

APPENDIX G: INDIVIDUAL ANIMAL WEEKLY BODY WEIGHTS

PRODUCT IDENTIFICATION

Silk Fibroin

Individual Animal Body Weights
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male		Bodyweight (g)					
0 mg/kg/day Group 1	Day(s) Relative to Start Date						
	1	8	15	22	29	30	
7001	240	282	330	382	428	399	
7002	222	271	326	371	410	380	
7003	226	266	314	344	407	360	
7004	226	273	322	342	389	355	
7005	245	275	365	423	481	444	
7006	220	245	320	374	441	389	
7007	235	283	326	391	436	402	
7008	212	266	316	365	406	379	
7009	250	304	350	401	434	404	
7010	243	301	352	405	454	432	
Mean	231.9	275.6	332.1	380.2	428.6	394.4	
SD	12.5	17.3	17.4	26.5	26.9	28.4	
N	10	10	10	10	10	10	

Individual Animal Body Weights
PSL Study Number 51651 - A 28 Day Oral Gavage Toxicity Study in Rats

Sex: Male Bodyweight (g)

125 mg/kg/day Group 2	Day(s) Relative to Start Date					
	1	8	15	22	29	30
7021	247	269	333	364	397	371
7022	223	291	339	399	431	412
7023	226	283	327	378	413	379
7024	212	257	295	338	374	336
7025	225	270	311	364	395	372
7026	241	296	340	380	413	391
7027	221	276	325	389	440	420
7028	239	287	336	388	408	383
7029	248	288	331	380	420	389
7030	240	285	337	374	410	384
Mean	232.2	282.2	327.5	372.8	410.1	383.7
SD	12.3	11.6	14.2	15.6	18.7	23.1
N	10	10	10	10	10	10

Individual Animal Body Weights
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male		Bodyweight (g)					
250 mg/kg/day Group 3	Day(s) Relative to Start Date						
	1	8	15	22	29	30	
7041	240	295	340	391	430	406	
7042	239	293	345	399	430	408	
7043	224	285	344	390	420	407	
7044	211	260	324	369	407	383	
7045	226	265	315	344	393	352	
7046	247	300	346	391	436	395	
7047	230	282	325	365	395	373	
7048	253	308	357	401	440	409	
7049	243	290	340	382	423	400	
7050	217	267	315	358	392	364	
Mean	233.0	284.5	335.2	379.1	416.6	389.7	
SD	13.8	16.0	14.4	18.9	18.4	20.6	
N	10	10	10	10	10	10	

Individual Animal Body Weights
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male	Bodyweight (g)	Day(s) Relative to Start Date					
		1	8	15	22	29	30
500 mg/kg/day Group 4							
7061	211	269	327	376	419	385	
7062	244	312	359	413	447	415	
7063	250	306	358	400	436	409	
7064	232	303	367	420	466	419	
7065	233	292	334	386	426	402	
7066	225	279	329	375	425	388	
7067	240	290	340	385	447	413	
7068	223	285	330	381	459	406	
7069	217	260	303	355	396	370	
7070	242	303	361	415	463	427	
Mean	231.7	289.9	340.8	392.6	438.2	403.4	
SD	12.6	16.9	20.1	20.5	22.3	17.5	
N	10	10	10	10	10	10	

Individual Animal Body Weights
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Bodyweight (g)

0 mg/kg/day Group 1	Day(s) Relative to Start Date					
	1	8	15	22	29	31
7011	181	208	220	236	245	233
7012	208	220	242	270	282	261
7013	200	211	221	235	245	228
7014	215	240	270	290	295	274
7015	222	240	255	271	282	266
7016	225	248	247	275	279	275
7017	197	221	247	254	253	246
7018	190	207	226	239	250	232
7019	205	224	255	259	275	253
7020	198	224	247	245	280	247
Mean	204.2	224.3	243.2	256.3	268.5	251.5
SD	13.9	14.2	16.0	17.2	18.4	17.3
N	10	10	10	10	10	10

Individual Animal Body Weights
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Bodyweight (g)

125 mg/kg/day Group 2	Day(s) Relative to Start Date					
	1	8	15	22	29	31
7031	188	201	213	224	238	201
7032	209	231	267	273	305	284
7033	203	212	232	246	256	244
7034	226	240	260	266	284	262
7035	206	232	250	257	269	250
7036	196	208	220	215	230	220
7037	197	207	223	241	250	238
7038	212	234	243	270	280	262
7039	223	250	283	301	320	291
7040	191	211	218	231	238	225
Mean	204.9	222.6	240.9	252.4	267.0	247.7
SD	12.8	16.7	23.7	26.1	30.1	28.2
N	10	10	10	10	10	10

Individual Animal Body Weights
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Bodyweight (g)

250 mg/kg/day Group 3	Day(s) Relative to Start Date					
	1	8	15	22	29	31
7051	210	234	248	253	282	259
7052	217	243	271	291	306	289
7053	234	258	268	287	301	260
7054	199	222	247	265	283	270
7055	194	217	237	255	262	250
7056	187	200	212	228	235	218
7057	208	223	233	253	271	251
7058	202	217	237	240	249	239
7059	206	231	237	258	262	252
7060	196	219	225	240	242	230
Mean	205.3	225.4	241.5	257.0	268.3	253.8
SD	13.3	16.0	18.0	19.9	23.9	21.9
N	10	10	10	10	10	10

Individual Animal Body Weights
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

500 mg/kg/day Group 4	Day(s) Relative to Start Date					
	Sex: Female Bodyweight (g)					
	1	8	15	22	29	31
7071	207	217	246	268	304	267
7072	218	230	261	280	311	276
7073	189	200	218	240	248	229
7074	185	212	222	235	242	232
7075	213	237	250	258	264	260
7076	206	235	242	265	277	256
7077	197	214	232	239	271	244
7078	200	216	234	237	257	242
7079	229	246	266	297	305	287
7080	205	207	226	238	253	240
Mean	205.9	221.4	239.7	255.7	273.2	253.3
SD	11.8	14.8	16.2	21.5	25.3	19.2
N	10	10	10	10	10	10

APPENDIX H: INDIVIDUAL ANIMAL MEAN DAILY BODY WEIGHT GAIN

PRODUCT IDENTIFICATION

Silk Fibroin

Individual Animal Mean Daily Body Weight Gain
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Mean Daily Body Weight Gain (g/day)

0 mg/kg/day Group 1	Day(s) Relative to Start Date			
	1 → 8	8 → 15	15 → 22	22 → 29
7001	6.0	6.9	7.4	6.6
7002	7.0	7.9	6.4	5.6
7003	5.7	6.9	4.3	9.0
7004	6.7	7.0	2.9	6.7
7005	4.3	12.9	8.3	8.3
7006	3.6	10.7	7.7	9.6
7007	6.9	6.1	9.3	6.4
7008	7.7	7.1	7.0	5.9
7009	7.7	6.6	7.3	4.7
7010	8.3	7.3	8.1	6.4
Mean	6.38	7.93	6.87	6.91
SD	1.52	2.14	1.93	1.55
N	10	10	10	10

Individual Animal Mean Daily Body Weight Gain
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Mean Daily Body Weight Gain (g/day)

125 mg/kg/day Group 2	Day(s) Relative to Start Date			
	1 → 8	8 → 15	15 → 22	22 → 29
7021	6.0	6.3	4.4	4.7
7022	9.7	6.9	7.7	5.4
7023	8.1	6.3	7.3	5.0
7024	6.4	5.4	6.1	5.1
7025	6.4	5.9	7.6	4.4
7026	7.9	6.3	5.7	4.7
7027	7.9	7.1	9.0	7.3
7028	6.9	7.0	4.6	5.7
7029	5.7	6.1	7.0	5.7
7030	6.4	7.4	5.3	5.1
Mean	7.14	6.47	6.47	5.33
SD	1.23	0.62	1.49	0.81
N	10	10	10	10

Individual Animal Mean Daily Body Weight Gain
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male Mean Daily Body Weight Gain (g/day)

250 mg/kg/day Group 3	Day(s) Relative to Start Date			
	1 → 8	8 → 15	15 → 22	22 → 29
7041	7.9	6.4	7.3	5.6
7042	7.7	7.6	7.6	4.4
7043	6.7	8.4	6.6	4.3
7044	7.0	8.1	6.4	5.4
7045	5.6	7.1	4.1	7.0
7046	7.6	6.6	6.4	6.4
7047	7.4	6.1	5.7	4.3
7048	7.9	7.0	6.3	5.6
7049	6.7	7.1	6.0	5.9
7050	7.1	6.9	6.3	4.7
Mean	7.36	7.24	6.27	5.36
SD	0.84	0.92	0.93	0.93
N	10	10	10	10

Individual Animal Mean Daily Body Weight Gain
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Male 500 mg/kg/day Group 4	Day(s) Relative to Start Date			
	1 → 8	8 → 15	15 → 22	22 → 29
7061	8.3	8.3	7.0	6.1
7062	9.7	6.7	7.7	4.9
7063	8.0	7.4	6.0	5.0
7064	10.1	9.1	7.6	6.6
7065	8.4	6.0	7.4	5.6
7066	7.7	7.1	6.6	7.1
7067	7.1	7.1	7.9	7.4
7068	8.9	6.4	8.7	9.7
7069	6.1	6.1	7.4	5.9
7070	8.7	8.3	7.7	6.9
Mean	8.31	7.27	7.40	6.51
SD	1.17	1.03	0.74	1.42
N	10	10	10	10

Individual Animal Mean Daily Body Weight Gain
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Mean Daily Body Weight Gain (g/day)

0 mg/kg/day Group 1	Day(s) Relative to Start Date			
	1 → 8	8 → 15	15 → 22	22 → 29
7011	3.9	1.7	2.3	1.3
7012	1.7	3.1	4.0	1.7
7013	1.6	1.4	2.0	1.4
7014	3.6	4.3	1.4	2.1
7015	2.6	2.1	2.3	1.6
7016	3.3	-0.1	4.0	0.6
7017	3.4	3.7	1.0	-0.1
7018	2.4	3.0	1.4	1.7
7019	2.6	4.4	0.6	2.3
7020	3.7	3.3	-0.3	5.0
Mean	2.87	2.70	1.87	1.76
SD	0.82	1.42	1.37	1.35
N	10	10	10	10

Individual Animal Mean Daily Body Weight Gain
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Mean Daily Body Weight Gain (g/day)

125 mg/kg/day Group 2	Day(s) Relative to Start Date			
	1 → 8	8 → 15	15 → 22	22 → 29
7031	1.9	1.7	1.6	2.0
7032	3.1	5.1	0.9	4.6
7033	1.3	2.9	2.0	1.4
7034	2.0	2.9	0.9	2.6
7035	3.9	2.6	1.0	1.7
7036	1.9	1.7	-0.7	2.1
7037	1.4	2.3	2.6	1.3
7038	3.1	1.3	3.9	1.4
7039	3.9	4.7	2.6	2.7
7040	2.9	1.0	1.9	1.0
Mean	2.53	2.61	1.64	2.09
SD	0.96	1.38	1.25	1.03
N	10	10	10	10

Individual Animal Mean Daily Body Weight Gain
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Mean Daily Body Weight Gain (g/day)

250 mg/kg/day Group 3	Day(s) Relative to Start Date			
	1 → 8	8 → 15	15 → 22	22 → 29
7051	3.4	2.0	0.7	4.1
7052	3.7	4.0	2.9	2.1
7053	3.4	1.4	2.7	2.0
7054	3.3	3.6	2.6	2.6
7055	3.3	2.9	2.6	1.0
7056	1.9	1.7	2.3	1.0
7057	2.1	1.4	2.9	2.6
7058	2.1	2.9	0.4	1.3
7059	3.6	0.9	3.0	0.6
7060	3.3	0.9	2.1	0.3
Mean	3.01	2.16	2.21	1.76
SD	0.68	1.11	0.91	1.16
N	10	10	10	10

Individual Animal Mean Daily Body Weight Gain
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Mean Daily Body Weight Gain (g/day)

500 mg/kg/day Group 4	Day(s) Relative to Start Date			
	1 → 8	8 → 15	15 → 22	22 → 29
7071	1.4	4.1	3.1	5.1
7072	1.7	4.4	2.7	4.4
7073	1.6	2.6	3.1	1.1
7074	2.4	1.4	1.9	1.0
7075	3.4	1.9	1.1	0.9
7075	4.1	1.0	3.3	1.7
7077	2.4	2.6	1.0	4.6
7078	2.3	2.6	0.4	2.9
7079	2.4	2.9	4.4	1.1
7080	0.3	2.7	1.7	2.1
Mean	2.21	2.61	2.29	2.50
SD	1.07	1.07	1.25	1.65
N	10	10	10	10

APPENDIX I: FOOD CONSUMPTION BY CAGE

PRODUCT IDENTIFICATION

Silk Fibroin

Food Consumption by Cage
P&L Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Group	Sex	Cage	No In Cage	Day numbers relative to Start Date									
				From: To:	1 0	6 6	8 13	13 15	15 20	20 22	22 27	27 29	
1	m	1	2	23.9	24.5	27.3	27.8	29.9	26.8	29.3	27.8		
		2	2	24.2	22.3	25.6	26.3	25.6	24.8	26.3	24.8		
		3	2	26.3	18.8	29.3	33.3	31.9	28.3	33.3	31.8		
		4	2	23.8	24.8	25.4	28.5	28.2	29.3	30.5	27.1		
		5	2	27.4	28.5	29.4	30.8	28.8	28.5	29.6	29.5		
				Mean	25.12	23.60	27.40	29.78	28.88	27.50	29.80	28.20	
				S.D.	1.63	3.85	1.93	2.28	2.31	1.79	2.51	2.61	
				N	5	5	5	5	5	5	5	5	

* = Result to left has an associated comment or marker
Food consumption units are g/animal/day

Group 1 - 0 mg/kg/day Group 1 Group 2 - 125 mg/kg/day Group 2
Group 3 - 250 mg/kg/day Group 3 Group 4 - 500 mg/kg/day Group 4

Food Consumption by Cage
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

		Day numbers relative to Start Date										
Group	Sex	Cage	No In Cage	From:	1	6	8	13	15	20	22	27
				To:	6	6	13	15	20	22	27	29
2	m	11	2		25.3	25.8	27.6	29.0	28.0	23.5	27.9	23.5
		12	2		25.0	26.3	26.4	28.3	27.9	28.3	28.5	27.5
		13	2		26.1	27.5	27.0	30.0	32.3	28.5	29.8	27.0
		14	2		23.2	24.5	25.6	27.8	26.1	23.8	26.4	26.0
		15	2		24.4	23.5	26.9	29.8	27.0	26.0	27.1	25.0
				Mean	24.80	25.50	26.70	28.95	28.26	26.00	27.94	25.80
				S.D.	1.08	1.55	0.75	0.96	2.39	2.38	1.31	1.60
				N	5	5	5	5	5	5	5	5

* = Result to left has an associated comment or marker
Food consumption units are g/animal/day

Group 1 - 0 mg/kg/day Group 1 Group 2 - 125 mg/kg/day Group 2
Group 3 - 250 mg/kg/day Group 3 Group 4 - 500 mg/kg/day Group 4

Food Consumption by Cage
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Group	Sex	Cage	No. In Cage	From: To:	Day numbers relative to Start Date							
					1 6	6 8	8 13	13 15	15 20	20 22	22 27	27 29
3	m	21	2		24.4	28.5	27.7	29.5	27.1	27.8	28.4	25.0
		22	2		27.7	27.0	29.1	33.5	30.7	28.3	30.3	29.0
		23	2		24.2	25.0	27.4	28.0	27.3	27.3	27.1	28.3
		24	2		27.9	28.3	30.6	30.5	29.6	27.5	28.6	27.8
		25	2		24.4	22.8	27.0	30.3	28.0	27.5	29.9	27.8
				Mean	25.72	26.30	28.36	30.35	28.54	27.65	28.86	27.55
				S.D.	1.98	2.42	1.48	2.01	1.56	0.38	1.28	1.51
				N	5	5	5	5	5	5	5	5

* = Result to left has an associated comment on marker
Food consumption units are g/animal/day

Group 1 - 0 mg/kg/day Group 1 Group 2 - 125 mg/kg/day Group 2
Group 3 - 250 mg/kg/day Group 3 Group 4 - 500 mg/kg/day Group 4

Food Consumption by Cage
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Group	Sex	Cage	No. In Cage	Day numbers relative to Start Date								
				From: To:	1 6	6 8	8 13	13 15	15 20	20 22	22 27	27 29
4	m	31	2		26.6	30.0	29.2	29.0	28.9	30.3	30.5	27.5
		32	2		28.4	29.0	30.5	33.0	29.6	30.5	32.3	28.3
		33	2		25.9	26.8	27.7	28.5	28.8	26.0	29.0	27.5
		34	2		25.0	26.8	27.3	26.8	30.6	31.3	31.8	32.8
		35	2		24.9	27.3	28.1	29.3	29.7	30.0	30.9	30.8
				Mean	26.16	27.95	28.56	29.30	29.52	29.60	30.90	29.35
				S.D.	1.45	1.47	1.30	2.29	0.73	2.07	1.28	2.32
				N	5	5	5	5	5	5	5	5

* = Result to left has an associated comment or marker
Food consumption units are g/animal/day

Group 1 - 0 mg/kg/day Group 1 Group 2 - 125 mg/kg/day Group 2
Group 3 - 250 mg/kg/day Group 3 Group 4 - 500 mg/kg/day Group 4

Food Consumption by Cage
PSL Study Number 51651 - A 28 Day Oral Gavage Toxicity Study in Rats

		Day numbers relative to Start Date												
Group	Sex	Cage	No. in Cage	From:	1	6	8	13	15	20	22	27	27	
				To:	6	8	13	15	20	22	27	28		
1	F	6	2		20.3	20.5	20.7	22.8	20.8	20.5	22.0	19.3		
					19.8	19.5	20.1	22.0	20.9	19.8	20.4	20.0		
		8	2		22.0	19.3	22.9	21.3	21.6	19.3	22.1	18.8		
					18.6	17.5	18.6	20.0	17.8	17.5	17.9	15.3		
		10	2		21.4	22.0	22.1	24.3	20.3	17.3	20.6	20.0		
					Mean	20.42	19.75	20.88	22.20	20.28	18.85	20.60	18.65	
					S.D.	1.34	1.66	1.69	1.62	1.46	1.42	1.70	1.97	
					N	5	5	5	5	5	5	5	5	

* = Result to left has an associated comment or marker
Food consumption units are g/animal/day

Group 1 - 0 mg/kg/day Group 1 Group 2 - 125 mg/kg/day Group 2
Group 3 - 250 mg/kg/day Group 3 Group 4 - 500 mg/kg/day Group 4

Food Consumption by Cage
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Group	Sex	Cage	No. In Cage	Day numbers relative to Start Date							
				From: To:	1 6	6 8	8 13	13 15	15 20	20 22	22 27
2	F	16	2	18.6	18.8	19.8	22.0	19.5	17.0	19.8	20.3
			2	20.8	20.5	21.2	24.8	21.2	19.8	21.0	18.8
			2	18.6	18.0	19.1	22.8	18.1	13.3	17.0	18.5
			2	20.1	18.5	20.9	22.5	21.4	20.0	22.6	18.5
			2	20.0	18.8	20.2	22.8	20.5	18.5	21.0	18.5
			Mean	19.62	18.90	20.24	22.95	20.14	17.70	20.28	18.90
			S.D.	0.98	0.95	0.84	1.05	1.36	2.76	2.09	0.76
			N	5	5	5	5	5	5	5	5

* = Result to left has an associated comment or marker
Food consumption units are g/animal/day

Group 1 - 0 mg/kg/day Group 1 Group 2 - 125 mg/kg/day Group 2
Group 3 - 250 mg/kg/day Group 3 Group 4 - 500 mg/kg/day Group 4

Food Consumption by Cage
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Group	Sex	Cage	No In Cage	Day numbers relative to Start Date									
				From: To:	1 6	6 8	8 13	13 15	15 20	20 22	22 27	27 29	
3	f	26	2		22.2	21.5	22.6	23.5	22.3	20.8	22.7	21.3	
		27	2		20.3	21.3	20.9	21.5	20.3	18.8	20.9	20.0	
		28	2		18.4	18.3	18.9	22.0	19.6	20.0	20.6	18.5	
		29	2		19.8	19.0	19.7	20.3	19.3	18.0	20.5	16.8	
		30	2		18.7	17.5	18.0	20.0	18.3	18.0	18.3	17.0	
				Mean	19.88	19.50	20.02	21.45	19.96	19.10	20.60	18.70	
				S.D.	1.51	1.79	1.79	1.42	1.48	1.23	1.57	1.93	
				N	5	5	5	5	5	5	5	5	

* = Result to left has an associated comment or marker
Food consumption units are g/animal/day

Group 1 - 0 mg/kg/day Group 1 Group 2 - 125 mg/kg/day Group 2
Group 3 - 250 mg/kg/day Group 3 Group 4 - 500 mg/kg/day Group 4

Food Consumption by Cage
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Group	Sex	Cage	No In Cage	Day numbers relative to Start Date								
				From: To:	1 6	6 8	8 13	13 15	15 20	20 22	22 27	27 29
4	f	36	2		23.7	21.8	21.5	25.0	23.8	25.0	24.8	23.8
		37	2		18.7	18.5	28.1	24.3	21.0	19.3	20.9	19.5
		38	2		21.6	22.5	20.9	24.0	21.6	19.0	22.5	21.3
		39	2		20.3	21.5	19.7	24.5	20.6	17.5	21.5	23.3
		40	2		20.1	20.5	20.4	20.8	19.9	18.8	20.6	20.5
				Mean	20.88	20.95	20.52	23.70	21.38	19.90	22.06	21.65
				S.D.	1.88	1.55	0.70	1.69	1.49	2.93	1.69	1.81
				N	5	5	5	5	5	5	5	5

* = Result to left has an associated comment or marker
Food consumption units are g/animal/day

Group 1 - 0 mg/kg/day Group 1 Group 2 - 125 mg/kg/day Group 2
Group 3 - 250 mg/kg/day Group 3 Group 4 - 500 mg/kg/day Group 4

APPENDIX J: CLINICAL PATHOLOGY

PRODUCT IDENTIFICATION

Silk Fibroin

Submitted by:

Eurofins Advinus
21 & 22 Phase II, Peenya Industrial Area
Bengaluru, 560 058, India



CLINICAL PATHOLOGY PHASE REPORT

STUDY TITLE

SILK FIBROIN: A 28-DAY ORAL GAVAGE TOXICITY STUDY IN RATS

PSL STUDY NUMBER: 51651

EUROFINS ADVINUS STUDY PHASE NUMBER: G18871

PRINCIPAL INVESTIGATOR: K. C. JAYACHANDRA, M.V.Sc., DABT

**PATHOLOGY PHASE REPORT COMPLETED ON
01 APRIL 2020**

SPONSOR

**CAMBRIDGE CROPS, INC
444 SOMERVILLE AVE,
SOMERVILLE, MA 02143**

TEST FACILITY

**PRODUCT SAFETY LABS
2394 US HIGHWAY 130
DAYTON, NEW JERSEY 08810**

TEST SITE

**EUROFINS ADVINUS LIMITED
#21 & 22, PEENYA INDUSTRIAL AREA - PHASE II
BENGALURU- 560 058, INDIA**

**PSL Study No.: 51651
Eurofins Advinus Study Phase No.: G18871_PATH/Clinical Pathology Phase Report
Copy No. 1/1**

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5/1/2019

GLP COMPLIANCE STATEMENT AND DECLARATION

PSI Study No. : 51651

Eurofins Advinus Study Phase No. : G18871


Eurofins Advinus Study Phase Code : PATH

Principal Investigator : Dr. K. C. Jayachandran

Location : Department of Safety Assessment, Pathology section, Eurofins Advinus Limited, Bengaluru, India

I hereby confirm that the Phase of Clinical Pathology data interpretation of the above mentioned study was performed and documented in compliance with ICH (DIA, Q1.P. 2) CPD Part 5A, 1987 which is compatible with OECD Principles of Good Laboratory Practice (as revised in 1997) published in ENVIRONMENTAL HEALTH, OECD, Nov. 1998. A copy of audited clinical pathology data generated at the PSI was provided for the preparation of clinical pathology data interpretation phase report.

It is assured that the reported results faithfully represent the raw data generated at PSI during the experimental work. No circumstances have been left unreported which may have affected the quality or integrity of the data or which might have a potential bearing on the validity and reproducibility of this study phase.


 K. C. Jayachandran, M V Sc., D.Phil
 Principal Investigator, Pathology Section
 Dept. of Safety Assessment
 Eurofins Advinus Limited, Bengaluru

Date

PSI Study No.: 51651
 Eurofins Advinus Study Phase No.: G18871_PATH/Clinical Pathology Phase Report
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QUALITY ASSURANCE STATEMENT

The clinical pathology data interpretation phase (Eurofins Advintus Study phase No. G18871) of PSL Study No. 51651 entitled "S01 Program A 28-Day Oral Coverage Lottery Study in Rats" was inspected in accordance with U.S. FDA GLP-21 CFR Part 312, 1987 which is compatible with OECD Principles of Good Laboratory Practice (as revised in 1997) published in ENV/MR/CHEM (98)17, OECD, Paris, 1998.

The clinical pathology data interpretation phase report was reviewed and findings reported to Principal Investigator, Study Director, Lead QAU, Test Site Management, and Test Facility Management on the dates shown below:

Inspection / Audit		Reporting to Principal Investigator and Test Site Management	Reporting to Study Director, Lead QAU and Test Facility Management
Date	Phase	Date	Date
14 November 2019	Initiation Phase Study plan review	14 November 2019	13 November 2019
20 February 2020	Reporting Phase Initial clinical pathology phase report review	20 February 2020	20 February 2020
01 April 2020	Final clinical pathology phase report review	01 April 2020	01 April 2020

Report review was performed according to the Standard Operating Procedures of the test site's Quality Assurance Unit. The report of the clinical pathology data interpretation phase of the study was inspected against the approved study plan and pertinent raw data provided by the study director, and it accurately reflects this data.

