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	409	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	289	333	384	397	371
7022	229	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	359	392	364
Mean	233.0	284.5	335.2	379.1	416.6	389.7
SD	13.6	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)

500 mg/kg/day Group 4	Day(s) Relative to Start Date					
	1	8	15	22	29	30
7061	211	269	327	376	419	385
7062	244	312	359	413	447	415
7063	250	306	358	400	435	409
7064	232	303	367	420	466	419
7065	233	292	334	386	425	402
7066	225	279	329	375	425	388
7067	240	290	340	395	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	280	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	228	239	250	232
7019	206	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	205	232	250	257	269	250
7036	195	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	280
7054	199	222	247	265	283	270
7055	194	217	237	255	262	250
7056	187	200	212	228	235	218
7057	208	229	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	226.4	241.5	257.0	269.3	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

Sex: Female Bodyweight (g)

500 mg/kg/day Group 4	Day(s) Relative to Start Date					
	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	195	212	222	235	242	232
7075	213	237	250	258	264	260
7076	206	235	242	255	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	6.39	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	7.5	4.4
7043	8.7	8.4	5.6	4.3
7044	7.0	9.1	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 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
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
7076	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
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: / To:	1 6	6 8	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	28.3	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	27.3
		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	29.70	28.88	27.50	29.80	28.20
				S.D.	1.63	3.85	1.93	2.29	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: / To:	1 / 6	6 / 8	8 / 13	13 / 15	15 / 20	20 / 22	22 / 27	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	26.8
		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

Day numbers relative to Start Date

Group	Sex	Cage	No in Cage	From: / To:	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 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: / 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.	1.43	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: / To:	1 / 6	6 / 8	8 / 13	13 / 15	15 / 20	20 / 22	22 / 27	27 / 29
1	F	6	2		20.3	20.5	20.7	22.8	20.8	20.5	22.0	19.3
		7	2		19.8	19.5	20.1	22.8	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
		9	2		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

Day numbers relative to Start Date

Group	Sex	Cage	No In Cage	From: / To:	1 / 6	6 / 8	8 / 13	13 / 15	15 / 20	20 / 22	22 / 27	27 / 29
2	f	16	2		18.6	18.8	19.8	22.0	19.5	17.0	19.8	20.3
		17	2		20.8	20.5	21.2	24.8	21.2	19.8	21.0	18.8
		18	2		18.6	18.0	19.1	22.8	18.1	13.3	17.0	18.5
		19	2		20.1	18.5	20.9	22.5	21.4	20.0	22.6	18.5
		20	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

Day numbers relative to Start Date

Group	Sex	Cage	No In Cage	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	1.49	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

Day numbers relative to Start Date

Group	Sex	Cage	No In Cage	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	20.1	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

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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

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GLP COMPLIANCE STATEMENT AND DECLARATION

PSL Study No.	: 51651
Eurofins Advinus Study Phase No.	: G18871
Eurofins Advinus Study Phase Code	: PATH
Principal Investigator	: Dr K C Jayachandra
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 FCS, FDA GLP 21 CFR Part 58, 1987 which is comparable with OECD Principles of Good Laboratory Practice (as revised in 1997) published in ENV/MC/CHEM (98)17, OECD, Paris, 1998. A copy of audited clinical pathology data generated at the PSL 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 PSL 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.

[redacted]

K C Jayachandra, M V Sc., DAHT
Principal Investigator, Pathology Section
Dept. of Safety Assessment
Eurofins Advinus Limited, Bengaluru

Date:

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QUALITY ASSURANCE STATEMENT

The clinical pathology data interpretation phase (Eurofins Advinus Study phase No. G18871) of PSL Study No. 51651 entitled "Oral Repeat 28-Day Oral Gavage Toxicity Study in Rats" was inspected in accordance with U.S. FDA GLP 21 CFR Part 58, 1987 which is comparable with OECD Principles of Good Laboratory Practice (as revised in 1997) published in ENV/MC/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	15 November 2019
26 February 2020	Reporting Phase Draft clinical pathology phase report review	28 February 2020	29 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 the data.

[redacted]

Satish Murigod, M.Sc., RQAP-GLP — Date
Head, QAU-GLP
Eurofins Advinus Limited,
Bengaluru

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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 reticulocyte
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

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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	K. C. Jayachandra, M.V.Sc., DABT Pathologist, Pathology Department of Safety Assessment
Report Review	S. K. Vijayasarathi, 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

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1. 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: RhondaKrick@productsafetylabs.com

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Study Phase Schedule

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

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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.

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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 (BILI)	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

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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

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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.

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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).

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9. TABLES

TABLE 1. Summary of Haematology Parameters - Males

Refer Appendix 1

Group		RBC	WBC	Hgb	HCT	MCV?	MCH?	[illegible]	PLT?	[illegible]
		[illegible]	[illegible]	(g/dL)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
1 (Control)	N	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Mean	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Std.Dev.	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	N	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Mean	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Std.Dev.	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	N	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Mean	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Std.Dev.	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	N	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Mean	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Std.Dev.	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

TABLE 1 contd. Summary of Hematology Parameters Males

Group		ALYM	AMON	ALUS	ABAS	ALUC	ARET	MCHC
Control	(n)	10	10	10	10	10	10	10
	Mean	7.945	0.59	0.056	0.029	0.154	226.6	30.01
	Sdev	1.9954	0.703	0.0560	0.0218	0.0500	36.57	0.540
2	(n)	10	10	10	10	10	10	10
	Mean	[illegible]	0.29	0.072	0.025	0.160	206.5	30.00
	Sdev	2.5629	0.118	[illegible]	0.0108	[illegible]	29.30	0.751
	(n)	10	10	10	10	10	10	10
	Mean	7.166	0.28	0.066	0.025	0.129	224.8	30.18
	Sdev	1.4543	[illegible]	0.0400	0.0118	0.0482	28.11	0.437
4	(n)	10	10	10	10	10	10	10
	Mean	[illegible]	0.29	0.056	0.021	0.116	243.2	27.42
	Sdev	[illegible]	[illegible]	0.0305	0.0091	0.0375	52.97	[illegible]

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TABLE 2. Summary of Haematology Parameters Females

Refer Appendix 1

Group		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Control	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Mean	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Mean	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Mean	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
4	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Mean	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

TABLE 2 contd. Summary of Haematology Parameters Females

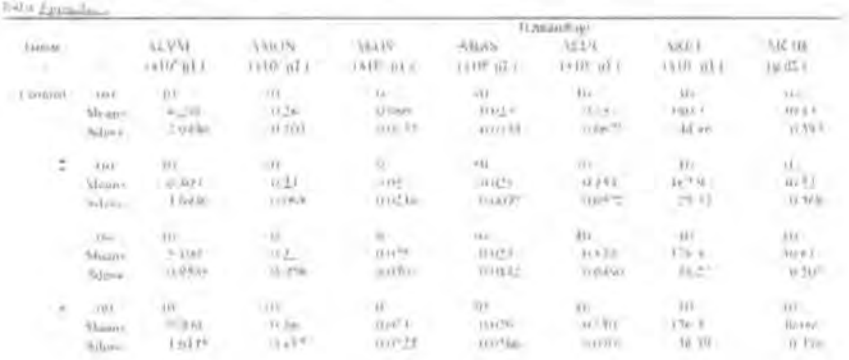

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TABLE 3. Summary of Coagulation Parameters - Males

[illegible]

Coagulation

Group		APTT (sec)	PT (sec)
Control	[illegible]	[illegible]	10
	Mean	[illegible]	9.6
	[illegible]	[illegible]	0.28
	[illegible]	10	10
	Mean	[illegible]	9.5
	[illegible]	[illegible]	0.25
[illegible]	[illegible]	[illegible]	9
	Mean	[illegible]	9.4
	[illegible]	[illegible]	0.40
[illegible]	[illegible]	[illegible]	10
	Mean	[illegible]	9.6
	[illegible]	[illegible]	0.25

TABLE 4. Summary of Coagulation Parameters – Females

Group		APTT (SEC)	PT (SEC)
Control	(N)	[illegible]	[illegible]
	Mean	[illegible]	9.1
	Sdev	[illegible]	[illegible]
[illegible]	(N)	[illegible]	[illegible]
	Mean	[illegible]	[illegible]
	Sdev	[illegible]	[illegible]
[illegible]	(N)	[illegible]	[illegible]
	Mean	[illegible]	9.1
	Sdev	[illegible]	[illegible]
[illegible]	(N)	[illegible]	[illegible]
	Mean	[illegible]	[illegible]
	Sdev	[illegible]	0.18

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TABLE 5. Summary of Clinical Chemistry Parameters - Males

Refer [illegible]

