

Table 6 - continued Hematological findings

Group and dose	Differential leukocyte count												
	Eosinophils (10 ³ /μL)	Neutrophils (10 ³ /μL)	Lymphocytes (10 ³ /μL)	Basophils (10 ³ /μL)	Monocytes (10 ³ /μL)	Large unstained cells (10 ³ /μL)	N	Mean	S.D.				
Anti-KLH antibody 3 mg/kg	6	6	6	6	6	6	6	0.07	1.46	7.44	0.02	0.14	0.10
	±0.03	±0.74	±0.99	±0.01	±0.05	±0.03							
Anti-HMGB1 antibody 0.75 mg/kg	6	6	6	6	6	6	6	0.06	1.20	7.62	0.02	0.14	0.13
	±0.03	±0.48	±2.03	±0.01	±0.03	±0.06							
Anti-HMGB1 antibody 1.5 mg/kg	6	6	6	6	6	6	6	0.05	0.82	6.36	0.02	0.11	0.07
	±0.02	±0.34	±0.88	±0.01	±0.03	±0.02							
Anti-HMGB1 antibody 3.0 mg/kg	6	6	6	6	6	6	6	0.07	1.14	8.58	0.03	0.17	0.10
	±0.02	±0.30	±1.57	±0.01	±0.09	±0.03							

Not significantly different from Anti-KLH antibody group.

Table 7 Biochemical findings

Group and dose	T.Protein (g/dL)	α 1-Globulin (g/dL)	α 2-Globulin (g/dL)	β -Globulin (g/dL)	γ -Globulin (g/dL)	Albumin (g/dL)	T.Bilirubin (mg/dL)	AST (IU/L)	ALT (IU/L)
Anti-KLH antibody 3 mg/kg	N	6	6	6	6	6	6	6	6
	Mean	5.1	0.91	0.39	0.72	0.21	2.85	86	19
	S.D.	± 0.2	± 0.05	± 0.02	± 0.03	± 0.05	± 0.12	± 0.0	± 2
Anti-HMGB1 antibody 0.75 mg/kg	N	6	6	6	6	6	6	6	6
	Mean	5.0	0.88	0.38	0.70	0.20	2.86	85	20
	S.D.	± 0.1	± 0.14	± 0.02	± 0.03	± 0.07	± 0.08	± 0.0	± 1
Anti-HMGB1 antibody 1.5 mg/kg	N	6	6	6	6	6	6	6	6
	Mean	5.0	0.91	0.38	0.71	0.17	2.86	79	21
	S.D.	± 0.2	± 0.10	± 0.04	± 0.06	± 0.03	± 0.09	± 0.0	± 3
Anti-HMGB1 antibody 3.0 mg/kg	N	6	6	6	6	6	6	6	6
	Mean	5.0	0.84	0.40	0.72	0.17	2.89	85	23
	S.D.	± 0.2	± 0.06	± 0.04	± 0.05	± 0.02	± 0.10	± 0.0	± 4

Not significantly different from Anti-KLH antibody group.

Table 7 - continued Biochemical findings

Group and dose	N	ALP (IU/L)	T.Cholesterol (mg/dL)	Triglycerides (mg/dL)	Phospholipids (mg/dL)	Glucose (mg/dL)	BUN (mg/dL)	Creatinine (mg/dL)	IP (mg/dL)	Ca (mg/dL)
Anti-KLH antibody 3 mg/kg	N	6	6	6	6	6	6	6	6	6
	Mean	587	83	66	142	104	12.7	0.3	9.7	9.8
	S.D.	±142	±12	±23	±17	±15	±2.4	±0.0	±0.6	±0.2
Anti-HMGB1 antibody 0.75 mg/kg	N	6	6	6	6	6	6	6	6	6
	Mean	542	87	50	138	104	12.1	0.3	9.6	9.9
	S.D.	±40	±11	±17	±17	±5	±1.3	±0.0	±0.4	±0.2
Anti-HMGB1 antibody 1.5 mg/kg	N	6	6	6	6	6	6	6	6	6
	Mean	665	82	53	141	99	14.4	0.3	9.7	9.7
	S.D.	±89	±18	±26	±22	±11	±2.3	±0.0	±0.9	±0.2
Anti-HMGB1 antibody 3.0 mg/kg	N	6	6	6	6	6	6	6	6	6
	Mean	482	80	52	136	102	12.2	0.3	10.0	9.7
	S.D.	±69	±13	±31	±21	±16	±2.7	±0.0	±1.1	±0.2

Not significantly different from Anti-KLH antibody group.