Srinath Murugesu, M.Sc., RQA/GLP
Head, QAU-GLP
Eurofins Advintus Limited,
Bengaluru

Date:



LIST OF ABBREVIATIONS AND SYMBOLS

General

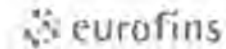
or -	no data
Hemol.	hemolyzed
INS. /INS-I	insufficient sample
N	number of values used in calculation
NCOAG. /NO CO	not coagulated
SDevs	standard deviation
Sligh.	slightly cloudy
Trace	- trace intact
TI	trace intact
TH	trace hemolyzed
Moderat	Moderate

Hematology

ABAS	- absolute basophil
AEOS	absolute eosinophil
ALUC	absolute large unstained cell
ALYM	absolute lymphocyte
AMON	absolute monocyte
ANEU	absolute neutrophil (all forms)
ARET	absolute reticuloocyte
HCT	hematocrit
HGB	Hemoglobin
LUC	Large unstained cells
MCH	- mean corpuscular (cell) hemoglobin
MCHC	- mean corpuscular (cell) hemoglobin concentration
MCV	- mean corpuscular (cell) volume
PLT	- platelet count
RBC	red blood cell count
RDW	- red cell distribution width
WBC	- white blood cell count

Coagulation

APTT	activated partial thromboplastin time
PT	prothrombin time
COAG	- No Coagulation



LIST OF ABBREVIATIONS AND SYMBOLS contd.

Clinical Chemistry

ALB	albumin
ALKP	alkaline phosphatase
ALT	alanine aminotransferase
AST	aspartate aminotransferase
BUN	urea nitrogen
CA	calcium
CHOL	cholesterol
Cl	chloride
CREAT	creatinine
GLOB	globulin
GLU	glucose
K	potassium
NA	sodium
PHOS	inorganic phosphorous
SDH	sorbitol dehydrogenase
TBIL	total bilirubin
TP	total protein
TRIG	triglycerides

Urinalysis

BACT	Bacteria
D	Dark
L	Light
QUAL	quality
SG	specific gravity
TL	Trace Low
UBIL	urine bilirubin
UBLO	urine blood
UCLA	clarity
UCOL	color
UGLU	urine glucose
ULEU	urine leukocyte
UKET	urine ketone
UPRO	urine total protein
URO	urobilinogen
UVOL	Volume
YEL	Yellow
WNL	Within Normal Limits



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**TEST SITE STUDY PERSONNEL**

TEST SITE	Eurofins Advinus Limited # 21 & 22, Peenya Industrial Area – Phase II, Bengaluru 560058 India
Principal Investigator	R. C. Jayachandra, M.V.Sc., DABT Pathologist, Pathology Department of Safety Assessment
Report Review	S. K. Vijayasarithi, M.V.Sc., Ph.D., FIATP Department of Safety Assessment
Test site management:	Rajiv Malik Eurofins Advinus Limited Nos 21 & 22, Peenya Industrial Area – Phase II, Bengaluru, 560 058, India
Test site QA	Muktha Bhagavan, M.Sc., RQAP-GLP Deputy Head, Quality Assurance Unit-GLP Eurofins Advinus Limited, Bengaluru
Report compilation:	M. Tejaswini, B.Sc. Electronic Data Processing (EDP) Department of Safety Assessment



I. STUDY PHASE DETAILS

Study Title	Silk Fibroin: A 28-Day Oral Gavage Toxicity Study in Rats
Study Phase	Pathology
Test Facility Study Number	51651
Test Site Study Phase No.	G18871
Test Facility	Product Safety Labs, LLC (PSL) 2394 US Highway 130 Dayton, New Jersey 08810
Test Site	Eurofins Advinus Limited # 21 & 22, Peenya Industrial Area – Phase II, Bengaluru 560058 India
Sponsor	Cambridge Crops, Inc 444 Somerville Ave, Somerville, MA 02143
Sponsor Representative	Laith Abu-Taleb Cambridge Crops, Inc 444 Somerville Ave, Somerville, MA 02143 Tel: 301-580-3965 Email: laith@cambridgecrops.com
Study Director	Raghavendra Gowda, Ph.D Study Director Tel: 732-438-5100 x1542 Email: RaghavendraGowda@productSafetyLabs.com
Lead QAU	Rhonda S. Krick, BS Director, Quality Assurance Product Safety Labs Email: RhondaS.Krick@productSafetyLabs.com



Study Phase Schedule

Study Phase Initiation Date	12 November 2019
Final pathology Phase Report (Study Phase Completion Date)	01 April 2020



2. OBJECTIVE

The objective of this study was to evaluate the potential sub-chronic toxicity of Silk Fibroin in male and female rats likely to arise from repeated exposure, via oral gavage, over a test period of at least 28 days. A no-observed-adverse-effect-level (NOAEL) was determined. This clinical pathology phase report includes interpretation of hematology, coagulation, clinical chemistry and urinalysis data and the conclusions drawn from respective data.

3. STUDY DESIGN

Experimental procedures applicable to clinical pathology are summarized in the tables below. More details can be found in the final study report.

The selected male and female rats were assigned to control and various treated groups as shown below:

Group	Number of Rats Males/Females	Oral Gavage Dose of Test Substance (mg/kg/day)	Dose Volume (mL/kg)	Concentration (mg/mL) ^b
1	10/10	0 (Vehicle control) ^a	10	0
2	10/10	125		12.5
3	10/10	250		25
4	10/10	500		50

a: Distilled water

b: Appropriate concentration of the test substance as received in vehicle to achieve the target dose level

4. METHODS

4.1. Clinical Pathology Investigations

4.1.1 Sample Collection

Clinical pathology analyses were conducted on samples collected on Days 30 (males) and 31 (females) for hematology, coagulation, clinical chemistry, and urinalysis. The samples were analyzed at PSL (Test facility) and the electronic copies of the results were shared with Eurofins Advinus (Test site) for interpretation of the data.

4.1.2 Hematology and Coagulation

Complete blood counts, including reticulocytes, were determined on an ADVIA 120 Hematology System. Coagulation times were determined on a Siemens Sysmex CA620 automated coagulation system.



The following hematological and coagulation parameters were determined by PSL and the electronic copies of results were shared with test site for inclusion in the clinical pathology phase report:

erythrocyte count (RBC)	hemoglobin concentration (HGB)
hematocrit (HCT)	mean corpuscular volume (MCV)
mean corpuscular hemoglobin (MCH)	red cell distribution width (RDW)
absolute reticulocyte count (ARET)	platelet count (PLT)
total white blood cell (WBC) and differential leukocyte count	
mean corpuscular hemoglobin concentration (MCHC) was calculated	

prothrombin time (PT)
activated partial thromboplastin time (APTT)

4.1.3 Clinical Chemistry

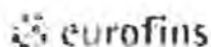
The following parameters were determined on a COBAS C311 automated clinical chemistry analyzer at PSL and the electronic copies of results were shared with test site for inclusion in the pathology phase report:

serum aspartate aminotransferase (AST)	serum alanine aminotransferase (ALT)
sorbitol dehydrogenase (SDH)	alkaline phosphatase (ALKP)
total bilirubin (BILL)	urine nitrogen (BUN)
blood creatinine (CREAT)	total cholesterol (CHOL)
triglycerides (TRIG)	fasting glucose (GLUC)
total serum protein (TP)	albumin (ALB)
globulin (GLOB)	calcium (CALC)
inorganic phosphorus (IPHS)	sodium (NA)
potassium (K)	chloride (CL)

4.1.4 Urinalysis

The following parameters were determined at PSL and the electronic copies of results were shared with test site for inclusion in the pathology phase report:

quality (QUAL)	pH	ketone (KET)
color (COL)	glucose (UGLC)	bilirubin (UBIL)
clarity (CLAR)	specific gravity (SG)	blood (BLD)
volume (UVOL)	protein (UMTP)	urobilinogen (URO)
microscopic urine sediment examination		



5. RESULTS AND DISCUSSION

5.1. CLINICAL PATHOLOGY

5.1.1 HEMATOLOGY

Refer Tables 1 and 2, Appendix 1

There were no test substance-related changes in hematology parameters.

All the changes in hematology were considered unrelated to test substance, because they occurred sporadically, were considered due to biological variance among rats as magnitude of variation was minimal

5.1.2 COAGULATION

Refer Tables 3 and 4, Appendix 2

There were no test substance-related changes in coagulation parameters

5.1.3 CLINICAL CHEMISTRY

Refer Tables 5 and 6, Appendix 3

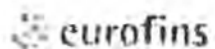
There were no test substance-related changes in clinical chemistry parameters

All the changes in clinical chemistry were considered unrelated to test substance, because they occurred sporadically, were considered due to biological variance among rats as magnitude of variation was minimal

5.1.4 URINALYSIS

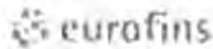
Refer Tables 7 and 8, Appendix 4

There were no test substance-related changes in urinalysis parameters



6. SUMMARY

Administration of test substance Silk Fibroin by oral gavage route in Sprague Dawley rats for at least 28 consecutive days at dose levels of 0, 125, 250 and 500 mg/kg/day did not induce any test substance-related changes in hematology, coagulation, clinical chemistry and urinalysis parameters.



7. ARCHIVES

Eurofins Advinus has archived the following documents of the study such as copy of the study plan, study plan amendments, draft clinical pathology phase report, the original signed pathology phase report (copy 1/1) and correspondence generated at Eurofins Advinus for the clinical pathology phase for at least 9 years following the completion of the study phase. Archiving beyond 9 years will be decided after consulting the Sponsor.

8. REPORT DISTRIBUTION

An electronic PDF copy (1/1) of pathology phase report generated at the Test Site was sent to the study director/Test Facility (PSL). The original signed final pathology phase report (1/1) was archived at the Test site (Eurofins Advinus).



9. TABLES



TABLE L Summary of Hematology Parameters - Males

Parameter	Baseline		Week 12		Week 24		Week 36		Week 48	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
WBC	7.5	1.5	7.5	1.5	7.5	1.5	7.5	1.5	7.5	1.5
Hemoglobin	14.5	1.5	14.5	1.5	14.5	1.5	14.5	1.5	14.5	1.5
Hematocrit	45.0	4.0	45.0	4.0	45.0	4.0	45.0	4.0	45.0	4.0
Platelets	250	50	250	50	250	50	250	50	250	50
Neutrophils	60	10	60	10	60	10	60	10	60	10
Lymphocytes	35	5	35	5	35	5	35	5	35	5
Monocytes	3	1	3	1	3	1	3	1	3	1
Eosinophils	1	0.5	1	0.5	1	0.5	1	0.5	1	0.5
Reticulocytes	0.5	0.2	0.5	0.2	0.5	0.2	0.5	0.2	0.5	0.2

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TABLE 1 contd. Summary of Hematology Parameters Males

Group	n	Hematology						
		ALYM (x10 ⁹ /L)	ASPN (x10 ⁹ /L)	ALQS (x10 ⁹ /L)	AMAS (x10 ⁹ /L)	ALUC (x10 ⁹ /L)	ARE1 (x10 ⁹ /L)	MLDC (g/dL)
Control	00	00	00	00	00	00	00	00
	Mean	7.915	11.89	0.056	0.029	0.154	220.6	50.00
	SD	1.7857	0.700	0.0360	0.0319	0.0500	36.57	0.540
I	00	00	00	00	00	00	00	00
	Mean	7.628	11.29	0.0712	0.025	0.160	206.5	50.00
	SD	1.5629	0.118	0.0335	0.0308	0.0577	29.50	0.751
II	00	00	00	00	00	00	00	00
	Mean	7.195	11.28	0.066	0.025	0.129	224.4	50.00
	SD	1.4523	0.096	0.0290	0.0118	0.0482	25.11	0.437
A	00	00	00	00	00	00	00	00
	Mean	7.126	11.29	0.056	0.023	0.116	243.2	27.42
	SD	1.5376	0.060	0.0303	0.0221	0.0375	52.97	0.156



TABLE 2. Summary of Haematology Parameters - Females

Group	N	Hb		Hct		Hgb		RBC		WBC	
		(g/dL)	(g/dL)	(%)	(%)	(g/dL)	(g/dL)	(10 ¹² /L)	(10 ⁹ /L)	(10 ⁹ /L)	(10 ⁹ /L)
Control	Mean	10.0	10.0	30.0	30.0	10.0	10.0	10.0	10.0	10.0	10.0
	SD	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
	Range	8.0-12.0	8.0-12.0	25.0-35.0	25.0-35.0	8.0-12.0	8.0-12.0	8.0-12.0	8.0-12.0	8.0-12.0	8.0-12.0
1	Mean	10.0	10.0	30.0	30.0	10.0	10.0	10.0	10.0	10.0	10.0
	SD	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
	Range	8.0-12.0	8.0-12.0	25.0-35.0	25.0-35.0	8.0-12.0	8.0-12.0	8.0-12.0	8.0-12.0	8.0-12.0	8.0-12.0
2	Mean	10.0	10.0	30.0	30.0	10.0	10.0	10.0	10.0	10.0	10.0
	SD	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
	Range	8.0-12.0	8.0-12.0	25.0-35.0	25.0-35.0	8.0-12.0	8.0-12.0	8.0-12.0	8.0-12.0	8.0-12.0	8.0-12.0
3	Mean	10.0	10.0	30.0	30.0	10.0	10.0	10.0	10.0	10.0	10.0
	SD	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
	Range	8.0-12.0	8.0-12.0	25.0-35.0	25.0-35.0	8.0-12.0	8.0-12.0	8.0-12.0	8.0-12.0	8.0-12.0	8.0-12.0
4	Mean	10.0	10.0	30.0	30.0	10.0	10.0	10.0	10.0	10.0	10.0
	SD	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
	Range	8.0-12.0	8.0-12.0	25.0-35.0	25.0-35.0	8.0-12.0	8.0-12.0	8.0-12.0	8.0-12.0	8.0-12.0	8.0-12.0



TABLE 2 contd. Summary of Haematology Parameters Females

Parameter	Units							
	WBC ($\times 10^9/l$)	LYM ($\times 10^9/l$)	PLT ($\times 10^9/l$)	HGB (g/dl)	HCT ($\%$)	MCV (fl)	MCH (pg)	MCHC (g/dl)
1 (control)	Unit	U/L	U/L	U/L	U/L	U/L	U/L	U/L
	Mean	9.200	0.24	0.060	10.20	33.3	100.0	30.30
	SD	2.940	0.03	0.003	0.030	0.60	1.40	0.30
2	Unit	U/L	U/L	U/L	U/L	U/L	U/L	U/L
	Mean	9.000	0.21	0.02	10.20	33.3	100.0	30.30
	SD	1.600	0.00	0.000	0.000	0.00	0.00	0.00
3	Unit	U/L	U/L	U/L	U/L	U/L	U/L	U/L
	Mean	7.100	0.20	0.00	10.20	33.3	100.0	30.30
	SD	0.950	0.00	0.000	0.000	0.00	0.00	0.00
4	Unit	U/L	U/L	U/L	U/L	U/L	U/L	U/L
	Mean	9.000	0.20	0.00	10.20	33.3	100.0	30.30
	SD	1.600	0.00	0.000	0.000	0.00	0.00	0.00

Cefuroxime

TABLE 3. Summary of Coagulation Parameters - Males

Parameter	Cefuroxime	
	APTT (sec)	PT (sec)
Baseline	Mean	10.8
	SD	1.0
	95%	9.23
Day 14	Mean	10.8
	SD	1.0
	95%	9.23
Day 28	Mean	10.8
	SD	1.0
	95%	9.23

curafins

TABLE 4. Summary of Coagulation Parameters – Fvivalpy

Group	APTT (sec)		PT (sec)	
	Mean	SD	Mean	SD
Control	30	3.0	10	1.0
	Mean	30.1	9.1	1.0
	SD	3.1	0.7	0.7
100	30	3.0	10	1.0
	Mean	30.2	9.0	1.0
	SD	3.12	0.10	0.10
500	30	3.0	10	1.0
	Mean	30.9	9.1	1.0
	SD	3.17	0.10	0.10
1000	30	3.0	10	1.0
	Mean	30.9	9.0	1.0
	SD	3.10	0.10	0.10



TABLE 5. Summary of Clinical Chemistry Parameters - Males

Refer Appendix 3

Group n	N4 (n=10)	K (n=10)	L (n=10)	Serum Chemistry						
				AS (U/L)	ALT (U/L)	ALP (U/L)	BUN (mg/dL)	Cr (mg/dL)	Urea (mg/dL)	
Control	min	0	0	0	0	0	0	0	0	
	Mean	102.4	8.097	98.67	6.0	27.04	152.5	1.0	0.51	36.9
	Stdev	3.11	0.0181	2.32	11.54	6.236	77.24	0.08	0.02	1.69
J	min	0	0	0	0	0	0	0	0	
	Mean	103.9	7.42	99.18	7.8	28.53	151.1	1.1	0.6	38.9
	Stdev	1.03	0.0202	2.32	11.98	6.084	23.8	0.08	0.04	0.2
S	min	0	0	0	0	0	0	0	0	
	Mean	101.2	7.499	98.57	6.7	24.69	113.5	1.0	0.22	33.1
	Stdev	2.72	0.067	1.54	11.1	3.295	35.71	0.09	0.07	0.65
4	min	0	0	0	0	0	0	0	0	
	Mean	102.0	7.07	98.60	6.1	21.98	112	1.08	0.16	36.0
	Stdev	3.96	0.077	2.72	9.8	1.282	54.14	0.0	0.25	1.15



TABLE 5 (cont'd). Summary of Clinical Chemistry Parameters - Males

L0290	Unit	Eurofins Chemistry								
		GLU	GLY	GLY	GLY	UREA	UREA	UREA	UREA	UREA
		mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL
1	Mean	100	100	100	100	100	100	100	100	100
	SD	15	15	15	15	15	15	15	15	15
	CV	15%	15%	15%	15%	15%	15%	15%	15%	15%
2	Mean	100	100	100	100	100	100	100	100	100
	SD	15	15	15	15	15	15	15	15	15
	CV	15%	15%	15%	15%	15%	15%	15%	15%	15%
3	Mean	100	100	100	100	100	100	100	100	100
	SD	15	15	15	15	15	15	15	15	15
	CV	15%	15%	15%	15%	15%	15%	15%	15%	15%



TABLE 6. Summary of Clinical Chemistry Parameters - Females

See Appendix 2

Parameter	U	L	Clinical Chemistry							
			U (mmol/L)	L (mmol/L)	U (mmol/L)	L (mmol/L)	U (mmol/L)	L (mmol/L)	U (mmol/L)	L (mmol/L)
Creatinine	U	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Mean	133.8	5.25	84.75	47.5	27.500	62.5	3.5	10.0	5.0
	SD	8.00	10.50	13.00	7.00	7.500	50.0	1.0	1.50	0.50
Urea	U	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Mean	120.8	3.00	59.0	30.0	22.000	64.0	3.0	10.0	5.0
	SD	8.00	10.00	13.00	7.00	7.500	50.0	1.0	1.50	0.50
Urea Nitrogen	U	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Mean	120.4	3.00	59.0	30.0	22.000	64.0	3.0	10.0	5.0
	SD	8.00	10.00	13.00	7.00	7.500	50.0	1.0	1.50	0.50
Urea Nitrogen	U	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Mean	120.4	3.00	59.0	30.0	22.000	64.0	3.0	10.0	5.0
	SD	8.00	10.00	13.00	7.00	7.500	50.0	1.0	1.50	0.50



TABLE 6 contd. Summary of Clinical Chemistry Parameters - Females

Refer Appendix 1

Group	n	CRLA1 (ng/dL)	cGAs (ng/dL)	pTbAs (ng/dL)	Serum Chemistry		SGLT (U/L)	IP (ng/dL)	ALB (g/dL)	S-CRE (ng/dL)
					Mean	SD				
Control	n	0	0	0	0	0	0	0	0	0
	Mean	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	SD	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1	n	0	0	0	0	0	0	0	0	0
	Mean	0.250	121.8	4.25	0.002	11.9	9.65	5.72	4.66	2.06
	SD	0.265	21.72	0.53	0.015	12.02	2.170	0.592	0.525	0.257
2	n	0	0	0	0	0	0	0	0	0
	Mean	0.000	133.6	7.85	0.002	12.2	10.16	6.00	4.50	1.96
	SD	0.000	51.33	1.211	0.015	9.82	5.055	0.321	0.652	0.320
3	n	0	0	0	0	0	0	0	0	0
	Mean	0.225	124.8	4.37	0.000	11.5	11.69	6.82	4.69	2.15
	SD	0.011	11.03	0.21	0.010	17.51	17.409	0.583	0.399	0.279

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TABLE 7. Summary of Clinical Analysis of Urine - Males

Group	n	pH		Specific Gravity	
		Mean (SD)	SD	Mean (SD)	SD
Control	n	10	0.0	1.000	0.000
	Mean	6.20	0.70	1.015	0.06
	SD	0.080	0.150	0.000	0.000
A	n	10	0.0	1.000	0.000
	Mean	6.20	0.60	1.020	0.07
	SD	0.080	0.170	0.000	0.000
B	n	10	0.0	1.000	0.000
	Mean	6.20	0.70	1.020	0.07
	SD	0.080	0.150	0.000	0.000
C	n	10	0.0	1.000	0.000
	Mean	6.20	0.60	1.020	0.07
	SD	0.080	0.170	0.000	0.000

curafins

TABLE 8. Summary of Clinical Analysis of Urine - Females

Group	ITT (N)	ITT (n)	ITT (%)	Analysis	
				ITT (n)	ITT (%)
1	ITT	9	9	9	9
	Major	0/20	0/11	0/27.3	0/17
	Minor	0/200	0/100	0/50.0	0/55
2	ITT	8	8	8	8
	Major	0/20	0/11	0/27.3	0/17
	Minor	0/200	0/100	0/50.0	0/55
3	ITT	10	10	10	10
	Major	0/20	0/11	0/27.3	0/17
	Minor	0/200	0/100	0/50.0	0/55
4	ITT	0	0	0	0
	Major	0/20	0/11	0/27.3	0/17
	Minor	0/200	0/100	0/50.0	0/55

EUROFINS

10 APPENDICES

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APPENDIX 1. Individual Animal Haematology Parameters

Animal No.	Sex	Day Tissue Week n	Study Phase	WBC (x10 ⁹ /L)	RBC (x10 ¹² /L)	HGB (g/dL)	HCT (%)	HbA (g/L)	HbF (%)	HbT (g/L)	
											WBC (x10 ⁹ /L)
7001	D	51	1	10.5	5.13	9.48	9.27	45.7	51.7	67.3	18.0
7002	F	51	1	10.5	5.13	9.32	8.12	78.1	51.0	65.5	19.0
7003	F	51	1	10.5	5.13	9.08	8.76	43.7	49.8	62.0	18.9
7004	F	51	1	10.5	5.13	8.44	6.22	15.6	33.3	49.3	17.6
7005	F	51	1	10.5	5.13	8.33	11.23	10.0	52.2	66.0	19.2
7006	F	51	1	10.5	5.13	8.61	11.04	16.7	50.0	63.1	19.4
7007	F	51	1	10.5	5.13	8.13	10.89	19.1	40.8	62.0	18.2
7008	D	51	1	10.5	5.13	7.99	12.78	33.4	42.5	63.1	20.5
7009	D	51	1	10.5	5.13	8.36	7.41	18.7	32.9	61.2	18.8
7010	F	51	1	10.5	5.13	8.25	10.62	15.6	51.1	62.2	18.9
7021	F	51	2	10.5	5.13	8.91	10.18	16.7	54.8	64.1	19.0
7022	F	51	2	10.5	5.13	8.02	10.15	15.4	51.0	61.0	19.2
7023	F	51	2	10.5	5.13	8.15	11.09	14.3	50.9	62.2	19.0
7024	F	51	2	10.5	5.13	7.85	8.84	11.4	48.0	62.9	18.5
7025	F	51	2	10.5	5.13	9.42	7.83	49.3	56.2	64.1	17.8
7026	F	51	2	10.5	5.13	9.00	13.31	17.0	47.0	63.8	18.9
7027	F	51	2	10.5	5.13	8.80	10.02	15.2	50.1	61.7	19.1
7028	F	51	2	10.5	5.13	1.81	0.90	10.0	38.3	61.1	17.5
7029	F	51	2	10.5	5.13	3.17	0.44	11.7	25.0	61.1	18.7
7030	F	51	2	10.5	5.13	8.11	10.14	18.4	49.0	62.2	19.0
7041	F	51	3	10.5	5.13	8.68	7.41	15.4	50.8	66.1	20.1
7042	F	51	3	10.5	5.13	8.23	7.82	10.7	57.2	64.0	19.1
7043	F	51	3	10.5	5.13	8.53	9.83	16.4	55.1	66.1	19.2
7044	F	51	3	10.5	5.13	7.95	10.08	15.1	49.1	64.2	19.0

TI = Drawing Phase

S = Scheduled Animal Entry; F = Unscheduled Animal Entry; N = Scheduled Necropsy; n = Unscheduled Necropsy



