

Neurotoxicity

Positive Control Data in Rats



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	<u>Date Range</u>
Adult Neurotoxicity Positive Control Data	1989 - 2009

Contact: Elise M. Lewis, Ph.D.

**Director of Reproductive and Neurobehavioral Toxicology
Charles River Preclinical Services Pennsylvania**

Phone: 267.532.3741

Fax: 215.443.8587

Email: elise.lewis@crl.com

TESTING FACILITY POSITIVE CONTROL DATA

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1. Introduction

This appendix contains tabulated summaries of positive control studies conducted at Charles River Laboratories Preclinical Services, Pennsylvania for adult neurotoxicity evaluations. As noted in Table 1, this site first conducted the first positive control study for adult neurotoxicity testing in 1989: this appendix contains summaries of the data from an earlier evaluation of the motor activity system (012-058) and from one of the evaluations of positive controls (012-206) using the functional observational battery.

Table 1. Neurotoxicity Positive Control Studies

Study	In-Life Start	Test Substance	Dosage Information			Evaluations		
			mg/kg	mL/kg	Number of Dosages	FOB	Motor Activity	Neuropathology
012-006	12/1989	acrylamide	50	1	7	√		
		physostigmine	0.75	1.5	1			
		DDT	75	1	1			
012-011	05/1991	d-amphetamine	0.75, 1.5, 4	1	1		√	
		chlorpromazine	1, 2, 4	1	1			
012-014	09/1991	acrylamide	40	1	9	√	√	√
		IDPN	200	1	3			
		carbaryl	75	5	1			
		DDT	75	5	1			
		triadimefon	200	5	1			
012-015	03/1992	DDT	75	1	1	√		
012-016	04/1992	d-amphetamine	0.5, 1, 4	1	1		√	
		chlorpromazine	1, 2, 4	1	1			
012-017	05/1992	acrylamide	40	1	9	√		
		IDPN	200	1	3			
		carbaryl	40	5	1			
		DDT	75	1	1			
		d-amphetamine	4	1	1			
012-022	10/1992	carbaryl	40, 200	5	1	√		
012-037	06/1994	acrylamide	45	1	10	√		
		IDPN	250	1	4			
		carbaryl	40	5	1			
		DDT	75	1	1			
		d-amphetamine	4	1	1			
012-056	11/1995	acrylamide	45	1	10	√		
		IDPN	250	1	5			
		carbaryl	40	1	1			
		DDT	75	1	1			
		d-amphetamine	4	1	1			
012-058	04/1996	acrylamide	45	1	10		√	√
		d-amphetamine	0.75	1	1			
		MK-801	10	1	1			
		trimethyltin	8	1	1			
012-061	10/1996	acrylamide	30	1	17	√		
		carbaryl	50, 100	2	1			
		DDT	100	2	1			
		MK-801	0.25	1	1			
		trimethyltin	8	1	2			
012-075	03/1998	acrylamide	30	1	17	√		
		carbaryl	100	4	1			
		DDT	100	2	1			
		MK-801	0.3	1	1			
		trimethyltin	8	1	1			

Table 1. Neurotoxicity Positive Control Studies

Study	In-Life Start	Test Substance	Dosage Information			Evaluations		
			mg/kg	mL/kg	Number of Dosages	FOB	Motor Activity	Neuropathology
012-081	11/2000	acrylamide	30	1	10	√		
		carbaryl	100	4	1			
		d-amphetamine	4	1	1			
		DDT	100	2	1			
		IDPN	250	1	5			
012-081X	12/2001	carbaryl	100	4	1	√		
012-104	05/2002	carbaryl	100	4	1	√		
		chlorpromazine	6	1	1			
		d-amphetamine	4	1	1			
		DDT	75	2	1			
		IDPN	250	1	4/5			
012-104X	05/2003	carbaryl	100	4	1	√		
		DDT	75	2	1			
		carbaryl	100	4	1			
		chlorpromazine	6	1	1			
		d-amphetamine	4	1	1			
		DDT	75	2	1			
		IDPN	250	1	5			
012-134	08/2004	carbaryl	100	4	1	√		
		chlorpromazine	6	1	1			
		d-amphetamine	4	1	1			
		DDT	75	2	1			
		IDPN	250	1	5			
012-143	06/2005	carbaryl	100	4	1	√		
		chlorpromazine	6	1	1			
		d-amphetamine	4	1	1			
		DDT	75	2	1			
		IDPN	250	1	5			
012-155	04/2006	IDPN	75	10	3		√	
		IDPN	150	10	3			
		IDPN	225	10	3			
		IDPN	300	10	3			
		carbaryl	100	4	1			
		chlorpromazine	6	1	1			
		d-amphetamine	4	1	1			
		DDT	75	2	1			
		IDPN	250	1	5			
012-173	04/2007	carbaryl	100	4	1	√		
		chlorpromazine	6	1	1			
		d-amphetamine	4	1	1			
		DDT	75	2	1			
		IDPN	250	1	5			
012-188	01/2008	carbaryl	100	4	1	√		
		chlorpromazine	6	1	1			
		d-amphetamine	4	1	1			
		DDT	75	2	1			
		IDPN	250	1	5			
012-198	07/2008	carbaryl	100	4	1	√		
		chlorpromazine	6	1	1			
		d-amphetamine	4	1	1			
		DDT	75	2	1			
		IDPN	250	1	5			
012-206	02/2009	carbaryl	100	4	1	√		
		chlorpromazine	6	1	1			
		d-amphetamine	4	1	1			
		DDT	75	2	1			
		IDPN	250	1	5			

2. Study 012-058: Neurotoxicity Evaluation of Positive Control Substances in Crl:CD®BR VAF/Plus® Rats

The purpose of this study was to evaluate positive control substances using tests of motor activity and auditory startle habituation and by neurohistological examination. The study was one component of the positive control data collected by the Testing Facility in accordance with the testing guidelines of the U.S. Environmental Protection Agency (EPA). Five Crl:CD BR VAF/Plus (Sprague-Dawley) rats per sex were randomly assigned to each of five dosage groups given the vehicle or one of four test substances. Motor activity was evaluated in three of the five dosage groups, and those results are presented in this summary.

2.1. Methods

2.1.1. Regulatory Compliance

The EPA Good Laboratory Practices (GLPs) were used as the basis for conduct of the study; however, the Quality Assurance Unit did not inspect phases of the study and the prescribed practices regarding characterization and handling of the test substances were modified: Samples of the test solutions/suspensions were not taken for analyses of concentration, stability or homogeneity.

2.1.2. Description of Test Substances, Lot Numbers, Suppliers and Storage

Acrylamide (2-Propenamide; Sigma Chemical Co., Lot 75H0474), a white crystalline powder, was received at the Testing Facility on 07 NOV 95, and stored at room temperature, protected from light.

d-Amphetamine [D-(-)-2-Amino-6-Phosphonohexanoic Acid; Sigma Chemical Co., Lot 75H3787], a white powder, was received at the Testing Facility on 17 NOV 95, and stored at room temperature, protected from light.

The vehicle was 0.9% Sodium Chloride Injection, USP (Baxter Healthcare Corporation, Lot C304717) received at the Testing Facility on 30 JAN 96, and stored at room temperature.

2.1.3. Preparations of Dosing Formulations

Concentrations of 0 mg/mL (0.9% Sodium Chloride for Injection, Vehicle), 45 mg/mL (acrylamide) and 0.75 mg/mL (d-amphetamine) were administered via intraperitoneal injection at a dosage volume of 1 mL/kg.

Acrylamide (Group II) and the vehicle (Group I) were administered once every day for 10 days. The vehicle was also administered to Group I prior to the third motor activity test on the tenth – and last – day of dosage for the rats given acrylamide, and again prior to the fourth motor activity test 3 days after the end of the dosage period for the rats in Group II. d-Amphetamine (Group III) was administered prior to the second, third and fourth motor activity tests.

2.1.4. Testing Procedure

Motor activity was evaluated in four test sessions.

- Session 1. Before the first day of dosage administration in all groups;
- Session 2. As soon as possible after dosage on the eighth day of dosage administration for Groups I and II and after the first dose for Group III;
- Session 3. On the tenth day of dosage for Groups I and II and after the second dose for Group III;
- Session 4. Three days after the tenth – and last – dosage for Group II and after rats in Groups I and III each were injected with another dose.

The movements of each rat were monitored by a passive infrared sensor mounted outside a stainless-steel wire-bottomed cage (40.6 x 25.4 x 17.8 cm). Each test session was 1.5 hours in duration with the number of movements and time spent in movement tabulated at each five-minute interval. The apparatus monitored a rack of up to 32 cages and sensors during each session, with each rat tested in the same location on the rack across test sessions.

As a result of equipment failure, one test was invalid (Group II male rat 17960). This occurrence is noted in the raw data and the tables. On days 1 or 7 of observation (16 APR 96), motor activity data were not recorded for male rats 17951 (Group I), 17956 (Group II) and 17961 (Group III). This deviation did not adversely affect the outcome or interpretation of the study because the missing data were distributed across dosage groups.

2.1.5. Statistical Methods

Data from the motor activity tests, with repeated measurements within a session, were analyzed using an Analysis of Variance with Repeated Measures. A significant effect ($P \leq 0.05$) in that test appeared as an effect of Test Substance (a difference between groups in the total across all measurements in a session) or as an interaction between Test Substance and Block (a difference between groups at specific measurement periods). The Test Substance effect was significant, the totals for the control group and the groups given the different test substances were compared using Dunnett's Test. The Test Substance x Block interaction was significant, an Analysis of Variance Test was used to

evaluate the data at each measurement period, and a significant result ($P \leq 0.05$) was followed by a comparison of the groups using Dunnett's Test.

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 1 (PAGE 1): MOTOR ACTIVITY - SUMMARY - MALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0(VEHICLE)	II 45(ACRYLAMIDE)	III 0.75(d-AMPHETAMINE)
PREDOSAGE				
NUMBER OF RATS	N	5	5	5
NUMBER OF MOVEMENTS				
BLOCK 1	MEAN ± S.D.	71.4 ± 9.5	58.2 ± 16.8	69.2 ± 5.0
BLOCK 2	MEAN ± S.D.	68.6 ± 6.8	53.0 ± 20.0	66.4 ± 7.2
BLOCK 3	MEAN ± S.D.	69.8 ± 12.1	60.0 ± 18.8	73.2 ± 9.7
BLOCK 4	MEAN ± S.D.	64.2 ± 3.7	53.8 ± 11.7	69.8 ± 9.8
BLOCK 5	MEAN ± S.D.	69.6 ± 7.5	60.8 ± 17.2	69.6 ± 8.9
BLOCK 6	MEAN ± S.D.	53.2 ± 18.5	60.2 ± 16.2	71.0 ± 8.5
BLOCK 7	MEAN ± S.D.	64.8 ± 4.9	61.6 ± 15.5	70.6 ± 7.6
BLOCK 8	MEAN ± S.D.	62.2 ± 3.1	59.8 ± 16.8	68.2 ± 15.2
BLOCK 9	MEAN ± S.D.	64.0 ± 12.1	49.6 ± 13.5	72.2 ± 11.4
BLOCK 10	MEAN ± S.D.	67.2 ± 9.4	58.2 ± 16.3	72.6 ± 10.6
BLOCK 11	MEAN ± S.D.	66.6 ± 10.3	51.6 ± 8.6	65.2 ± 10.5
BLOCK 12	MEAN ± S.D.	58.2 ± 10.7	55.2 ± 16.2	64.2 ± 8.6
BLOCK 13	MEAN ± S.D.	58.4 ± 10.1	53.6 ± 10.7	62.2 ± 25.1
BLOCK 14	MEAN ± S.D.	71.0 ± 6.0	52.2 ± 15.0	51.4 ± 34.4
BLOCK 15	MEAN ± S.D.	58.8 ± 14.6	54.8 ± 20.8	57.0 ± 33.7
BLOCK 16	MEAN ± S.D.	39.4 ± 23.5	39.6 ± 33.7	55.2 ± 28.9
BLOCK 17	MEAN ± S.D.	13.4 ± 25.6	32.8 ± 29.2	44.8 ± 31.8
BLOCK 18	MEAN ± S.D.	10.6 ± 23.7	19.6 ± 20.1	31.2 ± 26.5
TOTAL	MEAN ± S.D.	1031.4 ± 55.3	934.6 ± 242.1	1134.0 ± 196.8

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 1 (PAGE 2): MOTOR ACTIVITY - SUMMARY - MALE RATS

DOSAGE GROUP			I		II		III	
DOSAGE (MG/KG/DAY)			0(VEHICLE)		45(ACRYLAMIDE)		0.75(d-AMPHETAMINE)	
PREDOSAGE								
NUMBER OF RATS		N	5		5		5	
TIME (SECONDS) SPENT IN MOVEMENT								
BLOCK 1	MEAN ± S.D.		195.6 ± 21.8		217.2 ± 37.0		207.2 ± 28.9	
BLOCK 2	MEAN ± S.D.		160.2 ± 33.2		190.8 ± 43.1		174.4 ± 41.7	
BLOCK 3	MEAN ± S.D.		155.6 ± 23.6		187.0 ± 48.2		169.0 ± 17.1	
BLOCK 4	MEAN ± S.D.		145.2 ± 11.3		156.0 ± 36.4		145.2 ± 27.7	
BLOCK 5	MEAN ± S.D.		139.4 ± 14.4		161.2 ± 28.8		133.8 ± 12.4	
BLOCK 6	MEAN ± S.D.		115.4 ± 53.7		156.2 ± 39.9		152.2 ± 29.1	
BLOCK 7	MEAN ± S.D.		139.6 ± 22.8		152.8 ± 41.9		131.0 ± 27.9	
BLOCK 8	MEAN ± S.D.		137.0 ± 37.7		175.6 ± 24.2		124.4 ± 49.4	
BLOCK 9	MEAN ± S.D.		112.4 ± 35.1		142.6 ± 52.2		148.6 ± 28.5	
BLOCK 10	MEAN ± S.D.		119.8 ± 28.8		150.6 ± 46.4		144.8 ± 15.7	
BLOCK 11	MEAN ± S.D.		136.2 ± 46.1		153.2 ± 43.4		119.6 ± 33.7	
BLOCK 12	MEAN ± S.D.		95.0 ± 18.8		125.2 ± 28.9		110.2 ± 62.7	
BLOCK 13	MEAN ± S.D.		107.8 ± 40.9		129.6 ± 47.0		89.2 ± 49.4	
BLOCK 14	MEAN ± S.D.		109.2 ± 26.1		116.2 ± 27.1		92.8 ± 63.4	
BLOCK 15	MEAN ± S.D.		103.4 ± 60.6		98.6 ± 39.2		115.4 ± 76.8	
BLOCK 16	MEAN ± S.D.		59.4 ± 45.8		79.6 ± 83.6		93.0 ± 64.4	
BLOCK 17	MEAN ± S.D.		18.0 ± 39.7		47.0 ± 43.8		55.8 ± 53.9	
BLOCK 18	MEAN ± S.D.		14.6 ± 32.6		27.0 ± 32.2		55.0 ± 57.7	
TOTAL	MEAN ± S.D.		2063.8 ± 355.4		2466.4 ± 427.5		2261.6 ± 543.6	

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 1 (PAGE 3): MOTOR ACTIVITY - SUMMARY - MALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0(VEHICLE)	II 45(ACRYLAMIDE)	III 0.75(d-AMPHETAMINE)
SESSION 2				
NUMBER OF RATS	N	5	5	5
NUMBER OF MOVEMENTS				
BLOCK 1	MEAN ± S.D.	71.8 ± 8.8	66.0 ± 14.9	66.2 ± 6.4
BLOCK 2	MEAN ± S.D.	70.6 ± 10.3	32.0 ± 29.2*	68.4 ± 7.9
BLOCK 3	MEAN ± S.D.	74.4 ± 15.3	25.6 ± 33.0*	76.2 ± 15.2
BLOCK 4	MEAN ± S.D.	66.4 ± 11.6	21.4 ± 29.6**	71.6 ± 2.3
BLOCK 5	MEAN ± S.D.	66.8 ± 6.4	9.0 ± 11.9**	79.2 ± 13.5
BLOCK 6	MEAN ± S.D.	62.8 ± 6.9	9.8 ± 11.0**	75.0 ± 7.0
BLOCK 7	MEAN ± S.D.	60.0 ± 13.6	7.6 ± 6.9**	77.8 ± 13.2
BLOCK 8	MEAN ± S.D.	36.6 ± 29.5	2.8 ± 1.9*	70.6 ± 5.8*
BLOCK 9	MEAN ± S.D.	29.8 ± 30.4	12.2 ± 11.8	74.0 ± 7.6**
BLOCK 10	MEAN ± S.D.	18.6 ± 26.1	10.8 ± 8.9	77.2 ± 7.1**
BLOCK 11	MEAN ± S.D.	18.8 ± 26.4	8.0 ± 3.5	72.0 ± 6.8**
BLOCK 12	MEAN ± S.D.	11.6 ± 23.8	5.6 ± 4.3	69.8 ± 14.7**
BLOCK 13	MEAN ± S.D.	1.6 ± 1.8	10.8 ± 10.9	71.2 ± 18.0**
BLOCK 14	MEAN ± S.D.	14.4 ± 22.3	8.4 ± 7.8	67.6 ± 23.4**
BLOCK 15	MEAN ± S.D.	9.6 ± 17.8	6.0 ± 9.6	63.4 ± 10.5**
BLOCK 16	MEAN ± S.D.	15.0 ± 28.0	9.6 ± 12.1	70.0 ± 11.3**
BLOCK 17	MEAN ± S.D.	1.8 ± 1.1	12.2 ± 13.1	62.8 ± 23.2**
BLOCK 18	MEAN ± S.D.	2.6 ± 5.3	8.8 ± 6.6	68.8 ± 22.5**
TOTAL	MEAN ± S.D.	633.2 ± 106.0	266.6 ± 114.4**	1281.8 ± 146.9**

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

* Significantly different from the vehicle control group value ($P \leq 0.05$).

** Significantly different from the vehicle control group value ($P \leq 0.01$).

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 1 (PAGE 4): MOTOR ACTIVITY - SUMMARY - MALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0(VEHICLE)	II 45(ACRYLAMIDE)	III 0.75(d-AMPHETAMINE)
SESSION 2				
NUMBER OF RATS	N	5	5	5
TIME (SECONDS) SPENT IN MOVEMENT				
BLOCK 1	MEAN ± S.D.	177.4 ± 27.0	154.2 ± 65.1	225.0 ± 22.7
BLOCK 2	MEAN ± S.D.	144.4 ± 40.9	84.4 ± 92.5	203.4 ± 47.9
BLOCK 3	MEAN ± S.D.	125.2 ± 32.3	62.8 ± 86.4	196.4 ± 50.5
BLOCK 4	MEAN ± S.D.	139.8 ± 61.0	42.6 ± 77.4*	207.0 ± 33.3
BLOCK 5	MEAN ± S.D.	111.6 ± 35.0	12.6 ± 20.9**	180.4 ± 41.0*
BLOCK 6	MEAN ± S.D.	109.4 ± 47.1	10.4 ± 14.8**	214.8 ± 15.9**
BLOCK 7	MEAN ± S.D.	103.2 ± 45.1	5.6 ± 5.1**	182.0 ± 27.2**
BLOCK 8	MEAN ± S.D.	57.4 ± 67.4	1.8 ± 2.5	185.2 ± 32.5**
BLOCK 9	MEAN ± S.D.	59.4 ± 66.8	10.4 ± 10.5	163.6 ± 43.1**
BLOCK 10	MEAN ± S.D.	25.4 ± 38.6	16.6 ± 29.4	149.0 ± 39.5**
BLOCK 11	MEAN ± S.D.	24.8 ± 34.3	8.2 ± 6.1	190.0 ± 29.9**
BLOCK 12	MEAN ± S.D.	12.8 ± 27.0	4.6 ± 5.8	147.6 ± 45.7**
BLOCK 13	MEAN ± S.D.	1.6 ± 2.3	11.8 ± 15.7	126.2 ± 38.6**
BLOCK 14	MEAN ± S.D.	13.2 ± 21.8	9.2 ± 10.2	125.8 ± 48.6**
BLOCK 15	MEAN ± S.D.	6.8 ± 13.6	7.8 ± 15.2	135.6 ± 62.8**
BLOCK 16	MEAN ± S.D.	16.6 ± 35.4	7.4 ± 8.5	106.4 ± 44.7**
BLOCK 17	MEAN ± S.D.	2.0 ± 2.9	11.2 ± 13.9	123.0 ± 71.4**
BLOCK 18	MEAN ± S.D.	3.0 ± 6.2	5.2 ± 4.9	120.6 ± 64.6**
TOTAL	MEAN ± S.D.	1134.0 ± 409.6	466.8 ± 347.3	2982.0 ± 571.8**

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

* Significantly different from the vehicle control group value ($P \leq 0.05$).

** Significantly different from the vehicle control group value ($P \leq 0.01$).

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 1 (PAGE 5): MOTOR ACTIVITY - SUMMARY - MALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0(VEHICLE)	II 45(ACRYLAMIDE)	III 0.75(d-AMPHETAMINE)
SESSION 3				
NUMBER OF RATS	N	5	5	5
NUMBER OF MOVEMENTS				
BLOCK 1	MEAN ± S.D.	70.0 ± 12.1	62.0 ± 20.6	57.0 ± 5.6
BLOCK 2	MEAN ± S.D.	66.4 ± 7.2	47.8 ± 39.1	66.6 ± 3.7
BLOCK 3	MEAN ± S.D.	72.8 ± 12.4	19.8 ± 24.3**	72.8 ± 8.6
BLOCK 4	MEAN ± S.D.	68.6 ± 9.4	10.4 ± 15.6**	74.8 ± 9.0
BLOCK 5	MEAN ± S.D.	65.2 ± 9.0	10.2 ± 7.2**	75.4 ± 2.2
BLOCK 6	MEAN ± S.D.	44.0 ± 28.7	9.2 ± 3.3*	72.0 ± 8.3*
BLOCK 7	MEAN ± S.D.	39.0 ± 25.9	8.2 ± 7.5*	69.4 ± 10.7*
BLOCK 8	MEAN ± S.D.	33.0 ± 31.7	17.0 ± 16.5	73.0 ± 2.4*
BLOCK 9	MEAN ± S.D.	32.2 ± 35.3	10.6 ± 8.0	67.4 ± 8.0*
BLOCK 10	MEAN ± S.D.	25.0 ± 30.4	23.6 ± 29.2	71.2 ± 14.8*
BLOCK 11	MEAN ± S.D.	9.4 ± 11.1	19.6 ± 21.7	72.6 ± 3.8**
BLOCK 12	MEAN ± S.D.	2.0 ± 1.6	5.0 ± 2.1	75.6 ± 2.3**
BLOCK 13	MEAN ± S.D.	1.8 ± 1.5	18.8 ± 15.4*	73.4 ± 7.8**
BLOCK 14	MEAN ± S.D.	4.2 ± 1.9	14.8 ± 12.4	72.8 ± 11.2**
BLOCK 15	MEAN ± S.D.	3.2 ± 4.6	8.0 ± 8.7	75.2 ± 12.4**
BLOCK 16	MEAN ± S.D.	6.4 ± 9.0	12.0 ± 8.4	66.8 ± 18.2**
BLOCK 17	MEAN ± S.D.	0.4 ± 0.9	20.4 ± 11.3	55.4 ± 27.9**
BLOCK 18	MEAN ± S.D.	1.6 ± 1.8	12.4 ± 11.2	56.6 ± 34.1**
TOTAL	MEAN ± S.D.	545.2 ± 139.8	329.8 ± 135.5*	1248.0 ± 81.0**

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

* Significantly different from the vehicle control group value ($P \leq 0.05$).

** Significantly different from the vehicle control group value ($P \leq 0.01$).

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 1 (PAGE 6): MOTOR ACTIVITY - SUMMARY - MALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0(VEHICLE)	II 45(ACRYLAMIDE)	III 0.75(d-AMPHETAMINE)
SESSION 3				
NUMBER OF RATS	N	5	5	5
TIME (SECONDS) SPENT IN MOVEMENT				
BLOCK 1	MEAN ± S.D.	176.0 ± 45.4	115.8 ± 65.6	232.6 ± 42.7
BLOCK 2	MEAN ± S.D.	160.6 ± 32.3	81.4 ± 78.8	223.4 ± 48.1
BLOCK 3	MEAN ± S.D.	148.4 ± 21.2	39.6 ± 70.8**	201.8 ± 35.0
BLOCK 4	MEAN ± S.D.	147.8 ± 33.0	14.0 ± 30.2**	203.8 ± 34.3*
BLOCK 5	MEAN ± S.D.	121.2 ± 12.8	7.8 ± 5.1**	205.6 ± 28.8**
BLOCK 6	MEAN ± S.D.	74.0 ± 58.5	5.8 ± 4.8*	204.0 ± 36.7**
BLOCK 7	MEAN ± S.D.	58.2 ± 43.3	7.0 ± 9.4	187.8 ± 45.4**
BLOCK 8	MEAN ± S.D.	44.2 ± 44.0	19.2 ± 18.8	208.6 ± 24.8**
BLOCK 9	MEAN ± S.D.	34.4 ± 36.4	8.8 ± 5.3	187.6 ± 49.5**
BLOCK 10	MEAN ± S.D.	29.4 ± 39.6	31.6 ± 39.2	170.6 ± 48.5**
BLOCK 11	MEAN ± S.D.	9.2 ± 12.7	21.4 ± 28.6	175.0 ± 38.2**
BLOCK 12	MEAN ± S.D.	0.6 ± 0.5	2.4 ± 1.8	159.8 ± 42.0**
BLOCK 13	MEAN ± S.D.	0.6 ± 0.9	18.2 ± 11.2	153.8 ± 38.7**
BLOCK 14	MEAN ± S.D.	2.6 ± 2.7	14.8 ± 13.2	159.2 ± 31.9**
BLOCK 15	MEAN ± S.D.	1.2 ± 1.6	5.6 ± 8.7	151.4 ± 45.4**
BLOCK 16	MEAN ± S.D.	7.0 ± 14.0	9.8 ± 8.2	114.6 ± 56.1**
BLOCK 17	MEAN ± S.D.	0.0 ± 0.0	20.8 ± 13.8	91.0 ± 60.3**
BLOCK 18	MEAN ± S.D.	0.2 ± 0.4	12.4 ± 17.3	114.8 ± 78.5**
TOTAL	MEAN ± S.D.	1015.6 ± 240.5	436.4 ± 199.3	3145.4 ± 641.2**

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

* Significantly different from the vehicle control group value ($P \leq 0.05$).

** Significantly different from the vehicle control group value ($P \leq 0.01$).

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 1 (PAGE 7): MOTOR ACTIVITY - SUMMARY - MALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0(VEHICLE)	II 45(ACRYLAMIDE)	III 0.75(d-AMPHETAMINE)
SESSION 4				
NUMBER OF RATS	N	5	3a	5
NUMBER OF MOVEMENTS				
BLOCK 1	MEAN ± S.D.	73.0 ± 10.8	44.3 ± 44.0	60.6 ± 6.1
BLOCK 2	MEAN ± S.D.	70.2 ± 13.1	35.3 ± 31.0*	63.4 ± 3.8
BLOCK 3	MEAN ± S.D.	69.4 ± 8.8	7.7 ± 12.4**	72.0 ± 4.7
BLOCK 4	MEAN ± S.D.	59.6 ± 6.2	6.3 ± 7.8**	69.0 ± 6.6
BLOCK 5	MEAN ± S.D.	71.4 ± 14.7	17.0 ± 25.2**	74.6 ± 10.4
BLOCK 6	MEAN ± S.D.	64.4 ± 14.0	9.3 ± 4.0**	69.2 ± 7.2
BLOCK 7	MEAN ± S.D.	53.2 ± 18.1	8.0 ± 5.6**	74.4 ± 8.0*
BLOCK 8	MEAN ± S.D.	35.0 ± 28.6	3.7 ± 5.5	75.2 ± 13.4*
BLOCK 9	MEAN ± S.D.	24.6 ± 30.7	3.7 ± 1.2	78.2 ± 5.2**
BLOCK 10	MEAN ± S.D.	18.4 ± 32.8	12.7 ± 12.9	74.4 ± 8.8**
BLOCK 11	MEAN ± S.D.	16.6 ± 29.3	5.7 ± 6.6	77.6 ± 9.2**
BLOCK 12	MEAN ± S.D.	14.8 ± 26.4	10.7 ± 8.4	78.6 ± 6.4**
BLOCK 13	MEAN ± S.D.	18.4 ± 28.9	1.0 ± 1.0	74.0 ± 7.4**
BLOCK 14	MEAN ± S.D.	11.4 ± 20.0	2.0 ± 2.0	76.4 ± 12.2**
BLOCK 15	MEAN ± S.D.	16.6 ± 31.2	10.3 ± 15.3	74.2 ± 3.8**
BLOCK 16	MEAN ± S.D.	9.0 ± 19.6	0.3 ± 0.6	78.0 ± 4.2**
BLOCK 17	MEAN ± S.D.	16.8 ± 19.3	3.3 ± 5.8	74.4 ± 10.2**
BLOCK 18	MEAN ± S.D.	8.4 ± 15.6	8.3 ± 8.0	76.4 ± 9.5**
TOTAL	MEAN ± S.D.	651.2 ± 174.8	189.7 ± 143.5**	1320.6 ± 76.9**

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

a. Excludes values for rats that were found dead.

* Significantly different from the vehicle control group value ($P \leq 0.05$).

** Significantly different from the vehicle control group value ($P \leq 0.01$).

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 1 (PAGE 8): MOTOR ACTIVITY - SUMMARY - MALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0(VEHICLE)	II 45(ACRYLAMIDE)	III 0.75(d-AMPHETAMINE)
SESSION 4				
NUMBER OF RATS	N	5	3a	5
TIME (SECONDS) SPENT IN MOVEMENT				
BLOCK 1	MEAN ± S.D.	170.4 ± 38.9	69.3 ± 78.8*	233.0 ± 25.3
BLOCK 2	MEAN ± S.D.	148.8 ± 42.7	55.7 ± 48.5*	217.2 ± 36.6*
BLOCK 3	MEAN ± S.D.	134.4 ± 25.8	6.3 ± 11.0**	211.2 ± 3.3**
BLOCK 4	MEAN ± S.D.	116.8 ± 35.3	5.0 ± 7.8**	202.0 ± 25.7**
BLOCK 5	MEAN ± S.D.	113.6 ± 25.2	24.0 ± 39.8**	200.6 ± 20.5**
BLOCK 6	MEAN ± S.D.	91.2 ± 19.6	7.7 ± 6.4**	186.0 ± 33.3**
BLOCK 7	MEAN ± S.D.	82.6 ± 57.2	11.0 ± 13.4	174.4 ± 35.8*
BLOCK 8	MEAN ± S.D.	49.0 ± 50.5	3.3 ± 5.8	204.2 ± 20.9**
BLOCK 9	MEAN ± S.D.	26.2 ± 37.8	1.3 ± 0.6	167.6 ± 35.8**
BLOCK 10	MEAN ± S.D.	34.6 ± 73.5	28.7 ± 43.7	169.8 ± 13.4**
BLOCK 11	MEAN ± S.D.	18.4 ± 36.2	4.0 ± 4.6	172.8 ± 26.3**
BLOCK 12	MEAN ± S.D.	15.0 ± 27.5	9.3 ± 8.6	157.4 ± 18.3**
BLOCK 13	MEAN ± S.D.	21.4 ± 31.9	0.0 ± 0.0	179.0 ± 37.1**
BLOCK 14	MEAN ± S.D.	12.2 ± 23.5	0.3 ± 0.6	139.4 ± 13.2**
BLOCK 15	MEAN ± S.D.	25.8 ± 43.3	10.7 ± 18.5	143.2 ± 39.2**
BLOCK 16	MEAN ± S.D.	11.6 ± 25.9	0.0 ± 0.0	139.6 ± 36.6**
BLOCK 17	MEAN ± S.D.	26.8 ± 38.6	2.7 ± 4.6	148.0 ± 49.4**
BLOCK 18	MEAN ± S.D.	5.4 ± 11.5	5.3 ± 5.0	157.6 ± 40.5**
TOTAL	MEAN ± S.D.	1104.2 ± 279.4	244.7 ± 212.3**	3203.0 ± 301.0**

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

a. Excludes values for rats that were found dead.

* Significantly different from the vehicle control group value ($P \leq 0.05$).