Table 7 - continued Biochemical findings

Group and dose	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)
Anti-KLH antibody	N	6	6
3 mg/kg	Mean	144.2	102.7
	S.D.	±0.9	±1.4
Anti-HMGB1 antibody	N	6	6
0.75 mg/kg	Mean	145.5	103.4
	S.D.	±1.1	±0.9
Anti-HMGB1 antibody	N	6	6
1.5 mg/kg	Mean	145.5	103.9
	S.D.	±1.3	±1.2
Anti-HMGB1 antibody	N	6	6
3.0 mg/kg	Mean	145.5	102.5
	S.D.	±1.2	±1.7

Not significantly different from Anti-KLH antibody group.

Table 8 Necropsy findings

Organs and findings	Group and dose				Number of animals
	Anti-KLH antibody 3 mg/kg	Anti-HMGB1 antibody 0.75 mg/kg	Anti-HMGB1 antibody 1.5 mg/kg	Anti-HMGB1 antibody 3.0 mg/kg	
All organs and tissues	NR	NR	NR	NR	6

No appreciable changes in all other organs and tissues.

Table 9 Absolute and relative organ weights

Group and dose	Final body weight		Brain		Pituitary		Submaxillary glands	
	N	(g)	(g)	(g/100 gB.W.)	(mg)	(mg/100 gB.W.)	(g)	(g/100 gB.W.)
Anti-KLH antibody 3 mg/kg	N	6	6	6	6	6	6	6
	Mean	215.2	2.02	0.94	8.8	4.1	0.44	0.21
	S.D.	±7.4	±0.03	±0.04	±0.9	±0.3	±0.02	±0.01
Anti-HMGB1 antibody 0.75 mg/kg	N	6	6	6	6	6	6	6
	Mean	214.6	1.99	0.93	9.7	4.5	0.43	0.20
	S.D.	±5.5	±0.07	±0.04	±0.9	±0.4	±0.03	±0.01
Anti-HMGB1 antibody 1.5 mg/kg	N	6	6	6	6	6	6	6
	Mean	215.8	2.06	0.96	9.0	4.2	0.44	0.20
	S.D.	±8.1	±0.05	±0.03	±1.0	±0.4	±0.02	±0.01
Anti-HMGB1 antibody 3.0 mg/kg	N	6	6	6	6	6	6	6
	Mean	213.5	2.01	0.94	9.6	4.5	0.43	0.20
	S.D.	±9.2	±0.07	±0.05	±1.5	±0.5	±0.06	±0.02

Not significantly different from Anti-KLH antibody group.

Table 9 - continued Absolute and relative organ weights

Group and dose	Thyroids		Heart		Lungs		Thymus	
	(mg)	(mg/100 gB.W.)	(g)	(g/100 gB.W.)	(g)	(g/100 gB.W.)	(g)	(g/100 gB.W.)
Anti-KLH antibody 3 mg/kg	N	6	6	6	6	6	6	6
	Mean	15.8	7.3	0.98	0.46	1.08	0.50	0.61
	S.D.	±2.2	±1.0	±0.08	±0.04	±0.03	±0.03	±0.15
Anti-HMGB1 antibody 0.75 mg/kg	N	6	6	6	6	6	6	6
	Mean	15.5	7.2	1.02	0.48	1.10	0.51	0.64
	S.D.	±2.2	±0.9	±0.06	±0.02	±0.07	±0.04	±0.08
Anti-HMGB1 antibody 1.5 mg/kg	N	6	6	6	6	6	6	6
	Mean	15.1	7.0	1.02	0.47	1.09	0.51	0.59
	S.D.	±1.8	±0.8	±0.11	±0.04	±0.05	±0.02	±0.11
Anti-HMGB1 antibody 3.0 mg/kg	N	6	6	6	6	6	6	6
	Mean	15.3	7.2	1.01	0.48	1.10	0.52	0.67
	S.D.	±1.2	±0.6	±0.04	±0.02	±0.06	±0.03	±0.12

Not significantly different from Anti-KLH antibody group.