Group #		Serum Chemistry Na [illegible]	K [illegible]	Cl [illegible]	AST [illegible]	ALT [illegible]	ALKP [illegible]	BUN (mg/dl)	[illegible] (mg/dl)	CHOL [illegible]
Control	Cnt	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Mean	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Stdev	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
2	Cnt	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Mean	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Stdev	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
3	Cnt	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Mean	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Stdev	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
4	Cnt	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Mean	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Stdev	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

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TABLE 5 contd. Summary of Clinical Chemistry Parameters – Males

Refer Appendix 1

Group		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
1 Control	N	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Mean	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Std Dev	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
2	N	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Mean	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Std Dev	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
3	N	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Mean	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Std Dev	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
4	N	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Mean	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Std Dev	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

TABLE 6. Summary of Clinical Chemistry Parameters - Females

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TABLE 6 contd. Summary of Clinical Chemistry Parameters - Females

Refer [illegible]

Group		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
		Serum Chemistry								
Control	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Mean	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Stdev	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Mean	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Stdev	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Mean	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Stdev	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Mean	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Stdev	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

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TABLE 7. Summary of Clinical Analysis of Urine - Males

Group		URO (EU/dL)	pH	SG	[illegible] (mL)	Urinalysis UPRO (mg/dL)
Control	[illegible]	10	10	10	10	10
	Means	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Sdevs	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
2	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	10
	Means	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Sdevs	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	10	[illegible]	[illegible]	[illegible]	[illegible]
	Means	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Sdevs	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Means	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Sdevs	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

TABLE 8. Summary of Clinical Analysis of Urine – Females

Group		[illegible]	pH	SG	[illegible]	[illegible]
1 Control	N	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Mean	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	SD	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
2	N	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Mean	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	SD	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	N	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Mean	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	SD	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	N	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Mean	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	SD	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

10 APPENDICES

APPENDIX 1. Individual Animal Haematology Parameters

Animal #	Sex	Dosage Group #	Day/Week of Phase	Status Num Name	RBC (x10^6/uL)	WBC (x10^3/uL)	HGB (g/dL)	HCT (%)	MCV (fL)	MCH (pg)
7001	D M	Ctrl	30 S	S I [illegible]	8.44	9.27	15.7	51.7	61.7	18.6
7002	D M	Ctrl	30 S	S I [illegible]	[illegible]	8.12	15.1	51.0	65.[illegible]	19.0
7003	D M	Ctrl	30 S	S I [illegible]	8.08	8.76	15.7	49.8	62.0	16.9
7004	D M	Ctrl	30 S	S I	8.44	6.22	15.6	51.3	60.3	17.6
7005	D M	Ctrl	30 S	S I	8.31	11.23	[illegible]	55.2	66.0	19.2
7006	D M	Ctrl	30 S	S I [illegible]	8.6[illegible]	12.00	16.[illegible]	50.0	55.6	19.8
7007	D M	Ctrl	30 S	S I	8.13	10.99	15.[illegible]	50.9	62.[illegible]	19.2
7008	D M	Ctrl	30 S	S I	7.76	12.70	15.9	52.5	61.1	20.5
7009	D M	Ctrl	30 S	S I [illegible]	8.36	7.41	15.7	52.9	63.2	19.8
7010	D M	Ctrl	30 S	S I	8.25	10.87	15.6	51.1	62.2	18.9
7021	D M	2	30 S	S I [illegible]	8.91	11.18	16.7	54.9	61.1	17.0
7022	D M	2	30 S	S I [illegible]	8.02	10.15	15.9	51.5	63.9	19.2
7023	D M	2	30 S	S I [illegible]	8.14	13.89	15.3	50.7	62.2	19.0
7024	D M	2	30 S	S I	7.65	8.84	14.9	48.2	62.9	19.5
7025	D M	2	30 S	S I	9.15	5.83	16.3	56.2	61.4	17.8
7026	D M	2	30 S	S I [illegible]	9.00	13.31	[illegible]	[illegible]	63.8	18.9
7027	D M	2	30 S	S I [illegible]	8.01	10.92	15.2	50.1	61.[illegible]	19.1
7028	D M	2	30 S	S I [illegible]	8.51	8.90	[illegible]	58.1	61.1	18.[illegible]
7029	D M	2	30 S	S I	[illegible]	8.44	14.7	45.0	61.1	18.7
7030	D M	2	30 S	S I	8.61	10.14	15.4	50.9	62.2	19.0
7041	D M	3	30 S	S I [illegible]	8.[illegible]	7.41	15.[illegible]	50.6	60.2	20.1
7042	D M	3	30 S	S I	8.23	7.82	15.7	53.2	64.0	19.1
7043	D M	3	30 S	S I [illegible]	8.87	9.84	16.4	55.1	64.1	19.2
7044	D M	3	30 S	S I	7.95	10.78	15.4	51.1	64.2	19.[illegible]

D = Dosing Phase

S = Scheduled Animal Removal; U = Unscheduled Animal Removal; S = Scheduled Necropsy; u = Unscheduled Necropsy

APPENDIX 1 contd. Individual Animal Haematology Parameters

Animal #	Sex	Group	Day Week of Phase	[illegible] Name	RBC ($x10^6/\mu L$)	WBC ($x10^3/\mu L$)	HGB (g/dL)	HCT (%)	MCV (fL)	MCH (pg)
7045	D M	3	[illegible]	[illegible]	7.82	8.13	15.4	50.7	64.1	19.7
7046	D M	3	[illegible]	[illegible]	7.71	8.15	15.4	49.6	67.2	21.0
7047	D M	3	[illegible]	[illegible]	8.74	5.74	16.5	51.1	67.7	18.9
7048	D M	3	[illegible]	[illegible]	8.43	11.54	16.1	54.4	64.2	19.1
7049	D M	3	[illegible]	[illegible]	8.56	14.55	16.5	53.1	62.4	19.0
7050	D M	3	[illegible]	[illegible]	9.27	8.07	17.1	56.8	61.1	18.4
7061	D M	4	[illegible]	[illegible]	7.89	[illegible]	16.8	52.4	66.7	20.3
7062	D M	4	[illegible]	[illegible]	7.55	[illegible]	15.1	48.1	64.0	20.0
7063	D M	4	[illegible]	[illegible]	7.40	10.23	13.6	47.2	63.7	18.4
7064	D M	4	[illegible]	[illegible]	8.43	9.05	16.3	53.3	65.8	19.3
7065	D M	4	[illegible]	[illegible]	7.88	11.44	17.2	49.3	62.6	19.5
7066	D M	4	[illegible]	[illegible]	7.37	9.23	14.7	47.8	64.9	19.9
7067	D M	4	[illegible]	[illegible]	8.07	9.07	[illegible]	[illegible]	[illegible]	[illegible]
7069	D M	4	[illegible]	[illegible]	7.88	7.01	15.8	50.8	64.3	19.6
7068	D M	4	[illegible]	[illegible]	7.63	8.07	17.3	52.0	68.7	19.8
7070	D M	4	[illegible]	[illegible]	8.06	6.70	15.0	54.1	65.1	19.1
7011	D F	Ctrl	[illegible]	[illegible]	8.09	[illegible]	16.5	51.2	60.8	20.3
7012	D F	Ctrl	[illegible]	[illegible]	8.57	4.14	15.8	[illegible]	61.4	18.2
7013	D F	Ctrl	[illegible]	[illegible]	8.47	[illegible]	16.0	52.0	61.5	18.9
7014	D F	Ctrl	[illegible]	[illegible]	7.68	[illegible]	15.5	45.1	61.6	18.8
7015	D F	Ctrl	[illegible]	[illegible]	7.58	8.23	14.3	45.5	60.0	18.8
7016	D F	Ctrl	[illegible]	[illegible]	8.55	[illegible]	15.0	51.0	61.7	18.6
7017	D F	Ctrl	[illegible]	[illegible]	8.60	[illegible]	16.4	51.5	61.9	18.0
7018	D F	Ctrl	[illegible]	[illegible]	8.21	[illegible]	15.1	49.9	60.7	18.4

D = Dosing Phase

S = Scheduled [illegible] [illegible] Animal [illegible] [illegible] [illegible]

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APPENDIX 1 contd. Individual Animal Haematology Parameters

