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
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	9
	1	0	0	0	0	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 - 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
1	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	9
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	8	7	5

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

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
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	9
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
40	0	10	10	7	7	5
	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/excreations

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	9
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
40	0	10	10	8	6	5
	1	0	0	0	1	0
	2	0	0	0	0	0
	3	0	0	0	0	0

Key to Tables 7 and 8

Standard key to functional observation data

Parameters assessed and scoring criteria of sensorimotor responses in the functional observation are described as follows:

Sensorimotor responses

Parameters	Scoring criteria
Visual placing	0: Normal response 1: Slight decrease 2: Marked decrease
Approach response	-2: Marked decrease -1: Slight decrease 0: Normal response 1: Slight increase 2: Marked increase
Auditory response	-2: Marked decrease -1: Slight decrease 0: Normal response 1: Slight increase 2: Marked increase
Touch response	-2: Marked decrease -1: Slight decrease 0: Normal response 1: Slight increase 2: Marked increase
Pain response	-2: Marked decrease -1: Slight decrease 0: Normal response 1: Slight increase 2: Marked increase
Aerial righting reflex	0: Normal reflex 1: Slight decrease 2: Marked decrease 3: No reflex

Table 7 - 1 Functional observation - Summary data in male rats

Motor activity at 4 weeks of treatment

Dose (mg/kg/day)		Counts/10 min						Total
		0-10	10-20	20-30	30-40	40-50	50-60	
0	Mean	1590	1083	572	202	91	124	3662
	S.D.	370	369	560	243	156	140	1536
	N	10	10	10	10	10	10	10
1	Mean	1467	1035	480	286	59	209	3536
	S.D.	328	290	263	262	86	253	1097
	N	10	10	10	10	10	10	10
8	Mean	1573	967	488	242	103	94	3466
	S.D.	296	306	406	318	170	124	1303
	N	10	10	10	10	10	10	10
40	Mean	1588	1180	858	635	253	35	4548
	S.D.	393	216	217	193	216	42	1015
	N	4	4	4	4	4	4	4

S.D.: Standard deviation.
N: Number of animals.

Table 7 - 2 Functional observation - Summary data in male rats

Grip strength at 4 weeks of treatment (g)

Dose (mg/kg/day)		Forelimb	Hindlimb
0	Mean	785	481
	S.D.	52	46
	N	10	10
1	Mean	718	479
	S.D.	51	35
	N	10	10
8	Mean	773	487
	S.D.	74	40
	N	10	10
40	Mean	794	489
	S.D.	56	45
	N	4	4

S.D.: Standard deviation.
N: Number of animals.

Table 7 - 3 Functional observation - Summary data in male rats

Sensorimotor responses at 4 weeks of treatment

Dose (mg/kg/day)	Score	Visual placing	Approach response	Auditory response	Touch response	Pain response	Aerial righting reflex
0	-2		0	0	0	0	
	-1		0	0	0	0	
	0	10	10	10	10	9	10
	1	0	0	0	0	1	0
	2	0	0	0	0	0	0
	3						0
1	-2		0	0	0	0	
	-1		0	0	0	0	
	0	10	10	10	10	9	10
	1	0	0	0	0	1	0
	2	0	0	0	0	0	0
	3						0
8	-2		0	0	0	0	
	-1		0	0	0	0	
	0	10	10	10	10	10	10
	1	0	0	0	0	0	0
	2	0	0	0	0	0	0
	3						0
40	-2		0	0	0	0	
	-1		0	0	0	0	
	0	4	4	4	4	4	4
	1	0	0	0	0	0	0
	2	0	0	0	0	0	0
	3						0

Table 8 - 1 Functional observation - Summary data in female rats

Motor activity at 4 weeks of treatment

Dose (mg/kg/day)		Counts/10 min						
		0-10	10-20	20-30	30-40	40-50	50-60	Total
0	Mean	1646	1164	702	297	246	193	4246
	S.D.	272	280	326	311	280	354	1250
	N	10	10	10	10	10	10	10
1	Mean	1757	1053	474	270	268	255	4076
	S.D.	299	303	429	309	270	227	1177
	N	10	10	10	10	10	10	10
8	Mean	1586	1104	732	298	91	144	3955
	S.D.	311	300	311	208	156	193	801
	N	9	9	9	9	9	9	9
40	Mean	1458	939	689	506	267	79	3937
	S.D.	500	538	620	614	519	168	2420
	N	5	5	5	5	5	5	5

S.D.: Standard deviation.
N: Number of animals.

