

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

Clinical signs	Dose (mg/kg/day)	0	8	40	200/100
	No. of animals examined	8	8	8	8
No abnormalities detected		8	8	8	2
Appearance:					
Emaciation		0	0	0	2
Posture/Body position:					
Abdominal distention		0	0	0	1
Behavior:					
Decreased spontaneous motor activity		0	0	0	3
Respiration:					
Abnormal respiratory sound		0	0	0	3
Consciousness/Nervous system:					
Sedation		0	0	0	1
Muscle weakness		0	0	0	4 *
Body temperature:					
Hypothermy		0	0	0	2
Excretion:					
Loose stool		0	0	0	2
Fur :					
perioral region:Soiled fur		0	0	0	3
external genital region:Soiled fur		0	0	0	3
Eye/Eyelid (eyelid):					
Ptosis		0	0	0	1

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

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

Clinical signs	Dose (mg/kg/day)	0	8	40	100
	No. of animals examined	10	10	10	10
No abnormalities detected		10	10	10	7
Posture/Body position:					
Abdominal distention		0	0	0	1
Respiration:					
Abnormal respiratory sound		0	0	0	2
Consciousness/Nervous system:					
Sedation		0	0	0	1
Muscle weakness		0	0	0	1
Body temperature:					
Hypothermy		0	0	0	1
Eye/Eyelid (eyelid):					
Ptosis		0	0	0	1
Mouth (oral cavity):					
Salivation		0	0	0	1

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
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	10	10	10	10
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
200/100	0	10	8	6	6	6
	1	0	0	1	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	0	0	0
	0	0	0	0	2	2
	1	10	10	10	8	8
	2	0	0	0	0	0
8	-2	0	0	0	0	0
	-1	0	0	0	0	1
	0	2	3	8	8	5
	1	8	7	2	2	4
	2	0	0	0	0	0
				**		
40	-2	0	0	0	0	0
	-1	0	0	0	0	1
	0	1	1	1	5	3
	1	9	9	9	5	6
	2	0	0	0	0	0
200/100	-2	0	0	0	0	0
	-1	0	0	0	0	1
	0	2	0	4	3	1
	1	7	8	3	3	4
	2	1	0	0	0	0
			*			

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

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	2	4	5	7
	1	1	2	4	3	2
	2	1	3	1	1	0
	3	1	0	1	1	1
	4	0	2	0	0	0
	5	2	1	0	0	0
	6	3	0	0	0	0
	7	1	0	0	0	0
	8	0	0	0	0	0
	9	0	0	0	0	0
8	0	1	7	10	9	8
	1	4	2	0	0	1
	2	2	0	0	1	1
	3	0	1	0	0	0
	4	1	0	0	0	0
	5	0	0	0	0	0
	6	1	0	0	0	0
	7	0	0	0	0	0
	8	0	0	0	0	0
	9	1	0	0	0	0
40	0	1	6	8	8	7
	1	2	1	0	2	1
	2	2	2	1	0	1
	3	3	1	0	0	0
	4	0	0	0	0	0
	5	1	0	1	0	1
	6	1	0	0	0	0
	7	0	0	0	0	0
	8	0	0	0	0	0
	9	0	0	0	0	0
200/100	0	1	1	6	6	5
	1	1	4	1	0	1
	2	1	1	0	0	0
	3	3	0	0	0	0
	4	1	2	0	0	0
	5	1	0	0	0	0
	6	2	0	0	0	0
	7	0	0	0	0	0
	8	0	0	0	0	0
	9	0	0	0	0	0

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

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	10	10	10	10
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
8	0	9	10	10	10	10
	1	1	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
40	0	9	10	10	10	10
	1	1	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
200/100	0	10	6	4	6	5
	1	0	1	2	0	1
	2	0	0	1	0	0
	3	0	1	0	0	0

**

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

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	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
8	0	1	0	0	0	0
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
	N	9	10	10	10	10
40	0	1	0	0	0	0
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
	N	9	10	10	10	10
200/100	0	0	2	3	0	1
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
	N	10	6	4	6	5

**

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

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	6	0	3	8	5
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
	N	4	10	7	2	5
8	0	6	1	1	4	5
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
	N	4	9	9	6	5
40	0	5	2	5	6	3
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
	N	5	8	5	4	7
200/100	0	5	4	3	5	5
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
	N	5	4	4	1	1

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

Table 5 - 7

Detailed clinical observation - Summary data in male rats

Handling: Salivation

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
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	10	10	10	10
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
200/100	0	10	8	7	5	6
	1	0	0	0	1	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
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	10	10	10	10
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
200/100	0	10	8	6	6	6
	1	0	0	1	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0