APPENDIX 1 contd. Individual Animal Haematology Parameters

Animal #	Sex	Age	Study Week	Phase	Species	Strain	Hb (g/dL)	Hct (%)	Hct/Cr (L/g)	Hb 1 (%)	WBC (x10 ⁹ /L)	MPV (fl)
7055	D	M	3	03	S	1	9.82	4.11	1.54	92.7	92.1	19.7
7036	D	M	3	03	S	1	7.71	4.15	18.4	10.6	87.3	21.0
7043	D	M	3	03	S	1	8.74	5.61	10.0	9.1	87.7	18.4
7048	D	M	3	03	S	1	8.43	10.54	10.1	84.4	86.2	19.1
7049	D	M	3	03	S	1	8.56	11.55	10.7	83.1	87.8	19.0
7050	D	M	3	03	S	1	8.22	8.07	17.1	86.6	84.1	18.4
7061	D	M	4	03	S	1	7.89	8.0	16.0	82.4	86.7	20.3
7062	D	M	4	03	S	1	7.55	7.00	15.1	48.1	84.0	70.0
7063	D	M	4	03	S	1	7.40	10.25	13.0	44.2	83.0	16.9
7064	D	M	4	03	S	1	8.43	7.00	10.2	83.8	85.0	19.1
7065	D	M	4	03	S	1	7.88	10.44	15.2	49.7	82.0	19.7
7066	D	M	4	03	S	1	7.87	9.23	14.7	37.8	82.0	19.9
7067	D	M	4	03	S	1	8.02	9.07	17.1	37.0	81.0	19.3
7069	D	M	4	03	S	1	7.80	7.00	15.0	50.0	84.1	19.0
7069	D	M	4	03	S	1	7.83	8.00	17.1	32.0	86.7	19.0
7070	D	M	4	03	S	1	8.06	10.00	15.0	54.1	85.1	19.1
7071	D	M	5	03	S	1	8.09	8.00	16.0	39.2	80.0	18.1
7072	D	M	5	03	S	1	8.57	1.04	15.0	7.0	80.8	18.1
7073	D	M	5	03	S	1	8.47	10.00	10.0	72.0	81.4	19.0
7074	D	M	5	03	S	1	7.88	8.00	14.0	43.1	81.6	18.4
7075	D	M	5	03	S	1	7.50	8.21	14.1	43.1	80.0	18.5
7076	D	M	5	03	S	1	8.55	8.00	15.0	51.0	81.8	18.4
7077	D	M	5	03	S	1	8.64	8.00	10.8	51.5	81.0	18.0
7078	D	M	5	03	S	1	8.21	4.00	13.1	39.0	82.7	19.4

D: Mating Phase

S: Solidated Sprague Dawley; M: Male; D: Female; Hb: Hemoglobin; Hct: Hematocrit; Hct/Cr: Hematocrit/Creatinine; WBC: White Blood Cells; MPV: Mean Platelet Volume



APPENDIX 1 contd. Individual Animal Haematology Parameters

Animal #	Sex	Day Group Week	Study Phase	Sex- Name	RBC (x10 ¹² /µL)	WBC (x10 ⁹ /µL)	HGB (g/dL)	HCT (%)	MCV (fL)	MPV (fL)
7014	D	1	1	S 1 1	7.09	7.71	14.4	49.0	69.1	19.0
7020	D	1	1	S 1 1	8.92	11.94	15.8	52.0	59.6	17.9
7051	D	1	1	S 1 1	7.39	7.72	15.7	51.8	69.6	18.2
7072	D	1	1	S 1 1	7.68	7.41	14.5	48.1	63.1	18.3
7073	D	1	1	S 1 1	8.47	7.61	15.2	51.7	60.6	19.1
7074	D	1	1	S 1 1	7.57	7.07	13.7	46.0	60.3	18.1
7075	D	1	1	S 1 1	8.51	7.11	15.7	50.5	59.4	18.2
7076	D	1	1	S 1 1	8.78	7.11	16.1	52.1	59.6	18.3
7077	D	1	1	S 1 1	7.89	9.11	14.5	48.1	59.1	18.5
7078	D	1	1	S 1 1	8.66	8.77	16.1	53.2	61.9	18.7
7079	D	1	1	S 1 1	8.56	7.71	15.1	47.1	55.1	18.0
7080	D	1	1	S 1 1	9.56	7.81	15.1	51.4	56.4	19.9
7087	D	1	1	S 1 1	7.18	6.75	13.7	45.5	63.8	18.4
7092	D	1	1	S 1 1	7.67	7.61	14.8	47.1	60.1	18.9
7097	D	1	1	S 1 1	9.16	7.27	14.8	48.3	59.1	17.8
7098	D	1	1	S 1 1	8.09	6.95	13.7	47.0	58.0	18.1
7099	D	1	1	S 1 1	7.82	5.79	13.1	42.7	54.7	18.2
7096	D	1	1	S 1 1	4.81	6.29	10.1	53.3	107.5	18.3
7097	D	1	1	S 1 1	7.56	7.11	13.7	44.6	59.1	18.1
7098	D	1	1	S 1 1	9.03	7.15	14.7	52.4	60.2	18.4
7099	D	1	1	S 1 1	8.66	7.11	15.1	51.4	61.8	18.9
7099	D	1	1	S 1 1	8.93	8.85	16.8	55.7	61.7	18.8
7071	D	1	1	S 1 1	7.92	7.28	14.1	50.9	64.1	19.1
7072	D	1	1	S 1 1	7.75	7.04	13.1	50.0	64.0	19.5

D = Dosing Phase

1 = Scheduled Animal Return, 2 = UnScheduled Animal Return, N = Scheduled Necropsy, n = UnScheduled Necropsy

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APPENDIX 1 cont'd. Individual Animal Haematology Parameters

Visit #	Sex	Day Group Week	Screen		RBC (x10 ¹² /mL)	WBC (x10 ⁹ /µL)	Hgb (g/dL)	Hct (%)	MCV (fL)	MCH (pg)
			Pre- Study	Post- Study						
7071	♂	4	NA	NA	7.26	3.03	11.1	37.20	67.20	10.3
7073	♂	1	NA	NA	7.76	3.87	11.2	37.6	69.2	10.3
7078	♂	1	NA	NA	8.11	0.99	19.4	40.1	62.2	10.7
7079	♂	1	NA	NA	8.11	12.03	17.1	52.0	64.1	10.4
7072	♂	3	NA	NA	8.96	7.67	16.2	42.9	69.0	10.7
7076	♂	1	NA	NA	8.87	3.84	26.4	53.1	60.1	10.6
7074	♂	3	NA	NA	8.11	3.09	11.2	31.0	56.8	17.8
7080	♂	4	NA	NA	8.11	3.31	11.4	39.1	67.8	11.3

H = Unknown Phase

S = Scheduled Animal Exam, U = Unscheduled Animal Exam, N = Scheduled Necropsy, U = Unscheduled Necropsy

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APPENDIX I contd. Individual Animal Haematology Parameters

Animal #	Sex	Day		RDW (%)	PLT (x10 ⁹ /l)	ASPT (x10 ⁹ /l)	ALYM (x10 ⁹ /l)	AMON (x10 ⁹ /l)	ABOS (x10 ⁹ /l)	ABAS (x10 ⁹ /l)	ALUC (x10 ⁹ /l)	
		Intake	Phase									Week
7001	D M	100	10.5	S 1.1	12.1	0.29	1.11	7.79	0.1	3.19	0.07	0.16
7002	D M	100	10.5	S 1.1	12.0	0.09	1.50	0.30	0.2	3.09	0.02	0.14
7003	D M	100	10.5	S 1.1	17.3	0.04	1.00	0.49	0.5	0.14	0.0	0.06
7004	D M	100	10.5	S 1.1	12.1	0.04	0.07	4.43	0.2	0.01	0.02	0.07
7005	D M	100	10.5	S 1.1	13.4	0.04	1.14	9.49	0.1	0.03	0.03	0.11
7006	D M	100	10.5	S 1.1	17.4	0.03	0.00	0.0	0.1	0.01	0.00	0.23
7007	D M	100	10.5	S 1.1	13.4	0.02	1.00	8.45	0.0	0.01	0.01	0.16
7008	D M	100	10.5	S 1.1	12.6	0.00	1.10	0.07	0.4	0.0	0.0	0.10
7009	D M	100	10.5	S 1.1	12.9	0.00	0.00	0.23	0.3	0.01	0.02	0.14
7010	D M	100	10.5	S 1.1	17.0	0.03	1.04	0.03	0.4	0.10	0.05	0.19
7021	D M	2	10.5	S 1.1	13.0	0.02	1.10	1.16	0.2	0.00	0.05	0.07
7022	D M	2	10.5	S 1.1	11.0	0.01	1.14	0.10	0.3	0.0	0.02	0.12
7023	D M	2	10.5	S 1.1	12.2	0.01	1.76	11.78	0.4	0.15	0.04	0.22
7024	D M	2	10.5	S 1.1	11.0	0.00	1.04	0.29	0.2	0.00	0.01	0.05
7025	D M	2	10.5	S 1.1	12.5	0.00	0.05	1.45	0.1	0.03	0.02	0.06
7026	D M	2	10.5	S 1.1	16.4	0.03	1.15	11.26	0.4	0.06	0.04	0.12
7027	D M	2	10.5	S 1.1	11.5	0.00	1.00	0.16	0.3	0.00	0.00	0.1
7028	D M	2	10.5	S 1.1	12.4	0.03	0.06	0.17	0.3	0.07	0.05	0.16
7029	D M	2	10.5	S 1.1	11.0	0.02	0.04	0.00	0.3	0.0	0.00	0.14
7030	D M	2	10.5	S 1.1	12.0	0.00	0.00	0.10	0.3	0.0	0.01	0.10
7041	D M	4	10.5	S 1.1	11.0	0.00	0.00	0.24	0.2	0.00	0.01	0.10
7042	D M	4	10.5	S 1.1	11.0	0.00	0.00	0.10	0.2	0.00	0.02	0.11
7043	D M	4	10.5	S 1.1	11.0	0.00	1.22	0.00	0.1	0.00	0.00	0.13
7044	D M	4	10.5	S 1.1	11.0	0.00	0.00	0.11	0.3	0.00	0.0	0.10

D - Dosing Phase

S - Scheduled Animal Exam, U - Unscheduled Animal Exam, N - Scheduled Necropsy, n - Unscheduled Necropsy



APPENDIX 1 contd. Individual Animal Haematology Parameters

Screening	Sex	Age	Hb		Hct	PCV	RBC	HbA	HbF	HbE	HbS	HbT	
			(g/dl)	(g/dl)									
7005	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.2	0.20	0.01	1.96
7006	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	1.11
7007	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.2	0.00	0.02	0.23
7008	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7009	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7010	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7011	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7012	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7013	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7014	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7015	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7016	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7017	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7018	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7019	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7020	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7021	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7022	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7023	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7024	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7025	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7026	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7027	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7028	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7029	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7030	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7031	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7032	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7033	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7034	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7035	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7036	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7037	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10
7038	D	33	1	10.5	31.1	31.0	599	1.54	0.00	0.1	0.00	0.01	0.10

D - Dosing Phase

1 - Screened (non-dosed) - 2 - Dosed (Animal 1) - 3 - Dosed (Animal 2) - 4 - Dosed (Animal 3)

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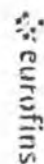
APPENDIX I contd. Individual Animal Hematology Parameters

Cohort	Sex	Age	Day on treatment	Sex	Spleen Weight (g)	RBCs (x 10 ¹² /L)	Hct (%)	Hgb (g/dL)	PLT (x 10 ⁹ /L)	WBC (x 10 ⁹ /L)	GLY (g/dL)	BUN (mg/dL)	ALB (g/dL)	ALP (U/L)	ALT (U/L)	MCH (pg)
01	M	1	11	5	1.70	—	—	0.07	—	—	—	—	—	—	—	—
01	F	1	11	5	—	—	—	0.07	—	—	—	—	—	—	—	0.14
01	M	2	11	5	—	—	—	0.06	—	—	—	—	—	—	—	0.7
01	F	2	11	5	—	—	—	0.04	—	—	—	—	—	—	—	0.27
01	M	4	11	5	—	—	—	0.06	—	—	—	—	—	—	—	0.18
01	F	4	11	5	—	—	—	0.07	—	—	—	—	—	—	—	0.1
01	M	8	11	5	10.8	—	—	0.06	—	—	—	—	—	—	—	0.10
01	F	8	11	5	—	—	—	0.05	—	—	—	—	—	—	—	0.12

Standard Animal Room, Eurofins Animal Health, Eurofins Eurofins, Eurofins Eurofins, Eurofins Eurofins

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APPENDIX 1 (contd.) Individual Animal Haematology Parameters

Animal ID	Sex	Age	Weight (kg)	Hemoglobin (g/dL)		Hematocrit (%)	Hemoglobin A1c (%)	Mean Corpuscular Volume (fL)
				Baseline	Study			
7000	M	1.91	50.8	5.1.3	22.9	51.4	104.4	
7001	M	1.81	50.5	5.1.3	22.8	51.2	104.2	
7002	M	1.81	50.2	5.1.3	22.7	51.1	104.1	
7003	M	1.81	50.1	5.1.3	22.6	51.0	104.0	
7004	M	1.81	50.0	5.1.3	22.5	50.9	103.9	
7005	M	1.81	49.9	5.1.3	22.4	50.8	103.8	
7006	M	1.81	49.8	5.1.3	22.3	50.7	103.7	
7007	M	1.81	49.7	5.1.3	22.2	50.6	103.6	
7008	M	1.81	49.6	5.1.3	22.1	50.5	103.5	
7009	M	1.81	49.5	5.1.3	22.0	50.4	103.4	
7010	M	1.81	49.4	5.1.3	21.9	50.3	103.3	
7011	M	1.81	49.3	5.1.3	21.8	50.2	103.2	
7012	M	1.81	49.2	5.1.3	21.7	50.1	103.1	
7013	M	1.81	49.1	5.1.3	21.6	50.0	103.0	
7014	M	1.81	49.0	5.1.3	21.5	49.9	102.9	
7015	M	1.81	48.9	5.1.3	21.4	49.8	102.8	
7016	M	1.81	48.8	5.1.3	21.3	49.7	102.7	
7017	M	1.81	48.7	5.1.3	21.2	49.6	102.6	
7018	M	1.81	48.6	5.1.3	21.1	49.5	102.5	
7019	M	1.81	48.5	5.1.3	21.0	49.4	102.4	
7020	M	1.81	48.4	5.1.3	20.9	49.3	102.3	
7021	M	1.81	48.3	5.1.3	20.8	49.2	102.2	
7022	M	1.81	48.2	5.1.3	20.7	49.1	102.1	
7023	M	1.81	48.1	5.1.3	20.6	49.0	102.0	
7024	M	1.81	48.0	5.1.3	20.5	48.9	101.9	
7025	M	1.81	47.9	5.1.3	20.4	48.8	101.8	
7026	M	1.81	47.8	5.1.3	20.3	48.7	101.7	
7027	M	1.81	47.7	5.1.3	20.2	48.6	101.6	
7028	M	1.81	47.6	5.1.3	20.1	48.5	101.5	
7029	M	1.81	47.5	5.1.3	20.0	48.4	101.4	
7030	M	1.81	47.4	5.1.3	19.9	48.3	101.3	
7031	M	1.81	47.3	5.1.3	19.8	48.2	101.2	
7032	M	1.81	47.2	5.1.3	19.7	48.1	101.1	
7033	M	1.81	47.1	5.1.3	19.6	48.0	101.0	
7034	M	1.81	47.0	5.1.3	19.5	47.9	100.9	

18 - Missing Data

% = Statistical Analysis Group 1. 20% Inclusion Analysis Group. % = Inclusion Grouping. # = Inclusion Grouping.

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APPENDIX 4 (Contd.) Individual Animal Haematology Parameters

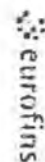
Investigator	Sex	Age	Weight (kg)	Sex	Strain	ARRT (KCP/µl)	ARRT (g/dl)
7055	14 M	3	30.3	♀	1	508	10.3
7056	14 M	3	30.7	♂	1	216	33.0
7057	14 M	3	30.3	♀	1	226	30.2
7058	14 M	3	30.3	♀	1	225	29.8
7059	14 M	3	31.3	♀	1	235	32.2
7060	14 M	3	30.7	♂	1	212	30.2
7061	14 M	3	30.5	♀	1	171	30.6
7062	14 M	3	30.3	♀	1	208	31.4
7063	14 M	3	30.7	♂	1	224	29.0
7064	14 M	3	30.8	♂	1	196	29.7
7065	14 M	3	30.9	♂	1	204	30.6
7066	14 M	3	31.1	♂	1	230	31.2
7067	14 M	3	30.4	♂	1	183	30.2
7068	14 M	3	30.3	♂	1	182	29.8
7069	14 M	3	30.3	♀	1	197	30.1
7070	14 M	3	30.7	♀	1	214	29.0
7071	14 F	3	30.9	♂	1	183	30.8
7072	14 F	3	30.9	♀	1	175	29.0
7073	14 F	3	31.3	♀	1	211	30.1
7074	14 F	3	31.3	♂	1	166	29.8
7075	14 F	3	30.5	♂	1	172	30.6
7076	14 F	3	31.1	♂	1	162	29.7
7077	14 F	3	31.0	♀	1	179	29.8
7078	14 F	3	31.0	♂	1	164	30.5

14 - Fasting Phase

5 - Adrenalectomized Animal Room 2 - Cerebrally Adrenalectomized Animal Room 3 - Adrenalectomized Neurotoxic - Cerebrally Adrenalectomized

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APPENDIX 1 (cont'd) Individual Animal Haematology Parameters

Animal ID	Sex	Day of Phase	Sex- Age	WBC ($\times 10^9$ /L)	RBC ($\times 10^{12}$ /L)
0001	M	1	10	11.1	50.9
0002	M	1	10	11.0	50.3
0003	F	2	10	11.1	50.5
0004	F	3	10	11.0	50.7
0005	F	4	10	11.1	51.1
0006	F	5	10	11.0	50.6
0007	F	6	10	11.0	50.6
0008	F	7	10	11.0	50.7
0009	F	8	10	11.0	50.8
0010	F	9	10	11.0	50.8
0011	F	10	10	11.0	50.8
0012	F	11	10	11.0	50.8
0013	F	12	10	11.0	50.8
0014	F	13	10	11.0	50.8
0015	F	14	10	11.0	50.8
0016	F	15	10	11.0	50.8
0017	F	16	10	11.0	50.8
0018	F	17	10	11.0	50.8
0019	F	18	10	11.0	50.8
0020	F	19	10	11.0	50.8
0021	F	20	10	11.0	50.8
0022	F	21	10	11.0	50.8
0023	F	22	10	11.0	50.8
0024	F	23	10	11.0	50.8
0025	F	24	10	11.0	50.8
0026	F	25	10	11.0	50.8
0027	F	26	10	11.0	50.8
0028	F	27	10	11.0	50.8
0029	F	28	10	11.0	50.8
0030	F	29	10	11.0	50.8
0031	F	30	10	11.0	50.8
0032	F	31	10	11.0	50.8
0033	F	32	10	11.0	50.8
0034	F	33	10	11.0	50.8
0035	F	34	10	11.0	50.8
0036	F	35	10	11.0	50.8
0037	F	36	10	11.0	50.8
0038	F	37	10	11.0	50.8
0039	F	38	10	11.0	50.8
0040	F	39	10	11.0	50.8
0041	F	40	10	11.0	50.8
0042	F	41	10	11.0	50.8
0043	F	42	10	11.0	50.8
0044	F	43	10	11.0	50.8
0045	F	44	10	11.0	50.8
0046	F	45	10	11.0	50.8
0047	F	46	10	11.0	50.8
0048	F	47	10	11.0	50.8
0049	F	48	10	11.0	50.8
0050	F	49	10	11.0	50.8
0051	F	50	10	11.0	50.8
0052	F	51	10	11.0	50.8
0053	F	52	10	11.0	50.8
0054	F	53	10	11.0	50.8
0055	F	54	10	11.0	50.8
0056	F	55	10	11.0	50.8
0057	F	56	10	11.0	50.8
0058	F	57	10	11.0	50.8
0059	F	58	10	11.0	50.8
0060	F	59	10	11.0	50.8
0061	F	60	10	11.0	50.8
0062	F	61	10	11.0	50.8
0063	F	62	10	11.0	50.8
0064	F	63	10	11.0	50.8
0065	F	64	10	11.0	50.8
0066	F	65	10	11.0	50.8
0067	F	66	10	11.0	50.8
0068	F	67	10	11.0	50.8
0069	F	68	10	11.0	50.8
0070	F	69	10	11.0	50.8
0071	F	70	10	11.0	50.8
0072	F	71	10	11.0	50.8
0073	F	72	10	11.0	50.8
0074	F	73	10	11.0	50.8
0075	F	74	10	11.0	50.8
0076	F	75	10	11.0	50.8
0077	F	76	10	11.0	50.8
0078	F	77	10	11.0	50.8
0079	F	78	10	11.0	50.8
0080	F	79	10	11.0	50.8
0081	F	80	10	11.0	50.8
0082	F	81	10	11.0	50.8
0083	F	82	10	11.0	50.8
0084	F	83	10	11.0	50.8
0085	F	84	10	11.0	50.8
0086	F	85	10	11.0	50.8
0087	F	86	10	11.0	50.8
0088	F	87	10	11.0	50.8
0089	F	88	10	11.0	50.8
0090	F	89	10	11.0	50.8
0091	F	90	10	11.0	50.8
0092	F	91	10	11.0	50.8
0093	F	92	10	11.0	50.8
0094	F	93	10	11.0	50.8
0095	F	94	10	11.0	50.8
0096	F	95	10	11.0	50.8
0097	F	96	10	11.0	50.8
0098	F	97	10	11.0	50.8
0099	F	98	10	11.0	50.8
0100	F	99	10	11.0	50.8
0101	F	100	10	11.0	50.8

0 = Unknown Phase

2 = Subtotal Animal Count; 3 = Total Subtotal Animal Count; N = Calculated Neutrophils; n = Unsubstituted Neutrophils

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APPENDIX I (cont'd). Individual Animal Haematology Parameters

Animal ID	Sex	Day Group Week of Phase	Scoring Score	ADFI (g/d)	ADFI (g/d)
7074	♂	4	11.7	2.1	30.5
7074	♂	4	11.7	2.1	29.5
7075	♂	4	11.7	1.1	30.0
7075	♂	4	11.7	1.1	29.2
7077	♂	4	11.8	1.1	30.7
7077	♂	4	11.8	1.1	30.0
7078	♂	4	11.8	1.1	29.8
7080	♂	4	11.7	1.1	30.0

7077

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PKC Study 3 vs. PKC1
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APPENDIX 2. Individual Animal Coagulation Parameters

Animal ID	Sex	Age	Weight (kg)	Day of Phase	Fibrinogen (g/dl)	Partial Thromboplastin Time (sec)	APTT (sec)	PT (sec)
7001	D.M.	1	30.5	5.1	—	—	—	—
7002	D.M.	1	30.5	5.1	—	—	—	—
7003	D.M.	1	30.5	5.1	—	—	—	—
7004	D.M.	1	30.5	5.1	—	—	—	—
7005	D.M.	1	30.5	5.1	—	—	—	—
7006	D.M.	1	30.5	5.1	—	—	—	—
7007	D.M.	1	30.5	5.1	—	—	—	—
7008	D.M.	1	30.5	5.1	—	—	—	—
7009	D.M.	1	30.5	5.1	—	—	—	—
7010	D.M.	1	30.5	5.1	—	—	—	—
7011	D.M.	1	30.5	5.1	—	—	—	—
7012	D.M.	1	30.5	5.1	—	—	—	—
7013	D.M.	1	30.5	5.1	—	—	—	—
7014	D.M.	1	30.5	5.1	—	—	—	—
7015	D.M.	1	30.5	5.1	—	—	—	—
7016	D.M.	1	30.5	5.1	—	—	—	—
7017	D.M.	1	30.5	5.1	—	—	—	—
7018	D.M.	1	30.5	5.1	—	—	—	—
7019	D.M.	1	30.5	5.1	—	—	—	—
7020	D.M.	1	30.5	5.1	—	—	—	—
7021	D.M.	1	30.5	5.1	—	—	—	—
7022	D.M.	1	30.5	5.1	—	—	—	—
7023	D.M.	1	30.5	5.1	—	—	—	—
7024	D.M.	1	30.5	5.1	—	—	—	—
7025	D.M.	1	30.5	5.1	—	—	—	—
7026	D.M.	1	30.5	5.1	—	—	—	—
7027	D.M.	1	30.5	5.1	—	—	—	—
7028	D.M.	1	30.5	5.1	—	—	—	—
7029	D.M.	1	30.5	5.1	—	—	—	—
7030	D.M.	1	30.5	5.1	—	—	—	—
7031	D.M.	1	30.5	5.1	—	—	—	—
7032	D.M.	1	30.5	5.1	—	—	—	—
7033	D.M.	1	30.5	5.1	—	—	—	—
7034	D.M.	1	30.5	5.1	—	—	—	—
7035	D.M.	1	30.5	5.1	—	—	—	—
7036	D.M.	1	30.5	5.1	—	—	—	—
7037	D.M.	1	30.5	5.1	—	—	—	—
7038	D.M.	1	30.5	5.1	—	—	—	—
7039	D.M.	1	30.5	5.1	—	—	—	—
7040	D.M.	1	30.5	5.1	—	—	—	—
7041	D.M.	1	30.5	5.1	—	—	—	—
7042	D.M.	1	30.5	5.1	—	—	—	—
7043	D.M.	1	30.5	5.1	—	—	—	—
7044	D.M.	1	30.5	5.1	—	—	—	—
7045	D.M.	1	30.5	5.1	—	—	—	—

Day 1: Baseline

S: Scheduled Animal Screen; U: Unscheduled Animal Screen; N: Scheduled Necropsy; U: Unscheduled Necropsy

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Eurofins Advisory Study Phase # 1: 018572; PAT (Clinical Pathology) Photo Report
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APPENDIX 2 contd. Individual Animal Coagulation Parameters

Animal ID	Sex	Days		APTT (sec)	PT (sec)
		Correct Week	Score		
7074	♂	1	11.7	8.1	9
7075	♂	1	11.9	8.3	9
7076	♂	1	11.8	8.4	9
7077	♂	1	11.4	8.1	9
7078	♂	1	11.7	8.1	9
7079	♂	1	11.0	8.1	9
7080	♂	1	11.1	8.1	9
7081	♂	1	11.5	8.1	9
7082	♂	1	11.7	8.1	9
7083	♂	1	11.4	8.1	9
7084	♂	1	11.4	8.2	9
7085	♂	1	11.3	8.1	9
7086	♂	1	11.7	8.1	9
7087	♂	1	11.7	8.1	9
7088	♂	1	11.5	8.1	9
7089	♂	1	11.5	8.1	9
7090	♂	1	11.2	8.1	9
7091	♂	1	11.7	8.1	9
7092	♂	1	11.4	8.1	9
7093	♂	1	11.4	8.1	9
7094	♂	1	11.4	8.1	9
7095	♂	1	11.4	8.1	9
7096	♂	1	11.2	8.1	9
7097	♂	1	11.2	8.1	9
7098	♂	1	11.7	8.1	9
7099	♂	1	11.5	8.1	9
7100	♂	1	11.7	8.1	9
7101	♂	1	11.8	8.1	9
7102	♂	4	11.8	8.1	9