** Significantly different from the vehicle control group value ($P \leq 0.01$).

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:CD®BR VAF/Plus® RATS

TABLE 2 (PAGE 1): MOTOR ACTIVITY - SUMMARY - FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0(VEHICLE)	II 45(ACRYLAMIDE)	III 0.75(d-AMPHETAMINE)
PREDOSAGE				
NUMBER OF RATS	N	5	5	5
NUMBER OF MOVEMENTS				
BLOCK 1	MEAN ± S.D.	65.2 ± 12.0	75.4 ± 7.9	71.4 ± 10.9
BLOCK 2	MEAN ± S.D.	72.4 ± 11.0	77.0 ± 7.4	70.0 ± 6.7
BLOCK 3	MEAN ± S.D.	70.4 ± 10.6	73.8 ± 10.4	66.0 ± 10.1
BLOCK 4	MEAN ± S.D.	71.8 ± 12.5	77.2 ± 5.6	70.0 ± 13.8
BLOCK 5	MEAN ± S.D.	70.8 ± 17.0	73.8 ± 8.7	72.6 ± 12.0
BLOCK 6	MEAN ± S.D.	69.2 ± 6.2	68.4 ± 12.7	69.8 ± 17.6
BLOCK 7	MEAN ± S.D.	68.0 ± 6.4	79.6 ± 8.8	53.8 ± 30.0
BLOCK 8	MEAN ± S.D.	61.8 ± 30.2	67.8 ± 16.2	50.6 ± 31.0
BLOCK 9	MEAN ± S.D.	50.6 ± 28.7	64.8 ± 24.0	50.2 ± 31.8
BLOCK 10	MEAN ± S.D.	54.4 ± 30.6	58.4 ± 17.8	35.0 ± 28.2
BLOCK 11	MEAN ± S.D.	49.8 ± 32.1	66.8 ± 19.1	54.4 ± 30.5
BLOCK 12	MEAN ± S.D.	56.6 ± 20.2	56.4 ± 15.8	49.0 ± 29.5
BLOCK 13	MEAN ± S.D.	57.8 ± 16.0	39.8 ± 29.0	32.6 ± 21.2
BLOCK 14	MEAN ± S.D.	45.0 ± 36.0	44.8 ± 38.0	26.0 ± 21.8
BLOCK 15	MEAN ± S.D.	30.0 ± 28.4	38.2 ± 34.9	11.4 ± 18.9
BLOCK 16	MEAN ± S.D.	27.4 ± 24.4	29.2 ± 38.3	9.8 ± 9.7
BLOCK 17	MEAN ± S.D.	12.8 ± 12.6	20.6 ± 35.3	13.6 ± 20.2
BLOCK 18	MEAN ± S.D.	9.0 ± 17.4	14.8 ± 27.0	20.0 ± 31.3
TOTAL	MEAN ± S.D.	943.0 ± 163.9	1026.8 ± 271.2	826.2 ± 209.9

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 2 (PAGE 2): MOTOR ACTIVITY - SUMMARY - FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0(VEHICLE)	II 45(ACRYLAMIDE)	III 0.75(d-AMPHETAMINE)
PREDOSAGE				
NUMBER OF RATS	N	5	5	5
TIME (SECONDS) SPENT IN MOVEMENT				
BLOCK 1	MEAN ± S.D.	226.8 ± 16.0	216.2 ± 12.2	203.4 ± 23.1
BLOCK 2	MEAN ± S.D.	191.2 ± 14.0	177.6 ± 33.2	185.0 ± 30.2
BLOCK 3	MEAN ± S.D.	186.2 ± 19.4	195.2 ± 32.3	160.8 ± 32.4
BLOCK 4	MEAN ± S.D.	162.8 ± 24.5	154.6 ± 32.3	145.8 ± 63.7
BLOCK 5	MEAN ± S.D.	178.4 ± 25.4	162.0 ± 35.4	138.4 ± 29.7
BLOCK 6	MEAN ± S.D.	136.4 ± 32.7	126.4 ± 39.9	109.8 ± 18.6
BLOCK 7	MEAN ± S.D.	120.8 ± 31.5	120.6 ± 20.4	95.8 ± 56.6
BLOCK 8	MEAN ± S.D.	108.4 ± 61.5	100.6 ± 36.4	75.2 ± 57.7
BLOCK 9	MEAN ± S.D.	89.4 ± 65.8	98.4 ± 48.9	74.2 ± 46.3
BLOCK 10	MEAN ± S.D.	100.0 ± 66.9	91.8 ± 54.7	69.0 ± 72.5
BLOCK 11	MEAN ± S.D.	84.4 ± 70.0	105.8 ± 75.6	78.6 ± 48.4
BLOCK 12	MEAN ± S.D.	74.4 ± 57.6	78.2 ± 58.9	64.2 ± 46.1
BLOCK 13	MEAN ± S.D.	108.2 ± 26.5	47.0 ± 44.8	34.8 ± 32.3
BLOCK 14	MEAN ± S.D.	46.4 ± 38.6	57.2 ± 53.8	29.2 ± 31.2
BLOCK 15	MEAN ± S.D.	70.6 ± 80.7	48.6 ± 46.4	19.4 ± 39.0
BLOCK 16	MEAN ± S.D.	32.4 ± 35.9	32.2 ± 51.9	6.4 ± 8.0
BLOCK 17	MEAN ± S.D.	7.8 ± 9.3	18.4 ± 37.8	18.0 ± 32.1
BLOCK 18	MEAN ± S.D.	6.4 ± 13.2	10.0 ± 21.2	34.8 ± 62.9
TOTAL	MEAN ± S.D.	1931.0 ± 437.6	1840.8 ± 477.6	1542.8 ± 410.2

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 2 (PAGE 3): MOTOR ACTIVITY - SUMMARY - FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0(VEHICLE)	II 45(ACRYLAMIDE)	III 0.75(d-AMPHETAMINE)
SESSION 2				
NUMBER OF RATS	N	5	5	5
NUMBER OF MOVEMENTS				
BLOCK 1	MEAN ± S.D.	67.6 ± 6.1	71.4 ± 12.6	59.2 ± 5.0
BLOCK 2	MEAN ± S.D.	74.8 ± 12.4	75.2 ± 10.0	60.2 ± 9.4
BLOCK 3	MEAN ± S.D.	73.8 ± 11.4	55.6 ± 34.4	67.2 ± 12.4
BLOCK 4	MEAN ± S.D.	56.6 ± 14.2	14.4 ± 20.6**	70.2 ± 13.2
BLOCK 5	MEAN ± S.D.	52.8 ± 29.3	15.0 ± 9.3*	68.2 ± 10.4
BLOCK 6	MEAN ± S.D.	58.4 ± 10.0	16.0 ± 18.7**	62.6 ± 15.1
BLOCK 7	MEAN ± S.D.	56.0 ± 14.8	9.0 ± 9.0**	75.2 ± 18.0
BLOCK 8	MEAN ± S.D.	40.4 ± 28.9	12.6 ± 14.0	63.4 ± 12.7
BLOCK 9	MEAN ± S.D.	24.8 ± 30.0	20.8 ± 34.3	67.8 ± 13.5
BLOCK 10	MEAN ± S.D.	13.0 ± 20.8	15.4 ± 17.5	68.0 ± 15.8**
BLOCK 11	MEAN ± S.D.	18.4 ± 21.7	6.8 ± 3.3	67.0 ± 13.6**
BLOCK 12	MEAN ± S.D.	36.6 ± 28.5	18.0 ± 17.6	65.4 ± 8.0
BLOCK 13	MEAN ± S.D.	37.2 ± 14.1	26.6 ± 21.1	74.4 ± 13.9**
BLOCK 14	MEAN ± S.D.	34.6 ± 25.2	40.4 ± 42.1	70.0 ± 13.7
BLOCK 15	MEAN ± S.D.	23.2 ± 30.3	20.2 ± 19.3	61.2 ± 13.2*
BLOCK 16	MEAN ± S.D.	19.6 ± 31.8	8.8 ± 8.2	69.8 ± 8.9**
BLOCK 17	MEAN ± S.D.	3.4 ± 3.1	9.8 ± 10.0	66.8 ± 10.0**
BLOCK 18	MEAN ± S.D.	16.0 ± 31.4	16.2 ± 16.7	69.4 ± 9.2**
TOTAL	MEAN ± S.D.	707.2 ± 122.1	452.2 ± 167.8*	1206.0 ± 173.7**

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

* Significantly different from the vehicle control group value ($P \leq 0.05$).

** Significantly different from the vehicle control group value ($P \leq 0.01$).

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:CD®BR VAF/Plus® RATS

TABLE 2 (PAGE 4): MOTOR ACTIVITY - SUMMARY - FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0(VEHICLE)	II 45(ACRYLAMIDE)	III 0.75(d-AMPHETAMINE)
SESSION 2				
NUMBER OF RATS	N	5	5	5
TIME (SECONDS) SPENT IN MOVEMENT				
BLOCK 1	MEAN ± S.D.	207.6 ± 18.5	131.8 ± 50.0**	250.8 ± 6.0
BLOCK 2	MEAN ± S.D.	168.8 ± 27.0	106.2 ± 45.5*	243.2 ± 26.0**
BLOCK 3	MEAN ± S.D.	138.6 ± 23.9	67.4 ± 45.6**	231.8 ± 24.4**
BLOCK 4	MEAN ± S.D.	134.4 ± 48.6	11.2 ± 15.2**	222.6 ± 35.8**
BLOCK 5	MEAN ± S.D.	81.8 ± 50.9	14.2 ± 13.3*	233.8 ± 20.6**
BLOCK 6	MEAN ± S.D.	84.4 ± 24.5	12.6 ± 19.6**	218.8 ± 43.8**
BLOCK 7	MEAN ± S.D.	82.8 ± 39.1	3.8 ± 5.9**	210.6 ± 36.0**
BLOCK 8	MEAN ± S.D.	60.6 ± 52.0	13.0 ± 15.1	214.2 ± 38.8**
BLOCK 9	MEAN ± S.D.	22.6 ± 24.0	22.8 ± 43.2	211.8 ± 40.3**
BLOCK 10	MEAN ± S.D.	7.0 ± 12.9	11.0 ± 16.0	201.8 ± 50.3**
BLOCK 11	MEAN ± S.D.	16.2 ± 23.3	4.0 ± 3.4	189.6 ± 45.4**
BLOCK 12	MEAN ± S.D.	48.6 ± 45.9	16.2 ± 19.6	155.2 ± 62.8**
BLOCK 13	MEAN ± S.D.	47.6 ± 30.9	19.8 ± 21.5	163.6 ± 48.3**
BLOCK 14	MEAN ± S.D.	46.6 ± 41.8	49.8 ± 61.6	194.8 ± 47.3**
BLOCK 15	MEAN ± S.D.	30.0 ± 44.3	19.0 ± 26.4	170.2 ± 46.9**
BLOCK 16	MEAN ± S.D.	13.6 ± 24.9	3.8 ± 4.3	157.0 ± 52.6**
BLOCK 17	MEAN ± S.D.	1.0 ± 0.7	5.8 ± 6.4	157.8 ± 55.4**
BLOCK 18	MEAN ± S.D.	14.2 ± 29.5	11.4 ± 16.0	157.8 ± 56.8**
TOTAL	MEAN ± S.D.	1206.4 ± 265.4	523.8 ± 277.3*	3585.4 ± 633.6**

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

* Significantly different from the vehicle control group value ($P \leq 0.05$).

** Significantly different from the vehicle control group value ($P \leq 0.01$).

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 2 (PAGE 5): MOTOR ACTIVITY - SUMMARY - FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0(VEHICLE)	II 45(ACRYLAMIDE)	III 0.75(d-AMPHETAMINE)
SESSION 3				
NUMBER OF RATS	N	5	5	5
NUMBER OF MOVEMENTS				
BLOCK 1	MEAN ± S.D.	59.4 ± 12.9	63.2 ± 25.2	57.6 ± 9.1
BLOCK 2	MEAN ± S.D.	63.4 ± 10.3	22.8 ± 23.5**	62.0 ± 6.2
BLOCK 3	MEAN ± S.D.	67.6 ± 11.6	7.0 ± 9.2**	69.0 ± 13.4
BLOCK 4	MEAN ± S.D.	62.4 ± 7.3	8.0 ± 13.0**	69.8 ± 13.0
BLOCK 5	MEAN ± S.D.	60.4 ± 5.9	6.0 ± 9.6**	71.4 ± 12.0
BLOCK 6	MEAN ± S.D.	34.8 ± 26.0	6.2 ± 5.9	65.8 ± 18.2*
BLOCK 7	MEAN ± S.D.	46.6 ± 12.0	11.6 ± 11.1**	69.4 ± 9.6*
BLOCK 8	MEAN ± S.D.	40.4 ± 25.7	12.0 ± 11.6	71.8 ± 17.1*
BLOCK 9	MEAN ± S.D.	36.8 ± 33.6	4.0 ± 3.1	67.8 ± 13.4
BLOCK 10	MEAN ± S.D.	22.8 ± 31.9	4.4 ± 5.4	69.8 ± 15.2**
BLOCK 11	MEAN ± S.D.	24.8 ± 34.1	4.2 ± 2.6	74.0 ± 9.4**
BLOCK 12	MEAN ± S.D.	11.6 ± 13.5	15.0 ± 10.4	63.6 ± 10.0**
BLOCK 13	MEAN ± S.D.	16.2 ± 16.0	4.0 ± 2.6	70.4 ± 9.9**
BLOCK 14	MEAN ± S.D.	2.2 ± 2.5	12.0 ± 18.8	66.0 ± 18.0**
BLOCK 15	MEAN ± S.D.	1.2 ± 1.3	4.0 ± 3.8	55.8 ± 29.6**
BLOCK 16	MEAN ± S.D.	0.2 ± 0.4	8.0 ± 8.3	51.4 ± 31.1**
BLOCK 17	MEAN ± S.D.	4.0 ± 2.9	9.4 ± 8.7	46.8 ± 30.0**
BLOCK 18	MEAN ± S.D.	2.0 ± 1.9	19.0 ± 8.7	51.0 ± 29.8**
TOTAL	MEAN ± S.D.	556.8 ± 106.5	220.8 ± 99.9**	1153.4 ± 76.9**

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

* Significantly different from the vehicle control group value ($P \leq 0.05$).

** Significantly different from the vehicle control group value ($P \leq 0.01$).

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 2 (PAGE 6): MOTOR ACTIVITY - SUMMARY - FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0(VEHICLE)	II 45(ACRYLAMIDE)	III 0.75(d-AMPHETAMINE)
SESSION 3				
NUMBER OF RATS	N	5	5	5
TIME (SECONDS) SPENT IN MOVEMENT				
BLOCK 1	MEAN ± S.D.	220.0 ± 14.7	99.6 ± 76.6**	253.8 ± 10.4
BLOCK 2	MEAN ± S.D.	194.0 ± 30.8	21.0 ± 30.7**	243.0 ± 15.9*
BLOCK 3	MEAN ± S.D.	146.4 ± 34.6	3.6 ± 5.9**	234.8 ± 17.8**
BLOCK 4	MEAN ± S.D.	113.2 ± 37.3	12.4 ± 27.2**	224.4 ± 29.9**
BLOCK 5	MEAN ± S.D.	86.4 ± 42.2	8.0 ± 15.7**	206.0 ± 31.6**
BLOCK 6	MEAN ± S.D.	40.4 ± 40.8	3.4 ± 3.5	219.0 ± 32.9**
BLOCK 7	MEAN ± S.D.	67.0 ± 41.3	8.0 ± 6.2*	191.6 ± 42.7**
BLOCK 8	MEAN ± S.D.	49.8 ± 30.7	9.8 ± 15.3	206.4 ± 40.4**
BLOCK 9	MEAN ± S.D.	43.0 ± 46.3	1.8 ± 2.0	186.6 ± 43.8**
BLOCK 10	MEAN ± S.D.	24.0 ± 31.8	2.2 ± 3.5	180.6 ± 41.1**
BLOCK 11	MEAN ± S.D.	25.8 ± 37.0	2.2 ± 2.5	175.0 ± 47.9**
BLOCK 12	MEAN ± S.D.	7.2 ± 9.2	11.6 ± 10.3	177.4 ± 38.1**
BLOCK 13	MEAN ± S.D.	10.8 ± 11.6	1.6 ± 1.8	150.6 ± 54.3**
BLOCK 14	MEAN ± S.D.	1.8 ± 3.0	15.4 ± 29.5	155.2 ± 65.6**
BLOCK 15	MEAN ± S.D.	0.6 ± 1.3	2.4 ± 2.5	133.6 ± 80.1**
BLOCK 16	MEAN ± S.D.	0.0 ± 0.0	4.6 ± 4.8	112.6 ± 74.2**
BLOCK 17	MEAN ± S.D.	2.0 ± 1.9	8.6 ± 10.3	93.0 ± 78.3*
BLOCK 18	MEAN ± S.D.	0.6 ± 0.9	12.4 ± 7.1	109.6 ± 78.8**
TOTAL	MEAN ± S.D.	1033.0 ± 237.3	228.6 ± 209.0*	3253.2 ± 708.8**

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

* Significantly different from the vehicle control group value ($P \leq 0.05$).

** Significantly different from the vehicle control group value ($P \leq 0.01$).

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 2 (PAGE 7): MOTOR ACTIVITY - SUMMARY - FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0(VEHICLE)	II 45(ACRYLAMIDE)	III 0.75(d-AMPHETAMINE)
SESSION 4				
NUMBER OF RATS	N	5	5	5
NUMBER OF MOVEMENTS				
BLOCK 1	MEAN ± S.D.	70.8 ± 4.4	45.4 ± 35.8**	56.4 ± 9.2
BLOCK 2	MEAN ± S.D.	67.8 ± 7.4	31.4 ± 16.8**	65.0 ± 6.4*
BLOCK 3	MEAN ± S.D.	64.6 ± 13.6	5.4 ± 4.9**	65.6 ± 16.7*
BLOCK 4	MEAN ± S.D.	55.6 ± 19.2	8.4 ± 12.2**	59.8 ± 14.0**
BLOCK 5	MEAN ± S.D.	54.6 ± 23.5	12.6 ± 18.1*	63.0 ± 20.9**
BLOCK 6	MEAN ± S.D.	51.4 ± 30.4	1.6 ± 1.8**	59.6 ± 14.1**
BLOCK 7	MEAN ± S.D.	34.2 ± 41.1	14.6 ± 16.6	68.4 ± 12.9**
BLOCK 8	MEAN ± S.D.	26.8 ± 34.5	9.0 ± 10.3	67.0 ± 11.4**
BLOCK 9	MEAN ± S.D.	29.4 ± 34.1	8.4 ± 9.9	67.6 ± 15.7**
BLOCK 10	MEAN ± S.D.	29.8 ± 29.6	3.6 ± 2.5	69.6 ± 11.4**
BLOCK 11	MEAN ± S.D.	36.2 ± 34.5	15.6 ± 14.2	65.2 ± 16.1*
BLOCK 12	MEAN ± S.D.	25.6 ± 31.5	15.0 ± 25.3	67.2 ± 14.8**
BLOCK 13	MEAN ± S.D.	25.2 ± 32.8	4.4 ± 4.8	68.0 ± 17.4**
BLOCK 14	MEAN ± S.D.	21.4 ± 23.0	2.2 ± 3.8	70.4 ± 11.3**
BLOCK 15	MEAN ± S.D.	26.2 ± 35.9	7.2 ± 9.0	67.8 ± 9.3**
BLOCK 16	MEAN ± S.D.	20.2 ± 16.3	5.2 ± 5.3	68.8 ± 8.0**
BLOCK 17	MEAN ± S.D.	19.8 ± 20.8	6.6 ± 4.0	73.2 ± 12.1**
BLOCK 18	MEAN ± S.D.	21.2 ± 25.5	16.6 ± 21.6	63.8 ± 14.3**
TOTAL	MEAN ± S.D.	680.8 ± 247.5	213.2 ± 70.0*	1186.4 ± 170.9**

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

* Significantly different from the vehicle control group value ($P \leq 0.05$).

** Significantly different from the vehicle control group value ($P \leq 0.01$).

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 2 (PAGE 8): MOTOR ACTIVITY - SUMMARY - FEMALE RATS

DOSAGE GROUP DOSAGE (MG/KG/DAY)		I 0(VEHICLE)	II 45(ACRYLAMIDE)	III 0.75(d-AMPHETAMINE)
SESSION 4				
NUMBER OF RATS	N	5	5	5
TIME (SECONDS) SPENT IN MOVEMENT				
BLOCK 1	MEAN ± S.D.	195.0 ± 21.4	73.4 ± 73.3	260.2 ± 11.9
BLOCK 2	MEAN ± S.D.	187.8 ± 28.0	31.4 ± 25.7**	235.6 ± 18.8
BLOCK 3	MEAN ± S.D.	147.2 ± 62.6	2.6 ± 4.7**	222.0 ± 30.6
BLOCK 4	MEAN ± S.D.	95.2 ± 45.0	5.8 ± 9.8**	240.8 ± 30.6
BLOCK 5	MEAN ± S.D.	73.8 ± 38.2	8.6 ± 14.4*	218.4 ± 42.3
BLOCK 6	MEAN ± S.D.	63.8 ± 37.0	0.8 ± 1.3**	239.0 ± 24.6
BLOCK 7	MEAN ± S.D.	48.6 ± 66.1	9.6 ± 11.4	199.2 ± 59.5
BLOCK 8	MEAN ± S.D.	39.0 ± 53.6	4.2 ± 5.4	204.4 ± 41.4*
BLOCK 9	MEAN ± S.D.	50.4 ± 68.0	5.0 ± 8.0	190.6 ± 38.0*
BLOCK 10	MEAN ± S.D.	47.6 ± 68.4	1.0 ± 1.0	169.4 ± 61.5**
BLOCK 11	MEAN ± S.D.	67.0 ± 85.0	10.8 ± 11.3	181.2 ± 52.1
BLOCK 12	MEAN ± S.D.	27.2 ± 35.3	16.4 ± 33.9	166.8 ± 39.1*
BLOCK 13	MEAN ± S.D.	20.8 ± 26.7	2.8 ± 3.6	184.0 ± 50.8*
BLOCK 14	MEAN ± S.D.	24.0 ± 28.3	0.8 ± 1.8	172.4 ± 62.8**
BLOCK 15	MEAN ± S.D.	24.2 ± 40.6	4.2 ± 5.8	169.2 ± 50.4*
BLOCK 16	MEAN ± S.D.	19.4 ± 19.6	4.2 ± 5.5	164.8 ± 37.3**
BLOCK 17	MEAN ± S.D.	28.8 ± 35.3	4.6 ± 3.4	177.8 ± 46.4**
BLOCK 18	MEAN ± S.D.	19.4 ± 26.6	14.4 ± 19.7	135.2 ± 74.9*
TOTAL	MEAN ± S.D.	1179.2 ± 490.9	200.6 ± 117.7**	3531.0 ± 679.6**

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

* Significantly different from the vehicle control group value ($P \leq 0.05$).

** Significantly different from the vehicle control group value ($P \leq 0.01$).

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 3 (PAGE 1): MOTOR ACTIVITY - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP I		0.9% SALINE		0(VEHICLE) MG/KG/DAY		PREDOSAGE	
RAT NUMBER		17951	17952	17953	17954	17955	
NUMBER OF MOVEMENTS							
BLOCK	1	77	65	83	59	73	
BLOCK	2	74	67	75	58	69	
BLOCK	3	77	55	86	68	63	
BLOCK	4	64	59	69	63	66	
BLOCK	5	81	70	68	60	69	
BLOCK	6	62	61	67	55	21	
BLOCK	7	60	69	61	63	71	
BLOCK	8	63	57	62	64	65	
BLOCK	9	63	66	44	74	73	
BLOCK	10	67	65	58	63	83	
BLOCK	11	62	77	61	78	55	
BLOCK	12	59	66	70	53	43	
BLOCK	13	58	67	56	43	68	
BLOCK	14	74	62	68	77	74	
BLOCK	15	33	65	68	62	66	
BLOCK	16	7	50	35	71	34	
BLOCK	17	2	6	0	59	0	
BLOCK	18	0	0	0	53	0	
TOTAL		983	1027	1031	1123	993	

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 3 (PAGE 2): MOTOR ACTIVITY - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP I		0.9% SALINE		0(VEHICLE) MG/KG/DAY		PREDOSAGE
RAT NUMBER		17951	17952	17953	17954	17955
TIME (SECONDS) SPENT IN MOVEMENT						
BLOCK 1	187	224	174	213	180	
BLOCK 2	149	210	151	171	120	
BLOCK 3	142	192	159	156	129	
BLOCK 4	141	162	131	148	144	
BLOCK 5	148	152	149	120	128	
BLOCK 6	126	187	125	101	38	
BLOCK 7	109	171	149	131	138	
BLOCK 8	107	202	135	117	124	
BLOCK 9	81	143	68	133	137	
BLOCK 10	96	165	98	131	109	
BLOCK 11	163	162	165	134	57	
BLOCK 12	107	110	108	81	69	
BLOCK 13	76	170	128	75	90	
BLOCK 14	75	125	91	115	140	
BLOCK 15	24	102	115	192	84	
BLOCK 16	2	56	72	127	40	
BLOCK 17	0	1	0	89	0	
BLOCK 18	0	0	0	73	0	
TOTAL	1733	2534	2018	2307	1727	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.						

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 3 (PAGE 3): MOTOR ACTIVITY - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP II		ACRYLAMIDE		45 MG/KG/DAY		PREDOSAGE
RAT NUMBER		17956	17957	17958	17959	17960
NUMBER OF MOVEMENTS						
BLOCK 1	76	67	59	31	58	
BLOCK 2	62	61	74	22	46	
BLOCK 3	75	71	71	30	53	
BLOCK 4	54	60	64	34	57	
BLOCK 5	76	57	73	33	65	
BLOCK 6	78	47	74	41	61	
BLOCK 7	75	54	73	38	68	
BLOCK 8	72	70	74	39	44	
BLOCK 9	51	40	70	35	52	
BLOCK 10	54	63	77	33	64	
BLOCK 11	63	51	51	39	54	
BLOCK 12	54	63	74	30	55	
BLOCK 13	52	70	42	47	57	
BLOCK 14	56	43	71	32	59	
BLOCK 15	80	71	49	28	46	
BLOCK 16	70	60	6	0	62	
BLOCK 17	61	55	3	0	45	
BLOCK 18	21	22	4	0	51	
TOTAL	1130	1025	1009	512	997	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.						

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 3 (PAGE 4): MOTOR ACTIVITY - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP II		ACRYLAMIDE		45 MG/KG/DAY		PREDOSAGE
RAT NUMBER		17956	17957	17958	17959	17960
TIME (SECONDS) SPENT IN MOVEMENT						
BLOCK 1	217	224	164	268	213	
BLOCK 2	211	152	146	250	195	
BLOCK 3	177	118	187	252	201	
BLOCK 4	141	132	119	205	183	
BLOCK 5	155	130	139	196	186	
BLOCK 6	156	103	138	210	174	
BLOCK 7	127	95	163	200	179	
BLOCK 8	149	182	159	212	176	
BLOCK 9	162	78	117	218	138	
BLOCK 10	129	139	128	233	124	
BLOCK 11	161	115	133	225	132	
BLOCK 12	100	142	116	167	101	
BLOCK 13	124	114	62	179	169	
BLOCK 14	71	120	116	135	139	
BLOCK 15	163	107	67	85	71	
BLOCK 16	197	74	3	0	124	
BLOCK 17	90	80	0	0	65	
BLOCK 18	23	32	1	0	79	
TOTAL	2553	2137	1958	3035	2649	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.						

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:CD®BR VAF/Plus® RATS

TABLE 3 (PAGE 5): MOTOR ACTIVITY - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP III		d-AMPHETAMINE		0.75 MG/KG/DAY		PREDOSAGE	
RAT NUMBER		17961	17962	17963	17964	17965	
NUMBER OF MOVEMENTS							
BLOCK	1	74	69	70	61	72	
BLOCK	2	75	68	68	66	55	
BLOCK	3	86	61	72	68	79	
BLOCK	4	71	68	73	55	82	
BLOCK	5	70	68	71	57	82	
BLOCK	6	77	63	80	61	74	
BLOCK	7	63	77	73	62	78	
BLOCK	8	50	77	84	54	76	
BLOCK	9	74	68	80	55	84	
BLOCK	10	67	69	78	61	88	
BLOCK	11	63	56	55	73	79	
BLOCK	12	56	71	63	56	75	
BLOCK	13	27	64	60	62	98	
BLOCK	14	0	74	62	35	86	
BLOCK	15	0	60	65	71	89	
BLOCK	16	6	53	77	70	70	
BLOCK	17	0	53	25	73	73	
BLOCK	18	2	51	11	27	65	
TOTAL		861	1170	1167	1067	1405	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.							

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 3 (PAGE 6): MOTOR ACTIVITY - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP III		d-AMPHETAMINE		0.75 MG/KG/DAY		PREDOSAGE	
RAT NUMBER		17961	17962	17963	17964	17965	
TIME (SECONDS) SPENT IN MOVEMENT							
BLOCK	1	186	173	222	209	246	
BLOCK	2	144	146	190	151	241	
BLOCK	3	176	174	145	160	190	
BLOCK	4	152	142	159	100	173	
BLOCK	5	125	121	129	149	145	
BLOCK	6	113	129	171	174	174	
BLOCK	7	94	108	153	148	152	
BLOCK	8	54	122	175	104	167	
BLOCK	9	171	118	165	117	172	
BLOCK	10	122	146	162	138	156	
BLOCK	11	118	72	117	124	167	
BLOCK	12	48	133	76	86	208	
BLOCK	13	16	87	121	76	146	
BLOCK	14	0	133	90	74	167	
BLOCK	15	0	114	216	123	124	
BLOCK	16	3	65	94	172	131	
BLOCK	17	0	43	15	92	129	
BLOCK	18	0	80	8	46	141	
TOTAL		1522	2106	2408	2243	3029	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.							

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 3 (PAGE 7): MOTOR ACTIVITY - INDIVIDUAL DATA - MALE RATS

	DOSAGE GROUP I	0.9% SALINE			0(VEHICLE) MG/KG/DAY	SESSION 2
RAT NUMBER	17951	17952	17953	17954	17955	
NUMBER OF MOVEMENTS						
BLOCK 1	73	58	81	77	70	
BLOCK 2	83	68	79	65	58	
BLOCK 3	88	68	75	89	52	
BLOCK 4	81	57	74	67	53	
BLOCK 5	60	66	62	76	70	
BLOCK 6	51	69	64	65	65	
BLOCK 7	84	58	52	54	52	
BLOCK 8	16	75	14	62	16	
BLOCK 9	1	70	0	29	49	
BLOCK 10	0	58	0	2	33	
BLOCK 11	0	39	0	0	55	
BLOCK 12	0	4	0	0	54	
BLOCK 13	0	4	0	1	3	
BLOCK 14	0	4	8	54	6	
BLOCK 15	0	7	0	41	0	
BLOCK 16	4	5	1	65	0	
BLOCK 17	2	2	0	3	2	
BLOCK 18	0	12	1	0	0	
TOTAL	543	724	511	750	638	

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 3 (PAGE 8): MOTOR ACTIVITY - INDIVIDUAL DATA - MALE RATS

	DOSAGE GROUP I	0.9% SALINE			0(VEHICLE) MG/KG/DAY	SESSION 2
RAT NUMBER	17951	17952	17953	17954	17955	
TIME (SECONDS) SPENT IN MOVEMENT						
BLOCK 1	202	196	171	184	134	
BLOCK 2	170	202	132	114	104	
BLOCK 3	149	150	105	144	78	
BLOCK 4	98	219	115	189	78	
BLOCK 5	72	148	115	143	80	
BLOCK 6	59	170	78	147	93	
BLOCK 7	85	174	68	121	68	
BLOCK 8	11	165	17	83	11	
BLOCK 9	0	149	0	40	108	
BLOCK 10	0	88	0	1	38	
BLOCK 11	0	69	0	0	55	
BLOCK 12	0	3	0	0	61	
BLOCK 13	0	5	0	0	3	
BLOCK 14	0	3	5	52	6	
BLOCK 15	0	3	0	31	0	
BLOCK 16	1	2	0	80	0	
BLOCK 17	0	2	0	7	1	
BLOCK 18	0	14	1	0	0	
TOTAL	847	1762	807	1336	918	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.						

