

2. 学会発表

なし

H. 知的財産権の出願・取得状況

1. 特許取得

なし

2. 実用新案登録

なし

3. その他

なし

Table 1 - 1 Mortality - Cumulative death rates in male rats

Dose (mg/kg/day)	Week				
	1	2	3	4	5
0	0 <sup>a</sup> /10 <sup>b</sup>	0/10	0/10	0/10	0/10
1	0/10	0/10	0/10	0/10	0/10
8	0/10	0/10	0/10	0/10	0/10
40	3/10	4/10	6/10	6/10	6/10

<sup>a</sup>: Cumulative number of animals found dead or killed *in extremis* during the treatment period.

<sup>b</sup>: Effective number of animals at each week.

Table 1 - 2 Mortality - Cumulative death rates in male rats  
Immunized group

Dose (mg/kg/day)	Week			
	1	2	3	4
0	0 <sup>a</sup> /8 <sup>b</sup>	0/8	0/8	0/8
1	0/8	0/8	0/8	0/8
8	0/8	0/8	0/8	0/8
40	1/8	3/8	3/8	5/8

<sup>a</sup>: Cumulative number of animals found dead or killed *in extremis* during the treatment period.

<sup>b</sup>: Effective number of animals at each week.

Table 2 - 1 Mortality - Cumulative death rates in female rats

Dose (mg/kg/day)	Week				
	1	2	3	4	5
0	0 <sup>a</sup> /10 <sup>b</sup>	0/10	0/10	0/10	0/10
1	0/10	0/10	0/10	0/10	0/10
8	0/10	0/10	0/10	1/10	1/10
40	0/10	2/10	3/10	5/10	5/10

<sup>a</sup>: Cumulative number of animals found dead or killed *in extremis* during the treatment period.

<sup>b</sup>: Effective number of animals at each week.

Table 2 - 2 Mortality - Cumulative death rates in female rats  
Immunized group

Dose (mg/kg/day)	Week			
	1	2	3	4
0	0 <sup>a</sup> /8 <sup>b</sup>	0/8	0/8	0/8
0.2	0/8	0/8	0/8	0/8
1	0/8	0/8	0/8	0/8
8	0/8	0/8	0/8	0/8
24	0/8	0/8	1/8	1/8

<sup>a</sup>: Cumulative number of animals found dead or killed *in extremis* during the treatment period.

<sup>b</sup>: Effective number of animals at each week.

Table 3 - 1 General clinical observation - Incidence of signs in male rats

Clinical signs	Dose (mg/kg/day)	0	1	8	40
	No. of animals examined	10	10	10	10
No abnormalities detected		10	10	7	3
Appearance:					
Emaciation		0	0	0	1
Posture/Body position:					
Abdominal distention		0	0	0	6 **
Behavior:					
Decreased spontaneous motor activity		0	0	0	1
Respiration:					
Abnormal respiratory sound		0	0	3	7 **
Consciousness/Nervous system:					
Sedation		0	0	0	3
Body temperature:					
Hypothermy		0	0	0	4 *
Excretion:					
Loose stool		0	0	0	1
Fur:					
perinasal region:Soiled fur		0	0	0	4 *
perioral region:Soiled fur		0	0	0	1
external genital region:Soiled fur		0	0	0	5 *
Mouth (oral cavity):					
Salivation		0	0	0	3

Significantly different from control: \*,  $p \leq 0.05$ ; \*\*,  $p \leq 0.01$ .

Table 3 - 2      General clinical observation - Incidence of signs in male rats  
Immunized group

Clinical signs	Dose (mg/kg/day)	0	1	8	40
	No. of animals examined	8	8	8	8
No abnormalities detected		8	8	8	0
Appearance:					
Emaciation		0	0	0	1
Posture/Body position:					
Abdominal distention		0	0	0	4 *
Respiration:					
Abnormal respiratory sound		0	0	0	8 **
Body temperature:					
Hypothermy		0	0	0	2
Excretion:					
Loose stool		0	0	0	5 *
Fur:					
perinasal region:Soiled fur		0	0	0	2
perioral region:Soiled fur		0	0	0	3
external genital region:Soiled fur		0	0	0	6 **

Significantly different from control: \*,  $p \leq 0.05$ ; \*\*,  $p \leq 0.01$ .