Animal #	Sex	Group	Day Week of Phase	Session Name	RBC (x10^6/µL)	WBC (x10^3/µL)	HGB (g/dL)	HCT (%)	MCV (fL)	MCH (pg)
7019	D F	Ctrl	31.5	S 1 1	7.09	7.71	14.4	49.6	64.?	19.6
7020	D F	Ctrl	31.5	S 1 1	8.92	11.94	15.8	52.0	59.6	17.9
7021	D F		31.5	S 1 1	7.39	[illegible]	[illegible]	44.8	60.6	18.5
7022	D F		31.5	S 1 1	7.64	4.41	14.4	48.1	[illegible]	18.9
7033	D F	2	31.5	S 1 1	8.47	3.66	[illegible]	51.3	60.6	19.1
7034	D F	2	31.5	S 1 1	[illegible]	7.07	14.7	46.8	[illegible]	18.1
7035	D F		31.5	S 1 1	8.51	7.13	[illegible]	50.5	59.4	18.2
7036	D F		31.5	S 1 1	8.78	7.14	16.1	52.4	59.6	18.3
7037	D F		31.5	S 1 1	7.81	9.11	[illegible]	48.1	59.1	18.5
7038	D F	2	31.5	S 1 1	8.66	8.47	16.1	53.2	61.9	18.7
7049	D F		31.5	S 1 1	8.56	[illegible]	15.0	[illegible]	62.1	18.6
7050	D F	2	31.5	S 1 1	9.36	7.86	[illegible]	54.4	56.8	16.9
7051	D F	3	31.5	S 1 1	7.19	6.75	[illegible]	43.8	59.8	19.8
7052	D F	3	31.5	S 1 1	7.62	5.61	14.6	47.1	60.3	18.9
7053	D F	3	31.5	S 1 1	9.16	7.25	13.8	38.3	59.3	17.8
7054	D F		31.5	S 1 1	8.09	6.95	[illegible]	51.0	61.0	19.?
7055	D F		31.5	S 1 1	7.64	5.73	14.1	[illegible]	59.7	18.?
7056	D F	3	31.5	S 1 1	4.81	6.25	[illegible]	53.3	60.3	18.3
7057	D F	4	31.5	S 1 1	7.56	[illegible]	13	44.6	59.?	18.1
7058	D F	3	31.5	S 1 1	9.03	7.15	[illegible]	53.4	60.2	18.4
7059	D F		31.5	S 1 1	8.66	[illegible]	15.1	53.?	61.8	18.9
7060	D F	3	31.5	S 1 1	8.91	8.85	16.8	55.2	61.?	18.9
7071	D F	4	31.5	S 1 1	7.94	5.28	[illegible]	50.9	64.?	19.?
7072	D F	4	31.5	S 1 1	7.75	7.04	[illegible]	50.0	64.?	19.5

D = Dosing Phase

S = Scheduled Animal Room, U = UnScheduled Animal Room, N = Scheduled Necropsy, n = UnScheduled Necropsy

APPENDIX 1 contd. Individual Animal Haematology Parameters

Animal #	Sex	Group	Day Week	Status	RBC (x10⁶/µL)	WBC (x10³/µL)	HGB (g/dL)	HCT (%)	MCV (fL)	MCH (pg)
[illegible]	[illegible]	4	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	12.03	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	7.87	[illegible]	42.9	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

D: Dosing Phase

S: Scheduled Autopsy Room; U: UnScheduled Autopsy Room; N: Scheduled Necropsy; #: UnScheduled Necropsy

APPENDIX I contd. Individual Animal Haematology Parameters

Animal #	Sex	Group	Day Week of Phase	Necropsy Status	RDW (%)	PLT (x10³/µL)	ANEU (x10³/µL)	ALYM (x10³/µL)	AMON (x10³/µL)	AEOS (x10³/µL)	ABAS (x10³/µL)	ALUC (x10³/µL)
7001	D M	Ctrl	16.5	S 1 1	12.1	1126	1.31	7.34	0.3	0.14	[illegible]	0.16
7002	D M	Ctrl	16.5	S 1 1	12.0	0994	1.50	9.50	0.2	0.08	0.02	0.15
7003	D M	Ctrl	16.5	S 1 1	17.3	1051	1.06	6.99	0.5	0.11	0.01	0.16
7004	D M	Ctrl	16.5	S 1 1	12.1	1004	0.97	4.93	0.2	0.03	0.02	0.17
7005	D M	Ctrl	16.5	S 1 1	12.4	1244	1.14	9.99	0.1	0.05	0.04	0.31
7006	D M	Ctrl	16.5	S 1 1	[illegible]	1130	1.09	[illegible]	0.1	0.04	0.09	0.25
7007	D M	Ctrl	16.5	S 1 1	12.4	1242	1.36	8.85	0.9	0.02	0.02	0.16
7008	D M	Ctrl	16.5	S 1 1	12.6	1100	1.14	10.37	0.5	[illegible]	0.01	0.19
7009	D M	Ctrl	16.5	S 1 1	12.9	1308	0.60	6.23	0.3	0.02	0.02	0.14
7010	D M	Ctrl	16.5	S 1 1	15.0	1071	1.44	8.81	0.4	0.14	0.07	0.19
7021	D M	2	16.5	S 1 1	13.6	1085	1.30	4.56	0.2	0.04	0.07	0.07
7022	D M	2	16.5	S 1 1	11.9	1311	1.12	8.10	0.3	0.05	0.02	0.12
7023	D M	2	16.5	S 1 1	12.2	1166	1.76	11.78	0.4	0.15	0.04	0.22
7024	D M	2	16.5	S 1 1	[illegible]	[illegible]	1.01	6.29	0.2	0.08	0.01	0.09
7025	D M	2	16.5	S 1 1	12.5	1290	0.65	4.65	0.1	0.05	0.02	0.16
7026	D M	2	16.5	S 1 1	16.4	1057	1.35	11.36	0.4	0.06	0.04	0.13
7027	D M	2	16.5	S 1 1	[illegible]	1145	1.07	4.76	0.3	0.05	0.01	0.11
7028	D M	2	16.5	S 1 1	12.4	1263	0.96	8.17	0.3	0.07	0.07	0.16
7029	D M	2	16.5	S 1 1	12.2	1247	0.52	5.01	0.3	0.03	0.01	0.14
7030	D M	2	16.5	S 1 1	[illegible]	1214	0.97	8.16	0.3	0.06	0.02	0.19
7041	D M	3	16.5	S 1 1	11.6	1265	0.67	6.24	0.2	0.05	0.03	0.10
7042	D M	3	16.5	S 1 1	12	1137	0.79	6.70	0.2	0.07	0.02	0.11
7043	D M	3	16.5	S 1 1	11	1103	1.22	[illegible]	0.3	0.16	0.03	0.13
7044	D M	3	16.5	S 1 1	[illegible]	[illegible]	0.93	6.51	0.3	0.05	0.01	0.10

D = Dosing Phase

S = Scheduled Animal Room, U = UnScheduled Animal Room, N = Scheduled Necropsy, U = UnScheduled Necropsy

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Copy No. 1/1

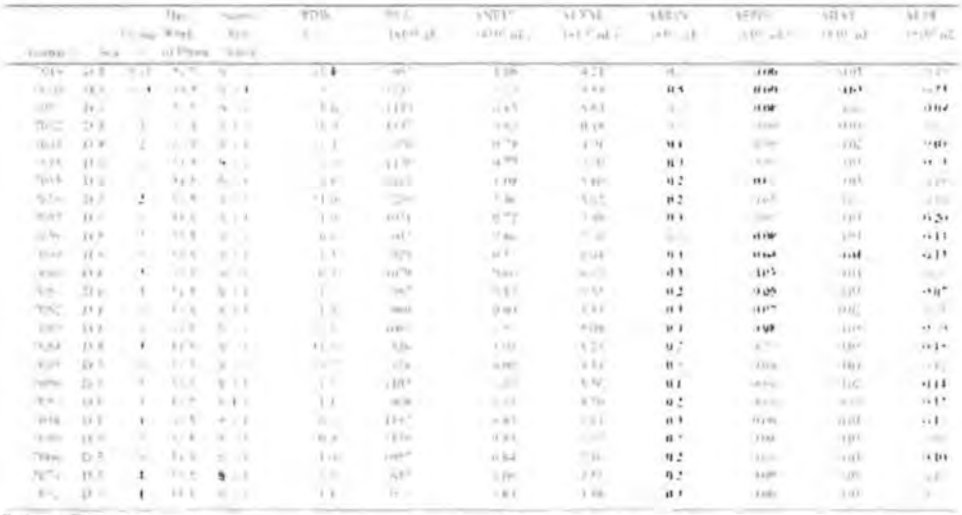
APPENDIX 4 contd. Individual Animal Haematology Parameters