Table 9 - continued Absolute and relative organ weights

Group and dose	Liver		Spleen		Kidneys		Adrenals		
	(g)	(g/100 gB.W.)	(g)	(g/100 gB.W.)	(g)	(g/100 gB.W.)	(mg)	(mg/100 gB.W.)	
Anti-KLH antibody 3 mg/kg	N	6	6	6	6	6	6	6	
	Mean	7.76	3.60	0.69	0.32	1.96	0.91	52.0	24.1
	S.D.	±0.62	±0.17	±0.14	±0.06	±0.10	±0.04	±5.2	±2.0
Anti-HMGB1 antibody 0.75 mg/kg	N	6	6	6	6	6	6	6	
	Mean	7.57	3.53	0.71	0.33	1.97	0.92	48.9	22.8
	S.D.	±0.32	±0.07	±0.08	±0.04	±0.14	±0.06	±5.4	±2.6
Anti-HMGB1 antibody 1.5 mg/kg	N	6	6	6	6	6	6	6	
	Mean	7.58	3.52	0.69	0.32	1.97	0.91	50.5	23.4
	S.D.	±0.32	±0.11	±0.09	±0.04	±0.18	±0.07	±5.0	±2.0
Anti-HMGB1 antibody 3.0 mg/kg	N	6	6	6	6	6	6	6	
	Mean	7.45	3.49	0.70	0.33	2.02	0.94	47.9	22.4
	S.D.	±0.54	±0.14	±0.06	±0.03	±0.24	±0.08	±3.9	±1.4

Not significantly different from Anti-KLH antibody group.

Table 9 - continued Absolute and relative organ weights

Group and dose	Seminal vesicle		Prostate		Epididymides		Testes	
	(\bar{x})	(\bar{x} /100 gB.W.)	(\bar{x})	(\bar{x} /100 gB.W.)	(\bar{x})	(\bar{x} /100 gB.W.)	(\bar{x})	(\bar{x} /100 gB.W.)
Anti-KLH antibody 3 mg/kg	N	6	6	6	6	6	6	6
	Mean	0.51	0.24	0.23	0.11	0.32	0.15	2.32
	S.D.	± 0.11	± 0.05	± 0.03	± 0.02	± 0.01	± 0.01	± 0.08
Anti-HMGB1 antibody 0.75 mg/kg	N	6	6	6	6	6	6	6
	Mean	0.56	0.26	0.22	0.10	0.33	0.16	2.45
	S.D.	± 0.09	± 0.04	± 0.05	± 0.02	± 0.03	± 0.01	± 0.18
Anti-HMGB1 antibody 1.5 mg/kg	N	6	6	6	6	6	6	6
	Mean	0.54	0.25	0.24	0.11	0.32	0.15	2.42
	S.D.	± 0.03	± 0.01	± 0.03	± 0.01	± 0.03	± 0.01	± 0.10
Anti-HMGB1 antibody 3.0 mg/kg	N	6	6	6	6	6	6	6
	Mean	0.57	0.27	0.21	0.10	0.31	0.15	2.44
	S.D.	± 0.04	± 0.02	± 0.04	± 0.02	± 0.03	± 0.02	± 0.13

Not significantly different from Anti-KLH antibody group.

