which was color-coded for exposure level identification and contained study number and animal number information.

2.9. VETERINARY CARE

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

2.10. HUSBANDRY DURING NON-EXPOSURE PERIODS

2.10.1. FACILITIES MANAGEMENT/ANIMAL HUSBANDRY

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

2.10.2. HOUSING

Animals were individually housed in suspended, stainless steel wire mesh cages during the study.

2.10.3. FEED

Certified Rodent Diet, No. 5002; (Meal) (PMI Nutrition International, St. Louis, Missouri) was available without restriction. Fresh feed was presented weekly.

2.10.4. FEED ANALYSIS

Analysis of each feed lot used during this study was performed by the manufacturer. Results are maintained on file at the testing facility. There were no known contaminants in the feed that were expected to interfere with the objectives of this study.

2.10.5. WATER

Water (Elizabethtown Water Company, Westfield, New Jersey) was available without restriction via an automated watering system.

2.10.6. WATER ANALYSIS

Water analyses are conducted by Elizabethtown Water Company, Westfield, New Jersey (Raritan - Millstone Plant) to ensure that water meets standards specified under the EPA Federal Safe Drinking Water Act Regulations (40 CFR Part 141). In addition, water samples are collected biannually from representative rooms in the testing facility; chemical and microbiological water analyses are conducted on these samples by a subcontract laboratory. Results of all water analyses are maintained on file at the testing facility. There were no known contaminants in the water that were expected to interfere with the results of this study.

2.10.7. ENVIRONMENTAL CONDITIONS

Light/Dark Cycle

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

Temperature

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

Desired Range:	18 to 26 °C
Actual Range:	20.0 to 23.8 °C
Daily Average Range:	20.7 to 21.2 °C

Relative Humidity

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

Desired Range:	30 to 70%
Actual Range:	46.11 to 81.89%
Daily Average Range:	50.45 to 53.49%

2.11. HUSBANDRY DURING EXPOSURE

2.11.1. HOUSING

Animals were individually housed in stainless steel, wire mesh cages within 1000-Liter stainless steel and glass whole-body exposure chambers. The placement of each animal in the chamber was rotated at each exposure to ensure uniform exposure of the animals. A description of the animal rotation is included in the raw data.

2.11.2. FEED

None was provided during exposure.

2.11.3. WATER

None was provided during exposure.

2.11.4. ENVIRONMENTAL CONDITIONS

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

Temperature

Desired Range:	20 to 24 °C
Actual Range:	22 to 24 °C

Relative Humidity

Desired Range:	40 to 60%
Actual Range:	53 to 61%

2.12. TEST SUBSTANCE ADMINISTRATION AND CHAMBER OPERATION

2.12.1. ROUTE OF ADMINISTRATION

Inhalation, as a gas, via whole-body exposure.

2.12.2. FREQUENCY AND DURATION OF ADMINISTRATION

The test substance was administered for 6 hours per day for 7 consecutive days per week for 14 or 15 days.

2.12.3. PRE-STUDY TRIALS

Trials were performed (at least two 6-hour periods) to evaluate the optimal set of conditions and equipment to generate a stable and uniform atmosphere at the targeted exposure levels. During this time, samples were taken to determine the distribution of the test substance in the exposure chamber.

2.12.4. CHAMBER OPERATION

The whole-body exposure chambers each had a volume of 1000 Liters. Each chamber was operated dynamically under slight negative pressure at a minimum calibrated flow rate of 200 Liters per minute. The final airflow was set to provide at least one air change (calculated by dividing the chamber volume by the airflow rate) in 5.0 minutes (12 air changes/hour) and a T_{99} equilibrium time (calculated by multiplying the air change by the exponential factor 4.6) of at most 23 minutes. The chamber airflow rate, total flow rate, time for air change and 99% equilibrium time (T_{99}) for each group are summarized below.

Group	Airflow Rate (Lpm)	Air Change (min)	T_{99} (min)
1	227	4.4	20.2
2	215	4.7	21.6
3	207	4.8	22.1
4	210	4.8	22.1

This chamber size and airflow rates were considered adequate to maintain the animal loading factor below 5% and the oxygen level at 19% or higher. At the end of the exposure, all animals remained in chamber for a minimum of 30 minutes. During this time, the chamber was operated at the same flow rate as used during the exposure using clean air only. Recordings of airflow rate and static pressure were made every half-hour during the exposure.

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

Refer to Figures 1 & 2 and Appendix I for equipment details.

2.12.5. EXPOSURE PROCEDURE

Group 1

Animals were exposed to room air only.

Groups 2, 3 and 4

The test substance was delivered from a single cylinder, through a regulator and two backpressure gauges, and branched, via ¼" tubing, to the three exposure chambers. For each chamber, ¼" tubing directed the test substance to a flowmeter, regulated by a metering valve, and into the inlet of a 1000-Liter stainless steel and glass whole-body exposure chamber.

Refer to Figures 1 & 2 and Appendix I for equipment details.

2.13. EXPOSURE CHAMBER SAMPLING

2.13.1. CHAMBER SAMPLING

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

Refer to Appendices I & J for equipment details.

2.13.2. PARTICLE SIZE DISTRIBUTION ANALYSIS

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

Refer to Appendix I for equipment details.

2.13.3. NOMINAL CONCENTRATION

The nominal exposure concentration (ppm) was calculated by dividing the average test substance flow (ccm) during the exposure by the average chamber airflow (Lpm).

$$\text{Nominal (ppm)} = \frac{\text{Test Substance Flow (ccm)} \times 1000}{\text{Total Chamber Airflow (Lpm)}}$$

2.13.4. CHAMBER AND EXPOSURE ROOM ENVIRONMENT

Chamber oxygen levels (maintained at least 19%) were measured pretest and at the beginning, middle and end of the study. Air samples were taken in the vapor generation area pretest and at the beginning, middle and end of the study. Light (maintained approximately 30 – 40 foot-candles at 1.0 meter above the floor) and noise levels (maintained below 85 decibels) in the exposure room were measured pretest and at the beginning, middle and end of the study.

Refer to Appendix I for equipment details.

2.14. EXPERIMENTAL EVALUATIONS

2.14.1. VIABILITY CHECKS (CAGE-SIDE)

Animals were observed in their cages for mortality and general condition twice daily (once in the morning and once in the afternoon).

2.14.2. PHYSICAL EXAMINATIONS

All visible animals were observed as a group at least once during each exposure.

Each animal was removed from its cage and examined twice pretest (including on the first day of exposures) and once per week during the study period. Examinations included, but were not limited to, evaluation of skin and fur, eyes, nose, oral cavity, abdomen and external genitalia, occurrence of secretions and excretions, and autonomic activity (e.g., lacrimation, piloerection, pupil size, unusual respiratory pattern). Changes in gait, posture and response to handling, as well as the presence of clonic or tonic movements, stereotypy (e.g., excessive grooming, repetitive circling) or bizarre behavior (e.g., self-mutilation, walking backward) were recorded.

2.14.3. BODY WEIGHT

Animals were removed from their cages and weighed twice pretest (including on the first day of exposures) and weekly during treatment. Terminal, fasted body weights were obtained just prior to necropsy.

2.14.4. FEED CONSUMPTION

Feed consumption was measured during the week prior to exposures and weekly during the study. Feed was available without restriction 7 days/week, except during exposures and terminal fasting. Animals were presented with full feeders of known weight. After 6 or 7 days, the feeders were reweighed and the resulting weight subtracted from the initial feeder weight to obtain the grams of feed consumed per animal over the 6 or 7-day period. Feed consumption was measured (weighed) weekly, beginning one week prior to treatment.

Calculation

Feed Consumption (g/kg/day) =

$$\frac{\text{grams of feed consumed}}{\text{body weight (kg)}^{a}} \div 6 \text{ or } 7 \text{ days}$$

[a]The average of the current and previous weight was used.

2.15. POSTMORTEM

2.15.1. NECROPSY INFORMATION

Necropsy was performed on 10 animals/sex/group after animals were treated for 14 or 15 days. Animals were fasted overnight prior to necropsy. A necropsy schedule was established in order to assure that approximately equal numbers of males and females were examined on each day of necropsy and that examination of animals of both sexes were performed at similar times of the day throughout the necropsy period.

Method of Euthanasia

Exsanguination following carbon dioxide inhalation.

2.15.2. MACROSCOPIC EXAMINATIONS

Complete macroscopic postmortem examinations were performed on all animals. The macroscopic examination included examination of the external surface and all orifices; the external surfaces of the brain and spinal cord; the organs and tissues of the cranial, thoracic, abdominal and pelvic cavities and neck; and the remainder of the carcass for the presence of macroscopic morphologic abnormalities. Special attention was paid to the organs of the reproductive system.

2.15.3. ORGAN WEIGHTS

Organs indicated in Table I (below) were weighed for all animals at the scheduled necropsies. Prior to weighing, the organs were carefully dissected and properly trimmed to remove adipose and other contiguous tissues in a uniform manner. Organs were weighed as soon as possible after dissection in order to avoid drying. Paired organs were weighed together.

2.15.4. TISSUES PRESERVED

The tissues listed in Table I (below) were obtained at the scheduled sacrifice interval and preserved for all animals. No microscopic examination was performed.

TABLE I

ORGAN NAME	WEIGHED	PRESERVED
adrenal glands	X	X
aorta (thoracic)		X
bone (sternum, femur)		X
bone marrow (rib)		X

ORGAN NAME	WEIGHED	PRESERVED
brain (medulla, pons, cerebrum and cerebellum)	X	X
epididymides	X	X
esophagus		X
eyes with optic nerve		X
heart	X	X
kidneys	X	X
lacrimal glands		X
large intestine (cecum, colon, rectum)		X
larynx		X
liver	X	X
lungs (with mainstem bronchi)	X	X
lymph nodes (mesenteric, mediastinal)		X
mammary gland		X
muscle (*Biceps femoris*)		X
nasopharyngeal tissue		X
nerve (sciatic)		X
ovaries	X	X
pancreas		X
pituitary gland	X	X
prostate gland		X
salivary glands with submandibular lymph node		X
seminal vesicles	X	X
skin		X
small intestine (duodenum, ileum, jejunum)		X
spinal cord (cervical, thoracic, lumbar)		X
spleen	X	X
stomach		X
testes	X	X
thymic region	X	X

ORGAN NAME	WEIGHED	PRESERVED
thyroid/parathyroid glands		X
trachea		X
urinary bladder		X
uterus (body/horns) with cervix	X	X
Zymbal's gland		X
tissues with macroscopic findings		X

Preservatives

All tissues - 10% neutral buffered formalin.
Eyes were placed in glutaraldehyde/paraformaldehyde initially and then retained in 10% formalin. Testes and epididymides were placed in Modified Davidson's solution initially and then retained in 10% formalin. Lungs and urinary bladder were infused with formalin prior to their immersion into a larger volume of the same fixative.

Smear preparations of the marrow from the rib were air dried and fixed in absolute methanol.

2.16. STATISTICAL ANALYSIS

The following parameters were analyzed statistically:

body weight
feed consumption
organ weights

2.16.1. METHOD OF ANALYSIS

Mean values of all dose groups were compared to the mean value for the control group at each time interval.

Evaluation of equality of group means was made by the appropriate statistical method, followed by a multiple comparison test if needed. Bartlett's test (Sokal and Rohlf, 1995) was performed to determine if groups had equal variances. For all parameters except organ weights, if the variances were equal, parametric procedures were used; if not, nonparametric procedures were used. Organ weight data was analyzed only by parametric methods. The parametric method was the standard one-way analysis of variance (ANOVA) using the F ratio to assess significance (Dunlap and Duffy, 1975). If significant differences among the means were indicated, additional tests were used to determine which means were significantly different from the control: Dunnett's (Dunlap et al., 1981), or Cochran and Cox's modified t-test (Cochran and Cox, 1959). The nonparametric method was the Kruskal-Wallis test (Kruskal and Wallis, 1952, 1953) and if differences were indicated, Pairwise Comparison with Bonferroni Correction (Games and Howell, 1976) were used to determine which means differed from control. Bartlett's test for equality of variance was conducted at the 1% significance level; all other statistical tests were conducted at the 5% and 1% significance levels.

2.17. DATA STORAGE

All raw data, and preserved specimens, as well as the original study protocol and the original final report, are to be maintained in the Archives of the Testing Facility upon completion of the study. The Sponsor will determine the final disposition of these materials.

2.18. REGULATORY REFERENCES

2.18.1. TEST GUIDELINES

This study was not designed to meet regulatory requirements. It was designed to provide preliminary toxicity data for the test substance in order to determine appropriate exposure levels for a subsequent OECD 422 study.

2.18.2. GOOD LABORATORY PRACTICES

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

2.18.3. ANIMAL WELFARE ACT COMPLIANCE

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

2.19. PROTOCOL DEVIATIONS

No protocol deviations occurred during this study.

3. RESULTS AND DISCUSSION

3.1. TEST SUBSTANCE ANALYSIS

(Appendix N)

Prestudy GC analysis of the test substance showed a purity of 99.23% for butane. This value compared closely to the purity of 99.96% for the analytical standard of butane and the 99.5% purity as guaranteed by the supplier of the test substance.

3.2. CHAMBER MONITORING

(Appendices A, K & L)

Chamber distribution analyses (see Appendix K) showed that the test substance was evenly distributed within each chamber. Chamber monitoring (see Appendix L) showed that the chamber oxygen levels were at least 19%. Chamber room monitoring (see Appendix L) showed that no test substance was present in the room and that the sound and light levels were acceptable.

The target and mean (± standard deviation) analytical (IR) and nominal concentrations (see Appendix A) are summarized as follows:

Group	Test Substance	Target Concentration (ppm)	Analytical Concentration (ppm)	Nominal Concentration (ppm)
1	Air Control	0	0.00 ± 0.00	0 ± 0
2	Butane	90	91.26 ± 4.74	84.3 ± 0.0
3	Butane	900	910.5 ± 32.9	913 ± 4
4	Butane	9000	9197 ± 328	8581 ± 47

The analytically measured (IR) exposure levels of the airborne test substance were reasonably close to the targeted exposure levels. The differences between measured and nominal concentrations varied somewhat from the expected 1:1 ratio for this type of gas exposure. The exact cause of the differences was not determined but was probably a result of a combination of slight variances in the calibration of the chamber airflows and the calibration of the IR monitor. Chamber environmental conditions averaged 23°C temperature and 55% relative humidity.

Mean particle size distribution measurements for the exposures (see Appendix A) are summarized as follows:

Group	Test Substance	Mass Median Aerodynamic Diameter (µm)	Geometric Standard Deviation	Total Mass Concentration (mg/m^3)
1	Air Control	1.404	2.071	4.55E-03
2	Butane	1.781	2.119	4.85E-03
3	Butane	1.848	1.987	4.29E-03
4	Butane	2.754	2.011	5.89E-03

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

3.3. MORTALITY

(Appendix B)

All animals survived to termination.

3.4. CLINICAL OBSERVATIONS

3.4.1. EXPOSURE PERIODS

(Table 1)

The test animals were unremarkable during the exposure periods.

3.4.2. NON-EXPOSURE PERIODS

(Table 2 & Appendix C)

The test animals were generally unremarkable during the non-exposure periods. Scattered observations such as red staining of the snout were noted but were not attributed to treatment.

3.5. BODY WEIGHTS

(Figures 3-4, Tables 3–4 & Appendices D - E)

There were no statistically significant or exposure-related differences in absolute body weights or in body weight changes in the test substance exposed animals compared to the air control animals.

3.6. FEED CONSUMPTION

(Figure 5-6, Table 5 & Appendix F)

There were no statistically significant or exposure-related differences in feed consumption in the test substance exposed animals compared to the air control animals.

3.7. ORGAN WEIGHTS

(Table 6 & Appendix G)

There were no exposure-related differences in organ weights (absolute and relative to body weight or brain weight) in the test substance exposed animals compared to the air control animals. A statistically significant increase was noted in thymus-to-body-weight ratio for the 90 ppm exposed male animals. However, in the absence of an exposure level related pattern and any corresponding macroscopic postmortem findings, this difference was considered incidental.

3.8. MACROSCOPIC PATHOLOGY

(Table 7 & Appendix H)

No gross abnormalities related to test substance exposure were evident at necropsy examination. The macroscopic lesions noted were similar to those routinely encountered in animals of this age and species or were represented by individual animals and considered incidental findings.

4. CONCLUSION

Two weeks of exposure of rats to butane gas at exposure levels of 90, 900 and 9000 ppm resulted in no effects of exposure. Therefore, the 9000 ppm exposure level was a no observable effect level (NOEL) and was considered an acceptable high exposure level (limited by safety considerations for a flammable gas) for a subsequent OECD 422 study.

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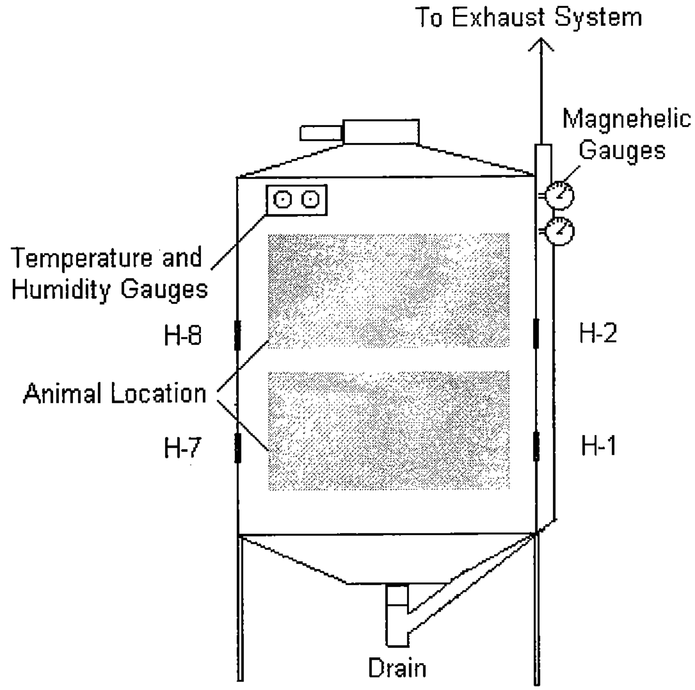
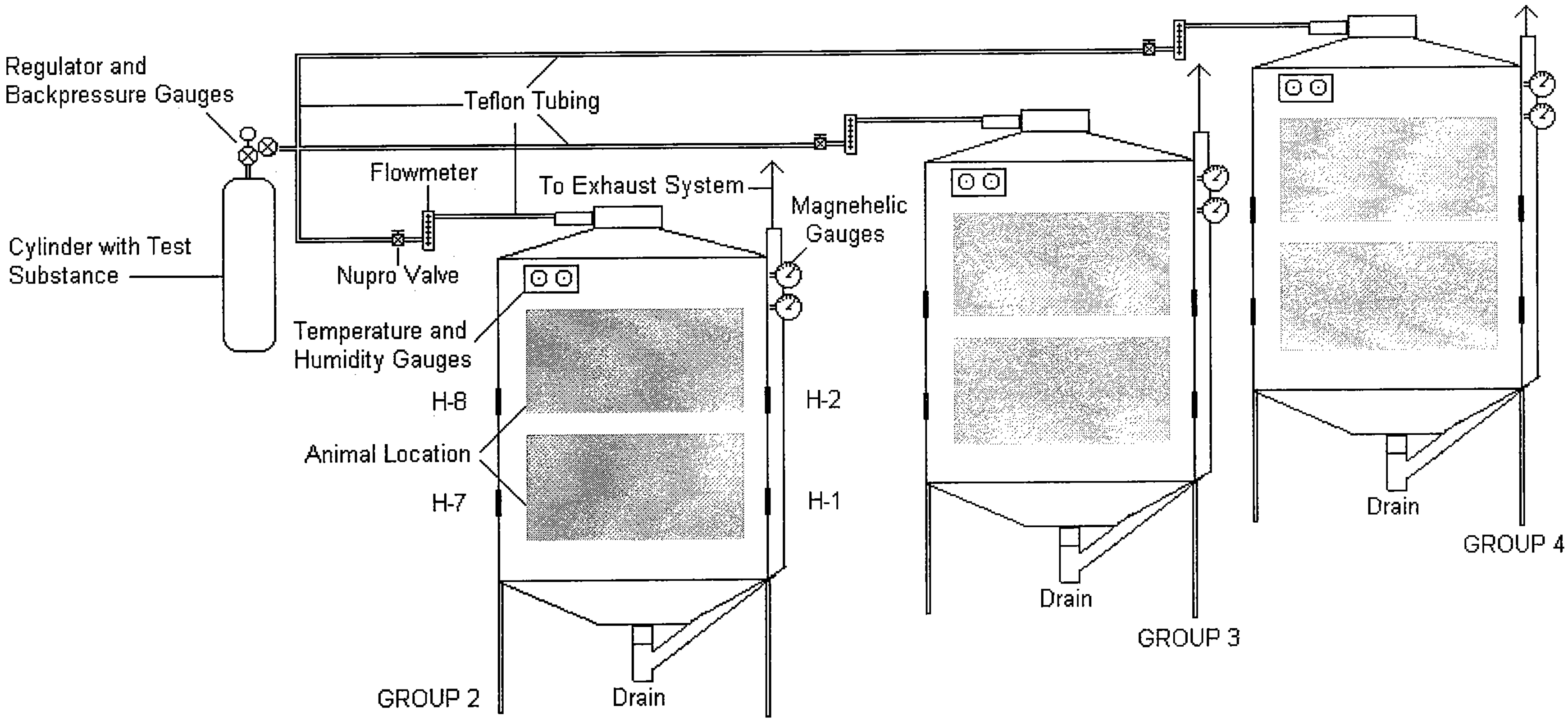
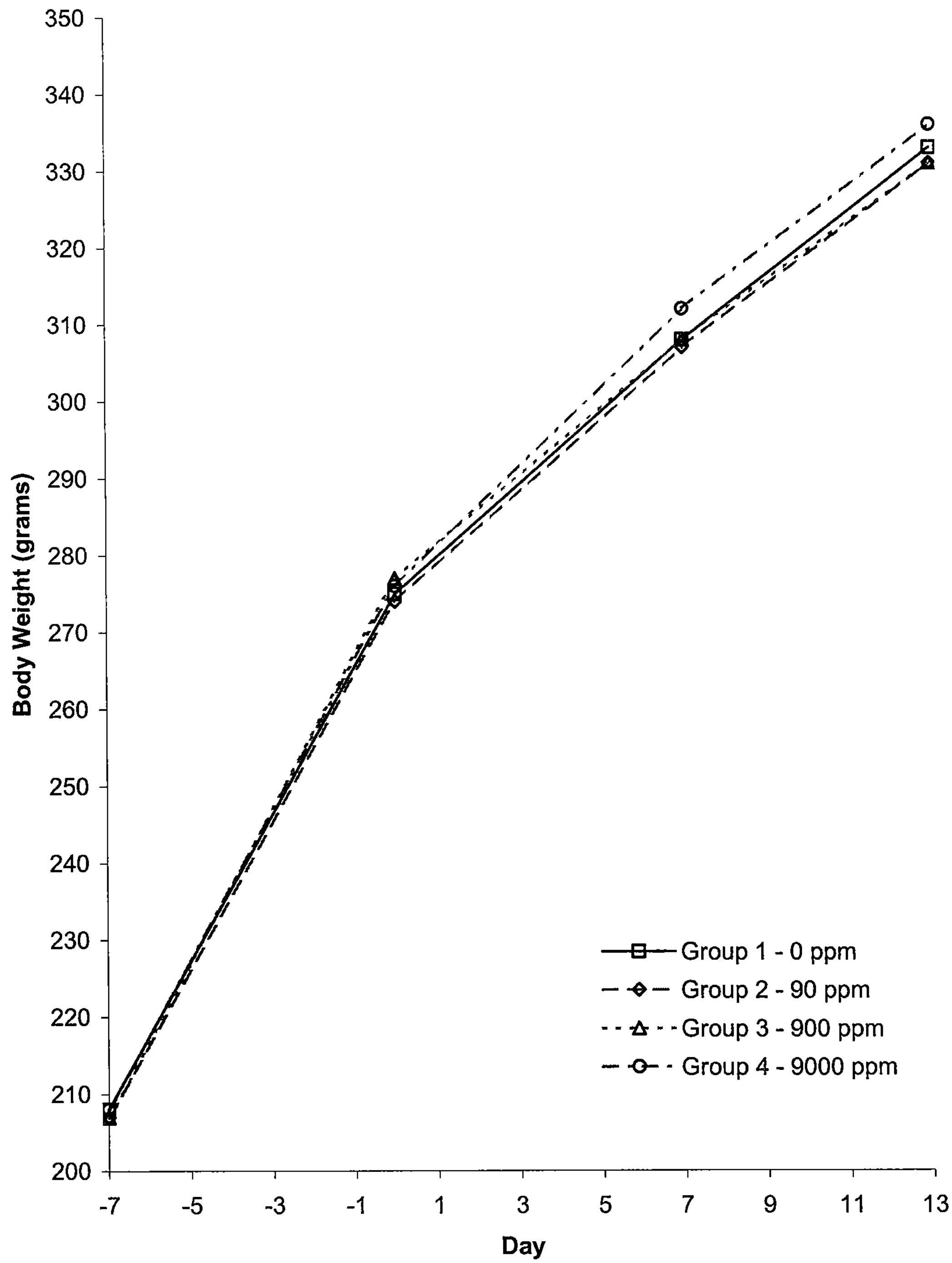
Group 1	Diagram of 1000-Liter Whole-Body Exposure Chamber and Generation System	Figure 1



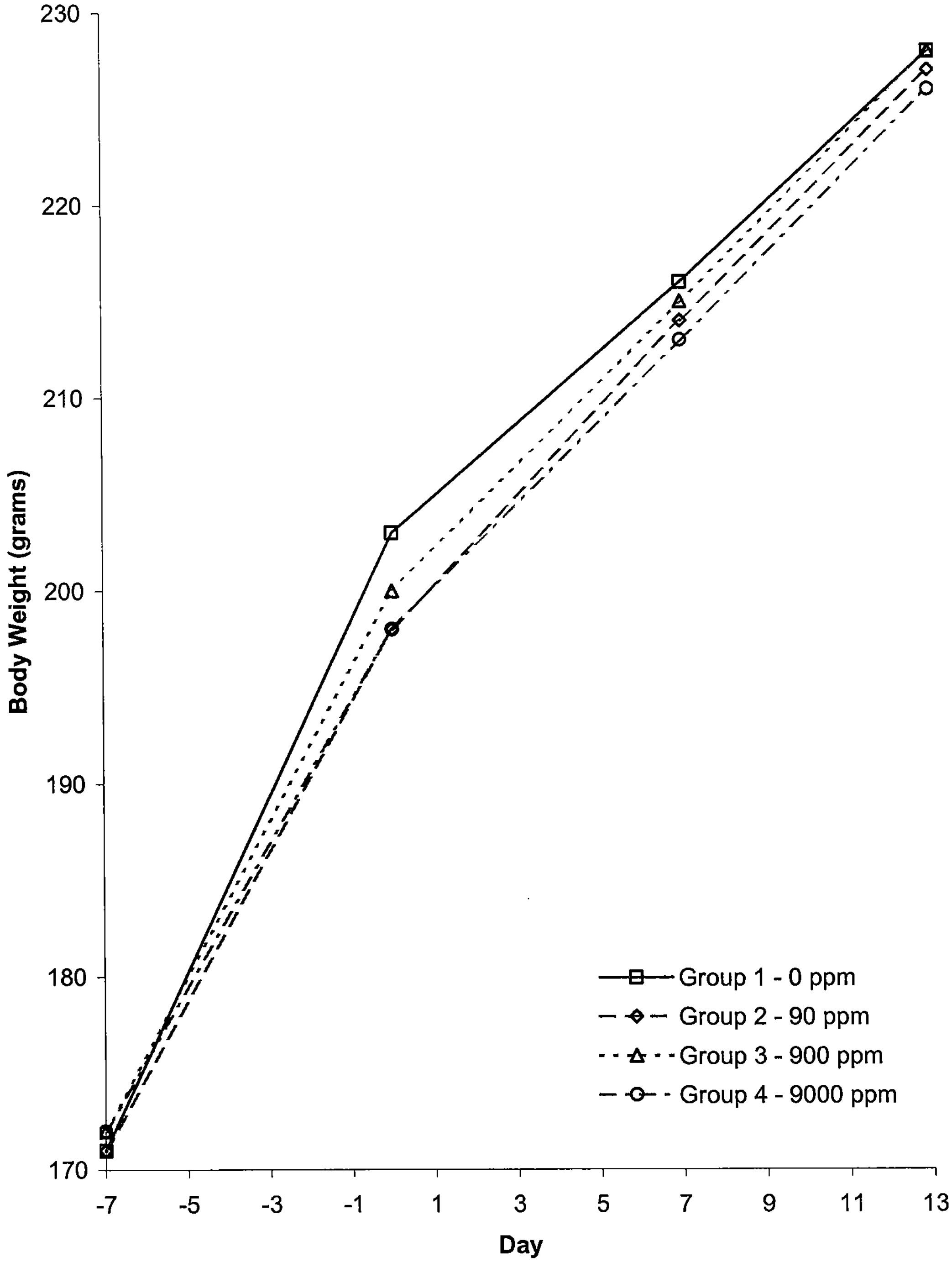
Groups 2, 3 & 4	Diagram of 1000-Liter Whole-Body Exposure Chamber and Generation System	Figure 2