U = Testing Point

N = Scheduled Animal Death U = Scheduled Animal Rescue S = Scheduled Sacrifice D = Unscheduled Sacrifice

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APPENDIX 2 (contd.) Individual Animal Coagulation Parameters

Treatment	Sex	Day (Study Week)	Study Phase	Serum Type Number	APTT	PT
					(sec)	(sec)
001	M	1	1	5.1.1	16	8
004	F	4	1	5.1.1	15	8
005	F	3	1	5.1.1	15	8
006	F	4	1	5.1.1	15	8
007	F	4	1	5.1.1	15	8
008	F	4	1	5.1.1	16	8
009	F	4	1	5.1.1	15	8
010	F	1	1	5.1.1	16	8

5) General Notes

5) Scheduled Animal Deaths: 1) Scheduled Animal Deaths: 0) Scheduled Deaths: 0) Scheduled Necropsies

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APPENDIX A Individual Animal Clinical Chemistry Parameters

Animal #	Sex	Creatinine (mg/dL)		BUN (mg/dL)	K ⁺ (mmol/L)	Ca ²⁺ (mmol/L)	Mg ²⁺ (mmol/L)	P _i (mg/dL)	Alb (g/L)	Total Protein (g/L)	Total Bilirubin (mg/dL)	AST (U/L)	ALT (U/L)	ALP (U/L)	GPT (U/L)
		Observed	Normal Range												
7050	U M	0.07	0.1-0.2	1.9	3.45	36.4	1.1	29.8	88	15	10.4	16	16	104	16
7060	U M	0.07	0.1-0.2	1.81	3.31	36.8	1.0	31.8	96	15	10.0	16	16	104	16
7070	U M	0.07	0.1-0.2	1.82	3.28	36.1	1.0	32.0	111	15	10.2	16	16	104	16
7080	U M	0.07	0.1-0.2	1.86	3.36	36.7	1.0	33.0	119	15	10.1	16	16	104	16
7090	U M	0.07	0.1-0.2	1.55	3.74	35.2	1.0	33.0	101	15	10.0	16	16	104	16
7100	U M	0.07	0.1-0.2	1.67	3.61	36.8	1.0	34.4	111	15	10.1	16	16	104	16
7110	U M	0.10	0.1-0.2	1.07	3.97	35.8	1.0	24.0	117	15	10.1	16	16	104	16
7120	U M	0.07	0.1-0.2	1.83	3.34	36.0	1.0	32.4	111	15	10.0	16	16	104	16
7130	U M	0.07	0.1-0.2	1.83	3.41	36.0	1.0	33.0	117	15	10.1	16	16	104	16
7140	U M	0.07	0.1-0.2	1.53	3.30	36.4	1.0	27.4	111	15	10.0	16	16	104	16
7150	U M	0.07	0.1-0.2	1.53	3.46	36.0	1.0	30.0	117	15	10.1	16	16	104	16
7160	U M	0.07	0.1-0.2	1.60	3.42	36.5	1.0	32.0	109	15	10.0	16	16	104	16
7170	U M	0.07	0.1-0.2	1.96	3.27	36.8	1.0	29.0	111	15	10.0	16	16	104	16
7180	U M	0.07	0.1-0.2	1.84	3.39	36.1	1.0	29.0	111	15	10.0	16	16	104	16
7190	U M	0.07	0.1-0.2	1.87	3.36	36.8	1.0	30.0	114	15	10.1	16	16	104	16
7200	U M	0.07	0.1-0.2	1.18	3.82	36.2	1.0	31.8	111	15	10.1	16	16	104	16
7210	U M	0.07	0.1-0.2	1.98	3.30	36.0	1.0	33.0	111	15	10.0	16	16	104	16
7220	U M	0.07	0.1-0.2	1.54	3.10	36.0	1.0	22.0	111	15	10.0	16	16	104	16
7230	U M	0.07	0.1-0.2	1.31	3.58	36.0	1.0	34.0	111	15	10.0	16	16	104	16
7240	U M	0.07	0.1-0.2	1.80	3.09	36.7	1.0	24.0	111	15	10.0	16	16	104	16
7250	U M	0.07	0.1-0.2	1.87	3.00	36.0	1.0	30.0	111	15	10.0	16	16	104	16
7260	U M	0.07	0.1-0.2	1.82	3.40	36.0	1.0	29.0	111	15	10.0	16	16	104	16
7270	U M	0.07	0.1-0.2	1.67	3.48	36.0	1.0	30.0	111	15	10.0	16	16	104	16
7280	U M	0.07	0.1-0.2	1.89	3.43	36.7	1.0	29.0	111	15	10.0	16	16	104	16

D = Dosing Phase

U = Unfasted, F = Fasted, M = Male, F = Female, N = Not Determined, P = Postmortem, S = Serum, U = Urine



APPE NDIX 3 contd. Individual Animal Clinical Chemistry Parameters

Animal #	Sex	Age	Strain	No. of Blood Samples	No. of Animals	Urea (mmol/L)	Creatinine (µmol/L)	AST (U/L)	ALT (U/L)	ALP (U/L)	BUN (mg/dL)	Cr (mg/dL)
7047	♂	007	S	144	14	38.3	17	203.0	1	12	3.3	0.3
7048	♀	007	S	153	14	34.7	17	224.0	14	17	3.4	0.4
7049	♂	007	S	141	14	23.8	18.1	203.0	17	13	3.0	0.3
7050	♂	007	S	140	14	37.4	18	223.0	18	13	3.1	0.3
7051	♂	007	S	145	14	36.5	18.3	214.0	17	12	3.1	0.3
7052	♂	007	S	139	14	29	17.9	233.0	128	17	3.0	0.3
7053	♂	007	S	147	14	32.7	17.4	123.0	130	13	3.0	0.3
7054	♂	007	S	140	14	33.0	17.4	203.0	10	13	3.0	0.3
7055	♂	007	S	142	14	43.1	18.4	193.0	17	14	3.1	0.3
7056	♂	007	S	144	14	34.4	18.2	103.0	11	14	3.0	0.3
7057	♂	007	S	140	14	31.1	18.1	213.0	11	14	3.0	0.3
7058	♂	007	S	140	14	31.1	18.1	213.0	11	14	3.0	0.3
7059	♂	007	S	141	14	31.1	18.1	213.0	11	14	3.0	0.3
7060	♂	007	S	141	14	31.1	18.1	213.0	11	14	3.0	0.3
7061	♂	007	S	141	14	31.1	18.1	213.0	11	14	3.0	0.3
7062	♂	007	S	141	14	31.1	18.1	213.0	11	14	3.0	0.3
7063	♂	007	S	141	14	31.1	18.1	213.0	11	14	3.0	0.3
7064	♂	007	S	141	14	31.1	18.1	213.0	11	14	3.0	0.3
7065	♂	007	S	141	14	31.1	18.1	213.0	11	14	3.0	0.3
7066	♂	007	S	141	14	31.1	18.1	213.0	11	14	3.0	0.3
7067	♂	007	S	141	14	31.1	18.1	213.0	11	14	3.0	0.3
7068	♂	007	S	141	14	31.1	18.1	213.0	11	14	3.0	0.3
7069	♂	007	S	141	14	31.1	18.1	213.0	11	14	3.0	0.3
7070	♂	007	S	141	14	31.1	18.1	213.0	11	14	3.0	0.3
7071	♂	007	S	141	14	31.1	18.1	213.0	11	14	3.0	0.3
7072	♂	007	S	141	14	31.1	18.1	213.0	11	14	3.0	0.3
7073	♂	007	S	141	14	31.1	18.1	213.0	11	14	3.0	0.3
7074	♂	007	S	141	14	31.1	18.1	213.0	11	14	3.0	0.3
7075	♂	007	S	141	14	31.1	18.1	213.0	11	14	3.0	0.3
7076	♂	007	S	141	14	31.1	18.1	213.0	11	14	3.0	0.3
7077	♂	007	S	141	14	31.1	18.1	213.0	11	14	3.0	0.3
7078	♂	007	S	141	14	31.1	18.1	213.0	11	14	3.0	0.3
7079	♂	007	S	141	14	31.1	18.1	213.0	11	14	3.0	0.3
7080	♂	007	S	141	14	31.1	18.1	213.0	11	14	3.0	0.3

SD = Standard Deviation

1 = Investigator Assay Error 2 = Laboratory Assay Error 3 = Investigator Sample Error 4 = Investigator Sample Error



APPENDIX 3 contd. Individual Animal Clinical Chemistry Parameters

Animal ID	Sex	Days on-treat	Week of Phase	Study Day	WBC (x10 ⁹ /L)	Hb (g/dL)	PCV (%)	PLT (x10 ⁹ /L)	AST (U/L)	ALT (U/L)	ALP (U/L)	BUN (mg/dL)	Cr (mg/dL)
5019	011	1	10.0	8	11.0	6.42	42.5	41	14.06	10	15	0.7	
4756	011	1	10.0	8	11.0	5.15	36.4	111	11.00	40	16	0.4	
4757	011	1	10.0	8	11.0	11	11	56.8	41	10.40	12	0.9	
5092	011	1	10.0	8	11.0	10.0	27.4	50	17.01	11	11	0.9	
5051	011	1	10.0	8	11.0	11	11	99.0	128	24.00	10	1.1	
5103	011	1	10.0	8	11.0	5.67	43.7	95	17.50	15	11	0.5	
4109	011	1	10.0	8	11.0	7.17	119.8	63	15.00	11	14	0.1	
5054	011	1	10.0	8	11.0	6.29	43.5	70	17.10	15	11	0.1	
4777	011	1	10.0	8	11.0	6.95	74.0	84	10	6.7	11	0.6	
5118	011	1	10.0	8	11.0	6.1	11.5	6.7	7.00	10	11	0.6	
5031	011	1	10.0	8	11.0	6.29	22.7	66	12.00	15	14	0.3	
5069	011	1	10.0	8	11.0	6.34	36.7	59	14.00	11	14	1.1	
5051	011	1	10.0	8	11.0	6.6	36	59	14.00	10	14	0.6	
5097	011	1	10.0	8	11.0	6.11	47	68	17.01	11	11	0.1	
5049	011	1	10.0	8	11.0	6.46	24.1	69	13.00	14	11	0.1	
5114	011	1	10.0	8	11.0	7.39	44.6	65	10.40	10	11	0.1	
5085	011	1	10.0	8	11.0	6.18	31	59	17.01	11	11	0.1	
5066	011	1	10.0	8	11.0	6.08	47.2	26.7	10.00	10	11	0.5	
5097	011	1	10.0	8	11.0	5.91	116.7	68	10.01	11	11	0.1	
5066	011	1	10.0	8	11.0	7.16	117.7	11	17.04	15	17	1.8	
5068	011	1	10.0	8	11.0	6.26	11	11.3	11.00	11	11	0.3	
5061	011	1	10.0	8	11.0	6.4	11	10.1	16.01	11	11	0.6	
5075	011	1	10.0	8	11.0	6.16	47.1	17	11.01	10	11	1.1	
5077	011	1	10.0	8	11.0	5.17	29.4	110	16.01	11	11	0.1	

U = micromol/L

2 = Significant Animal Review, 1 = Not Significant Animal Review, N = Not Assessed/Not Reported, 0 = DGS, tested but not reported

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APPENDIX 3 cont'd: Individual Animal Clinical Chemistry (Continued)

Animal #	Sex	Age	Weight (kg)	Species	Strain	Urea (mg/dL)	Cr (mg/dL)	BUN (mg/dL)	ALT (U/L)	ALP (U/L)	BUN (mg/dL)	Cr (mg/dL)
7071	011	1	11.0	S	1	27	—	301	40	25.00	11	—
7071	011	1	11.0	S	1	—	0.25	0.0	40	2.00	—	0.0
7075	011	1	11.0	S	1	—	0.68	0.0	40	17.00	11	—
7075	011	1	11.0	S	1	—	7.85	102.0	57	120.00	11	0.0
7075	011	1	11.0	S	1	—	2.21	0.0	—	—	—	—
7075	011	1	11.0	S	1	141	—	15.6	22	20.00	11	10.0
7075	011	1	11.0	S	1	140	—	—	—	50.00	11	—
7075	011	1	11.0	S	1	100	—	—	—	30.00	10	10.0

Legend:

1 = randomized Animal B (m); 0 = Unrandomized Animal B (m); S = randomized Subject; 0 = Unrandomized Subject



APPENDIX 3 (cont'd): Individual Animal Clinical Chemistry Parameters

Sample ID	Sex	Age	Weight (kg)	Phase	Sampling Day	ALT (U/L)	AST (U/L)	BUN (mg/dL)	Creat (mg/dL)	SUN (mg/dL)	SUN (mg/dL)	Urea (mg/dL)
9001	D	M	1.01	0.0	0.0	40	170	20	0.0	0.0	0.0	0.0
9002	D	M	1.09	0.0	0.0	38	170	19	0.0	0.0	0.0	0.0
9003	D	M	1.01	0.0	0.0	40	170	19	0.0	0.0	0.0	0.0
9004	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9005	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9006	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9007	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9008	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9009	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9010	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9011	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9012	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9013	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9014	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9015	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9016	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9017	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9018	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9019	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9020	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9021	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9022	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9023	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9024	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9025	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9026	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9027	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9028	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9029	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9030	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9031	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9032	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9033	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9034	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0
9035	D	M	1.01	0.0	0.0	37	170	19	0.0	0.0	0.0	0.0

U: Urine; P: Plasma

ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; BUN: Blood Urea Nitrogen; Creat: Creatinine



APPENDIX 3 contd. Individual Annual Clinical Chemistry Parameters

Subject ID	Sex	Age (Years)	Weight (kg)	Height (cm)	CRP (mg/L)	Urea (mg/dL)	Uric Acid (mg/dL)	Protein (mg/dL)	Albumin (g/L)	Bilirubin (mg/dL)	ALT (U/L)	AST (U/L)
7007	M	42	78.5	178	0.2	10	4.5	0.6	3.8	0.1	15	18
7008	M	43	80.2	180	0.1	12	5.0	0.5	3.5	0.1	18	20
7009	M	44	75.0	175	0.3	11	4.8	0.7	3.6	0.1	16	19
7010	M	45	82.0	185	0.2	13	5.2	0.6	3.7	0.1	17	21
7011	M	46	79.5	182	0.1	14	5.5	0.5	3.4	0.1	19	22
7012	M	47	81.0	183	0.2	15	5.8	0.6	3.5	0.1	20	23
7013	M	48	77.0	178	0.3	16	6.0	0.7	3.6	0.1	21	24
7014	M	49	83.0	188	0.2	17	6.2	0.6	3.7	0.1	22	25
7015	M	50	80.0	185	0.1	18	6.5	0.5	3.8	0.1	23	26
7016	M	51	78.0	182	0.2	19	6.8	0.6	3.9	0.1	24	27
7017	M	52	84.0	190	0.1	20	7.0	0.5	4.0	0.1	25	28
7018	M	53	81.0	187	0.2	21	7.2	0.6	4.1	0.1	26	29
7019	M	54	79.0	184	0.3	22	7.5	0.7	4.2	0.1	27	30
7020	M	55	85.0	192	0.2	23	7.8	0.6	4.3	0.1	28	31
7021	M	56	82.0	189	0.1	24	8.0	0.5	4.4	0.1	29	32
7022	M	57	80.0	186	0.2	25	8.2	0.6	4.5	0.1	30	33
7023	M	58	78.0	183	0.3	26	8.5	0.7	4.6	0.1	31	34
7024	M	59	84.0	191	0.2	27	8.8	0.6	4.7	0.1	32	35
7025	M	60	81.0	188	0.1	28	9.0	0.5	4.8	0.1	33	36
7026	M	61	79.0	185	0.2	29	9.2	0.6	4.9	0.1	34	37
7027	M	62	85.0	193	0.1	30	9.5	0.5	5.0	0.1	35	38
7028	M	63	82.0	190	0.2	31	9.8	0.6	5.1	0.1	36	39
7029	M	64	80.0	187	0.3	32	10.0	0.7	5.2	0.1	37	40
7030	M	65	86.0	195	0.2	33	10.2	0.6	5.3	0.1	38	41
7031	M	66	83.0	192	0.1	34	10.5	0.5	5.4	0.1	39	42
7032	M	67	81.0	189	0.2	35	10.8	0.6	5.5	0.1	40	43
7033	M	68	79.0	186	0.3	36	11.0	0.7	5.6	0.1	41	44
7034	M	69	85.0	194	0.2	37	11.2	0.6	5.7	0.1	42	45
7035	M	70	82.0	191	0.1	38	11.5	0.5	5.8	0.1	43	46
7036	M	71	80.0	188	0.2	39	11.8	0.6	5.9	0.1	44	47
7037	M	72	86.0	196	0.1	40	12.0	0.5	6.0	0.1	45	48
7038	M	73	83.0	193	0.2	41	12.2	0.6	6.1	0.1	46	49
7039	M	74	81.0	190	0.3	42	12.5	0.7	6.2	0.1	47	50
7040	M	75	87.0	198	0.2	43	12.8	0.6	6.3	0.1	48	51
7041	M	76	84.0	195	0.1	44	13.0	0.5	6.4	0.1	49	52
7042	M	77	82.0	192	0.2	45	13.2	0.6	6.5	0.1	50	53
7043	M	78	80.0	189	0.3	46	13.5	0.7	6.6	0.1	51	54
7044	M	79	86.0	197	0.2	47	13.8	0.6	6.7	0.1	52	55
7045	M	80	83.0	194	0.1	48	14.0	0.5	6.8	0.1	53	56
7046	M	81	81.0	191	0.2	49	14.2	0.6	6.9	0.1	54	57
7047	M	82	79.0	188	0.3	50	14.5	0.7	7.0	0.1	55	58
7048	M	83	85.0	196	0.2	51	14.8	0.6	7.1	0.1	56	59
7049	M	84	82.0	193	0.1	52	15.0	0.5	7.2	0.1	57	60
7050	M	85	80.0	190	0.2	53	15.2	0.6	7.3	0.1	58	61
7051	M	86	86.0	198	0.1	54	15.5	0.5	7.4	0.1	59	62
7052	M	87	83.0	195	0.2	55	15.8	0.6	7.5	0.1	60	63
7053	M	88	81.0	192	0.3	56	16.0	0.7	7.6	0.1	61	64
7054	M	89	87.0	200	0.2	57	16.2	0.6	7.7	0.1	62	65
7055	M	90	84.0	197	0.1	58	16.5	0.5	7.8	0.1	63	66
7056	M	91	82.0	194	0.2	59	16.8	0.6	7.9	0.1	64	67
7057	M	92	80.0	191	0.3	60	17.0	0.7	8.0	0.1	65	68
7058	M	93	86.0	199	0.2	61	17.2	0.6	8.1	0.1	66	69
7059	M	94	83.0	196	0.1	62	17.5	0.5	8.2	0.1	67	70
7060	M	95	81.0	193	0.2	63	17.8	0.6	8.3	0.1	68	71
7061	M	96	79.0	190	0.3	64	18.0	0.7	8.4	0.1	69	72
7062	M	97	85.0	198	0.2	65	18.2	0.6	8.5	0.1	70	73
7063	M	98	82.0	195	0.1	66	18.5	0.5	8.6	0.1	71	74
7064	M	99	80.0	192	0.2	67	18.8	0.6	8.7	0.1	72	75
7065	M	100	86.0	200	0.1	68	19.0	0.5	8.8	0.1	73	76

U = Urea; Crp = CRP

† = Abnormal; ** = Abnormal; *** = Abnormal; **** = Abnormal



APPENDIX J contd. Individual Animal Clinical Chemistry Parameters

Sampl. #	Sex	Age	Weight (kg)	Temp. (°C)	HR (b/min)	PR (b/min)	MAP (mmHg)	SpO ₂ (%)	FiO ₂ (%)	PaO ₂ (mmHg)	PaCO ₂ (mmHg)	pH	pCO ₂ (kPa)	pO ₂ (kPa)	BE (mmol/L)	TC (mmol/L)	Trig (mmol/L)	Chol (mmol/L)	Urea (mmol/L)	Cr (µmol/L)	BUN (mg/dL)	Ca (mmol/L)	Alb (g/L)	Gluc (mmol/L)	Ins (µU/mL)	ACT (sec)	PT (sec)	APTT (sec)	INR	APTT/APTT _{ref}	APTT/INR				
7076	♂	1	6.21	37.8	5	3	93	100	21	100	33	7.4	10.1	13.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0		
7079	♂	1	6.11	37.8	3	3	95	100	21	100	33	7.4	10.1	13.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
7083	♂	1	6.18	37.8	3	3	93	100	21	100	33	7.4	10.1	13.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7084	♂	1	6.18	37.8	3	3	94	100	21	100	33	7.4	10.1	13.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7088	♂	1	6.13	37.8	3	3	95	100	21	100	33	7.4	10.1	13.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7090	♂	1	6.13	37.8	3	3	95	100	21	100	33	7.4	10.1	13.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7091	♂	1	6.13	37.8	3	3	95	100	21	100	33	7.4	10.1	13.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7092	♂	1	6.13	37.8	3	3	95	100	21	100	33	7.4	10.1	13.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7093	♂	1	6.13	37.8	3	3	95	100	21	100	33	7.4	10.1	13.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7094	♂	1	6.13	37.8	3	3	95	100	21	100	33	7.4	10.1	13.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7095	♂	1	6.13	37.8	3	3	95	100	21	100	33	7.4	10.1	13.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7096	♂	1	6.13	37.8	3	3	95	100	21	100	33	7.4	10.1	13.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7097	♂	1	6.13	37.8	3	3	95	100	21	100	33	7.4	10.1	13.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7098	♂	1	6.13	37.8	3	3	95	100	21	100	33	7.4	10.1	13.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7099	♂	1	6.13	37.8	3	3	95	100	21	100	33	7.4	10.1	13.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7100	♂	1	6.13	37.8	3	3	95	100	21	100	33	7.4	10.1	13.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7101	♂	1	6.13	37.8	3	3	95	100	21	100	33	7.4	10.1	13.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

D: Urinary Data

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APPENDIX 3 contd. Individual Annual Clinical Chemistry Parameters

AMPHO B	Site	Sex	Age	Weight (kg)	* Hb (g/L)		* AST (U/L)	* ALT (U/L)	* Bilirubin (mg/dL)	* BUN (mg/dL)	* Cr (mg/dL)	* eGFR (mL/min/1.73m ²)
					Observed	Normal						
5000	1117	M	31	67.1	13.1	100	17	10	0.00	11	0.8	100
5000	1117	F	34	67.0	12.0	100	17	10	0.00	11	0.8	100
5000	1117	M	31	67.0	12.0	100	17	10	0.00	11	0.8	100
5000	1117	M	31	67.0	12.0	100	17	10	0.00	11	0.8	100
5000	1117	F	34	67.0	12.0	100	17	10	0.00	11	0.8	100
5000	1117	M	31	67.0	12.0	100	17	10	0.00	11	0.8	100
5000	1117	F	34	67.0	12.0	100	17	10	0.00	11	0.8	100
5000	1117	M	31	67.0	12.0	100	17	10	0.00	11	0.8	100
5000	1117	F	34	67.0	12.0	100	17	10	0.00	11	0.8	100

D. Events

Adverse Event (AE) | Serious Adverse Event (SAE) | SAE of Interest (SOI) | Unexpected Adverse Event (UAE)



APPENDIX 3 (contd.) Individual Annual Clinical Chemistry Parameters

Study ID	Day	Time	Sample	Unit	SIU	LAB
			Phase		(U/L)	(U/L)
7000	D-M	1.00	00*	S	3.5	7.0
7001	D-M	1.00	00*	S	3.5	1.0
7002	D-M	1.00	00*	S	3.7	3.0
7003	D-M	1.00	00*	S, L, T	3.0	1.0
7004	D-M	1.00	00*	S	3.3	2.3
7005	D-M	1.00	00*	S	4.5	7.1
7006	D-M	1.00	00*	S	3.3	2.2
7007	D-M	1.00	00*	S, L, T	3.3	—
7008	D-M	1.00	00*	S, L	4.5	7.1
7009	D-M	1.00	00*	S, L	3.5	3.1
7010	D-M	1.00	00*	S, L	3.5	2.1
7011	D-M	1.00	00*	S, L	3.5	2.1
7012	D-M	2.00	00*	S, L	4.0	—
7013	D-M	2.00	00*	S, L	3.5	—
7014	D-M	2.00	00*	S, L	3.5	—
7015	D-M	2.00	00*	S, L	3.5	—
7016	D-M	3.00	00*	S, L	4.0	7.1
7017	D-M	3.00	00*	S, L	3.5	—
7018	D-M	3.00	00*	S, L	3.5	—
7019	D-M	3.00	00*	S, L	3.5	—
7020	D-M	3.00	00*	S, L	3.5	—
7021	D-M	3.00	00*	S, L	3.5	—
7022	D-M	3.00	00*	S, L	3.5	—
7023	D-M	3.00	00*	S, L	3.5	—
7024	D-M	3.00	00*	S, L	3.5	—
7025	D-M	3.00	00*	S, L	3.5	—
7026	D-M	3.00	00*	S, L	3.5	—
7027	D-M	3.00	00*	S, L	3.5	—
7028	D-M	3.00	00*	S, L	3.5	—
7029	D-M	3.00	00*	S, L	3.5	—
7030	D-M	3.00	00*	S, L	3.5	—
7031	D-M	3.00	00*	S, L	3.5	—
7032	D-M	3.00	00*	S, L	3.5	—
7033	D-M	3.00	00*	S, L	3.5	—
7034	D-M	3.00	00*	S, L	3.5	—
7035	D-M	3.00	00*	S, L	3.5	—

