

Table 7 Necropsy in male microminipigs

Study No. SBL703-023

Findings	Group Animal No.	1				2				3				
		1	5	16	17	6	7	9	10	11	12	13	14	15
Pericardial cavity														
Retention, pericardial fluid		-	-	-	-	-	-	-	-	-	-	-	P	P
Aorta														
White striation, abdominal aorta		-	-	-	-	-	-	-	-	-	-	-	P	P
Heart														
Red focus, epicardium		-	-	-	-	-	-	-	-	-	-	-	P	P
Carotid artery														
Thickening, vascular wall		-	-	-	-	-	-	-	P	-	-	-	-	-
Nodule, intravascular		-	-	-	-	-	-	-	-	-	-	P	-	-
Induration, vascular wall		-	-	-	-	-	-	-	-	-	-	-	P	P
Kidney														
Cyst, left		-	P	-	-	-	-	-	-	-	-	-	-	-

Notes) - : No abnormal changes P : Non-graded changes

Table 8-2

Organ weight in male microminipigs (End of the dosing period)

Study No. SBL703-023

Group	Animal No.	Liver g	Kidn.R g	Kidn.L g	Kidn.R&L g	Epid.R g	Epid.L g	Epid.R&L g	Sem.V. g	Prost. g	Omentum g	Mes.adip. g
1	1	466.3	61.4	63.9	125.3	13.2	13.2	26.4	114.2	9.9	37.6	129.5
	5	172.2	19.7	19.9	39.6	12.8	13.6	26.4	47.4	8.1	1.3	23.7
	16	305.1	34.4	35.0	69.4	15.1	15.6	30.7	40.2	9.1	7.4	57.9
	17	453.7	40.4	37.3	77.7	12.6	11.8	24.4	68.2	6.2	12.2	80.6
	Mean	349.33	38.98	39.03	78.00	13.43	13.55	26.98	67.50	8.33	14.63	72.93
	±S.D.	138.93	17.30	18.29	35.52	1.14	1.57	2.66	33.32	1.60	15.95	44.38
2	6	412.3	63.7	65.9	129.6	10.7	11.7	22.4	75.5	11.3	88.8	296.8
	7	433.1	49.9	51.8	101.7	15.2	17.9	33.1	71.7	9.2	45.7	113.6
	9	323.2	42.9	43.4	86.3	16.0	18.0	34.0	103.7	14.1	18.5	107.2
	10	401.7	67.3	62.1	129.4	15.5	15.7	31.2	305.9	14.6	33.1	132.2
	Mean	392.58	55.95	55.80	111.75	14.35	15.83	30.18	139.20	12.30*	46.53	162.45
	±S.D.	48.05	11.49	10.19	21.44	2.46	2.95	5.31	112.05	2.53	30.30	90.19
3	11	490.3	53.6	57.6	111.2	13.9	14.8	28.7	235.7	12.2	32.3	105.7
	12	424.9	44.8	45.5	90.3	13.1	12.5	25.6	106.8	11.2	56.2	86.7
	13	366.6	51.0	50.3	101.3	19.9	20.9	40.8	86.7	14.3	32.3	168.4
	14	268.2	32.9	34.9	67.8	24.4	21.2	45.6	343.4	10.1	13.4	46.0
	15	320.1	51.9	54.0	105.9	13.5	13.4	26.9	296.9	16.6	27.6	88.3
Mean	374.02	46.84	48.46	95.30	16.96	16.56	33.52	213.90*	12.88**	32.36	99.02	
	±S.D.	86.99	8.47	8.81	17.19	5.01	4.18	9.07	113.78	2.59	15.42	44.54

Notes) Kidn.R : Kidney (Right) Kidn.L : Kidney (Left) Kidn.R&L : Kidney (Right&Left)
Epid.R : Epididymis (Right) Epid.L : Epididymis (Left) Epid.R&L : Epididymis (Right&Left)
Sem.V. : Seminal vesicle Prost. : Prostate Omentum : Omentum
Mes.adip. : Mesenteric adipose tissue (including mesenteric lymph node)

* P<0.05 , ** P<0.01 : Significantly different from Group 1.

