

Table 1-2 Clinical signs in female rats

Group	Dose (mg/kg)	Grade	Water for injection			ACQ			ACQ					
			0	1	2 3 +	0	1	2 3 +	0	1	2 3 +			
Day	Item													
0	No abnormal signs		8	8	8	8	8	8	8	8	8	8	8	8
1	No abnormal signs		8	8	8	8	8	8	8	8	8	8	8	8
2	No abnormal signs		8	8	8	8	8	8	8	8	8	8	8	8
3	No abnormal signs		8	8	8	8	8	8	8	8	8	8	8	8
4	No abnormal signs		8	8	8	8	8	8	8	8	8	8	8	8
5	No abnormal signs		8	8	8	8	8	8	8	8	8	8	8	8
6	No abnormal signs		8	8	8	8	8	8	8	8	8	8	8	8
7	No abnormal signs		8	8	8	8	8	8	8	8	8	8	8	8
8	No abnormal signs		8	8	8	8	8	8	8	8	8	8	8	8
9	No abnormal signs		8	8	8	8	8	8	8	8	8	8	8	8
10	No abnormal signs		8	8	8	8	8	8	8	8	8	8	8	8
11	No abnormal signs		8	8	8	8	8	8	8	8	8	8	8	8
12	No abnormal signs		8	8	8	8	8	8	8	8	8	8	8	8
13	No abnormal signs		8	8	8	8	8	8	8	8	8	8	8	8
14	No abnormal signs		8	8	8	8	8	8	8	8	8	8	8	8
15	No abnormal signs		8	8	8	8	8	8	8	8	8	8	8	8
16	No abnormal signs		8	8	8	8	8	8	8	8	8	8	8	8
17	No abnormal signs		8	8	8	8	8	8	8	8	8	8	8	8
18	No abnormal signs		8	8	8	8	8	8	8	8	8	8	8	8
19	No abnormal signs		8	8	8	8	8	8	8	8	8	8	8	8
20	No abnormal signs		8	8	8	8	8	8	8	8	8	8	8	8

Numerals represent the number of animals.

Table 1-3 Clinical signs in male rats (Administration site)

Group	Number of animals	Item	Day of administration (Before administration)																																
			0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20												
Water for injection	8		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0							
ACQ (10 mg/kg)	8	Crust	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1						
ACQ (100 mg/kg)	8	Thickening	0	0	0	0	0	1	1	5	7	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	7						
		Hemorrhage	0	0	0	0	0	0	0	0	0	0	1	2	3	5	6	6	6	6	6	6	6	6	6	6	6	6	6	7					
		Loss	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	4	0	0	4	0	0	4	0	0	2							
		Ulcer	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	5	5	5	5	5	5	5	5	5	6	6	7				
ACQ (300 mg/kg)	8	Thickening	0	0	0	0	0	0	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8					
		Hemorrhage	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	2	3	3	3	3	3	3	3	3	3	7	6					
		Loss	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0				
		Ulcer	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1		

Numerals represent the number of animals.

Table 1-4 Clinical signs in female rats (Administration site)

Study No.: SBL101-001

Group	Number of animals	Item	Day of administration (Before administration)																				
			0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Water for injection	8		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
ACQ (10 mg/kg)	8	Crust	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
ACQ (100 mg/kg)	8	Thickening	0	0	0	0	0	0	2	3	7	8	8	8	8	8	8	8	8	8	8	8	
		Hemorrhage	0	0	0	0	0	0	0	0	0	2	3	3	6	7	7	7	7	7	7	7	7
		Loss	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	5	0	0	1	1	0
		Ulcer	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	6	6	6	6	7	8
ACQ (300 mg/kg)	8	Thickening	0	0	0	0	0	0	8	8	8	8	8	8	8	8	8	8	8	8	8	8	
		Hemorrhage	0	0	0	0	0	0	0	0	0	0	1	1	3	3	3	3	3	3	6	6	6
		Loss	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
		Ulcer	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	2

Numerals represent the number of animals.

Table 2-1 Body weight (g) in male rats

Group	Water for injection	ACQ		ACQ
		10	100	
Pre	193.8± 3.9(8)	194.0± 4.0(8)	194.3± 4.1(8)	194.0± 3.9(8)
1W	228.8±14.3(8)	226.8± 9.7(8)	201.5± 9.4(8)**	201.9± 6.7(8)**
2W	266.8±21.0(8)	259.1±13.0(8)	231.1± 9.4(8)**	233.5± 8.6(8)**
3W	287.0±23.6(8)	277.4±11.0(8)	236.8±11.6(8)**	242.9±11.8(8)**

Values are expressed as the mean ± S.D. (N).