IT - Listing #79w

N = Scheduled Annual Blood; * = Unscheduled Annual Blood; S = Scheduled Urinary Copy; L = Unscheduled Urinary Copy



APPENDIX 3 (cont): Individual Annual Clinical Chemistry Parameters

Annual #	Sex	Tox		Sera		ALT	CRP
		Urea	Cr	Alb	Ca		
7045	F	30.5	2.1	3.0	3.2		
7046	F	30.5	2.1	3.0	3.2		
7047	F	30.5	2.1	3.0	3.2		
7048	F	30.5	2.1	3.0	3.2		
7049	F	30.5	2.1	3.0	3.2		
7050	F	30.5	2.1	3.0	3.2		
7051	F	30.5	2.1	3.0	3.2		
7052	F	30.5	2.1	3.0	3.2		
7053	F	30.5	2.1	3.0	3.2		
7054	F	30.5	2.1	3.0	3.2		
7055	F	30.5	2.1	3.0	3.2		
7056	F	30.5	2.1	3.0	3.2		
7057	F	30.5	2.1	3.0	3.2		
7058	F	30.5	2.1	3.0	3.2		
7059	F	30.5	2.1	3.0	3.2		
7060	F	30.5	2.1	3.0	3.2		
7061	F	30.5	2.1	3.0	3.2		
7062	F	30.5	2.1	3.0	3.2		
7063	F	30.5	2.1	3.0	3.2		
7064	F	30.5	2.1	3.0	3.2		
7065	F	30.5	2.1	3.0	3.2		
7066	F	30.5	2.1	3.0	3.2		
7067	F	30.5	2.1	3.0	3.2		
7068	F	30.5	2.1	3.0	3.2		
7069	F	30.5	2.1	3.0	3.2		
7070	F	30.5	2.1	3.0	3.2		
7071	F	30.5	2.1	3.0	3.2		
7072	F	30.5	2.1	3.0	3.2		
7073	F	30.5	2.1	3.0	3.2		
7074	F	30.5	2.1	3.0	3.2		
7075	F	30.5	2.1	3.0	3.2		
7076	F	30.5	2.1	3.0	3.2		
7077	F	30.5	2.1	3.0	3.2		
7078	F	30.5	2.1	3.0	3.2		
7079	F	30.5	2.1	3.0	3.2		
7080	F	30.5	2.1	3.0	3.2		

D = Missing Data

S = Scheduled Annual Screen 1-4 = Scheduled Annual Screen 5 = Scheduled Screening 6-10 = Scheduled Screening

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APPENDIX 3 (cont'd). Individual Animal Clinical Chemistry Parameters

Animal	Sex	Age	Weight (kg)	Phase	ALT (U/L)	ALP (U/L)
001	♂	3.5	3.2	S-1	12	49
002	♂	4.0	3.8	S-1	18	5
003	♂	3.5	3.5	S-1	18	100
004	♂	3.5	3.5	S-1	15.0	5.0
005	♂	3.5	3.5	S-1	15.0	100
006	♂	3.5	3.5	S-1	15.0	200
007	♂	3.5	3.5	S-1	15.0	200
008	♂	3.5	3.5	S-1	15.0	200
009	♂	3.5	3.5	S-1	15.0	200
010	♂	3.5	3.5	S-1	15.0	200
011	♂	3.5	3.5	S-1	15.0	200
012	♂	3.5	3.5	S-1	15.0	200
013	♂	3.5	3.5	S-1	15.0	200
014	♂	3.5	3.5	S-1	15.0	200
015	♂	3.5	3.5	S-1	15.0	200
016	♂	3.5	3.5	S-1	15.0	200
017	♂	3.5	3.5	S-1	15.0	200
018	♂	3.5	3.5	S-1	15.0	200
019	♂	3.5	3.5	S-1	15.0	200
020	♂	3.5	3.5	S-1	15.0	200
021	♂	3.5	3.5	S-1	15.0	200
022	♂	3.5	3.5	S-1	15.0	200
023	♂	3.5	3.5	S-1	15.0	200
024	♂	3.5	3.5	S-1	15.0	200
025	♂	3.5	3.5	S-1	15.0	200
026	♂	3.5	3.5	S-1	15.0	200
027	♂	3.5	3.5	S-1	15.0	200
028	♂	3.5	3.5	S-1	15.0	200
029	♂	3.5	3.5	S-1	15.0	200
030	♂	3.5	3.5	S-1	15.0	200
031	♂	3.5	3.5	S-1	15.0	200
032	♂	3.5	3.5	S-1	15.0	200

U = Urea Nitrogen

S = Scheduled Animal Room; 1 = Experimental Animal Room; N = Necropsy; S = Scheduled Surgery; 0 = Scheduled Surgery

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APPENDIX J (cont'd) Individual Animal Clinical Chemistry Parameters

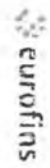
Treatment	Sex	Age at Phase Start	Days on Study	Weight kg	Sex	Sex Score	ALT (U/L)	
							Observed	Adjusted
001	♂	1	51.3	0.1	♂	1	5.1	2.4
002	♂	1	51.5	0.1	♂	1
003	♂	1	51.5	0.1	♂	1	1.1	...
004	♂	1	51.5	0.1	♂	1	2.2	...
005	♂	1	51.5	0.1	♂	1	2.9	...
006	♂	1	51.5	0.1	♂	1	1.1	...
007	♂	1	51.5	0.1	♂	1	4.5	2.1
008	♂	1	51.5	0.1	♂	1

0 - Learning Phase

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APPENDIX 4 Individual Animal Clinical Analysis of Ulfine

Study No.	Sex	Age	Weight (kg)	Phase	Ulfine	Ulfine	SPs (mg/dL)	Ulfine (mg/dL)	Ulfine (ng/mL)	Ulfine (ng/mL)	Ulfine (ng/mL)	Ulfine (ng/mL)	Ulfine (ng/mL)
001	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
002	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
003	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
004	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
005	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
006	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
007	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
008	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
009	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
010	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
011	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
012	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
013	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
014	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
015	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
016	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
017	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
018	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
019	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
020	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
021	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
022	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
023	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
024	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
025	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
026	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
027	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
028	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
029	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
030	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
031	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
032	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
033	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
034	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
035	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
036	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
037	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
038	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
039	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
040	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
041	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
042	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
043	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
044	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
045	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
046	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
047	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
048	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
049	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---
050	M	1	3.5	1	Ulfine	Ulfine	---	---	---	---	---	---	---

U: Urinary Phase

1: Subcutaneous Injection; 2: Intravenous Injection; 3: Intramuscular Injection; 4: Intraperitoneal Injection



APPENDIX 4 (contd.) Individual Animal Clinical Analysis of Urine

Study ID	Sex	Day	Week	Phase	Cat	Protein	pH	Specific Gravity	Bilirubin	pH	pH	pH
507	D	1	1	1	POS	POS	POS	POS	POS	POS	POS	POS
507	D	1	1	1	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0	0	0.00	0.00
507	D	1	1	2	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0	0	0.00	0.00
507	D	1	1	3	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0	0	0.00	0.00
507	D	1	1	4	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0	0	0.00	0.00
507	D	1	1	5	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0	0	0.00	0.00
507	D	1	1	6	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0	0	0.00	0.00
507	D	1	1	7	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0	0	0.00	0.00
507	D	1	1	8	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0	0	0.00	0.00
507	D	1	1	9	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0	0	0.00	0.00
507	D	1	1	10	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0	0	0.00	0.00

U. Basing

Signature Animal Report U. Basing Individual Animal Report W. Schmalzer Signature U. Basing Animal Report



APPENDIX I continued, Individual Annual Clinical Analysis of Urine

Year/Visit	Sex	Age	Weight (kg)	Height (cm)	Urea Nitrogen (mg/dL)	Creatinine (mg/dL)	BUN:Cr	PPVT (mmHg)	Urea Nitrogen (mg/dL)	Urea Nitrogen (mg/dL)
7001	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7002	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7003	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7004	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7005	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7006	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7007	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7008	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7009	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7010	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7011	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7012	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7013	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7014	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7015	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7016	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7017	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7018	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7019	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7020	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7021	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7022	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7023	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7024	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7025	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7026	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7027	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7028	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7029	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7030	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7031	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7032	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7033	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7034	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7035	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7036	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7037	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7038	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7039	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7040	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7041	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7042	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7043	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL
7044	F	51	100	167	1.1	1.1	1.0	85	1.1	WNL

U: Urinary; P: Plasma

WNL: within normal limits; BUN: Blood Urea Nitrogen; Cr: Creatinine; PPVT: Pulmonary Vascular Pressure; WNL: within normal limits

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APPENDIX 1 contd. Individual Amniotic Chemical Analysis of Fetus

Amniotic #	Sex	Day of Group	Week of Gestation	Weight (g)	PLG (%)	CHOL (mg/dl)	GLU (mg/dl)	UREA (mg/dl)	PSca	17-OH-DHEA
7027	F	M	3	00.7	8.0	1.11	ND	ND	ND	ND
7028	F	M	3	00.8	8.0	1.12	ND	ND	ND	ND
7029	F	M	3	00.9	8.0	1.13	ND	ND	ND	ND
7030	F	M	3	00.8	8.0	1.14	ND	ND	ND	ND
7031	F	M	3	00.9	8.0	1.15	ND	ND	ND	ND
7032	F	M	3	00.8	8.0	1.16	ND	ND	ND	ND
7033	F	M	3	00.9	8.0	1.17	ND	ND	ND	ND
7034	F	M	3	00.8	8.0	1.18	ND	ND	ND	ND
7035	F	M	3	00.9	8.0	1.19	ND	ND	ND	ND
7036	F	M	3	00.8	8.0	1.20	ND	ND	ND	ND
7037	F	M	3	00.9	8.0	1.21	ND	ND	ND	ND
7038	F	M	3	00.8	8.0	1.22	ND	ND	ND	ND
7039	F	M	3	00.9	8.0	1.23	ND	ND	ND	ND
7040	F	M	3	00.8	8.0	1.24	ND	ND	ND	ND
7041	F	M	3	00.9	8.0	1.25	ND	ND	ND	ND
7042	F	M	3	00.8	8.0	1.26	ND	ND	ND	ND
7043	F	M	3	00.9	8.0	1.27	ND	ND	ND	ND
7044	F	M	3	00.8	8.0	1.28	ND	ND	ND	ND
7045	F	M	3	00.9	8.0	1.29	ND	ND	ND	ND
7046	F	M	3	00.8	8.0	1.30	ND	ND	ND	ND
7047	F	M	3	00.9	8.0	1.31	ND	ND	ND	ND
7048	F	M	3	00.8	8.0	1.32	ND	ND	ND	ND
7049	F	M	3	00.9	8.0	1.33	ND	ND	ND	ND
7050	F	M	3	00.8	8.0	1.34	ND	ND	ND	ND
7051	F	M	3	00.9	8.0	1.35	ND	ND	ND	ND
7052	F	M	3	00.8	8.0	1.36	ND	ND	ND	ND
7053	F	M	3	00.9	8.0	1.37	ND	ND	ND	ND
7054	F	M	3	00.8	8.0	1.38	ND	ND	ND	ND
7055	F	M	3	00.9	8.0	1.39	ND	ND	ND	ND
7056	F	M	3	00.8	8.0	1.40	ND	ND	ND	ND
7057	F	M	3	00.9	8.0	1.41	ND	ND	ND	ND
7058	F	M	3	00.8	8.0	1.42	ND	ND	ND	ND
7059	F	M	3	00.9	8.0	1.43	ND	ND	ND	ND
7060	F	M	3	00.8	8.0	1.44	ND	ND	ND	ND
7061	F	M	3	00.9	8.0	1.45	ND	ND	ND	ND
7062	F	M	3	00.8	8.0	1.46	ND	ND	ND	ND
7063	F	M	3	00.9	8.0	1.47	ND	ND	ND	ND
7064	F	M	3	00.8	8.0	1.48	ND	ND	ND	ND
7065	F	M	3	00.9	8.0	1.49	ND	ND	ND	ND
7066	F	M	3	00.8	8.0	1.50	ND	ND	ND	ND
7067	F	M	3	00.9	8.0	1.51	ND	ND	ND	ND
7068	F	M	3	00.8	8.0	1.52	ND	ND	ND	ND
7069	F	M	3	00.9	8.0	1.53	ND	ND	ND	ND
7070	F	M	3	00.8	8.0	1.54	ND	ND	ND	ND
7071	F	M	3	00.9	8.0	1.55	ND	ND	ND	ND
7072	F	M	3	00.8	8.0	1.56	ND	ND	ND	ND
7073	F	M	3	00.9	8.0	1.57	ND	ND	ND	ND
7074	F	M	3	00.8	8.0	1.58	ND	ND	ND	ND
7075	F	M	3	00.9	8.0	1.59	ND	ND	ND	ND
7076	F	M	3	00.8	8.0	1.60	ND	ND	ND	ND
7077	F	M	3	00.9	8.0	1.61	ND	ND	ND	ND
7078	F	M	3	00.8	8.0	1.62	ND	ND	ND	ND
7079	F	M	3	00.9	8.0	1.63	ND	ND	ND	ND
7080	F	M	3	00.8	8.0	1.64	ND	ND	ND	ND
7081	F	M	3	00.9	8.0	1.65	ND	ND	ND	ND
7082	F	M	3	00.8	8.0	1.66	ND	ND	ND	ND
7083	F	M	3	00.9	8.0	1.67	ND	ND	ND	ND
7084	F	M	3	00.8	8.0	1.68	ND	ND	ND	ND
7085	F	M	3	00.9	8.0	1.69	ND	ND	ND	ND
7086	F	M	3	00.8	8.0	1.70	ND	ND	ND	ND
7087	F	M	3	00.9	8.0	1.71	ND	ND	ND	ND
7088	F	M	3	00.8	8.0	1.72	ND	ND	ND	ND
7089	F	M	3	00.9	8.0	1.73	ND	ND	ND	ND
7090	F	M	3	00.8	8.0	1.74	ND	ND	ND	ND
7091	F	M	3	00.9	8.0	1.75	ND	ND	ND	ND
7092	F	M	3	00.8	8.0	1.76	ND	ND	ND	ND
7093	F	M	3	00.9	8.0	1.77	ND	ND	ND	ND
7094	F	M	3	00.8	8.0	1.78	ND	ND	ND	ND
7095	F	M	3	00.9	8.0	1.79	ND	ND	ND	ND
7096	F	M	3	00.8	8.0	1.80	ND	ND	ND	ND
7097	F	M	3	00.9	8.0	1.81	ND	ND	ND	ND
7098	F	M	3	00.8	8.0	1.82	ND	ND	ND	ND
7099	F	M	3	00.9	8.0	1.83	ND	ND	ND	ND
7100	F	M	3	00.8	8.0	1.84	ND	ND	ND	ND
7101	F	M	3	00.9	8.0	1.85	ND	ND	ND	ND
7102	F	M	3	00.8	8.0	1.86	ND	ND	ND	ND
7103	F	M	3	00.9	8.0	1.87	ND	ND	ND	ND
7104	F	M	3	00.8	8.0	1.88	ND	ND	ND	ND
7105	F	M	3	00.9	8.0	1.89	ND	ND	ND	ND
7106	F	M	3	00.8	8.0	1.90	ND	ND	ND	ND
7107	F	M	3	00.9	8.0	1.91	ND	ND	ND	ND
7108	F	M	3	00.8	8.0	1.92	ND	ND	ND	ND
7109	F	M	3	00.9	8.0	1.93	ND	ND	ND	ND
7110	F	M	3	00.8	8.0	1.94	ND	ND	ND	ND
7111	F	M	3	00.9	8.0	1.95	ND	ND	ND	ND
7112	F	M	3	00.8	8.0	1.96	ND	ND	ND	ND
7113	F	M	3	00.9	8.0	1.97	ND	ND	ND	ND
7114	F	M	3	00.8	8.0	1.98	ND	ND	ND	ND
7115	F	M	3	00.9	8.0	1.99	ND	ND	ND	ND
7116	F	M	3	00.8	8.0	2.00	ND	ND	ND	ND

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7 - Sex: M = Male; F = Female; N = Not Specified; S = Stillborn; D = Deceased

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APPENDIX 4 contd. Individual Animal Clinical Analysis of Urine