Table 8-4

Relative organ weight in male microminipigs (End of the dosing period)

Study No. SBL703-023

Group	Animal No.	Liver g/kg	Kidn.R g/kg	Kidn.L g/kg	Kidn.R&L g/kg	Epid.R g/kg	Epid.L g/kg	Epid.R&L g/kg	Sem.V. g/kg	Prost. g/kg	Omentum g/kg	Mes.adip. g/kg
1	1	16.08	2.12	2.20	4.32	0.46	0.46	0.91	3.94	0.34	1.3	4.5
	5	15.80	1.81	1.83	3.63	1.17	1.25	2.42	4.35	0.74	0.1	2.2
	16	12.40	1.40	1.42	2.82	0.61	0.63	1.25	1.63	0.37	0.3	2.4
	17	17.93	1.60	1.47	3.07	0.50	0.47	0.96	2.70	0.25	0.5	3.2
	Mean	15.553	1.733	1.730	3.460	0.685	0.703	1.385	3.155	0.425	0.55	3.08
	±S.D.	2.304	0.308	0.363	0.666	0.329	0.373	0.706	1.235	0.216	0.53	1.04
2	6	10.77	1.66	1.72	3.38	0.28	0.31	0.58	1.97	0.30	2.3	7.7
	7	14.83	1.71	1.77	3.48	0.52	0.61	1.13	2.46	0.32	1.6	3.9
	9	15.25	2.02	2.05	4.07	0.75	0.85	1.60	4.89	0.67	0.9	5.1
	10	13.39	2.24	2.07	4.31	0.52	0.52	1.04	10.20	0.49	1.1	4.4
	Mean	13.560	1.908	1.903	3.810	0.518	0.573	1.088	4.880	0.445	1.48*	5.28*
	±S.D.	2.023	0.273	0.183	0.451	0.192	0.224	0.418	3.769	0.173	0.62	1.69
3	11	18.43	2.02	2.17	4.18	0.52	0.56	1.08	8.86	0.46	1.2	4.0
	12	17.34	1.83	1.86	3.69	0.53	0.51	1.04	4.36	0.46	2.3	3.5
	13	14.96	2.08	2.05	4.13	0.81	0.85	1.67	3.54	0.58	1.3	6.9
	14	12.96	1.59	1.69	3.28	1.18	1.02	2.20	16.59	0.49	0.6	2.2
	15	10.85	1.76	1.83	3.59	0.46	0.45	0.91	10.06	0.56	0.9	3.0
	Mean	14.908	1.856	1.920	3.774	0.700	0.678	1.380	8.682*	0.510	1.26	3.92
	±S.D.	3.106	0.199	0.190	0.380	0.301	0.245	0.544	5.234	0.057	0.64	1.79

Notes) Kidn.R : Kidney (Right) Kidn.L : Kidney (Left) Kidn.R&L : Kidney (Right&Left)
Epid.R : Epididymis (Right) Epid.L : Epididymis (Left) Epid.R&L : Epididymis (Right&Left)
Sem.V. : Seminal vesicle Prost. : Prostate Omentum : Omentum
Mes.adip. : Mesenteric adipose tissue (including mesenteric lymph node)

* P<0.05 : Significantly different from Group 1.

Group	Animal No.	Sign code	Day of dosing																			
			7	8	9	10	1	2	3	4	5	6	7	8								
1	2	cG	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9
		fB	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9
		3	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9
		4	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9

Notes) - : No abnormal signs + : Non-graded signs 1 : Slight 2 : Moderate 3 : Severe
 cG:Lateral position fB:Hypothermia

Group	Animal No.	Sign code	Day of dosing															
			1 4	5	6	7	8	9	2 0	3	4	5	6	7	8	9		
1	2	cG	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
		fB	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
		3	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
		4	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

Notes) - : No abnormal signs + : Non-graded signs 1 : Slight 2 : Moderate 3 : Severe
 cG:Lateral position fB:Hypothermia

Group	Animal No.	Sign code	Day of dosing												No. of days						
			8	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3			
1	2	cG																1	0	0	0
		fB																1	0	0	0
																					(1)
																					0
																					(1)

Notes) - : No abnormal signs + : Non-graded signs 1 : Slight 2 : Moderate 3 : Severe
 () : Total number of days observed
 cG:Lateral position fB:Hypothermia

Appendix 2-1 Body weight (kg) in male microminipigs

Study No. SBL703-023

Group	Animal No.	Pre	1w	2w	3w	4w	5w	6w	7w	8w	9w	10w	11w	12w	13w
1	2	4.0	3.9	4.0	4.1	4.2	4.2	4.3	4.4	4.3	4.3	4.3	4.3	4.4	4.4
	3	4.7	4.7	4.7	4.9	5.3	5.3	5.6	5.8	6.1	6.2	6.4	6.6	6.9	7.1
	4	3.1	3.1	3.1	3.0	3.1	2.9	2.9	2.9	2.8	2.7	2.5	2.4		
	Mean	3.93	3.90	3.93	4.00	4.20	4.13	4.27	4.37	4.40	4.40	4.40	4.43	5.65	5.75
	±S.D.	0.80	0.80	0.80	0.95	1.10	1.20	1.35	1.45	1.65	1.75	1.95	2.10		