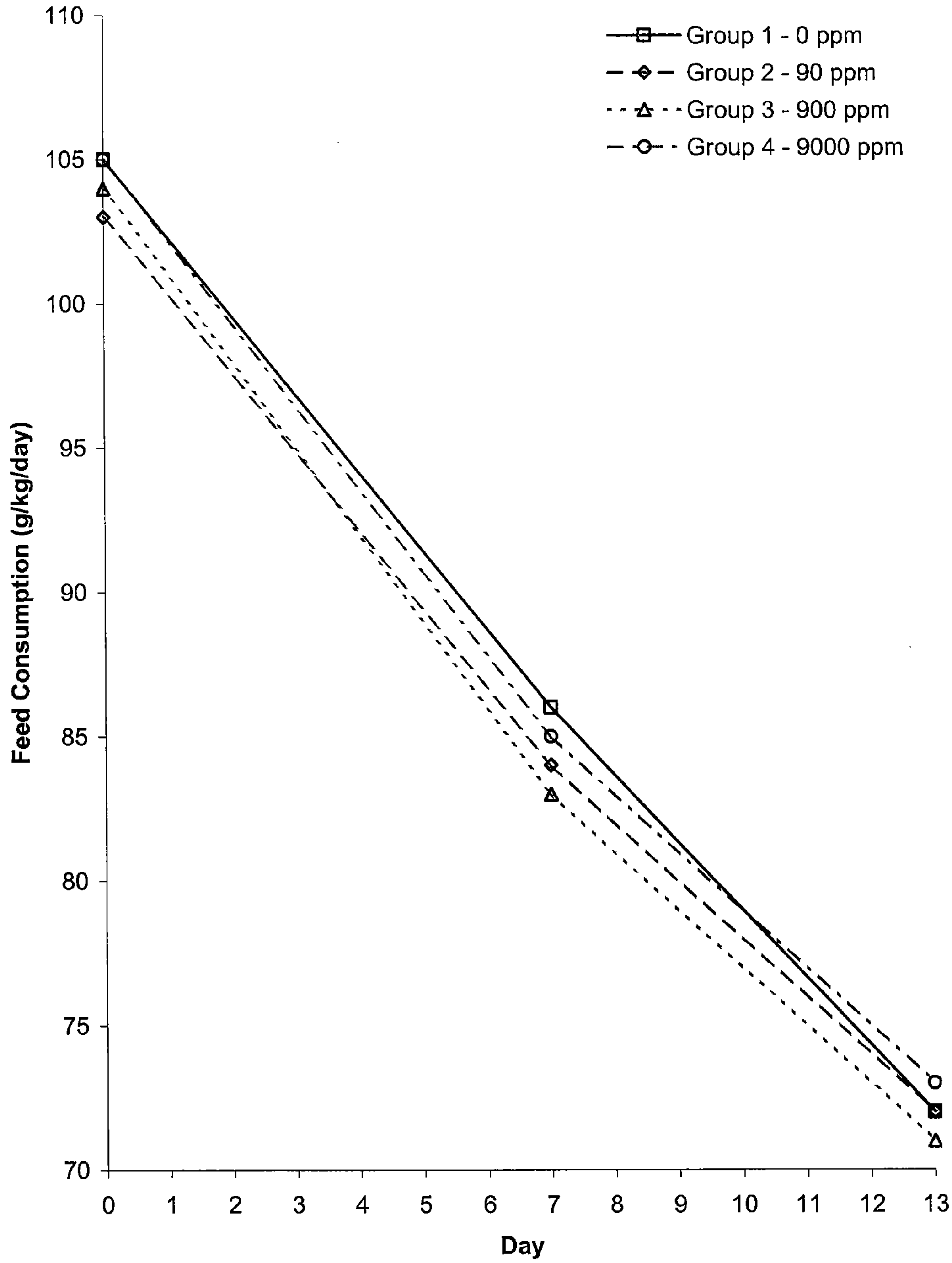
Males	Mean Body Weights	Figure 3



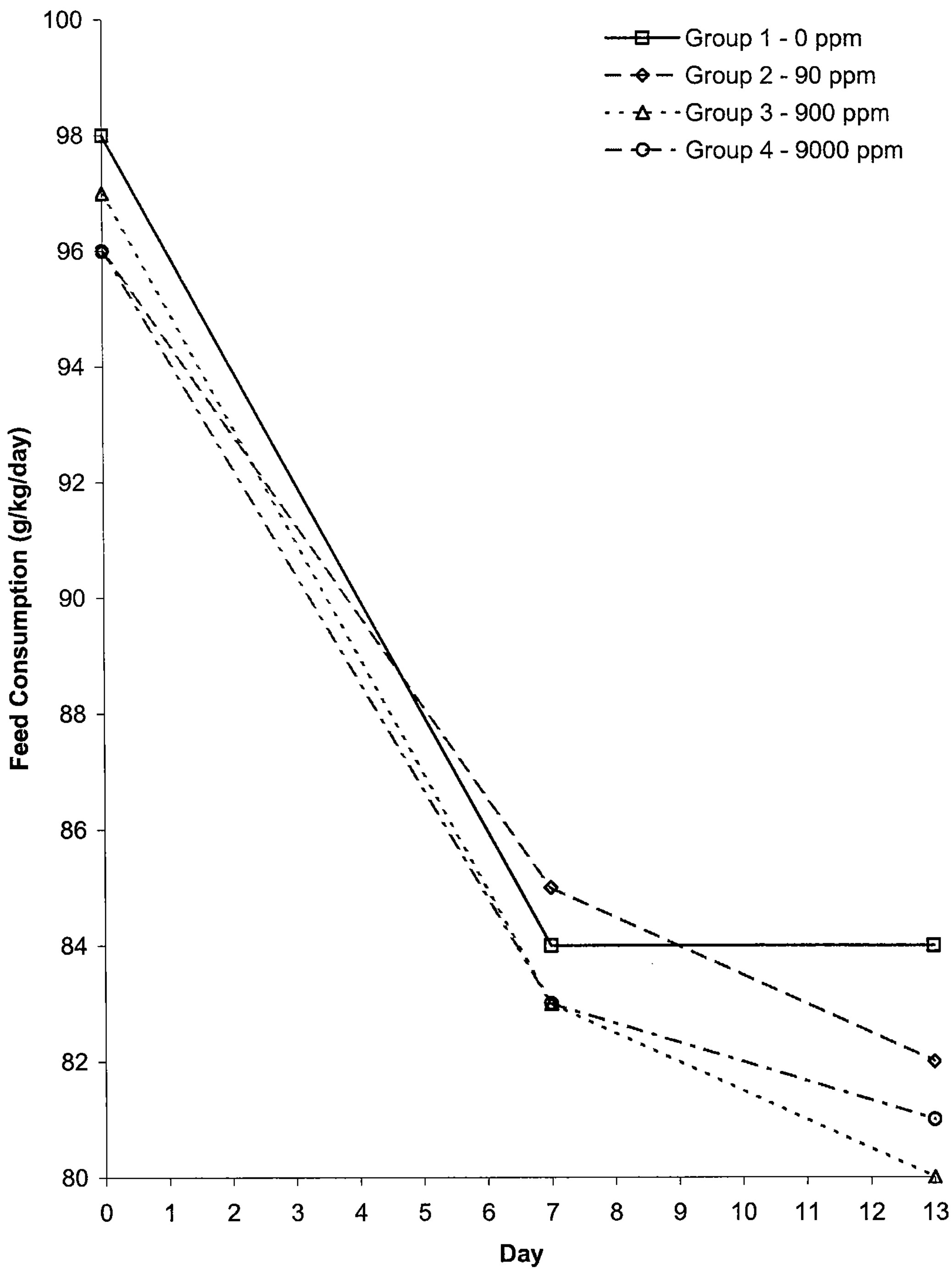
Females	Mean Body Weights	Figure 4



Males	Mean Feed Consumption	Figure 5



Females	Mean Feed Consumption	Figure 6



	General Preface	

General Notes

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

	Summary of In-Chamber Observations														Table 1
Exposure Number	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**
Group 1 – 0 ppm															
Normal Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All	All	All
Group 2 – 90 ppm															
Normal Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All	All	All
Group 3 – 900 ppm															
Normal Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All	All	All
Group 4 – 9000 ppm															
Normal Within Normal Limits	All	All	All	All	All	All	All	All	All	All	All	All	All	All	All

All = 100% of the animals exhibiting a given observation.

	Summary of Clinical Observations Preface	Table 2

For summarization purposes, descriptive comments [i.e., location of scab(s) and/or sore(s), etc.] are not presented in this table. These data are contained in the study raw data if needed.

Total represents a cumulative total of all animals with the indicated observation one or more times during the study.

Corresponding exposure levels for each group were as follows:

Group 1 - 0 ppm
Group 2 - 90 ppm
Group 3 - 900 ppm
Group 4 - 9000 ppm

TABLE 2

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

MALES

SUMMARY OF CLINICAL OBSERVATIONS

	GROUP#	DAY OF STUDY -7	0	7	13	14	15	TOTAL
# OF ANIMALS EXAMINED	1	10	10	10	10	5	5	
	2	10	10	10	10	5	5	
	3	10	10	10	10	5	5	
	4	10	10	10	10	5	5	
NORMAL								
WITHIN NORMAL LIMITS	1	10	10	8	8	0	0	10
	2	10	10	10	10	0	0	10
	3	10	10	8	9	0	0	10
	4	10	10	9	9	0	0	10
DEAD								
Terminal Sacrifice	1	0	0	0	0	5	5	10
	2	0	0	0	0	5	5	10
	3	0	0	0	0	5	5	10
	4	0	0	0	0	5	5	10
DERMAL GENERAL								
Ulceration - Cervical	1	0	0	1	1	0	0	1
	2	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0
Scab(s)	1	0	0	1	1	0	0	1
	2	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0
Alopecia - Extremities/Snout	1	0	0	1	1	0	0	1
	2	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0
	4	0	0	1	1	0	0	1

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TABLE 2

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

MALES

SUMMARY OF CLINICAL OBSERVATIONS

	GROUP#	DAY OF STUDY -7	0	7	13	14	15	TOTAL
# OF ANIMALS EXAMINED	1	10	10	10	10	5	5	
	2	10	10	10	10	5	5	
	3	10	10	10	10	5	5	
	4	10	10	10	10	5	5	
RED STAINS - SNOUT	1	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0
	3	0	0	1	0	0	0	1
	4	0	0	0	0	0	0	0
OCULAR								
Chromodacryorrhea - Unilateral	1	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0
	3	0	0	1	1	0	0	1
	4	0	0	0	0	0	0	0

TABLE 2

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

FEMALES SUMMARY OF CLINICAL OBSERVATIONS

	GROUP#	DAY OF STUDY -7	0	7	13	14	15	TOTAL
# OF ANIMALS EXAMINED	1	10	10	10	10	5	5	
	2	10	10	10	10	5	5	
	3	10	10	10	10	5	5	
	4	10	10	10	10	5	5	
NORMAL								
WITHIN NORMAL LIMITS	1	10	10	8	8	0	0	10
	2	10	10	8	8	0	0	10
	3	10	10	7	7	0	0	10
	4	10	10	9	9	0	0	10
DEAD								
Terminal Sacrifice	1	0	0	0	0	5	5	10
	2	0	0	0	0	5	5	10
	3	0	0	0	0	5	5	10
	4	0	0	0	0	5	5	10
DERMAL GENERAL								
Scab(s)	1	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0
	3	0	0	1	1	0	0	1
	4	0	0	0	0	0	0	0
Alopecia - Extremities/Snout	1	0	0	1	1	0	0	1
	2	0	0	1	1	0	0	1
	3	0	0	3	3	0	0	3
	4	0	0	1	1	0	0	1
RED STAINS - SNOUT	1	0	0	1	1	0	0	1
	2	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0

TABLE 2

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

FEMALES

SUMMARY OF CLINICAL OBSERVATIONS

	GROUP#	DAY OF STUDY -7	0	7	13	14	15	TOTAL
# OF ANIMALS EXAMINED	1	10	10	10	10	5	5	
	2	10	10	10	10	5	5	
	3	10	10	10	10	5	5	
	4	10	10	10	10	5	5	
Alopecia - General	1	0	0	0	0	0	0	0
	2	0	0	1	1	0	0	1
	3	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0

TABLE 3

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

MALES MEAN BODY WEIGHTS (GRAMS)

	DOSE GROUP:	1	2	3	4
	DOSE LEVEL (PPM):	0	90	900	9000
DAY -7	MEAN	208	207	207	208
	S.D.	8.2	9.7	8.7	7.3
	N	10	10	10	10
DAY 0	MEAN	275	274	277	276
	S.D.	11.8	10.1	9.0	12.8
	N	10	10	10	10
DAY 7	MEAN	308	307	308	312
	S.D.	11.8	8.7	13.3	17.4
	N	10	10	10	10
DAY 13	MEAN	333	331	331	336
	S.D.	17.6	10.7	15.3	22.8
	N	10	10	10	10

No statistically significant differences

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TABLE 3

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

FEMALES

MEAN BODY WEIGHTS (GRAMS)

	DOSE GROUP:	1	2	3	4
	DOSE LEVEL (PPM):	0	90	900	9000
DAY -7	MEAN	171	171	172	172
	S.D.	8.2	7.8	7.9	7.9
	N	10	10	10	10
DAY 0	MEAN	203	198	200	198
	S.D.	10.5	8.1	12.1	10.7
	N	10	10	10	10
DAY 7	MEAN	216	214	215	213
	S.D.	14.5	8.7	10.3	9.3
	N	10	10	10	10
DAY 13	MEAN	228	227	228	226
	S.D.	14.6	10.8	10.9	9.8
	N	10	10	10	10

No statistically significant differences

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TABLE 4

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

MALES — MEAN BODY WEIGHT CHANGE FROM BASELINE (GRAMS)

		DOSE GROUP:	1	2	3	4
		DOSE LEVEL (PPM):	0	90	900	9000
DAY	0 TO 7	MEAN	33	33	32	36
		S.D.	5.9	3.3	8.2	8.2
		N	10	10	10	10
DAY	0 TO 13	MEAN	58	57	54	59
		S.D.	10.2	5.7	14.3	14.0
		N	10	10	10	10

No statistically significant differences

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TABLE 4

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

FEMALES

MEAN BODY WEIGHT CHANGE FROM BASELINE (GRAMS)

	DOSE GROUP: DOSE LEVEL (PPM):	1 0	2 90	3 900	4 9000
DAY 0 TO 7	MEAN	13	16	14	15
	S.D.	9.4	6.2	6.0	5.4
	N	10	10	10	10
DAY 0 TO 13	MEAN	25	29	28	28
	S.D.	8.1	7.4	6.1	8.6
	N	10	10	10	10

No statistically significant differences

TABLE 5

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

MALES

MEAN FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

	DOSE GROUP:	1	2	3	4
	DOSE LEVEL (PPM):	0	90	900	9000
DAY 0	MEAN	105	103	104	105
	S.D.	3.9	5.5	4.8	2.7
	N	10	9	10	10
DAY 7	MEAN	86	84	83	85
	S.D.	4.9	5.4	4.9	2.9
	N	9	10	8	9
DAY 13	MEAN	72	72	71	73
	S.D.	3.7	1.9	6.8	3.4
	N	10	9	9	10

No statistically significant differences

TABLE 5

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

FEMALES MEAN FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

		DOSE GROUP:	1	2	3	4
		DOSE LEVEL (PPM):	0	90	900	9000
DAY	0	MEAN	98	96	97	96
		S.D.	6.7	4.6	6.5	6.7
		N	10	10	10	10
DAY	7	MEAN	84	85	83	83
		S.D.	7.7	4.0	4.9	4.2
		N	10	10	10	10
DAY	13	MEAN	84	82	80	81
		S.D.	8.1	1.7	3.7	3.8
		N	10	10	10	10

No statistically significant differences

	Mean Organ Weights Preface	Table 6

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Key to Abbreviations:

g	=	Grams
wt.	=	Weight
observ.	=	Observed

Corresponding exposure levels for each group were as follows:

Group 1	-	0 ppm
Group 2	-	90 ppm
Group 3	-	900 ppm
Group 4	-	9000 ppm

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Group	Terminal Body wt. (g)	Adrenal Glands	Brain	Epididymides	Heart	Kidneys	Liver	Lungs
Male Animals								
1								
Mean:	309.1	0.0701	2.1366	0.9055	1.2596	3.3632	11.2665	1.8929
Standard deviation:	18.5	0.0091	0.1118	0.0678	0.0521	0.1948	0.8728	0.2237
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
2								
Mean:	309.9	0.0669	2.1457	0.9167	1.2490	3.5231	11.2858	1.9188
Standard deviation:	7.8	0.0065	0.0907	0.0807	0.0827	0.3106	0.8842	0.1234
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3								
Mean:	308.7	0.0668	2.1157	0.9157	1.2287	3.4532	11.1262	1.9514
Standard deviation:	15.9	0.0094	0.0781	0.0769	0.1095	0.3328	0.6532	0.2107
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
4								
Mean:	310.3	0.0706	2.1146	0.9180	1.2409	3.4795	11.9273	1.9407
Standard deviation:	23.0	0.0082	0.0959	0.1177	0.1199	0.3542	1.5663	0.1743
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)

*(+) = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance
%($) = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

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Group	Terminal Body wt. (g)	Pituitary gland	Seminal vesicles	Spleen	Testes	Thymus
			Male Animals			
1						
Mean:	309.1	0.0103	1.0527	0.7378	3.2380	0.5517
Standard deviation:	18.5	0.0020	0.1878	0.1088	0.2473	0.1306
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)
2						
Mean:	309.9	0.0102	1.0206	0.6855	3.2907	0.6950
Standard deviation:	7.8	0.0018	0.2589	0.0927	0.1152	0.1771
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)
3						
Mean:	308.7	0.0096	0.9701	0.7167	3.2418	0.5483
Standard deviation:	15.9	0.0015	0.1966	0.1302	0.2421	0.1252
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)
4						
Mean:	310.3	0.0123	1.1260	0.7423	3.1751	0.5093
Standard deviation:	23.0	0.0023	0.2226	0.2212	0.3097	0.1068
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)

*(+) = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance
%($) = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

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Group	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs	Ovaries
F e m a l e A n i m a l s								
1								
M e a n:	212.6	0.0824	2.0426	0.9307	2.4616	8.6266	1.7845	0.1199
Standard deviation:	13.6	0.0120	0.1045	0.0811	0.2699	0.9889	0.2454	0.0195
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
2								
M e a n:	212.0	0.0761	2.0489	0.9193	2.3977	8.3758	1.7555	0.1183
Standard deviation:	8.1	0.0081	0.0870	0.1083	0.2068	0.9293	0.1884	0.0117
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3								
M e a n:	210.3	0.0746	2.0375	0.9144	2.3323	7.9702	1.7077	0.1088
Standard deviation:	11.5	0.0108	0.1003	0.0570	0.2308	0.8089	0.2722	0.0159
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
4								
M e a n:	208.8	0.0816	2.0233	0.8985	2.3711	8.3570	1.7848	0.1154
Standard deviation:	7.6	0.0124	0.0811	0.0534	0.1959	0.7493	0.3264	0.0209
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)

*(+) = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance
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Group	Terminal Body wt. (g)	Pituitary gland	Spleen	Thymus	Uterus
Female Animals					
1					
Mean:	212.6	0.0145	0.4941	0.5151	0.5587
Standard deviation:	13.6	0.0019	0.0663	0.0934	0.0705
Number of observ. :	(10)	(10)	(10)	(10)	(10)
2					
Mean:	212.0	0.0133	0.5512	0.5597	0.6087
Standard deviation:	8.1	0.0015	0.0948	0.1000	0.2015
Number of observ. :	(10)	(10)	(10)	(10)	(10)
3					
Mean:	210.3	0.0138	0.5177	0.4853	0.6667
Standard deviation:	11.5	0.0021	0.0776	0.0825	0.1780
Number of observ. :	(10)	(10)	(10)	(10)	(10)
4					
Mean:	208.8	0.0142	0.5362	0.4504	0.5501
Standard deviation:	7.6	0.0020	0.0727	0.0518	0.0769
Number of observ. :	(10)	(10)	(10)	(10)	(10)

*(+) = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance
%($) = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

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Group		Terminal Body wt. (g)	Adrenal Glands	Brain	Epididymides	Heart	Kidneys	Liver	Lungs
Male Animals									
1	Mean:	309.1	0.0228	0.6931	0.2938	0.4085	1.0910	3.6462	0.6150
	Standard deviation:	18.5	0.0035	0.0496	0.0277	0.0246	0.0851	0.2232	0.0862
	Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
2	Mean:	309.9	0.0216	0.6924	0.2961	0.4032	1.1364	3.6421	0.6196
	Standard deviation:	7.8	0.0024	0.0227	0.0285	0.0273	0.0896	0.2724	0.0448
	Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3	Mean:	308.7	0.0217	0.6867	0.2976	0.3984	1.1228	3.6089	0.6323
	Standard deviation:	15.9	0.0032	0.0360	0.0322	0.0334	0.1394	0.2176	0.0615
	Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
4	Mean:	310.3	0.0228	0.6853	0.2970	0.4001	1.1238	3.8601	0.6311
	Standard deviation:	23.0	0.0028	0.0641	0.0404	0.0270	0.1071	0.5935	0.0414
	Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)

*(+) = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance
%($) = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

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Group	Terminal Body wt. (g)	Pituitary gland	Seminal vesicles	Spleen	Testes	Thymus
Male Animals						
1						
Mean:	309.1	0.0034	0.3409	0.2386	1.0511	0.1773
Standard deviation:	18.5	0.0008	0.0608	0.0313	0.1056	0.0348
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)
2						
Mean:	309.9	0.0033	0.3299	0.2215	1.0625	0.2242*
Standard deviation:	7.8	0.0006	0.0859	0.0318	0.0474	0.0554
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)
3						
Mean:	308.7	0.0031	0.3149	0.2329	1.0541	0.1773
Standard deviation:	15.9	0.0005	0.0638	0.0449	0.1106	0.0377
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)
4						
Mean:	310.3	0.0039	0.3648	0.2414	1.0266	0.1631
Standard deviation:	23.0	0.0007	0.0773	0.0852	0.1070	0.0274
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)

*(+) = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance
%($) = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

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Group	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs	Ovaries
Female Animals								
1								
Mean:	212.6	0.0389	0.9633	0.4379	1.1575	4.0595	0.8409	0.0564
Standard deviation:	13.6	0.0060	0.0611	0.0274	0.1027	0.4009	0.1161	0.0088
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
2								
Mean:	212.0	0.0359	0.9678	0.4338	1.1319	3.9511	0.8285	0.0559
Standard deviation:	8.1	0.0034	0.0515	0.0500	0.0971	0.4087	0.0859	0.0057
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3								
Mean:	210.3	0.0354	0.9713	0.4351	1.1095	3.7926	0.8114	0.0517
Standard deviation:	11.5	0.0042	0.0636	0.0205	0.0956	0.3575	0.1143	0.0068
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
4								
Mean:	208.8	0.0391	0.9699	0.4307	1.1355	4.0061	0.8572	0.0554
Standard deviation:	7.6	0.0057	0.0498	0.0289	0.0837	0.3857	0.1700	0.0105
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)

*(+) = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance
%($) = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

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Group	Terminal Body wt. (g)	Pituitary gland	Spleen	Thymus	Uterus
Female Animals					
1					
Mean:	212.6	0.0069	0.2326	0.2430	0.2637
Standard deviation:	13.6	0.0010	0.0297	0.0444	0.0364
Number of observ. :	(10)	(10)	(10)	(10)	(10)
2					
Mean:	212.0	0.0063	0.2599	0.2634	0.2873
Standard deviation:	8.1	0.0008	0.0436	0.0416	0.0947
Number of observ. :	(10)	(10)	(10)	(10)	(10)
3					
Mean:	210.3	0.0066	0.2464	0.2316	0.3178
Standard deviation:	11.5	0.0009	0.0374	0.0423	0.0884
Number of observ. :	(10)	(10)	(10)	(10)	(10)
4					
Mean:	208.8	0.0068	0.2571	0.2164	0.2633
Standard deviation:	7.6	0.0010	0.0370	0.0302	0.0342
Number of observ. :	(10)	(10)	(10)	(10)	(10)

*(+) = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance
%($) = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

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Group	Terminal Body wt. (g)	Adrenal Glands	Brain	Epididymides	Heart	Kidneys	Liver	Lungs
Male Animals								
1								
Mean:	309.1	3.2969	100.0000	42.4978	59.1157	157.8305	528.5156	88.7258
Standard deviation:	18.5	0.5005	0.0000	4.1002	4.2130	12.7271	48.9553	10.7292
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
2								
Mean:	309.9	3.1248	100.0000	42.8070	58.3277	164.1024	526.5806	89.5767
Standard deviation:	7.8	0.3432	0.0000	4.3306	4.8568	11.3044	43.2084	7.0764
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3								
Mean:	308.7	3.1623	100.0000	43.2824	58.0917	163.5371	526.3789	92.3645
Standard deviation:	15.9	0.4665	0.0000	3.3585	5.0583	18.3315	34.4989	10.9394
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
4								
Mean:	310.3	3.3517	100.0000	43.4754	58.7346	164.4068	564.7740	92.3062
Standard deviation:	23.0	0.4941	0.0000	5.7519	5.5639	13.0502	75.7504	11.3656
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(9)

*(+) = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance
%($) = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

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Group	Terminal Body wt. (g)	Pituitary gland	Seminal vesicles	Spleen	Testes	Thymus
Male Animals						
1						
Mean:	309.1	0.4839	49.2407	34.6479	151.9882	25.8206
Standard deviation:	18.5	0.0963	8.4807	5.7044	14.8294	5.9914
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)
2						
Mean:	309.9	0.4744	47.7910	32.0771	153.6751	32.6000
Standard deviation:	7.8	0.0865	12.8491	5.0731	9.6626	8.9052
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)
3						
Mean:	308.7	0.4537	45.7370	33.8516	153.3421	25.9785
Standard deviation:	15.9	0.0613	8.3428	5.9277	11.8202	6.1405
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)
4						
Mean:	310.3	0.5809	53.1617	35.1070	150.2226	24.2120
Standard deviation:	23.0	0.1147	9.9136	10.2888	13.6547	5.6996
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)

*(+) = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance
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Group	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs	Ovaries
Female Animals								
1								
Mean:	212.6	4.0471	100.0000	45.5944	120.5404	422.8045	87.4052	5.9002
Standard deviation:	13.6	0.6639	0.0000	3.6978	12.3952	48.6271	11.7340	1.1017
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
2								
Mean:	212.0	3.7239	100.0000	44.8308	117.0894	408.7192	85.8067	5.7842
Standard deviation:	8.1	0.4677	0.0000	4.6178	9.5995	41.5741	9.9256	0.6569
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
3								
Mean:	210.3	3.6683	100.0000	44.9249	114.6700	391.7837	83.8030	5.3658
Standard deviation:	11.5	0.5873	0.0000	2.7710	12.4206	42.1405	12.3352	0.9686
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)
4								
Mean:	208.8	4.0413	100.0000	44.4199	117.1798	412.9518	88.6999	5.7289
Standard deviation:	7.6	0.6451	0.0000	2.2901	8.2604	31.2799	18.7634	1.1305
Number of observ. :	(10)	(10)	(10)	(10)	(10)	(10)	(10)	(10)

*(+) = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance
%($) = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