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 3 (PAGE 9): MOTOR ACTIVITY - INDIVIDUAL DATA - MALE RATS

	DOSAGE GROUP II		ACRYLAMIDE		45 MG/KG/DAY	SESSION 2
RAT NUMBER	17956	17957	17958	17959	17960	
NUMBER OF MOVEMENTS						
BLOCK 1	67	41	80	74	68	
BLOCK 2	60	5	11	17	67	
BLOCK 3	67	0	2	3	56	
BLOCK 4	68	1	34	2	2	
BLOCK 5	28	0	0	13	4	
BLOCK 6	27	0	14	2	6	
BLOCK 7	0	3	18	9	8	
BLOCK 8	3	2	2	1	6	
BLOCK 9	6	1	26	4	24	
BLOCK 10	26	10	7	8	3	
BLOCK 11	7	6	13	4	10	
BLOCK 12	5	3	5	13	2	
BLOCK 13	3	12	0	28	11	
BLOCK 14	6	5	2	7	22	
BLOCK 15	1	4	0	2	23	
BLOCK 16	4	4	31	7	2	
BLOCK 17	5	9	35	2	10	
BLOCK 18	17	3	14	2	8	
TOTAL	400	109	294	198	332	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.						

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 3 (PAGE 10): MOTOR ACTIVITY - INDIVIDUAL DATA - MALE RATS

	DOSAGE GROUP II	ACRYLAMIDE		45 MG/KG/DAY		SESSION 2
RAT NUMBER	17956	17957	17958	17959	17960	
TIME (SECONDS) SPENT IN MOVEMENT						
BLOCK 1	228	50	152	178	163	
BLOCK 2	212	11	16	29	154	
BLOCK 3	174	0	0	1	139	
BLOCK 4	179	0	31	0	3	
BLOCK 5	49	0	0	12	2	
BLOCK 6	36	0	8	0	8	
BLOCK 7	0	2	11	11	4	
BLOCK 8	5	0	0	0	4	
BLOCK 9	6	0	19	3	24	
BLOCK 10	69	7	3	3	1	
BLOCK 11	6	4	6	6	19	
BLOCK 12	2	3	2	15	1	
BLOCK 13	3	6	0	39	11	
BLOCK 14	6	6	1	6	27	
BLOCK 15	1	3	0	0	35	
BLOCK 16	6	3	22	6	0	
BLOCK 17	3	8	35	0	10	
BLOCK 18	12	0	7	1	6	
TOTAL	997	103	313	310	611	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.						

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 3 (PAGE 11): MOTOR ACTIVITY - INDIVIDUAL DATA - MALE RATS

	DOSAGE GROUP III	d-AMPHETAMINE	0.75 MG/KG/DAY	SESSION 2	
RAT NUMBER	17961	17962	17963	17964	17965
NUMBER OF MOVEMENTS					
BLOCK 1	72	70	69	64	56
BLOCK 2	67	68	79	57	71
BLOCK 3	71	71	100	59	80
BLOCK 4	70	72	75	72	69
BLOCK 5	69	73	90	67	97
BLOCK 6	75	83	78	64	75
BLOCK 7	63	72	99	78	77
BLOCK 8	65	65	70	76	77
BLOCK 9	74	62	82	73	79
BLOCK 10	76	71	88	71	80
BLOCK 11	69	77	79	62	73
BLOCK 12	71	66	88	48	76
BLOCK 13	79	77	71	41	88
BLOCK 14	67	67	84	30	90
BLOCK 15	66	66	69	45	71
BLOCK 16	74	54	71	66	85
BLOCK 17	79	22	68	71	74
BLOCK 18	84	35	89	57	79
TOTAL	1291	1171	1449	1101	1397
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.					

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 3 (PAGE 12): MOTOR ACTIVITY - INDIVIDUAL DATA - MALE RATS

	DOSAGE GROUP III	d-AMPHETAMINE		0.75 MG/KG/DAY		SESSION 2
RAT NUMBER	17961	17962	17963	17964	17965	
TIME (SECONDS) SPENT IN MOVEMENT						
BLOCK 1	208	241	236	194	246	
BLOCK 2	225	254	178	133	227	
BLOCK 3	238	235	147	136	226	
BLOCK 4	231	227	185	159	233	
BLOCK 5	226	204	140	134	198	
BLOCK 6	242	206	206	216	204	
BLOCK 7	195	183	156	156	220	
BLOCK 8	233	188	157	153	195	
BLOCK 9	214	131	127	139	207	
BLOCK 10	189	142	121	103	190	
BLOCK 11	239	170	162	190	189	
BLOCK 12	155	137	169	77	200	
BLOCK 13	161	105	121	76	168	
BLOCK 14	165	105	138	52	169	
BLOCK 15	225	81	152	70	150	
BLOCK 16	151	43	82	113	143	
BLOCK 17	201	13	166	105	130	
BLOCK 18	185	21	135	98	164	
TOTAL	3683	2686	2778	2304	3459	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.						

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 3 (PAGE 13): MOTOR ACTIVITY - INDIVIDUAL DATA - MALE RATS

	DOSAGE GROUP I		0.9% SALINE		0(VEHICLE) MG/KG/DAY		SESSION 3
RAT NUMBER	17951	17952	17953	17954	17955		
NUMBER OF MOVEMENTS							
BLOCK 1	82	53	76	77	62		
BLOCK 2	71	72	67	68	54		
BLOCK 3	83	87	73	58	63		
BLOCK 4	83	67	61	60	72		
BLOCK 5	64	60	61	81	60		
BLOCK 6	12	65	18	78	47		
BLOCK 7	28	44	0	64	59		
BLOCK 8	0	55	0	69	41		
BLOCK 9	0	22	0	73	66		
BLOCK 10	7	2	0	54	62		
BLOCK 11	0	5	0	17	25		
BLOCK 12	2	3	1	0	4		
BLOCK 13	1	4	0	2	2		
BLOCK 14	6	4	1	5	5		
BLOCK 15	11	3	0	2	0		
BLOCK 16	1	22	3	6	0		
BLOCK 17	0	0	0	2	0		
BLOCK 18	0	0	4	3	1		
TOTAL	451	568	365	719	623		

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 3 (PAGE 14): MOTOR ACTIVITY - INDIVIDUAL DATA - MALE RATS

	DOSAGE GROUP I	0.9% SALINE	0(VEHICLE) MG/KG/DAY	SESSION 3	
RAT NUMBER	17951	17952	17953	17954	17955
TIME (SECONDS) SPENT IN MOVEMENT					
BLOCK 1	189	228	179	181	103
BLOCK 2	169	206	153	159	116
BLOCK 3	132	181	159	136	134
BLOCK 4	162	171	110	181	115
BLOCK 5	118	137	125	124	102
BLOCK 6	13	103	25	156	73
BLOCK 7	33	86	0	110	62
BLOCK 8	0	102	0	64	55
BLOCK 9	0	32	0	56	84
BLOCK 10	5	1	0	53	88
BLOCK 11	0	2	0	15	29
BLOCK 12	1	1	0	0	1
BLOCK 13	0	2	0	0	1
BLOCK 14	2	3	0	1	7
BLOCK 15	3	3	0	0	0
BLOCK 16	0	32	1	2	0
BLOCK 17	0	0	0	0	0
BLOCK 18	0	0	1	0	0
TOTAL	827	1290	753	1238	970
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.					

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 3 (PAGE 15): MOTOR ACTIVITY - INDIVIDUAL DATA - MALE RATS

	DOSAGE GROUP II	ACRYLAMIDE		45 MG/KG/DAY		SESSION 3
RAT NUMBER	17956	17957	17958	17959	17960	
NUMBER OF MOVEMENTS						
BLOCK 1	67	28	84	63	68	
BLOCK 2	66	74	87	0	12	
BLOCK 3	61	5	22	1	10	
BLOCK 4	2	2	8	2	38	
BLOCK 5	8	2	20	15	6	
BLOCK 6	7	15	8	8	8	
BLOCK 7	2	0	13	18	8	
BLOCK 8	24	2	42	4	13	
BLOCK 9	8	1	23	12	9	
BLOCK 10	0	1	33	70	14	
BLOCK 11	8	14	58	12	6	
BLOCK 12	5	7	2	7	4	
BLOCK 13	5	17	45	16	11	
BLOCK 14	3	33	22	7	9	
BLOCK 15	5	2	23	8	2	
BLOCK 16	1	5	18	19	17	
BLOCK 17	16	21	39	9	17	
BLOCK 18	5	5	22	3	27	
TOTAL	293	234	569	274	279	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.						

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 3 (PAGE 16): MOTOR ACTIVITY - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP II		ACRYLAMIDE		45 MG/KG/DAY		SESSION 3	
RAT NUMBER		17956	17957	17958	17959	17960	
TIME (SECONDS) SPENT IN MOVEMENT							
BLOCK 1		208	26	126	94	125	
BLOCK 2		177	90	136	0	4	
BLOCK 3		165	1	25	0	7	
BLOCK 4		1	0	1	0	68	
BLOCK 5		10	1	13	11	4	
BLOCK 6		3	14	2	4	6	
BLOCK 7		1	0	4	23	7	
BLOCK 8		37	2	41	2	14	
BLOCK 9		15	1	9	12	7	
BLOCK 10		0	0	43	94	21	
BLOCK 11		7	9	72	15	4	
BLOCK 12		5	3	0	2	2	
BLOCK 13		12	20	37	13	9	
BLOCK 14		1	32	20	2	19	
BLOCK 15		1	0	21	4	2	
BLOCK 16		0	4	17	19	9	
BLOCK 17		21	14	43	6	20	
BLOCK 18		5	2	13	0	42	
TOTAL		669	219	623	301	370	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.							

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 3 (PAGE 17): MOTOR ACTIVITY - INDIVIDUAL DATA - MALE RATS

	DOSAGE GROUP III	d-AMPHETAMINE	0.75 MG/KG/DAY	SESSION 3	
RAT NUMBER	17961	17962	17963	17964	17965
NUMBER OF MOVEMENTS					
BLOCK 1	63	54	63	54	51
BLOCK 2	72	62	68	65	66
BLOCK 3	80	73	72	59	80
BLOCK 4	78	73	81	60	82
BLOCK 5	76	75	76	78	72
BLOCK 6	76	73	73	80	58
BLOCK 7	76	80	70	52	69
BLOCK 8	72	72	75	76	70
BLOCK 9	60	64	77	61	75
BLOCK 10	75	69	93	52	67
BLOCK 11	69	71	75	70	78
BLOCK 12	78	76	77	75	72
BLOCK 13	72	76	85	64	70
BLOCK 14	65	80	64	66	89
BLOCK 15	78	69	58	80	91
BLOCK 16	75	85	37	73	64
BLOCK 17	80	68	10	48	71
BLOCK 18	93	61	1	57	71
TOTAL	1338	1281	1155	1170	1296
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.					

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 3 (PAGE 18): MOTOR ACTIVITY - INDIVIDUAL DATA - MALE RATS

	DOSAGE GROUP III		d-AMPHETAMINE		0.75 MG/KG/DAY	SESSION 3
RAT NUMBER	17961	17962	17963	17964	17965	
TIME (SECONDS) SPENT IN MOVEMENT						
BLOCK 1	240	264	232	161	266	
BLOCK 2	236	259	237	139	246	
BLOCK 3	189	230	219	146	225	
BLOCK 4	214	221	206	145	233	
BLOCK 5	207	232	177	176	236	
BLOCK 6	164	226	203	174	253	
BLOCK 7	192	210	185	115	237	
BLOCK 8	214	222	176	192	239	
BLOCK 9	243	192	159	120	224	
BLOCK 10	181	211	147	99	215	
BLOCK 11	174	224	130	147	200	
BLOCK 12	186	144	115	135	219	
BLOCK 13	174	164	130	101	200	
BLOCK 14	165	147	169	114	201	
BLOCK 15	187	190	105	99	176	
BLOCK 16	172	119	21	131	130	
BLOCK 17	118	153	3	57	124	
BLOCK 18	180	140	0	71	183	
TOTAL	3436	3548	2614	2322	3807	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.						

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 3 (PAGE 19): MOTOR ACTIVITY - INDIVIDUAL DATA - MALE RATS

	DOSAGE GROUP I	0.9% SALINE			0(VEHICLE) MG/KG/DAY	SESSION 4
RAT NUMBER	17951	17952	17953	17954	17955	
NUMBER OF MOVEMENTS						
BLOCK 1	78	69	89	61	68	
BLOCK 2	74	80	82	65	50	
BLOCK 3	60	60	73	75	79	
BLOCK 4	65	63	64	51	55	
BLOCK 5	87	85	52	69	64	
BLOCK 6	58	84	52	74	54	
BLOCK 7	69	75	33	48	41	
BLOCK 8	18	25	4	75	53	
BLOCK 9	3	9	2	74	35	
BLOCK 10	0	1	0	76	15	
BLOCK 11	1	5	4	69	4	
BLOCK 12	2	4	4	62	2	
BLOCK 13	0	4	0	20	68	
BLOCK 14	2	1	6	1	47	
BLOCK 15	2	9	0	0	72	
BLOCK 16	1	0	0	0	44	
BLOCK 17	0	9	11	14	50	
BLOCK 18	0	1	0	5	36	
TOTAL	520	584	476	839	837	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.						

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 3 (PAGE 20): MOTOR ACTIVITY - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP I		0.9% SALINE		0(VEHICLE) MG/KG/DAY		SESSION 4	
RAT NUMBER		17951	17952	17953	17954	17955	
TIME (SECONDS) SPENT IN MOVEMENT							
BLOCK 1	176	213	167	188	108		
BLOCK 2	148	193	136	182	85		
BLOCK 3	119	180	125	128	120		
BLOCK 4	150	154	101	109	70		
BLOCK 5	108	157	95	111	97		
BLOCK 6	89	118	63	95	91		
BLOCK 7	81	180	47	69	36		
BLOCK 8	15	29	1	124	76		
BLOCK 9	1	5	0	88	37		
BLOCK 10	0	0	0	166	7		
BLOCK 11	0	4	4	83	1		
BLOCK 12	0	7	3	64	1		
BLOCK 13	0	8	0	23	76		
BLOCK 14	1	0	6	0	54		
BLOCK 15	3	25	0	0	101		
BLOCK 16	0	0	0	0	58		
BLOCK 17	0	11	14	14	95		
BLOCK 18	0	0	0	1	26		
TOTAL	891	1284	762	1445	1139		
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.							

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 3 (PAGE 21): MOTOR ACTIVITY - INDIVIDUAL DATA - MALE RATS

	DOSAGE GROUP II	ACRYLAMIDE		45 MG/KG/DAY		SESSION 4
RAT NUMBER	17956	17957	17958a	17959	17960b	
NUMBER OF MOVEMENTS						
BLOCK 1	89	1		43	0	
BLOCK 2	48	0		58	0	
BLOCK 3	1	0		22	0	
BLOCK 4	4	0		15	0	
BLOCK 5	46	0		5	0	
BLOCK 6	13	5		10	0	
BLOCK 7	2	9		13	0	
BLOCK 8	0	1		10	0	
BLOCK 9	5	3		3	0	
BLOCK 10	27	2		9	0	
BLOCK 11	13	0		4	0	
BLOCK 12	15	1		16	0	
BLOCK 13	1	0		2	0	
BLOCK 14	2	0		4	0	
BLOCK 15	2	1		28	0	
BLOCK 16	0	1		0	0	
BLOCK 17	0	0		10	0	
BLOCK 18	9	0		16	0	
TOTAL	277	24		268	0	

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

a. Rat 17958 was found dead on day 12 of study.

b. Rat 17960 was found dead on day 13 of study (during Motor Activity evaluation); values excluded from group averages and statistical analyses.

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 3 (PAGE 22): MOTOR ACTIVITY - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP II		ACRYLAMIDE		45 MG/KG/DAY		SESSION 4	
RAT NUMBER		17956	17957	17958a	17959	17960b	
TIME (SECONDS) SPENT IN MOVEMENT							
BLOCK 1	155	0		53	0		
BLOCK 2	78	0		89	0		
BLOCK 3	0	0		19	0		
BLOCK 4	1	0		14	0		
BLOCK 5	70	0		2	0		
BLOCK 6	15	5		3	0		
BLOCK 7	0	7		26	0		
BLOCK 8	0	0		10	0		
BLOCK 9	2	1		1	0		
BLOCK 10	79	1		6	0		
BLOCK 11	9	0		3	0		
BLOCK 12	17	0		11	0		
BLOCK 13	0	0		0	0		
BLOCK 14	0	0		1	0		
BLOCK 15	0	0		32	0		
BLOCK 16	0	0		0	0		
BLOCK 17	0	0		8	0		
BLOCK 18	6	0		10	0		
TOTAL	432	14		288	0		

TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.

a. Rat 17958 was found dead on day 12 of study.

b. Rat 17960 was found dead on day 13 of study (during Motor Activity evaluation); values excluded from group averages and statistical analyses.

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 3 (PAGE 23): MOTOR ACTIVITY - INDIVIDUAL DATA - MALE RATS

DOSAGE GROUP III		d-AMPHETAMINE		0.75 MG/KG/DAY		SESSION 4	
RAT NUMBER		17961	17962	17963	17964	17965	
NUMBER OF MOVEMENTS							
BLOCK 1		55	68	66	59	55	
BLOCK 2		62	63	68	58	66	
BLOCK 3		80	69	72	71	68	
BLOCK 4		70	66	64	80	65	
BLOCK 5		80	71	90	67	65	
BLOCK 6		73	63	75	60	75	
BLOCK 7		85	71	71	65	80	
BLOCK 8		67	81	94	59	75	
BLOCK 9		77	82	79	70	83	
BLOCK 10		64	69	84	72	83	
BLOCK 11		88	78	85	66	71	
BLOCK 12		84	86	74	71	78	
BLOCK 13		77	72	81	78	62	
BLOCK 14		82	68	95	65	72	
BLOCK 15		74	72	80	70	75	
BLOCK 16		83	77	77	72	81	
BLOCK 17		77	71	88	76	60	
BLOCK 18		85	83	81	63	70	
TOTAL		1363	1310	1424	1222	1284	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.							

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 3 (PAGE 24): MOTOR ACTIVITY - INDIVIDUAL DATA - MALE RATS

	DOSAGE GROUP III	d-AMPHETAMINE		0.75 MG/KG/DAY		SESSION 4
RAT NUMBER	17961	17962	17963	17964	17965	
TIME (SECONDS) SPENT IN MOVEMENT						
BLOCK 1	254	231	225	196	259	
BLOCK 2	226	222	237	154	247	
BLOCK 3	209	208	210	213	216	
BLOCK 4	210	190	212	165	233	
BLOCK 5	203	183	191	191	235	
BLOCK 6	176	192	217	134	211	
BLOCK 7	158	167	190	131	226	
BLOCK 8	228	202	182	186	223	
BLOCK 9	174	172	168	112	212	
BLOCK 10	181	181	173	149	165	
BLOCK 11	208	163	168	138	187	
BLOCK 12	146	175	156	134	176	
BLOCK 13	197	162	130	177	229	
BLOCK 14	145	117	152	141	142	
BLOCK 15	119	112	143	132	210	
BLOCK 16	96	164	106	153	179	
BLOCK 17	203	106	135	197	99	
BLOCK 18	150	176	105	143	214	
TOTAL	3283	3123	3100	2846	3663	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.						

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:CD®BR VAF/Plus® RATS

TABLE 4 (PAGE 1): MOTOR ACTIVITY - INDIVIDUAL DATA - FEMALE RATS

	DOSAGE GROUP I	0.9% SALINE	0(VEHICLE) MG/KG/DAY	PREDOSAGE	
RAT NUMBER	17976	17977	17978	17979	17980
NUMBER OF MOVEMENTS					
BLOCK 1	76	59	80	53	58
BLOCK 2	90	65	76	68	63
BLOCK 3	78	62	84	69	59
BLOCK 4	73	61	92	62	71
BLOCK 5	96	59	81	58	60
BLOCK 6	69	79	65	63	70
BLOCK 7	66	68	63	79	64
BLOCK 8	10	87	79	67	66
BLOCK 9	1	74	61	53	64
BLOCK 10	1	78	65	69	59
BLOCK 11	0	60	75	77	37
BLOCK 12	43	28	69	75	68
BLOCK 13	69	68	66	55	31
BLOCK 14	71	13	79	62	0
BLOCK 15	42	0	46	62	0
BLOCK 16	50	2	39	46	0
BLOCK 17	21	1	13	29	0
BLOCK 18	0	3	40	2	0
TOTAL	856	867	1173	1049	770
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.					

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 4 (PAGE 2): MOTOR ACTIVITY - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP I		0.9% SALINE		0(VEHICLE) MG/KG/DAY		PREDOSAGE
RAT NUMBER	17976	17977	17978	17979	17980	
TIME (SECONDS) SPENT IN MOVEMENT						
BLOCK 1	220	223	221	255	215	
BLOCK 2	169	198	197	205	187	
BLOCK 3	175	220	172	180	184	
BLOCK 4	127	186	149	181	171	
BLOCK 5	162	183	144	206	197	
BLOCK 6	91	181	125	145	140	
BLOCK 7	79	143	102	158	122	
BLOCK 8	6	149	113	111	163	
BLOCK 9	0	164	68	144	71	
BLOCK 10	0	147	75	171	107	
BLOCK 11	0	54	115	186	67	
BLOCK 12	39	13	78	165	77	
BLOCK 13	128	99	111	135	68	
BLOCK 14	87	12	76	57	0	
BLOCK 15	64	0	94	195	0	
BLOCK 16	35	0	40	87	0	
BLOCK 17	14	0	4	21	0	
BLOCK 18	0	1	30	1	0	
TOTAL	1396	1973	1914	2603	1769	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.						

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 4 (PAGE 3): MOTOR ACTIVITY - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP II		ACRYLAMIDE		45 MG/KG/DAY		PREDOSAGE
RAT NUMBER		17981	17982	17983	17984	17985
NUMBER OF MOVEMENTS						
BLOCK 1	81	76	64	72	84	
BLOCK 2	85	70	74	71	85	
BLOCK 3	91	73	63	69	73	
BLOCK 4	84	78	71	72	81	
BLOCK 5	84	76	60	76	73	
BLOCK 6	81	49	73	63	76	
BLOCK 7	83	92	69	74	80	
BLOCK 8	79	69	68	41	82	
BLOCK 9	67	80	74	23	80	
BLOCK 10	78	36	71	44	63	
BLOCK 11	89	38	74	60	73	
BLOCK 12	68	30	69	55	60	
BLOCK 13	53	1	74	20	51	
BLOCK 14	84	9	59	0	72	
BLOCK 15	70	0	66	1	54	
BLOCK 16	92	0	17	0	37	
BLOCK 17	83	2	1	14	3	
BLOCK 18	63	1	5	4	1	
TOTAL	1415	780	1052	759	1128	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.						

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 4 (PAGE 4): MOTOR ACTIVITY - INDIVIDUAL DATA - FEMALE RATS

	DOSAGE GROUP II	ACRYLAMIDE			45 MG/KG/DAY	PREDOSAGE
RAT NUMBER	17981	17982	17983	17984	17985	
TIME (SECONDS) SPENT IN MOVEMENT						
BLOCK 1	217	203	236	211	214	
BLOCK 2	139	219	204	157	169	
BLOCK 3	154	199	204	178	241	
BLOCK 4	125	200	148	126	174	
BLOCK 5	139	169	200	114	188	
BLOCK 6	137	114	145	65	171	
BLOCK 7	116	118	122	95	152	
BLOCK 8	147	83	99	52	122	
BLOCK 9	96	90	135	23	148	
BLOCK 10	151	26	142	52	88	
BLOCK 11	154	20	209	59	87	
BLOCK 12	99	18	170	55	49	
BLOCK 13	60	0	114	13	48	
BLOCK 14	98	3	68	0	117	
BLOCK 15	103	0	66	0	74	
BLOCK 16	123	0	12	0	26	
BLOCK 17	86	0	1	4	1	
BLOCK 18	48	0	1	1	0	
TOTAL	2192	1462	2276	1205	2069	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.						

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 4 (PAGE 5): MOTOR ACTIVITY - INDIVIDUAL DATA - FEMALE RATS

	DOSAGE GROUP III	d-AMPHETAMINE	0.75 MG/KG/DAY	PREDOSAGE	
RAT NUMBER	17986	17987	17988	17989	17990
NUMBER OF MOVEMENTS					
BLOCK 1	87	57	67	73	73
BLOCK 2	69	61	70	80	70
BLOCK 3	70	49	67	76	68
BLOCK 4	84	47	70	75	74
BLOCK 5	64	60	82	88	69
BLOCK 6	71	41	82	69	86
BLOCK 7	5	51	75	57	81
BLOCK 8	1	59	74	42	77
BLOCK 9	0	52	72	45	82
BLOCK 10	0	51	70	14	40
BLOCK 11	5	57	71	53	86
BLOCK 12	11	33	69	46	86
BLOCK 13	0	24	40	54	45
BLOCK 14	0	27	34	57	12
BLOCK 15	0	44	0	12	1
BLOCK 16	0	25	9	12	3
BLOCK 17	0	45	0	23	0
BLOCK 18	0	27	0	72	1
TOTAL	467	810	952	948	954
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.					

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 4 (PAGE 6): MOTOR ACTIVITY - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP III		d-AMPHETAMINE		0.75 MG/KG/DAY		PREDOSAGE	
RAT NUMBER		17986	17987	17988	17989	17990	
TIME (SECONDS) SPENT IN MOVEMENT							
BLOCK	1	176	206	229	184	222	
BLOCK	2	162	154	219	175	215	
BLOCK	3	154	171	208	119	152	
BLOCK	4	147	54	205	118	205	
BLOCK	5	103	165	173	130	121	
BLOCK	6	117	102	138	89	103	
BLOCK	7	3	147	124	84	121	
BLOCK	8	0	115	146	43	72	
BLOCK	9	0	104	116	61	90	
BLOCK	10	0	167	120	8	50	
BLOCK	11	6	79	111	65	132	
BLOCK	12	6	43	78	63	131	
BLOCK	13	0	31	30	88	25	
BLOCK	14	0	32	32	78	4	
BLOCK	15	0	89	0	7	1	
BLOCK	16	0	20	6	5	1	
BLOCK	17	0	74	0	16	0	
BLOCK	18	0	29	0	145	0	
TOTAL		874	1782	1935	1478	1645	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.							

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 4 (PAGE 7): MOTOR ACTIVITY - INDIVIDUAL DATA - FEMALE RATS

	DOSAGE GROUP I	0.9% SALINE	0(VEHICLE) MG/KG/DAY	SESSION 2	
RAT NUMBER	17976	17977	17978	17979	17980
NUMBER OF MOVEMENTS					
BLOCK 1	69	74	71	58	66
BLOCK 2	95	70	78	65	66
BLOCK 3	90	71	80	67	61
BLOCK 4	71	59	63	33	57
BLOCK 5	4	67	81	60	52
BLOCK 6	68	46	67	61	50
BLOCK 7	58	41	74	41	66
BLOCK 8	54	1	68	19	60
BLOCK 9	66	0	47	1	10
BLOCK 10	5	2	50	7	1
BLOCK 11	5	2	45	39	1
BLOCK 12	14	1	43	69	56
BLOCK 13	15	42	32	48	49
BLOCK 14	5	57	32	16	63
BLOCK 15	2	43	0	4	67
BLOCK 16	0	7	12	3	76
BLOCK 17	0	2	5	2	8
BLOCK 18	72	0	6	2	0
TOTAL	693	585	854	595	809
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.					

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 4 (PAGE 8): MOTOR ACTIVITY - INDIVIDUAL DATA - FEMALE RATS

	DOSAGE GROUP I	0.9% SALINE	0(VEHICLE) MG/KG/DAY	SESSION 2	
RAT NUMBER	17976	17977	17978	17979	17980
TIME (SECONDS) SPENT IN MOVEMENT					
BLOCK 1	205	207	179	228	219
BLOCK 2	162	144	154	170	214
BLOCK 3	140	174	115	118	146
BLOCK 4	128	139	134	67	204
BLOCK 5	0	123	78	82	126
BLOCK 6	59	67	77	101	118
BLOCK 7	74	35	134	62	109
BLOCK 8	84	0	81	14	124
BLOCK 9	51	0	44	0	18
BLOCK 10	2	1	30	2	0
BLOCK 11	1	0	28	52	0
BLOCK 12	12	0	43	111	77
BLOCK 13	10	51	23	83	71
BLOCK 14	2	100	30	20	81
BLOCK 15	0	44	0	4	102
BLOCK 16	0	3	6	1	58
BLOCK 17	0	1	1	1	2
BLOCK 18	67	0	3	1	0
TOTAL	997	1089	1160	1117	1669
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.					

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 4 (PAGE 9): MOTOR ACTIVITY - INDIVIDUAL DATA - FEMALE RATS

	DOSAGE GROUP II		ACRYLAMIDE		45 MG/KG/DAY	SESSION 2
RAT NUMBER	17981	17982	17983	17984	17985	
NUMBER OF MOVEMENTS						
BLOCK 1	83	53	66	83	72	
BLOCK 2	77	65	90	67	77	
BLOCK 3	91	53	43	6	85	
BLOCK 4	18	0	1	4	49	
BLOCK 5	22	0	22	19	12	
BLOCK 6	48	5	11	15	1	
BLOCK 7	1	10	24	6	4	
BLOCK 8	4	3	18	35	3	
BLOCK 9	82	6	9	6	1	
BLOCK 10	44	1	19	10	3	
BLOCK 11	6	4	8	12	4	
BLOCK 12	7	1	23	46	13	
BLOCK 13	50	16	47	19	1	
BLOCK 14	96	18	75	8	5	
BLOCK 15	54	5	16	13	13	
BLOCK 16	5	0	18	17	4	
BLOCK 17	4	8	26	11	0	
BLOCK 18	2	13	17	44	5	
TOTAL	694	261	533	421	352	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.						

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 4 (PAGE 10): MOTOR ACTIVITY - INDIVIDUAL DATA - FEMALE RATS

	DOSAGE GROUP II	ACRYLAMIDE		45 MG/KG/DAY		SESSION 2
RAT NUMBER	17981	17982	17983	17984	17985	
TIME (SECONDS) SPENT IN MOVEMENT						
BLOCK 1	144	76	207	133	99	
BLOCK 2	149	68	161	66	87	
BLOCK 3	122	56	60	2	97	
BLOCK 4	18	0	0	3	35	
BLOCK 5	34	0	20	11	6	
BLOCK 6	47	1	6	9	0	
BLOCK 7	0	4	14	1	0	
BLOCK 8	4	0	24	34	3	
BLOCK 9	100	6	5	2	1	
BLOCK 10	38	0	13	3	1	
BLOCK 11	3	3	2	10	2	
BLOCK 12	3	0	28	45	5	
BLOCK 13	42	10	44	3	0	
BLOCK 14	123	11	111	2	2	
BLOCK 15	66	4	9	5	11	
BLOCK 16	1	0	9	8	1	
BLOCK 17	1	7	16	5	0	
BLOCK 18	0	7	10	39	1	
TOTAL	895	253	739	381	351	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.						

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 4 (PAGE 11): MOTOR ACTIVITY - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP III		d-AMPHETAMINE		0.75 MG/KG/DAY		SESSION 2	
RAT NUMBER		17986	17987	17988	17989	17990	
NUMBER OF MOVEMENTS							
BLOCK 1		63	63	61	51	58	
BLOCK 2		57	48	65	58	73	
BLOCK 3		61	57	61	69	88	
BLOCK 4		87	66	61	56	81	
BLOCK 5		66	62	75	56	82	
BLOCK 6		60	58	52	54	89	
BLOCK 7		76	65	75	56	104	
BLOCK 8		72	48	73	51	73	
BLOCK 9		82	50	67	60	80	
BLOCK 10		72	59	59	56	94	
BLOCK 11		81	62	61	50	81	
BLOCK 12		67	56	77	60	67	
BLOCK 13		67	63	69	75	98	
BLOCK 14		72	63	63	59	93	
BLOCK 15		71	51	56	49	79	
BLOCK 16		85	63	69	64	68	
BLOCK 17		81	56	62	62	73	
BLOCK 18		80	56	73	65	73	
TOTAL		1300	1046	1179	1051	1454	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.							

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 4 (PAGE 12): MOTOR ACTIVITY - INDIVIDUAL DATA - FEMALE RATS

	DOSAGE GROUP III	d-AMPHETAMINE		0.75 MG/KG/DAY		SESSION 2
RAT NUMBER	17986	17987	17988	17989	17990	
TIME (SECONDS) SPENT IN MOVEMENT						
BLOCK 1	254	244	245	258	253	
BLOCK 2	267	244	208	269	228	
BLOCK 3	259	213	217	258	212	
BLOCK 4	214	235	166	261	237	
BLOCK 5	232	246	212	262	217	
BLOCK 6	220	248	157	270	199	
BLOCK 7	208	217	205	262	161	
BLOCK 8	192	235	164	265	215	
BLOCK 9	163	249	194	258	195	
BLOCK 10	208	221	134	269	177	
BLOCK 11	179	225	167	245	132	
BLOCK 12	132	205	153	222	64	
BLOCK 13	140	189	140	235	114	
BLOCK 14	160	243	201	236	134	
BLOCK 15	151	204	152	231	113	
BLOCK 16	146	197	165	204	73	
BLOCK 17	138	163	171	235	82	
BLOCK 18	152	195	136	227	79	
TOTAL	3415	3973	3187	4467	2885	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.						