Appendix 2-2 Body weight (kg) in male microminipigs

Study No. SBL703-023

Group	Animal No.	14w	15w	16w	17w	18w	19w	20w	21w	22w	23w	24w	25w	26w	27w
1	2	4.4	4.2	4.1	4.1	3.9	4.1	4.0	3.8	4.1	3.8	4.0	4.0	3.9	3.8
	3	7.1	7.1	7.0	7.1	7.0	6.9	6.8	6.7	6.7	6.5	6.8	7.0	6.6	6.4
	4														
	Mean	5.75	5.65	5.55	5.60	5.45	5.50	5.40	5.25	5.40	5.15	5.40	5.50	5.25	5.10

Group	Animal No.	RBC (10 ⁶ /μL)									
		Pre	2w	4w	8w	12w	16w	20w	24w	28w	32w
1	2	7.55	7.52	7.29	7.84	8.04	7.43	6.67	6.04	6.65	
	3	7.07	8.19	7.64	8.06	6.59	7.94	7.94	7.38	6.92	7.06
	4	8.74	8.72	7.12	8.23						
	Mean	7.787	8.143	7.350	8.043	7.315	7.685	7.305	6.710	6.785	
	±S.D.	0.860	0.601	0.265	0.196						

Note) RBC : Erythrocyte count

Group	Animal No.	Hb (g/dL)									
		Pre	2w	4w	8w	12w	16w	20w	24w	28w	32w
1	2	13.7	14.6	14.4	15.5	16.0	14.7	13.2	12.1	13.5	
	3	13.4	15.3	14.8	15.9	13.3	16.2	16.1	15.0	14.4	15.1
	4	14.8	15.6	13.9	16.2						
	Mean	13.97	15.17	14.37	15.87	14.65	15.45	14.65	13.55	13.95	
	±S.D.	0.74	0.51	0.45	0.35						

Note) Hb : Hemoglobin concentration

Group	Animal No.	Ht (%)									
		Pre	2w	4w	8w	12w	16w	20w	24w	28w	32w
1	2	42.5	45.2	43.8	45.7	46.8	41.8	37.5	34.6	37.2	
	3	40.7	46.2	46.6	47.2	38.7	45.8	46.1	42.9	40.0	41.1
	4	46.8	47.8	41.5	46.8						
	Mean	43.33	46.40	43.97	46.57	42.75	43.80	41.80	38.75	38.60	
	±S.D.	3.13	1.31	2.55	0.78						

Note) Ht : Hematocrit value

Group	Animal No.	MCV (fL)									
		Pre	2w	4w	8w	12w	16w	20w	24w	28w	32w
1	2	56.3	60.1	60.0	58.3	58.3	56.2	56.2	57.3	56.0	
	3	57.5	56.4	61.0	58.5	58.7	57.6	58.0	58.1	57.9	58.3
	4	53.5	54.8	58.2	56.8						
	Mean ±S.D.	55.77 2.05	57.10 2.72	59.73 1.42	57.87 0.93	58.50	56.90	57.10	57.70	56.95	

Note) MCV : Mean corpuscular volume

Group	Animal No.	MCH (pg)									
		Pre	2w	4w	8w	12w	16w	20w	24w	28w	32w
1	2	18.1	19.5	19.8	19.8	20.0	19.8	19.8	20.0	20.3	
	3	18.9	18.6	19.3	19.7	20.2	20.5	20.3	20.3	20.9	21.4
	4	17.0	17.8	19.5	19.7						
	Mean	18.00	18.63	19.53	19.73	20.10	20.15	20.05	20.15	20.60	
	±S.D.	0.95	0.85	0.25	0.06						

Note) MCH : Mean corpuscular hemoglobin

Group	Animal No.	MCHC (g/dL)									
		Pre	2w	4w	8w	12w	16w	20w	24w	28w	32w
1	2	32.2	32.4	33.0	34.0	34.3	35.1	35.2	34.9	36.2	
	3	32.9	33.0	31.7	33.6	34.5	35.5	35.0	35.0	36.1	36.7
	4	31.7	32.6	33.4	34.7						
	Mean	32.27	32.67	32.70	34.10	34.40	35.30	35.10	34.95	36.15	
	±S.D.	0.60	0.31	0.89	0.56						

Note) MCHC : Mean corpuscular hemoglobin concentration