

# **Reproductive and Behavioral Evaluations in Crl:CD-1<sup>®</sup> (ICR) Mice**

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# CLINICAL LABORATORY PARAMETERS FOR CRL:CD® (SD) RATS

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## **INTRODUCTION AND PURPOSE**

Guidelines for assessing developmental toxicity have been developed by the Expert Working Group (Safety) of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) under consultation with regulatory parties, in accordance with the ICH process. These guidelines suggest exposure of both the mature adult and juvenile animals at all stages of development from conception through sexual maturity and into the following generation. The rationale for this testing regimen is to allow for the detection of immediate and latent drug effects across development and one generation. The guidelines state that these toxicity tests are to be conducted in a mammalian species. Typically the rat is used as there are ample historical control data available for the rats and also most testing facilities are familiar with the rat model. However, by mere virtue of a rat's size, a rat study requires more test article than a comparable study in the mouse. As test article availability can be a limiting factor in the timing of a study and study delays can stall the drug development process, it may be useful to conduct developmental toxicity studies in the mouse. Additionally, for some drug classes, the mouse is a more appropriate model.

To this end, Charles River Laboratories has started to compile historical control data on mouse developmental and reproductive toxicity parameters. As always, our purpose in preparing this compilation is to offer the study director or reviewing toxicologist a range of control values of various developmental, behavioral and functional parameters measured in standard developmental toxicity studies. It is our hope that these data will provide the foundation for a more detailed and encompassing future data compilation. The strength and usefulness of this type of publication depend on the number of contributors, their comments and their suggestions for improvement. Please contact Mary Giknis at [mlagiknis@verizon.net](mailto:mlagiknis@verizon.net) with your helpful suggestions and for instructions on how you can contribute data to a future document.

## **COMMON STUDY PARAMETERS**

The data presented here are from studies conducted between 1997 and 2006. All studies used Crl:CD-1®(ICR) mice from four different Charles River production sites (Portage, MI; Kingston, NY; Raleigh, NC; or St. Constant, Quebec, Canada). Mice in these studies were from the control groups of studies where the test materials were administered using the dietary, gavage, intramuscular injection, subcutaneous injection, or intravenous route.

Mice in these studies were housed appropriately as outlined in the *Guide for Care and Use of Laboratory Animals*; National Academy Press, 1996 and had free access to water. All animals were fed a diet of Purina Mills Lab Chow. The animal rooms were generally maintained at an average temperature of 72 +/- 5° F. with an average relative humidity of 30-70%. A 12hr/12hr light/dark cycle was employed in all studies. Minor variations in environmental conditions were noted but were not considered by those performing the studies to have had any effect on the quality and integrity of the studies.

## **DATA PRESENTED**

### **ESTROUS CYCLING AND COHABITATION DATA**

The estrous cycling data was collected from 609 mice from a total of 27 studies. Vaginal lavage was performed using saline and microscopic slides were prepared for estrus evaluation. The stage of estrus was determined by a trained technician based on the number and types of cells present in the washing sample. The estrous cycling data are presented in Table 1.

### **SPERM MOTILITY AND SPERM COUNT DATA**

The data presented here are from a total of 294 mice from 12 studies and were collected using a Hamilton Thorne Computer Assisted Semen Analyzer, Hamilton Thorne IVOS. The necropsy and sample preparations were done in accordance with the Standard Operating Procedures of the testing facility. During the sample preparation extreme care was used to keep all materials that came in contact with the sperm at a constant temperature of 36 +/- 1°C. In addition, the pH of the media used in sample preparation was maintained at 7.2 +/- 0.1 by frequent checking and adjustment with either 1N HCL or 1N NaOH to maintain the target pH. These data were derived from separate motility and concentration analyses of sperm cells from the left cauda epididymis. The sperm evaluation data are presented in Table 2.

### **NATURAL DELIVERY DATA**

The natural delivery and pup survival data were compiled from a total of 177 litters from nine studies and represent observations from delivery through Postnatal Day 22. For these data, the day on which a vaginal plug was found was designated as Gestational Day 0 and the day of birth was designated as Postnatal Day 0. These data are presented in Table 3.