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 4 (PAGE 13): MOTOR ACTIVITY - INDIVIDUAL DATA - FEMALE RATS

	DOSAGE GROUP I	0.9% SALINE	0(VEHICLE) MG/KG/DAY	SESSION 3	
RAT NUMBER	17976	17977	17978	17979	17980
NUMBER OF MOVEMENTS					
BLOCK 1	70	49	76	55	47
BLOCK 2	69	63	77	50	58
BLOCK 3	67	54	86	64	67
BLOCK 4	72	63	53	58	66
BLOCK 5	52	66	58	60	66
BLOCK 6	6	68	33	53	14
BLOCK 7	40	42	33	56	62
BLOCK 8	46	70	0	36	50
BLOCK 9	57	2	0	52	73
BLOCK 10	34	0	6	0	74
BLOCK 11	73	1	0	1	49
BLOCK 12	20	6	1	0	31
BLOCK 13	12	0	4	27	38
BLOCK 14	3	2	0	6	0
BLOCK 15	0	3	0	1	2
BLOCK 16	0	0	0	1	0
BLOCK 17	4	8	0	5	3
BLOCK 18	1	1	4	4	0
TOTAL	626	498	431	529	700
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.					

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 4 (PAGE 14): MOTOR ACTIVITY - INDIVIDUAL DATA - FEMALE RATS

	DOSAGE GROUP I	0.9% SALINE	0(VEHICLE) MG/KG/DAY	SESSION 3	
RAT NUMBER	17976	17977	17978	17979	17980
TIME (SECONDS) SPENT IN MOVEMENT					
BLOCK 1	213	211	213	246	217
BLOCK 2	153	221	169	212	215
BLOCK 3	94	153	136	187	162
BLOCK 4	98	139	56	124	149
BLOCK 5	60	146	40	111	75
BLOCK 6	3	101	22	63	13
BLOCK 7	28	54	45	73	135
BLOCK 8	56	73	0	44	76
BLOCK 9	67	1	0	38	109
BLOCK 10	52	0	3	0	65
BLOCK 11	80	0	0	0	49
BLOCK 12	10	4	0	0	22
BLOCK 13	6	0	3	17	28
BLOCK 14	1	1	0	7	0
BLOCK 15	0	3	0	0	0
BLOCK 16	0	0	0	0	0
BLOCK 17	2	5	0	2	1
BLOCK 18	0	0	2	1	0
TOTAL	923	1112	689	1125	1316
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.					

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 4 (PAGE 15): MOTOR ACTIVITY - INDIVIDUAL DATA - FEMALE RATS

	DOSAGE GROUP II		ACRYLAMIDE		45 MG/KG/DAY	SESSION 3
RAT NUMBER	17981	17982	17983	17984	17985	
NUMBER OF MOVEMENTS						
BLOCK 1	54	27	89	61	85	
BLOCK 2	4	20	58	0	32	
BLOCK 3	22	4	9	0	0	
BLOCK 4	2	0	31	2	5	
BLOCK 5	4	0	23	1	2	
BLOCK 6	5	0	4	16	6	
BLOCK 7	9	31	7	3	8	
BLOCK 8	6	12	32	4	6	
BLOCK 9	4	2	4	1	9	
BLOCK 10	8	2	12	0	0	
BLOCK 11	2	6	7	1	5	
BLOCK 12	11	2	28	23	11	
BLOCK 13	5	0	7	5	3	
BLOCK 14	9	0	45	6	0	
BLOCK 15	0	2	7	9	2	
BLOCK 16	7	22	7	0	4	
BLOCK 17	11	15	20	0	1	
BLOCK 18	16	20	6	24	29	
TOTAL	179	165	396	156	208	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.						

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 4 (PAGE 16): MOTOR ACTIVITY - INDIVIDUAL DATA - FEMALE RATS

	DOSAGE GROUP II	ACRYLAMIDE		45 MG/KG/DAY		SESSION 3
RAT NUMBER	17981	17982	17983	17984	17985	
TIME (SECONDS) SPENT IN MOVEMENT						
BLOCK 1	58	11	217	104	108	
BLOCK 2	2	8	74	0	21	
BLOCK 3	14	1	3	0	0	
BLOCK 4	1	0	61	0	0	
BLOCK 5	3	0	36	1	0	
BLOCK 6	4	0	3	9	1	
BLOCK 7	5	17	11	1	6	
BLOCK 8	6	2	37	3	1	
BLOCK 9	2	0	2	0	5	
BLOCK 10	3	0	8	0	0	
BLOCK 11	0	2	3	0	6	
BLOCK 12	8	0	26	18	6	
BLOCK 13	1	0	3	4	0	
BLOCK 14	4	0	68	5	0	
BLOCK 15	0	1	4	6	1	
BLOCK 16	4	10	9	0	0	
BLOCK 17	14	5	24	0	0	
BLOCK 18	20	5	5	18	14	
TOTAL	149	62	594	169	169	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.						

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 4 (PAGE 17): MOTOR ACTIVITY - INDIVIDUAL DATA - FEMALE RATS

	DOSAGE GROUP III		d-AMPHETAMINE		0.75 MG/KG/DAY	SESSION 3
RAT NUMBER	17986	17987	17988	17989	17990	
NUMBER OF MOVEMENTS						
BLOCK 1	54	49	55	57	73	
BLOCK 2	59	59	68	55	69	
BLOCK 3	80	49	70	64	82	
BLOCK 4	79	53	82	59	76	
BLOCK 5	82	68	66	56	85	
BLOCK 6	49	62	80	49	89	
BLOCK 7	67	64	73	59	84	
BLOCK 8	90	65	60	54	90	
BLOCK 9	73	59	61	57	89	
BLOCK 10	69	59	54	74	93	
BLOCK 11	90	66	73	72	69	
BLOCK 12	80	61	54	65	58	
BLOCK 13	64	66	61	76	85	
BLOCK 14	81	61	61	86	41	
BLOCK 15	83	63	64	64	5	
BLOCK 16	62	42	70	81	2	
BLOCK 17	36	59	62	77	0	
BLOCK 18	54	57	68	76	0	
TOTAL	1252	1062	1182	1181	1090	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.						

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 4 (PAGE 18): MOTOR ACTIVITY - INDIVIDUAL DATA - FEMALE RATS

	DOSAGE GROUP III	d-AMPHETAMINE		0.75 MG/KG/DAY		SESSION 3
RAT NUMBER	17986	17987	17988	17989	17990	
TIME (SECONDS) SPENT IN MOVEMENT						
BLOCK 1	270	247	244	258	250	
BLOCK 2	262	228	230	258	237	
BLOCK 3	216	257	220	249	232	
BLOCK 4	214	253	203	259	193	
BLOCK 5	166	216	203	252	193	
BLOCK 6	212	233	183	268	199	
BLOCK 7	157	240	156	236	169	
BLOCK 8	177	240	166	258	191	
BLOCK 9	184	212	138	246	153	
BLOCK 10	133	219	171	227	153	
BLOCK 11	184	212	153	222	104	
BLOCK 12	189	185	153	230	130	
BLOCK 13	138	151	150	233	81	
BLOCK 14	162	196	160	213	45	
BLOCK 15	149	154	145	219	1	
BLOCK 16	72	155	161	174	1	
BLOCK 17	29	121	121	194	0	
BLOCK 18	59	154	139	196	0	
TOTAL	2973	3673	3096	4192	2332	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.						

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 4 (PAGE 19): MOTOR ACTIVITY - INDIVIDUAL DATA - FEMALE RATS

	DOSAGE GROUP I	0.9% SALINE	0(VEHICLE) MG/KG/DAY	SESSION 4	
RAT NUMBER	17976	17977	17978	17979	17980
NUMBER OF MOVEMENTS					
BLOCK 1	78	71	70	66	69
BLOCK 2	73	70	76	60	60
BLOCK 3	75	69	41	66	72
BLOCK 4	81	57	27	58	55
BLOCK 5	85	57	25	39	67
BLOCK 6	81	47	2	58	69
BLOCK 7	11	90	0	4	66
BLOCK 8	1	68	0	4	61
BLOCK 9	9	70	0	5	63
BLOCK 10	45	74	8	19	3
BLOCK 11	11	72	12	76	10
BLOCK 12	0	59	6	61	2
BLOCK 13	1	69	4	52	0
BLOCK 14	3	43	0	49	12
BLOCK 15	0	4	3	41	83
BLOCK 16	30	2	6	22	41
BLOCK 17	41	12	0	3	43
BLOCK 18	47	4	4	0	51
TOTAL	672	938	284	683	827
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.					

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 4 (PAGE 20): MOTOR ACTIVITY - INDIVIDUAL DATA - FEMALE RATS

	DOSAGE GROUP I	0.9% SALINE	0(VEHICLE) MG/KG/DAY	SESSION 4	
RAT NUMBER	17976	17977	17978	17979	17980
TIME (SECONDS) SPENT IN MOVEMENT					
BLOCK 1	175	198	171	217	214
BLOCK 2	165	209	161	225	179
BLOCK 3	142	207	44	161	182
BLOCK 4	136	92	24	92	132
BLOCK 5	92	118	18	56	85
BLOCK 6	91	70	1	66	91
BLOCK 7	4	141	0	1	97
BLOCK 8	0	91	0	0	104
BLOCK 9	2	135	0	1	114
BLOCK 10	53	164	3	18	0
BLOCK 11	7	118	9	193	8
BLOCK 12	0	59	5	72	0
BLOCK 13	0	51	4	49	0
BLOCK 14	1	50	0	59	10
BLOCK 15	0	1	0	26	94
BLOCK 16	20	0	7	19	51
BLOCK 17	62	10	0	0	72
BLOCK 18	35	2	1	0	59
TOTAL	985	1716	448	1255	1492
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.					

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 4 (PAGE 21): MOTOR ACTIVITY - INDIVIDUAL DATA - FEMALE RATS

	DOSAGE GROUP II	ACRYLAMIDE	45 MG/KG/DAY	SESSION 4	
RAT NUMBER	17981	17982	17983	17984	17985
NUMBER OF MOVEMENTS					
BLOCK 1	12	68	70	76	1
BLOCK 2	34	49	31	39	4
BLOCK 3	5	2	14	3	3
BLOCK 4	10	0	0	29	3
BLOCK 5	9	1	44	9	0
BLOCK 6	0	4	1	3	0
BLOCK 7	4	40	23	3	3
BLOCK 8	23	17	2	1	2
BLOCK 9	25	1	4	2	10
BLOCK 10	0	3	4	7	4
BLOCK 11	20	1	35	2	20
BLOCK 12	0	6	6	60	3
BLOCK 13	2	2	12	6	0
BLOCK 14	1	0	0	1	9
BLOCK 15	2	18	16	0	0
BLOCK 16	1	1	14	5	5
BLOCK 17	2	4	9	12	6
BLOCK 18	47	1	3	0	32
TOTAL	197	218	288	258	105
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.					

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 4 (PAGE 22): MOTOR ACTIVITY - INDIVIDUAL DATA - FEMALE RATS

	DOSAGE GROUP II	ACRYLAMIDE		45 MG/KG/DAY		SESSION 4
RAT NUMBER	17981	17982	17983	17984	17985	
TIME (SECONDS) SPENT IN MOVEMENT						
BLOCK 1	6	68	126	167	0	
BLOCK 2	19	53	21	63	1	
BLOCK 3	0	0	11	1	1	
BLOCK 4	4	0	0	23	2	
BLOCK 5	4	0	34	5	0	
BLOCK 6	0	3	1	0	0	
BLOCK 7	3	23	21	1	0	
BLOCK 8	11	9	1	0	0	
BLOCK 9	19	0	1	1	4	
BLOCK 10	0	0	2	1	2	
BLOCK 11	13	0	27	0	14	
BLOCK 12	0	2	3	77	0	
BLOCK 13	0	1	8	5	0	
BLOCK 14	0	0	0	0	4	
BLOCK 15	0	11	10	0	0	
BLOCK 16	0	0	13	2	6	
BLOCK 17	0	4	8	8	3	
BLOCK 18	37	0	0	0	35	
TOTAL	116	174	287	354	72	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.						

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 4 (PAGE 23): MOTOR ACTIVITY - INDIVIDUAL DATA - FEMALE RATS

	DOSAGE GROUP III		d-AMPHETAMINE		0.75 MG/KG/DAY	SESSION 4
RAT NUMBER	17986	17987	17988	17989	17990	
NUMBER OF MOVEMENTS						
BLOCK 1	62	44	56	68	52	
BLOCK 2	56	62	66	68	73	
BLOCK 3	68	47	63	58	92	
BLOCK 4	64	47	56	50	82	
BLOCK 5	54	38	73	57	93	
BLOCK 6	59	55	45	56	83	
BLOCK 7	58	69	57	69	89	
BLOCK 8	68	59	64	58	86	
BLOCK 9	70	58	46	80	84	
BLOCK 10	66	57	62	84	79	
BLOCK 11	63	51	50	74	88	
BLOCK 12	69	52	52	80	83	
BLOCK 13	72	51	51	74	92	
BLOCK 14	82	57	63	68	82	
BLOCK 15	64	62	58	80	75	
BLOCK 16	78	65	59	66	76	
BLOCK 17	80	59	62	78	87	
BLOCK 18	55	68	80	72	44	
TOTAL	1188	1001	1063	1240	1440	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.						

PROTOCOL 012-058: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CrI:CD®BR VAF/Plus® RATS

TABLE 4 (PAGE 24): MOTOR ACTIVITY - INDIVIDUAL DATA - FEMALE RATS

DOSAGE GROUP III		d-AMPHETAMINE		0.75 MG/KG/DAY		SESSION 4	
RAT NUMBER		17986	17987	17988	17989	17990	
TIME (SECONDS) SPENT IN MOVEMENT							
BLOCK 1		251	267	271	244	268	
BLOCK 2		203	246	236	248	245	
BLOCK 3		177	246	222	254	211	
BLOCK 4		194	263	259	263	225	
BLOCK 5		165	265	198	258	206	
BLOCK 6		225	241	264	260	205	
BLOCK 7		128	244	221	259	144	
BLOCK 8		147	226	214	254	181	
BLOCK 9		145	243	206	195	164	
BLOCK 10		109	240	206	191	101	
BLOCK 11		129	249	191	208	129	
BLOCK 12		155	178	209	186	106	
BLOCK 13		162	238	185	224	111	
BLOCK 14		126	216	222	213	85	
BLOCK 15		146	185	217	205	93	
BLOCK 16		142	180	216	168	118	
BLOCK 17		174	208	219	187	101	
BLOCK 18		81	189	165	208	33	
TOTAL		2859	4124	3921	4025	2726	
TOTAL = SUM OF BLOCKS; EACH BLOCK CONSISTS OF A 5 MINUTE PERIOD.							

3. STUDY 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN CRL:(CD)SD RATS

The purpose of this study was to evaluate positive control substances using a functional observational battery (FOB). The study is one component of the certification of technicians conducting the FOB, in accordance with the testing guidelines of the U.S. Environmental Protection Agency (EPA).

3.1. Methods

3.1.1. Regulatory Compliance

The EPA Good Laboratory Practices were used as the basis for conducting the study with the following exceptions: the Quality Assurance Unit did not inspect phases of the study and samples of the test solutions/suspensions were not taken for analyses of concentration, stability or homogeneity. The Quality Assurance Unit audited the study at its completion.

3.1.2. Test Substances and Vehicle Information

Test Substance	Description	Lot Number	Date Received	Supplier	Expiration Date
Chlorpromazine ^a	White to off-white powder	017K1244	12 AUG 08	Sigma ^b	02 DEC 10
Carbaryl	White to light tan, crystalline powder	395-65B	23 JUN 08	Chem Service ^c	JAN 11
DDT ^d	White powder	02230KY	23 JAN 09	Sigma ^b	23 JAN 10
IDPN ^e	Clear slightly yellow liquid	A013811501	24 JUN 08	Acros Organics ^f	24 JUN 09
d-Amphetamine ^g	White powder	106K1828	29 MAR 07	Sigma ^b	FEB 10

- a. Chlorpromazine hydrochloride (CPZ)
- b. Sigma-Aldrich Co., St. Louis, MO
- c. Chem Service, Inc., West Chester, PA
- d. 1,1-Bis[4-chlorophenyl]-2,2,2-trichloroethane, 98% (4, 4-DDT)
- e. 3,3'-Iminodipropionitrile, 99+% (IDPN)
- f. Acros Organics, Fair Lawn, NJ.
- g. d-Amphetamine Sulfate

Bulk test substances were stored in light resistant glass containers at room temperature. Prepared solutions were stored in light resistant containers and refrigerated until used.

Vehicle	Description	Lot Number	Date Received	Supplier	Expiration Date
0.9% Sodium Chloride for Injection, USP	Clear, colorless liquid	J8C525	10 JUN 08	B. Braun ^a	SEP 2010
Corn Oil	Clear Yellow-Green Liquid	028K0044	01 NOV 08	Sigma ^b	01 NOV 09

- a. B Braun Medical Inc., Irvine, CA.
- b. Sigma-Aldrich, Inc., St. Louis, MO.

Bulk vehicles were stored at room temperature. Vehicles aliquotted for dosage were stored refrigerated.

The intraperitoneal route of administration was selected for Chlorpromazine, IDPN, d-Amphetamine because it is a common route for administration of these test substances in toxicity studies. The oral route of administration was selected for Carbaryl because previous studies conducted at the Testing Facility had shown that Carbaryl was effective when administered orally. The oral route of administration was selected for DDT because it is the common route for administration of this test substance in toxicity studies.

The saline was administered once every day for five consecutive days (simultaneously with the IDPN); a sixth dosage was administered simultaneously with the (Chlorpromazine). The IDPN was administered once every day for five consecutive days. The corn oil, Chlorpromazine, d Amphetamine, Carbaryl and DDT were administered once.

Dosage Group	Dosage (mg/kg/day)	Concentration ^a (mg/ml)	Dosage Volume (mL/kg)	Number of Rats per Sex	Assigned Rat Numbers	
					Male	Female
I	0 (Vehicle, 0.9% Saline)	0	1	4	12407, 12419, 12422, 12423	12456, 12465, 12467, 12468
II	0 (Vehicle, Mazola® Corn Oil)	0	4	4	12413, 12414, 12420, 12424	12457, 12460, 12469, 12478
III	250 (IDPN)	250	1	4	12401, 12404, 12406, 12421	12454, 12458, 12466, 12472
IV	6.0 (Chlorpromazine)	6.0	1	4	12409, 12410, 12425, 12426	12451, 12463, 12464, 12471
V	4.0 (d-Amphetamine)	4.0	1	4	12403, 12411, 12415, 12416	12452, 12455, 12475, 12476
VI	100 (Carbaryl)	25	4	4	12405, 12408, 12412, 12428	12453, 12459, 12474, 12477
VII	75 (DDT)	37.5	2	4	12402, 12417, 12418, 12427	12461, 12462, 12470, 12473

a. The test substances were considered 100% active for the purpose of test substance calculations.

3.1.3. Testing Procedures

Before the start of the preadministration period, a randomization procedure was performed to assign the rats to two vehicle control groups and five groups administered the test substances (four rats per sex per dosage group). A second set of randomization procedures were performed to assign seven rats of each sex to each of the four technicians who would be conducting the FOB examinations. Each of the dosage groups was separated into two replicates with the dosage schedule for each replicate separated by two days, to allow sufficient time for the functional observational battery.

The FOB assessed the following parameters:

1. Lacrimation, salivation, palpebral closure, prominence of the eye, papillary response to light, piloerection, respiration, and urination and defecation (autonomic functions).

2. Sensorimotor responses to auditory, tactile and painful stimuli (reactivity and sensitivity).
3. Reactions to handling and behavior in the open field (excitability).
4. Gait pattern in the open field, severity of gait abnormalities, proprioceptive positioning, air righting reaction and landing foot splay (gait and sensorimotor coordination).
5. Forelimb and hindlimb grip strength.
6. Abnormal clinical observations not sufficiently specified in the measurement scales for the parameters specified above. These observations would include, but not be limited to: general appearance (*e.g.*, changes in skin, fur, and mucous membranes; presence or absence of discharge; emaciation; dehydration), body position and posture (*e.g.*, hunchback posture), neuromuscular system (*e.g.*, tremor, convulsion, muscular contractions, hypotonia, hypertonia), and behavior (*e.g.*, headshaking, gyration, autophagia, backward motion, abnormal vocalization).

The sequence of testing proceeded from those with least interaction with the rats to those tests requiring the most interaction. After observations were made in the home cage each rat was placed in an area enclosed by a wall approximately 25 cm high. The rat was observed in this area for approximately two minutes at which time observations that can be made without handling the rat (for example, some autonomic functions, gait pattern, excitability, number of rears and some clinical observations) were recorded. Sensorimotor responses to visual (approach of a blunt end of a pen), auditory (click generated by a paper clip), tactile (touching the rump with the blunt end of a pen) and painful (tail pinch) stimuli were then evaluated. The final sequence of tests included evaluations of proprioceptive positioning, air righting, pupillary response to light, forelimb and hindlimb grip strength, and body temperature.

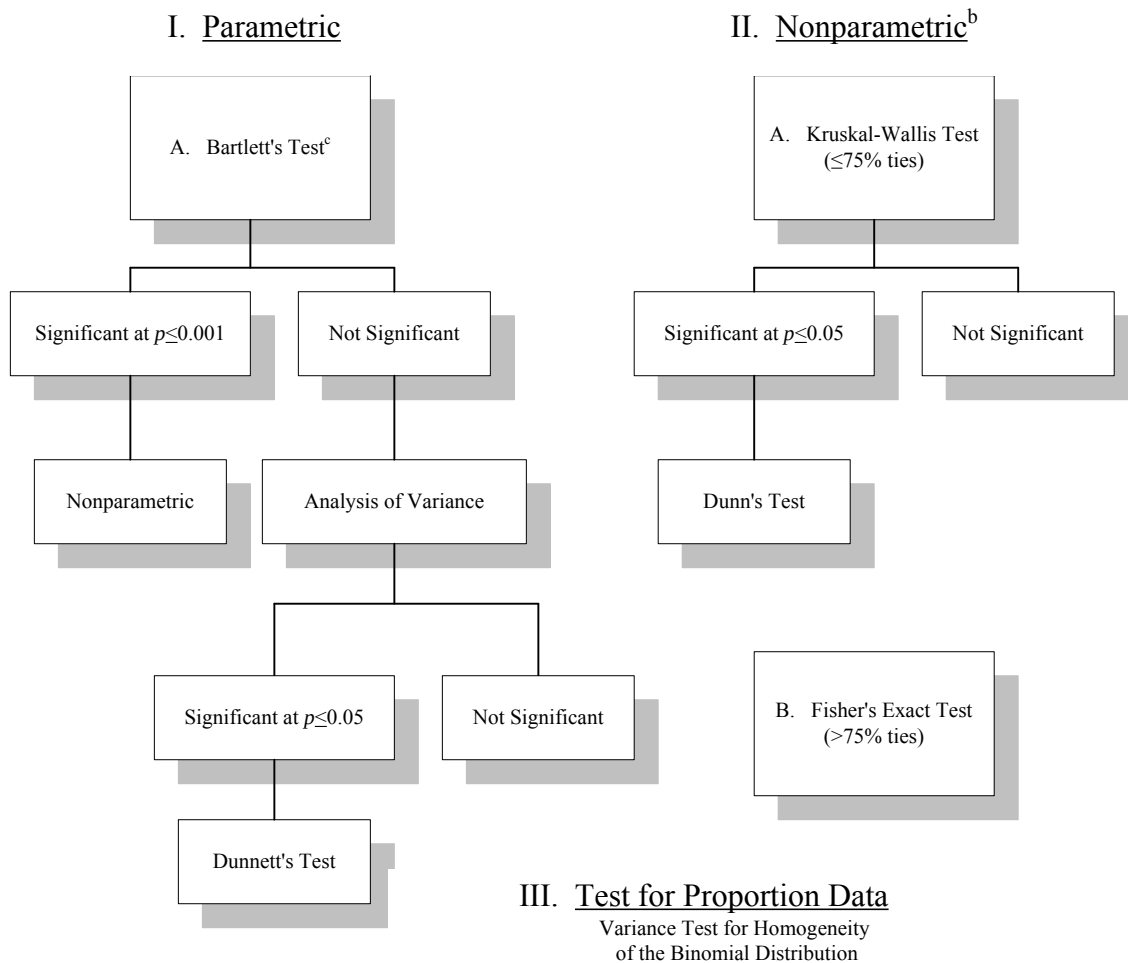
Observations were made by individuals who were unaware of the dosage group of the rat observed. Information regarding the dosage group was hidden during the conduct of the FOB, and the sequence of rats was changed for each test session. Only one of the individuals conducting the testing handled each rat throughout the FOB, and each individual handled at least one rat in each dosage group. Where possible, observations were made and recorded independently by all the individuals conducting the testing. Observations that could be made only by the person handling the rat (for example, reaction to removal, reaction to handling and the pupillary response to light) were made only by the handler.

A measurement of body temperature will be taken on each occasion that a rat is evaluated in the FOB. The measurement will be made using a rectal probe (Physitemp Instruments Model RET-2) and digital thermometer (Physitemp Instruments Model Bat-10 R LOP) at the completion of the FOB in each rat.

3.1.4. Statistical Methods

Data from the primary observer (the person handling each rat) was tabulated. Predosage FOB data for all groups were combined to compare baseline performance of male and female rats. In the summary of groups after dosage, data from the male and female rats were combined to increase statistical power in the analyses of those items in the FOB for which the differences between male and female rats in the predosage examination were not statistically significant ($p>0.05$).

Type of Test^a



-
- a. Statistically significant probabilities are reported as either $p \leq 0.05$ or $p \leq 0.01$.
 - b. Proportion data are not included in this category.
 - c. Test for homogeneity of variance.

Means and standard deviations were computed by dosage group and sex for continuous data such as body weight, feed consumption or test items in the FOB continuous values (for example, grip strength and landing foot splay). As outlined in the schematic for this section, these data were analyzed using parametric tests, if appropriate [Bartlett's test is not significant ($p > 0.001$)]. Rank scores and data with a small number of counts were analyzed using nonparametric tests. Clinical signs and other descriptive observations were converted to proportions and then analyzed as contingency tables.

For purposes of tabulation and statistical comparisons, rats in Group V (d-Amphetamine) were compared to rats in Group II (corn oil), rather than the saline control group (Group I). Group II was referred to as the control group, rather than the vehicle control group in the joint tabulation of data from these groups.

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TABLE A1 (PAGE 1): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - PREDOSAGE - PART A

PREDOSAGE:		MALES	FEMALES
RATS TESTED	N	28	28
HOME CAGE BEHAVIOR			
1: Sleeping	N	15	12
2: Awake, Immobile	N	12	9
3: Normal movement	N	1	7**
4: Unusual posture	N	0	0
5: Unusual behavior	N	0	0
ALTERATIONS (HOME CAGE)			
1: None	N	28	28
2: Stereotyped behavior	N	0	0
3: Bizarre behavior	N	0	0
4: Limb twitches/tremor	N	0	0
5: Whole body tremor/spasm	N	0	0
6: Unusual posture	N	0	0
7: Tonic-clonic seizure	N	0	0
REACTION TO REMOVAL			
(1) Sits quietly	N	22	24
(2) Vocalization	N	2	1
(3) Runs or freezes	N	4	3
(4) Tail or throat rattles	N	0	0
	MEAN SCORE	1.4	1.2
REACTION TO HANDLING			
(1) No resistance	N	25	28
(2) Vocalization	N	3	0
(3) Tense	N	0	0
(4) Squirring	N	0	0
	MEAN SCORE	1.1	1.0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

** Significantly different from the male group value ($p \leq 0.01$).

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE A1 (PAGE 2): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - PREDOSAGE - PART A

PREDOSAGE:		MALES	FEMALES
RATS TESTED	N	28	28
REARS IN OPEN FIELD	MEAN±S.D.	4.6 ± 2.7	7.7 ± 3.6**
DEFECATION IN OPEN FIELD			
1: None	N	25	28
2: Feces normal	N	3	0
3: Soft or liquid feces	N	0	0
URINATION IN OPEN FIELD			
(1) None	N	5	20
(2) Normal urination	N	23	8
(3) Excess urination	N	0	0
	MEAN SCORE	1.8	1.3**
LEVEL OF AROUSAL			
(1) Stuporous	N	0	0
(2) Sluggish	N	0	0
(3) Apparently normal	N	28	28
(4) Sudden darting	N	0	0
(5) Freezing, vocalization	N	0	0
	MEAN SCORE	3.0	3.0
ALTERATIONS (OPEN FIELD)			
1: None	N	28	28
2: Stereotyped behavior	N	0	0
3: Bizarre behavior	N	0	0
4: Limb twitches/tremor	N	0	0
5: Whole body tremor/spasm	N	0	0
6: Unusual posture	N	0	0
7: Tonic-clonic seizure	N	0	0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

** Significantly different from the male group value ($p \leq 0.01$).

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE A1 (PAGE 3): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - PREDOSAGE - PART A

PREDOSAGE:		MALES	FEMALES
RATS TESTED	N	28	28
GAIT PATTERN			
1: Apparently normal	N	28	28
2: Ataxic	N	0	0
3: Limbs splay or drag	N	0	0
4: Spastic, tip-toe	N	0	0
5: Duck-walk	N	0	0
6: Scissors gait	N	0	0
GAIT ABNORMALITY, SEVERITY			
(1) Normal gait	N	28	28
(2) Slight	N	0	0
(3) Moderate	N	0	0
(4) Extreme	N	0	0
MEAN SCORE		1.0	1.0
PALPEBRAL CLOSURE			
(1) Wide open	N	28	28
(2) Slightly drooping	N	0	0
(3) Half-closed	N	0	0
(4) Completely shut	N	0	0
MEAN SCORE		1.0	1.0
PROMINENCE OF THE EYE			
1: Normal	N	28	28
2: Exophthalmos	N	0	0
3: Enophthalmos	N	0	0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE A1 (PAGE 4): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - PREDOSAGE - PART A

PREDOSAGE:		MALES	FEMALES
RATS TESTED	N	28	28
LACRIMATION			
(1) No excess	N	28	28
(2) Excess at eyelid margin	N	0	0
(3) Margin persistently damp	N	0	0
(4) Extends beyond margin	N	0	0
	MEAN SCORE	1.0	1.0
SALIVATION			
(1) No excess	N	28	28
(2) Margin of mouth wet	N	0	0
(3) 1/4 to 1/2 submandibular	N	0	0
(4) Entire submandibular	N	0	0
	MEAN SCORE	1.0	1.0
PILOERECTION	N	0	0
ABNORMAL RESPIRATION	N	0	0
APPEARANCE			
(1) Clean and groomed	N	26	28
(2) Unkempt	N	2	0
(3) Urine and/or fecal stain	N	0	0
	MEAN SCORE	1.1	1.0
VISUAL REACTION			
(1) None	N	0	1
(2) Orienting	N	28	27
(3) Startle	N	0	0
(4) More energetic reaction	N	0	0
(5) Attacks	N	0	0
	MEAN SCORE	2.0	2.0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE A1 (PAGE 5): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - PREDOSAGE - PART A

PREDOSAGE:		MALES	FEMALES
RATS TESTED	N	28	28
TACTILE REACTION			
(1) None	N	0	0
(2) Orienting	N	25	28
(3) Startle	N	3	0
(4) More energetic reaction	N	0	0
(5) Attacks	N	0	0
	MEAN SCORE	2.1	2.0
AUDITORY REACTION			
(1) None	N	0	0
(2) Orienting	N	0	1
(3) Startle	N	28	27
(4) More energetic reaction	N	0	0
(5) Intense vocalization	N	0	0
	MEAN SCORE	3.0	3.0
TAIL-PINCH REACTION			
(1) None	N	1	0
(2) Orienting	N	23	21
(3) Startle	N	3	7
(4) More energetic reaction	N	0	0
(5) Attacks	N	1	0
	MEAN SCORE	2.2	2.2
VISUAL PLACING RESPONSE			
(1) Early extension	N	28	28
(2) Extension after contact	N	0	0
(3) No extension	N	0	0
	MEAN SCORE	1.0	1.0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE A1 (PAGE 6): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - PREDOSAGE - PART A

PREDOSAGE:		MALES	FEMALES
RATS TESTED	N	28	28
AIR RIGHTING RESPONSE			
(1) All feet land on ground	N	28	27
(2) Lands on side	N	0	1
(3) Lands on back	N	0	0
	MEAN SCORE	1.0	1.0
PUPIL RESPONSE TO LIGHT			
	N	28	28
FORELIMB GRIP TEST			
Maximum (G)	MEAN±S.D.	706.8 ± 186.9	643.8 ± 210.5
Average (G)	MEAN±S.D.	619.8 ± 177.9	560.1 ± 169.3
HINDLIMB GRIP TEST			
Maximum (G)	MEAN±S.D.	602.3 ± 145.6	471.1 ± 156.0**
Average (G)	MEAN±S.D.	536.3 ± 128.3	417.7 ± 137.7**
LANDING FOOT SPLAY			
Average (CM)	MEAN±S.D.	7.65 ± 2.09	6.24 ± 1.68**
BODY TEMPERATURE (°C)			
	MEAN±S.D.	37.03 ± 0.50	37.60 ± 0.70**
BODY WEIGHT (G)	MEAN±S.D.	411.1 ± 14.5	244.9 ± 9.2**

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

** Significantly different from the male group value ($p \leq 0.01$).

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE B1 (PAGE 1): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS I AND III - PART A

THREE DAYS AFTER LAST DOSAGE:			
GROUP		I	III
DOSAGE (MG/KG/DAY)a		0 (VEHICLE, 0.9% SALINE)	250 (IDPN)
RATS TESTED	N	8	8
HOME CAGE BEHAVIOR (MALE)			
1: Sleeping	N	2	3
2: Awake, Immobile	N	2	0
3: Normal movement	N	0	1
4: Unusual posture	N	0	0
5: Unusual behavior	N	0	0
HOME CAGE BEHAVIOR (FEMALE)			
1: Sleeping	N	2	1
2: Awake, Immobile	N	2	1
3: Normal movement	N	0	2
4: Unusual posture	N	0	0
5: Unusual behavior	N	0	0
ALTERATIONS (HOME CAGE)			
1: None	N	8	8
2: Stereotyped behavior	N	0	0
3: Bizarre behavior	N	0	0
4: Limb twitches/tremor	N	0	0
5: Whole body tremor/spasm	N	0	0
6: Unusual posture	N	0	0
7: Tonic-clonic seizure	N	0	0
REACTION TO REMOVAL			
(1) Sits quietly	N	7	8
(2) Vocalization	N	1	0
(3) Runs or freezes	N	0	0
(4) Tail or throat rattles	N	0	0
MEAN SCORE		1.1	1.0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on days 1 through 5 and day 8 of study for Group I. Dosage occurred on days 1 through 5 of study for Group III.