Table 4 - 1 General clinical observation - Incidence of signs in female rats

Clinical signs	Dose (mg/kg/day)	0	1	8	40
	No. of animals examined	10	10	10	10
No abnormalities detected		10	10	8	0
Appearance:					
Emaciation		0	0	1	5 *
Posture/Body position:					
Abdominal distention		0	0	1	6 **
Behavior:					
Decreased spontaneous motor activity		0	0	0	1
Respiration:					
Abnormal respiratory sound		0	0	2	10 **
Body temperature:					
Hypothermy		0	0	0	4 *
Excretion:					
Loose stool		0	0	1	3
Fur:					
perinasal region:Soiled fur		0	0	0	2
perioral region:Soiled fur		0	0	0	3
external genital region:Soiled fur		0	0	0	7 **

Significantly different from control: \*,  $p \leq 0.05$ ; \*\*,  $p \leq 0.01$ .



Table 4 - 2      General clinical observation - Incidence of signs in female rats  
Immunized group

Clinical signs	Dose (mg/kg/day)	0	0.2	1	8	24
	No. of animals examined	8	8	8	8	8
No abnormalities detected		8	8	8	7	2
Appearance:						
Emaciation		0	0	0	0	1
Posture/Body position:						
Abdominal distention		0	0	0	0	4 *
Behavior:						
Decreased spontaneous motor activity		0	0	0	0	1
Respiration:						
Bradypnea		0	0	0	0	1
Abnormal respiratory sound		0	0	0	1	5 *
Consciousness/Nervous system:						
Sedation		0	0	0	0	2
Fur:						
whole body:Piloerection		0	0	0	0	1
perinasal region:Soiled fur		0	0	0	0	1
perioral region:Soiled fur		0	0	0	0	1
external genital region:Soiled fur		0	0	0	0	1

\* and \*\*: Significantly different from the control at 5 and 1% levels of probability, respectively.

Table 5 - 1

Detailed clinical observation - Summary data in male rats

Open field: Piloerection

Dose (mg/kg/day)	Score	Week				
		-1	1	2	3	4
0	0	10	10	10	10	10
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
1	0	10	10	10	10	10
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
8	0	10	10	10	10	10
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
40	0	10	7	5	4	4
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0

Table 5 - 2 Detailed clinical observation - Summary data in male rats

Open field: Exploration

Dose (mg/kg/day)	Score	Week				
		-1	1	2	3	4
0	-2	0	0	0	0	0
	-1	0	0	2	2	6
	0	0	5	6	5	4
	1	10	5	2	3	0
	2	0	0	0	0	0
1	-2	0	0	0	0	0
	-1	0	0	0	0	2
	0	0	4	8	4	5
	1	10	6	2	6	3
	2	0	0	0	0	0
8	-2	0	0	0	0	0
	-1	0	0	1	1	3
	0	0	6	5	4	4
	1	10	4	4	5	3
	2	0	0	0	0	0
40	-2	0	0	0	0	0
	-1	0	0	1	1	3
	0	1	4	4	2	1
	1	9	3	0	1	0
	2	0	0	0	0	0

Table 5 - 3

Detailed clinical observation - Summary data in male rats

Open field: Rearing

Dose (mg/kg/day)	Score	Week				
		-1	1	2	3	4
0	0	1	6	7	7	8
	1	0	1	2	2	1
	2	0	2	0	1	1
	3	2	1	0	0	0
	4	4	0	1	0	0
	5	1	0	0	0	0
	6	1	0	0	0	0
	7	0	0	0	0	0
	8	1	0	0	0	0
1	0	0	5	8	3	6
	1	2	4	2	4	4
	2	1	1	0	2	0
	3	0	0	0	0	0
	4	2	0	0	1	0
	5	3	0	0	0	0
	6	2	0	0	0	0
	7	0	0	0	0	0
	8	0	0	0	0	0
8	0	1	8	8	7	8
	1	1	1	1	2	0
	2	1	1	0	0	1
	3	0	0	0	1	0
	4	5	0	0	0	1
	5	2	0	1	0	0
	6	0	0	0	0	0
	7	0	0	0	0	0
	8	0	0	0	0	0
40	0	1	6	5	4	4
	1	3	1	0	0	0
	2	2	0	0	0	0
	3	0	0	0	0	0
	4	3	0	0	0	0
	5	0	0	0	0	0
	6	0	0	0	0	0
	7	1	0	0	0	0
	8	0	0	0	0	0

Table 5 - 4

Detailed clinical observation - Summary data in male rats

Open field: Count of defecation

Dose (mg/kg/day)	Score	Week				
		-1	1	2	3	4
0	0	10	9	10	10	10
	1	0	1	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
1	0	9	10	9	10	10
	1	1	0	1	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
8	0	10	10	10	10	10
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
40	0	10	7	5	4	4
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0

Table 5 - 5

## Detailed clinical observation - Summary data in male rats

Open field: Feces excreted

Dose (mg/kg/day)	Score	Week				
		-1	1	2	3	4
0	0	0	1	0	0	0
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
	N	10	9	10	10	10
1	0	1	0	1	0	0
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
	N	9	10	9	10	10
8	0	0	0	0	0	0
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
	N	10	10	10	10	10
40	0	0	0	0	0	0
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
	N	10	7	5	4	4