Table 8 - 2 Functional observation - Summary data in female rats

Grip strength at 4 weeks of treatment (g)

Dose (mg/kg/day)		Forelimb	Hindlimb
0	Mean	621	381
	S.D.	41	21
	N	10	10
1	Mean	639	383
	S.D.	77	38
	N	10	10
8	Mean	628	382
	S.D.	49	25
	N	9	9
40	Mean	542	377
	S.D.	99	53
	N	5	5

S.D.: Standard deviation.
N: Number of animals.

Table 8 - 3 Functional observation - Summary data in female rats

Sensorimotor responses at 4 weeks of treatment

Dose (mg/kg/day)	Score	Visual placing	Approach response	Auditory response	Touch response	Pain response	Aerial righting reflex
0	-2		0	0	0	0	
	-1		0	0	0	0	
	0	10	10	10	10	10	9
	1	0	0	0	0	0	1
	2	0	0	0	0	0	0
	3						0
1	-2		0	0	0	0	
	-1		0	0	0	0	
	0	10	10	10	10	10	10
	1	0	0	0	0	0	0
	2	0	0	0	0	0	0
	3						0
8	-2		0	0	0	0	
	-1		0	0	0	0	
	0	9	9	9	9	9	9
	1	0	0	0	0	0	0
	2	0	0	0	0	0	0
	3						0
40	-2		0	0	0	0	
	-1		0	0	0	0	
	0	5	5	5	5	5	5
	1	0	0	0	0	0	0
	2	0	0	0	0	0	0
	3						0

Table 9 - 1 Body weight - Group mean values in male rats

(g)

Dose (mg/kg/day)		Week 0[a]	1	2	3	4
0	Mean	226	265	293	313	328
	S.D.	7	10	12	15	18
	N	10	10	10	10	10
1	Mean	225	263	291	309	330
	S.D.	7	7	12	15	17
	N	10	10	10	10	10
8	Mean	226	259	285	305	323
	S.D.	7	13	16	18	22
	N	10	10	10	10	10
40	Mean	226	245	255	300	314
	S.D.	7	35	48	17	18
	N	10	7	6	4	4

[a]: Week before initiation of treatment.
S.D.: Standard deviation.
N: Number of animals examined.

Table 9 - 2 Body weight - Group mean values in male rats
Immunized group

(g)

Dose (mg/kg/day)		Week 0[a]	1	2	3	4
0	Mean	208	251	292	320	343
	S.D.	4	4	8	10	14
	N	8	8	8	8	8
1	Mean	207	254	294	322	349
	S.D.	4	8	8	11	12
	N	8	8	8	8	8
8	Mean	208	249	285	310	332
	S.D.	4	5	9	12	16
	N	8	8	8	8	8
40	Mean	208	240	255 *	272 **	290 **
	S.D.	4	17	40	25	41
	N	8	7	5	5	3

[a]: Week before initiation of treatment.
S.D.: Standard deviation.
N: Number of animals examined.
Significantly different from control: *, p <= 0.05; **, p <= 0.01.