Table 10 Histopathological findings

Organs and findings	Group and dose																			
	Anti-KLH antibody 3 mg/kg			Anti-HMGB1 antibody 0.75 mg/kg			Anti-HMGB1 antibody 1.5 mg/kg			Anti-HMGB1 antibody 3.0 mg/kg										
	-	+	++	+	++	+++	-	+	++	+	++	+++	-	+	++	+	++	+++	Total	
	Number of animals																			
	6			6			6			6			6			6			Total	
Digestive system																				
Tongue			NR(6)			(0)														
Esophagus			NR(6)			(0)														
Stomach			NR(6)			(0)														
Duodenum			NR(6)			(0)														
Jejunum			NR(6)			(0)														
Ileum			NR(6)			(0)														
Cecum			NR(6)			(0)														
Colon			NR(6)			(0)														
Rectum			NR(6)			(0)														
Submaxillary gland			NR(6)			(0)														
Sublingual gland			NR(6)			(0)														
Parotid gland			NR(6)			(0)														
Liver			NR(6)			(0)														
Pancreas			NR(6)			(0)														
Respiratory system																				
Trachea			NR(6)			(0)														
Lung			(6)			(0)														
Metaplasia,osseous	5	1	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
Embolus,hair	5	1	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
Accumulation,foam cell,alveolus	6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hematopoietic system																				
Thymus			NR(6)			(0)														
Submaxillary lymph node			NR(6)			(0)														
Mesenteric lymph node			NR(6)			(0)														
Spleen			(6)			(0)														
Hematopoiesis,extramedullary	4	2	0	0	0	0	2	2	0	0	0	0	0	0	0	0	0	0	0	0
Bone marrow (sternum)			NR(6)			(0)														
Bone marrow (femur)			NR(6)			(0)														
Cardiovascular system																				
Heart			NR(6)			(0)														
Aorta			NR(6)			(0)														

Grade sign: -, none; +, mild; ++, moderate; +++, marked.
 NR: no remarkable changes.
 Figures in parentheses are number of animals with tissues examined histopathologically.

Table 10 - continued Histopathological findings

Organs and findings	Group and dose						Group and dose						Group and dose								
	Anti-KLH antibody 3 mg/kg		Anti-HMGB1 antibody 0.75 mg/kg		Anti-HMGB1 antibody 1.5 mg/kg		Anti-HMGB1 antibody 3.0 mg/kg		Anti-KLH antibody 3 mg/kg		Anti-HMGB1 antibody 0.75 mg/kg		Anti-HMGB1 antibody 1.5 mg/kg		Anti-HMGB1 antibody 3.0 mg/kg						
	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total	
Number of animals	6						6						6								
Urinary system																					
Kidney																					
Dilatation,pelvic cavity	5	1	(6)	0	1			(0)	0	0	6	0	0	0	0	6	0	0	0	0	0
Urinary bladder			NR(6)		(0)					NR(6)					NR(6)						NR(6)
Genital system																					
Testis																					
Epididymis			NR(6)		(0)					NR(6)					NR(6)						NR(6)
Cellular infiltration,lymphocyte			(6)		(0)					(6)					(6)						(6)
Prostate	6	0	0	0	0	5	1	0	0	1	6	0	0	0	0	6	0	0	0	0	0
Seminal vesicle			NR(6)		(0)					NR(6)					NR(6)						NR(6)
Mammary gland			NR(6)		(0)					NR(6)					NR(6)						NR(6)
Endocrine system																					
Pituitary																					
Cyst,intermediate lobe	5	1	(6)	0	1	5	1	0	0	1	6	0	0	0	0	6	0	0	0	0	0
Thyroid			(6)		(0)					(6)					(6)						(6)
Ectopic tissue,thymic	4	2	0	0	2	6	0	0	0	0	5	1	0	0	0	6	1	0	0	0	1
Remnant,ultimobranchial body	5	1	0	0	1	6	0	0	0	0	5	1	0	0	0	6	1	0	0	0	1
Para thyroid			NR(6)		(0)					NR(6)					NR(6)						NR(6)
Adrenal			NR(6)		(0)					NR(6)					NR(6)						NR(6)
Nervous system																					
Cerebrum			NR(6)		(0)					NR(6)					NR(6)						NR(6)
Cerebellum			NR(6)		(0)					NR(6)					NR(6)						NR(6)
Medulla oblongata			NR(6)		(0)					NR(6)					NR(6)						NR(6)
Spinal cord			NR(6)		(0)					NR(6)					NR(6)						NR(6)
Optic nerve			NR(6)		(0)					NR(6)					NR(6)						NR(6)
Sciatic nerve			NR(6)		(0)					NR(6)					NR(6)						NR(6)
Special sense organs																					
Eye			NR(6)		(0)					NR(6)					NR(6)						NR(6)
Harderian gland			NR(6)		(0)					NR(6)					NR(6)						NR(6)
Musculoskeletal system																					
M. biceps femoris			NR(6)		(0)					NR(6)					NR(6)						NR(6)
Sternum			NR(6)		(0)					NR(6)					NR(6)						NR(6)