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Group	Terminal Body wt. (g)	Pituitary gland	Spleen	Thymus	Uterus
			Female Animals		
1					
Mean:	212.6	0.7127	24.1826	25.2678	27.4335
Standard deviation:	13.6	0.0956	2.9550	4.7602	3.9068
Number of observ. :	(10)	(10)	(10)	(10)	(10)
2					
Mean:	212.0	0.6504	26.8606	27.3059	29.6705
Standard deviation:	8.1	0.0844	4.1270	4.6673	9.5260
Number of observ. :	(10)	(10)	(10)	(10)	(10)
3					
Mean:	210.3	0.6794	25.4606	23.9442	32.8497
Standard deviation:	11.5	0.1004	4.0048	4.6602	9.2346
Number of observ. :	(10)	(10)	(10)	(10)	(10)
4					
Mean:	208.8	0.6999	26.4993	22.2884	27.1482
Standard deviation:	7.6	0.0939	3.4112	2.7202	3.2818
Number of observ. :	(10)	(10)	(10)	(10)	(10)

*(+) = mean value of group was significantly different from control at P = 0.05(0.01) with Dunnett's test of significance
%($) = mean value of group was significantly different from control at P = 0.05(0.01) with Modified T test of significance

	Incidence Summary Report for Gross Necropsy Observations Preface	Table 7

Key to Abbreviations

LN	=	Lymph Node
Submandib/Max	=	Submandibular/Submaxillary

Corresponding exposure levels for each group were as follows:

Group 1	-	0 ppm
Group 2	-	90 ppm
Group 3	-	900 ppm
Group 4	-	9000 ppm

Huntingdon Life Sciences
Princeton Research Center
East Millstone, New Jersey
Terminal Sacrifice

Incidence Summary Report for Gross Necropsy Observations
Study number: 036143

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	-- Males --				-- Females --			
Group:	1	2	3	4	1	2	3	4
Number in group:	10	10	10	10	10	10	10	10
Within normal limits	8	8	8	8	9	8	9	9
Cecum								
Abnormal Contents	0	1	0	0	0	0	0	0
Ileum								
Abnormal Contents	0	1	0	0	0	0	0	0
Jejunum								
Abnormal Contents	0	1	0	0	0	0	0	0
Kidneys								
Dilated Pelvis	0	0	2	0	0	0	0	0
Lungs								
Discolored	0	2	0	1	0	1	0	1
Seminal vesicles								
Small	1	0	0	0	0	0	0	0
Skin-protocol								
Hair Thin/Absent	0	0	0	0	0	1	0	0
Spleen								
Irregular Surface	0	0	0	1	0	0	0	0
Discolored	0	0	0	1	0	0	0	0
Thymus								
Discolored	0	1	0	0	0	0	1	0
Urinary bladder								
Calculus	0	0	1	0	0	0	0	0
Thickened	0	0	1	0	0	0	0	0
Skin (other)								
Sore	1	0	0	0	0	0	0	0
Submandib/Max LN								
Enlarged	0	0	1	0	0	0	0	0
Lymph Node,other								
Enlarged	0	0	1	0	0	0	0	0

Huntingdon Life Sciences
Princeton Research Center
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Incidence Summary Report for Gross Necropsy Observations
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	-- Males --				-- Females --			
Group:	1	2	3	4	1	2	3	4
Number in group:	10	10	10	10	10	10	10	10
Extremity								
Hair thin/ absent	0	0	0	0	1	0	0	0

	Chamber Monitoring Results	Appendix A

Group 1 – 0 ppm (Air Control)														
Day	Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration Mean (ppm)	Individual (ppm)				Particle Size Determinations MMAD (µm)	GSD	TMC (mg/m³)	Chamber Environment Mean Temperature (°C)	Humidity (%)
0	8-Jul-03	1	0	0.00	0.00	0.00	0.00	0.00	0.931	2.230	8.19E-03	23	54
1	9-Jul-03	2	0	0.00	0.00	0.00	0.00	0.00	1.675	2.256	3.14E-03	24	55
2	10-Jul-03	3	0	0.00	0.00	0.00	0.00	0.00	1.055	2.412	3.37E-03	23	56
3	11-Jul-03	4	0	0.00	0.00	0.00	0.00	0.00	0.874	2.087	6.17E-03	23	55
4	12-Jul-03	5	0	0.00	0.00	0.00	0.00	0.00	3.764	2.341	2.18E-03	24	55
5	13-Jul-03	6	0	0.00	0.00	0.00	0.00	0.00	1.067	2.413	7.27E-03	23	55
6	14-Jul-03	7	0	0.00	0.00	0.00	0.00	0.00	1.546	2.127	1.51E-03	23	55
7	15-Jul-03	8	0	0.00	0.00	0.00	No Value	0.00	0.860	1.671	3.48E-03	23	55
8	16-Jul-03	9	0	0.00	0.00	0.00	0.00	0.00	0.952	2.022	4.03E-03	23	55
9	17-Jul-03	10	0	0.00	0.00	0.00	0.00	0.00	0.997	2.625	2.69E-03	24	54
10	18-Jul-03	11	0	0.00	0.00	0.00	0.00	0.00	2.107	2.111	2.39E-03	24	60
11	19-Jul-03	12	0	0.00	0.00	0.00	0.00	0.00	1.551	1.945	1.02E-03	23	56
12	20-Jul-03	13	0	0.00	0.00	0.00	0.00	0.00	2.118	2.160	1.20E-03	23	55
13	21-Jul-03	14	0	0.00	0.00	0.00	0.00	0.00	0.778	1.324	1.33E-02	23	55
14	22-Jul-03	15	0	0.00	0.00	0.00	0.00	0.00	0.791	1.340	8.28E-03	22	57
		Mean	**0**		**0.00**				**1.404**	**2.071**	**4.55E-03**	**23.2**	**55.5**
		S.D.	**0**		**0.00**				**0.796**	**0.374**	**3.44E-03**	**0.6**	**1.5**

Key: MMAD = Mass Median Aerodynamic Diameter; GSD = Geometric Standard Deviation; TMC = Total Mass Concentration; ppm = parts per million; µm = microns; mg/m³ = milligrams per cubic meter.

	Chamber Monitoring Results	Appendix A

Group 2 – 90 ppm														
Day	Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration					Particle Size Determinations			Chamber Environment Mean	
				Mean (ppm)	Individual (ppm)				MMAD (µm)	GSD	TMC (mg/m^3)	Temperature (°C)	Humidity (%)
0	8-Jul-03	1	84.3	88.48	90.5	88.2	77.9	97.3	1.496	2.749	1.11E-02	23	57
1	9-Jul-03	2	84.3	90.73	84.7	93.9	92.7	91.6	1.941	2.249	2.96E-03	23	57
2	10-Jul-03	3	84.3	90.73	92.7	88.2	92.7	89.3	3.558	3.118	5.56E-03	23	57
3	11-Jul-03	4	84.3	89.58	95.0	79.0	92.7	91.6	0.860	1.774	5.96E-03	23	57
4	12-Jul-03	5	84.3	90.48	93.9	90.5	88.2	89.3	1.477	2.231	9.60E-04	23	56
5	13-Jul-03	6	84.3	90.48	91.6	91.6	90.5	88.2	0.918	1.972	4.02E-03	23	56
6	14-Jul-03	7	84.3	92.45	91.6	91.6	93.9	92.7	3.381	2.163	3.06E-03	23	56
7	15-Jul-03	8	84.3	91.95	90.5	93.9	101	82.4	0.912	2.039	4.27E-03	23	56
8	16-Jul-03	9	84.3	90.73	88.2	92.7	92.7	89.3	0.889	1.694	3.59E-03	23	58
9	17-Jul-03	10	84.3	91.88	87.0	93.9	95.0	91.6	0.854	2.008	2.17E-03	23	56
10	18-Jul-03	11	84.3	92.73	89.3	87.0	97.3	97.3	2.417	2.151	2.98E-03	24	61
11	19-Jul-03	12	84.3	92.15	80.1	103	96.2	89.3	1.465	1.843	8.70E-04	23	58
12	20-Jul-03	13	84.3	93.88	95.0	97.3	92.7	90.5	4.966	2.568	1.78E-03	23	56
13	21-Jul-03	14	84.3	93.03	96.2	95.0	89.3	91.6	0.789	1.843	1.48E-02	23	57
14	22-Jul-03	15	84.3	89.60	95.0	93.9	83.6	85.9	0.795	1.376	8.69E-03	22	57
		Mean	**84.3**		**91.26**				**1.781**	**2.119**	**4.85E-03**	**23.0**	**57.0**
		S.D.	**0.0**		**4.74**				**1.268**	**0.437**	**3.92E-03**	**0.4**	**1.3**

Key: MMAD = Mass Median Aerodynamic Diameter; GSD = Geometric Standard Deviation; TMC = Total Mass Concentration; ppm = parts per million; µm = microns; mg/m^3 = milligrams per cubic meter.

	Chamber Monitoring Results	Appendix A

Group 3 – 900 ppm													
Day	Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration Mean (ppm)	Individual (ppm)				Particle Size Determinations MMAD (µm)	GSD	TMC (mg/m³)	Chamber Environment Mean Temperature (°C)	Humidity (%)
0	8-Jul-03	1	908	877.5	864	879	864	903	0.907	2.201	7.22E-03	23	54
1	9-Jul-03	2	915	890.5	902	870	870	920	1.192	2.066	2.16E-03	24	54
2	10-Jul-03	3	915	899.8	941	905	875	878	0.940	1.941	2.96E-03	23	55
3	11-Jul-03	4	915	896.8	878	893	909	907	0.844	1.669	5.44E-03	23	54
4	12-Jul-03	5	915	922.0	940	912	920	916	2.125	2.382	1.25E-03	23	54
5	13-Jul-03	6	915	916.5	917	918	918	913	0.952	1.667	2.78E-03	23	54
6	14-Jul-03	7	914	889.3	907	895	889	866	6.460	2.667	3.85E-03	23	53
7	15-Jul-03	8	915	896.8	922	910	874	881	0.876	1.914	3.64E-03	23	53
8	16-Jul-03	9	915	919.8	932	931	908	908	0.923	1.885	4.10E-03	23	53
9	17-Jul-03	10	915	921.5	920	928	916	922	1.764	2.442	3.18E-03	23	53
10	18-Jul-03	11	915	889.8	905	908	919	827	1.516	1.955	2.05E-03	24	59
11	19-Jul-03	12	915	911.8	928	904	919	896	0.990	1.486	5.76E-04	23	54
12	20-Jul-03	13	915	933.3	972	942	897	922	6.649	2.500	2.22E-03	23	54
13	21-Jul-03	14	915	924.5	945	918	909	926	0.784	1.564	1.40E-02	23	53
14	22-Jul-03	15	899	967.8	1060	989	907	915	0.796	1.463	8.92E-03	22	54
		Mean	**913**		**910.5**				**1.848**	**1.987**	**4.29E-03**	**23.1**	**54.1**
		S.D.	**4**		**32.9**				**1.950**	**0.384**	**3.47E-03**	**0.5**	**1.5**

Key: MMAD = Mass Median Aerodynamic Diameter; GSD = Geometric Standard Deviation; TMC = Total Mass Concentration; ppm = parts per million; µm = microns; mg/m³ = milligrams per cubic meter.

	Chamber Monitoring Results	Appendix A

Group 4 – 9000 ppm														
Day	Date	Exposure Number	Nominal (ppm)	Analytical Chamber Concentration Mean (ppm)	Individual (ppm)				Particle Size Determinations MMAD (µm)	GSD	TMC (mg/m³)	Chamber Environment Mean Temperature (°C)	Humidity (%)
0	8-Jul-03	1	8570	8998	9150	8840	8950	9050	0.859	1.593	5.91E-03	23	54
1	9-Jul-03	2	8570	8940	8810	8810	9070	9070	8.251	2.839	4.43E-03	23	55
2	10-Jul-03	3	8570	9283	9580	9440	9170	8940	0.986	1.656	2.15E-02	23	54
3	11-Jul-03	4	8570	9140	9120	9100	9120	9220	0.839	1.529	5.44E-03	23	54
4	12-Jul-03	5	8570	9100	9050	9180	9050	9120	1.533	1.946	1.06E-03	23	54
5	13-Jul-03	6	8570	9188	9220	9340	9120	9070	15.70	3.508	6.59E-03	23	54
6	14-Jul-03	7	8560	9185	9120	9140	9310	9170	1.220	1.886	1.18E-03	23	54
7	15-Jul-03	8	8570	9103	8970	9140	9180	9120	0.909	2.208	4.31E-03	23	54
8	16-Jul-03	9	8750	9100	7250	9600	9730	9820	0.915	1.795	4.16E-03	23	54
9	17-Jul-03	10	8570	9298	9150	9370	9320	9350	0.859	1.908	2.28E-03	23	54
10	18-Jul-03	11	8570	9430	9350	9300	9540	9530	2.410	2.075	3.30E-03	24	59
11	19-Jul-03	12	8570	9400	9420	9470	9400	9310	3.613	2.051	2.54E-03	23	55
12	20-Jul-03	13	8570	9188	9080	9120	9250	9300	1.622	2.086	8.12E-04	23	55
13	21-Jul-03	14	8570	9233	9100	9210	9350	9270	0.786	1.493	1.49E-02	23	54
14	22-Jul-03	15	8570	9370	9410	9420	9310	9340	0.806	1.598	1.00E-02	22	56
		Mean	**8581**		**9197**				**2.754**	**2.011**	**5.89E-03**	**23.0**	**54.7**
		S.D.	**47**		**328**				**4.073**	**0.536**	**5.68E-03**	**0.4**	**1.3**

Key: MMAD = Mass Median Aerodynamic Diameter; GSD = Geometric Standard Deviation; TMC = Total Mass Concentration; ppm = parts per million; µm = microns; mg/m³ = milligrams per cubic meter.

Huntingdon Life Sciences 03-6143

APPENDIX B

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

ANIMAL TERMINATION HISTORY

MALES GROUP 1 0 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
1211	Terminal Sacrifice	22-JUL-03	3	14
1212	Terminal Sacrifice	22-JUL-03	3	14
1213	Terminal Sacrifice	22-JUL-03	3	14
1214	Terminal Sacrifice	22-JUL-03	3	14
1215	Terminal Sacrifice	22-JUL-03	3	14
1216	Terminal Sacrifice	23-JUL-03	3	15
1217	Terminal Sacrifice	23-JUL-03	3	15
1218	Terminal Sacrifice	23-JUL-03	3	15
1219	Terminal Sacrifice	23-JUL-03	3	15
1220	Terminal Sacrifice	23-JUL-03	3	15

APPENDIX B

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

ANIMAL TERMINATION HISTORY

MALES GROUP 2 90 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
2211	Terminal Sacrifice	22-JUL-03	3	14
2212	Terminal Sacrifice	22-JUL-03	3	14
2213	Terminal Sacrifice	22-JUL-03	3	14
2214	Terminal Sacrifice	22-JUL-03	3	14
2215	Terminal Sacrifice	22-JUL-03	3	14
2216	Terminal Sacrifice	23-JUL-03	3	15
2217	Terminal Sacrifice	23-JUL-03	3	15
2218	Terminal Sacrifice	23-JUL-03	3	15
2219	Terminal Sacrifice	23-JUL-03	3	15
2220	Terminal Sacrifice	23-JUL-03	3	15

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APPENDIX B

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

ANIMAL TERMINATION HISTORY

MALES GROUP 3 900 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
3211	Terminal Sacrifice	22-JUL-03	3	14
3212	Terminal Sacrifice	22-JUL-03	3	14
3213	Terminal Sacrifice	22-JUL-03	3	14
3214	Terminal Sacrifice	22-JUL-03	3	14
3215	Terminal Sacrifice	22-JUL-03	3	14
3216	Terminal Sacrifice	23-JUL-03	3	15
3217	Terminal Sacrifice	23-JUL-03	3	15
3218	Terminal Sacrifice	23-JUL-03	3	15
3219	Terminal Sacrifice	23-JUL-03	3	15
3220	Terminal Sacrifice	23-JUL-03	3	15

APPENDIX B

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

ANIMAL TERMINATION HISTORY

MALES GROUP 4 9000 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
4211	Terminal Sacrifice	22-JUL-03	3	14
4212	Terminal Sacrifice	22-JUL-03	3	14
4213	Terminal Sacrifice	22-JUL-03	3	14
4214	Terminal Sacrifice	22-JUL-03	3	14
4215	Terminal Sacrifice	22-JUL-03	3	14
4216	Terminal Sacrifice	23-JUL-03	3	15
4217	Terminal Sacrifice	23-JUL-03	3	15
4218	Terminal Sacrifice	23-JUL-03	3	15
4219	Terminal Sacrifice	23-JUL-03	3	15
4220	Terminal Sacrifice	23-JUL-03	3	15

APPENDIX B

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

ANIMAL TERMINATION HISTORY

FEMALES GROUP 1 0 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
1711	Terminal Sacrifice	22-JUL-03	3	14
1712	Terminal Sacrifice	22-JUL-03	3	14
1713	Terminal Sacrifice	22-JUL-03	3	14
1714	Terminal Sacrifice	22-JUL-03	3	14
1715	Terminal Sacrifice	22-JUL-03	3	14
1716	Terminal Sacrifice	23-JUL-03	3	15
1717	Terminal Sacrifice	23-JUL-03	3	15
1718	Terminal Sacrifice	23-JUL-03	3	15
1719	Terminal Sacrifice	23-JUL-03	3	15
1720	Terminal Sacrifice	23-JUL-03	3	15

APPENDIX B

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

ANIMAL TERMINATION HISTORY

FEMALES GROUP 2 90 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
2711	Terminal Sacrifice	22-JUL-03	3	14
2712	Terminal Sacrifice	22-JUL-03	3	14
2713	Terminal Sacrifice	22-JUL-03	3	14
2714	Terminal Sacrifice	22-JUL-03	3	14
2715	Terminal Sacrifice	22-JUL-03	3	14
2716	Terminal Sacrifice	23-JUL-03	3	15
2717	Terminal Sacrifice	23-JUL-03	3	15
2718	Terminal Sacrifice	23-JUL-03	3	15
2719	Terminal Sacrifice	23-JUL-03	3	15
2720	Terminal Sacrifice	23-JUL-03	3	15

APPENDIX B

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

ANIMAL TERMINATION HISTORY

FEMALES GROUP 3 900 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
3711	Terminal Sacrifice	22-JUL-03	3	14
3712	Terminal Sacrifice	22-JUL-03	3	14
3713	Terminal Sacrifice	22-JUL-03	3	14
3714	Terminal Sacrifice	22-JUL-03	3	14
3715	Terminal Sacrifice	22-JUL-03	3	14
3716	Terminal Sacrifice	23-JUL-03	3	15
3717	Terminal Sacrifice	23-JUL-03	3	15
3718	Terminal Sacrifice	23-JUL-03	3	15
3719	Terminal Sacrifice	23-JUL-03	3	15
3720	Terminal Sacrifice	23-JUL-03	3	15

APPENDIX B

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

ANIMAL TERMINATION HISTORY

FEMALES GROUP 4 9000 PPM

ANIMAL#	TYPE OF DEATH	DATE OF DEATH	WEEK OF STUDY	STUDY DAY
4711	Terminal Sacrifice	22-JUL-03	3	14
4712	Terminal Sacrifice	22-JUL-03	3	14
4713	Terminal Sacrifice	22-JUL-03	3	14
4714	Terminal Sacrifice	22-JUL-03	3	14
4715	Terminal Sacrifice	22-JUL-03	3	14
4716	Terminal Sacrifice	23-JUL-03	3	15
4717	Terminal Sacrifice	23-JUL-03	3	15
4718	Terminal Sacrifice	23-JUL-03	3	15
4719	Terminal Sacrifice	23-JUL-03	3	15
4720	Terminal Sacrifice	23-JUL-03	3	15

	Individual Clinical Observations Preface	Appendix C

For summarization purposes, descriptive comments [i.e., location of scab(s) and sore(s), etc.] are not presented in this appendix. These data are contained in the study raw data if needed.

APPENDIX C

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 1 0 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY -7	0	7	13	14	15
1211	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
1212	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
1213	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
1214	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
1215	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
1216	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
1217	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
1218	WITHIN NORMAL LIMITS	P	P				
	Terminal Sacrifice						P
	DERMAL GENERAL: Ulceration - Cervical			P	P		
	DERMAL GENERAL: Scab(s)			P	P		
1219	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
1220	WITHIN NORMAL LIMITS	P	P				
	Terminal Sacrifice						P
	DERMAL GENERAL: Alopecia - Extremities/Snout			2	2		

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

APPENDIX C

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 2 90 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY	-7	0	7	13	14	15
2211	WITHIN NORMAL LIMITS		P	P	P	P		
	Terminal Sacrifice						P	
2212	WITHIN NORMAL LIMITS		P	P	P	P		
	Terminal Sacrifice						P	
2213	WITHIN NORMAL LIMITS		P	P	P	P		
	Terminal Sacrifice						P	
2214	WITHIN NORMAL LIMITS		P	P	P	P		
	Terminal Sacrifice						P	
2215	WITHIN NORMAL LIMITS		P	P	P	P		
	Terminal Sacrifice						P	
2216	WITHIN NORMAL LIMITS		P	P	P	P		
	Terminal Sacrifice							P
2217	WITHIN NORMAL LIMITS		P	P	P	P		
	Terminal Sacrifice							P
2218	WITHIN NORMAL LIMITS		P	P	P	P		
	Terminal Sacrifice							P
2219	WITHIN NORMAL LIMITS		P	P	P	P		
	Terminal Sacrifice							P
2220	WITHIN NORMAL LIMITS		P	P	P	P		
	Terminal Sacrifice							P

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

APPENDIX C

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 3 900 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY -7	0	7	13	14	15
3211	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
3212	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
3213	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
3214	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
3215	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
3216	WITHIN NORMAL LIMITS	P	P				
	Terminal Sacrifice						P
	OCULAR: Chromodacryorrhea - Unilateral			P	P		
3217	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
3218	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
3219	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
3220	WITHIN NORMAL LIMITS	P	P		P		
	Terminal Sacrifice						P
	DERMAL GENERAL: RED STAINS - SNOUT			1			

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

Huntingdon Life Sciences 03-6143

APPENDIX C

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

MALES GROUP 4 9000 PPM

ANIMAL#	OBSERVATIONS DAY OF STUDY	-7	0	7	13	14	15
4211	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
4212	WITHIN NORMAL LIMITS	P	P				
	Terminal Sacrifice					P	
	DERMAL GENERAL: Alopecia - Extremities/Snout			2	2		
4213	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
4214	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
4215	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
4216	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
4217	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
4218	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
4219	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
4220	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P

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

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APPENDIX C

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 1 0 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY -7	0	7	13	14	15
1711	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
1712	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
1713	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
1714	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
1715	WITHIN NORMAL LIMITS	P	P				
	Terminal Sacrifice					P	
	DERMAL GENERAL: RED STAINS - SNOUT			1	1		
1716	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
1717	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
1718	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
1719	WITHIN NORMAL LIMITS	P	P				
	Terminal Sacrifice						P
	DERMAL GENERAL: Alopecia - Extremities/Snout			3	3		
1720	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P

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

APPENDIX C

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 2 90 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY -7	0	7	13	14	15
2711	WITHIN NORMAL LIMITS	P	P				
	Terminal Sacrifice					P	
	DERMAL GENERAL: Alopecia - General			2	2		
2712	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
2713	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
2714	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
2715	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
2716	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
2717	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
2718	WITHIN NORMAL LIMITS	P	P				
	Terminal Sacrifice						P
	DERMAL GENERAL: Alopecia - Extremities/Snout			2	2		
2719	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
2720	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P

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

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APPENDIX C

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 3 900 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY -7	0	7	13	14	15
3711	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
3712	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
3713	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
3714	WITHIN NORMAL LIMITS	P	P				
	Terminal Sacrifice					P	
	DERMAL GENERAL: Alopecia - Extremities/Snout			2	2		
3715	WITHIN NORMAL LIMITS	P	P				
	Terminal Sacrifice					P	
	DERMAL GENERAL: Scab(s)			P	P		
	DERMAL GENERAL: Alopecia - Extremities/Snout			2	2		
3716	WITHIN NORMAL LIMITS	P	P				
	Terminal Sacrifice						P
	DERMAL GENERAL: Alopecia - Extremities/Snout			3	3		
3717	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
3718	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
3719	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P

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

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APPENDIX C

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 3 900 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY	-7	0	7	13	14	15
3720	WITHIN NORMAL LIMITS		P	P	P	P		
	Terminal Sacrifice							P

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

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APPENDIX C

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL CLINICAL OBSERVATIONS

FEMALES GROUP 4 9000 PPM

ANIMAL#	OBSERVATIONS	DAY OF STUDY: -7	0	7	13	14	15
4711	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
4712	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
4713	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
4714	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice					P	
4715	WITHIN NORMAL LIMITS	P	P				
	Terminal Sacrifice					P	
	DERMAL GENERAL: Alopecia - Extremities/Snout			2	2		
4716	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
4717	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
4718	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
4719	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P
4720	WITHIN NORMAL LIMITS	P	P	P	P		
	Terminal Sacrifice						P

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

APPENDIX D

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

MALES GROUP 1 0 PPM

	DAY OF STUDY			
ANIMAL#	-7	0	7	13
1211	214	283	310	335
1212	211	282	325	362
1213	201	264	299	320
1214	205	273	307	338
1215	214	288	320	350
1216	223	295	325	349
1217	199	262	295	313
1218	203	269	293	311
1219	197	260	301	316
1220	208	276	310	337
MEAN	208	275	308	333
S.D.	8.2	11.8	11.8	17.6
N	10	10	10	10

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APPENDIX D

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

MALES GROUP 2 90 PPM

	DAY OF STUDY			
ANIMAL#	-7	0	7	13
2211	219	281	310	328
2212	206	276	308	331
2213	214	280	314	348
2214	186	254	292	314
2215	212	289	322	344
2216	205	271	308	331
2217	217	284	311	339
2218	200	268	302	328
2219	208	274	307	329
2220	202	266	297	318
MEAN	207	274	307	331
S.D.	9.7	10.1	8.7	10.7
N	10	10	10	10

APPENDIX D

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

MALES GROUP 3 900 PPM

ANIMAL#	DAY OF STUDY -7	0	7	13
3211	213	286	315	326
3212	212	279	307	333
3213	208	274	291	307
3214	206	268	300	335
3215	202	273	300	327
3216	218	290	324	342
3217	190	263	290	307
3218	199	272	320	356
3219	216	290	327	341
3220	205	274	311	334
MEAN	207	277	308	331
S.D.	8.7	9.0	13.3	15.3
N	10	10	10	10

APPENDIX D

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

MALES GROUP 4 9000 PPM

	DAY OF STUDY			
ANIMAL#	-7	0	7	13
4211	202	268	302	337
4212	200	261	290	299
4213	220	301	335	361
4214	209	280	316	342
4215	213	287	336	364
4216	198	262	300	324
4217	209	276	316	340
4218	218	286	322	351
4219	206	267	286	298
4220	204	273	316	340
MEAN	208	276	312	336
S.D.	7.3	12.8	17.4	22.8
N	10	10	10	10

APPENDIX D

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

FEMALES GROUP 1 0 PPM

ANIMAL#	DAY OF STUDY -7	0	7	13
1711	180	207	234	241
1712	167	195	216	229
1713	178	214	232	243
1714	165	196	202	210
1715	174	218	228	234
1716	155	184	192	198
1717	171	200	210	226
1718	180	207	201	235
1719	176	212	227	241
1720	163	197	216	229
MEAN	171	203	216	228
S.D.	8.2	10.5	14.5	14.6
N	10	10	10	10

APPENDIX D

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

FEMALES GROUP 2 90 PPM

	DAY OF STUDY			
ANIMAL#	-7	0	7	13
2711	164	194	208	226
2712	161	188	204	208
2713	178	199	213	222
2714	169	199	212	230
2715	161	199	218	231
2716	183	213	232	248
2717	168	183	212	223
2718	175	201	211	218
2719	174	202	225	237
2720	179	197	206	225
MEAN	171	198	214	227
S.D.	7.8	8.1	8.7	10.8
N	10	10	10	10

APPENDIX D

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

FEMALES GROUP 3 900 PPM

	DAY OF STUDY			
ANIMAL#	-7	0	7	13
3711	179	221	227	236
3712	166	192	210	219
3713	169	190	209	221
3714	161	189	200	220
3715	168	195	216	224
3716	177	215	231	252
3717	178	211	223	234
3718	173	199	220	231
3719	162	187	203	215
3720	185	206	210	232
MEAN	172	200	215	228
S.D.	7.9	12.1	10.3	10.9
N	10	10	10	10