Animal ID	Sex	Age	Weight at Phase Start	Score at Phase Start	UCL A	UCL B	UCL C	UCL D	UCL E	UCL F	UCL G	UCL H	UCL I	UCL J	UCL K	UCL L	UCL M	UCL N	UCL O	UCL P	UCL Q	UCL R	UCL S	UCL T	UCL U	UCL V	UCL W	UCL X	UCL Y	UCL Z	UCL AA	UCL AB	UCL AC	UCL AD	UCL AE	UCL AF	UCL AG	UCL AH	UCL AI	UCL AJ	UCL AK	UCL AL	UCL AM	UCL AN	UCL AO	UCL AP	UCL AQ	UCL AR	UCL AS	UCL AT	UCL AU	UCL AV	UCL AW	UCL AX	UCL AY	UCL AZ	UCL BA	UCL BB	UCL BC	UCL BD	UCL BE	UCL BF	UCL BG	UCL BH	UCL BI	UCL BJ	UCL BK	UCL BL	UCL BM	UCL BN	UCL BO	UCL BP	UCL BQ	UCL BR	UCL BS	UCL BT	UCL BU	UCL BV	UCL BW	UCL BX	UCL BY	UCL BZ	UCL CA	UCL CB	UCL CC	UCL CD	UCL CE	UCL CF	UCL CG	UCL CH	UCL CI	UCL CJ	UCL CK	UCL CL	UCL CM	UCL CN	UCL CO	UCL CP	UCL CQ	UCL CR	UCL CS	UCL CT	UCL CU	UCL CV	UCL CW	UCL CX	UCL CY	UCL CZ	UCL DA	UCL DB	UCL DC	UCL DD	UCL DE	UCL DF	UCL DG	UCL DH	UCL DI	UCL DJ	UCL DK	UCL DL	UCL DM	UCL DN	UCL DO	UCL DP	UCL DQ	UCL DR	UCL DS	UCL DT	UCL DU	UCL DV	UCL DW	UCL DX	UCL DY	UCL DZ	UCL EA	UCL EB	UCL EC	UCL ED	UCL EE	UCL EF	UCL EG	UCL EH	UCL EI	UCL EJ	UCL EK	UCL EL	UCL EM	UCL EN	UCL EO	UCL EP	UCL EQ	UCL ER	UCL ES	UCL ET	UCL EU	UCL EV	UCL EW	UCL EX	UCL EY	UCL EZ	UCL FA	UCL FB	UCL FC	UCL FD	UCL FE	UCL FF	UCL FG	UCL FH	UCL FI	UCL FJ	UCL FK	UCL FL	UCL FM	UCL FN	UCL FO	UCL FP	UCL FQ	UCL FR	UCL FS	UCL FT	UCL FU	UCL FV	UCL FW	UCL FX	UCL FY	UCL FZ	UCL GA	UCL GB	UCL GC	UCL GD	UCL GE	UCL GF	UCL GG	UCL GH	UCL GI	UCL GJ	UCL GK	UCL GL	UCL GM	UCL GN	UCL GO	UCL GP	UCL GQ	UCL GR	UCL GS	UCL GT	UCL GU	UCL GV	UCL GW	UCL GX	UCL GY	UCL GZ	UCL HA	UCL HB	UCL HC	UCL HD	UCL HE	UCL HF	UCL HG	UCL HH	UCL HI	UCL HJ	UCL HK	UCL HL	UCL HM	UCL HN	UCL HO	UCL HP	UCL HQ	UCL HR	UCL HS	UCL HT	UCL HU	UCL HV	UCL HW	UCL HX	UCL HY	UCL HZ	UCL IA	UCL IB	UCL IC	UCL ID	UCL IE	UCL IF	UCL IG	UCL IH	UCL II	UCL IJ	UCL IK	UCL IL	UCL IM	UCL IN	UCL IO	UCL IP	UCL IQ	UCL IR	UCL IS	UCL IT	UCL IU	UCL IV	UCL IW	UCL IX	UCL IY	UCL IZ	UCL JA	UCL JB	UCL JC	UCL JD	UCL JE	UCL JF	UCL JG	UCL JH	UCL JI	UCL JJ	UCL JK	UCL JL	UCL JM	UCL JN	UCL JO	UCL JP	UCL JQ	UCL JR	UCL JS	UCL JT	UCL JU	UCL JV	UCL JW	UCL JX	UCL JY	UCL JZ	UCL KA	UCL KB	UCL KC	UCL KD	UCL KE	UCL KF	UCL KG	UCL KH	UCL KI	UCL KJ	UCL KK	UCL KL	UCL KM	UCL KN	UCL KO	UCL KP	UCL KQ	UCL KR	UCL KS	UCL KT	UCL KU	UCL KV	UCL KW	UCL KX	UCL KY	UCL KZ	UCL LA	UCL LB	UCL LC	UCL LD	UCL LE	UCL LF	UCL LG	UCL LH	UCL LI	UCL LJ	UCL LK	UCL LL	UCL LM	UCL LN	UCL LO	UCL LP	UCL LQ	UCL LR	UCL LS	UCL LT	UCL LU	UCL LV	UCL LW	UCL LX	UCL LY	UCL LZ	UCL MA	UCL MB	UCL MC	UCL MD	UCL ME	UCL MF	UCL MG	UCL MH	UCL MI	UCL MJ	UCL MK	UCL ML	UCL MN	UCL MO	UCL MP	UCL MQ	UCL MR	UCL MS	UCL MT	UCL MU	UCL MV	UCL MW	UCL MX	UCL MY	UCL MZ	UCL NA	UCL NB	UCL NC	UCL ND	UCL NE	UCL NF	UCL NG	UCL NH	UCL NI	UCL NJ	UCL NK	UCL NL	UCL NM	UCL NO	UCL NP	UCL NQ	UCL NR	UCL NS	UCL NT	UCL NU	UCL NV	UCL NW	UCL NX	UCL NY	UCL NZ	UCL OA	UCL OB	UCL OC	UCL OD	UCL OE	UCL OF	UCL OG	UCL OH	UCL OI	UCL OJ	UCL OK	UCL OL	UCL OM	UCL ON	UCL OO	UCL OP	UCL OQ	UCL OR	UCL OS	UCL OT	UCL OU	UCL OV	UCL OW	UCL OX	UCL OY	UCL OZ	UCL PA	UCL PB	UCL PC	UCL PD	UCL PE	UCL PF	UCL PG	UCL PH	UCL PI	UCL PJ	UCL PK	UCL PL	UCL PM	UCL PN	UCL PO	UCL PP	UCL PQ	UCL PR	UCL PS	UCL PT	UCL PU	UCL PV	UCL PW	UCL PX	UCL PY	UCL PZ	UCL QA	UCL QB	UCL QC	UCL QD	UCL QE	UCL QF	UCL QG	UCL QH	UCL QI	UCL QJ	UCL QK	UCL QL	UCL QM	UCL QN	UCL QO	UCL QP	UCL QQ	UCL QR	UCL QS	UCL QT	UCL QU	UCL QV	UCL QW	UCL QX	UCL QY	UCL QZ	UCL RA	UCL RB	UCL RC	UCL RD	UCL RE	UCL RF	UCL RG	UCL RH	UCL RI	UCL RJ	UCL RK	UCL RL	UCL RM	UCL RN	UCL RO	UCL RP	UCL RQ	UCL RR	UCL RS	UCL RT	UCL RU	UCL RV	UCL RW	UCL RX	UCL RY	UCL RZ	UCL SA	UCL SB	UCL SC	UCL SD	UCL SE	UCL SF	UCL SG	UCL SH	UCL SI	UCL SJ	UCL SK	UCL SL	UCL SM	UCL SN	UCL SO	UCL SP	UCL SQ	UCL SR	UCL SS	UCL ST	UCL SU	UCL SV	UCL SW	UCL SX	UCL SY	UCL SZ	UCL TA	UCL TB	UCL TC	UCL TD	UCL TE	UCL TF	UCL TG	UCL TH	UCL TI	UCL TJ	UCL TK	UCL TL	UCL TM	UCL TN	UCL TO	UCL TP	UCL TQ	UCL TR	UCL TS	UCL TT	UCL TU	UCL TV	UCL TW	UCL TX	UCL TY	UCL TZ	UCL UA	UCL UB	UCL UC	UCL UD	UCL UE	UCL UF	UCL UG	UCL UH	UCL UI	UCL UJ	UCL UK	UCL UL	UCL UM	UCL UN	UCL UO	UCL UP	UCL UQ	UCL UR	UCL US	UCL UT	UCL UY	UCL UZ	UCL VA	UCL VB	UCL VC	UCL VD	UCL VE	UCL VF	UCL VG	UCL VH	UCL VI	UCL VJ	UCL VK	UCL VL	UCL VM	UCL VN	UCL VO	UCL VP	UCL VQ	UCL VR	UCL VS	UCL VT	UCL VU	UCL VV	UCL VW	UCL VX	UCL VY	UCL VZ	UCL WA	UCL WB	UCL WC	UCL WD	UCL WE	UCL WF	UCL WG	UCL WH	UCL WI	UCL WJ	UCL WK	UCL WL	UCL WM	UCL WN	UCL WO	UCL WP	UCL WQ	UCL WR	UCL WS	UCL WT	UCL WU	UCL WV	UCL WW	UCL WX	UCL WY	UCL WZ	UCL XA	UCL XB	UCL XC	UCL XD	UCL XE	UCL XF	UCL XG	UCL XH	UCL XI	UCL XJ	UCL XK	UCL XL	UCL XM	UCL XN	UCL XO	UCL XP	UCL XQ	UCL XR	UCL XS	UCL XT	UCL XU	UCL XV	UCL XW	UCL XX	UCL XY	UCL XZ	UCL YA	UCL YB	UCL YC	UCL YD	UCL YE	UCL YF	UCL YG	UCL YH	UCL YI	UCL YJ	UCL YK	UCL YL	UCL YM	UCL YN	UCL YO	UCL YP	UCL YQ	UCL YR	UCL YS	UCL YT	UCL YU	UCL YV	UCL YW	UCL YX	UCL YY	UCL YZ	UCL ZA	UCL ZB	UCL ZC	UCL ZD	UCL ZE	UCL ZF	UCL ZG	UCL ZH	UCL ZI	UCL ZJ	UCL ZK	UCL ZL	UCL ZM	UCL ZN	UCL ZO	UCL ZP	UCL ZQ	UCL ZR	UCL ZS	UCL ZT	UCL ZU	UCL ZV	UCL ZW	UCL ZX	UCL ZY	UCL ZZ
7018	U	1	1.0	33.5	5.1	UCL AB	0.0	UCL BC	0.0	UCL CD	0.0	UCL DE	0.0	UCL EF	0.0	UCL FG	0.0	UCL GH	0.0	UCL HI	0.0	UCL IJ	0.0	UCL JK	0.0	UCL LM	0.0	UCL NO	0.0	UCL OP	0.0	UCL PQ	0.0	UCL RS	0.0	UCL TU	0.0	UCL VW	0.0	UCL XY	0.0	UCL Z	0.0	UCL AA	0.0	UCL BB	0.0	UCL CC	0.0	UCL DD	0.0	UCL EE	0.0	UCL FF	0.0	UCL GG	0.0	UCL HH	0.0	UCL II	0.0	UCL JJ	0.0	UCL KK	0.0	UCL LL	0.0	UCL MM	0.0	UCL NN	0.0	UCL OO	0.0	UCL PP	0.0	UCL QQ	0.0	UCL RR	0.0	UCL SS	0.0	UCL TT	0.0	UCL UU	0.0	UCL VV	0.0	UCL WW	0.0	UCL XX	0.0	UCL YY	0.0	UCL ZZ	0.0	UCL AAA	0.0	UCL BBB	0.0	UCL CCC	0.0	UCL DDD	0.0	UCL EEE	0.0	UCL FFF	0.0	UCL GGG	0.0	UCL HHH	0.0	UCL III	0.0	UCL JJJ	0.0	UCL KKK	0.0	UCL LLL	0.0	UCL MMM	0.0	UCL NNN	0.0	UCL OOO	0.0	UCL PPP	0.0	UCL QQQ	0.0	UCL RRR	0.0	UCL SSS	0.0	UCL TTT	0.0	UCL UUU	0.0	UCL VVV	0.0	UCL WWW	0.0	UCL XXX	0.0	UCL YYY	0.0	UCL ZZZ	0.0	UCL AAAA	0.0	UCL BBBB	0.0	UCL CCCC	0.0	UCL DDDD	0.0	UCL EEEE	0.0	UCL FFFF	0.0	UCL GGGG	0.0	UCL HHHH	0.0	UCL IIII	0.0	UCL JJJJ	0.0	UCL KKKK	0.0	UCL LLLL	0.0	UCL MMMM	0.0	UCL NNNN	0.0	UCL OOOO	0.0	UCL PPPP	0.0	UCL QQQQ	0.0	UCL RRRR	0.0	UCL SSSS	0.0	UCL TTTT	0.0	UCL UUUU	0.0	UCL VVVV	0.0	UCL WWWW	0.0	UCL XXXX	0.0	UCL YYYY	0.0	UCL ZZZZ	0.0	UCL AAAAA	0.0	UCL BBBBB	0.0	UCL CCCCC	0.0	UCL DDDDD	0.0	UCL EEEEE	0.0	UCL FFFFF	0.0	UCL GGGGG	0.0	UCL HHHHH	0.0	UCL IIIII	0.0	UCL JJJJJ	0.0	UCL KKKKK	0.0	UCL LLLLL	0.0	UCL MMMMM	0.0	UCL NNNNN	0.0	UCL OOOOO	0.0	UCL PPPPP	0.0	UCL QQQQQ	0.0	UCL RRRRR	0.0	UCL SSSSS	0.0	UCL TTTTT	0.0	UCL UUUUU	0.0	UCL VVVVV	0.0	UCL WWWWV	0.0	UCL XXXXX	0.0	UCL YYYYV	0.0	UCL ZZZZV	0.0	UCL AAAAAA	0.0	UCL BBBBBB	0.0	UCL CCCCCC	0.0	UCL DDDDDD	0.0	UCL EEEEEV	0.0	UCL FFFFFV	0.0	UCL GGGGGV	0.0	UCL HHHHHV	0.0	UCL IIIIIV	0.0	UCL JJJJJV	0.0	UCL KKKKKV	0.0	UCL LLLLLV	0.0	UCL MMMMMV	0.0	UCL NNNNNV	0.0	UCL OOOOOV	0.0	UCL PPPPPV	0.0	UCL QQQQQV	0.0	UCL RRRRRV	0.0	UCL SSSSSV	0.0	UCL TTTTTV	0.0	UCL UUUUV	0.0	UCL VVVVVV	0.0	UCL WWWWV	0.0	UCL XXXXV	0.0	UCL YYYYV	0.0	UCL ZZZZV	0.0	UCL AAAAAA	0.0	UCL BBBBBB	0.0	UCL CCCCCC	0.0	UCL DDDDDD	0.0	UCL EEEEEV	0.0	UCL FFFFFV	0.0	UCL GGGGGV	0.0	UCL HHHHHV	0.0	UCL IIIIIV	0.0	UCL JJJJJV	0.0	UCL KKKKKV	0.0	UCL LLLLLV	0.0	UCL MMMMMV	0.0	UCL NNNNNV	0.0	UCL OOOOOV	0.0	UCL PPPPPV	0.0	UCL QQQQQV	0.0	UCL RRRRRV	0.0	UCL SSSSSV	0.0	UCL TTTTTV	0.0	UCL UUUUV	0.0	UCL VVVVVV	0.0	UCL WWWWV	0.0	UCL XXXXV	0.0	UCL YYYYV	0.0	UCL ZZZZV	0.0	UCL AAAAAA	0.0	UCL BBBBBB	0.0	UCL CCCCCC	0.0	UCL DDDDDD	0.0	UCL EEEEEV	0.0	UCL FFFFFV	0.0	UCL GGGGGV	0.0	UCL HHHHHV	0.0	UCL IIIIIV	0.0	UCL JJJJJV	0.0	UCL KKKKKV	0.0	UCL LLLLLV	0.0	UCL MMMMMV	0.0	UCL NNNNNV	0.0	UCL OOOOOV	0.0	UCL PPPPPV	0.0	UCL QQQQQV	0.0	UCL RRRRRV	0.0	UCL SSSSSV	0.0	UCL TTTTTV	0.0	UCL UUUUV	0.0	UCL VVVVVV	0.0	UCL WWWWV	0.0	UCL XXXXV	0.0	UCL YYYYV	0.0	UCL ZZZZV	0.0	UCL AAAAAA	0.0	UCL BBBBBB	0.0	UCL CCCCCC	0.0	UCL DDDDDD	0.0	UCL EEEEEV	0.0	UCL FFFFFV	0.0	UCL GGGGGV	0.0	UCL HHHHHV	0.0	UCL IIIIIV	0.0	UCL JJJJJV	0.0	UCL KKKKKV	0.0	UCL LLLLLV	0.0	UCL MMMMMV	0.0	UCL NNNNNV	0.0	UCL OOOOOV	0.0	UCL PPPPPV	0.0	UCL QQQQQV	0.0	UCL RRRRRV	0.0	UCL SSSSSV	0.0	UCL TTTTTV	0.0	UCL UUUUV	0.0	UCL VVVVVV	0.0	UCL WWWWV	0.0	UCL XXXXV	0.0	UCL YYYYV	0.0	UCL ZZZZV	0.0	UCL AAAAAA	0.0	UCL BBBBBB	0.0	UCL CCCCCC	0.0	UCL DDDDDD	0.0	UCL EEEEEV	0.0	UCL FFFFFV	0.0	UCL GGGGGV	0.0	UCL HHHHHV	0.0	UCL IIIIIV	0.0	UCL JJJJJV	0.0	UCL KKKKKV	0.0	UCL LLLLLV	0.0	UCL MMMMMV	0.0	UCL NNNNNV	0.0	UCL OOOOOV	0.0	UCL PPPPPV	0.0	UCL QQQQQV	0.0	UCL RRRRRV	0.0	UCL SSSSSV	0.0	UCL TTTTTV	0.0	UCL UUUUV	0.0	UCL VVVVVV	0.0	UCL WWWWV	0.0	UCL XXXXV	0.0	UCL YYYYV	0.0	UCL ZZZZV	0.0	UCL AAAAAA	0.0	UCL BBBBBB	0.0	UCL CCCCCC	0.0	UCL DDDDDD	0.0	UCL EEEEEV	0.0	UCL FFFFFV	0.0	UCL GGGGGV	0.0	UCL HHHHHV	0.0	UCL IIIIIV	0.0	UCL JJJJJV	0.0	UCL KKKKKV	0.0	UCL LLLLLV	0.0	UCL MMMMMV	0.0	UCL NNNNNV	0.0	UCL OOOOOV	0.0	UCL PPPPPV	0.0	UCL QQQQQV	0.0	UCL RRRRRV	0.0	UCL SSSSSV	0.0	UCL TTTTTV	0.0	UCL UUUUV	0.0	UCL VVVVVV	0.0	UCL WWWWV	0.0	UCL XXXXV	0.0	UCL YYYYV	0.0	UCL ZZZZV	0.0	UCL AAAAAA	0.0	UCL BBBBBB	0.0	UCL CCCCCC	0.0	UCL DDDDDD	0.0	UCL EEEEEV	0.0	UCL FFFFFV	0.0																																																																																																																													



APPENDIX 4 (cont'd). Individual Annual Clinical Analysis of Urine

Animal	Sex	Age	Day of Cycle	Sexual Stage	UCLAB	UCLAB mg/L	UCLAB	UCLAB mg/dl	UCLAB
7074	F	1	15	2	NS	0.5	MDM	NS	NS
7074	F	1	2	5	CLAB	10	MDM	15	NS
7074	F	1	3	8	CLAB	15	MDM	20	NS
7076	F	2	15	5	CLAB	15	MDM	30	NS
7076	F	2	16	1	CLAB	12	DARK	0	NS
7076	F	2	17	4	CLAB	10	LIGHT	0	NS
7076	F	2	18	7	CLAB	25	DARK	0	NS
7080	F	2	11	10	CLAB	100	LIGHT	0	NS

UCLAB = Urinary Chloride Analysis

NS = Not Scheduled, Scheduled, Animal Deceased, Scheduled to Euthanize, or On Schedule to Euthanize

PG: Study 51651
Eurofins Advinus Study (Pilot Study) (Pilot) - Initial Pathology Report
Copy No. 1

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11. ANNEXURES



ANNEXURE 1: GLP Certificate

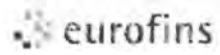
The summary of GLP accreditations received by the test facility from multiple Monitoring Authorities and the latest GLP certificate issued by the Indian National GLP Compliance Monitoring Authority are given below:

(i) Summary of Accreditations Received by the Test Facility from Multiple GLP Monitoring Authorities

GLP Monitoring Authority	Accreditation received in the year
Germany	1992, 1997, 2001, 2005 and 2010
Netherlands	1999, 2003, 2007 and 2009
India	2005, 2008, 2012, 2014 and 2017

Note:

1. The test facility was inspected/monitored as per the OECD GLP system by the respective Monitoring Authorities stated above, and maintained the accreditations continuously.
2. India accepted the OECD Council invitation and received the Full Adherence status for Mutual Acceptance of Data (MAD) in March 2011, and also became a member of the OECD GLP Working Group. As per the OECD provisions, the Monitoring Authorities in OECD member countries as well as those in Full Adherent countries would inspect test facilities in the respective countries for the purpose of monitoring and accreditation. Accordingly, since 2011, the test facility was inspected only by the Indian National GLP Compliance Monitoring Authority (NGC/MA) for monitoring and accreditation.



ANNEXURE 1 contd. GLP Certificate

(i) GLP Certificate India



ANNEXURE I contd. GLP Certificate





30/03/2017

ANNEXURE 1 contd. GLP Certificate

National GLP Compliance Monitoring Authority (NGCMA)

Annexure to Certificate of GLP Compliance No. GLP/C-111/2017

Areas of Expertise:

Physical/chemical testing including Phys. Chem. Analysis

Toxicity Studies

- Acute Toxicity
- Skin Irritation/Corrosion
- Eye Irritation
- Skin Sensitization
- Dermal Toxicity
- Inhalation Toxicity
- Sub-acute/ Sub-chronic Toxicity
- Chronic Toxicity
- Reproductive Toxicity
- Carcinogenicity Studies

Microbiology Studies

- Microbial Alteration Test (MART) Test
- Microbial Assay (MART) Test
- Sterility Test (MART) Test
- Spore Mutation Test (MART)

Environmental Toxicity Studies in Aquatic & Terrestrial Organisms

Studies on Biodegradability in Water, Soil, and Air Environment

- Biodegradability Study
- Environmental Fate Studies

Residue Studies

Analytical and Clinical Chemistry Testing

Others

- Biokinetic and Toxicokinetics
- Drug Metabolism and Pharmacokinetics & Tissue Distribution
- Safety Pharmacology
- PK and Immunogenicity Studies/ Studies

Types of Chemicals:

Industrial Chemicals, Pharmaceuticals, Veterinary Drugs, Pesticides, Cosmetics Products, Food Additives, Food Additives, CMOs, Solvents, Dyes/Pigments, Disinfectants, Packaging Materials, Nutritional Supplements and Medical Devices

Test Systems:

Yr. Mice, Rabbit, Guinea Pig, Dog, Goat, Chicken, Duck, Piglet, Hamster, Fresh Water Fish, Daphnia, Algae, Honeybee, Earthworm, *Ischiodora palustris*, *E. coli*, *Staph. aureus*, *Mycobacterium*, Cell line: Chinese hamster Ovary, ISH21 Cell Line, HEK 293 and Human Hepatoblastoma Liver cells Cell Line

000-40001-0000



[Redacted Signature]
Dr. Nandaj Sainmal
Head, NGCMA

APPENDIX K: ANIMAL NUMBERS, DOSE GROUPS, AND FATES

PRODUCT IDENTIFICATION

Silk Fibroin

Individual Animal Numbers, Dose Groups and Fates
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Group	Dose Level	Sex	Animal	Cage	Removal Day	Removal Week	Removal Date	Removal Time	Time Slot	Removal Symptom	Pathology Reason
1	0 mg/kg/day	Male	7001	1	30	5	05/12/19	8:25	-	Term	Term
			7002	1	30	5	05/12/19	8:25	-	Term	Term
			7003	2	30	5	05/12/19	8:25	-	Term	Term
			7004	2	30	5	05/12/19	8:25	-	Term	Term
			7005	3	30	5	05/12/19	8:25	-	Term	Term
			7006	3	30	5	05/12/19	8:25	-	Term	Term
			7007	4	30	5	05/12/19	8:25	-	Term	Term
			7008	4	30	5	05/12/19	8:25	-	Term	Term
			7009	5	30	5	05/12/19	8:25	-	Term	Term
			7010	5	30	5	05/12/19	8:25	-	Term	Term
1	0 mg/kg/day	Female	7011	6	31	5	06/12/19	8:02	-	Term	Term
			7012	6	31	5	06/12/19	8:02	-	Term	Term
			7013	7	31	5	06/12/19	8:02	-	Term	Term
			7014	7	31	5	06/12/19	8:02	-	Term	Term
			7015	8	31	5	06/12/19	8:02	-	Term	Term
			7016	8	31	5	06/12/19	8:03	-	Term	Term
			7017	9	31	5	06/12/19	8:03	-	Term	Term
			7018	9	31	5	06/12/19	8:03	-	Term	Term
			7019	10	31	5	06/12/19	8:03	-	Term	Term
			7020	10	31	5	06/12/19	8:03	-	Term	Term
2	125 mg/kg/day	Male	7021	11	30	5	05/12/19	8:26	-	Term	Term
			7022	11	30	5	05/12/19	8:26	-	Term	Term
			7023	12	30	5	05/12/19	8:26	-	Term	Term
			7024	12	30	5	05/12/19	8:26	-	Term	Term
			7025	13	30	5	05/12/19	8:26	-	Term	Term
			7026	13	30	5	05/12/19	8:26	-	Term	Term
			7027	14	30	5	05/12/19	8:26	-	Term	Term
			7028	14	30	5	05/12/19	8:26	-	Term	Term
			7029	15	30	5	05/12/19	8:26	-	Term	Term
			7030	15	30	5	05/12/19	8:26	-	Term	Term

Individual Animal Numbers, Dose Groups and Fates
PSL Study Number 51651 A 28-Day Oral Gavage Toxicity Study in Rats

Group	Dose Level	Sex	Animal	Cage	Removal Day	Removal Week	Removal Date	Removal Time	Time Slot	Removal Symptom	Pathology Reason
2	125 mg/kg/day	Female	7031	16	31	5	06/12/19	8:03	.	Term	Term
			7032	16	31	5	06/12/19	8:03	.	Term	Term
			7033	17	31	5	06/12/19	8:03	.	Term	Term
			7034	17	31	5	06/12/19	8:03	.	Term	Term
			7035	18	31	5	06/12/19	8:03	.	Term	Term
			7036	18	31	5	06/12/19	8:03	.	Term	Term
			7037	19	31	5	06/12/19	8:03	.	Term	Term
			7038	19	31	5	06/12/19	8:03	.	Term	Term
			7039	20	31	5	06/12/19	8:03	.	Term	Term
			7040	20	31	5	06/12/19	8:03	.	Term	Term
3	250 mg/kg/day	Male	7041	21	30	5	05/12/19	8:26	.	Term	Term
			7042	21	30	5	05/12/19	8:26	.	Term	Term
			7043	22	30	5	05/12/19	8:26	.	Term	Term
			7044	22	30	5	05/12/19	8:26	.	Term	Term
			7045	23	30	5	05/12/19	8:26	.	Term	Term
			7046	23	30	5	05/12/19	8:26	.	Term	Term
			7047	24	30	5	05/12/19	8:26	.	Term	Term
			7048	24	30	5	05/12/19	8:27	.	Term	Term
			7049	25	30	5	05/12/19	8:27	.	Term	Term
			7050	25	30	5	05/12/19	8:27	.	Term	Term
3	250 mg/kg/day	Female	7051	26	31	5	06/12/19	8:04	.	Term	Term
			7052	26	31	5	06/12/19	8:04	.	Term	Term
			7053	27	31	5	06/12/19	8:04	.	Term	Term
			7054	27	31	5	06/12/19	8:04	.	Term	Term
			7055	28	31	5	06/12/19	8:04	.	Term	Term
			7056	28	31	5	06/12/19	8:04	.	Term	Term
			7057	29	31	5	06/12/19	8:04	.	Term	Term
			7058	29	31	5	06/12/19	8:04	.	Term	Term
			7059	30	31	5	06/12/19	8:04	.	Term	Term
			7060	30	31	5	06/12/19	8:04	.	Term	Term

Individual Animal Numbers, Dose Groups and Fates
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Group	Dose Level	Sex	Animal	Cage	Removal Day	Removal Week	Removal Date	Removal Time	Time Slot	Removal Symptom	Pathology Reason
4	500 mg/kg/day	Male	7061	31	30	5	05/12/19	8:27	.	Term	Term
			7062	31	30	5	05/12/19	8:27	.	Term	Term
			7063	32	30	5	05/12/19	8:27	.	Term	Term
			7064	32	30	5	05/12/19	8:27	.	Term	Term
			7065	33	30	5	05/12/19	8:27	.	Term	Term
			7066	33	30	5	05/12/19	8:27	.	Term	Term
			7067	34	30	5	05/12/19	8:27	.	Term	Term
			7068	34	30	5	05/12/19	8:27	.	Term	Term
			7069	35	30	5	05/12/19	8:27	.	Term	Term
			7070	35	30	5	05/12/19	8:27	.	Term	Term
4	500 mg/kg/day	Female	7071	36	31	5	06/12/19	8:04	.	Term	Term
			7072	36	31	5	06/12/19	8:04	.	Term	Term
			7073	37	31	5	06/12/19	8:04	.	Term	Term
			7074	37	31	5	06/12/19	8:04	.	Term	Term
			7075	38	31	5	06/12/19	8:04	.	Term	Term
			7076	38	31	5	06/12/19	8:04	.	Term	Term
			7077	39	31	5	06/12/19	8:04	.	Term	Term
			7078	39	31	5	06/12/19	8:04	.	Term	Term
			7079	40	31	5	06/12/19	8:04	.	Term	Term
			7080	40	31	5	06/12/19	8:04	.	Term	Term

APPENDIX L: INDIVIDUAL ANIMAL NECROPSY OBSERVATIONS

PRODUCT IDENTIFICATION

Silk Fibroin

Individual Animal Necropsy Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Animal:	7001	Group:	1	Sex:	Male
		Dose:	0		
Necropsy Date: 12/5/2019					
Gross Pathology Observations [Correlation]:					
No observations found					
Any remaining protocol required tissues, which have been examined, have no visible lesions					
Animal:	7002	Group:	1	Sex:	Male
		Dose:	0		
Necropsy Date: 12/5/2019					
Gross Pathology Observations [Correlation]:					
No observations found					
Any remaining protocol required tissues, which have been examined, have no visible lesions					
Animal:	7003	Group:	1	Sex:	Male
		Dose:	0		
Necropsy Date: 12/5/2019					
Gross Pathology Observations [Correlation]:					
No observations found					
Any remaining protocol required tissues, which have been examined, have no visible lesions					
Animal:	7004	Group:	1	Sex:	Male
		Dose:	0		
Necropsy Date: 12/5/2019					
Gross Pathology Observations [Correlation]:					
No observations found					
Any remaining protocol required tissues, which have been examined, have no visible lesions					
Animal:	7005	Group:	1	Sex:	Male
		Dose:	0		
Necropsy Date: 12/5/2019					
Gross Pathology Observations [Correlation]:					
No observations found					
Any remaining protocol required tissues, which have been examined, have no visible lesions					
Animal:	7006	Group:	1	Sex:	Male
		Dose:	0		
Necropsy Date: 12/5/2019					
Gross Pathology Observations [Correlation]:					
No observations found					
Any remaining protocol required tissues, which have been examined, have no visible lesions					
Animal:	7007	Group:	1	Sex:	Male

Individual Animal Necropsy Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Dose: 0		
Necropsy Date: 12/5/2019		
Gross Pathology Observations [Correlation]:		
No observations found		
Any remaining protocol required tissues, which have been examined, have no visible lesions		
Animal: 7008	Group: 1	Sex: Male
Dose: 0		
Necropsy Date: 12/5/2019		
Gross Pathology Observations [Correlation]:		
No observations found		
Any remaining protocol required tissues, which have been examined, have no visible lesions		
Animal: 7009	Group: 1	Sex: Male
Dose: 0		
Necropsy Date: 12/5/2019		
Gross Pathology Observations [Correlation]:		
testes-combined : right: fixed		
epididymides-combined : right: small		
Any remaining protocol required tissues, which have been examined, have no visible lesions		
Animal: 7010	Group: 1	Sex: Male
Dose: 0		
Necropsy Date: 12/5/2019		
Gross Pathology Observations [Correlation]:		
No observations found		
Any remaining protocol required tissues, which have been examined, have no visible lesions		
Animal: 7011	Group: 1	Sex: Female
Dose: 0		
Necropsy Date: 12/6/2019		
Gross Pathology Observations [Correlation]:		
No observations found		
Any remaining protocol required tissues, which have been examined, have no visible lesions		
Animal: 7012	Group: 1	Sex: Female
Dose: 0		
Necropsy Date: 12/6/2019		
Gross Pathology Observations [Correlation]:		
No observations found		
Any remaining protocol required tissues, which have been examined, have no visible lesions		
Animal: 7013	Group: 1	Sex: Female

Individual Animal Necropsy Observations			
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats			
Necropsy Date: 12/6/2019		Dose: 0	
Gross Pathology Observations [Correlation]:			
uterus: fluid filled			
Any remaining protocol required tissues, which have been examined, have no visible lesions			
Animal: 7014	Group: 1	Sex: Female	Dose: 0
Necropsy Date: 12/6/2019			
Gross Pathology Observations [Correlation]:			
uterus: fluid filled			
Any remaining protocol required tissues, which have been examined, have no visible lesions			
Animal: 7015	Group: 1	Sex: Female	Dose: 0
Necropsy Date: 12/6/2019			
Gross Pathology Observations [Correlation]:			
No observations found			
Any remaining protocol required tissues, which have been examined, have no visible lesions			
Animal: 7016	Group: 1	Sex: Female	Dose: 0
Necropsy Date: 12/6/2019			
Gross Pathology Observations [Correlation]:			
No observations found			
Any remaining protocol required tissues, which have been examined, have no visible lesions			
Animal: 7017	Group: 1	Sex: Female	Dose: 0
Necropsy Date: 12/6/2019			
Gross Pathology Observations [Correlation]:			
No observations found			
Any remaining protocol required tissues, which have been examined, have no visible lesions			
Animal: 7018	Group: 1	Sex: Female	Dose: 0
Necropsy Date: 12/6/2019			
Gross Pathology Observations [Correlation]:			
uterus: fluid filled			
Any remaining protocol required tissues, which have been examined, have no visible lesions			
Animal: 7019	Group: 1	Sex: Female	Dose: 0

