

Table 5

Study No. B041794

Clinical Sign (F0 Lactation) - Summary  
 Sex : Female Time 10 : Before dosing

Test Substance Dose (mg/kg)	Findings	/Day					
		0	1	2	3	4	5
CCH 0	Number of animals	12	12	12	12	12	12
	No abnormality	12	12	12	12	12	12
CCH 10	Number of animals	11	11	11	11	11	11
	No abnormality	11	11	11	11	11	11
CCH 60	Number of animals	12	12	12	11	11	11
	No abnormality	11	11	11	11	11	11
	Total litter loss			1			
	Soiled perineal region	1	1	1			
CCH 300	Number of animals	12	12	12	12	12	12
	No abnormality	12	12	12	12	12	12

Table 5  
Table ContinuedClinical Sign (F0 Lactation) - Summary  
Sex : Female Time 20 : After dosing

Test Substance Dose (mg/kg)	Findings	/Day				
		0	1	2	3	4
CCH 0	Number of animals	12	12	12	12	12
	No abnormality	12	12	12	12	12
CCH 10	Number of animals	11	11	11	11	11
	No abnormality	11	11	11	11	11
CCH 60	Number of animals	12	12	11	11	11
	No abnormality	11	11	11	11	11
	Soiled perineal region	1	1			
CCH 300	Number of animals	12	12	12	12	12
	No abnormality	10	9	11	9	9
	Salivation	2	3	1	3	3

Table 6 Clinical Sign - Summary

Female †

Test Substance Dose(mg/kg)	Findings	Day Time	16		17		18		19		20		21		22		23		24		25		26		27		28		29		30		31		32	
			10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20		
CCH 0	Number of Animals		5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	
	No Abnormality		5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	
CCH 300	Number of Animals		5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	
	No Abnormality		5	4	5	4	5	4	5	4	5	4	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	
	Salivation	1	0	1	0	1	0	1	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	

†, Present; 1, Slight; 2, Moderate; 3, Severe;  
 Time 10, Before dosing; Time 20, After dosing;  
 #:Satellite animal

Table 6 Clinical Sign - Summary

Test Substance Dose(mg/kg)	Findings	Day Time	Female #																																	
			33 10	33 20	34 10	34 20	35 10	35 20	36 10	36 20	37 10	37 20	38 10	38 20	39 10	39 20	40 10	40 20	41 10	41 20	42 10	42 20	43	44	45	46	47	48	49	50	51	52	53	54	55	56
CCH 0	Number of Animals		5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	No Abnormality		5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
CCH 300	Number of Animals		5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	
	No Abnormality		5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	Salivation	1	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	0	0	0	0	0	0	0	0

+, Present; 1, Slight; 2, Moderate; 3, Severe;  
 Time 10, Before dosing; Time 20, After dosing;  
 #:Satellite animal

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Table 6 Clinical Sign - Summary

Female #

Test Substance Dose(mg/kg)	Findings	Day	57
CCH 0	Number of Animals		5
	No Abnormality		5
CCH 300	Number of Animals		5
	No Abnormality		5
	Salivation	1	0

+, Present; 1, Slight; 2, Moderate; 3, Severe;

#:Satellite animal

Table 7 Detailed Clinical Observations - Summary (Week -1)

Items	Sex:	Male				Female				
		Test Substance:	CCH	CCH	CCH	CCH	CCH	CCH	CCH	
		Dose (mg/kg):	0	10	60	300	0	10	60	300
		Number of Animals:	12	12	12	12	17	12	12	17
Home cage observations		(Criteria)								
Tremor	N		12	12	12	12	17	12	12	17
	1		0	0	0	0	0	0	0	0
	2		0	0	0	0	0	0	0	0
Clonic convulsion	N		12	12	12	12	17	12	12	17
	1		0	0	0	0	0	0	0	0
	2		0	0	0	0	0	0	0	0
Tonic convulsion	N		12	12	12	12	17	12	12	17
	1		0	0	0	0	0	0	0	0
	2		0	0	0	0	0	0	0	0
	3		0	0	0	0	0	0	0	0
	4		0	0	0	0	0	0	0	0
	5		0	0	0	0	0	0	0	0
Breathing	N		12	12	12	12	17	12	12	17
	1		0	0	0	0	0	0	0	0
	2		0	0	0	0	0	0	0	0
	3		0	0	0	0	0	0	0	0
	4		0	0	0	0	0	0	0	0
	5		0	0	0	0	0	0	0	0
Hand-held observations										
Reactivity on removal from the cage	1		0	0	0	0	0	0	0	0
	2		12	12	12	12	17	12	12	17
	3		0	0	0	0	0	0	0	0
	4		0	0	0	0	0	0	0	0
	5		0	0	0	0	0	0	0	0
	6		0	0	0	0	0	0	0	0

See Annex 12.7 for details of criteria.