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TABLE B1 (PAGE 2): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS I AND III - PART A

THREE DAYS AFTER LAST DOSAGE:			
GROUP		I	III
DOSAGE (MG/KG/DAY)a		0 (VEHICLE, 0.9% SALINE)	250 (IDPN)
RATS TESTED	N	8	8
REACTION TO HANDLING			
(1) No resistance	N	7	7
(2) Vocalization	N	1	0
(3) Tense	N	0	1
(4) Squirming	N	0	0
	MEAN SCORE	1.1	1.3
REARS IN OPEN FIELD (MALE)	MEAN±S.D.	1.3 ± 1.9	3.0 ± 2.9
REARS IN OPEN FIELD (FEMALE)	MEAN±S.D.	5.3 ± 4.6	0.8 ± 1.0*
DEFECATION IN OPEN FIELD			
1: None	N	8	5
2: Feces normal	N	0	3
3: Soft or liquid feces	N	0	0
URINATION IN OPEN FIELD (MALE)			
(1) None	N	1	2
(2) Normal urination	N	3	2
(3) Excess urination	N	0	0
	MEAN SCORE	1.8	1.5
URINATION IN OPEN FIELD (FEMALE)			
(1) None	N	3	2
(2) Normal urination	N	1	2
(3) Excess urination	N	0	0
	MEAN SCORE	1.3	1.5
LEVEL OF AROUSAL			
(1) Stuporous	N	0	0
(2) Sluggish	N	0	0
(3) Apparently normal	N	8	8
(4) Sudden darting	N	0	0
(5) Freezing, vocalization	N	0	0
	MEAN SCORE	3.0	3.0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on days 1 through 5 and day 8 of study for Group I. Dosage occurred on days 1 through 5 of study for Group III.

* Significantly different from the Group I value ($p \leq 0.05$).

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TABLE B1 (PAGE 3): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS I AND III - PART A

THREE DAYS AFTER LAST DOSAGE:			
GROUP		I	III
DOSAGE (MG/KG/DAY) ^a		0 (VEHICLE, 0.9% SALINE)	250 (IDPN)
RATS TESTED	N	8	8
ALTERATIONS (OPEN FIELD)			
1: None	N	8	0**
2: Stereotyped behavior	N	0	8**
3: Bizarre behavior	N	0	6**
4: Limb twitches/tremor	N	0	0
5: Whole body tremor/spasm	N	0	0
6: Unusual posture	N	0	7**
7: Tonic-clonic seizure	N	0	0
GAIT PATTERN			
1: Apparently normal	N	8	0**
2: AtaXic	N	0	8**
3: Limbs splay or drag	N	0	8**
4: Spastic, tip-toe	N	0	0
5: Duck-walk	N	0	0
6: Scissors gait	N	0	0
GAIT ABNORMALITY, SEVERITY			
(1) Normal gait	N	8	0
(2) Slight	N	0	2
(3) Moderate	N	0	5
(4) Extreme	N	0	1
MEAN SCORE		1.0	2.9**
PALPEBRAL CLOSURE			
(1) Wide open	N	8	8
(2) Slightly drooping	N	0	0
(3) Half-closed	N	0	0
(4) Completely shut	N	0	0
MEAN SCORE		1.0	1.0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on days 1 through 5 and day 8 of study for Group I. Dosage occurred on days 1 through 5 of study for Group III.

** Significantly different from the Group I value ($p \leq 0.01$).

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TABLE B1 (PAGE 4): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS I AND III - PART A

THREE DAYS AFTER LAST DOSAGE:			
GROUP		I	III
DOSAGE (MG/KG/DAY)a		0 (VEHICLE, 0.9% SALINE)	250 (IDPN)
RATS TESTED	N	8	8
PROMINENCE OF THE EYE			
1: Normal	N	8	8
2: Exophthalmos	N	0	0
3: Enophthalmos	N	0	0
LACRIMATION			
(1) No excess	N	8	8
(2) Excess at eyelid margin	N	0	0
(3) Margin persistently damp	N	0	0
(4) Extends beyond margin	N	0	0
MEAN SCORE		1.0	1.0
SALIVATION			
(1) No excess	N	8	8
(2) Margin of mouth wet	N	0	0
(3) 1/4 to 1/2 submandibular	N	0	0
(4) Entire submandibular	N	0	0
MEAN SCORE		1.0	1.0
PILOERECTION	N	0	0
ABNORMAL RESPIRATION	N	0	1
APPEARANCE			
(1) Clean and groomed	N	6	3
(2) Unkempt	N	2	4
(3) Urine and/or fecal stain	N	0	1
MEAN SCORE		1.3	1.8
VISUAL REACTION			
(1) None	N	0	0
(2) Orienting	N	7	8
(3) Startle	N	1	0
(4) More energetic reaction	N	0	0
(5) Attacks	N	0	0
MEAN SCORE		2.1	2.0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on days 1 through 5 and day 8 of study for Group I. Dosage occurred on days 1 through 5 of study for Group III.

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TABLE B1 (PAGE 5): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS I AND III - PART A

THREE DAYS AFTER LAST DOSAGE:			
GROUP		I	III
DOSAGE (MG/KG/DAY)a		0 (VEHICLE, 0.9% SALINE)	250 (IDPN)
RATS TESTED	N	8	8
TACTILE REACTION			
(1) None	N	0	4
(2) Orienting	N	8	4
(3) Startle	N	0	0
(4) More energetic reaction	N	0	0
(5) Attacks	N	0	0
	MEAN SCORE	2.0	1.5*
AUDITORY REACTION			
(1) None	N	0	6
(2) Orienting	N	0	2
(3) Startle	N	8	0
(4) More energetic reaction	N	0	0
(5) Intense vocalization	N	0	0
	MEAN SCORE	3.0	1.3**
TAIL-PINCH REACTION			
(1) None	N	1	1
(2) Orienting	N	7	6
(3) Startle	N	0	1
(4) More energetic reaction	N	0	0
(5) Attacks	N	0	0
	MEAN SCORE	1.9	2.0
VISUAL PLACING RESPONSE			
(1) Early extension	N	8	0
(2) Extension after contact	N	0	1
(3) No extension	N	0	7
	MEAN SCORE	1.0	2.9**
AIR RIGHTING RESPONSE			
(1) All feet land on ground	N	7	1b
(2) Lands on side	N	1	0b
(3) Lands on back	N	0	6b
	MEAN SCORE	1.1	2.7**b

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on days 1 through 5 and day 8 of study for Group I. Dosage occurred on days 1 through 5 of study for Group III.

b. Excludes values for rat 12421; testing was unable to be performed due to the condition of the rat.

* Significantly different from the Group I value ($p \leq 0.05$).

** Significantly different from the Group I value ($p \leq 0.01$).

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE B1 (PAGE 6): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS I AND III - PART A

THREE DAYS AFTER LAST DOSAGE:				
GROUP		I		III
DOSAGE (MG/KG/DAY) ^a		0 (VEHICLE, 0.9% SALINE)		250 (IDPN)
RATS TESTED	N	8		8
PUPIL RESPONSE TO LIGHT	N	8		8
FORELIMB GRIP TEST				
MaXimum (G)	MEAN±S.D.	494.4 ± 194.5		523.8 ± 164.1
Average (G)	MEAN±S.D.	425.9 ± 169.7		458.4 ± 134.0
HINDLIMB GRIP TEST (MALE)				
MaXimum (G)	MEAN±S.D.	571.3 ± 181.7		448.8 ± 100.9
Average (G)	MEAN±S.D.	556.9 ± 178.2		375.0 ± 54.5
HINDLIMB GRIP TEST (FEMALE)				
MaXimum (G)	MEAN±S.D.	580.0 ± 269.8		408.8 ± 114.6
Average (G)	MEAN±S.D.	498.1 ± 218.9		388.1 ± 99.9
LANDING FOOT SPLAY (MALE)				
Average (CM)	MEAN±S.D.	8.73 ± 1.43		10.26 ± 1.36
LANDING FOOT SPLAY (FEMALE)				
Average (CM)	MEAN±S.D.	6.09 ± 1.13		8.75 ± 1.80*
BODY TEMPERATURE (°C) (MALE)	MEAN±S.D.	36.50 ± 1.04		36.60 ± 0.57
BODY TEMPERATURE (°C) (FEMALE)	MEAN±S.D.	37.85 ± 0.30		37.43 ± 1.01
BODY WEIGHT (G) (MALE)	MEAN±S.D.	432.5 ± 23.8		348.8 ± 10.1**
BODY WEIGHT (G) (FEMALE)	MEAN±S.D.	255.5 ± 16.4		222.3 ± 8.3**

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on days 1 through 5 and day 8 of study for Group I. Dosage occurred on days 1 through 5 of study for Group III.

* Significantly different from the Group I value ($p \leq 0.05$).

** Significantly different from the Group I value ($p \leq 0.01$).

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE B1 (PAGE 7): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS I AND III - PART A

ONE WEEK AFTER THE FIRST OBSERVATION:			
GROUP		I	III
DOSAGE (MG/KG/DAY)a		0 (VEHICLE, 0.9% SALINE)	250 (IDPN)
RATS TESTED	N	8	8
HOME CAGE BEHAVIOR (MALE)			
1: Sleeping	N	3	2
2: Awake, Immobile	N	1	0
3: Normal movement	N	0	0
4: Unusual posture	N	0	0
5: Unusual behavior	N	0	2
HOME CAGE BEHAVIOR (FEMALE)			
1: Sleeping	N	1	3
2: Awake, Immobile	N	1	1
3: Normal movement	N	2	0
4: Unusual posture	N	0	0
5: Unusual behavior	N	0	0
ALTERATIONS (HOME CAGE)			
1: None	N	8	6
2: Stereotyped behavior	N	0	2
3: Bizarre behavior	N	0	0
4: Limb twitches/tremor	N	0	0
5: Whole body tremor/spasm	N	0	0
6: Unusual posture	N	0	0
7: Tonic-clonic seizure	N	0	0
REACTION TO REMOVAL			
(1) Sits quietly	N	7	7
(2) Vocalization	N	1	1
(3) Runs or freezes	N	0	0
(4) Tail or throat rattles	N	0	0
MEAN SCORE		1.1	1.1

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on days 1 through 5 and day 8 of study for Group I. Dosage occurred on days 1 through 5 of study for Group III.

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE B1 (PAGE 8): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS I AND III - PART A

ONE WEEK AFTER THE FIRST OBSERVATION:			
GROUP		I	III
DOSAGE (MG/KG/DAY)a		0 (VEHICLE, 0.9% SALINE)	250 (IDPN)
RATS TESTED	N	8	8
REACTION TO HANDLING			
(1) No resistance	N	7	7
(2) Vocalization	N	1	1
(3) Tense	N	0	0
(4) Squirming	N	0	0
	MEAN SCORE	1.1	1.1
REARS IN OPEN FIELD (MALE)	MEAN±S.D.	1.3 ± 1.3	5.3 ± 4.6
REARS IN OPEN FIELD (FEMALE)	MEAN±S.D.	7.0 ± 4.1	6.5 ± 2.6
DEFECATION IN OPEN FIELD			
1: None	N	7	6
2: Feces normal	N	1	2
3: Soft or liquid feces	N	0	0
URINATION IN OPEN FIELD (MALE)			
(1) None	N	0	2
(2) Normal urination	N	4	2
(3) Excess urination	N	0	0
	MEAN SCORE	2.0	1.5
URINATION IN OPEN FIELD (FEMALE)			
(1) None	N	4	3
(2) Normal urination	N	0	1
(3) Excess urination	N	0	0
	MEAN SCORE	1.0	1.3
LEVEL OF AROUSAL			
(1) Stuporous	N	0	0
(2) Sluggish	N	0	0
(3) Apparently normal	N	8	8
(4) Sudden darting	N	0	0
(5) Freezing, vocalization	N	0	0
	MEAN SCORE	3.0	3.0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on days 1 through 5 and day 8 of study for Group I. Dosage occurred on days 1 through 5 of study for Group III.

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE B1 (PAGE 9): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS I AND III - PART A

ONE WEEK AFTER THE FIRST OBSERVATION:			
GROUP		I	III
DOSAGE (MG/KG/DAY) ^a		0 (VEHICLE, 0.9% SALINE)	250 (IDPN)
RATS TESTED	N	8	8
ALTERATIONS (OPEN FIELD)			
1: None	N	8	0**
2: Stereotyped behavior	N	0	8**
3: Bizarre behavior	N	0	5**
4: Limb twitches/tremor	N	0	0
5: Whole body tremor/spasm	N	0	0
6: Unusual posture	N	0	3
7: Tonic-clonic seizure	N	0	0
GAIT PATTERN			
1: Apparently normal	N	8	0**
2: AtaXic	N	0	8**
3: Limbs splay or drag	N	0	7**
4: Spastic, tip-toe	N	0	0
5: Duck-walk	N	0	0
6: Scissors gait	N	0	0
GAIT ABNORMALITY, SEVERITY			
(1) Normal gait	N	8	0
(2) Slight	N	0	2
(3) Moderate	N	0	6
(4) Extreme	N	0	0
MEAN SCORE		1.0	2.8**
PALPEBRAL CLOSURE			
(1) Wide open	N	8	7
(2) Slightly drooping	N	0	1
(3) Half-closed	N	0	0
(4) Completely shut	N	0	0
MEAN SCORE		1.0	1.1

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on days 1 through 5 and day 8 of study for Group I. Dosage occurred on days 1 through 5 of study for Group III.

** Significantly different from the Group I value ($p \leq 0.01$).

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TABLE B1 (PAGE 10): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS I AND III - PART A

ONE WEEK AFTER THE FIRST OBSERVATION:			
GROUP		I	III
DOSAGE (MG/KG/DAY) ^a		0 (VEHICLE, 0.9% SALINE)	250 (IDPN)
RATS TESTED	N	8	8
PROMINENCE OF THE EYE			
1: Normal	N	8	8
2: Exophthalmos	N	0	0
3: Enophthalmos	N	0	0
LACRIMATION			
(1) No excess	N	8	8
(2) Excess at eyelid margin	N	0	0
(3) Margin persistently damp	N	0	0
(4) Extends beyond margin	N	0	0
MEAN SCORE		1.0	1.0
SALIVATION			
(1) No excess	N	8	8
(2) Margin of mouth wet	N	0	0
(3) 1/4 to 1/2 submandibular	N	0	0
(4) Entire submandibular	N	0	0
MEAN SCORE		1.0	1.0
PILOERECTION	N	0	0
ABNORMAL RESPIRATION	N	0	0
APPEARANCE			
(1) Clean and groomed	N	5	3
(2) Unkempt	N	3	3
(3) Urine and/or fecal stain	N	0	2
MEAN SCORE		1.4	1.9
VISUAL REACTION			
(1) None	N	0	1
(2) Orienting	N	8	7
(3) Startle	N	0	0
(4) More energetic reaction	N	0	0
(5) Attacks	N	0	0
MEAN SCORE		2.0	1.9

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on days 1 through 5 and day 8 of study for Group I. Dosage occurred on days 1 through 5 of study for Group III.

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE B1 (PAGE 11): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS I AND III - PART A

ONE WEEK AFTER THE FIRST OBSERVATION:			
GROUP		I	III
DOSAGE (MG/KG/DAY) ^a		0 (VEHICLE, 0.9% SALINE)	250 (IDPN)
RATS TESTED	N	8	8
TACTILE REACTION			
(1) None	N	0	2
(2) Orienting	N	8	6
(3) Startle	N	0	0
(4) More energetic reaction	N	0	0
(5) Attacks	N	0	0
	MEAN SCORE	2.0	1.8
AUDITORY REACTION			
(1) None	N	0	5
(2) Orienting	N	2	3
(3) Startle	N	6	0
(4) More energetic reaction	N	0	0
(5) Intense vocalization	N	0	0
	MEAN SCORE	2.8	1.4**
TAIL-PINCH REACTION			
(1) None	N	0	0
(2) Orienting	N	8	8
(3) Startle	N	0	0
(4) More energetic reaction	N	0	0
(5) Attacks	N	0	0
	MEAN SCORE	2.0	2.0
VISUAL PLACING RESPONSE			
(1) Early extension	N	8	0
(2) Extension after contact	N	0	0
(3) No extension	N	0	8
	MEAN SCORE	1.0	3.0**
AIR RIGHTING RESPONSE			
(1) All feet land on ground	N	7	b
(2) Lands on side	N	1	b
(3) Lands on back	N	0	b
	MEAN SCORE	1.1	b

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on days 1 through 5 and day 8 of study for Group I. Dosage occurred on days 1 through 5 of study for Group III.

b. Excludes values for eight rats in which testing was unable to be performed due to the condition of the rats.

** Significantly different from the Group I value ($p \leq 0.01$).

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TABLE B1 (PAGE 12): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS I AND III - PART A

ONE WEEK AFTER THE FIRST OBSERVATION:				
GROUP		I		III
DOSAGE (MG/KG/DAY) ^a		0 (VEHICLE, 0.9% SALINE)		250 (IDPN)
RATS TESTED	N	8		8
PUPIL RESPONSE TO LIGHT	N	8		8
FORELIMB GRIP TEST				
MaXimum (G)	MEAN±S.D.	575.6 ± 275.0		417.5 ± 133.9
Average (G)	MEAN±S.D.	485.0 ± 241.2		365.0 ± 93.8
HINDLIMB GRIP TEST (MALE)				
MaXimum (G)	MEAN±S.D.	618.8 ± 243.9		407.5 ± 97.5
Average (G)	MEAN±S.D.	548.8 ± 249.8		343.8 ± 68.5
HINDLIMB GRIP TEST (FEMALE)				
MaXimum (G)	MEAN±S.D.	483.8 ± 220.5		492.5 ± 205.1
Average (G)	MEAN±S.D.	438.1 ± 215.0		406.9 ± 125.2
LANDING FOOT SPLAY (MALE)				
Average (CM)	MEAN±S.D.	9.29 ± 4.32		b
LANDING FOOT SPLAY (FEMALE)				
Average (CM)	MEAN±S.D.	6.50 ± 1.51		6.75 ± ----
BODY TEMPERATURE (°C) (MALE)	MEAN±S.D.	36.98 ± 0.67		[1]c
BODY TEMPERATURE (°C) (FEMALE)	MEAN±S.D.	37.85 ± 0.41		37.43 ± 0.49
BODY WEIGHT (G) (MALE)	MEAN±S.D.	443.3 ± 29.5		38.00 ± 0.36
BODY WEIGHT (G) (FEMALE)	MEAN±S.D.	262.5 ± 16.8		355.5 ± 26.4**
				246.3 ± 13.6

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on days 1 through 5 and day 8 of study for Group I. Dosage occurred on days 1 through 5 of study for Group III.

b. Excludes values for four rats in which testing was unable to be performed due to the condition of the rats.

c. Excludes values for three rats in which testing was unable to be performed due to the condition of the rats.

** Significantly different from the Group I value ($p \leq 0.01$).

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE C1 (PAGE 1): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS I AND IV - PART A

THREE DAYS AFTER LAST DOSAGE (GROUP I) OR TARGETED TIME OF 60 TO 90 MINUTES POSTDOSAGE (GROUP IV):			
GROUP		I	IV
DOSAGE (MG/KG/DAY)a		0 (VEHICLE, 0.9% SALINE)	6.0 (CHLORPROMAZINE)
RATS TESTED	N	8	8
HOME CAGE BEHAVIOR (MALE)			
1: Sleeping	N	2	1
2: Awake, Immobile	N	2	3
3: Normal movement	N	0	0
4: Unusual posture	N	0	0
5: Unusual behavior	N	0	0
HOME CAGE BEHAVIOR (FEMALE)			
1: Sleeping	N	2	0
2: Awake, Immobile	N	2	3
3: Normal movement	N	0	0
4: Unusual posture	N	0	1
5: Unusual behavior	N	0	0
ALTERATIONS (HOME CAGE)			
1: None	N	8	7
2: Stereotyped behavior	N	0	0
3: Bizarre behavior	N	0	0
4: Limb twitches/tremor	N	0	0
5: Whole body tremor/spasm	N	0	0
6: Unusual posture	N	0	1
7: Tonic-clonic seizure	N	0	0
REACTION TO REMOVAL			
(1) Sits quietly	N	7	8
(2) Vocalization	N	1	0
(3) Runs or freezes	N	0	0
(4) Tail or throat rattles	N	0	0
	MEAN SCORE	1.1	1.0

n = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on days 1 through 5 and day 8 of study for Group I. Dosage occurred on day 1 of study for Group IV.

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE C1 (PAGE 2): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS I AND IV - PART A

THREE DAYS AFTER LAST DOSAGE (GROUP I) OR TARGETED TIME OF 60 TO 90 MINUTES POSTDOSAGE (GROUP IV):			
GROUP		I	IV
DOSAGE (MG/KG/DAY)a		0 (VEHICLE, 0.9% SALINE)	6.0 (CHLORPROMAZINE)
RATS TESTED	N	8	8
REACTION TO HANDLING			
(1) No resistance	N	7	8
(2) Vocalization	N	1	0
(3) Tense	N	0	0
(4) Squirming	N	0	0
	MEAN SCORE	1.1	1.0
REARS IN OPEN FIELD (MALE)	MEAN±S.D.	1.3 ± 1.9	2.0 ± 2.8
REARS IN OPEN FIELD (FEMALE)	MEAN±S.D.	5.3 ± 4.6	3.5 ± 4.5
DEFECATION IN OPEN FIELD			
1: None	N	8	8
2: Feces normal	N	0	0
3: Soft or liquid feces	N	0	0
URINATION IN OPEN FIELD (MALE)			
(1) None	N	1	0
(2) Normal urination	N	3	4
(3) Excess urination	N	0	0
	MEAN SCORE	1.8	2.0
URINATION IN OPEN FIELD (FEMALE)			
(1) None	N	3	3
(2) Normal urination	N	1	1
(3) Excess urination	N	0	0
	MEAN SCORE	1.3	1.3
LEVEL OF AROUSAL			
(1) Stuporous	N	0	0
(2) Sluggish	N	0	4
(3) Apparently normal	N	8	4
(4) Sudden darting	N	0	0
(5) Freezing, vocalization	N	0	0
	MEAN SCORE	3.0	2.5*

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on days 1 through 5 and day 8 of study for Group I. Dosage occurred on day 1 of study for Group IV.

* Significantly different from the Group I value ($p \leq 0.05$).

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE C1 (PAGE 3): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS I AND IV - PART A

THREE DAYS AFTER LAST DOSAGE (GROUP I) OR TARGETED TIME OF 60 TO 90 MINUTES POSTDOSAGE (GROUP IV):			
GROUP		I	IV
DOSAGE (MG/KG/DAY) ^a		0 (VEHICLE, 0.9% SALINE)	6.0 (CHLORPROMAZINE)
RATS TESTED	N	8	8
ALTERATIONS (OPEN FIELD)			
1: None	N	8	7
2: Stereotyped behavior	N	0	0
3: Bizarre behavior	N	0	0
4: Limb twitches/tremor	N	0	0
5: Whole body tremor/spasm	N	0	0
6: Unusual posture	N	0	1
7: Tonic-clonic seizure	N	0	0
GAIT PATTERN			
1: Apparently normal	N	8	5
2: AtaXic	N	0	0
3: Limbs splay or drag	N	0	2
4: Spastic, tip-toe	N	0	1
5: Duck-walk	N	0	0
6: Scissors gait	N	0	0
GAIT ABNORMALITY, SEVERITY			
(1) Normal gait	N	8	5
(2) Slight	N	0	3
(3) Moderate	N	0	0
(4) Extreme	N	0	0
MEAN SCORE		1.0	1.4
PALPEBRAL CLOSURE			
(1) Wide open	N	8	2
(2) Slightly drooping	N	0	6
(3) Half-closed	N	0	0
(4) Completely shut	N	0	0
MEAN SCORE		1.0	1.8**

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on days 1 through 5 and day 8 of study for Group I. Dosage occurred on day 1 of study for Group IV.

** Significantly different from the Group I value ($p \leq 0.01$).

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE C1 (PAGE 4): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS I AND IV - PART A

THREE DAYS AFTER LAST DOSAGE (GROUP I) OR TARGETED TIME OF 60 TO 90 MINUTES POSTDOSAGE (GROUP IV):			
GROUP		I	IV
DOSAGE (MG/KG/DAY) ^a		0 (VEHICLE, 0.9% SALINE)	6.0 (CHLORPROMAZINE)
RATS TESTED	N	8	8
PROMINENCE OF THE EYE			
1: Normal	N	8	8
2: Exophthalmos	N	0	0
3: Enophthalmos	N	0	0
LACRIMATION			
(1) No excess	N	8	8
(2) Excess at eyelid margin	N	0	0
(3) Margin persistently damp	N	0	0
(4) Extends beyond margin	N	0	0
MEAN SCORE		1.0	1.0
SALIVATION			
(1) No excess	N	8	8
(2) Margin of mouth wet	N	0	0
(3) 1/4 to 1/2 submandibular	N	0	0
(4) Entire submandibular	N	0	0
MEAN SCORE		1.0	1.0
PILOERECTION	N	0	0
ABNORMAL RESPIRATION	N	0	2
APPEARANCE			
(1) Clean and groomed	N	6	8
(2) Unkempt	N	2	0
(3) Urine and/or fecal stain	N	0	0
MEAN SCORE		1.3	1.0
VISUAL REACTION			
(1) None	N	0	4
(2) Orienting	N	7	4
(3) Startle	N	1	0
(4) More energetic reaction	N	0	0
(5) Attacks	N	0	0
MEAN SCORE		2.1	1.5*

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on days 1 through 5 and day 8 of study for Group I. Dosage occurred on day 1 of study for Group IV.

* Significantly different from the Group I value ($p \leq 0.05$).

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE C1 (PAGE 5): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS I AND IV - PART A

THREE DAYS AFTER LAST DOSAGE (GROUP I) OR TARGETED TIME OF 60 TO 90 MINUTES POSTDOSAGE (GROUP IV):			
GROUP		I	IV
DOSAGE (MG/KG/DAY)a		0 (VEHICLE, 0.9% SALINE)	6.0 (CHLORPROMAZINE)
RATS TESTED	N	8	8
TACTILE REACTION			
(1) None	N	0	2
(2) Orienting	N	8	6
(3) Startle	N	0	0
(4) More energetic reaction	N	0	0
(5) Attacks	N	0	0
MEAN SCORE		2.0	1.8
AUDITORY REACTION			
(1) None	N	0	0
(2) Orienting	N	0	2
(3) Startle	N	8	6
(4) More energetic reaction	N	0	0
(5) Intense vocalization	N	0	0
MEAN SCORE		3.0	2.8
TAIL-PINCH REACTION			
(1) None	N	1	1
(2) Orienting	N	7	6
(3) Startle	N	0	1
(4) More energetic reaction	N	0	0
(5) Attacks	N	0	0
MEAN SCORE		1.9	2.0
VISUAL PLACING RESPONSE			
(1) Early extension	N	8	6
(2) Extension after contact	N	0	2
(3) No extension	N	0	0
MEAN SCORE		1.0	1.3
AIR RIGHTING RESPONSE			
(1) All feet land on ground	N	7	8
(2) Lands on side	N	1	0
(3) Lands on back	N	0	0
MEAN SCORE		1.1	1.0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on days 1 through 5 and day 8 of study for Group I. Dosage occurred on day 1 of study for Group IV.

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE C1 (PAGE 6): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS I AND IV - PART A

THREE DAYS AFTER LAST DOSAGE (GROUP I) OR TARGETED TIME OF 60 TO 90 MINUTES POSTDOSAGE (GROUP IV):				
GROUP		I		IV
DOSAGE (MG/KG/DAY) ^a		0 (VEHICLE, 0.9% SALINE)		6.0 (CHLORPROMAZINE)
RATS TESTED	N	8		8
PUPIL RESPONSE TO LIGHT	N	8		8
FORELIMB GRIP TEST				
MaXimum (G)	MEAN±S.D.	494.4 ± 194.5		834.4 ± 286.1**
Average (G)	MEAN±S.D.	425.9 ± 169.7		674.1 ± 213.9*
HINDLIMB GRIP TEST (MALE)				
MaXimum (G)	MEAN±S.D.	571.3 ± 181.7		935.0 ± 257.0
Average (G)	MEAN±S.D.	556.9 ± 178.2		844.4 ± 217.7
HINDLIMB GRIP TEST (FEMALE)				
MaXimum (G)	MEAN±S.D.	580.0 ± 269.8		770.0 ± 344.6
Average (G)	MEAN±S.D.	498.1 ± 218.9		690.6 ± 300.9
LANDING FOOT SPLAY (MALE)				
Average (CM)	MEAN±S.D.	8.73 ± 1.43		11.26 ± 1.90
LANDING FOOT SPLAY (FEMALE)				
Average (CM)	MEAN±S.D.	6.09 ± 1.13		9.63 ± 1.61**
BODY TEMPERATURE (°C) (MALE)	MEAN±S.D.	36.5 ± 1.0		35.0 ± 0.8
BODY TEMPERATURE (°C) (FEMALE)	MEAN±S.D.	37.85 ± 0.30		36.85 ± 0.48**
BODY WEIGHT (G) (MALE)	MEAN±S.D.	432.5 ± 23.8		438.5 ± 24.6
BODY WEIGHT (G) (FEMALE)	MEAN±S.D.	255.5 ± 16.4		252.3 ± 10.7

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on days 1 through 5 and day 8 of study for Group I. Dosage occurred on day 1 of study for Group IV.

* Significantly different from the Group I value ($p \leq 0.05$).

** Significantly different from the Group I value ($p \leq 0.01$).

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE D1 (PAGE 1): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS II AND V - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE:			
GROUP		II	V
DOSAGE (MG/KG/DAY)a		0 (VEHICLE, CORN OIL)	4.0 (D-AMPHETAMINE)
RATS TESTED	N	8	8
HOME CAGE BEHAVIOR (MALE)			
1: Sleeping	N	0	0
2: Awake, Immobile	N	2	0
3: Normal movement	N	2	0
4: Unusual posture	N	0	0
5: Unusual behavior	N	0	4**
HOME CAGE BEHAVIOR (FEMALE)			
1: Sleeping	N	0	0
2: Awake, Immobile	N	3	0**
3: Normal movement	N	1	0
4: Unusual posture	N	0	0
5: Unusual behavior	N	0	4**
ALTERATIONS (HOME CAGE)			
1: None	N	8	0**
2: Stereotyped behavior	N	0	8**
3: Bizarre behavior	N	0	0
4: Limb twitches/tremor	N	0	0
5: Whole body tremor/spasm	N	0	0
6: Unusual posture	N	0	0
7: Tonic-clonic seizure	N	0	0
REACTION TO REMOVAL			
(1) Sits quietly	N	6	5
(2) Vocalization	N	1	3
(3) Runs or freezes	N	1	0
(4) Tail or throat rattles	N	0	0
	MEAN SCORE	1.4	1.4

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on day 1 of study.