Animal No.	Sex	Dose Level	Week of Phase	Sample Status	RDW (%)	PCT (x10⁹ /L)	ANEU (x10⁹ /L)	LYMPH (x10⁹ /L)	MONO (x10⁹ /L)	EOS (x10⁹ /L)	BASO (x10⁹ /L)	ATYP (x10⁹ /L)
5005	M	1	4	S	13.0	0.49	1.68	4.06	0.2	0.20	0.01	0.06
5006	M	1	13	S	13.1	0.51	1.84	4.04	0.2	0.21	0.01	0.11
5007	M	1	26	S	13.1	0.53	1.73	4.32	0.2	0.16	0.02	0.23
5008	M	1	52	S	13.1	0.52	1.62	4.03	0.2	0.19	0.01	0.10
5009	M	1	26	R	13.2	0.50	1.56	3.98	0.2	0.18	0.01	0.14
5010	M	1	52	R	13.4	0.54	1.71	4.11	0.2	0.19	0.01	0.08
5011	M	4	4	S	13.4	0.51	1.66	4.13	0.2	0.18	0.01	0.09
5012	M	4	13	S	13.3	0.50	1.59	4.01	0.2	0.17	0.01	0.10
5013	M	4	26	S	13.5	0.52	1.64	4.09	0.2	0.18	0.01	0.11
5014	M	4	52	S	13.6	0.53	1.70	4.14	0.2	0.19	0.01	0.09
5015	M	4	26	R	13.5	0.51	1.63	4.07	0.2	0.17	0.01	0.10
5016	M	4	52	R	13.7	0.54	1.72	4.16	0.2	0.18	0.01	0.11
5017	M	4	13	R	13.4	0.52	1.67	4.10	0.2	0.19	0.01	0.12
5018	M	4	4	R	13.3	0.50	1.60	4.05	0.2	0.18	0.01	0.08

D = Dosing Phase

S = Scheduled (control Group 1) / Unscheduled Animal Recovery N = Scheduled Necropsy R = Individual Recovery

APPENDIX 4 contd. Individual Animal Haematology Parameters



APPENDIX 4 contd. Individual Animal Haematology Parameters

Animal	Sex	Group	Day/Week	State	RDW	PLT	ANEU	ALYM	AMON	AEOS	ABAS	ALUC
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
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[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

[illegible]

Standard Animal Room [illegible] Predicted State [illegible]

APPENDIX [illegible] contd. Individual Animal Haematology Parameters

[illegible]	Sex	Group	Day Week of Phase	[illegible]	[illegible]	[illegible]
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[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
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[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

[illegible]

[illegible]

[illegible]

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APPENDIX [illegible] contd. Individual Animal Haematology Parameters

[illegible]	Sex	Group #	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
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[illegible]	M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
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[illegible]	F	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	F	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	F	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	F	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	F	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	F	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	F	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

[illegible]

[illegible]

[illegible] Study No.: 51651
[illegible]

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APPENDIX I contd Individual Animal Haematology Parameters

				Day of Study at Bleed	Sex	Sex	ARBC (x10^12/L)	MCH (pg)

1) Dosing Phase

2) Scheduled Animal Room 1 Unscheduled Animal Room No Isolated Necropsy Unscheduled Necropsy

APPENDIX [illegible] contd. Individual Animal Haematology Parameters

Animal #	Sex	Group	Day/Week of Phase	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	4	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	4	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	4	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	4	[illegible]	[illegible]	[illegible]	29.2
[illegible]	[illegible]	4	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	4	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	4	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	4	[illegible]	[illegible]	[illegible]	[illegible]

APPENDIX 2. Individual Animal Coagulation Parameters

			Hct	Sample	APTT	PT	
	Sex		at Plate				
	M						
	M						
	M						
	M						
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	M						

Clotting Abnormal

S = Satisfactory Normal Results; U = Unsatisfactory Normal Result; N = Not Initiated (Incomplete); X = Unsatisfactory Specimen

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APPENDIX 2 contd. Individual Animal Coagulation Parameters

Animal #	Sex	Group	Day Week of Phase	Event Name	APTT (sec)	PT (sec)
[illegible]	D M	3	[illegible]	S	NO CO	NO CO
[illegible]	D M	[illegible]	[illegible]	S	[illegible]	[illegible]
[illegible]	D M	[illegible]	[illegible]	S	[illegible]	[illegible]
[illegible]	D M	3	[illegible]	S	15	[illegible]
[illegible]	D M	[illegible]	[illegible]	S	18	[illegible]
[illegible]	D M	3	[illegible]	S	18	[illegible]
[illegible]	D M	4	[illegible]	S	22	[illegible]
[illegible]	D M	4	[illegible]	S	[illegible]	[illegible]
[illegible]	D M	4	[illegible]	S	[illegible]	[illegible]
[illegible]	D M	4	[illegible]	S	18	[illegible]
[illegible]	D M	4	[illegible]	S	18	[illegible]
[illegible]	D M	4	[illegible]	S	[illegible]	[illegible]
[illegible]	D M	4	[illegible]	S	18	[illegible]
[illegible]	D M	4	[illegible]	S	[illegible]	[illegible]
[illegible]	D M	4	[illegible]	S	17	[illegible]
[illegible]	D M	4	[illegible]	S	[illegible]	[illegible]
[illegible]	D F	[illegible]	[illegible]	S	[illegible]	[illegible]
[illegible]	D F	[illegible]	[illegible]	S	17	[illegible]
[illegible]	D F	[illegible]	[illegible]	S	[illegible]	[illegible]
[illegible]	D F	[illegible]	[illegible]	S	17	[illegible]
[illegible]	D F	[illegible]	[illegible]	S	[illegible]	[illegible]
[illegible]	D F	[illegible]	[illegible]	S	[illegible]	[illegible]
[illegible]	D F	[illegible]	[illegible]	S	[illegible]	[illegible]
[illegible]	D F	[illegible]	[illegible]	S	[illegible]	[illegible]

D = Dosing Phase

S = Scheduled Animal Room; U = Unscheduled Animal Room; S = Scheduled Necropsy; [illegible]

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APPENDIX 2 contd. Individual Animal Coagulation Parameters

Animal ID	Sex	Group	Day/Week of Phase	Scheduled Status	APTT (sec)	PT (sec)
[illegible]	[illegible]	Ctrl	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	Ctrl	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	17	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
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[illegible]	[illegible]	4	[illegible]	[illegible]	[illegible]	[illegible]

[illegible] Dosing Phase

[illegible] Scheduled Animal [illegible] [illegible] Scheduled Necropsy [illegible]

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APPENDIX 2 contd. Individual Animal Coagulation Parameters

[illegible]	[illegible]	[illegible]	Day Week of Phase	Scenario Status	APTT [illegible]	PT [illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
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[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

[illegible]

S = Scheduled Animal [illegible] U = Unscheduled Animal [illegible] Scheduled [illegible] Scheduled Necropsy

APPENDIX A Individual Animal Clinical Chemistry Parameters

Animal #	Sex	Dosage										
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

[illegible]

APPENDIX 3 contd. Individual Animal Clinical Chemistry Parameters

Animal #	Sex	Group	Day of Dosing	Terminal Body Weight (g)	ALT (U/L)	AST (U/L)	ALP (U/L)	GLDH (U/L)	TBIL (mg/dL)	CK (U/L)
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

[illegible]

[illegible]

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APPENDIX 3 contd. Individual Animal Clinical Chemistry Parameters

[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	AST [illegible]	ALT [illegible]	[illegible]	BUN (mg/dL)	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
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[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
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[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

[illegible]

[illegible]

PSL Study No.: 51651
Eurofins Advinus Study Phase No.: [illegible] PATH Clinical Pathology Phase Report
Copy No. [illegible]

APPENDIX 3 contd. Individual Animal Clinical Chemistry Parameters

Animal #	[illegible]	[illegible]	[illegible] of Plasma	[illegible] Start	Na (mmol/L)	K (mmol/L)	Cl (mmol/L)	AST (U/L)	ALT (U/L)	ALKP (U/L)	BUN (mg/dL)	CA (mg/dL)
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

[illegible]

[illegible] Scheduled Animal Room; [illegible] Unscheduled Animal Room; [illegible] Scheduled Necropsy; [illegible] Unscheduled Necropsy

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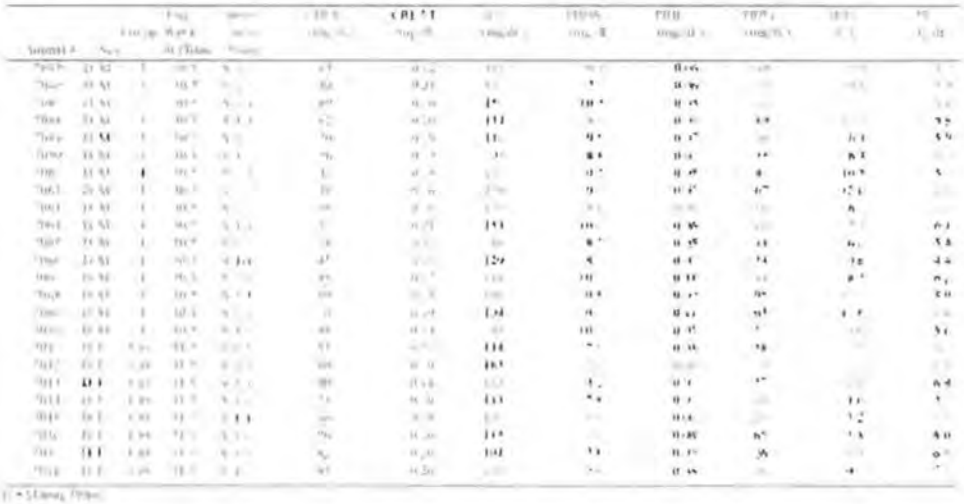
APPENDIX 3 contd. Individual Animal Clinical Chemistry Parameters