Table 10 - 1 Body weight - Group mean values in female rats

(g)

Dose (mg/kg/day)		Week 0[a]	1	2	3	4
0	Mean	146	167	186	196	203
	S.D.	6	9	8	10	10
	N	10	10	10	10	10
1	Mean	146	167	179	190	201
	S.D.	6	9	12	10	9
	N	10	10	10	10	10
8	Mean	146	160	172	179	192
	S.D.	6	7	15	20	8
	N	10	10	10	10	9
40	Mean	146	160	172	175 *	175 *
	S.D.	6	18	14	19	24
	N	10	10	8	7	5

[a]: Week before initiation of treatment.
S.D.: Standard deviation.
N: Number of animals examined.
Significantly different from control: *, p <= 0.05; **, p <= 0.01.

Table 10 - 2 Body weight - Group mean values in female rats
Immunized group

(g)

Dose (mg/kg/day)		Week 0[a]	1	2	3	4
0	Mean	147	166	183	196	206
	S.D.	4	9	12	13	13
	N	8	8	8	8	8
0.2	Mean	147	167	182	192	207
	S.D.	4	7	9	9	13
	N	8	8	8	8	8
1	Mean	147	165	179	193	206
	S.D.	3	7	8	9	9
	N	8	8	8	8	8
8	Mean	147	163	177	194	205
	S.D.	3	10	13	11	13
	N	8	8	8	8	8
24	Mean	147	159	172	188	200
	S.D.	4	19	30	19	28
	N	8	8	8	7	7

[a]: Week before initiation of treatment.
S.D.: Standard deviation.
N: Number of animals examined.

Table 11 Food consumption - Group mean values in male rats

(g/rat/day)

Dose (mg/kg/day)		Week 1	2	3	4	Average
0	Mean	22.0	23.1	22.5	22.3	22.5
	S.D.	1.8	2.2	1.6	1.8	
	N	10	10	10	10	
1	Mean	21.6	22.5	22.0	22.5	22.2
	S.D.	1.2	2.3	2.0	1.6	
	N	10	10	10	10	
8	Mean	20.8	21.7	21.9	21.8	21.6
	S.D.	1.9	3.1	2.0	2.0	
	N	10	10	10	10	
40	Mean	14.1 **	15.5 **	20.1	20.3	17.5
	S.D.	6.7	7.3	1.4	1.5	
	N	10	7	4	4	

S.D.: Standard deviation.

N: Number of animals examined.

Significantly different from control: *, $p <= 0.05$; **, $p <= 0.01$.

Table 12 Food consumption - Group mean values in female rats

(g/rat/day)

Dose (mg/kg/day)		Week 1		2	3		4		Average
0	Mean	17.5		17.7	17.9		17.8		17.7
	S.D.	1.3		1.5	1.3		1.3		
	N	10		10	10		10		
1	Mean	17.3		17.0	17.7		17.6		17.4
	S.D.	2.2		2.3	1.9		2.4		
	N	10		10	10		10		
8	Mean	15.4	**	15.7	16.1	*	15.8	*	15.8
	S.D.	1.0		1.6	1.1		1.3		
	N	10		10	10		9		
40	Mean	14.9		14.6	14.6		15.7		15.0
	S.D.	3.0		4.1	4.3		8.3		
	N	10		10	8		5		

S.D.: Standard deviation.

N: Number of animals examined.

Significantly different from control: *, p <= 0.05; **, p <= 0.01.

Table 13 Food efficiency - Group mean values in male rats

(%)

Dose (mg/kg/day) \ Week	1	2	3	4	Average
0	25.3	17.3	12.7	9.6	16.2
1	25.1	17.8	11.7	13.3	17.0
8	22.7	17.1	13.0	11.8	16.2
40	19.3	9.2	32.0	9.9	17.6

Food efficiency = (mean body weight gain from previous week/mean food consumption x 7) x 100.

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Table 14 Food efficiency - Group mean values in female rats

(%)

Dose (mg/kg/day) \ Week	1	2	3	4	Average
0	17.1	15.3	8.0	5.6	11.5
1	17.3	10.1	8.9	8.9	11.3
8	13.0	10.9	6.2	11.8	10.5
40	13.4	11.7	2.9	0.0	7.0

Food efficiency = (mean body weight gain from previous week/mean food consumption x 7) x 100.