Grade sign: -, none; +, mild; ++, moderate; +++, marked.

NR: no remarkable changes.

Figures in parentheses are number of animals with tissues examined histopathologically.

Table 10 – continued Histopathological findings

Organs and findings	Group and dose				Number of animals																																		
	Anti-KLH antibody 3 mg/kg	Anti-HMGB1 antibody 0.75 mg/kg	Anti-HMGB1 antibody 1.5 mg/kg	Anti-HMGB1 antibody 3.0 mg/kg	-	+	++	+++	Total	-	+	++	+++	Total	-	+	++	+++	Total																				
Musculoskeletal system																																							
Femur							NR(6)						(0)				NR(6)																						
Integumentary system																																							
Integument							NR(6)						(0)					NR(6)																					
Others																																							
Tail (treated site)							NR(6)						(0)					NR(6)																					

Grade sign: -, none; +, mild; ++, moderate; +++, marked.

NR: no remarkable changes.

Figures in parentheses are number of animals with tissues examined histopathologically.

Appendix 1 Individual clinical signs

Group and dose	Animal No.	Days													
		1		2		3		4		5		6		7	
		PRE	1 hr	PRE	1 hr	PRE	1 hr	PRE	1 hr	PRE	1 hr	PRE	1 hr	PRE	1 hr
Anti-KLH antibody 3 mg/kg	251	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	252	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	253	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	254	-	-	-	-	-	-	-	-	a	-	-	-	-	-
	255	-	-	-	-	-	-	-	-	-	-	-	-	a	-
	256	-	-	-	-	-	-	-	a	-	-	-	-	-	-
Anti-HMGB1 antibody 0.75 mg/kg	257	-	-	-	-	-	-	-	a	-	-	-	-	-	a
	258	-	-	-	-	-	-	-	a	-	-	-	-	-	-
	259	-	-	-	-	-	-	-	a	-	-	-	-	-	-
	260	-	-	-	-	-	-	-	a	-	-	-	-	-	a
	261	-	-	-	-	-	-	-	a	-	-	-	-	-	a
	262	-	-	-	-	-	-	-	a	-	-	-	-	-	a
Anti-HMGB1 antibody 1.5 mg/kg	263	-	-	-	-	-	-	-	a	-	-	-	-	-	-
	264	-	-	-	-	-	-	-	a	-	-	-	-	-	-
	265	-	-	-	-	-	-	-	a	-	-	-	-	-	-
	266	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	267	-	-	-	-	-	-	-	a	-	-	-	-	-	-
	268	-	-	-	-	-	-	-	a	-	-	-	-	-	-
Anti-HMGB1 antibody 3.0 mg/kg	269	-	-	-	-	-	-	-	-	-	-	-	-	a	-
	270	-	-	-	-	-	-	-	-	-	-	-	-	a	-
	271	-	-	-	-	-	-	-	a	-	-	-	-	-	-
	272	-	-	-	-	-	-	-	a	-	-	-	-	-	-
	273	-	-	-	-	-	-	-	a	-	-	-	-	-	-
	274	-	-	-	-	-	-	-	a	-	-	-	-	-	-

Clinical sign: -, No abnormality; a, Reddish urine.

PRE: before dosing.

1 hr: 0.5 to 1.5 hours after dosing.