Table 7 Detailed Clinical Observations - Summary (Week -1)

Items	Sex:	Male				Female			
		CCH	CCH	CCH	CCH	CCH	CCH	CCH	CCH
	Test Substance:	0	10	60	300	0	10	60	300
	Dose (mg/kg):	0	10	60	300	0	10	60	300
	Number of Animals:	12	12	12	12	17	12	12	17
Hand-held observations	(Criteria)								
Reactivity to handling	1	0	0	0	0	0	0	0	0
	2	12	12	12	12	17	12	12	17
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
Aggression	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Trauma	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Color of skin	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
Soiled fur	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Exophthalmos	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Palpebral closure	1	12	12	12	12	17	12	12	17
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
Color of conjunctiva	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
Secretion	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0

See Annex 12.7 for details of criteria.

Table 7 Detailed Clinical Observations - Summary (Week -1)

Items	Sex: Test Substance: Dose (mg/kg): Number of Animals:	Male				Female			
		CCH	CCH	CCH	CCH	CCH	CCH	CCH	CCH
		0	10	60	300	0	10	60	300
		12	12	12	12	17	12	12	17
Hand-held observations	(Criteria)								
Lacrimation	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
Salivation	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
Piloerection	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Pupil size	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
Open field observations									
Rearing	Mean	3.8	5.8	7.6	5.5	8.9	12.3	8.0	7.6
	S. D.	4.1	3.0	4.8	3.3	3.6	5.0	5.6	4.2
Arousal	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	12	12	12	12	17	12	12	17
	4	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0
Urination	N	8	11	10	8	14	10	9	16
	P	4	1	2	4	3	2	3	1

See Annex 12.7 for details of criteria.



Table 7 Detailed Clinical Observations - Summary (Week -1)

Items	Sex: Test Substance: Dose (mg/kg): Number of Animals:	Male				Female			
		CCH	CCH	CCH	CCH	CCH	CCH	CCH	CCH
		0	10	60	300	0	10	60	300
		12	12	12	12	17	12	12	17
Open field observations	(Criteria)								
Defecation	N	6	5	9	9	17	12	12	17
	P	6	7	3	3	0	0	0	0
Posture, body position	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0
Breathing	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0
Co-ordination movement	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Gait	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0
	6	0	0	0	0	0	0	0	0
	7	0	0	0	0	0	0	0	0
Tremor	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0

See Annex 12.7 for details of criteria.

Table 7 Detailed Clinical Observations - Summary (Week -1)

Items	Sex:	Male				Female			
		CCH	CCH	CCH	CCH	CCH	CCH	CCH	CCH
	Test Substance:	0	10	60	300	0	10	60	300
	Dose (mg/kg):	0	10	60	300	0	10	60	300
	Number of Animals:	12	12	12	12	17	12	12	17
Open field observations	(Criteria)								
Clonic convulsion	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
Tonic convulsion	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0
Stereotypy	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Bizarre behaviour	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0

See Annex 12.7 for details of criteria.

Table 7 Detailed Clinical Observations - Summary (Week 1)

Items	Sex:	Male				Female				
		CCH	CCH	CCH	CCH	CCH	CCH	CCH	CCH	
	Test Substance:	0	10	60	300	0	10	60	300	
	Dose (mg/kg):	0	10	60	300	0	10	60	300	
	Number of Animals:	12	12	12	12	17	12	12	17	
Home cage observations		(Criteria)								
Tremor	N	12	12	12	12	17	12	12	17	
	1	0	0	0	0	0	0	0	0	
	2	0	0	0	0	0	0	0	0	
Clonic convulsion	N	12	12	12	12	17	12	12	17	
	1	0	0	0	0	0	0	0	0	
	2	0	0	0	0	0	0	0	0	
Tonic convulsion	N	12	12	12	12	17	12	12	17	
	1	0	0	0	0	0	0	0	0	
	2	0	0	0	0	0	0	0	0	
	3	0	0	0	0	0	0	0	0	
	4	0	0	0	0	0	0	0	0	
	5	0	0	0	0	0	0	0	0	
Breathing	N	12	12	12	12	17	12	12	17	
	1	0	0	0	0	0	0	0	0	
	2	0	0	0	0	0	0	0	0	
	3	0	0	0	0	0	0	0	0	
	4	0	0	0	0	0	0	0	0	
	5	0	0	0	0	0	0	0	0	
Hand-held observations										
Reactivity on removal from the cage	1	0	0	0	0	0	0	0	0	
	2	12	12	12	12	17	12	12	17	
	3	0	0	0	0	0	0	0	0	
	4	0	0	0	0	0	0	0	0	
	5	0	0	0	0	0	0	0	0	
	6	0	0	0	0	0	0	0	0	