APPENDIX D

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHTS (GRAMS)

FEMALES GROUP 4 9000 PPM

	DAY OF STUDY			
ANIMAL#	-7	0	7	13
4711	161	188	200	212
4712	184	216	231	238
4713	179	209	218	231
4714	173	198	214	235
4715	172	185	212	228
4716	167	195	215	227
4717	166	189	206	220
4718	177	203	218	235
4719	178	209	219	224
4720	161	189	202	209
MEAN	172	198	213	226
S.D.	7.9	10.7	9.3	9.8
N	10	10	10	10

APPENDIX E

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHT CHANGE FROM BASELINE (GRAMS)

MALES GROUP 1 0 PPM

	DAY OF STUDY	
ANIMAL#	0-7	0-13
1211	27	52
1212	43	80
1213	35	56
1214	34	65
1215	31	62
1216	30	54
1217	33	51
1218	24	42
1219	41	56
1220	34	60
MEAN	33	58
S.D.	5.9	10.2
N	10	10

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APPENDIX E

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHT CHANGE FROM BASELINE (GRAMS)

MALES GROUP 2 90 PPM

	DAY OF STUDY	
ANIMAL#	0-7	0-13
2211	29	47
2212	32	55
2213	34	69
2214	38	60
2215	33	55
2216	37	60
2217	27	56
2218	34	60
2219	33	55
2220	31	52
MEAN	33	57
S.D.	3.3	5.7
N	10	10

APPENDIX E

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHT CHANGE FROM BASELINE (GRAMS)

MALES GROUP 3 900 PPM

	DAY OF STUDY	
ANIMAL#	0-7	0-13
3211	29	41
3212	28	55
3213	17	33
3214	32	67
3215	27	54
3216	35	53
3217	27	43
3218	48	84
3219	37	51
3220	37	60
MEAN	32	54
S.D.	8.2	14.3
N	10	10

APPENDIX E

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHT CHANGE FROM BASELINE (GRAMS)

MALES GROUP 4 9000 PPM

ANIMAL#	DAY OF STUDY 0-7	0-13
4211	34	69
4212	29	39
4213	34	60
4214	36	62
4215	49	77
4216	38	62
4217	40	64
4218	36	65
4219	19	31
4220	43	67
MEAN	36	59
S.D.	8.2	14.0
N	10	10

APPENDIX E

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHT CHANGE FROM BASELINE (GRAMS)

FEMALES GROUP 1 0 PPM

ANIMAL#	DAY OF STUDY 0-7	0-13
1711	28	35
1712	21	34
1713	18	29
1714	6	14
1715	10	16
1716	8	14
1717	10	26
1718	-6	28
1719	15	29
1720	19	31
MEAN	13	25
S.D.	9.4	8.1
N	10	10

APPENDIX E

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHT CHANGE FROM BASELINE (GRAMS)

FEMALES GROUP 2 90 PPM

ANIMAL#	DAY OF STUDY 0-7	0-13
2711	14	32
2712	16	20
2713	14	23
2714	13	31
2715	18	32
2716	19	35
2717	29	40
2718	9	16
2719	23	35
2720	8	28
MEAN	16	29
S.D.	6.2	7.4
N	10	10

APPENDIX E

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHT CHANGE FROM BASELINE (GRAMS)

FEMALES GROUP 3 900 PPM

ANIMAL#	DAY OF STUDY 0-7	0-13
3711	5	15
3712	18	27
3713	19	31
3714	11	32
3715	22	30
3716	16	37
3717	12	23
3718	21	32
3719	15	28
3720	4	26
MEAN	14	28
S.D.	6.0	6.1
N	10	10

APPENDIX E

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL BODY WEIGHT CHANGE FROM BASELINE (GRAMS)

FEMALES GROUP 4 9000 PPM

	DAY OF STUDY	
ANIMAL#	0-7	0-13
4711	11	24
4712	14	21
4713	9	23
4714	16	37
4715	28	43
4716	20	32
4717	16	30
4718	16	32
4719	10	15
4720	13	20
MEAN	15	28
S.D.	5.4	8.6
N	10	10

APPENDIX F

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

MALES GROUP 1 0 PPM

ANIMAL#	DAY OF STUDY 0	7	13
1211	105	80	68
1212	106	88	77
1213	105	86	73
1214	104	81	73
1215	102	87	72
1216	104	81	66
1217	114	96	79
1218	99	SF	71
1219	107	87	74
1220	102	84	72
MEAN	105	86	72
S.D.	3.9	4.9	3.7
N	10	9	10

SF=Spilled Feeder

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APPENDIX F

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

MALES GROUP 2 90 PPM

	DAY	OF STUDY	
ANIMAL#	0	7	13
2211	101	80	68
2212	108	96	74
2213	96	78	72
2214	110	85	71
2215	107	85	72
2216	94	79	70
2217	103	81	73
2218	SF	85	SF
2219	104	86	72
2220	107	81	74
MEAN	103	84	72
S.D.	5.5	5.4	1.9
N	9	10	9

SF=Spilled Feeder

APPENDIX F

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

MALES GROUP 3 900 PPM

ANIMAL#	DAY OF STUDY 0	7	13
3211	98	77	61
3212	98	77	65
3213	102	85	68
3214	103	79	73
3215	105	81	73
3216	101	85	67
3217	112	SF	82
3218	112	91	79
3219	102	SF	SF
3220	106	87	72
MEAN	104	83	71
S.D.	4.8	4.9	6.8
N	10	8	9

SF=Spilled Feeder

APPENDIX F

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

MALES GROUP 4 9000 PPM

	DAY OF STUDY		
ANIMAL#	0	7	13
4211	106	85	78
4212	106	84	68
4213	108	84	76
4214	103	84	72
4215	108	89	76
4216	107	85	71
4217	104	SF	74
4218	100	79	70
4219	102	82	70
4220	106	88	76
MEAN	105	85	73
S.D.	2.7	2.9	3.4
N	10	9	10

SF=Spilled Feeder

APPENDIX F

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

FEMALES GROUP 1 0 PPM

ANIMAL#	DAY OF STUDY 0	7	13
1711	103	91	89
1712	97	91	93
1713	83	67	66
1714	92	82	82
1715	100	78	77
1716	103	87	82
1717	93	81	83
1718	101	86	92
1719	105	94	88
1720	100	85	83
MEAN	98	84	84
S.D.	6.7	7.7	8.1
N	10	10	10

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APPENDIX F

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

FEMALES GROUP 2 90 PPM

	DAY OF STUDY		
ANIMAL#	0	7	13
2711	99	83	82
2712	95	82	79
2713	94	82	80
2714	94	88	83
2715	105	84	82
2716	95	83	81
2717	89	88	85
2718	96	81	80
2719	100	94	83
2720	92	82	80
MEAN	96	85	82
S.D.	4.6	4.0	1.7
N	10	10	10

APPENDIX F

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

FEMALES GROUP 3 900 PPM

	DAY	OF STUDY	
ANIMAL#	0	7	13
3711	106	77	78
3712	91	82	78
3713	89	85	74
3714	98	83	83
3715	106	91	83
3716	102	90	87
3717	97	77	76
3718	93	83	78
3719	99	88	78
3720	89	79	82
MEAN	97	83	80
S.D.	6.5	4.9	3.7
N	10	10	10

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APPENDIX F

BUTANE: A 2-WEEK RANGE-FINDING INHALATION TOXICITY
STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

INDIVIDUAL FEED CONSUMPTION VALUES (GRAMS/KG/DAY)

FEMALES GROUP 4 9000 PPM

	DAY OF STUDY		
ANIMAL#	0	7	13
4711	95	81	81
4712	85	74	74
4713	95	79	78
4714	97	85	83
4715	86	87	78
4716	96	84	81
4717	101	84	85
4718	102	79	82
4719	105	83	81
4720	101	88	88
MEAN	96	83	81
S.D.	6.7	4.2	3.8
N	10	10	10

	Individual Organ Weights Preface	Appendix G

Table of Contents

Key to Abbreviations:

g	=	Grams
wt.	=	Weight
observ.	=	Observed

Corresponding exposure levels for each group were as follows:

Group 1	-	0 ppm
Group 2	-	90 ppm
Group 3	-	900 ppm
Group 4	-	9000 ppm

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Summary statistics for absolute organ weights (g)
Study number: 036143

Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Epididymides	Heart	Kidneys	Liver
				Male	Animals			
1211/M	1/1	315.2	0.0659	2.3524	0.8831	1.2113	3.1219	11.2229
1212/M	1/1	340.9	0.0779	2.1161	0.8795	1.2700	3.3570	11.6739
1213/M	1/1	299.6	0.0790	2.1910	0.9257	1.2608	3.4802	11.5151
1214/M	1/1	318.0	0.0775	2.1084	0.9665	1.2132	3.3066	12.2463
1215/M	1/1	319.6	0.0697	1.9983	0.9914	1.3306	3.5357	11.8423
1216/M	1/1	327.1	0.0495	2.1709	0.9101	1.2702	3.3033	12.0146
1217/M	1/1	284.9	0.0787	2.0274	0.8899	1.1873	3.3937	11.4718
1218/M	1/1	284.0	0.0709	2.0245	0.9167	1.2354	2.9964	9.2720
1219/M	1/1	295.2	0.0662	2.2644	0.9488	1.2634	3.4867	10.4590
1220/M	1/1	306.7	0.0661	2.1123	0.7430	1.3537	3.6502	10.9466
Mean:		309.1	0.0701	2.1366	0.9055	1.2596	3.3632	11.2665
Standard deviation:		18.5	0.0091	0.1118	0.0678	0.0521	0.1948	0.8728
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
2211/M	2/1	319.4	0.0646	2.2967	0.8654	1.1422	4.0617	10.9283
2212/M	2/1	309.7	0.0625	2.1840	1.0840	1.3245	3.7540	13.1403
2213/M	2/1	317.9	0.0641	2.2234	0.9197	1.1599	3.3920	10.8492
2214/M	2/1	302.6	0.0610	2.0995	0.8533	1.1801	3.3302	11.1593
2215/M	2/1	320.0	0.0608	2.1256	0.7896	1.3772	3.4737	12.6763
2216/M	2/1	305.6	0.0819	2.1377	0.9519	1.2177	3.8766	11.2297
2217/M	2/1	313.8	0.0654	2.0576	0.9671	1.2600	3.5812	10.6859
2218/M	2/1	303.3	0.0733	2.0497	0.9585	1.3226	3.0247	10.5742
2219/M	2/1	309.7	0.0700	2.2511	0.8697	1.3191	3.5155	10.8418
2220/M	2/1	297.0	0.0656	2.0314	0.9075	1.1865	3.2210	10.7727
Mean:		309.9	0.0669	2.1457	0.9167	1.2490	3.5231	11.2858
Standard deviation:		7.8	0.0065	0.0907	0.0807	0.0827	0.3106	0.8842
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
3211/M	3/1	309.9	0.0735	2.0526	0.8468	1.0490	3.4371	11.7409
3212/M	3/1	302.1	0.0782	2.1076	1.0421	1.0998	3.1994	10.0777
3213/M	3/1	281.9	0.0637	2.0772	0.8616	1.1181	3.0949	11.6085
3214/M	3/1	319.9	0.0680	2.0819	0.9312	1.3690	3.4997	11.7516
3215/M	3/1	305.6	0.0552	2.1419	0.9204	1.3282	3.4571	10.7455
3216/M	3/1	320.3	0.0783	2.1902	0.9235	1.2178	3.1060	11.6090
3217/M	3/1	285.0	0.0627	2.0794	1.0082	1.2281	4.1334	10.1027
3218/M	3/1	332.7	0.0504	2.1039	0.8802	1.2351	3.2266	11.5125
3219/M	3/1	319.2	0.0645	2.2961	0.9598	1.3259	3.5222	11.3351
3220/M	3/1	310.1	0.0735	2.0265	0.7834	1.3156	3.8557	10.7784
Mean:		308.7	0.0668	2.1157	0.9157	1.2287	3.4532	11.1262
Standard deviation:		15.9	0.0094	0.0781	0.0769	0.1095	0.3328	0.6532
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
4211/M	4/1	313.8	0.0670	2.1305	0.6847	1.2013	3.4865	13.7471
4212/M	4/1	272.6	0.0714	2.1315	0.9163	1.0588	3.1494	14.3715
4213/M	4/1	333.2	0.0673	2.1488	1.0888	1.4134	4.0238	11.9388

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Epididymides	Heart	Kidneys	Liver
4214/M	4/1	319.6	0.0781	2.2367	1.0265	1.2462	3.5106	11.4703
4215/M	4/1	339.7	0.0819	1.9393	0.8634	1.2140	3.2473	12.6075
4216/M	4/1	294.4	0.0787	2.0552	0.8380	1.1840	3.2364	10.0543
4217/M	4/1	315.6	0.0747	1.9791	1.0385	1.2512	3.0148	10.9185
4218/M	4/1	321.9	0.0572	2.1934	0.9513	1.2521	3.6623	11.0562
4219/M	4/1	273.2	0.0590	2.1335	0.9201	1.1280	3.3904	9.7437
4220/M	4/1	319.1	0.0703	2.1981	0.8528	1.4597	4.0735	13.3654
Mean:		310.3	0.0706	2.1146	0.9180	1.2409	3.4795	11.9273
Standard deviation:		23.0	0.0082	0.0959	0.1177	0.1199	0.3542	1.5663
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)

Terminal Sacrifice

Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Lungs	Pituitary gland	Seminal vesicles	Spleen	Testes	Thymus
				Male Animals				
1211/M	1/1	315.2	2.1416	0.0085	1.1188	0.7923	3.1825	0.5652
1212/M	1/1	340.9	1.6885	0.0081	0.9070	0.6460	3.1699	0.6183
1213/M	1/1	299.6	1.6849	0.0131	1.2821	0.7165	3.4404	0.4756
1214/M	1/1	318.0	1.7039	0.0110	1.0169	0.7688	3.3235	0.5702
1215/M	1/1	319.6	1.7760	0.0098	1.2273	0.9145	3.2119	0.5488
1216/M	1/1	327.1	1.9340	0.0070	1.0082	0.8558	3.5390	0.8313
1217/M	1/1	284.9	2.0982	0.0112	0.7250	0.5998	3.5353	0.4740
1218/M	1/1	284.0	1.7591	0.0112	0.8421	0.7317	3.2329	0.3408
1219/M	1/1	295.2	1.8181	0.0130	1.1282	0.5717	3.0258	0.4627
1220/M	1/1	306.7	2.3251	0.0102	1.2716	0.7804	2.7185	0.6296
Mean:		309.1	1.8929	0.0103	1.0527	0.7378	3.2380	0.5517
Standard deviation:		18.5	0.2237	0.0020	0.1878	0.1088	0.2473	0.1306
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
2211/M	2/1	319.4	1.9118	0.0106	1.2358	0.6039	3.2996	0.4855
2212/M	2/1	309.7	1.8854	0.0094	0.9328	0.7649	3.4350	0.8041
2213/M	2/1	317.9	1.7445	0.0072	0.7420	0.5152	3.1865	0.5974
2214/M	2/1	302.6	2.0464	0.0109	1.2701	0.6481	3.1290	0.7226
2215/M	2/1	320.0	2.0351	0.0091	1.3044	0.7489	3.3123	1.0754
2216/M	2/1	305.6	1.9782	0.0124	0.9126	0.7674	3.2673	0.5566
2217/M	2/1	313.8	1.9268	0.0076	0.8635	0.7008	3.3272	0.8079
2218/M	2/1	303.3	1.6726	0.0118	0.9278	0.8232	3.4983	0.7194
2219/M	2/1	309.7	1.9802	0.0117	0.6319	0.6354	3.1637	0.4979
2220/M	2/1	297.0	2.0065	0.0109	1.3847	0.6467	3.2881	0.6835
Mean:		309.9	1.9188	0.0102	1.0206	0.6855	3.2907	0.6950
Standard deviation:		7.8	0.1234	0.0018	0.2589	0.0927	0.1152	0.1771
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
3211/M	3/1	309.9	1.6186	0.0110	0.8585	0.6142	3.2044	0.5221
3212/M	3/1	302.1	1.7778	0.0100	0.9698	0.5390	3.4866	0.4081
3213/M	3/1	281.9	1.9818	0.0093	0.9675	0.6736	3.2393	0.5490
3214/M	3/1	319.9	2.1316	0.0093	1.1390	0.8862	3.2970	0.7738
3215/M	3/1	305.6	1.9146	0.0109	1.1763	0.6859	3.0687	0.5665
3216/M	3/1	320.3	2.0573	0.0082	0.7355	0.8131	3.5781	0.6960
3217/M	3/1	285.0	1.7030	0.0074	0.9485	0.8876	3.5555	0.3934
3218/M	3/1	332.7	2.1413	0.0094	0.9440	0.5532	3.0097	0.5021
3219/M	3/1	319.2	1.9011	0.0122	1.3034	0.8291	3.1313	0.4327
3220/M	3/1	310.1	2.2869	0.0084	0.6585	0.6847	2.8475	0.6390
Mean:		308.7	1.9514	0.0096	0.9701	0.7167	3.2418	0.5483
Standard deviation:		15.9	0.2107	0.0015	0.1966	0.1302	0.2421	0.1252
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
4211/M	4/1	313.8	1.8824	0.0146	1.1858	0.7955	2.4943	0.4492
4212/M	4/1	272.6	1.6222	0.0077	0.7730	1.2778	3.1529	0.3804
4213/M	4/1	333.2	3.2118E	0.0119	1.0016	0.7877	3.5094	0.6081

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Lungs	Pituitary gland	Seminal vesicles	Spleen	Testes	Thymus
4214/M	4/1	319.6	1.7943	0.0128	1.2707	0.6609	3.3324	0.5207
4215/M	4/1	339.7	2.2244	0.0130	0.7684	0.6981	3.0630	0.5664
4216/M	4/1	294.4	1.9059	0.0155	1.4111	0.5094	3.1164	0.5134
4217/M	4/1	315.6	2.0161	0.0118	1.1163	0.6939	3.1199	0.6882
4218/M	4/1	321.9	2.0086	0.0126	1.1662	0.8606	3.5808	0.4918
4219/M	4/1	273.2	1.9163	0.0094	1.1813	0.4996	2.9928	0.3218
4220/M	4/1	319.1	2.0964	0.0132	1.3858	0.6392	3.3889	0.5527
Mean:		310.3	1.9407	0.0123	1.1260	0.7423	3.1751	0.5093
Standard deviation:		23.0	0.1743	0.0023	0.2226	0.2212	0.3097	0.1068
Number of observ. :		(10)	(9)	(10)	(10)	(10)	(10)	(10)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
Female Animals								
1711/F	1/1	228.7	0.0710	2.2952	1.0707	2.7404	8.7900	1.8767
1712/F	1/1	211.5	0.0802	2.0181	0.8404	2.5833	8.5814	1.5302
1713/F	1/1	231.0	0.0817	1.9719	0.9851	2.3488	8.4595	1.5889
1714/F	1/1	196.5	0.0729	2.0141	0.8293	2.2710	7.7408	1.8199
1715/F	1/1	218.1	0.0772	1.9660	0.9831	2.4026	8.4867	1.7021
1716/F	1/1	186.2	0.0790	1.9645	0.8545	1.9016	7.4343	1.4163
1717/F	1/1	213.5	0.0699	2.0381	0.8666	2.3625	7.5544	2.2704
1718/F	1/1	207.5	0.1027	1.9692	1.0033	2.8171	9.2688	2.0025
1719/F	1/1	220.5	0.1040	2.0426	0.9450	2.7072	10.7876	1.7977
1720/F	1/1	212.5	0.0849	2.1461	0.9289	2.4812	9.1624	1.8404
Mean:		212.6	0.0824	2.0426	0.9307	2.4616	8.6266	1.7845
Standard deviation:		13.6	0.0120	0.1045	0.0811	0.2699	0.9889	0.2454
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
2711/F	2/1	211.6	0.0634	2.1453	1.0802	2.7516	8.2688	1.7156
2712/F	2/1	200.0	0.0784	1.8888	0.7568	2.2165	7.1844	1.5128
2713/F	2/1	207.3	0.0729	2.1966	0.8930	2.2497	8.0699	1.8456
2714/F	2/1	212.1	0.0668	2.0846	0.8701	2.2870	9.3651	1.5911
2715/F	2/1	222.1	0.0793	2.0129	0.9855	2.4415	9.3753	1.9332
2716/F	2/1	227.1	0.0880	1.9999	0.8584	2.3765	7.8176	1.8659
2717/F	2/1	209.5	0.0699	1.9975	0.9666	2.5272	7.9415	2.0897
2718/F	2/1	205.5	0.0748	2.0074	0.7788	2.0585	7.0505	1.7641
2719/F	2/1	217.1	0.0867	2.0918	0.9439	2.4318	9.0727	1.4948
2720/F	2/1	207.2	0.0805	2.0646	1.0592	2.6368	9.6121	1.7417
Mean:		212.0	0.0761	2.0489	0.9193	2.3977	8.3758	1.7555
Standard deviation:		8.1	0.0081	0.0870	0.1083	0.2068	0.9293	0.1884
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
3711/F	3/1	219.7	0.0678	2.1991	0.9888	2.3880	8.2227	1.5182
3712/F	3/1	204.6	0.0763	1.9793	0.8637	2.3346	7.5475	1.4740
3713/F	3/1	197.4	0.0740	2.0800	0.8545	2.3406	7.0501	1.4607
3714/F	3/1	204.2	0.0683	1.9917	0.8267	1.9076	6.7107	1.8785
3715/F	3/1	208.2	0.0682	1.9919	0.9060	2.5042	7.6715	1.4838
3716/F	3/1	228.9	0.0916	1.8765	0.9538	2.5986	8.7607	1.6451
3717/F	3/1	219.1	0.0726	2.0384	0.9400	2.3063	7.9016	2.0553
3718/F	3/1	219.1	0.0810	2.1864	1.0004	2.6599	9.3878	2.1966
3719/F	3/1	191.1	0.0559	1.9608	0.9079	2.2276	8.6460	1.4942
3720/F	3/1	210.4	0.0898	2.0712	0.9025	2.0556	7.8037	1.8707
Mean:		210.3	0.0746	2.0375	0.9144	2.3323	7.9702	1.7077
Standard deviation:		11.5	0.0108	0.1003	0.0570	0.2308	0.8089	0.2722
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
4711/F	4/1	196.1	0.0820	1.8995	0.8924	2.1683	7.7800	2.1989
4712/F	4/1	219.0	0.0970	2.0564	0.9584	2.7608	8.8181	1.5529
4713/F	4/1	209.1	0.0800	2.0926	0.9353	2.2320	7.6531	1.6539

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
4714/F	4/1	215.2	0.0745	2.0910	0.9015	2.4639	8.3588	1.5114
4715/F	4/1	208.3	0.0614	2.0838	0.8915	2.3180	8.4617	1.5927
4716/F	4/1	210.3	0.0969	1.9377	0.7647	2.0682	7.5866	1.5103
4717/F	4/1	206.3	0.0809	2.0110	0.8915	2.4104	7.7436	2.3782
4718/F	4/1	214.7	0.0964	2.0402	0.9395	2.5003	9.6128	1.8394
4719/F	4/1	212.7	0.0668	1.9062	0.8839	2.3224	8.0363	2.0997
4720/F	4/1	196.5	0.0802	2.1143	0.9262	2.4669	9.5193	1.5109
Mean:		208.8	0.0816	2.0233	0.8985	2.3711	8.3570	1.7848
Standard deviation:		7.6	0.0124	0.0811	0.0534	0.1959	0.7493	0.3264
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)

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Summary statistics for absolute organ weights (g)
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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovaries	Pituitary gland	Spleen	Thymus	Uterus
				Female	Animals		
1711/F	1/1	228.7	0.0973	0.0131	0.5178	0.4980	0.5269
1712/F	1/1	211.5	0.1470	0.0130	0.4452	0.6166	0.6972
1713/F	1/1	231.0	0.1340	0.0138	0.5554	0.3843	0.4940
1714/F	1/1	196.5	0.0915	0.0177	0.4323	0.4344	0.5441
1715/F	1/1	218.1	0.1216	0.0159	0.4882	0.5991	0.5936
1716/F	1/1	186.2	0.1027	0.0119	0.4980	0.5182	0.4749
1717/F	1/1	213.5	0.1296	0.0154	0.4914	0.5237	0.5105
1718/F	1/1	207.5	0.1444	0.0130	0.3809	0.4200	0.6537
1719/F	1/1	220.5	0.1231	0.0148	0.5115	0.6785	0.5358
1720/F	1/1	212.5	0.1075	0.0167	0.6202	0.4781	0.5563
Mean:		212.6	0.1199	0.0145	0.4941	0.5151	0.5587
Standard deviation:		13.6	0.0195	0.0019	0.0663	0.0934	0.0705
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)
2711/F	2/1	211.6	0.1295	0.0147	0.4590	0.4727	0.4922
2712/F	2/1	200.0	0.1166	0.0153	0.4368	0.4540	0.4704
2713/F	2/1	207.3	0.1148	0.0129	0.7112	0.5707	0.4916
2714/F	2/1	212.1	0.1060	0.0111	0.6946	0.6773	0.6591
2715/F	2/1	222.1	0.1048	0.0143	0.5900	0.5797	0.4281
2716/F	2/1	227.1	0.1312	0.0125	0.5760	0.6471	0.5485
2717/F	2/1	209.5	0.1386	0.0122	0.5591	0.4668	0.6060
2718/F	2/1	205.5	0.1207	0.0138	0.4991	0.5347	0.4578
2719/F	2/1	217.1	0.1151	0.0147	0.5190	0.7334	0.9903
2720/F	2/1	207.2	0.1053	0.0114	0.4668	0.4603	0.9431
Mean:		212.0	0.1183	0.0133	0.5512	0.5597	0.6087
Standard deviation:		8.1	0.0117	0.0015	0.0948	0.1000	0.2015
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)
3711/F	3/1	219.7	0.0996	0.0164	0.6182	0.4238	0.6116
3712/F	3/1	204.6	0.0901	0.0164	0.4272	0.5204	0.6460
3713/F	3/1	197.4	0.1069	0.0112	0.3780	0.5105	0.4786
3714/F	3/1	204.2	0.0923	0.0113	0.4750	0.4612	1.1381
3715/F	3/1	208.2	0.1273	0.0112	0.6026	0.6912	0.7001
3716/F	3/1	228.9	0.1413	0.0145	0.5450	0.5065	0.6162
3717/F	3/1	219.1	0.1143	0.0156	0.5038	0.4595	0.6693
3718/F	3/1	219.1	0.1073	0.0153	0.5037	0.4023	0.6758
3719/F	3/1	191.1	0.1107	0.0126	0.5960	0.4277	0.5617
3720/F	3/1	210.4	0.0978	0.0139	0.5270	0.4501	0.5700
Mean:		210.3	0.1088	0.0138	0.5177	0.4853	0.6667
Standard deviation:		11.5	0.0159	0.0021	0.0776	0.0825	0.1780
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)
4711/F	4/1	196.1	0.1191	0.0163	0.4554	0.5053	0.4900
4712/F	4/1	219.0	0.1173	0.0149	0.5201	0.4160	0.6900
4713/F	4/1	209.1	0.1116	0.0171	0.6164	0.3866	0.6327

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovaries	Pituitary gland	Spleen	Thymus	Uterus
4714/F	4/1	215.2	0.0771	0.0160	0.4315	0.4515	0.5880
4715/F	4/1	208.3	0.0799	0.0142	0.5085	0.4451	0.4796
4716/F	4/1	210.3	0.1325	0.0128	0.4661	0.3635	0.4513
4717/F	4/1	206.3	0.1240	0.0130	0.5301	0.5144	0.4819
4718/F	4/1	214.7	0.1369	0.0110	0.6136	0.4849	0.5640
4719/F	4/1	212.7	0.1253	0.0121	0.5895	0.4338	0.5304
4720/F	4/1	196.5	0.1305	0.0142	0.6304	0.5024	0.5928
Mean:		208.8	0.1154	0.0142	0.5362	0.4504	0.5501
Standard deviation:		7.6	0.0209	0.0020	0.0727	0.0518	0.0769
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)

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Summary Statistics for % Organ to Body Weight
Study number: 036143

Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Epididymides	Heart	Kidneys	Liver
Male Animals								
1211/M	1/1	315.2	0.0209	0.7463	0.2802	0.3843	0.9905	3.5606
1212/M	1/1	340.9	0.0229	0.6207	0.2580	0.3725	0.9847	3.4244
1213/M	1/1	299.6	0.0264	0.7313	0.3090	0.4208	1.1616	3.8435
1214/M	1/1	318.0	0.0244	0.6630	0.3039	0.3815	1.0398	3.8510
1215/M	1/1	319.6	0.0218	0.6253	0.3102	0.4163	1.1063	3.7054
1216/M	1/1	327.1	0.0151	0.6637	0.2782	0.3883	1.0099	3.6731
1217/M	1/1	284.9	0.0276	0.7116	0.3124	0.4167	1.1912	4.0266
1218/M	1/1	284.0	0.0250	0.7129	0.3228	0.4350	1.0551	3.2648
1219/M	1/1	295.2	0.0224	0.7671	0.3214	0.4280	1.1811	3.5430
1220/M	1/1	306.7	0.0216	0.6887	0.2423	0.4414	1.1902	3.5692
Mean:		309.1	0.0228	0.6931	0.2938	0.4085	1.0910	3.6462
Standard deviation:		18.5	0.0035	0.0496	0.0277	0.0246	0.0851	0.2232
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
2211/M	2/1	319.4	0.0202	0.7191	0.2709	0.3576	1.2717	3.4215
2212/M	2/1	309.7	0.0202	0.7052	0.3500	0.4277	1.2121	4.2429
2213/M	2/1	317.9	0.0202	0.6994	0.2893	0.3649	1.0670	3.4128
2214/M	2/1	302.6	0.0202	0.6938	0.2820	0.3900	1.1005	3.6878
2215/M	2/1	320.0	0.0190	0.6643	0.2468	0.4304	1.0855	3.9613
2216/M	2/1	305.6	0.0268	0.6995	0.3115	0.3985	1.2685	3.6746
2217/M	2/1	313.8	0.0208	0.6557	0.3082	0.4015	1.1412	3.4053
2218/M	2/1	303.3	0.0242	0.6758	0.3160	0.4361	0.9973	3.4864
2219/M	2/1	309.7	0.0226	0.7269	0.2808	0.4259	1.1351	3.5007
2220/M	2/1	297.0	0.0221	0.6840	0.3056	0.3995	1.0845	3.6272
Mean:		309.9	0.0216	0.6924	0.2961	0.4032	1.1364	3.6421
Standard deviation:		7.8	0.0024	0.0227	0.0285	0.0273	0.0896	0.2724
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
3211/M	3/1	309.9	0.0237	0.6623	0.2732	0.3385	1.1091	3.7886
3212/M	3/1	302.1	0.0259	0.6976	0.3450	0.3641	1.0591	3.3359
3213/M	3/1	281.9	0.0226	0.7369	0.3056	0.3966	1.0979	4.1179
3214/M	3/1	319.9	0.0213	0.6508	0.2911	0.4279	1.0940	3.6735
3215/M	3/1	305.6	0.0181	0.7009	0.3012	0.4346	1.1313	3.5162
3216/M	3/1	320.3	0.0244	0.6838	0.2883	0.3802	0.9697	3.6244
3217/M	3/1	285.0	0.0220	0.7296	0.3538	0.4309	1.4503	3.5448
3218/M	3/1	332.7	0.0151	0.6324	0.2646	0.3712	0.9698	3.4603
3219/M	3/1	319.2	0.0202	0.7193	0.3007	0.4154	1.1034	3.5511
3220/M	3/1	310.1	0.0237	0.6535	0.2526	0.4243	1.2434	3.4758
Mean:		308.7	0.0217	0.6867	0.2976	0.3984	1.1228	3.6089
Standard deviation:		15.9	0.0032	0.0360	0.0322	0.0334	0.1394	0.2176
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
4211/M	4/1	313.8	0.0214	0.6789	0.2182	0.3828	1.1111	4.3808
4212/M	4/1	272.6	0.0262	0.7819	0.3361	0.3884	1.1553	5.2720
4213/M	4/1	333.2	0.0202	0.6449	0.3268	0.4242	1.2076	3.5831

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Summary Statistics for % Organ to Body Weight
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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Epididymides	Heart	Kidneys	Liver
4214/M	4/1	319.6	0.0244	0.6998	0.3212	0.3899	1.0984	3.5890
4215/M	4/1	339.7	0.0241	0.5709	0.2542	0.3574	0.9559	3.7114
4216/M	4/1	294.4	0.0267	0.6981	0.2846	0.4022	1.0993	3.4152
4217/M	4/1	315.6	0.0237	0.6271	0.3291	0.3965	0.9553	3.4596
4218/M	4/1	321.9	0.0178	0.6814	0.2955	0.3890	1.1377	3.4347
4219/M	4/1	273.2	0.0216	0.7809	0.3368	0.4129	1.2410	3.5665
4220/M	4/1	319.1	0.0220	0.6888	0.2673	0.4574	1.2766	4.1885
Mean:		310.3	0.0228	0.6853	0.2970	0.4001	1.1238	3.8601
Standard deviation:		23.0	0.0028	0.0641	0.0404	0.0270	0.1071	0.5935
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)

Terminal Sacrifice

Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Lungs	Pituitary gland	Seminal vesicles	Spleen	Testes	Thymus
				Male Animals				
1211/M	1/1	315.2	0.6794	0.0027	0.3549	0.2514	1.0097	0.1793
1212/M	1/1	340.9	0.4953	0.0024	0.2661	0.1895	0.9299	0.1814
1213/M	1/1	299.6	0.5624	0.0044	0.4279	0.2392	1.1483	0.1587
1214/M	1/1	318.0	0.5358	0.0035	0.3198	0.2418	1.0451	0.1793
1215/M	1/1	319.6	0.5557	0.0031	0.3840	0.2861	1.0050	0.1717
1216/M	1/1	327.1	0.5913	0.0021	0.3082	0.2616	1.0819	0.2541
1217/M	1/1	284.9	0.7365	0.0039	0.2545	0.2105	1.2409	0.1664
1218/M	1/1	284.0	0.6194	0.0039	0.2965	0.2576	1.1383	0.1200
1219/M	1/1	295.2	0.6159	0.0044	0.3822	0.1937	1.0250	0.1567
1220/M	1/1	306.7	0.7581	0.0033	0.4146	0.2545	0.8864	0.2053
Mean:		309.1	0.6150	0.0034	0.3409	0.2386	1.0511	0.1773
Standard deviation:		18.5	0.0862	0.0008	0.0608	0.0313	0.1056	0.0348
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
2211/M	2/1	319.4	0.5986	0.0033	0.3869	0.1891	1.0331	0.1520
2212/M	2/1	309.7	0.6088	0.0030	0.3012	0.2470	1.1091	0.2596
2213/M	2/1	317.9	0.5488	0.0023	0.2334	0.1621	1.0024	0.1879
2214/M	2/1	302.6	0.6763	0.0036	0.4197	0.2142	1.0340	0.2388
2215/M	2/1	320.0	0.6360	0.0028	0.4076	0.2340	1.0351	0.3361
2216/M	2/1	305.6	0.6473	0.0041	0.2986	0.2511	1.0691	0.1821
2217/M	2/1	313.8	0.6140	0.0024	0.2752	0.2233	1.0603	0.2575
2218/M	2/1	303.3	0.5515	0.0039	0.3059	0.2714	1.1534	0.2372
2219/M	2/1	309.7	0.6394	0.0038	0.2040	0.2052	1.0215	0.1608
2220/M	2/1	297.0	0.6756	0.0037	0.4662	0.2177	1.1071	0.2301
Mean:		309.9	0.6196	0.0033	0.3299	0.2215	1.0625	0.2242
Standard deviation:		7.8	0.0448	0.0006	0.0859	0.0318	0.0474	0.0554
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
3211/M	3/1	309.9	0.5223	0.0035	0.2770	0.1982	1.0340	0.1685
3212/M	3/1	302.1	0.5885	0.0033	0.3210	0.1784	1.1541	0.1351
3213/M	3/1	281.9	0.7030	0.0033	0.3432	0.2389	1.1491	0.1947
3214/M	3/1	319.9	0.6663	0.0029	0.3560	0.2770	1.0306	0.2419
3215/M	3/1	305.6	0.6265	0.0036	0.3849	0.2244	1.0042	0.1854
3216/M	3/1	320.3	0.6423	0.0026	0.2296	0.2539	1.1171	0.2173
3217/M	3/1	285.0	0.5975	0.0026	0.3328	0.3114	1.2475	0.1380
3218/M	3/1	332.7	0.6436	0.0028	0.2837	0.1663	0.9046	0.1509
3219/M	3/1	319.2	0.5956	0.0038	0.4083	0.2597	0.9810	0.1356
3220/M	3/1	310.1	0.7375	0.0027	0.2124	0.2208	0.9183	0.2061
Mean:		308.7	0.6323	0.0031	0.3149	0.2329	1.0541	0.1773
Standard deviation:		15.9	0.0615	0.0005	0.0638	0.0449	0.1106	0.0377
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
4211/M	4/1	313.8	0.5999	0.0047	0.3779	0.2535	0.7949	0.1431
4212/M	4/1	272.6	0.5951	0.0028	0.2836	0.4687	1.1566	0.1395
4213/M	4/1	333.2	0.9639E	0.0036	0.3006	0.2364	1.0532	0.1825

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Summary Statistics for % Organ to Body Weight
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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Lungs	Pituitary gland	Seminal vesicles	Spleen	Testes	Thymus
4214/M	4/1	319.6	0.5614	0.0040	0.3976	0.2068	1.0427	0.1629
4215/M	4/1	339.7	0.6548	0.0038	0.2262	0.2055	0.9017	0.1667
4216/M	4/1	294.4	0.6474	0.0053	0.4793	0.1730	1.0586	0.1744
4217/M	4/1	315.6	0.6388	0.0037	0.3537	0.2199	0.9886	0.2181
4218/M	4/1	321.9	0.6240	0.0039	0.3623	0.2674	1.1124	0.1528
4219/M	4/1	273.2	0.7014	0.0034	0.4324	0.1829	1.0955	0.1178
4220/M	4/1	319.1	0.6570	0.0041	0.4343	0.2003	1.0620	0.1732
Mean:		310.3	0.6311	0.0039	0.3648	0.2414	1.0266	0.1631
Standard deviation:		23.0	0.0414	0.0007	0.0773	0.0852	0.1070	0.0274
Number of observ. :		(10)	(9)	(10)	(10)	(10)	(10)	(10)

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Summary Statistics for % Organ to Body Weight
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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
				Female	Animals			
1711/F	1/1	228.7	0.0310	1.0036	0.4682	1.1983	3.8435	0.8206
1712/F	1/1	211.5	0.0379	0.9542	0.3974	1.2214	4.0574	0.7235
1713/F	1/1	231.0	0.0354	0.8536	0.4265	1.0168	3.6621	0.6878
1714/F	1/1	196.5	0.0371	1.0250	0.4220	1.1557	3.9393	0.9262
1715/F	1/1	218.1	0.0354	0.9014	0.4508	1.1016	3.8912	0.7804
1716/F	1/1	186.2	0.0424	1.0550	0.4589	1.0213	3.9926	0.7606
1717/F	1/1	213.5	0.0327	0.9546	0.4059	1.1066	3.5384	1.0634
1718/F	1/1	207.5	0.0495	0.9490	0.4835	1.3576	4.4669	0.9651
1719/F	1/1	220.5	0.0472	0.9263	0.4286	1.2278	4.8923	0.8153
1720/F	1/1	212.5	0.0400	1.0099	0.4371	1.1676	4.3117	0.8661
	Mean:	212.6	0.0389	0.9633	0.4379	1.1575	4.0595	0.8409
Standard deviation:		13.6	0.0060	0.0611	0.0274	0.1027	0.4009	0.1161
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
2711/F	2/1	211.6	0.0300	1.0138	0.5105	1.3004	3.9078	0.8108
2712/F	2/1	200.0	0.0392	0.9444	0.3784	1.1083	3.5922	0.7564
2713/F	2/1	207.3	0.0352	1.0596	0.4308	1.0852	3.8929	0.8903
2714/F	2/1	212.1	0.0315	0.9828	0.4102	1.0783	4.4154	0.7502
2715/F	2/1	222.1	0.0357	0.9063	0.4437	1.0993	4.2212	0.8704
2716/F	2/1	227.1	0.0387	0.8806	0.3780	1.0465	3.4424	0.8216
2717/F	2/1	209.5	0.0334	0.9535	0.4614	1.2063	3.7907	0.9975
2718/F	2/1	205.5	0.0364	0.9768	0.3790	1.0017	3.4309	0.8584
2719/F	2/1	217.1	0.0399	0.9635	0.4348	1.1201	4.1790	0.6885
2720/F	2/1	207.2	0.0389	0.9964	0.5112	1.2726	4.6390	0.8406
	Mean:	212.0	0.0359	0.9678	0.4338	1.1319	3.9511	0.8285
Standard deviation:		8.1	0.0034	0.0515	0.0500	0.0971	0.4087	0.0859
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
3711/F	3/1	219.7	0.0309	1.0010	0.4501	1.0869	3.7427	0.6910
3712/F	3/1	204.6	0.0373	0.9674	0.4221	1.1411	3.6889	0.7204
3713/F	3/1	197.4	0.0375	1.0537	0.4329	1.1857	3.5715	0.7400
3714/F	3/1	204.2	0.0334	0.9754	0.4048	0.9342	3.2863	0.9199
3715/F	3/1	208.2	0.0328	0.9567	0.4352	1.2028	3.6847	0.7127
3716/F	3/1	228.9	0.0400	0.8198	0.4167	1.1353	3.8273	0.7187
3717/F	3/1	219.1	0.0331	0.9304	0.4290	1.0526	3.6064	0.9381
3718/F	3/1	219.1	0.0370	0.9979	0.4566	1.2140	4.2847	1.0026
3719/F	3/1	191.1	0.0293	1.0261	0.4751	1.1657	4.5243	0.7819
3720/F	3/1	210.4	0.0427	0.9844	0.4289	0.9770	3.7090	0.8891
	Mean:	210.3	0.0354	0.9713	0.4351	1.1095	3.7926	0.8114
Standard deviation:		11.5	0.0042	0.0636	0.0205	0.0956	0.3575	0.1143
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
4711/F	4/1	196.1	0.0418	0.9686	0.4551	1.1057	3.9674	1.1213
4712/F	4/1	219.0	0.0443	0.9390	0.4376	1.2606	4.0265	0.7091
4713/F	4/1	209.1	0.0383	1.0008	0.4473	1.0674	3.6600	0.7910

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
4714/F	4/1	215.2	0.0346	0.9717	0.4189	1.1449	3.8842	0.7023
4715/F	4/1	208.3	0.0295	1.0004	0.4280	1.1128	4.0623	0.7646
4716/F	4/1	210.3	0.0461	0.9214	0.3636	0.9835	3.6075	0.7182
4717/F	4/1	206.3	0.0392	0.9748	0.4321	1.1684	3.7536	1.1528
4718/F	4/1	214.7	0.0449	0.9503	0.4376	1.1646	4.4773	0.8567
4719/F	4/1	212.7	0.0314	0.8962	0.4156	1.0919	3.7782	0.9872
4720/F	4/1	196.5	0.0408	1.0760	0.4713	1.2554	4.8444	0.7689
Mean:		208.8	0.0391	0.9699	0.4307	1.1355	4.0061	0.8572
Standard deviation:		7.6	0.0057	0.0498	0.0289	0.0837	0.3857	0.1700
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovaries	Pituitary gland	Spleen	Thymus	Uterus
				Female	Animals		
1711/F	1/1	228.7	0.0425	0.0057	0.2264	0.2178	0.2304
1712/F	1/1	211.5	0.0695	0.0061	0.2105	0.2915	0.3296
1713/F	1/1	231.0	0.0580	0.0060	0.2404	0.1664	0.2139
1714/F	1/1	196.5	0.0466	0.0090	0.2200	0.2211	0.2769
1715/F	1/1	218.1	0.0558	0.0073	0.2238	0.2747	0.2722
1716/F	1/1	186.2	0.0552	0.0064	0.2675	0.2783	0.2550
1717/F	1/1	213.5	0.0607	0.0072	0.2302	0.2453	0.2391
1718/F	1/1	207.5	0.0696	0.0063	0.1836	0.2024	0.3150
1719/F	1/1	220.5	0.0558	0.0067	0.2320	0.3077	0.2430
1720/F	1/1	212.5	0.0506	0.0079	0.2919	0.2250	0.2618
Mean:		212.6	0.0564	0.0069	0.2326	0.2430	0.2637
Standard deviation:		13.6	0.0088	0.0010	0.0297	0.0444	0.0364
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)
2711/F	2/1	211.6	0.0612	0.0069	0.2169	0.2234	0.2326
2712/F	2/1	200.0	0.0583	0.0077	0.2184	0.2270	0.2352
2713/F	2/1	207.3	0.0554	0.0062	0.3431	0.2753	0.2371
2714/F	2/1	212.1	0.0500	0.0052	0.3275	0.3193	0.3107
2715/F	2/1	222.1	0.0472	0.0064	0.2656	0.2610	0.1928
2716/F	2/1	227.1	0.0578	0.0055	0.2536	0.2849	0.2415
2717/F	2/1	209.5	0.0662	0.0058	0.2669	0.2228	0.2893
2718/F	2/1	205.5	0.0587	0.0067	0.2429	0.2602	0.2228
2719/F	2/1	217.1	0.0530	0.0068	0.2391	0.3378	0.4561
2720/F	2/1	207.2	0.0508	0.0055	0.2253	0.2222	0.4552
Mean:		212.0	0.0559	0.0063	0.2599	0.2634	0.2873
Standard deviation:		8.1	0.0057	0.0008	0.0436	0.0416	0.0947
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)
3711/F	3/1	219.7	0.0453	0.0075	0.2814	0.1929	0.2784
3712/F	3/1	204.6	0.0440	0.0080	0.2088	0.2543	0.3157
3713/F	3/1	197.4	0.0542	0.0057	0.1915	0.2586	0.2425
3714/F	3/1	204.2	0.0452	0.0055	0.2326	0.2259	0.5573
3715/F	3/1	208.2	0.0611	0.0054	0.2894	0.3320	0.3363
3716/F	3/1	228.9	0.0617	0.0063	0.2381	0.2213	0.2692
3717/F	3/1	219.1	0.0522	0.0071	0.2299	0.2097	0.3055
3718/F	3/1	219.1	0.0490	0.0070	0.2299	0.1836	0.3084
3719/F	3/1	191.1	0.0579	0.0066	0.3119	0.2238	0.2939
3720/F	3/1	210.4	0.0465	0.0066	0.2505	0.2139	0.2709
Mean:		210.3	0.0517	0.0066	0.2464	0.2316	0.3178
Standard deviation:		11.5	0.0068	0.0009	0.0374	0.0423	0.0884
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)
4711/F	4/1	196.1	0.0607	0.0083	0.2322	0.2577	0.2499
4712/F	4/1	219.0	0.0536	0.0068	0.2375	0.1900	0.3151
4713/F	4/1	209.1	0.0534	0.0082	0.2948	0.1849	0.3026

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovaries	Pituitary gland	Spleen	Thymus	Uterus
4714/F	4/1	215.2	0.0358	0.0074	0.2005	0.2098	0.2732
4715/F	4/1	208.3	0.0384	0.0068	0.2441	0.2137	0.2302
4716/F	4/1	210.3	0.0630	0.0061	0.2216	0.1728	0.2146
4717/F	4/1	206.3	0.0601	0.0063	0.2570	0.2493	0.2336
4718/F	4/1	214.7	0.0638	0.0051	0.2858	0.2259	0.2627
4719/F	4/1	212.7	0.0589	0.0057	0.2772	0.2039	0.2494
4720/F	4/1	196.5	0.0664	0.0072	0.3208	0.2557	0.3017
M e a n:		208.8	0.0554	0.0068	0.2571	0.2164	0.2633
Standard deviation:		7.6	0.0105	0.0010	0.0370	0.0302	0.0342
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Epididymides	Heart	Kidneys	Liver
				Male Animals				
1211/M	1/1	315.2	2.8014	100.0000	37.5404	51.4921	132.7113	477.0830
1212/M	1/1	340.9	3.6813	100.0000	41.5623	60.0161	158.6409	551.6705
1213/M	1/1	299.6	3.6057	100.0000	42.2501	57.5445	158.8407	525.5637
1214/M	1/1	318.0	3.6758	100.0000	45.8404	57.5413	156.8298	580.8338
1215/M	1/1	319.6	3.4880	100.0000	49.6122	66.5866	176.9354	592.6188
1216/M	1/1	327.1	2.2802	100.0000	41.9227	58.5103	152.1627	553.4387
1217/M	1/1	284.9	3.8818	100.0000	43.8937	58.5627	167.3917	565.8381
1218/M	1/1	284.0	3.5021	100.0000	45.2803	61.0225	148.0069	457.9897
1219/M	1/1	295.2	2.9235	100.0000	41.9007	55.7940	153.9790	461.8884
1220/M	1/1	306.7	3.1293	100.0000	35.1749	64.0865	172.8069	518.2314
Mean:		309.1	3.2969	100.0000	42.4978	59.1157	157.8305	528.5156
Standard deviation:		18.5	0.5005	0.0000	4.1002	4.2130	12.7271	48.9553
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
2211/M	2/1	319.4	2.8127	100.0000	37.6802	49.7322	176.8494	475.8262
2212/M	2/1	309.7	2.8617	100.0000	49.6337	60.6456	171.8864	601.6621
2213/M	2/1	317.9	2.8830	100.0000	41.3646	52.1679	152.5591	487.9554
2214/M	2/1	302.6	2.9055	100.0000	40.6430	56.2086	158.6187	531.5219
2215/M	2/1	320.0	2.8604	100.0000	37.1472	64.7911	163.4221	596.3634
2216/M	2/1	305.6	3.8312	100.0000	44.5292	56.9631	181.3444	525.3170
2217/M	2/1	313.8	3.1785	100.0000	47.0014	61.2364	174.0474	519.3381
2218/M	2/1	303.3	3.5761	100.0000	46.7629	64.5265	147.5679	515.8901
2219/M	2/1	309.7	3.1096	100.0000	38.6344	58.5980	156.1681	481.6223
2220/M	2/1	297.0	3.2293	100.0000	44.6736	58.4080	158.5606	530.3092
Mean:		309.9	3.1248	100.0000	42.8070	58.3277	164.1024	526.5806
Standard deviation:		7.8	0.3432	0.0000	4.3306	4.8568	11.3044	43.2084
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
3211/M	3/1	309.9	3.5808	100.0000	41.2550	51.1059	167.4510	572.0014
3212/M	3/1	302.1	3.7104	100.0000	49.4449	52.1826	151.8030	478.1600
3213/M	3/1	281.9	3.0666	100.0000	41.4789	53.8273	148.9939	558.8533
3214/M	3/1	319.9	3.2662	100.0000	44.7284	65.7572	168.1013	564.4652
3215/M	3/1	305.6	2.5772	100.0000	42.9712	62.0104	161.4034	501.6807
3216/M	3/1	320.3	3.5750	100.0000	42.1651	55.6022	141.8135	530.0430
3217/M	3/1	285.0	3.0153	100.0000	48.4851	59.0603	198.7785	485.8469
3218/M	3/1	332.7	2.3956	100.0000	41.8366	58.7053	153.3628	547.1981
3219/M	3/1	319.2	2.8091	100.0000	41.8013	57.7457	153.3993	493.6676
3220/M	3/1	310.1	3.6269	100.0000	38.6578	64.9198	190.2640	531.8727
Mean:		308.7	3.1623	100.0000	43.2824	58.0917	163.5371	526.3789
Standard deviation:		15.9	0.4665	0.0000	3.3585	5.0583	18.3315	34.4989
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
4211/M	4/1	313.8	3.1448	100.0000	32.1380	56.3858	163.6470	645.2523
4212/M	4/1	272.6	3.3498	100.0000	42.9885	49.6739	147.7551	674.2435
4213/M	4/1	333.2	3.1320	100.0000	50.6701	65.7763	187.2580	555.6032

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4214/M	4/1	319.6	3.4918	100.0000	45.8935	55.7160	156.9545	512.8225
4215/M	4/1	339.7	4.2232	100.0000	44.5212	62.5999	167.4470	650.1058
4216/M	4/1	294.4	3.8293	100.0000	40.7746	57.6100	157.4737	489.2127
4217/M	4/1	315.6	3.7744	100.0000	52.4734	63.2207	152.3319	551.6902
4218/M	4/1	321.9	2.6078	100.0000	43.3710	57.0849	166.9691	504.0668
4219/M	4/1	273.2	2.7654	100.0000	43.1263	52.8709	158.9126	456.7003
4220/M	4/1	319.1	3.1982	100.0000	38.7971	66.4074	185.3192	608.0433
M e a n:		310.3	3.3517	100.0000	43.4754	58.7346	164.4068	564.7740
Standard deviation:		23.0	0.4941	0.0000	5.7519	5.5639	13.0502	75.7504
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)

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				Male Animals				
1211/M	1/1	315.2	91.0389	0.3613	47.5599	33.6805	135.2874	24.0265
1212/M	1/1	340.9	79.7930	0.3828	42.8619	30.5279	149.7992	29.2188
1213/M	1/1	299.6	76.9010	0.5979	58.5167	32.7020	157.0242	21.7070
1214/M	1/1	318.0	80.8148	0.5217	48.2309	36.4637	157.6314	27.0442
1215/M	1/1	319.6	88.8756	0.4904	61.4172	45.7639	160.7316	27.4633
1216/M	1/1	327.1	89.0875	0.3224	46.4416	39.4214	163.0199	38.2929
1217/M	1/1	284.9	103.4922	0.5524	35.7601	29.5847	174.3761	23.3797
1218/M	1/1	284.0	86.8906	0.5532	41.5955	36.1423	159.6888	16.8338
1219/M	1/1	295.2	80.2906	0.5741	49.8234	25.2473	133.6248	20.4337
1220/M	1/1	306.7	110.0743	0.4829	60.1998	36.9455	128.6986	29.8064
Mean:		309.1	88.7258	0.4839	49.2407	34.6479	151.9882	25.8206
Standard deviation:		18.5	10.7292	0.0963	8.4807	5.7044	14.8294	5.9914
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
2211/M	2/1	319.4	83.2412	0.4615	53.8076	26.2943	143.6670	21.1390
2212/M	2/1	309.7	86.3278	0.4304	42.7106	35.0229	157.2802	36.8178
2213/M	2/1	317.9	78.4609	0.3238	33.3723	23.1717	143.3165	26.8688
2214/M	2/1	302.6	97.4708	0.5192	60.4954	30.8693	149.0355	34.4177
2215/M	2/1	320.0	95.7424	0.4281	61.3662	35.2324	155.8289	50.5928
2216/M	2/1	305.6	92.5387	0.5801	42.6907	35.8984	152.8418	26.0373
2217/M	2/1	313.8	93.6431	0.3694	41.9664	34.0591	161.7030	39.2642
2218/M	2/1	303.3	81.6022	0.5757	45.2652	40.1620	170.6738	35.0978
2219/M	2/1	309.7	87.9659	0.5197	28.0707	28.2262	140.5402	22.1181
2220/M	2/1	297.0	98.7743	0.5366	68.1648	31.8352	161.8638	33.6467
Mean:		309.9	89.5767	0.4744	47.7910	32.0771	153.6751	32.6000
Standard deviation:		7.8	7.0764	0.0865	12.8491	5.0731	9.6626	8.9052
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
3211/M	3/1	309.9	78.8561	0.5359	41.8250	29.9230	156.1142	25.4360
3212/M	3/1	302.1	84.3519	0.4745	46.0144	25.5741	165.4299	19.3633
3213/M	3/1	281.9	95.4073	0.4477	46.5771	32.4283	155.9455	26.4298
3214/M	3/1	319.9	102.3873	0.4467	54.7096	42.5669	158.3650	37.1680
3215/M	3/1	305.6	89.3879	0.5089	54.9185	32.0230	143.2700	26.4485
3216/M	3/1	320.3	93.9321	0.3744	33.5814	37.1245	163.3686	31.7779
3217/M	3/1	285.0	81.8986	0.3559	45.6141	42.6854	170.9868	18.9189
3218/M	3/1	332.7	101.7777	0.4468	44.8691	26.2940	143.0534	23.8652
3219/M	3/1	319.2	82.7969	0.5313	56.7658	36.1091	136.3747	18.8450
3220/M	3/1	310.1	112.8497	0.4145	32.4945	33.7873	140.5132	31.5322
Mean:		308.7	92.3645	0.4537	45.7370	33.8516	153.3421	25.9785
Standard deviation:		15.9	10.9394	0.0613	8.3428	5.9277	11.8202	6.1405
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
4211/M	4/1	313.8	88.3549	0.6853	55.6583	37.3387	117.0758	21.0843
4212/M	4/1	272.6	76.1060	0.3612	36.2655	59.9484	147.9193	17.8466
4213/M	4/1	333.2	149.4695E	0.5538	46.6121	36.6577	163.3191	28.2995