Appendix 2 Individual body weights

Group and dose	Animal No.	Body weight (g) on day				
		1	3	7		
Anti-KLH antibody 3 mg/kg	251	186.7	200.1	234.8		
	252	193.4	213.8	255.7		
	253	197.9	215.6	255.5		
	254	187.1	203.6	244.1		
	255	192.0	212.3	244.1		
	256	186.7	201.9	239.6		
Anti-HMGB1 antibody 0.75 mg/kg	257	187.1	207.2	239.0		
	258	194.5	216.1	249.6		
	259	193.0	209.7	245.1		
	260	189.8	208.5	248.5		
	261	192.1	212.0	254.9		
	262	187.8	203.8	236.1		
Anti-HMGB1 antibody 1.5 mg/kg	263	186.4	203.9	240.8		
	264	190.4	210.2	244.2		
	265	198.4	217.9	253.4		
	266	191.9	207.6	244.2		
	267	195.7	215.4	256.8		
	268	185.5	205.3	241.7		
Anti-HMGB1 antibody 3.0 mg/kg	269	191.6	208.4	245.6		
	270	191.9	206.0	237.7		
	271	200.9	219.9	260.2		
	272	190.4	206.5	246.5		
	273	187.0	202.1	234.6		
	274	183.4	200.6	235.8		

Appendix 3 Individual food consumption

Group and dose	Animal No.	Food consumption (g) on day				
		1	3	7		
Anti-KLH antibody 3 mg/kg	251	18.6	21.3	22.4		
	252	21.6	25.9	24.4		
	253	24.5	26.1	22.6		
	254	19.5	20.9	22.9		
	255	20.1	25.1	21.5		
	256	20.7	19.7	23.4		
Anti-HMGB1 antibody 0.75 mg/kg	257	20.7	21.3	23.5		
	258	22.5	26.0	25.6		
	259	22.6	24.4	24.7		
	260	22.2	22.9	23.5		
	261	23.1	23.5	27.2		
	262	21.4	23.7	24.6		
Anti-HMGB1 antibody 1.5 mg/kg	263	18.9	24.6	26.0		
	264	19.4	23.3	27.4		
	265	24.7	25.0	24.4		
	266	22.9	21.9	23.8		
	267	22.0	27.4	24.0		
	268	21.5	23.5	24.2		
Anti-HMGB1 antibody 3.0 mg/kg	269	21.4	23.5	25.0		
	270	21.7	22.4	21.5		
	271	23.5	26.9	26.5		
	272	20.5	23.9	25.1		
	273	19.6	22.0	22.9		
	274	23.1	22.4	23.0		

Appendix 4 Individual ophthalmological findings

Group and dose	Animal No.	Time in weeks	
		Before	Week 1
Anti-KLH antibody 3 mg/kg	251	-	-
	252	-	-
	253	-	-
	254	-	-
	255	-	-
	256	-	-
Anti-HMGB1 antibody 0.75 mg/kg	257	-	-
	258	-	-
	259	-	-
	260	-	-
	261	-	-
	262	-	-
Anti-HMGB1 antibody 1.5 mg/kg	263	-	-
	264	-	-
	265	-	-
	266	-	-
	267	-	-
	268	-	-
Anti-HMGB1 antibody 3.0 mg/kg	269	-	-
	270	-	-
	271	-	-
	272	-	-
	273	-	-
	274	-	-

Findings: -, No abnormality.