See Annex 12.7 for details of criteria.

Table 7 Detailed Clinical Observations - Summary (Week 1)

Items	Sex:	Male				Female			
		CCH	CCH	CCH	CCH	CCH	CCH	CCH	CCH
	Test Substance:	0	10	60	300	0	10	60	300
	Dose (mg/kg):	0	10	60	300	0	10	60	300
	Number of Animals:	12	12	12	12	17	12	12	17
Hand-held observations	(Criteria)								
Reactivity to handling	1	0	0	0	0	0	0	0	0
	2	12	12	12	12	17	12	12	17
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
Aggression	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Trauma	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Color of skin	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
Soiled fur	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Exophthalmos	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Palpebral closure	1	12	12	12	12	17	12	12	17
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
Color of conjunctiva	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
Secretion	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0

See Annex 12.7 for details of criteria.

Table 7 Detailed Clinical Observations - Summary (Week 1)

Items	Sex: Test Substance: Dose (mg/kg): Number of Animals:	Male				Female			
		CCH	CCH	CCH	CCH	CCH	CCH	CCH	CCH
		0	10	60	300	0	10	60	300
		12	12	12	12	17	12	12	17
Hand-held observations	(Criteria)								
Lacrimation	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
Salivation	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
Piloerection	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Pupil size	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
Open field observations									
Rearing	Mean	3.8	4.6	3.9	2.3	5.2	11.6	6.8	7.7
	S. D.	3.4	3.7	3.9	2.1	3.8	4.7	4.7	3.9
Arousal	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	12	12	12	12	17	12	12	17
	4	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0
Urination	N	8	7	8	9	15	12	12	17
	P	4	5	4	3	2	0	0	0

See Annex 12.7 for details of criteria.

Table 7 Detailed Clinical Observations - Summary (Week 1)

Items	Sex:	Male				Female			
		CCH	CCH	CCH	CCH	CCH	CCH	CCH	CCH
	Test Substance:	0	10	60	300	0	10	60	300
	Dose (mg/kg):	0	10	60	300	0	10	60	300
	Number of Animals:	12	12	12	12	17	12	12	17
Open field observations	(Criteria)								
Defecation	N	7	7	5	7	14	12	12	17
	P	5	5	7	5	3	0	0	0
Posture, body position	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0
Breathing	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0
Co-ordination movement	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Gait	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0
	6	0	0	0	0	0	0	0	0
	7	0	0	0	0	0	0	0	0
Tremor	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0

See Annex 12.7 for details of criteria.

Table 7 Detailed Clinical Observations - Summary (Week 1)

Items	Sex:	Male				Female			
		CCH	CCH	CCH	CCH	CCH	CCH	CCH	CCH
	Test Substance:	0	10	60	300	0	10	60	300
	Dose (mg/kg):	0	10	60	300	0	10	60	300
	Number of Animals:	12	12	12	12	17	12	12	17
Open field observations	(Criteria)								
Clonic convulsion	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
Tonic convulsion	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0
Stereotypy	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Bizarre behaviour	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0

See Annex 12.7 for details of criteria.