Table 5 - 9

Detailed clinical observation - Summary data in male rats

Handling: Reactivity of handling

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	10	10	10	10	10
	1	0	0	0	0	0
	2	0	0	0	0	0
8	-2	0	0	0	0	0
	-1	0	0	0	0	0
	0	10	10	10	10	10
	1	0	0	0	0	0
	2	0	0	0	0	0
40	-2	0	0	0	0	0
	-1	0	0	0	0	0
	0	10	10	10	10	10
	1	0	0	0	0	0
	2	0	0	0	0	0
200/100	-2	0	0	0	0	0
	-1	0	0	0	0	0
	0	10	8	7	6	6
	1	0	0	0	0	0
	2	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
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	10	10	10	10
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
100	0	10	10	10	9	9
	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	0	0
	1	10	9	9	9	10
	2	0	1	1	1	0
8	-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
40	-2	0	0	0	0	0
	-1	0	0	0	0	0
	0	0	0	0	0	1
	1	10	10	10	10	9
	2	0	0	0	0	0
100	-2	0	0	0	0	0
	-1	0	0	0	0	0
	0	0	0	0	0	2
	1	10	10	10	9	7
	2	0	0	0	0	0

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	3	3	1	0
	1	3	1	2	0	1
	2	3	1	0	3	2
	3	3	1	1	1	3
	4	0	1	2	2	0
	5	1	0	0	0	2
	6	0	2	1	1	1
	7	0	1	0	1	0
	8	0	0	0	0	1
	9	0	0	0	0	0
	10	0	0	0	0	0
	11	0	0	1	0	0
	12	0	0	0	1	0
8	0	2	0	1	0	1
	1	1	1	1	2	0
	2	3	2	3	1	1
	3	1	2	2	2	3
	4	0	1	0	2	3
	5	3	2	1	2	1
	6	0	2	2	0	1
	7	0	0	0	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
	12	0	0	0	0	0
40	0	1	1	2	0	1
	1	3	3	4	3	0
	2	0	3	2	4	6
	3	2	2	1	1	1
	4	3	0	1	2	2
	5	1	1	0	0	0
	6	0	0	0	0	0
	7	0	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
	12	0	0	0	0	0
100	0	0	0	2	2	2
	1	2	0	2	3	0
	2	2	5	4	2	3
	3	4	1	1	1	1
	4	1	1	0	1	3
	5	0	2	1	0	0
	6	0	1	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
	12	0	0	0	0	0

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

Table 6 - 4

Detailed clinical observation - Summary data in female rats

Open field: Count of defecation

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
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	10	10	10	10
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
100	0	10	10	10	9	9
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0

Table 6 - 5

Detailed clinical observation - Summary data in female rats

Open field: Feces excreted

Dose (mg/kg/day)	Score	Week				
		-1	1	2	3	4
0	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
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	10	10	10	10
100	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	9	9

Table 6 - 6

Detailed clinical observation - Summary data in female rats

Open field: Urine excreted

Dose (mg/kg/day)	Score	Week				
		-1	1	2	3	4
0	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
8	0	1	0	0	0	0
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
	N	9	10	10	10	10
40	0	0	1	0	0	2
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
	N	10	9	10	10	8
100	0	2	0	3	1	1
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
	N	8	10	7	8	8

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

Table 6 - 7

Detailed clinical observation - Summary data in female 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
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	10	10	10	10
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
100	0	10	10	9	9	9
	1	0	0	1	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0

Table 6 - 8

Detailed clinical observation - Summary data in female 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
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	10	10	10	10
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
100	0	10	10	10	8	8
	1	0	0	0	1	1
	2	0	0	0	0	0
	3	0	0	0	0	0

Table 6 - 9

Detailed clinical observation - Summary data in female rats

Handling: Reactivity of handling

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	10	10	10	10	10
	1	0	0	0	0	0
	2	0	0	0	0	0
8	-2	0	0	0	0	0
	-1	0	0	0	0	0
	0	10	10	10	10	10
	1	0	0	0	0	0
	2	0	0	0	0	0
40	-2	0	0	0	0	0
	-1	0	0	0	0	0
	0	10	10	10	9	10
	1	0	0	0	1	0
	2	0	0	0	0	0
100	-2	0	0	0	0	0
	-1	0	0	0	0	0
	0	10	10	10	9	9
	1	0	0	0	0	0
	2	0	0	0	0	0