Individual Animal Necropsy Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Necropsy Date: 12/6/2019		
Gross Pathology Observations [Correlation]:		
uterus: fluid filled		
Any remaining protocol required tissues, which have been examined, have no visible lesions		
Animal: 7020	Group: 1 Dose: 0	Sex: Female
Necropsy Date: 12/6/2019		
Gross Pathology Observations [Correlation]:		
No observations found		
Any remaining protocol required tissues, which have been examined, have no visible lesions		
Animal: 7021	Group: 2 Dose: 125	Sex: Male
Necropsy Date: 12/5/2019		
Gross Pathology Observations [Correlation]:		
No observations found		
Any remaining protocol required tissues, which have been examined, have no visible lesions		
Animal: 7022	Group: 2 Dose: 125	Sex: Male
Necropsy Date: 12/5/2019		
Gross Pathology Observations [Correlation]:		
No observations found		
Any remaining protocol required tissues, which have been examined, have no visible lesions		
Animal: 7023	Group: 2 Dose: 125	Sex: Male
Necropsy Date: 12/5/2019		
Gross Pathology Observations [Correlation]:		
No observations found		
Any remaining protocol required tissues, which have been examined, have no visible lesions		
Animal: 7024	Group: 2 Dose: 125	Sex: Male
Necropsy Date: 12/5/2019		
Gross Pathology Observations [Correlation]:		
No observations found		
Any remaining protocol required tissues, which have been examined, have no visible lesions		
Animal: 7025	Group: 2 Dose: 125	Sex: Male
Necropsy Date: 12/5/2019		

Individual Animal Necropsy Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7025	Group:	2	Sex:	Male
		Dose:	125		

Necropsy Date: 12/5/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7027	Group:	2	Sex:	Male
		Dose:	125		

Necropsy Date: 12/5/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7028	Group:	2	Sex:	Male
		Dose:	125		

Necropsy Date: 12/5/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7029	Group:	2	Sex:	Male
		Dose:	125		

Necropsy Date: 12/5/2019

Gross Pathology Observations [Correlation]:

testes-combined : right; small

testes-combined : flatcid

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7030	Group:	2	Sex:	Male
		Dose:	125		

Necropsy Date: 12/5/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7031	Group:	2	Sex:	Female
		Dose:	125		

Necropsy Date: 12/6/2019

Individual Animal Necropsy Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats**Gross Pathology Observations [Correlation]:**

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7032	Group:	2	Sex:	Female
		Dose:	125		

Necropsy Date: 12/6/2019

Gross Pathology Observations [Correlation]:

uterus : fluid filled

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7033	Group:	2	Sex:	Female
		Dose:	125		

Necropsy Date: 12/5/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7034	Group:	2	Sex:	Female
		Dose:	125		

Necropsy Date: 12/6/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7035	Group:	2	Sex:	Female
		Dose:	125		

Necropsy Date: 12/6/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7036	Group:	2	Sex:	Female
		Dose:	125		

Necropsy Date: 12/6/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7037	Group:	2	Sex:	Female
		Dose:	125		

Necropsy Date: 12/6/2019

Individual Animal Necropsy Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7038	Group:	2	Sex:	Female
		Dose:	125		

Necropsy Date: 12/6/2019

Gross Pathology Observations [Correlation]:

uterus: fluid filled

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7039	Group:	2	Sex:	Female
		Dose:	125		

Necropsy Date: 12/6/2019

Gross Pathology Observations [Correlation]:

uterus: fluid filled

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7040	Group:	2	Sex:	Female
		Dose:	125		

Necropsy Date: 12/6/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7041	Group:	3	Sex:	Male
		Dose:	250		

Necropsy Date: 12/5/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7042	Group:	3	Sex:	Male
		Dose:	250		

Necropsy Date: 12/5/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7043	Group:	3	Sex:	Male
		Dose:	250		

Necropsy Date: 12/5/2019

Individual Animal Necropsy Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal: 7044	Group: 3	Sex: Male
	Dose: 250	

Necropsy Date: 12/5/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal: 7045	Group: 3	Sex: Male
	Dose: 250	

Necropsy Date: 12/5/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal: 7046	Group: 3	Sex: Male
	Dose: 250	

Necropsy Date: 12/5/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal: 7047	Group: 3	Sex: Male
	Dose: 250	

Necropsy Date: 12/5/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal: 7048	Group: 3	Sex: Male
	Dose: 250	

Necropsy Date: 12/5/2019

Last Clinical Observations:

Eschar, Head, Superficial

Gross Pathology Observations [Correlation]:

non correlated finding; no correlated finding [Eschar, Head, Superficial (C)]

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal: 7049	Group: 3	Sex: Male
	Dose: 250	

Individual Animal Necropsy Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Necropsy Date: 12/5/2019		
Gross Pathology Observations [Correlation]:		
No observations found		
Any remaining protocol required tissues, which have been examined, have no visible lesions		
Animal: 7050	Group: 3 Dose: 250	Sex: Male
Necropsy Date: 12/5/2019		
Gross Pathology Observations [Correlation]:		
No observations found		
Any remaining protocol required tissues, which have been examined, have no visible lesions		
Animal: 7051	Group: 3 Dose: 250	Sex: Female
Necropsy Date: 12/6/2019		
Gross Pathology Observations [Correlation]:		
No observations found		
Any remaining protocol required tissues, which have been examined, have no visible lesions		
Animal: 7052	Group: 3 Dose: 250	Sex: Female
Necropsy Date: 12/6/2019		
Gross Pathology Observations [Correlation]:		
Uterus: fluid filled		
Any remaining protocol required tissues, which have been examined, have no visible lesions		
Animal: 7053	Group: 3 Dose: 250	Sex: Female
Necropsy Date: 12/6/2019		
Gross Pathology Observations [Correlation]:		
uterus: fluid filled		
Any remaining protocol required tissues, which have been examined, have no visible lesions		
Animal: 7054	Group: 3 Dose: 250	Sex: Female
Necropsy Date: 12/6/2019		
Gross Pathology Observations [Correlation]:		
No observations found		
Any remaining protocol required tissues, which have been examined, have no visible lesions		
Animal: 7055	Group: 3 Dose: 250	Sex: Female
Necropsy Date: 12/6/2019		

Individual Animal Necropsy Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7056	Group:	3	Sex:	Female
		Dose:	250		

Necropsy Date: 12/6/2019

Gross Pathology Observations [Correlation]:

uterus: fluid filled

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7057	Group:	3	Sex:	Female
		Dose:	250		

Necropsy Date: 12/6/2019

Gross Pathology Observations [Correlation]:

uterus: fluid filled

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7058	Group:	3	Sex:	Female
		Dose:	250		

Necropsy Date: 12/6/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7059	Group:	3	Sex:	Female
		Dose:	250		

Necropsy Date: 12/6/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7060	Group:	3	Sex:	Female
		Dose:	250		

Necropsy Date: 12/6/2019

Gross Pathology Observations [Correlation]:

uterus: fluid filled

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7061	Group:	4	Sex:	Male
		Dose:	500		

Necropsy Date: 12/5/2019

Individual Animal Necropsy Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal: 7062	Group: 4	Sex: Male
	Dose: 500	

Necropsy Date: 12/5/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal: 7063	Group: 4	Sex: Male
	Dose: 500	

Necropsy Date: 12/5/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal: 7064	Group: 4	Sex: Male
	Dose: 500	

Necropsy Date: 12/5/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal: 7065	Group: 4	Sex: Male
	Dose: 500	

Necropsy Date: 12/5/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal: 7066	Group: 4	Sex: Male
	Dose: 500	

Necropsy Date: 12/5/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal: 7067	Group: 4	Sex: Male
	Dose: 500	

Necropsy Date: 12/5/2019

Individual Animal Necropsy Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7068	Group:	4	Sex:	Male
		Dose:	500		

Necropsy Date: 12/5/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7069	Group:	4	Sex:	Male
		Dose:	500		

Necropsy Date: 12/5/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7070	Group:	4	Sex:	Male
		Dose:	500		

Necropsy Date: 12/5/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7071	Group:	4	Sex:	Female
		Dose:	500		

Necropsy Date: 12/6/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7072	Group:	4	Sex:	Female
		Dose:	500		

Necropsy Date: 12/6/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7073	Group:	4	Sex:	Female
		Dose:	500		

Necropsy Date: 12/6/2019

Individual Animal Necropsy Observations
PSL Study Number 51651 - A 28 Day Oral Gavage Toxicity Study in Rats

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7074	Group:	4	Sex:	Female
		Dose:	500		

Necropsy Date: 12/6/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7075	Group:	4	Sex:	Female
		Dose:	500		

Necropsy Date: 12/6/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7076	Group:	4	Sex:	Female
		Dose:	500		

Necropsy Date: 12/6/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7077	Group:	4	Sex:	Female
		Dose:	500		

Necropsy Date: 12/6/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7078	Group:	4	Sex:	Female
		Dose:	500		

Necropsy Date: 12/6/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal:	7079	Group:	4	Sex:	Female
		Dose:	500		

Necropsy Date: 12/6/2019

Individual Animal Necropsy Observations
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Gross Pathology Observations [Correlation]:

uterus: fluid filled

Any remaining protocol required tissues, which have been examined, have no visible lesions

Animal: 7080	Group: 4	Sex: Female
	Dose: 500	

Necropsy Date: 12/6/2019

Gross Pathology Observations [Correlation]:

No observations found

Any remaining protocol required tissues, which have been examined, have no visible lesions

APPENDIX M: INDIVIDUAL ANIMAL TERMINAL BODY AND ORGAN WEIGHTS

PRODUCT IDENTIFICATION

Silk Fibroin

Individual Animal Terminal Body and Organ Weights
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

0 mg/kg/day Group 1	Terminal BW (g)	Adrenal Glands Wt (g)	Brain Wt (g)	Heart Wt (g)	Kidneys Wt (g)	Liver Wt (g)	Spleen Wt (g)
	Day 31	Day 31	Day 31	Day 31	Day 31	Day 31	Day 31
	7011	233	0.079	1.96	0.86	1.86	7.35
7012	261	0.081	1.96	0.91	1.96	8.27	0.64
7013	228	0.086	2.11	0.96	2.12	7.68	0.61
7014	274	0.089	2.11	1.02	1.97	9.27	0.73
7015	266	0.084	2.02	0.96	1.89	8.79	0.55
7016	275	0.075	2.22	0.97	2.09	10.10	0.64
7017	246	0.092	1.94	0.91	1.98	8.33	0.60
7018	232	0.083	1.84	0.87	1.66	7.77	0.48
7019	253	0.067	1.81	0.91	1.98	8.96	0.50
7020	247	0.077	2.08	0.98	1.85	7.38	0.49
Mean	251.5	0.0813	2.006	0.935	1.936	8.390	0.577
SD	17.3	0.0073	0.128	0.061	0.131	0.894	0.080
N	10	10	10	10	10	10	10

Individual Animal Terminal Body and Organ Weights
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

0 mg/kg/day Group 1	Thymus Yt (g)	Thyroid-Parathyroid Yt (g)
	Day 31	Day 31
7011	0.448	0.019
7012	0.389	0.018
7013	0.520	0.026
7014	0.477	0.032
7015	0.446	0.022
7016	0.399	0.030
7017	0.382	0.015
7018	0.408	0.017
7019	0.443	0.025
7020	0.633	0.022
Mean	0.4545	0.0226
SD	0.0758	0.0056
N	10	10

Individual Animal Terminal Body and Organ Weights
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female		Day(s) Relative to Start Date					
125 mg/kg/day Group 2	Terminal BW (g)	Adrenal Glands Wt (g)	Brain Wt (g)	Heart Wt (g)	Kidneys Wt (g)	Liver Wt (g)	Spleen Wt (g)
	Day 31	Day 31	Day 31	Day 31	Day 31	Day 31	Day 31
	7031	201	0.067	1.88	0.80	1.55	6.80
7032	284	0.088	1.96	1.01	2.26	9.27	0.68
7033	244	0.078	2.26	0.93	1.82	8.59	0.44
7034	262	0.086	2.02	0.99	2.19	9.55	0.55
7035	250	0.102	2.17	0.87	1.78	9.21	0.62
7036	220	0.078	2.01	0.79	1.42	6.62	0.56
7037	238	0.067	1.98	0.89	1.83	7.18	0.57
7038	262	0.091	2.02	1.06	1.94	10.39	0.71
7039	291	0.078	1.90	1.28	2.10	9.67	0.69
7040	225	0.074	2.00	0.79	1.58	6.64	0.56
Mean	247.7	0.0829	2.020	0.941	1.847	8.382	0.582
SD	26.2	0.0099	0.115	0.153	0.281	1.430	0.095
N	10	10	10	10	10	10	10

Individual Animal Terminal Body and Organ Weights
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

125 mg/kg/day Group 2	Sex: Female Day(s) Relative to Start Date	
	Thymus Wt (g)	Thyroid-Parathyroid Wt (g)
	Day 31	Day 31
7031	0.295	0.032
7032	0.500	0.021
7033	0.461	0.028
7034	0.359	0.023
7035	0.329	0.025
7036	0.352	0.018
7037	0.403	0.023
7038	0.503	0.037
7039	0.325	0.026
7040	0.318	0.024
Mean	0.3845	0.0257
SD	0.0777	0.0055
N	10	10

Individual Animal Terminal Body and Organ Weights
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

250 mg/kg/day Group 3	Terminal BW (g)	Adrenal Glands Wt (g)	Brain Wt (g)	Heart Wt (g)	Kidneys Wt (g)	Liver Wt (g)	Spleen Wt (g)
	Day 31	Day 31	Day 31	Day 31	Day 31	Day 31	Day 31
	7051	259	0.093	1.98	0.92	1.95	8.32
7052	269	0.084	2.10	1.06	2.02	9.19	0.55
7053	260	0.091	2.04	0.97	2.00	8.79	0.60
7054	270	0.098	2.05	0.86	1.87	9.52	0.62
7055	250	0.080	2.02	1.00	1.88	9.78	0.56
7056	218	0.089	2.02	0.87	1.84	8.44	0.46
7057	251	0.069	2.01	0.93	2.03	8.50	0.52
7058	239	0.085	2.08	0.85	1.86	7.85	0.47
7059	252	0.084	2.09	0.99	1.88	8.99	0.51
7060	230	0.075	1.95	0.79	1.87	7.31	0.51
Mean	253.8	0.0808	2.035	0.924	1.920	8.669	0.529
SD	21.9	0.0078	0.046	0.082	0.073	0.750	0.053
N	10	10	10	10	10	10	10

Individual Animal Terminal Body and Organ Weights
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

250 mg/kg/day Group 3	Thymus Wt (g)	Thyroid-Panathyroid Wt (g)
	Day 31	Day 31
	7051	0.483
7052	0.421	0.022
7053	0.466	0.027
7054	0.425	0.024
7055	0.389	0.026
7056	0.475	0.030
7057	0.453	0.022
7058	0.396	0.023
7059	0.522	0.024
7060	0.302	0.022
Mean	0.4432	0.0243
SD	0.0824	0.0026
N	10	10

Individual Animal Terminal Body and Organ Weights
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

500 mg/kg/day Group 4	Terminal BW (g)	Adrenal Glands Wt (g)	Brain Wt (g)	Heart Wt (g)	Kidneys Wt (g)	Liver Wt (g)	Spleen Wt (g)
	Day 31	Day 31	Day 31	Day 31	Day 31	Day 31	Day 31
	7071	257	0.078	1.94	1.02	2.14	9.71
7072	276	0.077	2.29	1.05	1.98	9.57	0.67
7073	229	0.071	2.06	0.81	1.93	7.73	0.60
7074	232	0.078	1.93	0.90	1.67	7.49	0.50
7075	260	0.101	2.13	0.93	1.98	9.07	0.60
7076	256	0.088	1.97	0.92	1.82	8.52	0.72
7077	244	0.088	2.21	0.91	2.19	8.76	0.61
7078	242	0.085	2.07	0.85	1.67	9.12	0.54
7079	287	0.080	2.12	0.94	2.22	9.51	0.58
7080	240	0.065	2.03	0.84	1.67	5.98	0.51
Mean	253.3	0.0811	2.075	0.917	1.927	8.546	0.592
SD	19.2	0.0100	0.116	0.075	0.215	1.171	0.067
N	10	10	10	10	10	10	10

Individual Animal Terminal Body and Organ Weights
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

500 mg/kg/day Group 4	Thymus Wt (g)	Thyroid-Parathyroid Wt (g)
	Day 31	Day 31
	7071	0.378
7072	0.595	0.027
7073	0.461	0.026
7074	0.390	0.025
7075	0.549	0.025
7076	0.373	0.020
7077	0.451	0.030
7078	0.397	0.028
7079	0.431	0.034
7080	0.411	0.023
Mean	0.4426	0.0264
SD	0.0754	0.0038
N	10	10

APPENDIX N: INDIVIDUAL ANIMAL ORGAN-TO-BODY WEIGHT RATIOS

PRODUCT IDENTIFICATION

Silk Fibroin

Individual Animal Organ-To-Body Weight Ratio
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female		Day(s) Relative to Start Date					
0 mg/kg/day Group 1	Adrenal /TBW (Ratio)	Brain /TBW (Ratio)	Heart /TBW (Ratio)	Kidneys /TBW (Ratio)	Liver /TBW (Ratio)	Spleen /TBW (Ratio)	Thymus /TBW (Ratio)
	Day 31	Day 31	Day 31	Day 31	Day 31	Day 31	Day 31
7011	0.339	8.41	3.68	7.98	31.55	2.23	1.923
7012	0.310	7.51	3.48	7.51	31.69	2.46	1.490
7013	0.377	9.25	4.21	9.30	33.68	2.68	2.281
7014	0.325	7.70	3.72	7.19	33.83	2.66	1.741
7015	0.316	7.59	3.61	7.11	33.05	2.07	1.677
7016	0.273	8.07	3.53	7.60	36.73	2.33	1.451
7017	0.374	7.89	3.70	8.05	33.86	2.44	1.553
7018	0.358	7.93	3.75	7.16	33.49	2.11	1.759
7019	0.265	7.15	3.60	7.83	35.42	1.98	1.751
7020	0.312	8.42	3.97	7.49	29.88	1.98	2.563
Mean	0.3248	7.994	3.726	7.721	33.317	2.293	1.8188
SD	0.03893	0.592	0.217	0.647	1.957	0.261	0.3537
N	10	10	10	10	10	10	10

Individual Animal Organ-To-Body Weight Ratio
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female	Day(s) Relative to Start Date
0 mg/kg/day Group 1	Thyroid-Parathyroid /TBW (Ratio)
	Day 31
7011	0.8155
7012	0.6897
7013	1.1404
7014	1.1679
7015	0.8271
7016	1.0609
7017	0.6098
7018	0.7328
7019	0.9881
7020	0.6907
Mean	0.85527
SD	0.19509
N	10

Individual Animal Organ-To-Body Weight Ratio
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female		Day(s) Relative to Start Date						
125 mg/kg/day Group 2	Adrenal /TBW (Ratio)	Brain /TBW (Ratio)	Heart /TBW (Ratio)	Kidneys /TBW (Ratio)	Liver /TBW (Ratio)	Spleen /TBW (Ratio)	Thymus /TBW (Ratio)	
	Day 31	Day 31	Day 31	Day 31	Day 31	Day 31	Day 31	
7031	0.333	9.35	3.98	7.71	33.63	2.19	1.468	
7032	0.310	6.90	3.56	7.96	32.64	2.39	1.761	
7033	0.320	9.26	3.81	7.46	35.20	1.80	1.899	
7034	0.328	7.71	3.78	8.36	36.45	2.10	1.370	
7035	0.408	8.88	3.48	7.12	36.84	2.48	1.316	
7036	0.355	9.14	3.59	6.45	30.09	2.55	1.600	
7037	0.365	8.32	3.74	7.69	30.17	2.39	1.693	
7038	0.347	7.71	4.05	7.40	39.66	2.71	1.920	
7039	0.268	6.53	4.40	7.22	32.89	2.37	1.117	
7040	0.329	8.69	3.51	7.02	29.51	2.49	1.413	
Mean	0.3363	8.249	3.789	7.439	33.728	2.348	1.5547	
SD	0.0368	0.969	0.287	0.532	3.333	0.257	0.2623	
N	10	10	10	10	10	10	10	

Individual Animal Organ-To-Body Weight Ratio
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

125 mg/kg/day Group 2	Thyroid-Parathyroid /TBW (Ratio)
	Day 31
7031	1.5920
7032	0.7394
7033	1.1475
7034	0.8779
7035	1.0000
7036	0.8182
7037	0.9664
7038	1.4122
7039	0.8835
7040	1.0667
Mean	1.05138
SD	0.26845
N	10

Individual Animal Organ-To-Body Weight Ratio
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female		Day(s) Relative to Start Date					
250 mg/kg/day Group 3	Adrenal /TBW (Ratio)	Brain /TBW (Ratio)	Heart /TBW (Ratio)	Kidneys /TBW (Ratio)	Liver /TBW (Ratio)	Spleen /TBW (Ratio)	Thymus /TBW (Ratio)
	Day 31	Day 31	Day 31	Day 31	Day 31	Day 31	Day 31
	7051	0.320	7.64	3.56	7.53	32.12	1.89
7052	0.291	7.27	3.67	8.99	31.80	1.90	1.457
7053	0.325	7.29	3.46	7.14	31.39	2.14	1.664
7054	0.252	7.59	3.19	6.93	35.26	2.30	1.574
7055	0.320	8.08	4.00	7.52	39.12	2.24	1.556
7056	0.408	9.27	3.99	8.44	38.72	2.11	2.179
7057	0.275	8.01	3.71	8.09	33.86	2.07	1.805
7058	0.366	8.70	3.56	7.78	32.85	1.97	1.657
7059	0.333	8.29	3.93	7.46	35.87	2.02	2.468
7060	0.326	8.52	3.43	6.13	31.78	2.22	1.313
Mean	0.3206	8.066	3.649	7.801	34.268	2.086	1.7538
SD	0.0433	0.646	0.266	0.506	2.880	0.141	0.3460
N	10	10	10	10	10	10	10

Individual Animal Organ-To-Body Weight Ratio
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female Day(s) Relative to Start Date

250 mg/kg/day Group 3	Thyroid-Parathyroid /TBW (Ratio)
	Day 31
7051	0.8880
7052	0.7612
7053	0.9643
7054	0.8889
7055	1.0400
7056	1.3761
7057	0.8765
7058	0.9623
7059	0.9524
7060	0.9565
Mean	0.95663
SD	0.16191
N	10

Individual Animal Organ-To-Body Weight Ratio
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female		Day(s) Relative to Start Date					
500 mg/kg/day Group 4	Adrenal /TBW (Ratio)	Brain /TBW (Ratio)	Heart /TBW (Ratio)	Kidneys /TBW (Ratio)	Liver /TBW (Ratio)	Spleen /TBW (Ratio)	Thymus /TBW (Ratio)
	Day 31	Day 31	Day 31	Day 31	Day 31	Day 31	Day 31
	7071	0.292	7.27	3.82	8.01	36.37	2.21
7072	0.279	8.30	3.90	7.17	34.67	2.43	2.156
7073	0.310	9.00	3.54	8.43	33.76	2.62	2.013
7074	0.336	8.32	3.88	7.20	32.28	2.16	1.638
7075	0.388	8.19	3.58	7.62	34.88	2.31	2.112
7076	0.344	7.70	3.58	7.11	33.28	2.61	1.457
7077	0.361	9.06	3.73	8.98	35.90	2.50	1.848
7078	0.361	8.55	3.51	6.90	37.69	2.23	1.640
7079	0.279	7.36	3.28	7.74	33.14	2.02	1.502
7080	0.271	8.46	3.50	6.96	24.92	2.13	1.713
Mean	0.3211	8.222	3.623	7.611	33.689	2.341	1.7494
SD	0.0406	0.612	0.185	0.687	3.494	0.247	0.2707
N	10	10	10	10	10	10	10

Individual Animal Organ-To-Body Weight Ratio
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female	Day(s) Relative to Start Date
500 mg/kg/day Group 4	Thyroid-Parathyroid /TBW (Ratio) Day 31
7071	0.9738
7072	0.9783
7073	1.1354
7074	1.0776
7075	0.9615
7076	0.7813
7077	1.2295
7078	1.1570
7079	1.1847
7080	0.9563
Mean	1.04373
SD	0.13688
N	10

APPENDIX O: INDIVIDUAL ANIMAL ORGAN-TO-BRAIN WEIGHT RATIOS¹

PRODUCT IDENTIFICATION

Silk Fibroin

¹ [organ weight/brain weight]

Individual Animal Organ-To-Brain Weight Ratios
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

0 mg/kg/day Group 1	Sex: Female Day(s) Relative to Start Date						
	Adrenal /BrW (Ratio)	Heart /BrW (Ratio)	Kidneys /BrW (Ratio)	Liver /BrW (Ratio)	Spleen /BrW (Ratio)	Thymus /BrW (Ratio)	Thyroid-Parathyroid /BrW (Ratio)
	Day 31	Day 31	Day 31	Day 31	Day 31	Day 31	Day 31
7011	0.040	0.44	0.95	3.75	0.27	0.229	0.0010
7012	0.041	0.46	1.00	4.22	0.33	0.198	0.0009
7013	0.041	0.45	1.00	3.64	0.29	0.246	0.0012
7014	0.042	0.48	0.93	4.39	0.35	0.226	0.0015
7015	0.042	0.48	0.94	4.35	0.27	0.221	0.0011
7015	0.034	0.44	0.94	4.55	0.29	0.160	0.0014
7017	0.047	0.47	1.02	4.28	0.31	0.197	0.0008
7018	0.045	0.47	0.90	4.22	0.27	0.222	0.0009
7019	0.037	0.50	1.09	4.95	0.28	0.245	0.0014
7020	0.037	0.47	0.89	3.55	0.24	0.304	0.0011
Mean	0.0407	0.467	0.967	4.192	0.287	0.2268	0.00112
SD	0.0040	0.020	0.062	0.434	0.032	0.0345	0.00024
N	10	10	10	10	10	10	10