Appendix 5 Individual urinary findings

Group and dose	Animal No.	Urine volume (mL/24hr)	Specific gravity	Na (mEq/24hr)	K (mEq/24hr)	Cl (mEq/24hr)
Anti-KLH antibody 3 mg/kg	251	4.2	1.082	1.021	1.938	1.348
	252	5.9	1.066	1.104	2.086	1.484
	253	12.4	1.038	1.366	2.527	1.929
	254	4.9	1.072	1.069	1.927	1.423
	255	5.6	1.072	1.329	2.186	1.699
	256	7.0	1.058	1.302	2.232	1.680
Anti-HMGB1 antibody 0.75 mg/kg	257	7.8	1.050	1.147	2.118	1.502
	258	10.0	1.044	1.306	2.580	1.826
	259	4.3	1.062	0.774	1.507	1.161
	260	4.4	1.080	0.960	2.003	1.333
	261	14.3	1.034	1.376	2.737	1.991
	262	5.3	1.062	0.954	1.755	1.323
Anti-HMGB1 antibody 1.5 mg/kg	263	7.2	1.052	0.953	2.098	1.493
	264	6.5	1.064	1.169	2.192	1.645
	265	3.5	1.084	0.781	1.620	1.182
	266	4.9	1.074	1.017	1.907	1.472
	267	9.7	1.046	1.447	2.615	2.016
	268	7.8	1.050	1.109	2.118	1.576
Anti-HMGB1 antibody 3.0 mg/kg	269	6.4	1.050	0.919	1.926	1.329
	270	6.2	1.060	1.007	1.917	1.394
	271	6.3	1.068	1.299	2.306	1.716
	272	11.8	1.038	1.329	2.339	1.855
	273	3.4	1.072	0.584	1.363	0.932
	274	7.0	1.068	1.337	2.538	1.884

Appendix 5 - continued Individual urinary findings

Group and dose	Animal No.	Color	pH	Protein	Glucose	Ketone body	Bilirubin	Occult blood	Urobilinogen (mg/dL)
Anti-KLH antibody 3 mg/kg	251	Y	8.5	-	-	-	-	-	<1
	252	Y	8.5	-	-	-	-	-	<1
	253	Y	8.0	-	-	-	-	-	<1
	254	Y	8.0	-	-	-	-	-	<1
	255	Y	8.0	±	-	-	-	-	<1
	256	Y	8.5	-	-	-	-	-	<1
Anti-HMGB1 antibody 0.75 mg/kg	257	Y	8.5	-	-	-	-	-	<1
	258	Y	7.5	-	-	-	-	-	<1
	259	Y	8.5	-	-	-	-	-	<1
	260	Y	8.5	-	-	-	-	-	<1
	261	Y	8.5	-	-	-	-	-	<1
	262	Y	8.5	±	-	-	-	-	<1
Anti-HMGB1 antibody 1.5 mg/kg	263	Y	8.0	±	-	-	-	-	<1
	264	Y	8.0	-	-	-	-	-	<1
	265	Y	8.0	±	-	-	-	-	<1
	266	Y	8.5	±	-	-	-	-	<1
	267	Y	8.0	±	-	-	-	-	<1
	268	Y	8.0	-	-	-	-	-	<1
Anti-HMGB1 antibody 3.0 mg/kg	269	Y	8.5	-	-	-	-	-	<1
	270	Y	8.0	-	-	-	-	-	<1
	271	Y	8.5	±	-	-	-	-	<1
	272	Y	8.0	-	-	-	-	-	<1
	273	Y	8.0	±	-	-	-	-	<1
	274	Y	8.5	-	-	-	-	-	<1

Abbreviation: Y, yellow.
Grade sign: -, none; ±, trace; +, slight; ++, moderate; +++, severe; +++++, very severe.

Appendix 5 - continued Individual urinary findings

Group and dose	Animal No.	Urinary sediment					
		Epithelial cells	Erythrocytes	Leukocytes	Casts	Crystals	
Anti-KLH antibody 3 mg/kg	251	-	-	-	-	-	
	252	-	-	-	-	-	
	253	-	-	-	-	-	
	254	-	-	-	-	-	
	255	-	-	-	-	-	
	256	-	-	-	-	-	
Anti-HMGB1 antibody 0.75 mg/kg	257	-	-	-	-	-	
	258	-	-	-	-	-	
	259	-	-	-	-	-	
	260	-	-	-	-	-	
	261	-	-	-	-	-	
	262	-	-	-	-	-	
Anti-HMGB1 antibody 1.5 mg/kg	263	-	-	-	-	-	
	264	-	-	-	-	-	
	265	-	-	-	-	-	
	266	-	-	-	-	-	
	267	-	-	-	-	-	
	268	-	-	-	-	-	
Anti-HMGB1 antibody 3.0 mg/kg	269	-	-	-	-	-	
	270	-	-	-	-	-	
	271	-	-	-	-	-	
	272	-	-	-	-	-	
	273	-	-	-	-	-	
	274	-	-	-	-	-	

Grade signs are as follows.