Animal	Sex	Group	Week/Phase	Sacrifice Status	[illegible] (mg/dL)	CREAT (mg/dL)	[illegible]	[illegible]	PHOS (mg/dL)	TRIG (mg/dL)	SDH (U/L)	[illegible] (g/dL)
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

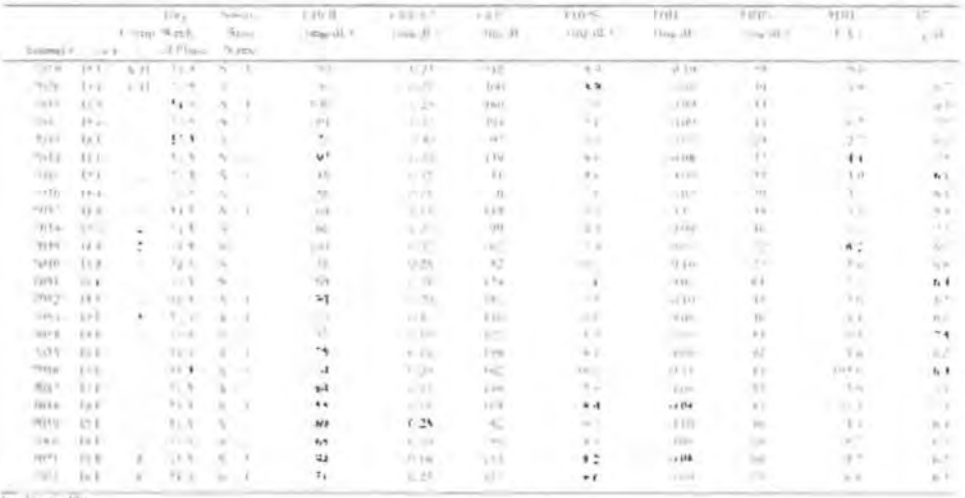
[illegible]: [illegible] Phase

[illegible]

APPENDIX 3 contd. Individual Animal Clinical Chemistry Parameters



APPENDIX J contd. Individual Animal Clinical Chemistry Parameters



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APPENDIX 3 contd.- Individual Animal Clinical Chemistry Parameters

Animal	Sex	[illegible]	[illegible] Week of Phase	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	1.25	[illegible]	[illegible]	[illegible]	29	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

[illegible]

[illegible]

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APPENDIX 3 contd. Individual Animal Clinical Chemistry Parameters

[illegible]	Sex	Group	Day/Week of Phase	[illegible]	[illegible]	[illegible]
[illegible]	DP M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	DP M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	DP M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	DP M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	DP M	[illegible]	[illegible]	[illegible]	[illegible]	2.3
[illegible]	DP M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	DP M	[illegible]	[illegible]	[illegible]	[illegible]	2.2
[illegible]	DP M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	DP M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	DP M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	DP M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	DP M	2	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	DP M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	DP M	2	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	DP M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	DP M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	DP M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	DP M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	DP M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	DP M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	DP M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	DP M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	DP M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	DP M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

DP = Dosing Phase

[illegible]

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APPENDIX 3 contd. Individual Animal Clinical Chemistry Parameters

Animal #	Sex	[illegible]	Day [illegible] Phase	Sample Name	ALB	GLOB
[illegible]	D M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	D M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	D M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	D M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	D M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	D M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	D M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	D M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	D M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	D M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	D M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	D M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	D M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	D M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	D M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	D M	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	D F	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	D F	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	D F	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	D F	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	D F	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	D F	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	D F	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	D F	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

D = Dosing Phase

S = Scheduled Animal Bleeds; U = Unscheduled Animal Bleeds; [illegible]

APPENDIX 5 contd. Individual Animal Clinical Chemistry Parameters

Animal	Sex	Day	Urine Stick	Urine Appearance	ALB (g/dL)	GLOB (g/dL)
001	M	1	3+	Yellow, Clear	3.2	4.9
002	M	1	4+	Yellow, Clear	3.3	4.7
003	M	1	3+	Yellow, Clear	3.4	4.6
004	M	1	3+	Yellow, Clear	3.3	4.8
005	M	1	3+	Yellow, Clear	3.3	4.7
006	M	1	3+	Yellow, Clear	3.3	4.6
007	M	1	3+	Yellow, Clear	3.3	4.6
008	M	1	3+	Yellow, Clear	3.3	4.6
009	M	1	3+	Yellow, Clear	3.3	4.6
010	M	1	3+	Yellow, Clear	3.3	4.6
011	M	1	3+	Yellow, Clear	3.3	4.6
012	M	1	3+	Yellow, Clear	3.3	4.6
013	M	1	3+	Yellow, Clear	3.3	4.6
014	M	1	3+	Yellow, Clear	3.3	4.6
015	M	1	3+	Yellow, Clear	3.3	4.6
016	M	1	3+	Yellow, Clear	3.3	4.6
017	M	1	3+	Yellow, Clear	3.3	4.6
018	M	1	3+	Yellow, Clear	3.3	4.6
019	M	1	3+	Yellow, Clear	3.3	4.6
020	M	1	3+	Yellow, Clear	3.3	4.6

D = Dosing Phase

S = Scheduled Animal Room | U = Unscheduled Animal Room | N = Scheduled Necropsy | U = Unscheduled Necropsy

APPENDIX 3 contd Individual Animal Clinical Chemistry Parameters

					Sex			

D - Dosing Phase

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APPENDIX 4 Individual Animal Clinical Analysis of Urine

[illegible]	Sex	[illegible]	[illegible]	Time	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	SMALL	NEGATIVE	[illegible]	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	SMALL	NEGATIVE	TRACE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	SMALL	NEGATIVE	[illegible]	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	[illegible]	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	[illegible]	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	SMALL	TRACE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	SMALL	TRACE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	[illegible]	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	[illegible]	[illegible]	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	2	[illegible]	[illegible]	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	SMALL	NEGATIVE	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	[illegible]	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	2	[illegible]	[illegible]	NEGATIVE	NEGATIVE	[illegible]	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	[illegible]	TRACE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	[illegible]	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	[illegible]	TRACE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	[illegible]	TRACE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	SMALL	NEGATIVE	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	[illegible]	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]

[illegible]

[illegible]

APPENDIX 4 contd. Individual Animal Clinical Analysis of Urine

Animal	Sex	Group	Day of Phase	Sample Time	UGLU	UPRO	UKET (mg/dL)	UBLD (mg/dL)	UBIL (EU/dL)	pH	SG	COL
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	30	NEGATIVE	NEGATIVE	0.2	[illegible]	[illegible]	YEL
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	SMALL	[illegible]	NEGATIVE	0.2	[illegible]	[illegible]	YEL
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	[illegible]	NEGATIVE	0.2	[illegible]	[illegible]	YEL
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	SMALL	15	NEGATIVE	0.2	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	0.2	[illegible]	[illegible]	YEL
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	15	NEGATIVE	0.2	[illegible]	[illegible]	YEL
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	0.2	[illegible]	[illegible]	YEL
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	15	NEGATIVE	0.2	[illegible]	[illegible]	YEL
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	MODERATE	NEGATIVE	NEGATIVE	0.2	[illegible]	[illegible]	YEL
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	0.2	[illegible]	[illegible]	YEL
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	0.2	[illegible]	[illegible]	YEL
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	[illegible]	NEGATIVE	0.2	[illegible]	[illegible]	YEL
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	0.2	[illegible]	[illegible]	YEL
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	15	NEGATIVE	0.2	[illegible]	[illegible]	YEL
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	[illegible]	NEGATIVE	0.2	[illegible]	[illegible]	YEL
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	30	TRACE	NEGATIVE	0.2	[illegible]	[illegible]	YEL
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	[illegible]	[illegible]	YEL
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	[illegible]	[illegible]	YEL
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	[illegible]	[illegible]	YEL
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	30	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	[illegible]	[illegible]	YEL
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	[illegible]	[illegible]	YEL
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	0.2	[illegible]	[illegible]	[illegible]