Table 7 Detailed Clinical Observations - Summary (Week 2)

Items	Sex:	Male				Female				
		CCH	CCH	CCH	CCH	CCH	CCH	CCH	CCH	
	Test Substance:	0	10	60	300	0	10	60	300	
	Dose (mg/kg):	0	10	60	300	0	10	60	300	
	Number of Animals:	12	12	12	12	17	12	12	17	
Home cage observations		(Criteria)								
Tremor	N	12	12	12	12	17	12	12	17	
	1	0	0	0	0	0	0	0	0	
	2	0	0	0	0	0	0	0	0	
Clonic convulsion	N	12	12	12	12	17	12	12	17	
	1	0	0	0	0	0	0	0	0	
	2	0	0	0	0	0	0	0	0	
Tonic convulsion	N	12	12	12	12	17	12	12	17	
	1	0	0	0	0	0	0	0	0	
	2	0	0	0	0	0	0	0	0	
	3	0	0	0	0	0	0	0	0	
	4	0	0	0	0	0	0	0	0	
	5	0	0	0	0	0	0	0	0	
Breathing	N	12	12	12	12	17	12	12	17	
	1	0	0	0	0	0	0	0	0	
	2	0	0	0	0	0	0	0	0	
	3	0	0	0	0	0	0	0	0	
	4	0	0	0	0	0	0	0	0	
	5	0	0	0	0	0	0	0	0	
Hand-held observations										
Reactivity on removal	1	0	0	0	0	0	0	0	0	
from the cage	2	12	12	12	12	17	12	12	17	
	3	0	0	0	0	0	0	0	0	
	4	0	0	0	0	0	0	0	0	
	5	0	0	0	0	0	0	0	0	
	6	0	0	0	0	0	0	0	0	

See Annex 12.7 for details of criteria.



Table 7 Detailed Clinical Observations - Summary (Week 2)

Items	Sex:	Male				Female			
		CCH	CCH	CCH	CCH	CCH	CCH	CCH	CCH
	Test Substance:	0	10	60	300	0	10	60	300
	Dose (mg/kg):	0	10	60	300	0	10	60	300
	Number of Animals:	12	12	12	12	17	12	12	17
Hand-held observations	(Criteria)								
Reactivity to handling	1	0	0	0	0	0	0	0	0
	2	12	12	12	12	17	12	12	17
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
Aggression	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Trauma	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Color of skin	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
Soiled fur	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Exophthalmos	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Palpebral closure	1	12	12	12	12	17	12	12	17
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
Color of conjunctiva	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
Secretion	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0

See Annex 12.7 for details of criteria.

Table 7 Detailed Clinical Observations - Summary (Week 2)

Items	Sex: Test Substance: Dose (mg/kg): Number of Animals:	Male				Female			
		CCH	CCH	CCH	CCH	CCH	CCH	CCH	CCH
		0	10	60	300	0	10	60	300
		12	12	12	12	17	12	12	17
Hand-held observations	(Criteria)								
Lacrimation	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
Salivation	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
Piloerection	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Pupil size	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
Open field observations									
Rearing	Mean	2.1	2.4	1.1	1.1	4.8	6.4	7.4	5.6
	S. D.	3.2	3.5	1.9	1.6	3.5	6.5	4.3	5.0
Arousal	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	12	12	12	12	17	12	12	17
	4	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0
Urination	N	10	9	12	11	17	12	12	17
	P	2	3	0	1	0	0	0	0

See Annex 12.7 for details of criteria.

Table 7 Detailed Clinical Observations - Summary (Week 2)

Items	Sex:	Male				Female			
		CCH	CCH	CCH	CCH	CCH	CCH	CCH	CCH
	Test Substance:	0	10	60	300	0	10	60	300
	Dose (mg/kg):	0	10	60	300	0	10	60	300
	Number of Animals:	12	12	12	12	17	12	12	17
Open field observations	(Criteria)								
Defecation	N	5	6	5	7	17	12	12	17
	P	7	6	7	5	0	0	0	0
Posture, body position	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0
Breathing	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0
Co-ordination movement	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Gait	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0
	6	0	0	0	0	0	0	0	0
	7	0	0	0	0	0	0	0	0
Tremor	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0

See Annex 12.7 for details of criteria.

Table 7 Detailed Clinical Observations - Summary (Week 2)

Items	Sex: Test Substance: Dose (mg/kg): Number of Animals:	Male				Female			
		CCH	CCH	CCH	CCH	CCH	CCH	CCH	CCH
		0	10	60	300	0	10	60	300
		12	12	12	12	17	12	12	17
Open field observations	(Criteria)								
Clonic convulsion	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
Tonic convulsion	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0
Stereotypy	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Bizarre behaviour	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0

See Annex 12.7 for details of criteria.