** P<0.01 : Significantly different from Water for injection.

Table 2-2 Body weight gain (g) in male rats

Group	Water for injection	ACQ		
		10	100	300
1w	35.0±13.1(8)	32.8± 8.3(8)	7.3± 8.9(8)**	7.9± 7.1(8)**
2w	38.0±10.0(8)	32.4± 7.1(8)	29.6± 4.3(8)	31.6± 7.5(8)
3w	20.3± 6.9(8)	18.3± 7.5(8)	5.6± 8.0(8)**	9.4± 6.6(8)*

Values are expressed as the mean ± S.D. (N).
 * P<0.05 , ** P<0.01 : Significantly different from Water for injection.

Table 2-3 Body weight (g) in female rats

Group	Water for injection	ACQ		
		10	100	300
Pre	149.1± 6.6 (8)	150.1± 6.0 (8)	149.0± 6.6 (8)	149.4± 5.4 (8)
1w	159.8±10.2 (8)	164.9± 6.9 (8)	151.9±11.3 (8)	157.3± 6.2 (8)
2w	175.3±11.9 (8)	183.4± 9.0 (8)	172.6± 8.2 (8)	177.0± 4.8 (8)
3w	188.8±14.0 (8)	195.3± 7.2 (8)	186.4±10.3 (8)	194.9± 9.5 (8)

Values are expressed as the mean ± S.D. (N).

* P<0.05 : Significantly different from Water for injection.

Table 2-4 Body weight gain (g) in female rats

Group	Water for injection	ACQ		
		10	100	300
1w	10.6± 9.8(8)	14.8± 5.7(8)	2.9± 5.8(8)	7.9± 4.1(8)
2w	15.5± 7.9(8)	18.5± 8.3(8)	20.8± 7.1(8)	19.8± 7.9(8)
3w	13.5± 6.4(8)	11.9± 4.3(8)	13.8± 3.2(8)	17.9± 7.0(8)

Values are expressed as the mean ± S.D. (N).
Not significantly different from Water for injection.

Table 3-1 Food consumption (g/day) in male rats

Group	Water for injection	ACQ		
		10	100	300
Pre	24.8± 1.5(8)	24.8± 0.9(8)	25.1± 2.0(8)	25.5± 2.1(8)
1w	24.0± 1.9(8)	24.8± 1.6(8)	21.4± 3.8(8)	20.8± 1.5(8)*
2w	27.3± 2.8(8)	26.4± 1.8(8)	26.0± 2.9(8)	24.4± 2.1(8)

Values are expressed as the mean ± S.D. (N).

* P<0.05 : Significantly different from Water for injection.

Table 3-2 Food consumption (g/day) in female rats

Group	Water for injection	ACQ		
		10	100	300
Pre	18.3± 2.7(8)	18.0± 1.9(8)	17.9± 1.2(8)	19.1± 2.9(8)
1w	18.6± 2.9(8)	19.0± 2.0(8)	19.4± 3.5(8)	18.3± 1.3(8)
2w	18.6± 2.7(8)	20.3± 1.3(8)	19.8± 1.8(8)	18.9± 2.0(8)

Values are expressed as the mean ± S.D. (N).
Not significantly different from Water for injection.

Gross ophthalmological examination

Grade

- 0 : No abnormal changes
- 1 : Slight
- 2 : Moderate
- 3 : Severe
- P : Non-graded change
- U : Unexamined

Table 4-1 Gross ophthalmological examination in male rats

Group	Water for injection	ACQ	ACQ	ACQ
Dose (mg/kg)		10	100	300
Week	Item	Grade		
Pre	No abnormal changes	8	8	8

Numerals represent the number of animals.

Table 4-2 Gross ophthalmological examination in female rats

Group	Water for injection	ACQ	ACQ	ACQ
Dose (mg/kg)	10	100	300	
Week	Item	Grade		
Pre	No abnormal changes	8	8	8

Numerals represent the number of animals.

Slit-lamp examination

Grade

- 0 : No abnormal changes
- 1 : Slight
- 2 : Moderate
- 3 : Severe
- P : Non-graded change
- U : Unexamined

Table 4-3 Slit-lamp examination in male rats

Group	Water for injection	ACQ	ACQ	ACQ
Dose (mg/kg)		10	100	300
Week	Grade			
Pre	No abnormal changes	8	8	8

Numerals represent the number of animals.

Table 4-4 Slit-lamp examination in female rats

Group	Water for injection	ACQ	ACQ	ACQ
Dose (mg/kg)		10	100	300
Week	Item	Grade		
Pre	No abnormal changes	8	8	8

Numerals represent the number of animals.

Fundusoscopic examination

Grade

- 0 : No abnormal changes
- 1 : Slight
- 2 : Moderate
- 3 : Severe
- P : Non-graded change
- U : Unexamined

Table 4-5 Funduscopic examination in male rats

Group	Water for injection	ACQ	ACQ	ACQ
Dose (mg/kg)		10	100	300
Week	Item	Grade		
Pre	No abnormal changes	8	8	8

Numerals represent the number of animals.