- Epithelial cells: -, < 3/field; +, 3/field ≤ and < 10/field; ++, 10/field ≤ and < 20/field; +++, ≥ 20/field.
- Erythrocytes: -, < 10/field; +, 10/field ≤ and < 30/field; ++, 30/field ≤ and < 100/field; +++, countless.
- Leukocytes: -, < 3/field; +, 3/field ≤ and < 20/field; ++, 20/field ≤ and < 40/field; +++, ≥ 40/field.
- Casts: -, none; +, ≥ 1/all field.
- Crystals: -, < 10/field; +, 10/field ≤ and < 20/field; ++, 20/field ≤ and < 30/field; +++, countless.

Appendix 6 Individual hematological findings

Group and dose	Animal No.	Leukoocytes	Erythrocytes	Hemoglobin	Hematocrit	MCV	MCH	MCHC	Reticulocyte	Platelets	PT
		(103/ μ L)	(104/ μ L)	(g/dL)	(%)	(fL)	(pg)	(g/dL)	(104/ μ L)	(104/ μ L)	(sec)
Anti-KLH antibody 3 mg/kg	251	10.64	709	14.1	42.3	59.7	19.8	33.2	46.1	128.7	13.4
	252	8.18	620	13.8	41.0	66.0	22.2	33.6	50.8	150.1	12.5
	253	9.92	611	13.3	39.9	65.3	21.7	33.3	48.3	116.5	12.1
	254	9.62	690	14.1	42.5	61.6	20.5	33.2	44.9	136.2	13.1
	255	7.68	667	13.8	41.1	61.5	20.6	33.5	36.7	136.9	12.2
	256	9.35	667	13.4	39.7	59.6	20.0	33.6	53.4	136.7	13.2
Anti-HMGB1 antibody 0.75 mg/kg	257	7.80	647	13.0	38.9	60.1	20.0	33.3	47.2	134.4	12.7
	258	13.02	647	13.1	39.1	60.5	20.2	33.4	47.9	135.3	12.3
	259	7.21	647	13.1	39.0	60.2	20.3	33.7	45.3	141.9	12.2
	260	7.62	698	13.9	41.2	59.0	19.8	33.6	51.0	149.2	11.5
	261	8.23	654	13.1	39.5	60.4	20.1	33.2	55.6	139.9	12.7
	262	11.05	680	13.3	40.4	59.5	19.6	32.9	59.2	141.8	12.9
Anti-HMGB1 antibody 1.5 mg/kg	263	6.98	621	12.6	37.9	60.9	20.2	33.2	43.5	130.2	11.9
	264	8.02	676	13.6	40.8	60.4	20.1	33.3	47.3	123.5	13.1
	265	8.37	634	13.7	41.9	66.0	21.6	32.7	54.5	123.3	12.6
	266	7.44	667	13.6	39.8	59.7	20.3	34.0	50.7	152.4	11.8
	267	7.02	633	12.8	38.2	60.4	20.2	33.5	50.6	146.3	12.5
	268	6.76	654	13.3	39.5	60.4	20.3	33.6	55.6	135.7	12.3
Anti-HMGB1 antibody 3.0 mg/kg	269	11.80	641	12.6	37.8	59.0	19.6	33.3	45.5	138.3	12.0
	270	11.83	652	12.9	39.0	59.8	19.8	33.2	45.0	143.0	12.8
	271	7.90	600	13.2	39.3	65.5	22.0	33.7	40.8	126.8	12.9
	272	11.37	630	13.7	41.6	66.0	21.8	33.1	53.6	134.6	11.7
	273	8.59	582	12.9	36.8	63.2	22.2	35.0	39.6	105.2	11.9
	274	9.03	648	13.8	40.8	63.0	21.3	33.8	44.7	137.6	12.5