** Significantly different from the Group II value ($p \leq 0.01$).

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE D1 (PAGE 2): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS II AND V - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE:			
GROUP		II	V
DOSAGE (MG/KG/DAY) ^a		0 (VEHICLE, CORN OIL)	4.0 (D-AMPHETAMINE)
RATS TESTED	N	8	8
REACTION TO HANDLING			
(1) No resistance	N	7	6
(2) Vocalization	N	1	2
(3) Tense	N	0	0
(4) Squirming	N	0	0
	MEAN SCORE	1.1	1.3
REARS IN OPEN FIELD (MALE)	MEAN±S.D.	4.0 ± 4.5	6.5 ± 2.4
REARS IN OPEN FIELD (FEMALE)	MEAN±S.D.	7.5 ± 5.7	7.5 ± 2.4
DEFECATION IN OPEN FIELD			
1: None	N	7	8
2: Feces normal	N	1	0
3: Soft or liquid feces	N	0	0
URINATION IN OPEN FIELD (MALE)			
(1) None	N	0	0
(2) Normal urination	N	4	4
(3) Excess urination	N	0	0
	MEAN SCORE	2.0	2.0
URINATION IN OPEN FIELD (FEMALE)			
(1) None	N	3	3
(2) Normal urination	N	1	1
(3) Excess urination	N	0	0
	MEAN SCORE	1.3	1.3
LEVEL OF AROUSAL			
(1) Stuporous	N	0	0
(2) Sluggish	N	0	0
(3) Apparently normal	N	8	8
(4) Sudden darting	N	0	0
(5) Freezing, vocalization	N	0	0
	MEAN SCORE	3.0	3.0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on day 1 of study.

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE D1 (PAGE 3): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS II AND V - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE:			
GROUP		II	V
DOSAGE (MG/KG/DAY) ^a		0 (VEHICLE, CORN OIL)	4.0 (D-AMPHETAMINE)
RATS TESTED	N	8	8
ALTERATIONS (OPEN FIELD)			
1: None	N	8	0**
2: Stereotyped behavior	N	0	8**
3: Bizarre behavior	N	0	0
4: Limb twitches/tremor	N	0	0
5: Whole body tremor/spasm	N	0	0
6: Unusual posture	N	0	6**
7: Tonic-clonic seizure	N	0	0
GAIT PATTERN			
1: Apparently normal	N	8	8
2: AtaXic	N	0	0
3: Limbs splay or drag	N	0	0
4: Spastic, tip-toe	N	0	0
5: Duck-walk	N	0	0
6: Scissors gait	N	0	0
GAIT ABNORMALITY, SEVERITY			
(1) Normal gait	N	8	8
(2) Slight	N	0	0
(3) Moderate	N	0	0
(4) Extreme	N	0	0
MEAN SCORE		1.0	1.0
PALPEBRAL CLOSURE			
(1) Wide open	N	8	8
(2) Slightly drooping	N	0	0
(3) Half-closed	N	0	0
(4) Completely shut	N	0	0
MEAN SCORE		1.0	1.0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on day 1 of study.

** Significantly different from the Group II value ($p \leq 0.01$).

TABLE D1 (PAGE 4): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS II AND V - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE:			
GROUP		II	V
DOSAGE (MG/KG/DAY) ^a		0 (VEHICLE, CORN OIL)	4.0 (D-AMPHETAMINE)
RATS TESTED	N	8	8
PROMINENCE OF THE EYE			
1: Normal	N	8	8
2: Exophthalmos	N	0	0
3: Enophthalmos	N	0	0
LACRIMATION			
(1) No excess	N	8	8
(2) Excess at eyelid margin	N	0	0
(3) Margin persistently damp	N	0	0
(4) Extends beyond margin	N	0	0
MEAN SCORE		1.0	1.0
SALIVATION			
(1) No excess	N	8	8
(2) Margin of mouth wet	N	0	0
(3) 1/4 to 1/2 submandibular	N	0	0
(4) Entire submandibular	N	0	0
MEAN SCORE		1.0	1.0
PILOERECTION	N	0	8**
ABNORMAL RESPIRATION	N	0	1
APPEARANCE			
(1) Clean and groomed	N	8	6
(2) Unkempt	N	0	0
(3) Urine and/or fecal stain	N	0	2
MEAN SCORE		1.0	1.5
VISUAL REACTION			
(1) None	N	0	0
(2) Orienting	N	8	8
(3) Startle	N	0	0
(4) More energetic reaction	N	0	0
(5) Attacks	N	0	0
MEAN SCORE		2.0	2.0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on day 1 of study.

** Significantly different from the Group II value ($p \leq 0.01$).

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE D1 (PAGE 5): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS II AND V - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE:			
GROUP		II	V
DOSAGE (MG/KG/DAY)a		0 (VEHICLE, CORN OIL)	4.0 (D-AMPHETAMINE)
RATS TESTED	N	8	8
TACTILE REACTION			
(1) None	N	0	0
(2) Orienting	N	8	8
(3) Startle	N	0	0
(4) More energetic reaction	N	0	0
(5) Attacks	N	0	0
MEAN SCORE		2.0	2.0
AUDITORY REACTION			
(1) None	N	0	0
(2) Orienting	N	0	1
(3) Startle	N	8	7
(4) More energetic reaction	N	0	0
(5) Intense vocalization	N	0	0
MEAN SCORE		3.0	2.9
TAIL-PINCH REACTION			
(1) None	N	0	0
(2) Orienting	N	8	7
(3) Startle	N	0	1
(4) More energetic reaction	N	0	0
(5) Attacks	N	0	0
MEAN SCORE		2.0	2.1
VISUAL PLACING RESPONSE			
(1) Early extension	N	8	8
(2) Extension after contact	N	0	0
(3) No extension	N	0	0
MEAN SCORE		1.0	1.0
AIR RIGHTING RESPONSE			
(1) All feet land on ground	N	7	5
(2) Lands on side	N	1	3
(3) Lands on back	N	0	0
MEAN SCORE		1.1	1.4

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on day 1 of study.

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TABLE D1 (PAGE 6): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS II AND V - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE:				
GROUP		II		V
DOSAGE (MG/KG/DAY) ^a		0 (VEHICLE, CORN OIL)		4.0 (D-AMPHETAMINE)
RATS TESTED	N	8		8
PUPIL RESPONSE TO LIGHT	N	8		8
FORELIMB GRIP TEST				
MaXimum (G)	MEAN±S.D.	712.5 ± 356.0		799.4 ± 265.5
Average (G)	MEAN±S.D.	601.6 ± 266.8		664.4 ± 202.8
HINDLIMB GRIP TEST (MALE)				
MaXimum (G)	MEAN±S.D.	676.3 ± 241.9		665.0 ± 268.2
Average (G)	MEAN±S.D.	610.0 ± 234.1		555.6 ± 197.7
HINDLIMB GRIP TEST (FEMALE)				
MaXimum (G)	MEAN±S.D.	631.3 ± 173.8		623.8 ± 234.5
Average (G)	MEAN±S.D.	550.6 ± 169.0		570.0 ± 208.6
LANDING FOOT SPLAY (MALE)				
Average (CM)	MEAN±S.D.	8.78 ± 2.28		8.39 ± 1.26
LANDING FOOT SPLAY (FEMALE)				
Average (CM)	MEAN±S.D.	6.30 ± 2.50		7.14 ± 2.96
BODY TEMPERATURE (°C) (MALE)	MEAN±S.D.	38.05 ± 0.10		38.40 ± 0.42
BODY TEMPERATURE (°C) (FEMALE)	MEAN±S.D.	38.23 ± 0.57		38.28 ± 0.17
BODY WEIGHT (G) (MALE)	MEAN±S.D.	433.5 ± 9.0		443.5 ± 19.8
BODY WEIGHT (G) (FEMALE)	MEAN±S.D.	254.5 ± 14.9		249.3 ± 9.0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on day 1 of study.

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE E1 (PAGE 1): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS II AND VI - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE:			
GROUP		II	VI
DOSAGE (MG/KG/DAY) ^a		0 (VEHICLE, CORN OIL)	100 (CARBARYL)
RATS TESTED	N	8	8
HOME CAGE BEHAVIOR (MALE)			
1: Sleeping	N	0	0
2: Awake, Immobile	N	2	0
3: Normal movement	N	2	0
4: Unusual posture	N	0	3**
5: Unusual behavior	N	0	4**
HOME CAGE BEHAVIOR (FEMALE)			
1: Sleeping	N	0	0
2: Awake, Immobile	N	3	0**
3: Normal movement	N	1	0
4: Unusual posture	N	0	4**
5: Unusual behavior	N	0	4**
ALTERATIONS (HOME CAGE)			
1: None	N	8	0**
2: Stereotyped behavior	N	0	0
3: Bizarre behavior	N	0	0
4: Limb twitches/tremor	N	0	0
5: Whole body tremor/spasm	N	0	8**
6: Unusual posture	N	0	7**
7: Tonic-clonic seizure	N	0	0
REACTION TO REMOVAL			
(1) Sits quietly	N	6	7
(2) Vocalization	N	1	1
(3) Runs or freezes	N	1	0
(4) Tail or throat rattles	N	0	0
	MEAN SCORE	1.4	1.1

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on day 1 of study.

** Significantly different from the Group II value ($p \leq 0.01$).

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE E1 (PAGE 2): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS II AND VI - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE:			
GROUP		II	VI
DOSAGE (MG/KG/DAY)a		0 (VEHICLE, CORN OIL)	100 (CARBARYL)
RATS TESTED	N	8	8
REACTION TO HANDLING			
(1) No resistance	N	7	8
(2) Vocalization	N	1	0
(3) Tense	N	0	0
(4) Squirming	N	0	0
	MEAN SCORE	1.1	1.0
REARS IN OPEN FIELD (MALE)	MEAN±S.D.	4.0 ± 4.5	0.0 ± 0.0*
REARS IN OPEN FIELD (FEMALE)	MEAN±S.D.	7.5 ± 5.7	0.3 ± 0.5*
DEFECATION IN OPEN FIELD			
1: None	N	7	7
2: Feces normal	N	1	1
3: Soft or liquid feces	N	0	0
URINATION IN OPEN FIELD (MALE)			
(1) None	N	0	0
(2) Normal urination	N	4	4
(3) Excess urination	N	0	0
	MEAN SCORE	2.0	2.0
URINATION IN OPEN FIELD (FEMALE)			
(1) None	N	3	1
(2) Normal urination	N	1	3
(3) Excess urination	N	0	0
	MEAN SCORE	1.3	1.8
LEVEL OF AROUSAL			
(1) Stuporous	N	0	0
(2) Sluggish	N	0	5
(3) Apparently normal	N	8	3
(4) Sudden darting	N	0	0
(5) Freezing, vocalization	N	0	0
	MEAN SCORE	3.0	2.4**

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on day 1 of study.

* Significantly different from the Group II value ($p \leq 0.05$).

** Significantly different from the Group II value ($p \leq 0.01$).

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE E1 (PAGE 3): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS II AND VI - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE:			
GROUP		II	VI
DOSAGE (MG/KG/DAY) ^a		0 (VEHICLE, CORN OIL)	100 (CARBARYL)
RATS TESTED	N	8	8
ALTERATIONS (OPEN FIELD)			
1: None	N	8	0**
2: Stereotyped behavior	N	0	0
3: Bizarre behavior	N	0	0
4: Limb twitches/tremor	N	0	1
5: Whole body tremor/spasm	N	0	8**
6: Unusual posture	N	0	8**
7: Tonic-clonic seizure	N	0	0
GAIT PATTERN			
1: Apparently normal	N	8	0**
2: AtaXic	N	0	7**
3: Limbs splay or drag	N	0	4**
4: Spastic, tip-toe	N	0	0
5: Duck-walk	N	0	0
6: Scissors gait	N	0	0
GAIT ABNORMALITY, SEVERITY			
(1) Normal gait	N	8	0
(2) Slight	N	0	6
(3) Moderate	N	0	2
(4) Extreme	N	0	0
MEAN SCORE		1.0	2.3**
PALPEBRAL CLOSURE			
(1) Wide open	N	8	8
(2) Slightly drooping	N	0	0
(3) Half-closed	N	0	0
(4) Completely shut	N	0	0
MEAN SCORE		1.0	1.0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on day 1 of study.

** Significantly different from the Group II value ($p \leq 0.01$).

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE E1 (PAGE 4): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS II AND VI - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE:			
GROUP		II	VI
DOSAGE (MG/KG/DAY) ^a		0 (VEHICLE, CORN OIL)	100 (CARBARYL)
RATS TESTED	N	8	8
PROMINENCE OF THE EYE			
1: Normal	N	8	8
2: Exophthalmos	N	0	0
3: Enophthalmos	N	0	0
LACRIMATION			
(1) No excess	N	8	4
(2) Excess at eyelid margin	N	0	3
(3) Margin persistently damp	N	0	1
(4) Extends beyond margin	N	0	0
	MEAN SCORE	1.0	1.6*
SALIVATION			
(1) No excess	N	8	3
(2) Margin of mouth wet	N	0	1
(3) 1/4 to 1/2 submandibular	N	0	4
(4) Entire submandibular	N	0	0
	MEAN SCORE	1.0	2.1**
PILOERECTION	N	0	0
ABNORMAL RESPIRATION	N	0	8**
APPEARANCE			
(1) Clean and groomed	N	8	6
(2) Unkempt	N	0	0
(3) Urine and/or fecal stain	N	0	2
	MEAN SCORE	1.0	1.5
VISUAL REACTION			
(1) None	N	0	6
(2) Orienting	N	8	2
(3) Startle	N	0	0
(4) More energetic reaction	N	0	0
(5) Attacks	N	0	0
	MEAN SCORE	2.0	1.3**

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on day 1 of study.

* Significantly different from the Group II value ($p \leq 0.05$).

** Significantly different from the Group II value ($p \leq 0.01$).

TABLE E1 (PAGE 5): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS II AND VI - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE:			
GROUP		II	VI
DOSAGE (MG/KG/DAY)a		0 (VEHICLE, CORN OIL)	100 (CARBARYL)
RATS TESTED	N	8	8
TACTILE REACTION			
(1) None	N	0	3
(2) Orienting	N	8	5
(3) Startle	N	0	0
(4) More energetic reaction	N	0	0
(5) Attacks	N	0	0
	MEAN SCORE	2.0	1.6
AUDITORY REACTION			
(1) None	N	0	0
(2) Orienting	N	0	5
(3) Startle	N	8	3
(4) More energetic reaction	N	0	0
(5) Intense vocalization	N	0	0
	MEAN SCORE	3.0	2.4**
TAIL-PINCH REACTION			
(1) None	N	0	4
(2) Orienting	N	8	4
(3) Startle	N	0	0
(4) More energetic reaction	N	0	0
(5) Attacks	N	0	0
	MEAN SCORE	2.0	1.5*
VISUAL PLACING RESPONSE			
(1) Early extension	N	8	4
(2) Extension after contact	N	0	4
(3) No extension	N	0	0
	MEAN SCORE	1.0	1.5*
AIR RIGHTING RESPONSE			
(1) All feet land on ground	N	7	3
(2) Lands on side	N	1	4
(3) Lands on back	N	0	1
	MEAN SCORE	1.1	1.8*

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on day 1 of study.

* Significantly different from the Group II value ($p \leq 0.05$).

** Significantly different from the Group II value ($p \leq 0.01$).

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE E1 (PAGE 6): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS II AND VI - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE:				
GROUP		II		VI
DOSAGE (MG/KG/DAY) ^a		0 (VEHICLE, CORN OIL)		100 (CARBARYL)
RATS TESTED	N	8		8
PUPIL RESPONSE TO LIGHT	N	8		8
FORELIMB GRIP TEST				
MaXimum (G)	MEAN±S.D.	712.5 ± 356.0		592.5 ± 222.1
Average (G)	MEAN±S.D.	601.6 ± 266.8		526.9 ± 191.8
HINDLIMB GRIP TEST (MALE)				
MaXimum (G)	MEAN±S.D.	676.3 ± 241.9		683.8 ± 196.0
Average (G)	MEAN±S.D.	610.0 ± 234.1		646.3 ± 182.6
HINDLIMB GRIP TEST (FEMALE)				
MaXimum (G)	MEAN±S.D.	631.3 ± 173.8		585.0 ± 74.9
Average (G)	MEAN±S.D.	550.6 ± 169.0		526.3 ± 66.1
LANDING FOOT SPLAY (MALE)				
Average (CM)	MEAN±S.D.	8.78 ± 2.28		9.24 ± 1.29
LANDING FOOT SPLAY (FEMALE)				
Average (CM)	MEAN±S.D.	6.30 ± 2.50		8.25 ± 1.61
BODY TEMPERATURE (°C) (MALE)	MEAN±S.D.	38.05 ± 0.10		34.10 ± 0.70**
BODY TEMPERATURE (°C) (FEMALE)	MEAN±S.D.	38.23 ± 0.57		33.13 ± 0.52**
BODY WEIGHT (G) (MALE)	MEAN±S.D.	433.5 ± 9.0		447.3 ± 20.7
BODY WEIGHT (G) (FEMALE)	MEAN±S.D.	254.5 ± 14.9		249.5 ± 20.0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on day 1 of study.

** Significantly different from the Group II value ($p \leq 0.01$).

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE F1 (PAGE 1): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS II AND VII - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE (GROUP II) OR TARGETED TIME OF 6 HOURS POSTDOSAGE (GROUP VII):			
GROUP		II	VII
DOSAGE (MG/KG/DAY)a		0 (VEHICLE, CORN OIL)	75 (DDT)
RATS TESTED	N	8	6b
HOME CAGE BEHAVIOR (MALE)			
1: Sleeping	N	0	0
2: Awake, Immobile	N	2	0
3: Normal movement	N	2	0
4: Unusual posture	N	0	0
5: Unusual behavior	N	0	3**
HOME CAGE BEHAVIOR (FEMALE)			
1: Sleeping	N	0	0
2: Awake, Immobile	N	3	0**
3: Normal movement	N	1	1
4: Unusual posture	N	0	0
5: Unusual behavior	N	0	2
ALTERATIONS (HOME CAGE)			
1: None	N	8	1**
2: Stereotyped behavior	N	0	0
3: Bizarre behavior	N	0	0
4: Limb twitches/tremor	N	0	0
5: Whole body tremor/spasm	N	0	5**
6: Unusual posture	N	0	0
7: Tonic-clonic seizure	N	0	0
REACTION TO REMOVAL			
(1) Sits quietly	N	6	4
(2) Vocalization	N	1	2
(3) Runs or freezes	N	1	0
(4) Tail or throat rattles	N	0	0
MEAN SCORE		1.4	1.3

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on day 1 of study.

b. Excludes values for male rat 12427 and female rat 12461, which were sacrificed due to adverse clinical observations.

** Significantly different from the Group II value ($p \leq 0.01$).

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE F1 (PAGE 2): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS II AND VII - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE (GROUP II) OR TARGETED TIME OF 6 HOURS POSTDOSAGE (GROUP VII):			
GROUP		II	VII
DOSAGE (MG/KG/DAY)a		0 (VEHICLE, CORN OIL)	75 (DDT)
RATS TESTED	N	8	6b
REACTION TO HANDLING			
(1) No resistance	N	7	5
(2) Vocalization	N	1	1
(3) Tense	N	0	0
(4) Squirming	N	0	0
	MEAN SCORE	1.1	1.2
REARS IN OPEN FIELD (MALE)	MEAN±S.D.	4.0 ± 4.5	1.3 ± 1.5
REARS IN OPEN FIELD (FEMALE)	MEAN±S.D.	7.5 ± 5.7	3.0 ± 2.6
DEFECATION IN OPEN FIELD			
1: None	N	7	5
2: Feces normal	N	1	1
3: Soft or liquid feces	N	0	0
URINATION IN OPEN FIELD (MALE)			
(1) None	N	0	1
(2) Normal urination	N	4	2
(3) Excess urination	N	0	0
	MEAN SCORE	2.0	1.7
URINATION IN OPEN FIELD (FEMALE)			
(1) None	N	3	3
(2) Normal urination	N	1	0
(3) Excess urination	N	0	0
	MEAN SCORE	1.3	1.0
LEVEL OF AROUSAL			
(1) Stuporous	N	0	0
(2) Sluggish	N	0	0
(3) Apparently normal	N	8	6
(4) Sudden darting	N	0	0
(5) Freezing, vocalization	N	0	0
	MEAN SCORE	3.0	3.0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on day 1 of study.

b. Excludes values for male rat 12427 and female rat 12461, which were sacrificed due to adverse clinical observations.

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE F1 (PAGE 3): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS II AND VII - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE (GROUP II) OR TARGETED TIME OF 6 HOURS POSTDOSAGE (GROUP VII):			
GROUP		II	VII
DOSAGE (MG/KG/DAY)a		0 (VEHICLE, CORN OIL)	75 (DDT)
RATS TESTED	N	8	6b
ALTERATIONS (OPEN FIELD)			
1: None	N	8	1**
2: Stereotyped behavior	N	0	0
3: Bizarre behavior	N	0	1
4: Limb twitches/tremor	N	0	0
5: Whole body tremor/spasm	N	0	5**
6: Unusual posture	N	0	0
7: Tonic-clonic seizure	N	0	0
GAIT PATTERN			
1: Apparently normal	N	8	6
2: AtaXic	N	0	0
3: Limbs splay or drag	N	0	0
4: Spastic, tip-toe	N	0	0
5: Duck-walk	N	0	0
6: Scissors gait	N	0	0
GAIT ABNORMALITY, SEVERITY			
(1) Normal gait	N	8	6
(2) Slight	N	0	0
(3) Moderate	N	0	0
(4) Extreme	N	0	0
	MEAN SCORE	1.0	1.0
PALPEBRAL CLOSURE			
(1) Wide open	N	8	6
(2) Slightly drooping	N	0	0
(3) Half-closed	N	0	0
(4) Completely shut	N	0	0
	MEAN SCORE	1.0	1.0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on day 1 of study.

b. Excludes values for male rat 12427 and female rat 12461, which were sacrificed due to adverse clinical observations.

** Significantly different from the Group II value ($p \leq 0.01$).

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE F1 (PAGE 4): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS II AND VII - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE (GROUP II) OR TARGETED TIME OF 6 HOURS POSTDOSAGE (GROUP VII):			
GROUP		II	VII
DOSAGE (MG/KG/DAY) ^a		0 (VEHICLE, CORN OIL)	75 (DDT)
RATS TESTED	N	8	6 ^b
PROMINENCE OF THE EYE			
1: Normal	N	8	6
2: Exophthalmos	N	0	0
3: Enophthalmos	N	0	0
LACRIMATION			
(1) No excess	N	8	6
(2) Excess at eyelid margin	N	0	0
(3) Margin persistently damp	N	0	0
(4) Extends beyond margin	N	0	0
MEAN SCORE		1.0	1.0
SALIVATION			
(1) No excess	N	8	6
(2) Margin of mouth wet	N	0	0
(3) 1/4 to 1/2 submandibular	N	0	0
(4) Entire submandibular	N	0	0
MEAN SCORE		1.0	1.0
PILOERECTION	N	0	0
ABNORMAL RESPIRATION	N	0	0
APPEARANCE			
(1) Clean and groomed	N	8	5
(2) Unkempt	N	0	0
(3) Urine and/or fecal stain	N	0	1
MEAN SCORE		1.0	1.3
VISUAL REACTION			
(1) None	N	0	1
(2) Orienting	N	8	5
(3) Startle	N	0	0
(4) More energetic reaction	N	0	0
(5) Attacks	N	0	0
MEAN SCORE		2.0	1.8

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on day 1 of study.

b. Excludes values for male rat 12427 and female rat 12461, which were sacrificed due to adverse clinical observations.

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE F1 (PAGE 5): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS II AND VII - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE (GROUP II) OR TARGETED TIME OF 6 HOURS POSTDOSAGE (GROUP VII):			
GROUP		II	VII
DOSAGE (MG/KG/DAY)a		0 (VEHICLE, CORN OIL)	75 (DDT)
RATS TESTED	N	8	6b
TACTILE REACTION			
(1) None	N	0	0
(2) Orienting	N	8	5
(3) Startle	N	0	1
(4) More energetic reaction	N	0	0
(5) Attacks	N	0	0
	MEAN SCORE	2.0	2.2
AUDITORY REACTION			
(1) None	N	0	0
(2) Orienting	N	0	0
(3) Startle	N	8	6
(4) More energetic reaction	N	0	0
(5) Intense vocalization	N	0	0
	MEAN SCORE	3.0	3.0
TAIL-PINCH REACTION			
(1) None	N	0	1
(2) Orienting	N	8	5
(3) Startle	N	0	0
(4) More energetic reaction	N	0	0
(5) Attacks	N	0	0
	MEAN SCORE	2.0	1.8
VISUAL PLACING RESPONSE			
(1) Early extension	N	8	6
(2) Extension after contact	N	0	0
(3) No extension	N	0	0
	MEAN SCORE	1.0	1.0
AIR RIGHTING RESPONSE			
(1) All feet land on ground	N	7	6
(2) Lands on side	N	1	0
(3) Lands on back	N	0	0
	MEAN SCORE	1.1	1.0

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on day 1 of study.

b. Excludes values for male rat 12427 and female rat 12461, which were sacrificed due to adverse clinical observations.

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

TABLE F1 (PAGE 6): FUNCTIONAL OBSERVATIONAL BATTERY - SUMMARY - MALE AND FEMALE RATS - GROUPS II AND VII - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE (GROUP II) OR TARGETED TIME OF 6 HOURS POSTDOSAGE (GROUP VII):				
GROUP		II		VII
DOSAGE (MG/KG/DAY) ^a		0 (VEHICLE, CORN OIL)		75 (DDT)
RATS TESTED	N	8		6 ^b
PUPIL RESPONSE TO LIGHT	N	8		6
FORELIMB GRIP TEST				
MaXimum (G)	MEAN±S.D.	712.5 ± 356.0		527.5 ± 126.8
Average (G)	MEAN±S.D.	601.6 ± 266.8		413.3 ± 58.3
HINDLIMB GRIP TEST (MALE)				
MaXimum (G)	MEAN±S.D.	676.3 ± 241.9		350.0 ± 206.9
Average (G)	MEAN±S.D.	610.0 ± 234.1		319.2 ± 200.8
HINDLIMB GRIP TEST (FEMALE)				
MaXimum (G)	MEAN±S.D.	631.3 ± 173.8		411.7 ± 229.4
Average (G)	MEAN±S.D.	550.6 ± 169.0		384.2 ± 211.3
LANDING FOOT SPLAY (MALE)				
Average (CM)	MEAN±S.D.	8.78 ± 2.28		7.03 ± 1.71
LANDING FOOT SPLAY (FEMALE)				
Average (CM)	MEAN±S.D.	6.30 ± 2.50		6.28 ± 0.90
BODY TEMPERATURE (°C) (MALE)	MEAN±S.D.	38.05 ± 0.10		38.93 ± 0.55*
BODY TEMPERATURE (°C) (FEMALE)	MEAN±S.D.	38.23 ± 0.57		38.67 ± 0.42
BODY WEIGHT (G) (MALE)	MEAN±S.D.	433.5 ± 9.0		439.7 ± 24.8
BODY WEIGHT (G) (FEMALE)	MEAN±S.D.	254.5 ± 14.9		258.3 ± 14.6

n: = Category number for descriptive test item.

(n) = Score assigned to graded test items; mean score was calculated by multiplying each score by the number of rats with that score and then dividing the sum of the products by the total number of rats

a. Dosage occurred on day 1 of study.

b. Excludes values for male rat 12427 and female rat 12461, which were sacrificed due to adverse clinical observations.

* Significantly different from the Group II value ($p \leq 0.05$).

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

APPENDIX A1 (PAGE 1): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - MALE RATS - PREDOSAGE - PART A

PREDOSAGE:														
RAT #	12407	12419	12422	12423	12413	12414	12420	12424	12401	12404	12406	12421	12409	12410
HOME CAGE BEHAVIOR	1	1	1	1	2	1	1	2	2	2	2	2	1	2
ALTERATIONS (HOME CAGE)	1	1	1	1	1	1	1	1	1	1	1	1	1	1
REACTION TO REMOVAL	1	1	3	1	1	1	1	1	1	2	1	1	1	1
REACTION TO HANDLING	1	1	1	1	1	1	1	1	1	1	1	1	1	1
REARS IN OPEN FIELD	6	5	3	8	7	6	2	5	0	3	0	6	3	8
DEFECATION IN OPEN FIELD	1	1	1	1	1	1	2	1	2	1	1	1	1	1
URINATION IN OPEN FIELD	2	2	2	2	2	2	1	1	2	2	2	1	2	2
LEVEL OF AROUSAL	3	3	3	3	3	3	3	3	3	3	3	3	3	3
ALTERATIONS (OPEN FIELD)	1	1	1	1	1	1	1	1	1	1	1	1	1	1
GAIT PATTERN	1	1	1	1	1	1	1	1	1	1	1	1	1	1
GAIT ABNORMALITY, SEVERITY	1	1	1	1	1	1	1	1	1	1	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1	1	1	1	1	1	1	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1	1	1	1	1	1	1	1	1	1	1
LACRIMATION	1	1	1	1	1	1	1	1	1	1	1	1	1	1
SALIVATION	1	1	1	1	1	1	1	1	1	1	1	1	1	1
PILOERECTION	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0	0	0	0	0	0	0	0	0	0	0
APPEARANCE	1	1	2	1	1	1	1	1	1	1	2	1	1	1
VISUAL REACTION	2	2	2	2	2	2	2	2	2	2	2	2	2	2
TACTILE REACTION	2	2	2	2	2	2	2	2	2	2	2	2	2	3
AUDITORY REACTION	3	3	3	3	3	3	3	3	3	3	3	3	3	3
TAIL-PINCH REACTION	2	2	3	2	2	2	2	2	2	5	2	2	2	3
VISUAL PLACING RESPONSE	1	1	1	1	1	1	1	1	1	1	1	1	1	1
AIR RIGHTING RESPONSE	1	1	1	1	1	1	1	1	1	1	1	1	1	1
PUPIL RESPONSE TO LIGHT	1	1	1	1	1	1	1	1	1	1	1	1	1	1
FORELIMB GRIP TEST #1 (G)	585	555	730	310	670	515	880	440	730	620	565	780	290	450
FORELIMB GRIP TEST #2 (G)	375	495	855	355	465	280	1100	755	960	385	510	730	565	510
HINDLIMB GRIP TEST #1 (G)	755	485	705	660	260	480	615	515	575	710	365	345	585	740
HINDLIMB GRIP TEST #2 (G)	420	360	385	580	235	350	365	570	850	700	400	365	525	735
LANDING FOOT SPLAY #1 (CM)	7.0	7.1	10.9	4.3	8.9	9.4	11.4	3.6	8.8	7.3	5.9	8.8	9.3	5.7
LANDING FOOT SPLAY #2 (CM)	6.7	7.4	9.1	5.2	9.2	6.9	10.3	4.5	11.5	5.8	5.9	5.0	10.0	8.8
BODY TEMPERATURE (°C)	37.2	36.4	37.3	36.8	36.9	36.6	37.1	37.3	37.3	37.4	37.2	36.9	36.9	37.3
BODY WEIGHT (G)	392	436	412	419	396	417	403	400	399	409	403	411	400	436
VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.														