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Lungs	Pituitary gland	Seminal vesicles	Spleen	Testes	Thymus
4214/M	4/1	319.6	80.2209	0.5723	56.8114	29.5480	148.9874	23.2798
4215/M	4/1	339.7	114.7012	0.6703	39.6226	35.9975	157.9436	29.2064
4216/M	4/1	294.4	92.7355	0.7542	68.6600	24.7859	151.6349	24.9805
4217/M	4/1	315.6	101.8695	0.5962	56.4044	35.0614	157.6424	34.7734
4218/M	4/1	321.9	91.5747	0.5745	53.1686	39.2359	163.2534	22.4218
4219/M	4/1	273.2	89.8195	0.4406	55.3691	23.4169	140.2766	15.0832
4220/M	4/1	319.1	95.3733	0.6005	63.0454	29.0797	154.1741	25.1444
Mean:		310.3	92.3062	0.5809	53.1617	35.1070	150.2226	24.2120
Standard deviation:		23.0	11.3656	0.1147	9.9136	10.2888	13.6547	5.6996
Number of observ. :		(10)	(9)	(10)	(10)	(10)	(10)	(10)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
				Female	Animals			
1711/F	1/1	228.7	3.0934	100.0000	46.6495	119.3970	382.9732	81.7663
1712/F	1/1	211.5	3.9740	100.0000	41.6431	128.0066	425.2218	75.8238
1713/F	1/1	231.0	4.1432	100.0000	49.9569	119.1136	429.0026	80.5771
1714/F	1/1	196.5	3.6195	100.0000	41.1747	112.7551	384.3305	90.3580
1715/F	1/1	218.1	3.9268	100.0000	50.0051	122.2075	431.6735	86.5768
1716/F	1/1	186.2	4.0214	100.0000	43.4971	96.7982	378.4322	72.0947
1717/F	1/1	213.5	3.4297	100.0000	42.5200	115.9168	370.6590	111.3979
1718/F	1/1	207.5	5.2153	100.0000	50.9496	143.0581	470.6886	101.6911
1719/F	1/1	220.5	5.0916	100.0000	46.2646	132.5370	528.1309	88.0104
1720/F	1/1	212.5	3.9560	100.0000	43.2832	115.6144	426.9326	85.7556
Mean:		212.6	4.0471	100.0000	45.5944	120.5404	422.8045	87.4052
Standard deviation:		13.6	0.6639	0.0000	3.6978	12.3952	48.6271	11.7340
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
2711/F	2/1	211.6	2.9553	100.0000	50.3519	128.2618	385.4380	79.9702
2712/F	2/1	200.0	4.1508	100.0000	40.0678	117.3497	380.3685	80.0932
2713/F	2/1	207.3	3.3188	100.0000	40.6537	102.4174	367.3814	84.0208
2714/F	2/1	212.1	3.2045	100.0000	41.7394	109.7093	449.2517	76.3264
2715/F	2/1	222.1	3.9396	100.0000	48.9592	121.2927	465.7609	96.0405
2716/F	2/1	227.1	4.4002	100.0000	42.9221	118.8309	390.8996	93.2997
2717/F	2/1	209.5	3.4994	100.0000	48.3905	126.5182	397.5720	104.6158
2718/F	2/1	205.5	3.7262	100.0000	38.7965	102.5456	351.2255	87.8798
2719/F	2/1	217.1	4.1448	100.0000	45.1238	116.2539	433.7270	71.4600
2720/F	2/1	207.2	3.8991	100.0000	51.3029	127.7148	465.5672	84.3602
Mean:		212.0	3.7239	100.0000	44.8308	117.0894	408.7192	85.8067
Standard deviation:		8.1	0.4677	0.0000	4.6178	9.5995	41.5741	9.9256
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
3711/F	3/1	219.7	3.0831	100.0000	44.9638	108.5899	373.9121	69.0373
3712/F	3/1	204.6	3.8549	100.0000	43.6366	117.9508	381.3217	74.4708
3713/F	3/1	197.4	3.5577	100.0000	41.0817	112.5289	338.9471	70.2260
3714/F	3/1	204.2	3.4292	100.0000	41.5073	95.7775	336.9333	94.3164
3715/F	3/1	208.2	3.4239	100.0000	45.4842	125.7192	385.1349	74.4917
3716/F	3/1	228.9	4.8814	100.0000	50.8287	138.4812	466.8639	87.6685
3717/F	3/1	219.1	3.5616	100.0000	46.1146	113.1427	387.6374	100.8291
3718/F	3/1	219.1	3.7047	100.0000	45.7556	121.6566	429.3725	100.4665
3719/F	3/1	191.1	2.8509	100.0000	46.3025	113.6067	440.9425	76.2036
3720/F	3/1	210.4	4.3357	100.0000	43.5738	99.2468	376.7719	90.3196
Mean:		210.3	3.6683	100.0000	44.9249	114.6700	391.7837	83.8030
Standard deviation:		11.5	0.5873	0.0000	2.7710	12.4206	42.1405	12.3352
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)
4711/F	4/1	196.1	4.3169	100.0000	46.9808	114.1511	409.5815	115.7621
4712/F	4/1	219.0	4.7170	100.0000	46.6057	134.2540	428.8125	75.5155
4713/F	4/1	209.1	3.8230	100.0000	44.6956	106.6616	365.7221	79.0357

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Adrenal Glands	Brain	Heart	Kidneys	Liver	Lungs
4714/F	4/1	215.2	3.5629	100.0000	43.1133	117.8336	399.7513	72.2812
4715/F	4/1	208.3	2.9465	100.0000	42.7824	111.2391	406.0707	76.4325
4716/F	4/1	210.3	5.0008	100.0000	39.4643	106.7348	391.5261	77.9429
4717/F	4/1	206.3	4.0229	100.0000	44.3312	119.8608	385.0622	118.2596
4718/F	4/1	214.7	4.7250	100.0000	46.0494	122.5517	471.1695	90.1578
4719/F	4/1	212.7	3.5044	100.0000	46.3697	121.8340	421.5875	110.1511
4720/F	4/1	196.5	3.7932	100.0000	43.8065	116.6769	450.2342	71.4610
Mean:		208.8	4.0413	100.0000	44.4199	117.1798	412.9518	88.6999
Standard deviation:		7.6	0.6451	0.0000	2.2901	8.2604	31.2799	18.7634
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)	(10)

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovaries	Pituitary gland	Spleen	Thymus	Uterus
				Female	Animals		
1711/F	1/1	228.7	4.2393	0.5708	22.5601	21.6975	22.9566
1712/F	1/1	211.5	7.2841	0.6442	22.0604	30.5535	34.5473
1713/F	1/1	231.0	6.7955	0.6998	28.1657	19.4888	25.0520
1714/F	1/1	196.5	4.5430	0.8788	21.4637	21.5679	27.0145
1715/F	1/1	218.1	6.1851	0.8087	24.8321	30.4730	30.1933
1716/F	1/1	186.2	5.2278	0.6058	25.3500	26.3782	24.1741
1717/F	1/1	213.5	6.3589	0.7556	24.1107	25.6955	25.0478
1718/F	1/1	207.5	7.3329	0.6602	19.3429	21.3285	33.1962
1719/F	1/1	220.5	6.0266	0.7246	25.0416	33.2175	26.2313
1720/F	1/1	212.5	5.0091	0.7782	28.8989	22.2776	25.9214
Mean:		212.6	5.9002	0.7127	24.1826	25.2678	27.4335
Standard deviation:		13.6	1.1017	0.0956	2.9550	4.7602	3.9068
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)
2711/F	2/1	211.6	6.0365	0.6852	21.3956	22.0342	22.9432
2712/F	2/1	200.0	6.1732	0.8100	23.1258	24.0364	24.9047
2713/F	2/1	207.3	5.2263	0.5873	32.3773	25.9811	22.3800
2714/F	2/1	212.1	5.0849	0.5325	33.3205	32.4906	31.6176
2715/F	2/1	222.1	5.2064	0.7104	29.3109	28.7992	21.2678
2716/F	2/1	227.1	6.5603	0.6250	28.8014	32.3566	27.4264
2717/F	2/1	209.5	6.9387	0.6108	27.9900	23.3692	30.3379
2718/F	2/1	205.5	6.0128	0.6875	24.8630	26.6364	22.8056
2719/F	2/1	217.1	5.5024	0.7027	24.8112	35.0607	47.3420
2720/F	2/1	207.2	5.1003	0.5522	22.6097	22.2949	45.6796
Mean:		212.0	5.7842	0.6504	26.8606	27.3059	29.6705
Standard deviation:		8.1	0.6569	0.0844	4.1270	4.6673	9.5260
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)
3711/F	3/1	219.7	4.5291	0.7458	28.1115	19.2715	27.8114
3712/F	3/1	204.6	4.5521	0.8286	21.5834	26.2921	32.6378
3713/F	3/1	197.4	5.1394	0.5385	18.1731	24.5433	23.0096
3714/F	3/1	204.2	4.6342	0.5674	23.8490	23.1561	57.1421
3715/F	3/1	208.2	6.3909	0.5623	30.2525	34.7005	35.1474
3716/F	3/1	228.9	7.5300	0.7727	29.0434	26.9917	32.8377
3717/F	3/1	219.1	5.6073	0.7653	24.7155	22.5422	32.8346
3718/F	3/1	219.1	4.9076	0.6998	23.0379	18.4001	30.9093
3719/F	3/1	191.1	5.6457	0.6426	30.3958	21.8125	28.6465
3720/F	3/1	210.4	4.7219	0.6711	25.4442	21.7314	27.5203
Mean:		210.3	5.3658	0.6794	25.4606	23.9442	32.8497
Standard deviation:		11.5	0.9686	0.1004	4.0048	4.6602	9.2346
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)
4711/F	4/1	196.1	6.2701	0.8581	23.9747	26.6017	25.7963
4712/F	4/1	219.0	5.7041	0.7246	25.2918	20.2295	33.5538
4713/F	4/1	209.1	5.3331	0.8172	29.4562	18.4746	30.2351

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Animal No/sex	Group/ Subgroup	Terminal Body wt. (g)	Ovaries	Pituitary gland	Spleen	Thymus	Uterus
4714/F	4/1	215.2	3.6872	0.7652	20.6361	21.5925	28.1205
4715/F	4/1	208.3	3.8343	0.6814	24.4025	21.3600	23.0156
4716/F	4/1	210.3	6.8380	0.6606	24.0543	18.7594	23.2905
4717/F	4/1	206.3	6.1661	0.6464	26.3600	25.5793	23.9632
4718/F	4/1	214.7	6.7101	0.5392	30.0755	23.7673	27.6444
4719/F	4/1	212.7	6.5733	0.6348	30.9254	22.7573	27.8250
4720/F	4/1	196.5	6.1723	0.6716	29.8160	23.7620	28.0377
Mean:		208.8	5.7289	0.6999	26.4993	22.2884	27.1482
Standard deviation:		7.6	1.1305	0.0939	3.4112	2.7202	3.2818
Number of observ. :		(10)	(10)	(10)	(10)	(10)	(10)

	Raw Data Listing of Gross Observations with Modifiers	Appendix H

Key to Abbreviations

LN	=	Lymph Node
Nose/Turb Sec 1	=	Nose/Turbinates Section 1
Nose/Turb Sec 2	=	Nose/Turbinates Section 2
Nose/Turb Sec 3	=	Nose/Turbinates Section 3
Nose/Turb Sec 4	=	Nose/Turbinates Section 4
SC	=	Spinal Cord
Submandib/Max	=	Submandibular/Submaxillary
V-DVTC	=	Ventral Diverticulum
V-SM-G	=	Ventral Seromucinous Glands

Corresponding exposure levels for each group were as follows:

Group 1	-	0 ppm
Group 2	-	90 ppm
Group 3	-	900 ppm
Group 4	-	9000 ppm

Note:

In the following table, nasopharyngeal tissue, as specified by the protocol, appears as Nose/Turb Sec 1, 2, 3 and 4 and larynx is presented as V-DVTC and V-SM-G. This is due to the fact that the Xybion protocol was entered with specific sections of each tissue delineated in the event that a microscopic examination was required.

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Animal number	Sex	Group/ Subgroup	Date data taken	Tissue / Observation(s) Locator, Color, General, Measurements, Severity levels			
1211	M	1/1	22-Jul-03	Within normal limits			
1212	M	1/1	22-Jul-03	Within normal limits			
1213	M	1/1	22-Jul-03	Within normal limits			
1214	M	1/1		Seminal vesicles			
			22-Jul-03	Small, Right, , , , Severe			
				Tissues marked 'Within normal limits':			
			22-Jul-03	Adrenal Glands	Aorta	Brain	Cecum
				Colon	Duodenum	Epididymides	Esophagus
				Eyes	Femur	Femoral Marrow	Heart
				Ileum	Jejunum	Kidneys	Lacrimal gland
				Larynx: V-SM-G	Larynx: V-DVTC	Liver	Lungs
				Mammary-protocol	Mediastinal LN	Mesenteric LN	Nerve
				Nose/Turb Sec 1	Nose/Turb Sec 2	Nose/Turb Sec 3	Nose/Turb Sec 4
				Optic nerve	Pancreas	Parathyroid	Pituitary gland
				Prostate	Rectum/Low Colon	Salivary glands	Skin-protocol
				Skeletal muscle	Cervical SC	Thoracic SC	Lumbar SC
				Spleen	Sternum	Sternal Marrow	Stomach
				Testes	Thymus	Thyroid gland	Trachea
				Urinary bladder	Zymbal's gland		
1215	M	1/1	22-Jul-03	Within normal limits			
1216	M	1/1	23-Jul-03	Within normal limits			
1217	M	1/1	23-Jul-03	Within normal limits			
1218	M	1/1		Skin (other)			
			23-Jul-03	Sore, Cervical, Red, Areas, 1.0 - 1.5 cm,			
				Tissues marked 'Within normal limits':			
			23-Jul-03	Adrenal Glands	Aorta	Brain	Cecum
				Colon	Duodenum	Epididymides	Esophagus
				Eyes	Femur	Femoral Marrow	Heart
				Ileum	Jejunum	Kidneys	Lacrimal gland
				Larynx: V-SM-G	Larynx: V-DVTC	Liver	Lungs
				Mammary-protocol	Mediastinal LN	Mesenteric LN	Nerve
				Nose/Turb Sec 1	Nose/Turb Sec 2	Nose/Turb Sec 3	Nose/Turb Sec 4
				Optic nerve	Pancreas	Parathyroid	Pituitary gland
				Prostate	Rectum/Low Colon	Salivary glands	Seminal vesicles
				Skin-protocol	Skeletal muscle	Cervical SC	Thoracic SC

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Animal number	Sex	Group/ Subgroup	Date data taken	Tissue / Observation(s) Locator, Color, General, Measurements, Severity levels
1218	M	1/1	23-Jul-03	Tissues marked 'Within normal limits': Lumbar SC, Spleen, Sternum, Sternal Marrow, Stomach, Testes, Thymus, Thyroid gland, Trachea, Urinary bladder, Zymbal's gland
1219	M	1/1	23-Jul-03	Within normal limits
1220	M	1/1	23-Jul-03	Within normal limits
2211	M	2/1	22-Jul-03	Within normal limits
2212	M	2/1	22-Jul-03	Within normal limits
2213	M	2/1		Cecum
			22-Jul-03	Abnormal Contents, , Black, Material, , Severe Thick
				Ileum
			22-Jul-03	Abnormal Contents, , Black, Material, , Severe Thick
				Jejunum
			22-Jul-03	Abnormal Contents, , Black, Material, , Severe Thick
				Lungs
			22-Jul-03	Discolored, Right diaphragmatic lobe, Tan, Focus, 0.2 - 0.5 cm, Slight
			22-Jul-03	Discolored, Right cardiac lobe, , Foci, </= 0.1 cm, Slight
				Tissues marked 'Within normal limits':
			22-Jul-03	Adrenal Glands, Aorta, Brain, Colon, Duodenum, Epididymides, Esophagus, Eyes, Femur, Femoral Marrow, Heart, Kidneys, Lacrimal gland, Larynx: V-SM-G, Larynx: V-DVTC, Liver, Mammary-protocol, Mediastinal LN, Mesenteric LN, Nerve, Nose/Turb Sec 1, Nose/Turb Sec 2, Nose/Turb Sec 3, Nose/Turb Sec 4, Optic nerve, Pancreas, Parathyroid, Pituitary gland, Prostate, Rectum/Low Colon, Salivary glands, Seminal vesicles, Skin-protocol, Skeletal muscle, Cervical SC, Thoracic SC, Lumbar SC, Spleen, Sternum, Sternal Marrow, Stomach, Testes, Thymus, Thyroid gland, Trachea, Urinary bladder, Zymbal's gland
2214	M	2/1	22-Jul-03 46	Within normal limits

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Animal number	Sex	Group/ Subgroup	Date data taken	Tissue / Observation(s) Locator, Color, General, Measurements, Severity levels			
2215	M	2/1		Lungs			
			22-Jul-03	Discolored, All lobes, Black, Foci, </= 0.1 cm, Slight			
				Thymus			
			22-Jul-03	Discolored, , Red, Foci, </= 0.1 cm, Slight			
				Tissues marked 'Within normal limits':			
			22-Jul-03	Adrenal Glands	Aorta	Brain	Cecum
				Colon	Duodenum	Epididymides	Esophagus
				Eyes	Femur	Femoral Marrow	Heart
				Ileum	Jejunum	Kidneys	Lacrimal gland
				Larynx: V-SM-G	Larynx: V-DVTC	Liver	Mammary-protocol
				Mediastinal LN	Mesenteric LN	Nerve	Nose/Turb Sec 1
				Nose/Turb Sec 2	Nose/Turb Sec 3	Nose/Turb Sec 4	Optic nerve
				Pancreas	Parathyroid	Pituitary gland	Prostate
				Rectum/Low Colon	Salivary glands	Seminal vesicles	Skin-protocol
				Skeletal muscle	Cervical SC	Thoracic SC	Lumbar SC
				Spleen	Sternum	Sternal Marrow	Stomach
				Testes	Thyroid gland	Trachea	Urinary bladder
				Zymbal's gland			
2216	M	2/1	23-Jul-03	Within normal limits			
2217	M	2/1	23-Jul-03	Within normal limits			
2218	M	2/1	23-Jul-03	Within normal limits			
2219	M	2/1	23-Jul-03	Within normal limits			
2220	M	2/1	23-Jul-03	Within normal limits			
3211	M	3/1	22-Jul-03	Within normal limits			
3212	M	3/1	22-Jul-03	Within normal limits			
3213	M	3/1	22-Jul-03	Within normal limits			
3214	M	3/1		Kidneys			
			22-Jul-03	Dilated Pelvis, Right, , , , Moderate			
				Submandib/Max LN			
			22-Jul-03	Enlarged, , , , , Moderate			
				Tissues marked 'Within normal limits':			
			22-Jul-03	Adrenal Glands	Aorta	Brain	Cecum
				Colon	Duodenum	Epididymides	Esophagus

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Animal number	Sex	Group/ Subgroup	Date data taken	Tissue / Observation(s) Locator, Color, General, Measurements, Severity levels			
3214	M	3/1	22-Jul-03	Tissues marked 'Within normal limits':			
				Eyes	Femur	Femoral Marrow	Heart
				Ileum	Jejunum	Lacrimal gland	Larynx: V-SM-G
				Larynx: V-DVTC	Liver	Lungs	Mammary-protocol
				Mediastinal LN	Mesenteric LN	Nerve	Nose/Turb Sec 1
				Nose/Turb Sec 2	Nose/Turb Sec 3	Nose/Turb Sec 4	Optic nerve
				Pancreas	Parathyroid	Pituitary gland	Prostate
				Rectum/Low Colon	Salivary glands	Seminal vesicles	Skin-protocol
				Skeletal muscle	Cervical SC	Thoracic SC	Lumbar SC
				Spleen	Sternum	Sternal Marrow	Stomach
				Testes	Thymus	Thyroid gland	Trachea
				Urinary bladder	Zymbal's gland		
3215	M	3/1	22-Jul-03	Within normal limits			
3216	M	3/1	23-Jul-03	Within normal limits			
3217	M	3/1		Kidneys			
			23-Jul-03	Dilated Pelvis, Bilateral, , , , Severe			
				Urinary bladder			
			23-Jul-03	Thickened, , , , , Severe			
			23-Jul-03	Calculus, Mucosa, , Firm, ,			
				Lymph Node,other			
			23-Jul-03	Enlarged, Left Iliac, , , , Moderate			
			23-Jul-03	Enlarged, Right Iliac, , , , Moderate			
				Tissues marked 'Within normal limits':			
			23-Jul-03	Adrenal Glands	Aorta	Brain	Cecum
				Colon	Duodenum	Epididymides	Esophagus
				Eyes	Femur	Femoral Marrow	Heart
				Ileum	Jejunum	Lacrimal gland	Larynx: V-SM-G
				Larynx: V-DVTC	Liver	Lungs	Mammary-protocol
				Mediastinal LN	Mesenteric LN	Nerve	Nose/Turb Sec 1
				Nose/Turb Sec 2	Nose/Turb Sec 3	Nose/Turb Sec 4	Optic nerve
				Pancreas	Parathyroid	Pituitary gland	Prostate
				Rectum/Low Colon	Salivary glands	Seminal vesicles	Skin-protocol
				Skeletal muscle	Cervical SC	Thoracic SC	Lumbar SC
				Spleen	Sternum	Sternal Marrow	Stomach
				Testes	Thymus	Thyroid gland	Trachea
				Zymbal's gland			
3218	M	3/1	23-Jul-03	Within normal limits			
3219	M	3/1	23-Jul-03	Within normal limits			

Huntingdon Life Sciences
Princeton Research Center
East Millstone, New Jersey
Terminal Sacrifice

Raw Data Listing of Gross Observations with Modifiers
Study number: 036143

Animal number	Sex	Group/ Subgroup	Date data taken	Tissue / Observation(s) Locator, Color, General, Measurements, Severity levels			
3220	M	3/1	23-Jul-03	Within normal limits			
4211	M	4/1	22-Jul-03	Within normal limits			
4212	M	4/1		Spleen			
			22-Jul-03	Irregular Surface, , , Rough, , Moderate			
			22-Jul-03	Discolored, , Tan, Foci, 0.2 - 0.5 cm, Moderate			
				Tissues marked 'Within normal limits':			
			22-Jul-03	Adrenal Glands	Aorta	Brain	Cecum
				Colon	Duodenum	Epididymides	Esophagus
				Eyes	Femur	Femoral Marrow	Heart
				Ileum	Jejunum	Kidneys	Lacrimal gland
				Larynx: V-SM-G	Larynx: V-DVTC	Liver	Lungs
				Mammary-protocol	Mediastinal LN	Mesenteric LN	Nerve
				Nose/Turb Sec 1	Nose/Turb Sec 2	Nose/Turb Sec 3	Nose/Turb Sec 4
				Optic nerve	Pancreas	Parathyroid	Pituitary gland
				Prostate	Rectum/Low Colon	Salivary glands	Seminal vesicles
				Skin-protocol	Skeletal muscle	Cervical SC	Thoracic SC
				Lumbar SC	Sternum	Sternal Marrow	Stomach
				Testes	Thymus	Thyroid gland	Trachea
				Urinary bladder	Zymbal's gland		
4213	M	4/1		Lungs			
			22-Jul-03	Discolored, All lobes, Red, , , Slight			
				Tissues marked 'Within normal limits':			
			22-Jul-03	Adrenal Glands	Aorta	Brain	Cecum
				Colon	Duodenum	Epididymides	Esophagus
				Eyes	Femur	Femoral Marrow	Heart
				Ileum	Jejunum	Kidneys	Lacrimal gland
				Larynx: V-SM-G	Larynx: V-DVTC	Liver	Mammary-protocol
				Mediastinal LN	Mesenteric LN	Nerve	Nose/Turb Sec 1
				Nose/Turb Sec 2	Nose/Turb Sec 3	Nose/Turb Sec 4	Optic nerve
				Pancreas	Parathyroid	Pituitary gland	Prostate
				Rectum/Low Colon	Salivary glands	Seminal vesicles	Skin-protocol
				Skeletal muscle	Cervical SC	Thoracic SC	Lumbar SC
				Spleen	Sternum	Sternal Marrow	Stomach
				Testes	Thymus	Thyroid gland	Trachea
				Urinary bladder	Zymbal's gland		
4214	M	4/1	22-Jul-03	Within normal limits			
4215	M	4/1	22-Jul-03	Within normal limits			

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Raw Data Listing of Gross Observations with Modifiers
Study number: 036143

Animal number	Sex	Group/ Subgroup	Date data taken	Tissue / Observation(s) Locator, Color, General, Measurements, Severity levels
4216	M	4/1	23-Jul-03	Within normal limits
4217	M	4/1	23-Jul-03	Within normal limits
4218	M	4/1	23-Jul-03	Within normal limits
4219	M	4/1	23-Jul-03	Within normal limits
4220	M	4/1	23-Jul-03	Within normal limits
1711	F	1/1	22-Jul-03	Within normal limits
1712	F	1/1	22-Jul-03	Within normal limits
1713	F	1/1	22-Jul-03	Within normal limits
1714	F	1/1	22-Jul-03	Within normal limits
1715	F	1/1	22-Jul-03	Within normal limits
1716	F	1/1	23-Jul-03	Within normal limits
1717	F	1/1	23-Jul-03	Within normal limits
1718	F	1/1	23-Jul-03	Within normal limits
1719	F	1/1		Extremity
			23-Jul-03	Hair thin/ absent, Both forepaws, , , , Severe
				Tissues marked 'Within normal limits':
			23-Jul-03	Adrenal Glands, Aorta, Brain, Cecum, Colon, Duodenum, Esophagus, Eyes, Femur, Femoral Marrow, Heart, Ileum, Jejunum, Kidneys, Lacrimal gland, Larynx: V-SM-G, Larynx: V-DVTC, Liver, Lungs, Mammary-protocol, Mediastinal LN, Mesenteric LN, Nerve, Nose/Turb Sec 1, Nose/Turb Sec 2, Nose/Turb Sec 3, Nose/Turb Sec 4, Optic nerve, Ovaries, Pancreas, Parathyroid, Pituitary gland, Rectum/Low Colon, Salivary glands, Skin-protocol, Skeletal muscle, Cervical SC, Thoracic SC, Lumbar SC, Spleen, Sternum, Sternal Marrow, Stomach, Thymus, Thyroid gland, Trachea, Urinary bladder, Uterus, Zymbal's gland

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Raw Data Listing of Gross Observations with Modifiers
Study number: 036143