D = Dosing Phase

[illegible] Unscheduled Sacrifice; N = Scheduled Necropsy [illegible]

eurofins

APPENDIX 4 contd. Individual Animal Clinical Analysis of Urine

Animal #	Sex	Group	Day/Week of Phase	[illegible]	BIL	[illegible]	KET mg/dL	GLU mg/dL	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	QNS	QNS	QNS	QNS	QNS	QNS	QNS	QNS
[illegible]	[illegible]		[illegible]	[illegible]	SMALL	SMALL	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]		[illegible]	[illegible]	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]		[illegible]	[illegible]	QNS	QNS	QNS	QNS	QNS	QNS	QNS	QNS
[illegible]	[illegible]		[illegible]	[illegible]	SMALL	[illegible]	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]		[illegible]	[illegible]	QNS	QNS	QNS	QNS	QNS	QNS	QNS	QNS
[illegible]	[illegible]		[illegible]	[illegible]	SMALL	SMALL	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]		[illegible]	[illegible]	NEGATIVE	[illegible]	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	SMALL	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]		[illegible]	[illegible]	NEGATIVE	SMALL	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]		[illegible]	[illegible]	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]		[illegible]	[illegible]	NEGATIVE	SMALL	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	[illegible]	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]		[illegible]	[illegible]	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	[illegible]	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	YI
[illegible]	[illegible]		[illegible]	[illegible]	SMALL	NEGATIVE	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]		[illegible]	[illegible]	SMALL	SMALL	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	SMALL	NEGATIVE	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]

[illegible]

[illegible]

eurofins

APPENDIX 4 contd. Individual Animal Clinical Analysis of Urine

[illegible]	[illegible]	[illegible]	Day, Week of Phase	[illegible]	[illegible]	[illegible]	[illegible] (mg/dL)	[illegible] (mg/dL)	[illegible]	pH	[illegible]	[illegible]
[illegible]	D F	1	[illegible]	[illegible]	INS	INS	INS	INS	INS	INS	INS	INS
[illegible]	D F	1	[illegible]	[illegible]	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	6	[illegible]	[illegible]	YEL
[illegible]	D F	1	[illegible]	[illegible]	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	YEL
[illegible]	D F	1	[illegible]	[illegible]	SMALL	NEGATIVE	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	D F	1	[illegible]	[illegible]	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	YEL
[illegible]	D F	1	[illegible]	[illegible]	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	YEL
[illegible]	D F	1	[illegible]	[illegible]	SMALL	[illegible]	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	D F	1	[illegible]	[illegible]	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	[illegible]	[illegible]	[illegible]	[illegible]

[illegible]

[illegible]

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APPENDIX [illegible] contd. Individual Animal Clinical Analysis of Urine

Animal	Sex	[illegible]	[illegible] of Phase	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	MEDIUM	[illegible]	WNL	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	DARK	[illegible]	WNL	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	MEDIUM	[illegible]	WNL	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	MEDIUM	[illegible]	WNL	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	MEDIUM	[illegible]	WNL	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	DARK	[illegible]	WNL	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	MEDIUM	[illegible]	WNL	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	MEDIUM	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	MEDIUM	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	WNL	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	WNL	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	DARK	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	DARK	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	MEDIUM	[illegible]	WNL	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	WNL	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	DARK	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	MEDIUM	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	WNL	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	DARK	[illegible]	WNL	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	MEDIUM	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	DARK	[illegible]	WNL	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	WNL	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	MEDIUM	[illegible]	WNL	

[illegible] Dosing Phase

[illegible]

[illegible]

APPENDIX [illegible] contd. Individual Animal Clinical Analysis of Urine

Animal #	Sex	Group	Day/Week of Phase	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	M	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	[illegible]	
[illegible]	M	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	MEDIUM	[illegible]	[illegible]	
[illegible]	M	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	[illegible]	
[illegible]	M	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	[illegible]	
[illegible]	M	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	MEDIUM	[illegible]	[illegible]	
[illegible]	M	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	[illegible]	
[illegible]	M	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	[illegible]	
[illegible]	M	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	MEDIUM	[illegible]	[illegible]	
[illegible]	M	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	[illegible]	
[illegible]	M	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	DARK	[illegible]	[illegible]	
[illegible]	M	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	MEDIUM	[illegible]	[illegible]	
[illegible]	M	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	DARK	[illegible]	[illegible]	
[illegible]	M	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	[illegible]	
[illegible]	M	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	MEDIUM	[illegible]	[illegible]	
[illegible]	M	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	[illegible]	
[illegible]	M	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	[illegible]	
[illegible]	F	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	MEDIUM	[illegible]	[illegible]	
[illegible]	F	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	[illegible]	
[illegible]	F	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	[illegible]	
[illegible]	F	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	[illegible]	
[illegible]	F	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	DARK	[illegible]	[illegible]	
[illegible]	F	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	[illegible]	
[illegible]	F	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	[illegible]	
[illegible]	F	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	[illegible]	

[illegible]

[illegible]

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APPENDIX 4 contd. Individual Animal Clinical Analysis of Urine

Animal	[illegible]	[illegible]	Days Worn at Phase	[illegible] Status	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	DARK	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	QNS	QNS	DARK	QNS	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	MEDIUM	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	QNS	QNS	DARK	QNS	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	DARK	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	QNS	QNS	DARK	QNS	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	DARK	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	DARK	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	DARK	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	DARK	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	DARK	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	MEDIUM	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	MEDIUM	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	MEDIUM	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	DARK	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	DARK	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	DARK	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	MEDIUM	[illegible]	[illegible]	
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	CLEAR	[illegible]	MEDIUM	[illegible]	[illegible]	

D = Dosing Phase

S = Scheduled Animal Result [illegible] Unscheduled Animal Result [illegible] Scheduled Necropsy [illegible] Unscheduled Necropsy

APPENDIX 4 contd. Individual Animal Clinical Analysis of Urine

Animal	Sex	Group	Day/Week of Phase	[illegible]	[illegible]	[illegible] (mL)	[illegible]	UPROT (mg/dL)	[illegible]	[illegible]
[illegible]	[illegible]	3	[illegible]	[illegible]	INS	INS	MEDIUM	INS	WNL	
7074	[illegible]	3	[illegible]	[illegible]	CLEAR	[illegible]	MEDIUM	[illegible]	WNL	
[illegible]	[illegible]	4	[illegible]	[illegible]	CLEAR	[illegible]	MEDIUM	[illegible]	WNL	
[illegible]	[illegible]	4	[illegible]	[illegible]	CLEAR	[illegible]	MEDIUM	[illegible]	WNL	
[illegible]	[illegible]	4	[illegible]	[illegible]	CLEAR	[illegible]	DARK	[illegible]	WNL	
[illegible]	[illegible]	4	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	WNL	
[illegible]	[illegible]	4	[illegible]	[illegible]	CLEAR	[illegible]	DARK	[illegible]	WNL	
[illegible]	[illegible]	4	[illegible]	[illegible]	CLEAR	[illegible]	LIGHT	[illegible]	WNL	

[illegible]

[illegible]

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11. ANNEXURES

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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 (NGCMA) for monitoring and accreditation

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ANNEXURE 1 contd. GLP Certificate

(i) GLP Certificate India

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ANNEXURE I contd. GLP Certificate

GOVERNMENT OF INDIA
Department of Science and Technology
National Good Laboratory Practice (GLP) Compliance Monitoring Authority (NGCMA)

Based on the inspection and the subsequent follow-up actions

Eurofins Advinus Limited
21&22 Phase II Peenya Industrial Area
Bengaluru – 560058

is certified capable of conducting the below-mentioned tests/studies in compliance with Organization for Economic Co-operation & Development (OECD) Principles of GLP

- **Physical-chemical Testing including Five batch analysis**
- **Toxicity Studies**
- **Mutagenicity Studies**
- **Environmental Toxicity Studies on Aquatic & Terrestrial Organisms**
- **Studies on Behaviour in Water, Soil, and Air; Bioaccumulation**
- **Residue Studies**
- **Analytical and Clinical Chemistry Testing**
- **Others**

The specific areas of expertise, types of chemicals and test systems are listed in annexure enclosed

Validity: November 07, 2017 – November 06, 2020

This certificate is subject to the condition that the test facility complies with the Terms & Conditions of the NGCMA's Document No. GLP/103 and OECD Principles of GLP

Certificate No: GLP/C/111/2017
Issue Date: 24.12.2017

[redacted]
(Dr. Neeraj Sharma)
Head, NGCMA

[redacted]

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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 Five Batch Analysis

Toxicity Studies

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

Mutagenicity Studies

- Chromosomal Aberration Test (in vitro/ in vivo)
- Micronucleus Assay (in vitro/ in vivo)
- Bacterial Reverse Mutation Assay (AMES Test)
- Gene Mutation Test (in vitro)

Environmental Toxicity Studies on Aquatic & Terrestrial Organisms

Studies on Behaviour in Water, Soil, and Air; Bioaccumulation

- Biodegradability Studies
- Environmental Fate Studies

Residue Studies

Analytical and Clinical Chemistry Testing

Others

- Bioanalytical and Toxicokinetics
- Drug Metabolism and Pharmacokinetics & Tissue Distribution
- Safety Pharmacology
- PK and Immunogenicity Analysis in Biologics