Table 7 Detailed Clinical Observations - Summary (Week 3)

Items	Sex:	Male				Female				
		CCH	CCH	CCH	CCH	CCH	CCH	CCH	CCH	
	Test Substance:	0	10	60	300	0	10	60	300	
	Dose (mg/kg):	0	10	60	300	0	10	60	300	
	Number of Animals:	12	12	12	12	17	12	12	17	
Home cage observations		(Criteria)								
Tremor	N	12	12	12	12	17	12	12	17	
	1	0	0	0	0	0	0	0	0	
	2	0	0	0	0	0	0	0	0	
Clonic convulsion	N	12	12	12	12	17	12	12	17	
	1	0	0	0	0	0	0	0	0	
	2	0	0	0	0	0	0	0	0	
Tonic convulsion	N	12	12	12	12	17	12	12	17	
	1	0	0	0	0	0	0	0	0	
	2	0	0	0	0	0	0	0	0	
	3	0	0	0	0	0	0	0	0	
	4	0	0	0	0	0	0	0	0	
	5	0	0	0	0	0	0	0	0	
Breathing	N	12	12	12	12	17	12	12	17	
	1	0	0	0	0	0	0	0	0	
	2	0	0	0	0	0	0	0	0	
	3	0	0	0	0	0	0	0	0	
	4	0	0	0	0	0	0	0	0	
	5	0	0	0	0	0	0	0	0	
Hand-held observations										
Reactivity on removal from the cage	1	0	0	0	0	0	0	0	0	
	2	12	12	12	12	17	12	12	17	
	3	0	0	0	0	0	0	0	0	
	4	0	0	0	0	0	0	0	0	
	5	0	0	0	0	0	0	0	0	
	6	0	0	0	0	0	0	0	0	

See Annex 12.7 for details of criteria.

Table 7 Detailed Clinical Observations - Summary (Week 3)

Items	Sex:	Male				Female			
		CCH	CCH	CCH	CCH	CCH	CCH	CCH	CCH
	Test Substance:	0	10	60	300	0	10	60	300
	Dose (mg/kg):	12	12	12	12	17	12	12	17
	Number of Animals:								
Hand-held observations	(Criteria)								
Reactivity to handling	1	0	0	0	0	0	0	0	0
	2	12	12	12	12	17	12	12	17
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
Aggression	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Trauma	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Color of skin	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
Soiled fur	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Exophthalmos	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Palpebral closure	1	12	12	12	12	17	12	12	17
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
Color of conjunctiva	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
Secretion	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0

See Annex 12.7 for details of criteria.

Table 7 Detailed Clinical Observations - Summary (Week 3)

Items	Sex: Test Substance: Dose (mg/kg): Number of Animals:	Male				Female			
		CCH	CCH	CCH	CCH	CCH	CCH	CCH	CCH
		0	10	60	300	0	10	60	300
		12	12	12	12	17	12	12	17
Hand-held observations	(Criteria)								
Lacrimation	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
Salivation	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
Piloerection	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Pupil size	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
Open field observations									
Rearing	Mean	1.3	1.0	3.3	4.4	3.2	4.9	3.0	2.4
	S. D.	2.1	2.1	4.0	2.7	3.3	4.3	3.1	2.1
Arousal	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	12	12	12	12	17	12	12	17
	4	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0
Urination	N	12	12	12	12	14	11	11	15
	P	0	0	0	0	3	1	1	2

See Annex 12.7 for details of criteria.

Table 7 Detailed Clinical Observations - Summary (Week 3)

Items	Sex: Test Substance: Dose (mg/kg): Number of Animals:	Male				Female			
		CCH	CCH	CCH	CCH	CCH	CCH	CCH	CCH
		0	10	60	300	0	10	60	300
		12	12	12	12	17	12	12	17
Open field observations	(Criteria)								
Defecation	N	11	12	9	12	13	12	12	17
	P	1	0	3	0	4	0	0	0
Posture, body position	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0
Breathing	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0
Co-ordination movement	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Gait	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0
	6	0	0	0	0	0	0	0	0
	7	0	0	0	0	0	0	0	0
Tremor	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0

See Annex 12.7 for details of criteria.



Table 7 Detailed Clinical Observations - Summary (Week 3)

Items	Sex:	Male				Female			
		CCH	CCH	CCH	CCH	CCH	CCH	CCH	CCH
	Test Substance:	0	10	60	300	0	10	60	300
	Dose (mg/kg):	0	10	60	300	0	10	60	300
	Number of Animals:	12	12	12	12	17	12	12	17
Open field observations	(Criteria)								
Clonic convulsion	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
Tonic convulsion	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0
Stereotypy	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Bizarre behaviour	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0

See Annex 12.7 for details of criteria.