Table 4-6 Funduscopic examination in female rats

Group	Water for injection	ACQ	ACQ	ACQ	ACQ
Dose(mg/kg)		10	100	300	
Week	Item	Grade			
Pre	No abnormal changes	8	8	8	8

Numerals represent the number of animals.

Hematology

RBC	($10^6/\text{mm}^3$)	Number of red blood cells
WBC	($10^3/\text{mm}^3$)	Number of white blood cells
Ht	(%)	Hematocrit value
Hb	(g/dL)	Hemoglobin concentration
Plat.	($10^3/\text{mm}^3$)	Number of blood platelets
MCV	(fL)	Mean corpuscular volume
MCH	(pg)	Mean corpuscular hemoglobin
MCHC	(g/dL)	Mean corpuscular hemoglobin concentration
Ret.	(%)	Reticulocyte ratio
Hemogram		
Eosino.	($10^3/\text{mm}^3$)	Number of eosinophilic leukocytes
Eosino.	(%)	Eosinophilic leukocyte ratio
Baso.	($10^3/\text{mm}^3$)	Number of basophilic leukocytes
Baso.	(%)	Basophilic leukocyte ratio
Mono.	($10^3/\text{mm}^3$)	Number of monocytes
Mono.	(%)	Monocyte ratio
Lymph.	($10^3/\text{mm}^3$)	Number of lymphocytes
Lymph.	(%)	Lymphocyte ratio
Neutro.	($10^3/\text{mm}^3$)	Neutrophil count
Neutro.	(%)	Neutrophil ratio
LUC	($10^3/\text{mm}^3$)	Large unstained cell count
LUC	(%)	Large unstained cell ratio
Blood coagulation test		
PT	(Sec)	Prothrombin time
APTT	(Sec)	Activated partial thromboplastin

Table 5-1 Hematology in male rats

Group	Dose (mg/kg)	N	Water for injection		ACQ		ACQ		ACQ	
			8	8	10	8	100	8	300	8
RBC	(10 ⁶ /mm ³)		7.603±0.354	7.653±0.342			6.909±0.412**			6.868±0.310**
WBC	(10 ³ /mm ³)		9.658±2.667	9.989±5.139			16.614±8.020			14.763±3.191
Ht	(%)		44.38±1.97	45.33±1.37			42.19±1.96			40.14±2.00**
Hb	(g/dL)		15.45±0.70	15.66±0.44			14.44±0.69**			13.64±0.65**
Plat.	(10 ³ /mm ³)		1184.8±176.0	1200.9±178.1			1427.8±116.8*			1889.0±219.4**
MCV	(fL)		58.41±1.96	59.29±1.01			61.11±1.69**			58.46±1.88
MCH	(pg)		20.34±0.76	20.51±0.48			20.90±0.71			19.86±0.67
MCHC	(g/dL)		34.84±0.46	34.58±0.41			34.23±0.56			33.99±0.54**
Ret.	(%)		2.91±0.59	2.79±0.67			3.49±0.96			4.46±0.73**
Eosino.	(10 ³ /mm ³)		0.055±0.033	0.065±0.050			0.085±0.083			0.036±0.024
Eosino.	(%)		0.56±0.33	0.61±0.34			0.45±0.28			0.25±0.20
Baso.	(10 ³ /mm ³)		0.036±0.017	0.034±0.024			0.055±0.036			0.058±0.019
Baso.	(%)		0.36±0.09	0.30±0.09			0.31±0.08			0.38±0.10
Mono.	(10 ³ /mm ³)		0.201±0.063	0.221±0.128			0.465±0.220*			0.758±0.350**
Mono.	(%)		2.08±0.44	2.28±0.89			2.98±1.07			5.09±2.03**
Lymph.	(10 ³ /mm ³)		6.844±2.658	7.224±2.630			5.235±2.539			5.949±1.680
Lymph.	(%)		70.13±11.13	75.64±8.33			32.66±7.16**			40.06±6.28**
Neutro.	(10 ³ /mm ³)		2.445±1.186	2.369±2.569			10.490±5.570**			7.476±1.988*
Neutro.	(%)		25.99±11.07	20.24±8.44			61.63±8.51**			50.73±8.17**
LUC	(10 ³ /mm ³)		0.079±0.026	0.080±0.045			0.284±0.227			0.488±0.211**
LUC	(%)		0.86±0.38	0.95±0.81			1.98±1.77			3.48±1.71*
PT	(Sec)		12.48±1.96	12.44±1.43			9.90±0.87*			9.04±0.59**
APTT	(Sec)		22.05±1.33	21.38±1.61			20.31±1.70*			19.55±0.66**

Values are expressed as the mean ± S.D.
 * P<0.05, ** P<0.01 : Significantly different from Water for injection.