Types of Chemicals:

Industrial Chemicals, Pharmaceuticals, Veterinary Drugs, Pesticides, Cosmetic Products, Food Additives, Feed Additives, GMOs, [illegible], [illegible], Devices, Packaging Materials, Nutraceuticals and Medical Devices

Test Systems:

Rat, Mice, Rabbit, Guinea Pig, Dog, Goat, Chicken, Quail, Pigeon, Hamster, Fresh Water Fish, Daphnia, Algae, Honeybee, Earthworm, Salmonella typhimurium, Escherichia coli, Mouse Lymphoma Cell line, Chinese Hamster Ovary (CHO) Cell Line, [illegible] and Human Hepatocellular Carcinoma Cell Line

[illegible]

(Dr. Neeraj Sharma)
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	8:25	.	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	8:03	.	Term	Term
			7052	26	31	5	06/12/19	8:03	.	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; flaccid
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

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: 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	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: 7021	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: 7022	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: 7023	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: 7024	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: 7025	Group: 2	Sex: Male
	Dose: 125	

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: 7026	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 : flaccid

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: 12/6/2019

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:

Escher, Head, Superficial

Gross Pathology Observations [Correlation]:

non correlated finding : no correlated finding [Escher, 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 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: 7051 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: 7052 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: 7053 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: 7054 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: 7055 Group: 3 Sex: Female
Dose: 250

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: 12/5/2019			

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	0.52
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	0.49
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	2.005	0.935	1.936	8.390	0.577
SD	17.3	0.0073	0.128	0.051	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 Wt (g) Day 31	Thyroid-Parathyroid Wt (g) Day 31
7011	0.448	0.019
7012	0.369	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	0.0058
N	10	10

Individual Animal Terminal Body and Organ Weights
PSL Study Number 51651 - A 28-Day Oral Gevage 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	0.44
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	0.087	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	28.2	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

Sex: Female Day(s) Relative to Start Date

125 mg/kg/day Group 2	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	0.49
7052	289	0.084	2.10	1.06	2.02	9.19	0.55
7053	280	0.091	2.04	0.97	2.00	8.79	0.60
7054	270	0.068	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-Parathyroid Wt (g)
	Day 31	Day 31
7051	0.483	0.023
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	0.0624	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	267	0.078	1.94	1.02	2.14	9.71	0.59
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	0.026
7072	0.595	0.027
7073	0.461	0.026
7074	0.380	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	3.69	7.98	31.55	2.23	1.923
7012	0.310	7.51	3.49	7.51	31.69	2.45	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	0.0383	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	1.0909
7017	0.6098
7018	0.7328
7019	0.9881
7020	0.8907
Mean	0.89527
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	33.83	2.19	1.458
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	8.68	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	0.366	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	8.89	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	0.999	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	1.5930
7032	0.7394
7033	1.1475
7034	0.8779
7035	1.0000
7036	0.8182
7037	0.9654
7038	1.4122
7039	0.8935
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	3.55	7.53	32.12	1.89	1.865
7052	0.291	7.27	3.67	6.99	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	0.356	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	8.13	31.78	2.22	1.313
Mean	0.3206	8.066	3.649	7.801	34.258	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	0.98663
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	1.416
7072	0.279	8.30	3.80	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	3.59	7.11	33.28	2.61	1.457
7077	0.361	9.06	3.73	8.98	35.90	2.50	1.848
7078	0.351	8.55	3.51	6.90	37.69	2.23	1.640
7079	0.279	7.39	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	0.13698
N	10

APPENDIX O: INDIVIDUAL ANIMAL ORGAN-TO-BRAIN WEIGHT RATIOS[1]

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

Sex: Female Day(s) Relative to Start Date

0 mg/kg/day Group 1	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
7016	0.034	0.44	0.94	4.55	0.29	0.180	0.0014
7017	0.047	0.47	1.02	4.29	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	0.82	3.62	0.23	0.157	0.0017
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	0.52	0.96	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	0.0012
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	0.0013
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	0.26	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	0.096	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

HSRL INC. HISTO-SCIENTIFIC RESEARCH LABORATORIES | HISTOLOGY PATHOLOGY ARCHIVES

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

TABLE OF CONTENTS

Final Pathology Report
Cambridge Chips, Inc
PSL Study Number 51651

1.0 GLP Compliance Statement- Histopathology Slide Preparation

The histological slide preparation portion of Product Safety Labs 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]

3/11/2

Craig [redacted]
Principal Investigator
Histo-Scientific Research Laboratories (HSRL)

Date

2.0 GLP Compliance Statement- Histopathology Evaluation

The histological slide evaluation portion of Product Safety Labs 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.

[redacted]

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

7 Jul 2020
Date

3/31/2020

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.

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)[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 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:

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

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 flaccid 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 macroscopic 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

[redacted]

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

Date

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

DocuSign Envelope ID: 08102655-6D6A-4B51-AF2F-A7160609C8AD

Expanded Summary Report of Histopathology

Study: [illegible]
Study Title: [illegible] 28 DAY ORAL GAVAGE TOXICITY STUDY [illegible]
Test Article: [illegible]

Males

	[illegible]	Control		1
	[illegible]		1	
	[illegible]		1	
	Number [illegible]	1		1
[illegible]	Number examined	10		
	Number [illegible]	9		
Microgranulomas	[illegible]			
[illegible]	Number examined	10		
	Number [illegible]	[illegible]		
[illegible]	Number examined	10		10
	[illegible]	10		[illegible]
[illegible]	Number examined	10	[illegible]	
	Number [illegible]	10	[illegible]	10
[illegible]	Number examined	10		10
	[illegible]			
[illegible]	[illegible]	10		
	Number [illegible]	10		

[illegible]

DocuSign Envelope ID: 08102655-6D6A-4B51-AF2F-A7160609C8AD

Expanded Summary Report of Histopathology [illegible]

Study: 51651
Study Title: [illegible] 28-DAY ORAL GAVAGE TOXICITY STUDY IN RATS
Test Article: [illegible]

Report Date: [illegible]

Males

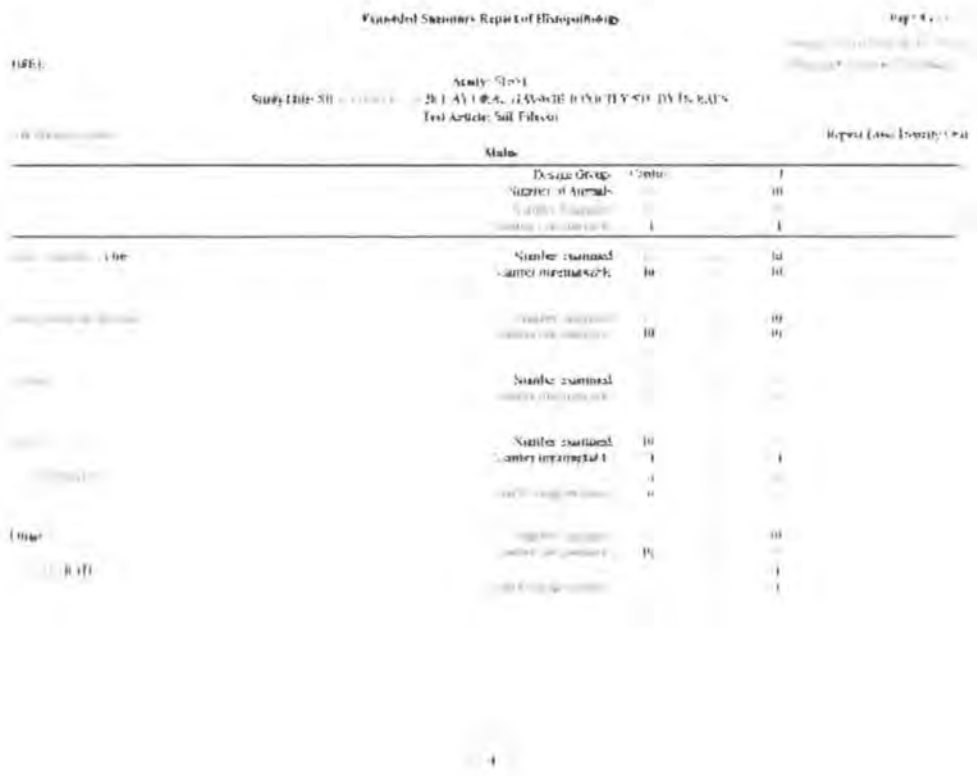
	Dosage Group	Control	[illegible]	[illegible]
	Number Examined	[illegible]	[illegible]	10
	[illegible]	[illegible]	[illegible]	10
	Number Unremarkable	[illegible]	[illegible]	[illegible]
Gland, Parathyroid	Number Examined	10	[illegible]	9
	Number Unremarkable	10	[illegible]	9
Gland, Pituitary	Number Examined	[illegible]	[illegible]	10
	Number Unremarkable	[illegible]	[illegible]	[illegible]
Gland, Prostate	Number Examined	[illegible]	[illegible]	10
	Number Unremarkable	[illegible]	[illegible]	[illegible]
[illegible]		[illegible]	[illegible]	1
	[illegible]	[illegible]	[illegible]	1
[illegible]	Number Examined	10	[illegible]	[illegible]
	Number Unremarkable	10	[illegible]	[illegible]
[illegible]	Number Examined	10	[illegible]	[illegible]
	Number Unremarkable	10	[illegible]	[illegible]
[illegible]		[illegible]	[illegible]	1
	[illegible]	[illegible]	[illegible]	1