Individual Animal Organ-To-Brain Weight Ratios
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female		Day(s) Relative to Start Date					
125 mg/kg/day Group 2	Adrenal /BrW (Ratio)	Heart /BrW (Ratio)	Kidneys /BrW (Ratio)	Liver /BrW (Ratio)	Spleen /BrW (Ratio)	Thymus /BrW (Ratio)	Thyroid-Parathyroid /BrW (Ratio)
	Day 31	Day 31	Day 31	Day 31	Day 31	Day 31	Day 31
	7031	0.036	0.43	0.62	3.62	0.23	0.157
7032	0.045	0.52	1.15	4.73	0.35	0.255	0.0011
7033	0.035	0.41	0.81	3.80	0.19	0.204	0.0012
7034	0.043	0.49	1.08	4.73	0.27	0.178	0.0011
7035	0.047	0.40	0.82	4.24	0.29	0.152	0.0012
7036	0.039	0.39	0.71	3.29	0.28	0.175	0.0009
7037	0.044	0.45	0.92	3.63	0.29	0.204	0.0012
7038	0.045	0.62	0.86	5.14	0.35	0.249	0.0018
7039	0.041	0.67	1.11	5.04	0.36	0.171	0.0014
7040	0.037	0.40	0.79	3.32	0.28	0.159	0.0012
Mean	0.0410	0.468	0.917	4.154	0.289	0.1903	0.00128
SD	0.0044	0.088	0.153	0.711	0.053	0.0371	0.00029
N	10	10	10	10	10	10	10

Individual Animal Organ-To-Brain Weight Ratios
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female		Day(s) Relative to Start Date					
250 mg/kg/day Group 3	Adrenal /BrW (Ratio)	Heart /BrW (Ratio)	Kidneys /BrW (Ratio)	Liver /BrW (Ratio)	Spleen /BrW (Ratio)	Thymus /BrW (Ratio)	Thyroid-Parathyroid /BrW (Ratio)
	Day 31	Day 31	Day 31	Day 31	Day 31	Day 31	Day 31
	7051	0.042	0.46	0.98	4.20	0.25	0.244
7052	0.040	0.50	0.96	4.38	0.26	0.200	0.0010
7053	0.045	0.48	0.98	4.31	0.29	0.228	0.0013
7054	0.033	0.42	0.91	4.64	0.30	0.207	0.0012
7055	0.040	0.50	0.93	4.84	0.28	0.193	0.0013
7056	0.044	0.43	0.91	4.18	0.23	0.235	0.0015
7057	0.034	0.46	1.01	4.23	0.26	0.225	0.0011
7058	0.041	0.41	0.89	3.77	0.23	0.190	0.0011
7059	0.040	0.47	0.90	4.30	0.24	0.298	0.0011
7060	0.038	0.40	0.95	3.73	0.26	0.154	0.0011
Mean	0.0397	0.454	0.944	4.258	0.260	0.2175	0.00119
SD	0.0037	0.036	0.040	0.339	0.026	0.0386	0.00013
N	10	10	10	10	10	10	10

Individual Animal Organ-To-Brain Weight Ratios
PSL Study Number 51651 - A 28-Day Oral Gavage Toxicity Study in Rats

Sex: Female		Day(s) Relative to Start Date					
500 mg/kg/day Group 4	Adrenal /BrW (Ratio)	Heart /BrW (Ratio)	Kidneys /BrW (Ratio)	Liver /BrW (Ratio)	Spleen /BrW (Ratio)	Thymus /BrW (Ratio)	Thyroid-Parathyroid /BrW (Ratio)
	Day 31	Day 31	Day 31	Day 31	Day 31	Day 31	Day 31
	7071	0.040	0.53	1.10	5.01	0.30	0.195
7072	0.034	0.46	0.86	4.18	0.29	0.260	0.0012
7073	0.034	0.39	0.94	3.75	0.29	0.224	0.0013
7074	0.040	0.47	0.87	3.89	0.20	0.197	0.0013
7075	0.047	0.44	0.93	4.26	0.28	0.258	0.0012
7076	0.045	0.47	0.92	4.32	0.37	0.199	0.0010
7077	0.040	0.41	0.99	3.96	0.28	0.204	0.0014
7078	0.041	0.41	0.81	4.41	0.26	0.192	0.0014
7079	0.038	0.44	1.05	4.49	0.27	0.203	0.0016
7080	0.032	0.41	0.82	2.95	0.25	0.202	0.0011
Mean	0.0391	0.443	0.929	4.120	0.286	0.2124	0.00127
SD	0.0048	0.039	0.066	0.544	0.033	0.0262	0.00015
N	10	10	10	10	10	10	10

APPENDIX P: HISTOPATHOLOGY

PRODUCT IDENTIFICATION

Silk Fibroin

Submitted By:

HSRL

Histo-Scientific Research Laboratories
5930 Main Street
Mount Jackson, VA 22842



PATHOLOGY REPORT
SILK FIBROIN: A 28-DAY ORAL GAVAGE TOXICITY STUDY IN RATS
Product Safety Labs (PSL) Study Number 51651

Prepared by

HSRL
Histo-Scientific Research Laboratories
5930 Main Street
Mount Jackson, VA 22842

Testing Facility

Product Safety Labs
2394 US Highway 130
Dayton, NJ 08810

Sponsor

Cambridge Crops, Inc
444 Somerville Ave
Somerville, MA 02143

March 31 2020

5930 Main Street 340.477.1448 phone www.hsrl.org
Mt. Jackson, VA 22842 340.477.1448 fax

Final Pathology Report
Cambridge Crops, Inc.
PSL Study Number 51651

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PSL Study Number 51651

4.0 GLP Compliance Statement- Histopathology Slide Preparation

The histological slide preparation portion of Product Safety Late Study Number 51651, which was performed at Histo-Scientific Research Laboratories (HSRL), 5930 Main Street, Mount Jackson, VA 22842, was conducted in compliance with U.S. FDA GLP- 21 CFR Part 58, 1987

[Redacted Signature]


Craig Lind
Principal Investigator
Histo-Scientific Research Laboratories (HSRL)

3/21/20
Date

Final Pathology Report
Cambridge-Cropas, Inc.
PSL Study Number 51651

2.8 GLP Compliance Statement- Histopathology Evaluation

The histological slide evaluation portion of Product Safety Lab. Study Number 51651 which was performed at Histo-Scientific Research Laboratories (HSRL), 5830 Main Street Mount Jackson, VA 22842 was conducted in compliance with U.S. FDA GLP 21 CFR Part 58, 1987


Christine E. Watson, MS, BVMS, MRCVS, DACVP
Principal Investigator
Histo-Scientific Research Laboratories (HSRL)

5/11/2020
Date

3/31/2020

Final Pathology Report
Cambridge Crops, Inc.
PSL Study Number 51651

3.0 Executive Summary

The objective of this study was to evaluate the potential subchronic toxicity of Silk Fibroin in male and female rats likely to arise from repeated exposure, via oral gavage, over a test period of at least 28 days. A no-observed-adverse-effect-level (NOAEL) was determined.

Methods: According to the protocol, 80 rats (40 male and 40 female) were assigned to four treatment groups. Following the in-life procedures, all animals were euthanized on Day 30/31 and subjected to a gross necropsy. Protocol-specified tissues were collected and forwarded to HSRL. Upon receipt, protocol-required tissues from both the control and high dose groups (Groups 1 and 4, respectively) and gross lesions from all animals were processed, embedded in paraffin, sectioned and stained with hematoxylin and eosin (H&E). The resulting microscopic slides were evaluated by Christine E. Watson, MS, BVMS, MRCVS, DACVP of HSRL. This pathology report by HSRL presents the results of the microscopic evaluation of protocol-required tissues and gross lesions from all animals.

Conclusion: The objective of this study was to evaluate the potential subchronic toxicity of Silk Fibroin in male and female rats likely to arise from repeated exposure, via oral gavage, over a test period of at least 28 days. A no-observed-adverse-effect-level (NOAEL) was determined.

Administration of Silk Fibroin via repeated exposure by oral gavage to control (Group 1) and high-dose (Group 4; 500 mg/kg/day) male and female rats was not associated with mortality. All animals survived to terminal sacrifice (Day 30/31). There were no test substance-related gross or microscopic findings.

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Cambridge Crops, Inc.
PSL Study Number 51651

4.0 Introduction

4.1 Protocol

This report presents the histopathology results of a study to evaluate the potential subchronic toxicity of Silk Fibroin administered via oral gavage to rats, PSL Study Number 51651, Cambridge Crops, Inc., Somerville, MA. All in-life procedures and tissue harvests were performed at Product Safety Labs under the direction of Raghavendra Gowda, Ph.D, Study Director. Histology was performed at HSRL and microscopic evaluation was completed by Christine E. Watson, MS, BVMS, MRCVS, DACVP at HSRL.

4.2 Objective

The objective of this study was to evaluate the potential subchronic toxicity of Silk Fibroin in male and female rats likely to arise from repeated exposure, via oral gavage, over a test period of at least 28 days. A no-observed-adverse-effect-level (NOAEL) was determined.

5.0 Methods

5.1 Compliance Statement

The histology and pathology portions of this study performed by HSRL were conducted in compliance with U.S. FDA GLP: 21 CFR Part 58, 1987.

5.2 Study Design

According to the protocol, 80 animals (40 male and 40 female) were enrolled in the study. The study design is further described in Table 1 as follows:

Table 1. Dose Levels

Group	Number Animals/Group (Male/Female)	Oral Gavage Dose of Test Substance (mg/kg/day)	Dose Volume (mL/kg)	Concentration (mg/mL) ^a
1	10/10	0 (Vehicle Control) ^a	10	0
2	10/10	125		12.5
3	10/10	250		25
4	10/10	500		50

^a Distilled Water

^b Appropriate concentrations of the test substance as received in vehicle to achieve the target dose level

5.3 Necropsy

At terminal sacrifice on Day 30/31, all animals were euthanized and subjected to a gross necropsy. Necropsies included examination of the external surface of the body, all orifices, musculoskeletal system, and the cranial, thoracic, abdominal and pelvic cavities, with their associated organs and tissues. At scheduled termination, the following organs were weighed: adrenals (combined), brain, epididymides (combined, males only), heart, kidneys (combined), liver, ovaries with oviducts (combined, females only), spleen, testes (combined, males only), thymus, and uterus (females only). The seminal vesicles with coagulating gland (combined, males only), thyroid/parathyroid, and ventral prostate (males only) were weighed fixed at HSRL. The following organs and tissues from all animals were preserved in 10% NBF:

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Cambridge Crops, Inc.
PSL Study Number 51651

accessory genital organs (prostate and seminal vesicles)	nasal turbinates
adrenals	nose
all gross lesions	ovaries
aorta	oviducts
bone (femur)	pancreas
bone marrow (from femur and sternum)	parathyroid
brain – sections including medulla/pons, cerebellar, and cerebral cortex	peripheral nerve (sciatic)
cecum	pharynx
cervix	pituitary gland
colon	rectum
duodenum	salivary glands (sublingual, submandibular, and parotid)
esophagus	skeletal muscle
Harderian gland	skin
heart	spinal cord – 3 levels: cervical, mid-thoracic, and lumbar
ileum with Peyer's patches	spleen
jejunum	sternum
kidneys	stomach
larynx	thymus
liver	thyroid
lungs	trachea
lymph node mandibular	urinary bladder
lymph node mesenteric	uterus
mammary gland	vagina

The epididymides, eyes, optic nerve, and testes were preserved in modified Davidson's fixative and then stored in ethanol.

5.4 Histological Processing

Collected tissues from all animals were forwarded to HSRL where the protocol-required tissues from both the control and high dose groups (Groups 1 and 4, respectively) and gross lesions from all animals were processed, embedded in paraffin, sectioned and stained with hematoxylin and eosin (H&E). Animal information from PSL's Gross Pathology Results was entered into Pristima[®] at HSRL. All microscopic slides were evaluated, and microscopic findings were entered directly into Pristima[®] by Christine E. Watson, MS, BVMS, MRCVS, DACVP of HSRL. Gross to microscopic correlations and the incidence of microscopic findings are presented in the Histopathology Incidence Tables portion of this report.

Within the Histopathology Incidence Tables, the following abbreviations apply:

M=Male
F=Female
1>=Minimal
2>=Mild
3>=Moderate
4>=Marked
5>=Severe

Within the Tissue Accountability Appendix, the following abbreviation applies:

SOPs=Standard Operating Procedures

3/31/2020

000847

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Cambridge Croys, Inc.
PSL Study Number 51651

6.0 Results

6.1 Animal Mortality

There were no unscheduled death animals among the animals submitted for histopathological evaluation.

6.2 Macroscopic Observations

The gross findings at terminal sacrifice on Day 30/31, were considered incidental, of the nature commonly observed in rats (background findings) and/or were of similar incidence in control and dosed rats and were not considered related to administration of Silk Fibroin.

Animals 7009 and 7029 had macroscopic findings of unilateral (right) small and/or fused testes correlated microscopically with testicular atrophy. Animal 7009 had macroscopic findings of small right epididymis that microscopically correlated epididymal atrophy. Females in Groups 1 through 4 with a microscopic finding of a fluid filled uterus was consistent with normal estrogen cycling of female rats.

6.3 Microscopic Observations

No Silk Fibroin-related microscopic findings were noted in terminal sacrifice animals on Day 30/31. The microscopic findings observed were considered incidental (background findings), of the nature commonly observed in rats and/or were of similar incidence and severity in the control and dosed animals and were not considered related to the administration of the test substance.

7.0 Conclusion

The objective of this study was to evaluate the potential subchronic toxicity of Silk Fibroin in male and female rats likely to arise from repeated exposure, via oral gavage, over a test period of at least 28 days. A no-observed-adverse-effect level (NOAEL) was determined.

Administration of Silk Fibroin via repeated exposure by oral gavage to control (Group 1) and high-dose (Group 4, 500 mg/kg/day) male and female rats was not associated with mortality. All animals survived to terminal sacrifice (Day 30/31). There were no test substance-related gross or microscopic findings.

Signature

Christine E. Watson, MS, BVMS, MRCVS, DACVP
Study Pathologist

Date

Final Pathology Report
Cambridge Crops, Inc.
PSL Study Number 51651

**Appendix A. Histopathology Incidence Tables (Expanded Summary Report of Histopathology Day
30/31 Animals)**

Expanded Summary Report of Histopathology

Study ID: 51651
 Sponsor: [Sponsor Name]
 Protocol: [Protocol Name]
 Site: [Site Name]

Male

System Organ Class	Primary Site	Frequency	Severity
Gastrointestinal disorders	Stomach (unspecified)	1	1
	Small intestine (unspecified)	0	0
Blood and blood forming organs	Erythrocyte count decreased	1	1
	Leucocyte count decreased	1	1
Musculoskeletal disorders	Joint pain	1	1
	Arthralgia	1	1
Nervous system disorders	Headache	1	1
	Dizziness	1	1
Respiratory disorders	Cough	1	1
	Pharyngitis	1	1
Skin disorders	Rash	1	1
	Pruritus	1	1
Total (All Sites)		10	10

Synopsis Summary Report of Histopathology

Page 1 of 1

001

Study Title: **Study Title: R...**
 Test Article: **Salt Electrolyte**

Report Date: **2010-01-01**

Pathology	Male		Female
	Number of Animals	Number of Lesions	
Stomach	10	4	1
Small Intestine	10	1	11
Colon	1	1	1
Rectum	10	0	11
Bladder	10	0	11
Uterus	10	0	11
Vagina	10	0	11
Endometrium	10	0	11
Myometrium	10	0	11
External Genitalia	10	0	11
Penis	10	0	11
Prostate Gland	10	0	11
Testis	10	0	11
Epididymis	10	0	11
Seminal Vesicle	10	0	11
Utricle	10	0	11
Preputial Gland	10	0	11
Subcutaneous Tissue	10	0	11
Skin	10	0	11
Muscle	10	0	11
Bone	10	0	11
Heart	10	0	11
Lung	10	0	11
Liver	10	0	11
Spleen	10	0	11
Thyroid Gland	10	0	11
Adipose Tissue	10	0	11
Other	10	0	11

Expanded Summary Report of Baseline Data

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PDF:

Study Title: **Study 51651 - A Phase 1, Single-Arm, Open-Label, Dose-Escalation Study of the Safety and Tolerability of the Anti-CD47 Antibody, SGN-CD47, in Patients with Solid Tumors**

Study ID: **51651**

Study ID:

Main:

Report Date: **12/15/2017**

Parameter	Design Group	Count	%
Total	Number of Animals	10	100
	% of CD47 Positive	10	100
Male	Number of Animals	1	10
	% of CD47 Positive	1	100
Female	Number of Animals	9	90
	% of CD47 Positive	9	100
Race	Number of Animals	10	100
	% of CD47 Positive	10	100
Ethnicity	Number of Animals	1	10
	% of CD47 Positive	1	100
Age	Number of Animals	10	100
	% of CD47 Positive	10	100
Weight	Number of Animals	10	100
	% of CD47 Positive	10	100

Expanded Summary Report of Histopathology

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HSRL

Study: 51651

Study Title: SILK FIBROIN: A 28-DAY ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Silk Fibroin

Rat/Sprague-Dawley

Repeat Dose Toxicity/Oral

	Males			
	Dosage Group	Control	2	4
	Number of Animals	10	1	10
	Number Examined	10	1	10
	Number Unremarkable	1	0	1
Lymph Node, Mandibular	Number examined	10	0	10
	Number unremarkable	10	0	10
Lymph Node, Mesenteric	Number examined	10	0	10
	Number unremarkable	10	0	10
Muscle, Skeletal	Number examined	10	0	10
	Number unremarkable	10	0	10
Nasal Turbinate	Number examined	10	0	10
	Number unremarkable	10	0	10
Nerve, Optic	Number examined	10	0	10
	Number unremarkable	10	0	10
Nerve, Peripheral (sciatic)	Number examined	10	0	10
	Number unremarkable	10	0	10

Expanded Summary Report of Histopathology

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Summary Report of Histopathology
Study Number 51651

Study Site: 4281 AY (USA, JAVASC) (IND: JY50, DV: 1000)
Test Article: 500, Falsolat

Category	Main	Report Line Number
Overall Summary	Overall Summary	1
	Overall Summary	2
	Overall Summary	3
Overall Summary	Overall Summary	4
	Overall Summary	5
Overall Summary	Overall Summary	6
	Overall Summary	7
Overall Summary	Overall Summary	8
	Overall Summary	9
Overall Summary	Overall Summary	10
	Overall Summary	11
Overall Summary	Overall Summary	12
	Overall Summary	13
Overall Summary	Overall Summary	14
	Overall Summary	15
Overall Summary	Overall Summary	16
	Overall Summary	17
Overall Summary	Overall Summary	18
	Overall Summary	19

Expanded Summary Report of Histopathology

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HSRL

Study: 51651

Study Title: SILK FIBROIN: A 28-DAY ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Silk Fibroin

Rat/Sprague-Dawley

Repeat Dose Toxicity/Oral

		Male			
		Dosage Group:	Control	2	4
		Number of Animals	10	1	10
		Number Examined	10	1	10
		Number Unremarkable	1	0	1
Trachea		Number examined	10	0	10
		Number unremarkable	10	0	10
Urinary Bladder		Number examined	10	0	10
		Number unremarkable	10	0	10

Expanded Summary Report of Histopathology

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HSRL

Study: 51651

Study Title: SILK FIBROIN: A 28-DAY ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Silk Fibroin

Rat/Spague-Dawley

Repeat Dose Toxicity/Oral

	Females			
	Control	2	3	4
	Number of Animals:	10	3	5
	Number Examined:	10	3	5
	Number Unrecoverable:	4	0	4
Artery, Aorta	Number examined:	10	0	0
	Number unrecoverable:	10	0	0
Bone Marrow	Number examined:	10	0	0
	Number unrecoverable:	10	0	0
Bone, Femur	Number examined:	10	0	0
	Number unrecoverable:	10	0	0
Bovine, Spleen	Number examined:	10	0	0
	Number unrecoverable:	10	0	0
Bronchus	Number examined:	10	0	0
	Number unrecoverable:	10	0	0
Cervix	Number examined:	10	0	0
	Number unrecoverable:	10	0	0

Expanded Summary Report of Histopathology

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HSRL

Study: 51651

Study Title: SILK FIBROIN: A 28-DAY ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Silk Fibroin

Rat/Sprague-Dawley

Repeat Dose Toxicity/Oral

	Females				
	Desage Group:	Control	2	3	4
	Number of Animals	10	3	5	10
	Number Examined	10	3	5	10
	Number Unremarkable	4	0	0	4
Esophagus	Number examined	10	0	0	10
	Number unremarkable	10	0	0	10
Eye	Number examined	10	0	0	10
	Number unremarkable	10	0	0	10
Gland, Adrenal	Number examined	10	0	0	10
	Number unremarkable	10	0	0	10
Gland, Harderian	Number examined	10	0	0	10
	Number unremarkable	10	0	0	10
Gland, Mammary	Number examined	10	0	0	10
	Number unremarkable	10	0	0	10
Gland, Parathyroid	Number examined	9	0	0	10
	Number unremarkable	9	0	0	10

Expanded Summary Report of Histopathology

Study Site ID	Study Site Name	Family	Number of Animals		
			1	2	3
		Female	0	0	0
		Male	0	0	0
		Total	0	0	0
		Female	0	0	0
		Male	0	0	0
		Total	0	0	0
		Female	0	0	0
		Male	0	0	0
		Total	0	0	0
		Female	0	0	0
		Male	0	0	0
		Total	0	0	0
		Female	0	0	0
		Male	0	0	0
		Total	0	0	0
		Female	0	0	0
		Male	0	0	0
		Total	0	0	0

Expanded Summary Report of Histopathology

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Protocol: 11-11-18-001

Page:

Page 1 of 1

Study ID: 11-11-18-001
Site ID: 11-11-18-001
Study Name: 11-11-18-001

Page:

Report Case ID: 11-11-18-001

	Female	Male	Both	Total
Female				
Design Group	2	1	1	
Number of Animals	1	1	1	3
Number of Samples	1	1	1	3
Number of Treatments	1	1	1	3
Male				
Number of Animals	0	0	0	0
Number of Samples	0	0	0	0
Number of Treatments	0	0	0	0
Both				
Number of Animals	2	1	1	4
Number of Samples	1	1	1	3
Number of Treatments	1	1	1	3
Total				
Number of Animals	2	1	1	4
Number of Samples	1	1	1	3
Number of Treatments	1	1	1	3
Number of Samples	1	1	1	3
Number of Treatments	1	1	1	3
Number of Animals	2	1	1	4
Number of Samples	1	1	1	3
Number of Treatments	1	1	1	3

Expanded Summary Report of Histopathology

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 Summary of Histopathology Findings
 Summary of Histopathology Findings

Study Site: **Study Title: 301 (U.S.) - A 28-DAY TOXICITY STUDY OF THE PHARMACOKINETICS AND PHARMACODYNAMICS OF THE TEST ARTICLE, SGLT2 INHIBITOR, IN MICE**

Sex (Species - male)	Histology				Report (Yes/No/Not Eval)
	Dosage Group	Number of Animals	Number of Animals	Number of Animals	
Male	Control	10	10	10	10
	Low Dose	10	10	10	10
Female	Control	10	10	10	10
	Low Dose	10	10	10	10
Male	Control	10	10	10	10
	Low Dose	10	10	10	10
Female	Control	10	10	10	10
	Low Dose	10	10	10	10
Male	Control	10	10	10	10
	Low Dose	10	10	10	10
Female	Control	10	10	10	10
	Low Dose	10	10	10	10

Expanded Summary Report of Histopathology

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ISRL

Study: 51651

Study Title: SILK FIBROIN: A 28-DAY ORAL GAVAGE TOXICITY STUDY IN RATS

Tax Article: Silk (Fibroin)

Rat/Sprague-Dawley

Repeat Dose Toxicity/Oral

	Females				
	Design Group:	Control	2	3	4
	Number of Animals:	10	3	5	10
	Number Examined:	10	3	5	10
	Number Unremarkable:	4	0	0	4
Nasal Turbinate	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Nerve, Optic	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Nerve, Trigeminal (somatic)	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Testis	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Ovary	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Oviduct	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10

Expanded Summary Report of Histopathology

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HRG:

Study Site:

Study Title: **Study 51651: A Phase 1/2 Study of the Safety and Efficacy of [Drug Name]**

HRG Reference:

Findings

HRG Reference:

Findings	Description	Number of Patients		Total
		Group 1	Group 2	
Adverse Events	Number of Adverse Events	1	1	2
	Number of Serious Adverse Events	0	0	0
Laboratory Abnormalities	Number of Abnormalities	1	1	2
	Number of Abnormalities	0	0	0
Immunogenicity	Number of Positive Results	0	0	0
	Number of Positive Results	0	0	0
Other	Number of Other Findings	0	0	0
	Number of Other Findings	0	0	0
Overall Summary	Number of Findings	1	1	2
	Number of Findings	0	0	0

Expanded Summary Report of Histopathology

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HSRL

Study: 51651

Study Title: SILK (TBROD): A 28-DAY ORAL GAVAGE TOXICITY STUDY IN RATS
Test Article: Silk Filtron

Rat/Sprague-Dawley

Repeat Dose Toxicity/Oral

	Females				
	Dosage Group	Control	2	3	4
	Number of Animals:	10	3	5	10
	Number Examined:	10	3	5	10
	Number Unremarkable:	4	0	0	4
Small Intestine, Jejunum	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Spinal Cord, Cervical	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Spinal Cord, Lumbar	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Spinal Cord, Midthoracic	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Spleen	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Stomach	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10

Expanded Summary Report of Histopathology

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ISRL

Study: 51651

Study Title: SILK FIBROIN: A 28-DAY ORAL GAVAGE TOXICITY STUDY IN RATS

Test Article: Silk Fibroin

Rat/Sprague-Dawley

Repeat Dose Toxicity/Oral

	Females				
	Dosage Group	Control	2	3	4
	Number of Animals	10	3	5	10
	Number Examined	10	3	5	10
	Number Unremarkable	4	0	0	4
Thymus	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Trachea	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Urinary Bladder	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Uterus	Number examined:	10	3	5	10
	Number unremarkable:	10	3	5	10
Vagina	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10