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

APPENDIX A1 (PAGE 2): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - MALE RATS - PREDOSAGE - PART A

PREDOSAGE:														
RAT #	12425	12426	12403	12411	12415	12416	12405	12408	12412	12428	12402	12417	12418	12427
HOME CAGE BEHAVIOR	1	1	1	1	2	1	1	1	2	2	1	2	2	3
ALTERATIONS (HOME CAGE)	1	1	1	1	1	1	1	1	1	1	1	1	1	1
REACTION TO REMOVAL	1	3	1	3	1	3	1	1	1	1	1	1	1	2
REACTION TO HANDLING	1	2	1	1	1	1	1	1	1	1	1	1	2	2
REARS IN OPEN FIELD	4	8	4	5	3	3	9	3	1	8	3	3	3	10
DEFECATION IN OPEN FIELD	1	1	1	1	1	1	1	1	1	1	1	1	2	1
URINATION IN OPEN FIELD	2	2	2	2	2	2	2	2	2	2	1	2	1	2
LEVEL OF AROUSAL	3	3	3	3	3	3	3	3	3	3	3	3	3	3
ALTERATIONS (OPEN FIELD)	1	1	1	1	1	1	1	1	1	1	1	1	1	1
GAIT PATTERN	1	1	1	1	1	1	1	1	1	1	1	1	1	1
GAIT ABNORMALITY, SEVERITY	1	1	1	1	1	1	1	1	1	1	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1	1	1	1	1	1	1	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1	1	1	1	1	1	1	1	1	1	1
LACRIMATION	1	1	1	1	1	1	1	1	1	1	1	1	1	1
SALIVATION	1	1	1	1	1	1	1	1	1	1	1	1	1	1
PILOERECTION	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0	0	0	0	0	0	0	0	0	0	0
APPEARANCE	1	1	1	1	1	1	1	1	1	1	1	1	1	1
VISUAL REACTION	2	2	2	2	2	2	2	2	2	2	2	2	2	2
TACTILE REACTION	2	2	3	2	2	2	2	2	2	2	2	2	3	2
AUDITORY REACTION	3	3	3	3	3	3	3	3	3	3	3	3	3	3
TAIL-PINCH REACTION	3	2	2	2	2	2	2	2	2	2	1	2	2	2
VISUAL PLACING RESPONSE	1	1	1	1	1	1	1	1	1	1	1	1	1	1
AIR RIGHTING RESPONSE	1	1	1	1	1	1	1	1	1	1	1	1	1	1
PUPIL RESPONSE TO LIGHT	1	1	1	1	1	1	1	1	1	1	1	1	1	1
FORELIMB GRIP TEST #1 (G)	805	940	455	755	395	725	325	360	730	710	360	905	790	995
FORELIMB GRIP TEST #2 (G)	520	1020	495	825	480	390	685	700	750	755	470	705	775	430
HINDLIMB GRIP TEST #1 (G)	505	595	595	615	815	520	445	660	425	545	645	720	355	700
HINDLIMB GRIP TEST #2 (G)	315	380	730	570	545	465	430	530	300	730	550	435	525	755
LANDING FOOT SPLAY #1 (CM)	7.3	8.9	6.6	11.4	7.6	8.1	3.6	7.9	5.2	6.4	7.3	7.3	9.0	12.4
LANDING FOOT SPLAY #2 (CM)	7.0	8.4	6.1	11.5	10.1	8.2	3.4	7.4	4.4	6.4	5.9	6.6	9.3	10.1
BODY TEMPERATURE (°C)	36.2	36.3	36.5	36.7	35.9	37.1	37.1	36.8	37.6	37.1	37.8	37.1	37.7	38.2
BODY WEIGHT (G)	392	406	394	438	410	428	391	426	412	424	408	428	396	426
VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.														

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

APPENDIX A2 (PAGE 1): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - FEMALE RATS - PREDOSAGE - PART A

PREDOSAGE:														
RAT #	12456	12465	12467	12468	12457	12460	12469	12478	12454	12458	12466	12472	12451	12463
HOME CAGE BEHAVIOR	3	1	2	1	2	2	1	2	3	1	1	2	3	1
ALTERATIONS (HOME CAGE)	1	1	1	1	1	1	1	1	1	1	1	1	1	1
REACTION TO REMOVAL	2	1	1	1	1	1	1	1	1	1	3	1	1	1
REACTION TO HANDLING	1	1	1	1	1	1	1	1	1	1	1	1	1	1
REARS IN OPEN FIELD	10	8a	8	11b	13	7	9	6	6	5	3	7	12	5
DEFECATION IN OPEN FIELD	1	1	1	1	1	1	1	1	1	1	1	1	1	1
URINATION IN OPEN FIELD	1	2	1	1	1	1	1	2	1	1	1	2	2	1
LEVEL OF AROUSAL	3	3	3	3	3	3	3	3	3	3	3	3	3	3
ALTERATIONS (OPEN FIELD)	1	1	1	1	1	1	1	1	1	1	1	1	1	1
GAIT PATTERN	1	1	1	1	1	1	1	1	1	1	1	1	1	1
GAIT ABNORMALITY, SEVERITY	1	1	1	1	1	1	1	1	1	1	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1	1	1	1	1	1	1	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1	1	1	1	1	1	1	1	1	1	1
LACRIMATION	1	1	1	1	1	1	1	1	1	1	1	1	1	1
SALIVATION	1	1	1	1	1	1	1	1	1	1	1	1	1	1
PILOERECTION	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0	0	0	0	0	0	0	0	0	0	0
APPEARANCE	1	1	1	1	1	1	1	1	1	1	1	1	1	1
VISUAL REACTION	2	2	2	2	2	2	2	1	2	2	2	2	2	2
TACTILE REACTION	2	2	2	2	2	2	2	2	2	2	2	2	2	2
AUDITORY REACTION	3	3	3	3	3	2	3	3	3	3	3	3	3	3
TAIL-PINCH REACTION	2	2	2	3	2	2	2	3	3	2	2	2	2	2
VISUAL PLACING RESPONSE	1	1	1	1	1	1	1	1	1	1	1	1	1	1
AIR RIGHTING RESPONSE	1	1	1	1	1	1	1	1	1	1	1	1	1	1
PUPIL RESPONSE TO LIGHT	1	1	1	1	1	1	1	1	1	1	1	1	1	1
FORELIMB GRIP TEST #1 (G)	385	465	425	400	560	760	495	610	230	960	615	610	465	610
FORELIMB GRIP TEST #2 (G)	350	630	435	740	650	885	480	640	325	580	610	625	320	540
HINDLIMB GRIP TEST #1 (G)	400	330	345	370	190	570	590	470	375	530	300	460	375	220
HINDLIMB GRIP TEST #2 (G)	450	390	260	285	255	680	460	430	365	520	265	735	455	340
LANDING FOOT SPLAY #1 (CM)	5.5	7.5	5.5	4.4	4.7	7.4	3.7	7.4	5.5	7.5	4.8	4.8	5.0	7.6
LANDING FOOT SPLAY #2 (CM)	6.1	5.9	3.9	6.1	4.9	8.6	3.6	7.6	3.7	6.8	5.8	4.5	6.1	7.9
BODY TEMPERATURE (°C)	38.8	38.3	37.6	38.3	38.1	38.4	37.5	37.2	37.3	37.0	37.7	37.8	37.1	37.5
BODY WEIGHT (G)	239	252	233	249	238	263	240	250	234	255	248	252	237	251

VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.

- Rat jumped out of the open field during the 2 minute observation period and was placed back into the open field.
- Rat jumped onto side of the open field during the 2 minute observation period and was placed back into the open field.

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

APPENDIX A2 (PAGE 2): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - FEMALE RATS - PREDOSAGE - PART A

PREDOSAGE:														
RAT #	12464	12471	12452	12455	12475	12476	12453	12459	12474	12477	12461	12462	12470	12473
HOME CAGE BEHAVIOR	2	1	2	1	1	3	1	1	2	3	3	3	1	2
ALTERATIONS (HOME CAGE)	1	1	1	1	1	1	1	1	1	1	1	1	1	1
REACTION TO REMOVAL	1	1	1	1	1	1	1	1	1	3	1	1	3	1
REACTION TO HANDLING	1	1	1	1	1	1	1	1	1	1	1	1	1	1
REARS IN OPEN FIELD	15	6	6	4	4	18a	4	4	9	7a	11	6	4	8
DEFECATION IN OPEN FIELD	1	1	1	1	1	1	1	1	1	1	1	1	1	1
URINATION IN OPEN FIELD	2	1	1	2	2	2	1	1	1	1	1	1	1	1
LEVEL OF AROUSAL	3	3	3	3	3	3	3	3	3	3	3	3	3	3
ALTERATIONS (OPEN FIELD)	1	1	1	1	1	1	1	1	1	1	1	1	1	1
GAIT PATTERN	1	1	1	1	1	1	1	1	1	1	1	1	1	1
GAIT ABNORMALITY, SEVERITY	1	1	1	1	1	1	1	1	1	1	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1	1	1	1	1	1	1	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1	1	1	1	1	1	1	1	1	1	1
LACRIMATION	1	1	1	1	1	1	1	1	1	1	1	1	1	1
SALIVATION	1	1	1	1	1	1	1	1	1	1	1	1	1	1
PILOERECTION	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0	0	0	0	0	0	0	0	0	0	0
APPEARANCE	1	1	1	1	1	1	1	1	1	1	1	1	1	1
VISUAL REACTION	2	2	2	2	2	2	2	2	2	2	2	2	2	2
TACTILE REACTION	2	2	2	2	2	2	2	2	2	2	2	2	2	2
AUDITORY REACTION	3	3	3	3	3	3	3	3	3	3	3	3	3	3
TAIL-PINCH REACTION	3	2	2	2	3	3	2	2	3	2	2	2	2	2
VISUAL PLACING RESPONSE	1	1	1	1	1	1	1	1	1	1	1	1	1	1
AIR RIGHTING RESPONSE	1	1	2	1	1	1	1	1	1	1	1	1	1	1
PUPIL RESPONSE TO LIGHT	1	1	1	1	1	1	1	1	1	1	1	1	1	1
FORELIMB GRIP TEST #1 (G)	760	680	855	585	500	950	735	315	205	675	510	360	360	990
FORELIMB GRIP TEST #2 (G)	505	660	790	1035	270	555	455	395	300	750	755	500	215	300
HINDLIMB GRIP TEST #1 (G)	610	525	295	635	320	310	270	465	535	315	220	360	650	745
HINDLIMB GRIP TEST #2 (G)	250	370	445	860	295	220	425	385	350	340	315	255	555	655
LANDING FOOT SPLAY #1 (CM)	8.2	5.7	5.8	10.6	11.6	4.3	6.3	5.9	6.9	7.1	7.1	4.4	7.8	5.7
LANDING FOOT SPLAY #2 (CM)	7.5	5.9	5.9	7.5	10.6	4.0	5.0	3.9	5.8	7.6	5.8	5.9	9.0	4.6
BODY TEMPERATURE (°C)	38.6	36.8	36.4	36.9	38.1	38.8	37.5	36.8	36.1	38.3	37.7	37.5	37.1	37.5
BODY WEIGHT (G)	234	252	235	251	240	240	231	242	243	265	238	253	236	255

VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.

a. Rat jumped onto side of the open field during the 2 minute observation period and was placed back into the open field.

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

APPENDIX B1 (PAGE 1): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - MALE RATS - GROUPS I AND III - PART A

THREE DAYS AFTER LAST DOSAGE:				
GROUP I	0 (VEHICLE, 0.9% SALINE) MG/KG/DAY			
RAT #	12407	12419	12422	12423
HOME CAGE BEHAVIOR	2	1	2	1
ALTERATIONS (HOME CAGE)	1	1	1	1
REACTION TO REMOVAL	1	1	2	1
REACTION TO HANDLING	1	1	2	1
REARS IN OPEN FIELD	0	1	0	4
DEFECATION IN OPEN FIELD	1	1	1	1
URINATION IN OPEN FIELD	2	2	2	1
LEVEL OF AROUSAL	3	3	3	3
ALTERATIONS (OPEN FIELD)	1	1	1	1
GAIT PATTERN	1	1	1	1
GAIT ABNORMALITY, SEVERITY	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1
LACRIMATION	1	1	1	1
SALIVATION	1	1	1	1
PILOERECTION	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0
APPEARANCE	1	1	2	1
VISUAL REACTION	2	2	2	2
TACTILE REACTION	2	2	2	2
AUDITORY REACTION	3	3	3	3
TAIL-PINCH REACTION	2	2	2	2
VISUAL PLACING RESPONSE	1	1	1	1
AIR RIGHTING RESPONSE	1	1	1	1
PUPIL RESPONSE TO LIGHT	1	1	1	1
FORELIMB GRIP TEST #1 (G)	430	545	705	375
FORELIMB GRIP TEST #2 (G)	325	810	565	250
HINDLIMB GRIP TEST #1 (G)	805	510	530	365
HINDLIMB GRIP TEST #2 (G)	780	585	525	355
LANDING FOOT SPLAY #1 (CM)	9.5	9.2	10.0	6.3
LANDING FOOT SPLAY #2 (CM)	9.8	8.3	9.6	7.1
BODY TEMPERATURE (°C)	35.0	36.6	37.1	37.3
BODY WEIGHT (G)	406	462	423	439
VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.				

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

APPENDIX B1 (PAGE 2): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - MALE RATS - GROUPS I AND III - PART A

THREE DAYS AFTER LAST DOSAGE:				
GROUP III				
250 (IDPN) MG/KG/DAY				
RAT #	12401	12404	12406	12421
HOME CAGE BEHAVIOR	1	3	1	1
ALTERATIONS (HOME CAGE)	1	1	1	1
REACTION TO REMOVAL	1	1	1	1
REACTION TO HANDLING	1	1	1	1
REARS IN OPEN FIELD	6	5	0	1
DEFECATION IN OPEN FIELD	2	1	2	1
URINATION IN OPEN FIELD	2	1	2	1
LEVEL OF AROUSAL	3	3	3	3
ALTERATIONS (OPEN FIELD)	2a, 3b, 6c	2d, 3b	2e, 3b, 6f	2g, 3b, 6f
GAIT PATTERN	2, 3h	2, 3h	2, 3h	2, 3h
GAIT ABNORMALITY, SEVERITY	4	3	2	2
PALPEBRAL CLOSURE	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1
LACRIMATION	1	1	1	1
SALIVATION	1	1	1	1
PILOERECTION	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0
APPEARANCE	2i	2j	1j	2k
VISUAL REACTION	2	2	2	2
TACTILE REACTION	1	2	2	1
AUDITORY REACTION	1	1	1	1
TAIL-PINCH REACTION	2	2	2	1
VISUAL PLACING RESPONSE	3	3	3	3
AIR RIGHTING RESPONSE	3	3	3	L
PUPIL RESPONSE TO LIGHT	1	1	1	1
FORELIMB GRIP TEST #1 (G)	600	440	365	730
FORELIMB GRIP TEST #2 (G)	610	490	350	305
HINDLIMB GRIP TEST #1 (G)	380	320	545	355
HINDLIMB GRIP TEST #2 (G)	275	345	255	525
LANDING FOOT SPLAY #1 (CM)	10.1	9.5	11.3	11.3
LANDING FOOT SPLAY #2 (CM)	9.2	7.8	11.8	11.1
BODY TEMPERATURE (°C)	36.8	36.0	37.3	36.3
BODY WEIGHT (G)	335	352	349	359

VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.

- a. Head bobbing, intermittent, moderate; head weaving, intermittent, extreme; circling to the right and left.
- b. Retropulsion.
- c. Low carriage.
- d. Head bobbing, intermittent, moderate; head weaving, intermittent, moderate.
- e. Head bobbing, intermittent, moderate; head weaving, intermittent, moderate; circling to the right.
- f. Hunched posture.
- g. Head bobbing, intermittent, moderate; head weaving, intermittent, moderate; circling to the right and left.
- h. Both fore and hindlimbs, splayed.
- i. Sparse hair coat, lower midline.
- j. Dehydration, mild.
- k. Cold to touch, whole body; sparse hair coat, right inguinal area.
- L. Testing was not performed due to condition of rat.

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

APPENDIX B1 (PAGE 3): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - MALE RATS - GROUPS I AND III - PART A

ONE WEEK AFTER THE FIRST OBSERVATION:				
GROUP I	0 (VEHICLE, 0.9% SALINE) MG/KG/DAY			
RAT #	12407	12419	12422	12423
HOME CAGE BEHAVIOR	1	1	2	1
ALTERATIONS (HOME CAGE)	1	1	1	1
REACTION TO REMOVAL	1	1	2	1
REACTION TO HANDLING	1	1	2	1
REARS IN OPEN FIELD	3	1	0	1
DEFECATION IN OPEN FIELD	1	1	2	1
URINATION IN OPEN FIELD	2	2	2	2
LEVEL OF AROUSAL	3	3	3	3
ALTERATIONS (OPEN FIELD)	1	1	1	1
GAIT PATTERN	1	1	1	1
GAIT ABNORMALITY, SEVERITY	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1
LACRIMATION	1	1	1	1
SALIVATION	1	1	1	1
PILOERECTION	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0
APPEARANCE	1	2	2	1
VISUAL REACTION	2	2	2	2
TACTILE REACTION	2	2	2	2
AUDITORY REACTION	3	3	3	3
TAIL-PINCH REACTION	2	2	2	2
VISUAL PLACING RESPONSE	1	1	1	1
AIR RIGHTING RESPONSE	1	1	1	1
PUPIL RESPONSE TO LIGHT	1	1	1	1
FORELIMB GRIP TEST #1 (G)	510	535	810	360
FORELIMB GRIP TEST #2 (G)	395	560	980	185
HINDLIMB GRIP TEST #1 (G)	875	535	580	395
HINDLIMB GRIP TEST #2 (G)	965	365	315	360
LANDING FOOT SPLAY #1 (CM)	8.4	8.4	15.6	4.8
LANDING FOOT SPLAY #2 (CM)	6.8	7.8	15.6	6.9
BODY TEMPERATURE (°C)	36.6	36.3	37.8	37.2
BODY WEIGHT (G)	406	478	446	443
VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.				

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

APPENDIX B1 (PAGE 4): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - MALE RATS - GROUPS I AND III - PART A

ONE WEEK AFTER THE FIRST OBSERVATION:				
GROUP III				
250 (IDPN) MG/KG/DAY				
RAT #	12401	12404	12406	12421
HOME CAGE BEHAVIOR	5	5	1	1
ALTERATIONS (HOME CAGE)	2a	2b	1	1
REACTION TO REMOVAL	1	1	1	1
REACTION TO HANDLING	1	1	1	1
REARS IN OPEN FIELD	10	3	0	8
DEFECATION IN OPEN FIELD	2	1	2	1
URINATION IN OPEN FIELD	2	2	1	1
LEVEL OF AROUSAL	3	3	3	3
ALTERATIONS (OPEN FIELD)	2c, 3d	2e, 3d, 6f	2c, 6f	2g, 6f
GAIT PATTERN	2, 3h	2	2, 3h	2, 3h
GAIT ABNORMALITY, SEVERITY	2	3	2	3
PALPEBRAL CLOSURE	1	1	1	2i
PROMINENCE OF THE EYE	1	1	1	1
LACRIMATION	1	1	1	1
SALIVATION	1	1	1	1
PILOERECTION	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0
APPEARANCE	2j	3k	2L	2m
VISUAL REACTION	2	2	2	1
TACTILE REACTION	2	2	2	1
AUDITORY REACTION	1	1	1	1
TAIL-PINCH REACTION	2	2	2	2
VISUAL PLACING RESPONSE	3	3	3	3
AIR RIGHTING RESPONSE	n	n	n	n
PUPIL RESPONSE TO LIGHT	1	1	1	1
FORELIMB GRIP TEST #1 (G)	400	390	415	230
FORELIMB GRIP TEST #2 (G)	365	495	400	595
HINDLIMB GRIP TEST #1 (G)	530	235	440	315
HINDLIMB GRIP TEST #2 (G)	330	345	295	260
LANDING FOOT SPLAY #1 (CM)	n	n	n	n
LANDING FOOT SPLAY #2 (CM)	n	n	n	n
BODY TEMPERATURE (°C)	37.7	37.9	36.8	37.3
BODY WEIGHT (G)	367	370	316	369

VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.

- Head bobbing, intermittent, moderate; head weaving, intermittent, moderate.
- Head bobbing, intermittent, slight; head weaving, intermittent, slight.
- Head bobbing, intermittent, moderate; head weaving, intermittent, moderate; circling to the right.
- Retropulsion.
- Head bobbing, intermittent, moderate; head weaving, intermittent, slight; circling to the right.
- Hunched posture.
- Head bobbing, intermittent, slight; head weaving, intermittent, moderate; circling to the left.
- Both fore and hindlimbs, splayed.
- Both eyes.
- Soft or liquid feces after two minute observation period; sparse hair coat, lower midline.
- Dehydration, mild.
- Dehydration, moderate.
- Dehydration, mild; sparse hair coat, right inguinal area.
- Testing was not performed due to condition of rat.

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

APPENDIX B2 (PAGE 1): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - FEMALE RATS - GROUPS I AND III - PART A

THREE DAYS AFTER LAST DOSAGE:				
GROUP I	0 (VEHICLE, 0.9% SALINE) MG/KG/DAY			
RAT #	12456	12465	12467	12468
HOME CAGE BEHAVIOR	1	2	2	1
ALTERATIONS (HOME CAGE)	1	1	1	1
REACTION TO REMOVAL	1	1	1	1
REACTION TO HANDLING	1	1	1	1
REARS IN OPEN FIELD	12	3	2	4
DEFECATION IN OPEN FIELD	1	1	1	1
URINATION IN OPEN FIELD	1	2	1	1
LEVEL OF AROUSAL	3	3	3	3
ALTERATIONS (OPEN FIELD)	1	1	1	1
GAIT PATTERN	1	1	1	1
GAIT ABNORMALITY, SEVERITY	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1
LACRIMATION	1	1	1	1
SALIVATION	1	1	1	1
PILOERECTION	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0
APPEARANCE	1	1	1	2
VISUAL REACTION	2	2	2	3
TACTILE REACTION	2	2	2	2
AUDITORY REACTION	3	3	3	3
TAIL-PINCH REACTION	2	2	2	1
VISUAL PLACING RESPONSE	1	1	1	1
AIR RIGHTING RESPONSE	1	1	1	2
PUPIL RESPONSE TO LIGHT	1	1	1	1
FORELIMB GRIP TEST #1 (G)	190	335	445	535
FORELIMB GRIP TEST #2 (G)	120	405	505	275
HINDLIMB GRIP TEST #1 (G)	915	660	275	330
HINDLIMB GRIP TEST #2 (G)	665	395	290	455
LANDING FOOT SPLAY #1 (CM)	5.2	6.3	4.8	7.6
LANDING FOOT SPLAY #2 (CM)	5.2	6.5	5.6	7.5
BODY TEMPERATURE (°C)	38.2	37.6	38.0	37.6
BODY WEIGHT (G)	236	257	253	276
VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.				

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

APPENDIX B2 (PAGE 2): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - FEMALE RATS - GROUPS I AND III - PART A

THREE DAYS AFTER LAST DOSAGE:				
GROUP III	250 (IDPN) MG/KG/DAY			
RAT #	12454	12458	12466	12472
HOME CAGE BEHAVIOR	2	1	3	3
ALTERATIONS (HOME CAGE)	1	1	1	1
REACTION TO REMOVAL	1	1	1	1
REACTION TO HANDLING	3	1	1	1
REARS IN OPEN FIELD	2	1	0	0
DEFECATION IN OPEN FIELD	2	1	1	1
URINATION IN OPEN FIELD	2	1	2	1
LEVEL OF AROUSAL	3	3	3	3
ALTERATIONS (OPEN FIELD)	2a, 6b	2c, 3d, 6e	2f, 6g	2h, 3d, 6e
GAIT PATTERN	2, 3i	2, 3i	2, 3j	2, 3i
GAIT ABNORMALITY, SEVERITY	3	3	3	3
PALPEBRAL CLOSURE	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1
LACRIMATION	1	1	1	1
SALIVATION	1	1	1	1
PILOERECTION	0	0	0	0
ABNORMAL RESPIRATION	0	1k	0	0
APPEARANCE	3	1L	2m	1n
VISUAL REACTION	2	2	2	2
TACTILE REACTION	2	2	1	1
AUDITORY REACTION	1	1	2	2
TAIL-PINCH REACTION	2	3	2	2
VISUAL PLACING RESPONSE	2	3	3	3
AIR RIGHTING RESPONSE	3	1	3	3
PUPIL RESPONSE TO LIGHT	1	1	1	1
FORELIMB GRIP TEST #1 (G)	380	520	760	335
FORELIMB GRIP TEST #2 (G)	305	350	575	220
HINDLIMB GRIP TEST #1 (G)	345	275	445	495
HINDLIMB GRIP TEST #2 (G)	315	280	515	435
LANDING FOOT SPLAY #1 (CM)	9.5	9.6	4.5	8.2
LANDING FOOT SPLAY #2 (CM)	7.6	11.5	8.2	10.9
BODY TEMPERATURE (°C)	38.4	37.6	36.0	37.7
BODY WEIGHT (G)	219	230	212	228

VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.

- Head bobbing, intermittent, moderate; head weaving, intermittent, moderate.
- Head tilt to the left; low carriage.
- Head bobbing, intermittent, moderate; head weaving, intermittent, moderate; circling to the right and left.
- Retropulsion.
- Low carriage.
- Head bobbing, intermittent, slight; head weaving, intermittent, slight; circling to the right.
- Hunched posture.
- Head bobbing, intermittent, moderate; head weaving, intermittent, moderate; circling to the right.
- Both fore and hindlimbs, splayed.
- Both hindlimbs, splayed.
- Tachypnea.
- Dehydration, mild.
- Tan feces, dehydration, mild.
- Vocalization to touch; dehydration, moderate.

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

APPENDIX B2 (PAGE 3): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - FEMALE RATS - GROUPS I AND III - PART A

ONE WEEK AFTER THE FIRST OBSERVATION:				
GROUP I	0 (VEHICLE, 0.9% SALINE) MG/KG/DAY			
RAT #	12456	12465	12467	12468
HOME CAGE BEHAVIOR	3	2	1	3
ALTERATIONS (HOME CAGE)	1	1	1	1
REACTION TO REMOVAL	1	1	1	1
REACTION TO HANDLING	1	1	1	1
REARS IN OPEN FIELD	11	3	4	10
DEFECATION IN OPEN FIELD	1	1	1	1
URINATION IN OPEN FIELD	1	1	1	1
LEVEL OF AROUSAL	3	3	3	3
ALTERATIONS (OPEN FIELD)	1	1	1	1
GAIT PATTERN	1	1	1	1
GAIT ABNORMALITY, SEVERITY	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1
LACRIMATION	1	1	1	1
SALIVATION	1	1	1	1
PILOERECTION	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0
APPEARANCE	1	1	1	2
VISUAL REACTION	2	2	2	2
TACTILE REACTION	2	2	2	2
AUDITORY REACTION	2	3	2	3
TAIL-PINCH REACTION	2	2	2	2
VISUAL PLACING RESPONSE	1	1	1	1
AIR RIGHTING RESPONSE	1	2	1	1
PUPIL RESPONSE TO LIGHT	1	1	1	1
FORELIMB GRIP TEST #1 (G)	225	430	455	1020
FORELIMB GRIP TEST #2 (G)	290	250	200	555
HINDLIMB GRIP TEST #1 (G)	615	530	330	265
HINDLIMB GRIP TEST #2 (G)	720	620	205	220
LANDING FOOT SPLAY #1 (CM)	4.6	6.4	9.6	5.8
LANDING FOOT SPLAY #2 (CM)	7.3	4.1	7.8	6.4
BODY TEMPERATURE (°C)	38.1	37.5	37.5	38.3
BODY WEIGHT (G)	243	263	260	284
VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.				

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

APPENDIX B2 (PAGE 4): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - FEMALE RATS - GROUPS I AND III - PART A

ONE WEEK AFTER THE FIRST OBSERVATION:				
GROUP III	250 (IDPN) MG/KG/DAY			
RAT #	12454	12458	12466	12472
HOME CAGE BEHAVIOR	1	1	2	1
ALTERATIONS (HOME CAGE)	1	1	1	1
REACTION TO REMOVAL	2	1	1	1
REACTION TO HANDLING	2	1	1	1
REARS IN OPEN FIELD	10	7	4	5a
DEFECATION IN OPEN FIELD	1	1	1	1
URINATION IN OPEN FIELD	2	1	1	1
LEVEL OF AROUSAL	3	3	3	3
ALTERATIONS (OPEN FIELD)	2b	2c,3d	2e,3d	2e,3d
GAIT PATTERN	2,3f	2,3f	2,3f	2,3g
GAIT ABNORMALITY, SEVERITY	3	3	3	3
PALPEBRAL CLOSURE	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1
LACRIMATION	1	1	1	1
SALIVATION	1	1	1	1
PILOERECTION	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0
APPEARANCE	3	1	1	1
VISUAL REACTION	2	2	2	2
TACTILE REACTION	2	1	2	2
AUDITORY REACTION	1	2	2	2
TAIL-PINCH REACTION	2	2	2	2
VISUAL PLACING RESPONSE	3	3	3	3
AIR RIGHTING RESPONSE	h	h	h	h
PUPIL RESPONSE TO LIGHT	1	1	1	1
FORELIMB GRIP TEST #1 (G)	160	275	575	315
FORELIMB GRIP TEST #2 (G)	205	300	365	355
HINDLIMB GRIP TEST #1 (G)	340	335	260	375
HINDLIMB GRIP TEST #2 (G)	755	440	235	515
LANDING FOOT SPLAY #1 (CM)	6.3	h	h	h
LANDING FOOT SPLAY #2 (CM)	7.2	h	h	h
BODY TEMPERATURE (°C)	37.8	38.5	38.0	37.7
BODY WEIGHT (G)	235	257	234	259

VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.

- Rat jumped onto side of the open field during the 2 minute observation period and was placed back into the open field.
- Head bobbing, intermittent, moderate; head weaving, intermittent, moderate; circling to the left.
- Head bobbing, intermittent, moderate; head weaving, intermittent, moderate; circling to the right and left.
- Retropulsion.
- Head bobbing, intermittent, moderate; head weaving, intermittent, moderate; circling to the right.
- Both fore and hindlimbs, splayed.
- Both hindlimbs, splayed.
- Testing was not performed due to condition of rat.

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

APPENDIX C1 (PAGE 1): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - MALE RATS - GROUPS I AND IV - PART A

THREE DAYS AFTER LAST DOSAGE:				
GROUP I	0 (VEHICLE, 0.9% SALINE) MG/KG/DAY			
RAT #	12407	12419	12422	12423
HOME CAGE BEHAVIOR	2	1	2	1
ALTERATIONS (HOME CAGE)	1	1	1	1
REACTION TO REMOVAL	1	1	2	1
REACTION TO HANDLING	1	1	2	1
REARS IN OPEN FIELD	0	1	0	4
DEFECATION IN OPEN FIELD	1	1	1	1
URINATION IN OPEN FIELD	2	2	2	1
LEVEL OF AROUSAL	3	3	3	3
ALTERATIONS (OPEN FIELD)	1	1	1	1
GAIT PATTERN	1	1	1	1
GAIT ABNORMALITY, SEVERITY	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1
LACRIMATION	1	1	1	1
SALIVATION	1	1	1	1
PILOERECTION	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0
APPEARANCE	1	1	2	1
VISUAL REACTION	2	2	2	2
TACTILE REACTION	2	2	2	2
AUDITORY REACTION	3	3	3	3
TAIL-PINCH REACTION	2	2	2	2
VISUAL PLACING RESPONSE	1	1	1	1
AIR RIGHTING RESPONSE	1	1	1	1
PUPIL RESPONSE TO LIGHT	1	1	1	1
FORELIMB GRIP TEST #1 (G)	430	545	705	375
FORELIMB GRIP TEST #2 (G)	325	810	565	250
HINDLIMB GRIP TEST #1 (G)	805	510	530	365
HINDLIMB GRIP TEST #2 (G)	780	585	525	355
LANDING FOOT SPLAY #1 (CM)	9.5	9.2	10.0	6.3
LANDING FOOT SPLAY #2 (CM)	9.8	8.3	9.6	7.1
BODY TEMPERATURE (°C)	35.0	36.6	37.1	37.3
BODY WEIGHT (G)	406	462	423	439
VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.				