Expanded Summary Report of Histopathology

Study Title: [illegible] DAYS IN RATS
Test Article: [illegible]

Males

	Dosage Group	Control	[illegible]	[illegible]
	Number of Animals	[illegible]	[illegible]	[illegible]
	Number Examined	[illegible]	[illegible]	[illegible]
	Number Unexamined	[illegible]	[illegible]	[illegible]
Gland, Salivary, [illegible]	Number Examined	[illegible]	[illegible]	[illegible]
	Number Unremarkable	[illegible]	[illegible]	[illegible]
Gland, Thyroid	Number Examined	[illegible]	[illegible]	[illegible]
	Number Unremarkable	[illegible]	[illegible]	[illegible]
[illegible]	Number Examined	[illegible]	[illegible]	[illegible]
	Number Unremarkable	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]
Kidney	Number Examined	[illegible]	[illegible]	[illegible]
	Number Unremarkable	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	Number Examined	[illegible]	[illegible]	[illegible]
	Number Unremarkable	[illegible]	[illegible]	[illegible]



Extended Summary Report of Histopathology

Study: [illegible]
Test Article: Soil Filtrate

Male

	Dosage Group	Control	1
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	[illegible]	1	1
[illegible] Liver	Number examined	[illegible]	10
	Number unremarkable	10	10
[illegible]	[illegible]	[illegible]	10
	[illegible]	10	10
[illegible]	Number examined	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]
[illegible]	Number examined	10	[illegible]
	Number incomplete	1	1
	[illegible]	1	[illegible]
	[illegible]	0	[illegible]
Lung	[illegible]	[illegible]	10
	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	1
	[illegible]	[illegible]	1

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

Study: [illegible]
Study Title: [illegible]
Test Article: [illegible]

Report Type: [illegible]

Male

	Dosage Group	Control		1
	Number of Animals	[illegible]		[illegible]
	[illegible]	[illegible]		[illegible]
	Number Examined	1		1
[illegible]	Number examined	10		[illegible]
	[illegible]	10		10
[illegible]	Number examined	10		[illegible]
	[illegible]	10		10
[illegible]	Number examined	[illegible]		[illegible]
	Number unremarkable		[illegible]	[illegible]
Thymus	Number examined	[illegible]		10
	[illegible]			[illegible]
[illegible]	[illegible]		0	2
	[illegible]		[illegible]	[illegible]
[illegible]	Number examined	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	Number examined	10	[illegible]	10
	[illegible]	[illegible]		[illegible]

Expanded Summary Report of Histopathology

Study: 51651

Study Title: [illegible]

Test Article: [illegible]

Males

	[illegible]	[illegible]	[illegible]	1
	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	0	1
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]		[illegible]	[illegible]	
	[illegible]		[illegible]	
[illegible]			[illegible]	1
	[illegible]	[illegible]	[illegible]	1
[illegible]	[illegible]	[illegible]	0	[illegible]
	[illegible]	[illegible]	[illegible]	10
[illegible]	[illegible]	[illegible]	[illegible]	10
	[illegible]	[illegible]		[illegible]
[illegible]	[illegible]	[illegible]		[illegible]
	[illegible]	[illegible]		[illegible]
[illegible]	[illegible]	[illegible]		[illegible]
	[illegible]	[illegible]	0	[illegible]

Expanded Summary Report of Histopathology

IISRI [illegible]

Study Title: [illegible]
Test Article: Salt [illegible]

Repeat Dose Toxicity [illegible]

Males

	[illegible]	Control	[illegible]	I
	[illegible]	10	I	10
	[illegible]	10	[illegible]	[illegible]
	Number Unremarkable	I	I	I
Spinal Cord, Lumbar	Number Examined	10	0	[illegible]
	[illegible]	10		10
Spinal Cord, Medulla	Number Examined	10		[illegible]
	Number Unremarkable	10	0	10
Spleen	Number Examined	[illegible]		[illegible]
	[illegible]			10
Stomach	Number Examined	10		[illegible]
	Number Unremarkable	[illegible]		10
[illegible]	Number Examined	10	I	[illegible]
	Number Unremarkable	4	0	[illegible]
[illegible]		I		[illegible]
	[illegible]	[illegible]		[illegible]
Thymus	Number Examined	10		10
	Number Unremarkable	[illegible]		10

Study: 51651
StudyTitle: SILK FIBROIN: A 28-DAY ORAL GAVAGE TOXICITY STUDY IN RATS
Test Article: Silk Fibroin

Rat/Sprague-Dawley

Males

	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

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
Artery, Aorta	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Bone Marrow	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Bone, Femur	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Bone, Sternum	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Brain	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Cervix	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10

Females

	Dosage Group:	Control	2	3	4
	Number of Animals:	10	3	5	10
	Number Examined:	10	3	5	10
	Number Unremarkable:	1	0	0	1
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: [illegible]
Study Title: [illegible] ORAL GAVAGE TOXICITY STUDY IN [illegible]
Test Article: [illegible]

Females

	Dosage Group	Control	2	3	4
	Number of Animals	10	[illegible]	[illegible]	10
	[illegible]	[illegible]	7	[illegible]	10
	[illegible]	1	[illegible]	[illegible]	1
Gland, Pituitary	[illegible]	10	[illegible]	[illegible]	[illegible]
	[illegible]	10	[illegible]	0	10
Gland, [illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Gland, Salivary [illegible]	Number Examined	[illegible]		0	[illegible]
	Number Unremarkable	[illegible]		0	10
[illegible]		1	[illegible]	[illegible]	0
	[illegible]	1	0	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]		[illegible]	[illegible]
	Number Unremarkable	[illegible]	[illegible]	0	[illegible]
Gland, Thyroid	[illegible]	[illegible]	[illegible]	0	10
	[illegible]	10	[illegible]	[illegible]	10
[illegible]	[illegible]	10	0	0	10
	[illegible]	8	[illegible]	[illegible]	[illegible]

Extended Summary Report of Histopathology

Females

Dosage Group		2		1
Number of Animals		1		
		1		1
	1	1		1
Number examined				
	1	2	1	
Number examined	1			
	1	1	1	1
Number examined	1			1
		1	1	1
		1		1
	1			
	1			

Expanded Summary Report of Histopathology

Study:
Test Article: Soil Poison

	Females				
	Dosage Group	Control			1
	Number of Animals	10	3	5	10
	Number Examined	1			1
	Number examined			0	
					10
Liver	number examined	10			10
				0	6
		3			1
	Total Examined	1			1
Lungs					
Lymph Node, Mandibular					
	Necrosis				
					10
Muscle, Skeletal					

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HSRL

Study: 51651
StudyTitle: SILK FIBROIN: A 28-DAY ORAL GAVAGE TOXICITY STUDY IN RATS
Test 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, Peripheral (sciatic)	Number examined:	10	0	0	10
	Number unremarkable:	10	0	0	10
Nose	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

Study: 51651

Study Title: [illegible]

Test Article: [illegible]

Females

	Dosage Group	Control	[illegible]	[illegible]	[illegible]
	Number of Animals	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	3	[illegible]	[illegible]
	[illegible]	1	[illegible]	[illegible]	1
[illegible]	Number Examined	[illegible]	[illegible]	[illegible]	[illegible]
	[illegible]	[illegible]	[illegible]	0	
[illegible]		1			
	[illegible]	1	[illegible]		[illegible]
[illegible]	[illegible]	[illegible]		[illegible]	[illegible]
	[illegible]	[illegible]		0	[illegible]
[illegible]	[illegible]	[illegible]		[illegible]	[illegible]
	[illegible]	[illegible]			
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Number Unexamined	[illegible]	0		[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
	Number Unremarkable	[illegible]		[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	0	0	[illegible]
	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Females

	Dosage Group:	Control	2	3	4
	Number of Animals:	10	5	5	10
	Number Examined:	10	5	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

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Study: 51651

StudyTitle: 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:	1	0	0	1
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