Animal number	Sex	Group/ Subgroup	Date data taken	Tissue / Observation(s) Locator, Color, General, Measurements, Severity levels			
1720	F	1/1	23-Jul-03	Within normal limits			
2711	F	2/1		Skin-protocol			
			22-Jul-03	Hair Thin/Absent, Abdominal, , , , Slight			
				Tissues marked 'Within normal limits':			
			22-Jul-03	Adrenal Glands	Aorta	Brain	Cecum
				Colon	Duodenum	Esophagus	Eyes
				Femur	Femoral Marrow	Heart	Ileum
				Jejunum	Kidneys	Lacrimal gland	Larynx: V-SM-G
				Larynx: V-DVTC	Liver	Lungs	Mammary-protocol
				Mediastinal LN	Mesenteric LN	Nerve	Nose/Turb Sec 1
				Nose/Turb Sec 2	Nose/Turb Sec 3	Nose/Turb Sec 4	Optic nerve
				Ovaries	Pancreas	Parathyroid	Pituitary gland
				Rectum/Low Colon	Salivary glands	Skeletal muscle	Cervical SC
				Thoracic SC	Lumbar SC	Spleen	Sternum
				Sternal Marrow	Stomach	Thymus	Thyroid gland
				Trachea	Urinary bladder	Uterus	Zymbal's gland
2712	F	2/1		Lungs			
			22-Jul-03	Discolored, All lobes, White, Foci, </= 0.1 cm, Slight			
				Tissues marked 'Within normal limits':			
			22-Jul-03	Adrenal Glands	Aorta	Brain	Cecum
				Colon	Duodenum	Esophagus	Eyes
				Femur	Femoral Marrow	Heart	Ileum
				Jejunum	Kidneys	Lacrimal gland	Larynx: V-SM-G
				Larynx: V-DVTC	Liver	Mammary-protocol	Mediastinal LN
				Mesenteric LN	Nerve	Nose/Turb Sec 1	Nose/Turb Sec 2
				Nose/Turb Sec 3	Nose/Turb Sec 4	Optic nerve	Ovaries
				Pancreas	Parathyroid	Pituitary gland	Rectum/Low Colon
				Salivary glands	Skin-protocol	Skeletal muscle	Cervical SC
				Thoracic SC	Lumbar SC	Spleen	Sternum
				Sternal Marrow	Stomach	Thymus	Thyroid gland
				Trachea	Urinary bladder	Uterus	Zymbal's gland
2713	F	2/1	22-Jul-03	Within normal limits			
2714	F	2/1	22-Jul-03	Within normal limits			
2715	F	2/1	22-Jul-03	Within normal limits			
2716	F	2/1	23-Jul-03	Within normal limits			
2717	F	2/1	23-Jul-03	Within normal limits			

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Raw Data Listing of Gross Observations with Modifiers
Study number: 036143

Animal number	Sex	Group/ Subgroup	Date data taken	Tissue / Observation(s) Locator, Color, General, Measurements, Severity levels			
2718	F	2/1	23-Jul-03	Within normal limits			
2719	F	2/1	23-Jul-03	Within normal limits			
2720	F	2/1	23-Jul-03	Within normal limits			
3711	F	3/1	22-Jul-03	Within normal limits			
3712	F	3/1	22-Jul-03	Within normal limits			
3713	F	3/1		Thymus			
			22-Jul-03	Discolored, Right lobe, Red, , , Slight			
				Tissues marked 'Within normal limits':			
			22-Jul-03	Adrenal Glands	Aorta	Brain	Cecum
				Colon	Duodenum	Esophagus	Eyes
				Femur	Femoral Marrow	Heart	Ileum
				Jejunum	Kidneys	Lacrimal gland	Larynx: V-SM-G
				Larynx: V-DVTC	Liver	Lungs	Mammary-protocol
				Mediastinal LN	Mesenteric LN	Nerve	Nose/Turb Sec 1
				Nose/Turb Sec 2	Nose/Turb Sec 3	Nose/Turb Sec 4	Optic nerve
				Ovaries	Pancreas	Parathyroid	Pituitary gland
				Rectum/Low Colon	Salivary glands	Skin-protocol	Skeletal muscle
				Cervical SC	Thoracic SC	Lumbar SC	Spleen
				Sternum	Sternal Marrow	Stomach	Thyroid gland
				Trachea	Urinary bladder	Uterus	Zymbal's gland
3714	F	3/1	22-Jul-03	Within normal limits			
3715	F	3/1	22-Jul-03	Within normal limits			
3716	F	3/1	23-Jul-03	Within normal limits			
3717	F	3/1	23-Jul-03	Within normal limits			
3718	F	3/1	23-Jul-03	Within normal limits			
3719	F	3/1	23-Jul-03	Within normal limits			
3720	F	3/1	23-Jul-03	Within normal limits			
4711	F	4/1	22-Jul-03	Within normal limits			
4712	F	4/1	22-Jul-03	Within normal limits			

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Raw Data Listing of Gross Observations with Modifiers
Study number: 036143

Animal number	Sex	Group/ Subgroup	Date data taken	Tissue / Observation(s) Locator, Color, General, Measurements, Severity levels			
4713	F	4/1	22-Jul-03	Within normal limits			
4714	F	4/1		Lungs			
			22-Jul-03	Discolored, All lobes, Red, Foci, </= 0.1 cm, Slight			
				Tissues marked 'Within normal limits':			
			22-Jul-03	Adrenal Glands	Aorta	Brain	Cecum
				Colon	Duodenum	Esophagus	Eyes
				Femur	Femoral Marrow	Heart	Ileum
				Jejunum	Kidneys	Lacrimal gland	Larynx: V-SM-G
				Larynx: V-DVTC	Liver	Mammary-protocol	Mediastinal LN
				Mesenteric LN	Nerve	Nose/Turb Sec 1	Nose/Turb Sec 2
				Nose/Turb Sec 3	Nose/Turb Sec 4	Optic nerve	Ovaries
				Pancreas	Parathyroid	Pituitary gland	Rectum/Low Colon
				Salivary glands	Skin-protocol	Skeletal muscle	Cervical SC
				Thoracic SC	Lumbar SC	Spleen	Sternum
				Sternal Marrow	Stomach	Thymus	Thyroid gland
				Trachea	Urinary bladder	Uterus	Zymbal's gland
4715	F	4/1	22-Jul-03	Within normal limits			
4716	F	4/1	23-Jul-03	Within normal limits			
4717	F	4/1	23-Jul-03	Within normal limits			
4718	F	4/1	23-Jul-03	Within normal limits			
4719	F	4/1	23-Jul-03	Within normal limits			
4720	F	4/1	23-Jul-03	Within normal limits			

	Equipment List	Appendix I

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

Compound Generator
Butane cylinder (MG Industries).

Flowmeters
Top Trak™ Mass Flow Meter, sizes 0-100 sccm, 0 – 1 and 0 – 10 Lpm, Model 821-1 (Sierra Instruments).
Flowmeter, size 0 - 20 Lpm (Dwyer®).

Pressure Gauges
MG Industries backpressure gauges, P/N 10206 and 10201.

Regulator
MG Industries, Series 300.

Valve
Metering Valve, Model SS-4L Series (Nupro® Co.).

Tubing
Teflon® size 1/4".
Plastic, size 1/4" and 1/2" (Norton, Baxter).
Stainless steel, size 1/2".

Vacuum Pump
Thomas Industries Inc., Model 707CM 50.
GAST® backpressure gauge, Model NA.

Air Analyzer
MIRAN® 1A-CVF Ambient Air Analyzer (Wilks) with a Cole Parmer Strip Chart Recorder, Model 201, and a Micronta® LCD Benchtop Digital Multimeter No. 22-195.
Balston® Microfibre™ Disposable Filter Unit, Grade DQ, was attached in-line.
Gas-tight syringes, size 0 – 1, 0 – 5 and 0 – 100 mL (Hamilton).

	Equipment List	Appendix I

Particle Sizer
TSI Aerodynamic Particle Sizer, Model 331001 and a DELL computer, Model 486P/25, equipped with an Epson LQ-570+ Dot matrix printer, Model P630B.

Environmental Monitoring
VWR Temperature and Humidity Gauge.
Oxygen/Gas Analyzer, Model 1214S (Gastech).
Digital Sound Level Meter, Model 840029 (SPER Scientific).
Photometer 1 Light Meter (Quantum Instruments).

Chamber Air Flow
Dwyer® Magnehelic® gauge, calibrated prestudy with Side Trak™ III, with Digital Meter, Model 831-N2 (Sierra Instruments Inc.).

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

	MIRAN® Calibration	Appendix J

Methodology for Butane

Settings: The instrument settings for the unit are summarized below:

Wavelength, microns	10.3
Pathlength, dial setting	4.87
Slit width, mm	1
Range, absorbance	1
Response, seconds	1
Gain	High
Chart speed, cm/min	1
Chart volts	1

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

Injection Volume (µL)	Calculated Concentration[1] (ppm)	Absorbance Operator 1 (volts)	Absorbance Operator 2 (volts)	Absorbance Average (volts)
390	69	0.0053	0.0060	0.0057
510	90	0.0085	0.0087	0.0086
5000	887	0.0778	0.0763	0.0771
51,000	9043	0.719	0.734	0.727
61,000	10816	0.837	0.854	0.846

[1]Calculated Conc. (ppm) = $\dfrac{\text{Volume injected (µL)}}{5.64\text{L}}$

where: 5.64L = volume of MIRAN® closed-loop

	MIRAN® Calibration	Appendix J

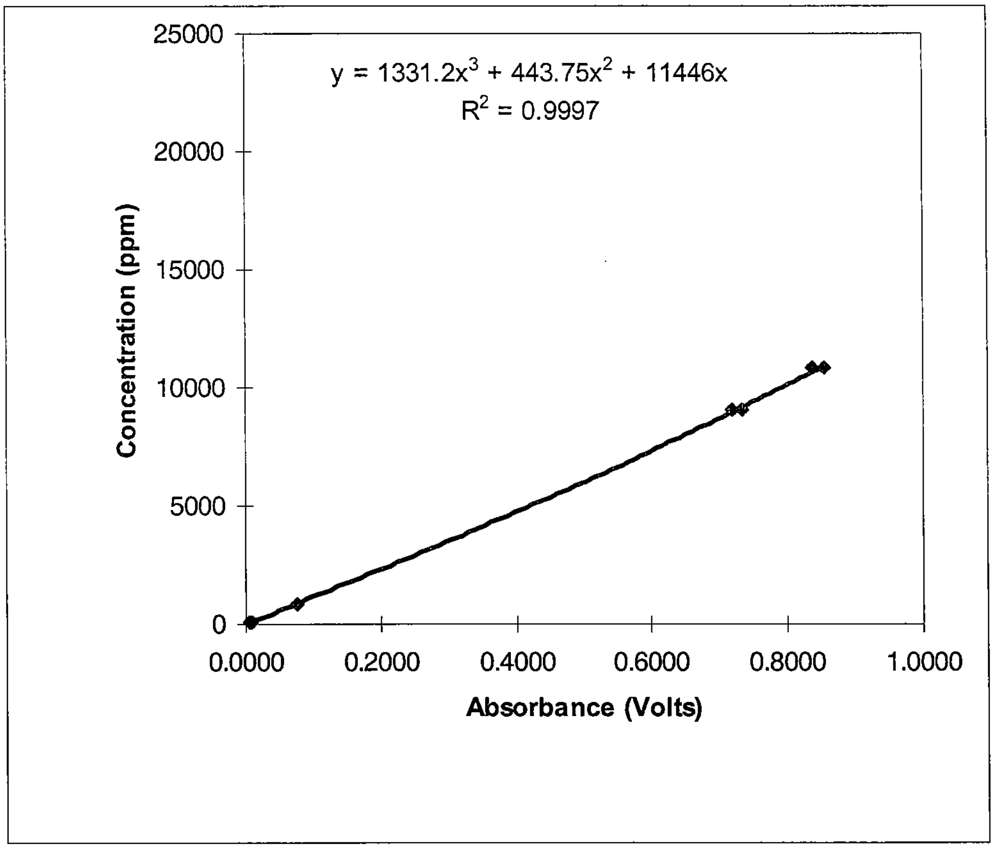
Calibration Checks: A three-point calibration check of the MIRAN® was performed prior to each exposure. The parameters are shown below:

Injection Volume (μL)	Calculated Concentration (ppm)	Expected Absorbance Reading (volts)	Acceptable Absorbance Range (volts)
510	90	0.0086	0.0073 – 0.0099
5000	887	0.0771	0.0655 – 0.887
51000	9043	0.727	0.618 – 0.836

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

	MIRAN® Calibration	Appendix J

Calibration Curve for Butane



	Chamber Distribution Results	Appendix K

Group (target)	Date	Port	IR Conc (ppm)	Ratio to H-1
2 (90 ppm)	2 July 2003	H-1	90.5	1.00
		H-2	93.9	1.04
		H-7	96.2	1.06
		H-8	85.9	0.95
3 (900 ppm)	2 July 2003	H-1	853	1.00
		H-2	745	0.87
		H-7	853	1.00
		H-8	853	1.00
	3 July 2003	H-1	724	1.00
		H-2	693	0.96
4 (9000 ppm)	2 July 2003	H-1	9200	1.00
		H-2	9210	1.00
		H-7	9220	1.00
		H-8	9250	1.01

	Chamber and Exposure Room Environmental Monitoring	Appendix L

Interval	Location	Test Substance (ppm)	Light (Ft Candles)	Noise (dB)	Oxygen (%)	Particle Sizing (mg/m^3)[a]
Pretest	Room	0	34.7	61.0	NM	
	Group 1	0	NM	NM	21	2.99×10^{-3}
	Group 2	0	NM	NM	21	1.55×10^{-3}
	Group 3	0	NM	NM	21	2.70×10^{-3}
	Group 4	0	NM	NM	21	1.77×10^{-3}
Exposure Day 1	Room	0	34.7	63.3	NM	
	Group 1	0	NM	NM	21	
	Group 2	88	NM	NM	21	
	Group 3	878	NM	NM	21	
	Group 4	8998	NM	NM	21	
Exposure Day 8	Room	0	33.9	61.2	NM	
	Group 1	0	NM	NM	21	
	Group 2	92	NM	NM	21	
	Group 3	897	NM	NM	21	
	Group 4	9103	NM	NM	21	
Exposure Day 14	Room	0	35.2	61.1	NM	
	Group 1	0	NM	NM	21	
	Group 2	93	NM	NM	21	
	Group 3	925	NM	NM	21	
	Group 4	9233	NM	NM	21	

NM = Not measured.
[a]Pretest results presented. For on-test results, see CMR (Appendix A).

Appendix M

PROTOCOL

BUTANE

A 2-WEEK RANGE-FINDING INHALATION TOXICITY STUDY IN THE RAT VIA WHOLE-BODY EXPOSURES

CONFIDENTIAL

HLS Study No.:	**03-6143**
Protocol No.:	**Final**
Date:	**30 June 2003**

PROTOCOL SIGNATURES / PREFACE

(Confidential Information - to be distributed on a need-to-know basis)

Study Title: Butane: A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Whole-Body Exposures

HLS Study No.: 03-6143

This is the Final Protocol. It has been reviewed and approved by:

1 July 03
Date

Gary M. Hoffman, B.A., DABT
Study Director
Huntingdon Life Sciences (HLS)
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30 June, 2003
Date

Thomas M. Gray, M.S., D.A.B.T.
Sponsor Representative
American Petroleum Institute (API)
Address: 1220 L Street, Northwest
Washington, D.C. 20005-4070
Phone No.: 202-682-8480
Fax No.: 202-682-8270
Email: grayt@api.com

TABLE OF CONTENTS

1. INTRODUCTION

HLS Study No.	03-6143
Study Title	Butane: A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Whole-Body Exposures
Testing Facility	Huntingdon Life Sciences 100 Mettlers Road P.O. Box 2360 East Millstone, NJ 08875-2360
Purpose	This study is designed to provide a preliminary assessment of the toxicity of the test substance when administered via whole-body inhalation to rats for 2 weeks in order to determine exposure levels for a subsequent OECD 422 inhalation study 03-4242.

2. STUDY PERSONNEL

Study Director	Gary M. Hoffman, B.A., DABT
Alternate Contact	Keith P. Hazelden, BSc, CBiol, MIBiol Director of Reproductive Toxicology x2590

Additional personnel will be documented in the study file and presented in the final report.

3. PROPOSED STUDY DATES

Study Initiation	Date Study Director signs protocol
Receipt of Test Animals	24 June 2003
First Day of Treatment	8 July 2003 (Experimental Start)
Last Day of Treatment	22 July 2003
Necropsy - Termination	22-23 July 2003
Experimental Completion	23 July 2003 (Date of last data collection)
Submission of Audited Draft Report	17 October 2003
Study Completion	Date final report is signed by Study Director

4. EXPERIMENTAL DESIGN

4.1. STUDY SUMMARY

Group	Test Substance	Exposure Level[a]	Number of Animals[b]	
		ppm	Males	Females
1	**Air Control**	0	10	10
2	**Butane**	90	10	10
3	**Butane**	900	10	10
4	**Butane**	9000	10	10

[a]Exposures will be 6 hours per day for 7 consecutive days per week for 2 weeks for a total of at least 14 exposures. Exposure levels are expressed as ppm of test substance. The exposures will be conducted via whole-body exposure.

[b]Complete postmortem evaluations will be performed on animals at termination of the study and on animals which are found dead or euthanized in a moribund condition during the course of the study.

The first day of exposures will be defined as Day 0 of the study.

4.2. JUSTIFICATION FOR ROUTE, DURATION AND FREQUENCY

The inhalation route is one of the potential routes of human exposure to this test substance. The duration of the study and frequency of exposures are considered to be the minimum necessary for determining exposure levels for a subsequent OECD 422 Study 03-4242.

4.3. JUSTIFICATION FOR TEST ANIMAL SELECTION

The rat is an animal model commonly utilized in toxicity studies as recommended in OECD and EPA guidelines. In addition, a historical database is available for comparative evaluation.

4.4. JUSTIFICATION FOR NUMBER OF ANIMALS

The number of animals in the protocol is considered to be the minimum necessary for scientific and statistical reasons in order to evaluate the data with sufficient confidence levels.

4.5. JUSTIFICATION FOR EXPOSURE LEVEL SELECTION

The exposure levels were selected based on prior results of minimal toxicity up to 1% (10000 ppm). Therefore, the high exposure level was established (for safety reasons) as 50% of the lower explosion limit (1.8% = 18000 ppm) for the test substance.

5. TEST SUBSTANCE

5.1. TEST SUBSTANCE: BUTANE

Test Substance Category: industrial gas

Description, lot number, storage, expiration date (if available) and handling procedures, as well as other pertinent information will be documented in the study data. The Testing Facility will purchase the test substance from a Sponsor approved vendor (MG Industries, Malvern PA). The test substance will be stored (ambient conditions) in an outside solvent shed except when in use in the inhalation laboratory. The test substance will be handled as a flammable gas.

5.2. IDENTIFICATION OF TEST SUBSTANCE

Unless otherwise noted, the identity, strength, purity, composition, stability and method of synthesis, fabrication and/or derivation of each batch of the test substance will be documented by the Supplier before its use in the study. This documentation will be maintained by the Supplier.

The Testing Facility will ensure that the location of the documentation of fabrication is provided in the report. Purity of the test substance will also be determined by the Testing Facility by assaying by GC before the study.

5.3. ARCHIVAL SAMPLES

An archival sample from each lot of test substance will be taken and stored in the Archives of the Sponsor (EPL Archives, Inc., 45610 Terminal Drive, Sterling, VA 20166). If multiple studies are conducted with the same test substance, a common archival sample may be taken and appropriately labeled.

5.4. ADMINISTRATION OF TEST SUBSTANCE

The test substance will be administered by whole-body inhalation exposure. The test substance will be administered as a gas (depending on the physical properties of the test substance) in the breathing air of the animals. The test atmosphere will be generated by an appropriate procedure determined during pre-study trials. The trials will be performed (at least two 6-hour periods) to evaluate the optimal set of conditions and equipment to generate a stable and uniform atmosphere at the target exposure levels. The method will be described in the raw data of the study and in the report.

The whole-body exposure chambers will each have a volume of approximately 1000 liters. Each chamber will be operated at a minimum flow rate of 200 liters per minute. The final airflow will be set to provide at least one air change in 5.0 minutes (12 air changes/hour) and a T_{99} equilibrium time of at most 23 minutes. This chamber size and air flowrate is considered adequate to maintain the animal loading factor below 5% and the oxygen level at 19% or higher. At the end of the exposure, all animals will remain in the chamber for a minimum of 30 minutes. During this time the chamber will be operated at approximately the same flow rate using clean air only.

5.5. EXPOSURE CONCENTRATION DETERMINATION

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

During each exposure, measurements of airborne concentrations of test substance in the animal's breathing zone will be performed at least four times using an appropriate sampling procedure and infrared spectrophotometric analytical procedure. Also prior to initiation of animal exposures, additional samples will be taken to determine the distribution of the test substance in the exposure chamber.

If more than the normal amount of trial time is required because of test substance generation or monitoring problems (80 technician hours), the Sponsor will be consulted prior to additional trials (additional cost).

5.6. PARTICLE SIZE DISTRIBUTION ANALYSIS

During each exposure, particle size determinations will be performed using a TSI Aerodynamic Particle Sizer to characterize the aerodynamic particle size distribution of any aerosol present.

5.7. CHAMBER AND EXPOSURE ROOM ENVIRONMENT

Chamber temperature, humidity, airflow rate and static pressure will be monitored continuously and recorded every 30 minutes during exposure. Chamber temperature and relative humidity will be maintained, to the maximum extent possible, between 20 to 24°C and 40 to 60%, respectively. Chamber oxygen levels (maintained at least 19%) will be measured pretest and at the beginning, middle and end of the study.

Air samples will be taken in the vapor generation area pretest and at the beginning, middle and end of the study. Light (maintained approximately 30-40 foot-candles at 1.0 meter above the floor) and noise levels (maintained below 85 decibels) in the exposure room will be measured pretest and at the beginning, middle and end of the study.

5.8. SUMMARY OF CHAMBER ACTIVITY

The minimum frequency of chamber activity is summarized below:

Activity	Frequency/chamber
Measured Test Substance Concentration	4X/day
Particle Size	1X/day
Temperature	13X/day
Relative Humidity	13X/day
Airflow Rate & Static Pressure	13X/day
Nominal Test Substance Concentration	1X/day
Rotation Pattern of Exposure Cages	1X/day
Loading/Unloading Verification	1X/day

5.9. FREQUENCY AND DURATION OF ADMINISTRATION

The test substance will be administered for 6 hours per day for 7 consecutive days per week for 2 weeks for a total of at least 14 exposures. Test substance administration will continue through the day prior to necropsy.

5.10. UNUSED TEST SUBSTANCE

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

6. TEST ANIMALS

6.1. SPECIES

Albino Rats (Outbred) Vaf/Plus®
Sprague-Dawley - derived (CD®)
Crl: CD (SD) IGS BR

6.2. SUPPLIER

Charles River Laboratories

Documentation of the specific breeding facility will be maintained in the study file.

6.3. ANIMAL REQUIREMENTS/SPECIFICATIONS

6.3.1. NUMBER OF ANIMALS ON STUDY

Total	Males	Females
80	40	40

6.3.2. AGE

Young adult (approximately 6 weeks at receipt; approximately 8 weeks (and no more than 9 weeks) at initiation of exposures.

6.3.3. WEIGHT

Approximately 200 to 300 grams (males) and 150 to 250 grams (females) at first exposure. Animals outside of this range may be used at the discretion of the Study Director.

6.4. ACCLIMATION PERIOD

Approximately 2 weeks; all animals will be checked for viability twice daily. Prior to assignment to study, all animals will be examined to ascertain suitability for study.

6.5. ANIMAL CARE AND HUSBANDRY

6.5.1. FACILITIES MANAGEMENT/ANIMAL HUSBANDRY

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

6.5.2. VETERINARY CARE

Animals will be monitored by the technical staff for any conditions requiring possible veterinary care. If any such conditions are identified, a staff veterinarian will be notified for an examination and evaluation. Animals will be treated as outlined in the Animal Welfare Act Compliance section of this protocol.

6.5.3. ENVIRONMENTAL CONDITIONS

Light/Dark Cycle

Twelve hour light/dark cycle provided via automatic timer.

Temperature

Temperature will be monitored in accordance with Testing Facility SOPs to ensure that the desired range of 18 to 26°C is maintained to the maximum extent possible.

Humidity

Humidity will be monitored in accordance with Testing Facility SOPs to ensure that the desired range of 30 to 70% is maintained to the maximum extent possible.

6.5.4. HOUSING

Animals will be individually housed in suspended, stainless steel wire mesh cages during the study.

6.5.5. FEED

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

6.5.6. WATER

Elizabethtown Water Company, Westfield, NJ; *ad libitum,* via automated watering system.

6.5.7. FEED ANALYSIS

Analytical certification of batches of feed provided by the manufacturer will be maintained on file at the Testing Facility. There are no known contaminants in the feed which are expected to interfere with the objectives of this study.

6.5.8. WATER ANALYSIS

Water analyses are conducted by Elizabethtown Water Company to assure that water meets standards specified under the EPA Federal Safe Drinking Water Act Regulations (40 CFR Part 141). Water analysis, provided by the supplier, will be maintained on file at the Testing Facility. In addition, chemical and microbiological analyses are conducted biannually on water samples collected from representative rooms in this facility. Results are maintained on file at the Testing Facility. There are no known contaminants which are expected to interfere with the objectives of this study.

6.5.9. ANIMAL ASSIGNMENT

More animals than required for the study will be purchased and acclimated. Animals considered suitable for study on the basis of pretest physical examinations, body weight data and any other pretest evaluations, will be randomly assigned to control or treated groups in an attempt to equalize mean group body weights. Individual weights of animals placed on test shall be within ±20% of the mean weight for each sex. Disposition of all animals not utilized in the study will be maintained in the study file.

6.5.10. IDENTIFICATION

Each animal will be assigned a temporary identification number upon receipt. After selection for study, each animal will be ear-tagged with a number assigned by the Testing Facility. This number plus the study number will comprise the unique animal number for each animal. If the tag is lost, it will be replaced. Each cage will be provided with a cage card which will be color coded for exposure level identification and will contain the study number and animal number.

6.5.11. ANIMAL HUSBANDRY/EXPOSURE

Housing:	Individually in cages.
Feed:	None.
Water:	None.

7. IN-LIFE EVALUATIONS

7.1. CLINICAL OBSERVATIONS

7.1.1. VIABILITY CHECKS (CAGE-SIDE)

Observations for mortality and general condition will be made at least twice daily (once in the morning and once in the afternoon). Animals in poor health or in a possible moribund condition will be identified for further monitoring and possible euthanasia.

7.1.2. PHYSICAL EXAMINATIONS

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

Out-of-Chamber: Each animal will be removed from its cage and examined at least once pretest and once per week during the study period. Examinations will include observations of general condition, skin and fur, eyes, nose, oral cavity, abdomen and external genitalia, occurrence of secretions and excretions, and autonomic activity (e.g., lacrimation, piloerection, pupil size, unusual respiratory pattern). Changes in gait, posture and response to handling as well as the presence of clonic or tonic movements, stereotypy (e.g., excessive grooming, repetitive circling) or bizarre behavior (e.g., self-mutilation, walking backward) will be recorded.

7.2. BODY WEIGHTS

Non-fasted body weights for each animal will be recorded at least once pretest, on the first day of exposures and once per week during the study period. Fasted weights will be obtained prior to necropsy.

7.3. FEED CONSUMPTION

Feed consumption will be measured (weighed) during the week prior to treatment initiation and once per week during the study period. Feed will be available without restriction 7 days/week except during exposures. Animals will be presented with weighed feeders at the scheduled intervals. After at least 5 days, the feeders will be reweighed and the resulting weight subtracted from the initial feeder weight to obtain the grams of feed consumed per animal per day. The grams consumed per kilogram of body weight per day will then be calculated for each animal.

8. POSTMORTEM EVALUATIONS

8.1. MACROSCOPIC PATHOLOGY

A complete macroscopic examination will be performed on all animals, including animals euthanized in a moribund condition or found dead; all abnormal observations will be recorded. The necropsy will consist of a careful examination of the external surface of the body, all orifices and the cranial, thoracic and abdominal cavities and their contents. Special attention should be paid to the organs of the reproduction system.

8.1.1. MORIBUND ANIMALS

Animals showing signs of severe debility, particularly if death appears imminent, will be humanely euthanized to prevent loss of tissues through autolysis.

8.1.2. TERMINAL NECROPSY

Necropsy will be performed on 10 animals/sex/group after animals have been treated for at least 14 days. Necropsy schedules will be established in order to assure that approximately equal numbers of males and females from each group will be examined at similar times of the day of necropsy.

8.2. METHOD OF EUTHANASIA

Exsanguination following carbon dioxide inhalation.

8.3. ORGAN WEIGHTS

Organs indicated below will be taken from all survivors at the scheduled necropsies, weighed, recorded and organ/body and organ/brain weight ratios calculated. Organs will not be weighed for animals found dead or euthanized in a moribund condition during the course of the study. Prior to weighing, all organs will be carefully dissected and properly trimmed to remove fat and other contiguous tissues in a uniform manner. Organs will be weighed as soon as possible after dissection to avoid drying. Paired organs will be weighed together.

adrenals	liver	seminal vesicles
brain	lungs	spleen
epididymides	ovaries	testes
heart	pituitary	thymus
kidneys		uterus

8.4. TISSUE PRESERVATION

Tissues listed in Appendix A will be obtained at necropsy and preserved for all animals.