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

APPENDIX C1 (PAGE 2): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - MALE RATS - GROUPS I AND IV - PART A

TARGETED TIME OF 60 TO 90 MINUTES POSTDOSAGE:				
GROUP IV	6.0 (CHLORPROMAZINE) MG/KG/DAY			
RAT #	12409	12410	12425	12426
HOME CAGE BEHAVIOR	2	2	2	1
ALTERATIONS (HOME CAGE)	1	1	1	1
REACTION TO REMOVAL	1	1	1	1
REACTION TO HANDLING	1	1	1	1
REARS IN OPEN FIELD	2	6	0	0
DEFECATION IN OPEN FIELD	1	1	1	1
URINATION IN OPEN FIELD	2	2	2	2
LEVEL OF AROUSAL	2	3	2	2
ALTERATIONS (OPEN FIELD)	6a	1	1	1
GAIT PATTERN	1	1	3b	1
GAIT ABNORMALITY, SEVERITY	1	1	2	1
PALPEBRAL CLOSURE	2c	1	2c	2c
PROMINENCE OF THE EYE	1	1	1	1
LACRIMATION	1	1	1	1
SALIVATION	1	1	1	1
PILOERECTION	0	0	0	0
ABNORMAL RESPIRATION	1d	0	0	0
APPEARANCE	1	1	1	1
VISUAL REACTION	1	2	2	1
TACTILE REACTION	1	2	2	1
AUDITORY REACTION	3	2	3	3
TAIL-PINCH REACTION	1	3	2	2
VISUAL PLACING RESPONSE	2	1	1	1
AIR RIGHTING RESPONSE	1	1	1	1
PUPIL RESPONSE TO LIGHT	1	1	1	1
FORELIMB GRIP TEST #1 (G)	860	860	840	510
FORELIMB GRIP TEST #2 (G)	610	495	1360	600
HINDLIMB GRIP TEST #1 (G)	975	900	1000	610
HINDLIMB GRIP TEST #2 (G)	1230	705	790	545
LANDING FOOT SPLAY #1 (CM)	9.6	7.6	13.1	12.7
LANDING FOOT SPLAY #2 (CM)	9.5	11.8	13.0	12.8
BODY TEMPERATURE (°C)	34.5	36.2	35.0	34.4
BODY WEIGHT (G)	419	474	426	435

VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.

- a. Low carriage.
- b. Both hindlimbs, splayed.
- c. Both eyes.
- d. Bradypnea.

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

APPENDIX C2 (PAGE 1): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - FEMALE RATS - GROUPS I AND IV - PART A

THREE DAYS AFTER LAST DOSAGE:				
GROUP I	0 (VEHICLE, 0.9% SALINE) MG/KG/DAY			
RAT #	12456	12465	12467	12468
HOME CAGE BEHAVIOR	1	2	2	1
ALTERATIONS (HOME CAGE)	1	1	1	1
REACTION TO REMOVAL	1	1	1	1
REACTION TO HANDLING	1	1	1	1
REARS IN OPEN FIELD	12	3	2	4
DEFECATION IN OPEN FIELD	1	1	1	1
URINATION IN OPEN FIELD	1	2	1	1
LEVEL OF AROUSAL	3	3	3	3
ALTERATIONS (OPEN FIELD)	1	1	1	1
GAIT PATTERN	1	1	1	1
GAIT ABNORMALITY, SEVERITY	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1
LACRIMATION	1	1	1	1
SALIVATION	1	1	1	1
PILOERECTION	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0
APPEARANCE	1	1	1	2
VISUAL REACTION	2	2	2	3
TACTILE REACTION	2	2	2	2
AUDITORY REACTION	3	3	3	3
TAIL-PINCH REACTION	2	2	2	1
VISUAL PLACING RESPONSE	1	1	1	1
AIR RIGHTING RESPONSE	1	1	1	2
PUPIL RESPONSE TO LIGHT	1	1	1	1
FORELIMB GRIP TEST #1 (G)	190	335	445	535
FORELIMB GRIP TEST #2 (G)	120	405	505	275
HINDLIMB GRIP TEST #1 (G)	915	660	275	330
HINDLIMB GRIP TEST #2 (G)	665	395	290	455
LANDING FOOT SPLAY #1 (CM)	5.2	6.3	4.8	7.6
LANDING FOOT SPLAY #2 (CM)	5.2	6.5	5.6	7.5
BODY TEMPERATURE (°C)	38.2	37.6	38.0	37.6
BODY WEIGHT (G)	236	257	253	276
VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.				

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

APPENDIX C2 (PAGE 2): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - FEMALE RATS - GROUPS I AND IV - PART A

TARGETED TIME OF 60 TO 90 MINUTES POSTDOSAGE:				
GROUP IV	6.0 (CHLORPROMAZINE) MG/KG/DAY			
RAT #	12451	12463	12464	12471
HOME CAGE BEHAVIOR	2	2	4	2
ALTERATIONS (HOME CAGE)	1	1	6a	1
REACTION TO REMOVAL	1	1	1	1
REACTION TO HANDLING	1	1	1	1
REARS IN OPEN FIELD	0	1	10	3
DEFECATION IN OPEN FIELD	1	1	1	1
URINATION IN OPEN FIELD	2	1	1	1
LEVEL OF AROUSAL	2	3	3	3
ALTERATIONS (OPEN FIELD)	1	1	1	1
GAIT PATTERN	3b	1	4c	1
GAIT ABNORMALITY, SEVERITY	2	1	2	1
PALPEBRAL CLOSURE	2d	1	2d	2d
PROMINENCE OF THE EYE	1	1	1	1
LACRIMATION	1	1	1	1
SALIVATION	1	1	1	1
PILOERECTION	0	0	0	0
ABNORMAL RESPIRATION	1e	0	0	0
APPEARANCE	1	1	1	1
VISUAL REACTION	1	2	2	1
TACTILE REACTION	2	2	2	2
AUDITORY REACTION	3	3	2	3
TAIL-PINCH REACTION	2	2	2	2
VISUAL PLACING RESPONSE	2	1	1	1
AIR RIGHTING RESPONSE	1	1	1	1
PUPIL RESPONSE TO LIGHT	1	1	1	1
FORELIMB GRIP TEST #1 (G)	415	410	650	1145
FORELIMB GRIP TEST #2 (G)	605	595	305	525
HINDLIMB GRIP TEST #1 (G)	980	220	815	750
HINDLIMB GRIP TEST #2 (G)	745	270	730	1015
LANDING FOOT SPLAY #1 (CM)	12.3	8.4	8.5	9.7
LANDING FOOT SPLAY #2 (CM)	11.5	8.5	8.5	9.6
BODY TEMPERATURE (°C)	36.5	37.4	37.1	36.4
BODY WEIGHT (G)	245	250	246	268

VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.

- a. Hunched posture.
- b. Both hindlimbs, splayed.
- c. Tip-toe walk, both hindlimbs.
- d. Both eyes.
- e. Tachypnea.

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

APPENDIX D1 (PAGE 1): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - MALE RATS - GROUPS II AND V - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE:				
GROUP II 0 (VEHICLE, CORN OIL) MG/KG/DAY				
RAT #	12413	12414	12420	12424
HOME CAGE BEHAVIOR	3	2	3	2
ALTERATIONS (HOME CAGE)	1	1	1	1
REACTION TO REMOVAL	1	1	1	1
REACTION TO HANDLING	1	1	1	1
REARS IN OPEN FIELD	10	1	0	5
DEFECATION IN OPEN FIELD	1	1	1	2
URINATION IN OPEN FIELD	2	2	2	2
LEVEL OF AROUSAL	3	3	3	3
ALTERATIONS (OPEN FIELD)	1	1	1	1
GAIT PATTERN	1	1	1	1
GAIT ABNORMALITY, SEVERITY	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1
LACRIMATION	1	1	1	1
SALIVATION	1	1	1	1
PILOERECTION	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0
APPEARANCE	1	1	1	1
VISUAL REACTION	2	2	2	2
TACTILE REACTION	2	2	2	2
AUDITORY REACTION	3	3	3	3
TAIL-PINCH REACTION	2	2	2	2
VISUAL PLACING RESPONSE	1	1	1	1
AIR RIGHTING RESPONSE	1	1	2	1
PUPIL RESPONSE TO LIGHT	1	1	1	1
FORELIMB GRIP TEST #1 (G)	365	755	690	485
FORELIMB GRIP TEST #2 (G)	520	695	765	255
HINDLIMB GRIP TEST #1 (G)	625	330	850	760
HINDLIMB GRIP TEST #2 (G)	345	355	740	875
LANDING FOOT SPLAY #1 (CM)	10.4	9.6	10.5	6.0
LANDING FOOT SPLAY #2 (CM)	9.6	10.0	9.4	4.7
BODY TEMPERATURE (°C)	38.1	37.9	38.1	38.1
BODY WEIGHT (G)	427	434	427	446
VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.				

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

APPENDIX D1 (PAGE 2): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - MALE RATS - GROUPS II AND V - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE:				
GROUP V				
4.0 (D-AMPHETAMINE) MG/KG/DAY				
RAT #	12403	12411	12415	12416
HOME CAGE BEHAVIOR	5	5	5	5
ALTERATIONS (HOME CAGE)	2a	2a	2a	2a
REACTION TO REMOVAL	2	2	1	1
REACTION TO HANDLING	1	2	1	1
REARS IN OPEN FIELD	9	5	8	4
DEFECATION IN OPEN FIELD	1	1	1	1
URINATION IN OPEN FIELD	2	2	2	2
LEVEL OF AROUSAL	3	3	3	3
ALTERATIONS (OPEN FIELD)	2a	2a, 6b	2a, 6b	2a, 6b
GAIT PATTERN	1	1	1	1
GAIT ABNORMALITY, SEVERITY	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1
LACRIMATION	1	1	1	1
SALIVATION	1	1	1	1
PILOERECTION	1	1	1	1
ABNORMAL RESPIRATION	0	1c	0	0
APPEARANCE	1	3	3	1
VISUAL REACTION	2	2	2	2
TACTILE REACTION	2	2	2	2
AUDITORY REACTION	2	3	3	3
TAIL-PINCH REACTION	2	2	2	2
VISUAL PLACING RESPONSE	1	1	1	1
AIR RIGHTING RESPONSE	1	1	2	1
PUPIL RESPONSE TO LIGHT	1	1	1	1
FORELIMB GRIP TEST #1 (G)	595	815	410	595
FORELIMB GRIP TEST #2 (G)	500	600	740	445
HINDLIMB GRIP TEST #1 (G)	490	350	330	1055
HINDLIMB GRIP TEST #2 (G)	610	545	450	615
LANDING FOOT SPLAY #1 (CM)	7.0	10.2	8.5	8.9
LANDING FOOT SPLAY #2 (CM)	6.8	9.7	8.7	7.3
BODY TEMPERATURE (°C)	38.8	38.2	37.9	38.7
BODY WEIGHT (G)	415	453	446	460

VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.

- a. Repetitive sniffing.
- b. Straub tail.
- c. Tachypnea.

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

APPENDIX D2 (PAGE 1): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - FEMALE RATS - GROUPS II AND V - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE:				
GROUP II 0 (VEHICLE, CORN OIL) MG/KG/DAY				
RAT #	12457	12460	12469	12478
HOME CAGE BEHAVIOR	2	3	2	2
ALTERATIONS (HOME CAGE)	1	1	1	1
REACTION TO REMOVAL	1	2	3	1
REACTION TO HANDLING	1	2	1	1
REARS IN OPEN FIELD	10	1	14	5
DEFECATION IN OPEN FIELD	1	1	1	1
URINATION IN OPEN FIELD	2	1	1	1
LEVEL OF AROUSAL	3	3	3	3
ALTERATIONS (OPEN FIELD)	1	1	1	1
GAIT PATTERN	1	1	1	1
GAIT ABNORMALITY, SEVERITY	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1
LACRIMATION	1	1	1	1
SALIVATION	1	1	1	1
PILOERECTION	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0
APPEARANCE	1	1a	1	1
VISUAL REACTION	2	2	2	2
TACTILE REACTION	2	2	2	2
AUDITORY REACTION	3	3	3	3
TAIL-PINCH REACTION	2	2	2	2
VISUAL PLACING RESPONSE	1	1	1	1
AIR RIGHTING RESPONSE	1	1	1	1
PUPIL RESPONSE TO LIGHT	1	1	1	1
FORELIMB GRIP TEST #1 (G)	375	1100	290	505
FORELIMB GRIP TEST #2 (G)	445	820	220	1340
HINDLIMB GRIP TEST #1 (G)	320	600	535	865
HINDLIMB GRIP TEST #2 (G)	445	340	615	685
LANDING FOOT SPLAY #1 (CM)	4.7	9.9	5.2	6.5
LANDING FOOT SPLAY #2 (CM)	3.7	9.9	5.2	5.3
BODY TEMPERATURE (°C)	38.3	37.9	39.0	37.7
BODY WEIGHT (G)	240	271	244	263
VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.				
a. Vocalization to touch.				

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

APPENDIX D2 (PAGE 2): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - FEMALE RATS - GROUPS II AND V - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE:				
GROUP V 4.0 (D-AMPHETAMINE) MG/KG/DAY				
RAT #	12452	12455	12475	12476
HOME CAGE BEHAVIOR	5	5	5	5
ALTERATIONS (HOME CAGE)	2a	2a	2a	2a
REACTION TO REMOVAL	2	1	1	1
REACTION TO HANDLING	1	1	1	2
REARS IN OPEN FIELD	6	10	5	9
DEFECATION IN OPEN FIELD	1	1	1	1
URINATION IN OPEN FIELD	1	1	1	2
LEVEL OF AROUSAL	3	3	3	3
ALTERATIONS (OPEN FIELD)	2a, 6b	2a	2a, 6b	2a, 6b
GAIT PATTERN	1	1	1	1
GAIT ABNORMALITY, SEVERITY	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1
LACRIMATION	1	1	1	1
SALIVATION	1	1	1	1
PILOERECTION	1	1	1	1
ABNORMAL RESPIRATION	0	0	0	0
APPEARANCE	1	1	1	1
VISUAL REACTION	2	2	2	2
TACTILE REACTION	2	2	2	2
AUDITORY REACTION	3	3	3	3
TAIL-PINCH REACTION	2	2	3	2
VISUAL PLACING RESPONSE	1	1	1	1
AIR RIGHTING RESPONSE	1	1	2	2
PUPIL RESPONSE TO LIGHT	1	1	1	1
FORELIMB GRIP TEST #1 (G)	1265	375	400	605
FORELIMB GRIP TEST #2 (G)	965	1150	630	540
HINDLIMB GRIP TEST #1 (G)	520	715	900	360
HINDLIMB GRIP TEST #2 (G)	355	660	700	350
LANDING FOOT SPLAY #1 (CM)	7.8	9.3	9.1	3.0
LANDING FOOT SPLAY #2 (CM)	6.9	9.5	8.7	2.8
BODY TEMPERATURE (°C)	38.1	38.2	38.3	38.5
BODY WEIGHT (G)	241	256	258	242

VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.

a. Repetitive sniffing.

b. Straub tail.

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

APPENDIX E1 (PAGE 1): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - MALE RATS - GROUPS II AND VI - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE:				
GROUP II 0 (VEHICLE, CORN OIL) MG/KG/DAY				
RAT #	12413	12414	12420	12424
HOME CAGE BEHAVIOR	3	2	3	2
ALTERATIONS (HOME CAGE)	1	1	1	1
REACTION TO REMOVAL	1	1	1	1
REACTION TO HANDLING	1	1	1	1
REARS IN OPEN FIELD	10	1	0	5
DEFECATION IN OPEN FIELD	1	1	1	2
URINATION IN OPEN FIELD	2	2	2	2
LEVEL OF AROUSAL	3	3	3	3
ALTERATIONS (OPEN FIELD)	1	1	1	1
GAIT PATTERN	1	1	1	1
GAIT ABNORMALITY, SEVERITY	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1
LACRIMATION	1	1	1	1
SALIVATION	1	1	1	1
PILOERECTION	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0
APPEARANCE	1	1	1	1
VISUAL REACTION	2	2	2	2
TACTILE REACTION	2	2	2	2
AUDITORY REACTION	3	3	3	3
TAIL-PINCH REACTION	2	2	2	2
VISUAL PLACING RESPONSE	1	1	1	1
AIR RIGHTING RESPONSE	1	1	2	1
PUPIL RESPONSE TO LIGHT	1	1	1	1
FORELIMB GRIP TEST #1 (G)	365	755	690	485
FORELIMB GRIP TEST #2 (G)	520	695	765	255
HINDLIMB GRIP TEST #1 (G)	625	330	850	760
HINDLIMB GRIP TEST #2 (G)	345	355	740	875
LANDING FOOT SPLAY #1 (CM)	10.4	9.6	10.5	6.0
LANDING FOOT SPLAY #2 (CM)	9.6	10.0	9.4	4.7
BODY TEMPERATURE (°C)	38.1	37.9	38.1	38.1
BODY WEIGHT (G)	427	434	427	446
VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.				

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATs

APPENDIX E1 (PAGE 2): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - MALE RATS - GROUPS II AND VI - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE:				
GROUP VI				
100 (CARBARYL) MG/KG/DAY				
RAT #	12405	12408	12412	12428
HOME CAGE BEHAVIOR	4,5	4,5	4,5	5
ALTERATIONS (HOME CAGE)	5a,6b	5a,6b	5a,6c	5a
REACTION TO REMOVAL	1	1	2	1
REACTION TO HANDLING	1	1	1	1
REARS IN OPEN FIELD	0	0	0	0
DEFECATION IN OPEN FIELD	1	2	1	1
URINATION IN OPEN FIELD	2	2	2	2
LEVEL OF AROUSAL	2	2	2	3
ALTERATIONS (OPEN FIELD)	5a,6d	4e,5f,6g	5a,6b	5a,6h
GAIT PATTERN	2,3i	2	2,3i	2
GAIT ABNORMALITY, SEVERITY	2	2	2	2
PALPEBRAL CLOSURE	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1
LACRIMATION	1	1	2j	1
SALIVATION	3	2	1	1
PILOERECTION	0	0	0	0
ABNORMAL RESPIRATION	1k	1L	1L	1L
APPEARANCE	1m	1n	1o	1p
VISUAL REACTION	1	1	1	1
TACTILE REACTION	2	1	2	2
AUDITORY REACTION	2	2	3	2
TAIL-PINCH REACTION	1	2	2	1
VISUAL PLACING RESPONSE	1	2	2	1
AIR RIGHTING RESPONSE	2	1	2	3
PUPIL RESPONSE TO LIGHT	1	1	1q	1
FORELIMB GRIP TEST #1 (G)	595	570	470	885
FORELIMB GRIP TEST #2 (G)	510	525	750	610
HINDLIMB GRIP TEST #1 (G)	760	400	530	750
HINDLIMB GRIP TEST #2 (G)	755	445	625	905
LANDING FOOT SPLAY #1 (CM)	10.3	8.7	7.3	10.4
LANDING FOOT SPLAY #2 (CM)	8.8	10.9	7.4	10.1
BODY TEMPERATURE (°C)	34.3	33.5	35.0	33.6
BODY WEIGHT (G)	417	459	462	451

VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.

- | | |
|--|---|
| a. Fasciculations, whole body. | m. Gasping; cold to touch, whole body. |
| b. Prostrate. | n. Cold to touch, whole body; chromorhinorrhea. |
| c. Low carriage. | o. Gasping; rales; excessive salivation, slight; cold to touch, whole body. |
| d. Head tilt to the right; low carriage. | p. Cold to touch, whole body. |
| e. Repetitive movements of the mouth. | q. Miosis, both eyes. |
| f. Fasciculations, whole body; head spasm, intermittent, moderate. | |
| g. Head tilt to the left; low carriage. | |
| h. Hunched posture. | |
| i. Both hindlimbs, splayed. | |
| j. Right eye. | |
| k. Bradypnea; rales. | |
| L. Bradypnea. | |

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

APPENDIX E2 (PAGE 1): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - FEMALE RATS - GROUPS II AND VI - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE:				
GROUP II				
0 (VEHICLE, CORN OIL) MG/KG/DAY				
RAT #	12457	12460	12469	12478
HOME CAGE BEHAVIOR	2	3	2	2
ALTERATIONS (HOME CAGE)	1	1	1	1
REACTION TO REMOVAL	1	2	3	1
REACTION TO HANDLING	1	2	1	1
REARS IN OPEN FIELD	10	1	14	5
DEFECATION IN OPEN FIELD	1	1	1	1
URINATION IN OPEN FIELD	2	1	1	1
LEVEL OF AROUSAL	3	3	3	3
ALTERATIONS (OPEN FIELD)	1	1	1	1
GAIT PATTERN	1	1	1	1
GAIT ABNORMALITY, SEVERITY	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1
LACRIMATION	1	1	1	1
SALIVATION	1	1	1	1
PILOERECTION	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0
APPEARANCE	1	1a	1	1
VISUAL REACTION	2	2	2	2
TACTILE REACTION	2	2	2	2
AUDITORY REACTION	3	3	3	3
TAIL-PINCH REACTION	2	2	2	2
VISUAL PLACING RESPONSE	1	1	1	1
AIR RIGHTING RESPONSE	1	1	1	1
PUPIL RESPONSE TO LIGHT	1	1	1	1
FORELIMB GRIP TEST #1 (G)	375	1100	290	505
FORELIMB GRIP TEST #2 (G)	445	820	220	1340
HINDLIMB GRIP TEST #1 (G)	320	600	535	865
HINDLIMB GRIP TEST #2 (G)	445	340	615	685
LANDING FOOT SPLAY #1 (CM)	4.7	9.9	5.2	6.5
LANDING FOOT SPLAY #2 (CM)	3.7	9.9	5.2	5.3
BODY TEMPERATURE (°C)	38.3	37.9	39.0	37.7
BODY WEIGHT (G)	240	271	244	263

VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.

a. Vocalization to touch.

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

APPENDIX E2 (PAGE 2): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - FEMALE RATS - GROUPS II AND VI - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE:				
GROUP VI				
100 (CARBARYL) MG/KG/DAY				
RAT #	12453	12459	12474	12477
HOME CAGE BEHAVIOR	4,5	4,5	4,5	4,5
ALTERATIONS (HOME CAGE)	5a,6b	5a,6b	5a,6b	5a,6b
REACTION TO REMOVAL	1	1	1	1
REACTION TO HANDLING	1	1	1	1
REARS IN OPEN FIELD	0	0	0	1
DEFECATION IN OPEN FIELD	1	1	1	1
URINATION IN OPEN FIELD	2	2	1	2
LEVEL OF AROUSAL	3	2	2	3
ALTERATIONS (OPEN FIELD)	5a,6c	5a,6c	5d,6e	5a,6f
GAIT PATTERN	2	2,3g	3g	2
GAIT ABNORMALITY, SEVERITY	2	3	3	2
PALPEBRAL CLOSURE	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1
LACRIMATION	2h	3i	1	2i
SALIVATION	3	3	3	1
PILOERECTION	0	0	0	0
ABNORMAL RESPIRATION	1j	1j	1j	1j
APPEARANCE	3k	1L	1k	3k
VISUAL REACTION	1	1	2	2
TACTILE REACTION	2	1	1	2
AUDITORY REACTION	3	2	2	3
TAIL-PINCH REACTION	2	1	1	2
VISUAL PLACING RESPONSE	2	1	2	1
AIR RIGHTING RESPONSE	2	1	2	1
PUPIL RESPONSE TO LIGHT	1	1	1	1
FORELIMB GRIP TEST #1 (G)	560	230	350	800
FORELIMB GRIP TEST #2 (G)	450	225	205	695
HINDLIMB GRIP TEST #1 (G)	405	665	450	465
HINDLIMB GRIP TEST #2 (G)	505	550	540	630
LANDING FOOT SPLAY #1 (CM)	6.1	8.9	9.2	8.5
LANDING FOOT SPLAY #2 (CM)	5.6	8.8	9.2	9.7
BODY TEMPERATURE (°C)	32.9	32.5	33.5	33.6
BODY WEIGHT (G)	228	240	256	274

VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.

- a. Fasciculations, whole body.
- b. Prostrate.
- c. Low carriage; hunched posture.
- d. Fasciculations, whole body; head spasm, intermittent, moderate.
- e. Hunched posture, prostrate.
- f. Hunched posture.
- g. Both hindlimbs, splayed.
- h. Left eye.
- i. Both eyes.
- j. Bradypnea.
- k. Cold to touch, whole body.
- L. Gasping; cold to touch, whole body.

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

APPENDIX F1 (PAGE 1): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - MALE RATS - GROUPS II AND VII - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE:				
GROUP II 0 (VEHICLE, CORN OIL) MG/KG/DAY				
RAT #	12413	12414	12420	12424
HOME CAGE BEHAVIOR	3	2	3	2
ALTERATIONS (HOME CAGE)	1	1	1	1
REACTION TO REMOVAL	1	1	1	1
REACTION TO HANDLING	1	1	1	1
REARS IN OPEN FIELD	10	1	0	5
DEFECATION IN OPEN FIELD	1	1	1	2
URINATION IN OPEN FIELD	2	2	2	2
LEVEL OF AROUSAL	3	3	3	3
ALTERATIONS (OPEN FIELD)	1	1	1	1
GAIT PATTERN	1	1	1	1
GAIT ABNORMALITY, SEVERITY	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1
LACRIMATION	1	1	1	1
SALIVATION	1	1	1	1
PILOERECTION	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0
APPEARANCE	1	1	1	1
VISUAL REACTION	2	2	2	2
TACTILE REACTION	2	2	2	2
AUDITORY REACTION	3	3	3	3
TAIL-PINCH REACTION	2	2	2	2
VISUAL PLACING RESPONSE	1	1	1	1
AIR RIGHTING RESPONSE	1	1	2	1
PUPIL RESPONSE TO LIGHT	1	1	1	1
FORELIMB GRIP TEST #1 (G)	365	755	690	485
FORELIMB GRIP TEST #2 (G)	520	695	765	255
HINDLIMB GRIP TEST #1 (G)	625	330	850	760
HINDLIMB GRIP TEST #2 (G)	345	355	740	875
LANDING FOOT SPLAY #1 (CM)	10.4	9.6	10.5	6.0
LANDING FOOT SPLAY #2 (CM)	9.6	10.0	9.4	4.7
BODY TEMPERATURE (°C)	38.1	37.9	38.1	38.1
BODY WEIGHT (G)	427	434	427	446
VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.				

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

APPENDIX F1 (PAGE 2): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - MALE RATS - GROUPS II AND VII - PART A

TARGETED TIME OF 6 HOURS POSTDOSAGE:				
GROUP VII		75 (DDT) MG/KG/DAY		
RAT #	12402	12417	12418	12427a
HOME CAGE BEHAVIOR	5	5	5	
ALTERATIONS (HOME CAGE)	5b	5b	5b	
REACTION TO REMOVAL	1	1	2	
REACTION TO HANDLING	1	1	2	
REARS IN OPEN FIELD	3	1	0	
DEFECATION IN OPEN FIELD	1	1	2	
URINATION IN OPEN FIELD	2	1	2	
LEVEL OF AROUSAL	3	3	3	
ALTERATIONS (OPEN FIELD)	5c	5b	3d, 5b	
GAIT PATTERN	1	1	1	
GAIT ABNORMALITY, SEVERITY	1	1	1	
PALPEBRAL CLOSURE	1	1	1	
PROMINENCE OF THE EYE	1	1	1	
LACRIMATION	1	1	1	
SALIVATION	1	1	1	
PILOERECTION	0	0	0	
ABNORMAL RESPIRATION	0	0	0	
APPEARANCE	1	1	1e	
VISUAL REACTION	2	1	2	
TACTILE REACTION	3	2	2	
AUDITORY REACTION	3	3	3	
TAIL-PINCH REACTION	2	1	2	
VISUAL PLACING RESPONSE	1	1	1	
AIR RIGHTING RESPONSE	1	1	1	
PUPIL RESPONSE TO LIGHT	1	1	1	
FORELIMB GRIP TEST #1 (G)	635	510	365	
FORELIMB GRIP TEST #2 (G)	345	230	395	
HINDLIMB GRIP TEST #1 (G)	515	195	175	
HINDLIMB GRIP TEST #2 (G)	585	175	270	
LANDING FOOT SPLAY #1 (CM)	6.2	6.1	10.7	
LANDING FOOT SPLAY #2 (CM)	6.1	5.8	7.3	
BODY TEMPERATURE (°C)	39.5	38.4	38.9	
BODY WEIGHT (G)	413	462	444	

VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.

- Rat 12427 was sacrificed on day 1 of study due to adverse clinical observations.
- Tremors, whole body, continuous, slight; twitches, whole body, intermittent, moderate.
- Tremors, whole body, continuous, slight.
- Spontaneous vocalization.
- Vocalization to touch.

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

APPENDIX F2 (PAGE 1): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - FEMALE RATS - GROUPS II AND VII - PART A

TARGETED TIME OF 30 TO 60 MINUTES POSTDOSAGE:				
GROUP II	0 (VEHICLE, CORN OIL) MG/KG/DAY			
RAT #	12457	12460	12469	12478
HOME CAGE BEHAVIOR	2	3	2	2
ALTERATIONS (HOME CAGE)	1	1	1	1
REACTION TO REMOVAL	1	2	3	1
REACTION TO HANDLING	1	2	1	1
REARS IN OPEN FIELD	10	1	14	5
DEFECATION IN OPEN FIELD	1	1	1	1
URINATION IN OPEN FIELD	2	1	1	1
LEVEL OF AROUSAL	3	3	3	3
ALTERATIONS (OPEN FIELD)	1	1	1	1
GAIT PATTERN	1	1	1	1
GAIT ABNORMALITY, SEVERITY	1	1	1	1
PALPEBRAL CLOSURE	1	1	1	1
PROMINENCE OF THE EYE	1	1	1	1
LACRIMATION	1	1	1	1
SALIVATION	1	1	1	1
PILOERECTION	0	0	0	0
ABNORMAL RESPIRATION	0	0	0	0
APPEARANCE	1	1a	1	1
VISUAL REACTION	2	2	2	2
TACTILE REACTION	2	2	2	2
AUDITORY REACTION	3	3	3	3
TAIL-PINCH REACTION	2	2	2	2
VISUAL PLACING RESPONSE	1	1	1	1
AIR RIGHTING RESPONSE	1	1	1	1
PUPIL RESPONSE TO LIGHT	1	1	1	1
FORELIMB GRIP TEST #1 (G)	375	1100	290	505
FORELIMB GRIP TEST #2 (G)	445	820	220	1340
HINDLIMB GRIP TEST #1 (G)	320	600	535	865
HINDLIMB GRIP TEST #2 (G)	445	340	615	685
LANDING FOOT SPLAY #1 (CM)	4.7	9.9	5.2	6.5
LANDING FOOT SPLAY #2 (CM)	3.7	9.9	5.2	5.3
BODY TEMPERATURE (°C)	38.3	37.9	39.0	37.7
BODY WEIGHT (G)	240	271	244	263
VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.				
a. Vocalization to touch.				

PROTOCOL 012-206: NEUROTOXICITY EVALUATION OF POSITIVE CONTROL SUBSTANCES IN Cr1:(CD)SD RATS

APPENDIX F2 (PAGE 2): FUNCTIONAL OBSERVATIONAL BATTERY - INDIVIDUAL DATA - FEMALE RATS - GROUPS II AND VII - PART A

TARGETED TIME OF 6 HOURS POSTDOSAGE:				
GROUP VII		75 (DDT) MG/KG/DAY		
RAT #	12461a	12462	12470	12473
HOME CAGE BEHAVIOR		3	5	5
ALTERATIONS (HOME CAGE)		1	5b	5c
REACTION TO REMOVAL		1	2	1
REACTION TO HANDLING		1	1	1
REARS IN OPEN FIELD		6	2	1
DEFECATION IN OPEN FIELD		1	1	1
URINATION IN OPEN FIELD		1	1	1
LEVEL OF AROUSAL		3	3	3
ALTERATIONS (OPEN FIELD)		1	5c	5d
GAIT PATTERN		1	1	1
GAIT ABNORMALITY, SEVERITY		1	1	1
PALPEBRAL CLOSURE		1	1	1
PROMINENCE OF THE EYE		1	1	1
LACRIMATION		1	1	1
SALIVATION		1	1	1
PILOERECTION		0	0	0
ABNORMAL RESPIRATION		0	0	0
APPEARANCE		1	1	3
VISUAL REACTION		2	2	2
TACTILE REACTION		2	2	2
AUDITORY REACTION		3	3	3
TAIL-PINCH REACTION		2	2	2
VISUAL PLACING RESPONSE		1	1	1
AIR RIGHTING RESPONSE		1	1	1
PUPIL RESPONSE TO LIGHT		1	1	1
FORELIMB GRIP TEST #1 (G)		245	305	395
FORELIMB GRIP TEST #2 (G)		710	520	305
HINDLIMB GRIP TEST #1 (G)		305	580	240
HINDLIMB GRIP TEST #2 (G)		250	675	255
LANDING FOOT SPLAY #1 (CM)		6.8	5.3	5.6
LANDING FOOT SPLAY #2 (CM)		5.7	5.5	8.8
BODY TEMPERATURE (°C)		38.2	39.0	38.8
BODY WEIGHT (G)		263	242	270

VALUES ARE THE QUANTITY, CATEGORY NUMBER, QUANTAL RESPONSE OR SCORE RECORDED FOR EACH ITEM IN THE BATTERY.

- Rat 12461 was sacrificed on day 1 of study due to adverse clinical observations.
- Tremors, whole body, continuous, moderate; twitches, head, intermittent, moderate.
- Tremors, whole body, continuous, moderate; twitches, whole body, intermittent, moderate.
- Tremors, whole body, continuous, moderate.