Table 5 - 6

## Detailed clinical observation - Summary data in male rats

Open field: Urine excreted

Dose (mg/kg/day)	Score	Week				
		-1	1	2	3	4
0	0	3	3	6	3	4
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
	N	7	7	4	7	6
1	0	0	2	0	0	2
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
	N	10	8	10	10	8
			**			
8	0	1	3	1	5	4
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
	N	9	7	9	5	6
			*			
40	0	1	1	1	1	1
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
	N	9	6	4	3	3

Significantly different from control: \*,  $p \leq 0.05$ ; \*\*,  $p \leq 0.01$ .

Table 5 - 7

Detailed clinical observation - Summary data in male rats

Handling: Salivasion

Dose (mg/kg/day)	Score	Week				
		-1	1	2	3	4
0	0	10	10	10	10	10
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
1	0	10	10	10	10	10
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
8	0	10	10	10	10	10
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
40	0	10	7	5	4	4
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0



Table 5 - 8

Detailed clinical observation - Summary data in male rats

Handling: Secretions/excretions

Dose (mg/kg/day)	Score	Week				
		-1	1	2	3	4
0	0	10	10	10	10	10
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
1	0	10	10	10	10	10
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
8	0	10	10	10	10	10
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
40	0	10	7	5	4	4
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0

Table 6 - 1

Detailed clinical observation - Summary data in female rats

Open field: Piloerection

Dose (mg/kg/day)	Score	Week				
		-1	1	2	3	4
0	0	10	10	10	10	10
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
1	0	10	10	10	10	10
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
8	0	10	10	10	9	9
	1	0	0	0	1	0
	2	0	0	0	0	0
	3	0	0	0	0	0
40	0	10	10	8	7	5
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0

Table 6 - 2 Detailed clinical observation - Summary data in female rats

## Open field: Exploration

Dose (mg/kg/day)	Score	Week				
		-1	1	2	3	4
0	-2	0	0	0	0	0
	-1	0	0	0	0	0
	0	0	0	0	1	0
	1	10	10	10	9	10
	2	0	0	0	0	0
1	-2	0	0	0	0	0
	-1	0	0	0	0	0
	0	0	0	2	1	0
	1	10	10	8	9	10
	2	0	0	0	0	0
8	-2	0	0	0	0	0
	-1	0	0	0	0	0
	0	0	1	1	4	3
	1	10	9	9	6	6
	2	0	0	0	0	0
40	-2	0	0	0	0	0
	-1	0	0	0	0	0
	0	0	2	3	3	3
	1	10	8	5	4	2
	2	0	0	0	0	0

Significantly different from control: \*,  $p \leq 0.05$ ; \*\*,  $p \leq 0.01$ .

Table 6 - 3

Detailed clinical observation - Summary data in female rats

Open field: Rearing

Dose (mg/kg/day)	Score	Week				
		-1	1	2	3	4
0	0	0	2	0	1	0
	1	1	1	0	2	3
	2	1	2	4	6	1
	3	1	2	4	0	2
	4	0	2	1	1	3
	5	3	1	1	0	0
	6	2	0	0	0	0
	7	0	0	0	0	1
	8	0	0	0	0	0
	9	1	0	0	0	0
	10	0	0	0	0	0
11	1	0	0	0	0	
1	0	0	1	1	0	1
	1	1	1	4	5	3
	2	4	6	2	2	3
	3	1	0	1	1	3
	4	1	0	2	2	0
	5	2	2	0	0	0
	6	0	0	0	0	0
	7	1	0	0	0	0
	8	0	0	0	0	0
	9	0	0	0	0	0
	10	0	0	0	0	0
11	0	0	0	0	0	
8	0	2	1	2	4	4
	1	1	4	4	3	2
	2	2	0	1	0	1
	3	2	4	0	2	0
	4	1	0	2	0	1
	5	1	0	0	0	1
	6	0	1	0	0	0
	7	1	0	1	1	0
	8	0	0	0	0	0
	9	0	0	0	0	0
	10	0	0	0	0	0
11	0	0	0	0	0	
40	0	0	2	3	4	2
	1	0	2	1	2	1
	2	1	3	2	1	0
	3	1	2	1	0	1
	4	1	0	0	0	1
	5	2	0	0	0	0
	6	2	1	0	0	0
	7	1	0	1	0	0
	8	0	0	0	0	0
	9	1	0	0	0	0
	10	0	0	0	0	0
11	1	0	0	0	0	

\*

Significantly different from control: \*,  $p \leq 0.05$ ; \*\*,  $p \leq 0.01$ .