Table 7 Detailed Clinical Observations - Summary (Week 4)

Items	Sex:	Male				Female				
		CCH	CCH	CCH	CCH	CCH	CCH	CCH	CCH	
	Test Substance:	0	10	60	300	0	10	60	300	
	Dose (mg/kg):	0	10	60	300	0	10	60	300	
	Number of Animals:	12	12	12	12	17	12	12	17	
Home cage observations		(Criteria)								
Tremor	N	12	12	12	12	17	12	12	17	
	1	0	0	0	0	0	0	0	0	
	2	0	0	0	0	0	0	0	0	
Clonic convulsion	N	12	12	12	12	17	12	12	17	
	1	0	0	0	0	0	0	0	0	
	2	0	0	0	0	0	0	0	0	
Tonic convulsion	N	12	12	12	12	17	12	12	17	
	1	0	0	0	0	0	0	0	0	
	2	0	0	0	0	0	0	0	0	
	3	0	0	0	0	0	0	0	0	
	4	0	0	0	0	0	0	0	0	
5	0	0	0	0	0	0	0	0		
Breathing	N	12	12	12	12	17	12	12	17	
	1	0	0	0	0	0	0	0	0	
	2	0	0	0	0	0	0	0	0	
	3	0	0	0	0	0	0	0	0	
	4	0	0	0	0	0	0	0	0	
5	0	0	0	0	0	0	0	0		
Hand-held observations										
Reactivity on removal from the cage	1	0	0	0	0	0	0	0	0	
	2	12	12	12	12	17	12	12	17	
	3	0	0	0	0	0	0	0	0	
	4	0	0	0	0	0	0	0	0	
	5	0	0	0	0	0	0	0	0	
	6	0	0	0	0	0	0	0	0	

See Annex 12.7 for details of criteria.

Table 7 Detailed Clinical Observations - Summary (Week 4)

Items	Sex: Test Substance: Dose (mg/kg): Number of Animals:	Male				Female			
		CCH	CCH	CCH	CCH	CCH	CCH	CCH	CCH
		0	10	60	300	0	10	60	300
		12	12	12	12	17	12	12	17
Hand-held observations	(Criteria)								
Reactivity to handling	1	0	0	0	0	0	0	0	0
	2	12	12	12	12	17	12	12	17
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
Aggression	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Trauma	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Color of skin	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
Soiled fur	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Exophthalmos	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Palpebral closure	1	12	12	12	12	17	12	12	17
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
Color of conjunctiva	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
Secretion	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0

See Annex 12.7 for details of criteria.

Table 7 Detailed Clinical Observations - Summary (Week 4)

Items	Sex: Test Substance: Dose (mg/kg): Number of Animals:	Male				Female			
		CCH	CCH	CCH	CCH	CCH	CCH	CCH	CCH
		0	10	60	300	0	10	60	300
		12	12	12	12	17	12	12	17
Hand-held observations	(Criteria)								
Lacrimation	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
Salivation	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
Piloerection	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Pupil size	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
Open field observations									
Rearing	Mean	3.6	3.0	3.0	3.0	2.5	6.5	6.4	5.8
	S. D.	3.4	3.2	5.1	2.7	2.6	6.5	5.0	5.3
Arousal	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	12	12	12	12	17	12	12	17
	4	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0
Urination	N	11	11	11	11	16	12	11	16
	P	1	1	1	1	1	0	1	1

See Annex 12.7 for details of criteria.

Table 7 Detailed Clinical Observations - Summary (Week 4)

Items	Sex: Test Substance: Dose (mg/kg): Number of Animals:	Male				Female			
		CCH	CCH	CCH	CCH	CCH	CCH	CCH	CCH
		0	10	60	300	0	10	60	300
		12	12	12	12	17	12	12	17
Open field observations	(Criteria)								
Defecation	N	7	10	12	12	14	12	12	17
	P	5	2	0	0	3	0	0	0
Posture, body position	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0
Breathing	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0
Co-ordination movement	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Gait	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0
	6	0	0	0	0	0	0	0	0
	7	0	0	0	0	0	0	0	0
Tremor	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0

See Annex 12.7 for details of criteria.