Eyes – glutaraldehyde/paraformaldehyde initially and then 10% neutral buffered formalin

Testes – modified Davidson's solution initially and then 10% neutral buffered formalin

All other tissues - 10% neutral buffered formalin

Note: Lungs and urinary bladder will be infused with formalin to ensure fixation.

8.5. MICROSCOPIC PATHOLOGY EVALUATIONS

No examinations are required. Authorization will be obtained from the Sponsor prior to performing any examinations. If tissues are examined, standard stains (hematoxylin and eosin) will be used. Special stains may be employed on selected tissues to aid in making a diagnosis at the discretion of the Study Pathologist. Special stains may also be employed at the request of the Sponsor (additional cost).

9. ARCHIVING OF RECORDS AND SPECIMENS

All data documenting experimental details and study procedures and observations will be recorded and maintained as raw data. At the completion of the study, all reports, raw data, preserved archival specimens and retained samples will be maintained in the Testing Facility's Archives for a period of 1 year after submission of the signed final report.

The Sponsor will be contacted in order to determine the final disposition of these materials. The Sponsor is responsible for all cost associated with the storage of these materials beyond one year from the issuance of the final report and for any costs associated with the shipment of these materials to the Sponsor or to any other facility designated by the Sponsor.

10. STATISTICAL ANALYSIS

10.1. ITEMS TO BE ANALYZED

The following will be compared for control and test substance-treated groups.

mean body weight values
mean feed consumption values
mean terminal organ weights, organ/body and organ/brain weight ratios

10.2. PROCEDURES

Evaluation of equality of group means will be made by the appropriate statistical method, followed by a multiple comparison test if needed. Bartlett's test (Bartlett, 1937; Sokal and Rohlf, 1995) will be performed to determine if groups have equal variances. For all parameters except organ weights, if the variances are equal, parametric procedures will be used; if not, nonparametric procedures will be used. Organ weight data will be analyzed only by parametric methods. The parametric method will be the standard one-way analysis of variance (ANOVA) using the F ratio to assess significance (Armitage, 1971; Dunlap and Duffy, 1975). If significant differences among the means are indicated, additional tests will be used to determine which means are significantly different from the control: Dunnett's (Dunlap et al., 1981; Dunnett, 1955, 1964), Williams (Williams, 1971, 1972), or Cochran and Cox's modified t-test (Cochran and Cox, 1959). The nonparametric method will be the Kruskal-Wallis test (Kruskal and Wallis, 1952, 1953) and if differences are indicated, Shirley's test (Shirley, 1977), Steel's test (Steel, 1959), or Pairwise Comparison with Bonferroni Correction (Games and Howell, 1976) will be used to determine which means differ from control. Bartlett's test for equality of variance will be conducted at the 1% significance level; all other statistical tests will be conducted at the 5% and 1% significance levels.

References for these procedures are:

Armitage, P. 1971. *Statistical Methods in Medical Research.* Oxford, UK: Blackwell Scientific Publications; Bartlett, M.S. 1937. Properties of sufficiency and statistical tests. *Proceedings of the Royal Society, Series A,* 160: 268-282; Cochran, W.G. and Cox, G.M. 1959. *Experimental Designs*, New York: John Wiley, pp. 100-102; Dunlap, W.P. and Duffy, J.A. 1975. Fortran IV Functions for Calculating Exact Probabilities Associated with Z, Chi-Square, T and F Values. *Behav. Res. Methods and Instrumentations* 7:59-60; Dunlap, W.P., Marx, M.S. and Agamy, G.G. 1981. Fortran IV functions for calculating probabilities associated with Dunnett's test. *Behav. Res. Methods and Instrumentation* 13: 363-366; Dunnett, C.W. 1955. A multiple comparison procedure for comparing several treatments with a control. *Journal of the American Statistical Association* 50: 1096-1121; Dunnett, C.W. 1964. New tables for multiple comparisons with a control. *Biometrics* 20-3: 482-491; Games, P.A. and Howell, J.F. 1976. Pairwise multiple comparison procedures with unequal n's and/or variances: a monte-carlo study. Journal of Educational Statistics 1: 113-125; Kruskal, W.H. and Wallis, W.A. 1952. Use of Ranks in one-criterion variance analysis. Journal of the American Statistical Association 47: 583-621; Kruskal, W.H. and Wallis, W.A. 1953. Errata for Kruskal-Wallis (1952) Journal of the American Statistical Association 48: 907-911; Shirley, E.A.C. 1977. A non-parametric equivalent of Williams' test for contrasting increasing dose levels of a treatment. Biometrics 33: 386-389; Sokal, R.R. and Rohlf, F.J. 1995. Biometry. 3rd Edition. San Francisco: W.H. Freeman pp. 369-371; Steel, R.G.D. 1959. A multiple comparison rank sum test: treatment versus control. *Biometrics* 15: 560-572.; Williams, D.A. 1971.

A test for differences between treatment means when several dose levels are compared with a zero dose control. Biometrics 27: 103-117; Williams, D.A. 1972. The comparison of several dose levels with a zero dose control. Biometrics 28: 519-531.

11. REPORTING

11.1. STATUS REPORTS

Periodic written (weekly) updates on study progress will be provided by the Study Director.

11.2. FINAL REPORT

One unbound hard copy and one electronic copy of a draft report will be submitted following termination of the study. After receipt and review of the Sponsor's comments, appropriate changes will be made and two hard copies and one electronic copy of a signed, final report will be issued. (Additional copies will be provided at additional cost). The report will minimally include:

Compliance Statement (including Sponsor signature line)
Quality Assurance Statement
Summary
Introduction
Experimental Design
Materials and Methods
Discussion of Study Results
Conclusion (including NOAEL statement, if applicable)
Tables of Exposure Data
Mortality Data
Individual animal termination history
Summary of daily animal observations (as appropriate)
Individual and summary tables of weekly physical examination data
Tables of mean and individual body weights
Tables of mean and individual feed consumption
Tables of mean and individual organ weights, organ/brain
and organ/body weight ratios
Individual and summary tables of macroscopic pathology findings
References for experimental methodology
Senior personnel participating in the study
Copy of study protocol and associated amendments

12. REGULATORY REFERENCES

12.1. TESTING GUIDELINES

This study is not designed to meet regulatory requirements. It is designed to provide preliminary toxicity data for the test substance in order to determine appropriate exposure levels for a subsequent OECD 422 inhalation study 03-4242.

12.2. GOOD LABORATORY PRACTICES

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

12.3. ANIMAL WELFARE ACT COMPLIANCE

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

1. The Sponsor's signature on this protocol documents that, for the study described, there are no generally accepted non-animal alternatives and the study does not unnecessarily duplicate previous experiments in regard to species, test substance, route of administration or duration of treatment.

2. All procedures used in this study have been designed to avoid discomfort, distress and pain to the animals. All methods are described in this study protocol or written laboratory standard operating procedures.

3. Any procedures outlined in this study which cause more than momentary or slight pain or distress to the animals will be performed with appropriate sedatives, analgesics or anesthetics unless the withholding of these agents is justified for scientific reasons, in writing by the Sponsor and the Study Director, in which case the procedure will continue for the minimum time necessary. Documentation of the justification for withholding treatment for pain

or distress and IACUC approval of the procedures will be made prior to study initiation on the IACUC Protocol Review Form.

4. Animals experiencing more than momentary or slight pain or distress due to test substance or injury or illness will be treated by the Testing Facility's veterinary staff with approved analgesics or agents to relieve pain after consultation with the Study Director and Sponsor. However, in emergency situations, the veterinary staff is authorized to administer emergency treatment as necessary. Any subsequent treatment or euthanasia will be administered after consultation with the Study Director. The Sponsor will be advised by the Study Director of all emergency situations in as timely a manner as possible.

5. Methods of euthanasia used during this study are in conformance with the above-referenced regulations.

12.4. INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC)

The IACUC Protocol Review Subcommittee has reviewed this protocol and found it to be in compliance with all appropriate regulations.

13. QUALITY ASSURANCE MONITORING

The Huntingdon Life Sciences Quality Assurance Unit will monitor the facilities, equipment, personnel, methods, practices, records and controls used in this study to assure that they are in conformance with this protocol, company SOPs, and the appropriate Good Laboratory Practice requirements.

14. ALTERATION IN STUDY DESIGN

Alterations of this protocol may be made as the study progresses. No changes in the protocol will be made without the consent of the Sponsor. In the event that the Sponsor authorizes a protocol change verbally, such changes will be honored by the Testing Facility and will be followed by a written verification. All protocol modifications will be signed by the Study Director and a Sponsor representative. Any modifications potentially affecting animal welfare will also be signed by 2 members of the Institutional Animal Care and Use Committee prior to the modification's implementation.

APPENDIX A
Tissues Preserved

Tissue	Preserved
adrenal gland	X
aorta (thoracic)	X
bone (sternum/femur)	X
bone marrow (rib) [a]	X
brain (medulla/pons, cerebrum and cerebellum)	X
epididymides	X
esophagus	X
eye (with optic nerve)	X
heart	X
kidneys	X
large intestine (cecum, colon, and rectum)	X
lacrimal gland	X
larynx	X
liver	X
lungs (with mainstem bronchi)	X
lymph nodes (mediastinal and mesenteric)	X
mammary gland	X
muscle (biceps femoris)	X
nasopharyngeal tissue	X
nerve (sciatic)	X
ovaries	X
pancreas	X
pituitary	X
prostate	X

Tissue	Preserved
salivary gland with submandibular lymph node	X
seminal vesicles	X
skin	X
small intestine (duodenum, jejunum, ileum)	X
spinal cord (cervical, thoracic, lumbar)	X
spleen	X
stomach	X
testes	X
thymic region	X
thyroid (with parathyroids)	X
trachea	X
urinary bladder	X
uterus (body/horns with cervix)	X
Zymbal's gland	X
gross lesions and tissue masses	X
target organs[b]	X

[a]Bone marrow smears will be prepared. They will only be evaluated (Sponsor approval, additional cost) if needed.

[b]Target organs will be designated by the Study Director, Pathologist and/or Sponsor based on experimental findings.

Protocol Amendment No. 1

Study Title: Butane: A 2-Week Range-Finding Inhalation Toxicity Study
in the Rat via Whole-Body Exposures

Changes

1. EXPOSURE CONCENTRATION DETERMINATION, page 4:

Revise: A nominal exposure concentration will be calculated daily, if possible. The **flow of test substance into the chamber and the** flow of air through the chamber will be monitored using appropriate calibrated equipment. ~~The test substance consumed during the exposure will be divided by the total volume of air passing through the chamber (volumetric flow rate times total exposure time) to give the nominal concentration.~~ **The average test substance flow during the exposure will be divided by the average chamber airflow to give the nominal concentration.**

2. TISSUE PRESERVATION, page 11:

Revise: Testes **and epididymides** – modified Davidson's solution initially and then 10% neutral buffered formalin

Reasons for Changes

1. Clarification of the procedure for calculating the nominal concentration for this gaseous test substance that is in cylinders too heavy to weigh before and after use.
2. Revision of the procedure for preservation of the epididymides.

Amendment approved by:

Gary M. Hoffman, B.A., DABT
Study Director

31 July 03
Date

Thomas M. Gray, M.S., DABT
Sponsor Representative

31 July 2003
Date

Protocol Amendment No. 2

Study Title: Butane: A 2-Week Range-Finding Inhalation Toxicity Study in the Rat via Whole-Body Exposures

Changes

1. Proposed Study Dates, page 1:

Revise:	Receipt of Test Animals	24 June 2003 **(Experimental Start)**
	First Day of Treatment	8 July 2003 ~~(Experimental Start)~~

2. Identification of Test Substance, page 5:
Add: ....Purity of the test substance will also be determined by the Testing Facility by assaying by GC before the study. **Stability of the test substance will also be determined by the Testing Facility by assaying by GC after the subsequent OECD 422 study 03-4242.**

3. Animal Requirements/Specifications, page 7:
Add: **Female rats will be nulliparous and non-pregnant.**

4. Statististical Analysis/Procedures, page 12:
Revise: Evaluation of equality of group means will be made by the appropriate statistical method, followed by a multiple comparison test if needed. Bartlett's test (Bartlett, 1937; Sokal and Rohlf, 1995) will be performed to determine if groups have equal variances. For all parameters except organ weights, if the variances are equal, parametric procedures will be used; if not, nonparametric procedures will be used. Organ weight data will be analyzed only by parametric methods. The parametric method will be the standard one-way analysis of variance (ANOVA) using the F ratio to assess significance (~~Armitage, 1971;~~ Dunlap and Duffy, 1975). If significant differences among the means are indicated, additional tests will be used to determine which means are significantly different from the control: Dunnett's (Dunlap et al., 1981; Dunnett, 1955, 1964), ~~Williams (Williams, 1971, 1972),~~ or Cochran and Cox's modified t-test (Cochran and Cox, 1959). The nonparametric method will be the Kruskal-Wallis test (Kruskal and Wallis, 1952, 1953) and if differences are indicated, ~~Shirley's test (Shirley, 1977)~~, ~~Steel's test (Steel, 1959)~~, or Pairwise Comparison with Bonferroni Correction (Games and Howell, 1976) will be used to determine which means differ from control. Bartlett's test for equality of variance will be conducted at the 1% significance level; all other statistical tests will be conducted at the 5% and 1% significance levels.

References for these procedures are:

~~Armitage, P. 1971. Statistical Methods in Medical Research. Oxford, UK: Blackwell Scientific Publications;~~ Bartlett, M.S. 1937. Properties of sufficiency and statistical tests.

Protocol Amendment No. 2

Proceedings of the Royal Society, Series A, 160: 268-282; Cochran, W.G. and Cox, G.M. 1959. *Experimental Designs*, New York: John Wiley, pp. 100-102; Dunlap, W.P. and Duffy, J.A. 1975. Fortran IV Functions for Calculating Exact Probabilities Associated with Z, Chi-Square, T and F Values. *Behav. Res. Methods and Instrumentations* 7:59-60; Dunlap, W.P., Marx, M.S. and Agamy, G.G. 1981. Fortran IV functions for calculating probabilities associated with Dunnett's test. *Behav. Res. Methods and Instrumentation* 13: 363-366; Dunnett, C.W. 1955. A multiple comparison procedure for comparing several treatments with a control. *Journal of the American Statistical Association* 50: 1096-1121; Dunnett, C.W. 1964. New tables for multiple comparisons with a control. *Biometrics* 20-3: 482-491; Games, P.A. and Howell, J.F. 1976. Pairwise multiple comparison procedures with unequal n's and/or variances: a monte-carlo study. Journal of Educational Statistics 1: 113-125; Kruskal, W.H. and Wallis, W.A. 1952. Use of Ranks in one-criterion variance analysis. Journal of the American Statistical Association 47: 583-621; Kruskal, W.H. and Wallis, W.A. 1953. Errata for Kruskal-Wallis (1952) Journal of the American Statistical Association 48: 907-911; ~~Shirley, E.A.C. 1977. A non-parametric equivalent of Williams' test for contrasting increasing dose levels of a treatment. Biometrics 33: 386-389;~~ Sokal, R.R. and Rohlf, F.J. 1995. Biometry. 3rd Edition. San Francisco: W.H. Freeman pp. 369-371; ~~Steel, R.G.D. 1959. A multiple comparison rank sum test: treatment versus control. Biometrics 15: 560-572.; Williams, D.A. 1971. A test for differences between treatment means when several dose levels are compared with a zero dose control. Biometrics 27: 103-117; Williams, D.A. 1972. The comparison of several dose levels with a zero dose control. Biometrics 28: 519-531.~~

Reasons for Changes

1. Correction of the Experimental Start Date as per OECD GLP's.
2. Clarification of how the stability of the test substance will be documented.
3. Oversight in original protocol.
4. Removal of statistical procedures and references not relevant to this study.

Amendment approved by:

Gary M. Hoffman, B.A., DABT
Study Director

28 oct 03
Date

Thomas M. Gray, M.S., DABT
Sponsor Representative

10/28/03
Date

STUDY TITLE

Analytical Report For:

Butane:
A 2 Week Range-Finding Inhalation Toxicity Study in the Rat Via Whole-Body Inhalation Exposures

AUTHOR

Yonggang Wang

REPORT DATE

14 August 2008

STUDY NUMBER

03-6143

	Analytical Report	Appendix N

SIGNATURES

Written by: ____________________ 14 Aug 08
Yonggang Wang, M.S. Date
Laboratory manager
Formulation Chemistry Services

Reviewed by: K A Saladdin 14 Aug 08
Kay Saladdin, B.S. Date
Associate Director
Formulation Chemistry Services

Approved by: ____________________ 14 Aug 08
Barbara A. Litzenberger, B.S., MT(ASCP) Date
Director
Analytical Services

Table of Contents

1. Summary

The test substance and the analytical standard (Butane) were analyzed ("pre-study") to determine the purity and stability of the test substance by comparison to the analytical standard. The analytical method was validated at Huntingdon Life Sciences (HLS). The analytical method involved gas bag sampling of the test substance and the analytical standard and quantification using Gas Chromatography with Flame Ionization Detection (FID).

2. Experimental Procedures

The analytical method (HLS-012-03) was validated by Formulation Chemistry at HLS. Details of the analytical method and the validation are maintained in this study file.

Gas bag sampling of the test substance and the analytical standard was performed in the Inhalation Department at HLS. The test substance and the analytical standard were analyzed using a Gas Chromatograph equipped with a HP Plot Q (30 m x 0.32 mm, 20 µm) column and Flame Ionization Detector (FID) to determine the purity of Butane test substance. HP 3396A integrator was used for data collection and Excel was used for processing the data.

Date of sample analysis is listed as follows:

Interval	Date Analyzed
"Pre-Study" Characterization	30 May 03

3. Results and Discussion

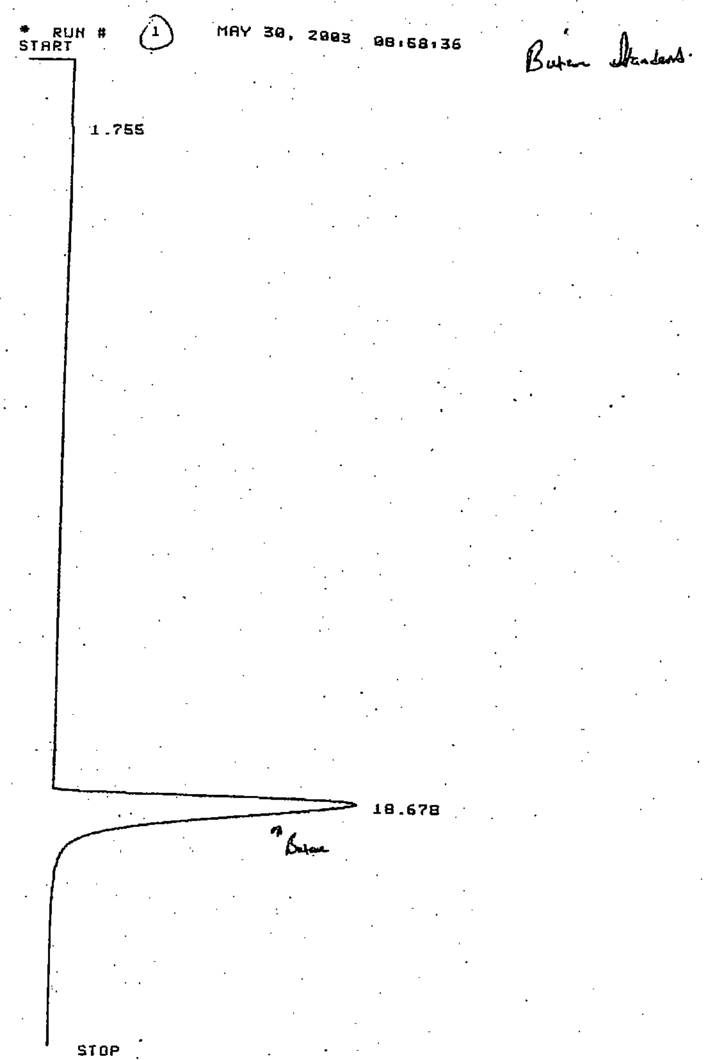
The test substance and analytical standard (Butane) were analyzed prior to the initiation of the study to determine the purity of the test substance. Stability of the test substance was analyzed on the subsequent study (03-4242). The results of the characterization are presented in Tables I and II. A typical chromatogram of Butane standard is presented in Figure I. A typical chromatogram of Butane test substance is presented in Figure II.

Table I: Characterization ("Pre-Study")

Sample ID	Area % of Ethane	Area % of Propane	Area % of Isobutane	Area % of Other Impurities	Area % of Butane Standard	Mean Area % of Butane Standard
Butane Standard	0.00	0.00	0.00	0.01	99.99	99.96
Butane Standard	0.00	0.00	0.00	0.06	99.94	
Butane Standard	0.00	0.00	0.00	0.05	99.95	

Sample ID	Area % of Ethane	Area % of Propane	Area % of Isobutane	Area % Other Impurities	Area % of Butane Substance	Mean Area % of Butane Test Substance
Butane Test Substance	0.02	0.12	0.69	0.01	99.16	99.23
Butane Test Substance	0.02	0.12	0.54	0.02	99.30	
Butane Test Substance	0.02	0.12	0.60	0.02	99.24	

Figure I. A Typical Gas Chromatogram of Butane Analytical Standard



RUN# 1 MAY 30, 2003 08:58:36

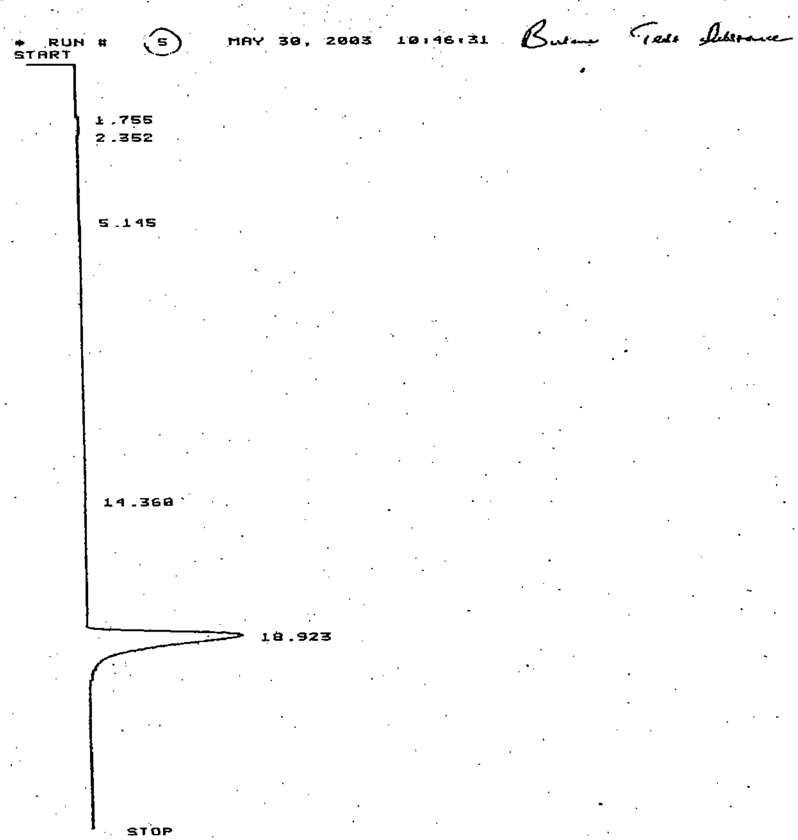
AREA%

RT	AREA	TYPE	WIDTH	AREA%
1.755	330	VB	.018	.01466
18.678	2250757	PV	.674	99.98534

TOTAL AREA=2251086
MUL FACTOR=1.0000E+00

Response (mV) vs Time (minutes)

Figure II. A Typical Gas Chromatogram of Butane Test Substance



RUN# 5 MAY 30, 2003 10:46:31

AREA%

RT	AREA	TYPE	WIDTH	AREA%
1.755	195	VB	.018	.02188
2.352	176	BB	.019	.01976
5.145	1098	BP	.085	.12321
14.360	4779	PV	.664	.53625
18.923	884943	BB	.566	99.29891

TOTAL AREA= 891191
MUL FACTOR=1.0000E+00

Response (mV) vs Time (minutes)

	Testing Facility Personnel	Appendix O

TITLE/DEPARTMENT	NAME/DEGREE
SENIOR VICE PRESIDENT, SAFETY ASSESSMENT	Sylvie J. Gosselin, D.V.M., Ph.D., Diplomate A.C.V.P.
DIRECTOR OF REPRODUCTIVE TOXICOLOGY	Keith P. Hazelden, B.Sc., M.I.Biol.
DIRECTOR, ANALYTICAL SERVICES	Barbara A. Litzenberger, B.S., M.T. (ASCP)
DIRECTOR, TOXICOLOGY OPERATIONS	Ian Vanterpool, F.I.A.T.
DIRECTOR, QUALITY ASSURANCE	Nicki S. Iacono, B.S.
STUDY DIRECTOR	Gary M. Hoffman, B.A., D.A.B.T.
STUDY MONITOR	Tara A. Gankiewicz, B.A.
VETERINARIAN	Teresa S. Kusznir, V.M.D.
MANAGER/SUPERVISOR	
Inhalation Toxicology	Robert Faust, B.S.
Pharmacy	Michael S. McCarthy
Analytical Services	Kay Saladdin, B.S.
Necropsy	G. Elizabeth Baxter, B.S.

	Report Amendments	Appendix P

There are no amendments for this report at this time.

	Report Amendments	Appendix OO

The following is a list of changes made to the final report.

Page No.	Change 1	Reason for Change
1, 290, 498	Study title on cover pages revised to: "Butane: Combined Repeated-Exposure Toxicity with Reproduction/Developmental Toxicity and Neurotoxicity Screening in Rats via Whole-Body Inhalation Exposures" Also, amended report date added and total number of pages revised.	Study title revised per sponsor request and protocol amendment to include developmental endpoints.
4	Inclusion of Quality Assurance Statement with Report Amendment audit and new signature/date.	Additional audit of report amendment.
5, 6	Study title on summary revised to: "Butane: Combined Repeated-Exposure Toxicity with Reproduction/Developmental Toxicity and Neurotoxicity Screening in Rats via Whole-Body Inhalation Exposures"	Study title revised per sponsor request and protocol amendment to include developmental endpoints.
	Also, last sentence of conclusion revised to read "Therefore, a no observed adverse effect level (NOAEL) of 9000 ppm was determined for this study's systemic, reproductive/developmental, and neonatal endpoints."	Reproduction reference clarified to include developmental endpoints per sponsor request and protocol amendment.
13	Section 2.3, footnote c: reference to reproduction study was revised to "reproduction/developmental study".	Reproduction reference clarified to include developmental endpoints per sponsor request and protocol amendment.
14	Section 2.4.3, Test Animal Selection: reference to reproduction toxicity was revised to "reproduction/developmental toxicity".	Reproduction reference clarified to include developmental endpoints per sponsor request and protocol amendment.
45	Section 4. Conclusion: Last sentence revised to read "Therefore, a no observed adverse effect level (NOAEL) of 9000 ppm was determined for this study's systemic, reproductive/developmental, and neonatal endpoints."	Reproduction reference clarified to include developmental endpoints per sponsor request and protocol amendment.

	Report Amendments	Appendix OO

Page No.	Change 1	Reason for Change
49	Notes on the General Preface were numbered to add the following as No. 2: The study title was revised to "Butane: Combined Repeated-Exposure Toxicity with Reproduction/Developmental Toxicity and Neurotoxicity Screening in Rats via Whole-Body Inhalation Exposures" effective 16 November 2009. Only the cover page and summary of the report were revised to reflect this change since all other pages were computer generated based on the original study title.	Note added to clarify why the study title was revised and what sections of the report were affected.
	Also, the original note was corrected from Days 14-20 - Mating to Days 14-28 - Mating.	Correction of typographical error.
689 - 783	Appendix KK, Neurobehavioral Positive Control Data for functional observational battery and motor activity was replaced.	Positive control data was replaced with up-dated information from amended reports. Notes were added to the preface pages (689 and 758) clarifying source of information.
784	Preface to Protocol and Protocol Amendments removed, and protocol renumbered as pages 784 - 819.	Blank preface page removed as unnecessary.
820	Protocol amendment no. 4 added to report.	Addition of Protocol Amendment No. 4 revising the study title.

Note: The total number of pages in the report has increased to 1012 due to the additional page of this report amendment.

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

14 mar 10
Date