### **PASSIVE AVOIDANCE TEST**

The Passive Avoidance Test data evaluates learning, short-term memory retention, long-term memory retention and hyperactivity. One male and one female were tested per litter. The apparatus used in these tests was a two-compartment stainless-steel chamber with hinged, clear Plexiglas® lids and a steel sliding door separating the compartments. One compartment was equipped with a bright light opposite the sliding door while the other compartment remained dark. The testing room remained dark during the testing session to enhance the effect of the chamber light. At the beginning of each trial, the mouse was placed in the compartment with the light, the sliding door opened and the chamber light turned on. The mouse was allowed to explore the apparatus until it entered the compartment without the light. Immediately after the mouse entered the dark compartment, the sliding door was closed, and a brief pulse of electric current (1mA) was delivered to the grid floor. The mouse was then removed and placed in a holding cage for 30 seconds, and the trial was repeated. Additional trials continued until the mouse remained in the compartment with the light for 60 seconds on two consecutive trials (the criterion for learning), or until 15 trials had been completed. The latency to enter the compartment without light or a maximum of 60 seconds was recorded for each trial. Each mouse was tested twice under these conditions with a one-week interval separating the tests. Passive Avoidance data obtained from four studies are presented for both sexes as individual study data in Table 4 and summarized in Table 5.

## **FUNCTIONAL OBSERVATION BATTERY**

In the Functional Observation Battery (FOB) testing begins with an assessment of behavior in the home cage, proceeding to observations of the mouse in an “open field” and ending with tests that require more interaction with the animal. The FOB is conducted by an observer unaware of the group assignment of each mouse and involves the assessment of the following parameters:

1. Lacrimation, salivation, palpebral closure, prominence of the eye, pupillary reaction to light, piloerection, respiration, and urination and defecation, and body temperature (autonomic functions).
2. Sensorimotor responses to visual, acoustic, tactile and painful stimuli (reactivity and sensitivity).
3. Reactions to handling and activity (including rearing) in the open field (excitability).
4. Gait pattern in the open field, severity of gait abnormalities, air righting reaction, visual placing response and landing foot splay (gait and sensorimotor coordination).
5. Forelimb and hindlimb grip tests.
6. Body weight.

Additional detailed clinical observations to supplement and/or complement the specific items in the FOB, included but were not limited to, identification of clinical signs related to general appearance (e.g., skin, fur, and mucous membranes (the presence or absence of discharge)), and further descriptions of alterations in body position and posture (e.g., hunchback posture), and behavior (e.g., tremors, convulsions, muscular contractions, stereotypical or repetitive behaviors, abnormal vocalization, and aggression).

Due to the limited number of studies included in these evaluations, the data are presented for each study and each timepoint evaluated. Summary data is then presented by grouping observations from all studies and timepoints. The individual study data are presented by sex in Tables 6 and 7, and are summarized in Tables 8 and 9.

## **MOTOR ACTIVITY ASSESSMENT**

Motor activity is monitored at specific time points during each study by an automated apparatus capable of detecting both increases and decreases in activity. In the 12 evaluations presented in this document, motor activity was monitored in one male and one female (whenever possible) per litter using a passive infrared sensor mounted outside a stainless-steel cage (40.6 X 25.4 X 17.8 cm) with Plexiglas® flooring. Each test session was 90 minutes in duration with the number of movements and the time spent in movement tabulated for each of eighteen five-minute intervals. The number of movements data are presented for both sexes by study and by timepoint in Tables 10 and 11, and summarized and presented by sex in Tables 12 and 13. The time in movement data, recorded in seconds, are presented by individual study and timepoint s in Tables 14 and 15 for males and females respectively and summarized by sex in Tables 16 and 17.

## **CALCULATIONS**

In general, simple descriptive statistics were employed. These included the mean, average, standard deviation and minimum and maximum value observed and standard calculations of percent.

## **ABBREVIATIONS**

Consec. = Consecutive

FOB = Functional Observational Battery

PD = Postnatal Day

M = Male

F = Female

Min. = Minimum

Max. = Maximum

## **ACKNOWLEDGEMENTS**

Our special thanks to the technicians who collected these data; the management personnel who compiled the data; and Joseph Frank, John F. Barnett, Jr., John A. Foss and Alan Hoberman for their data interpretations. Without the generous contributions of these individuals, this publication would not have been possible.

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**Table 1: Summary of Estrous Cycling Historical Control Data in Crl:CD1(ICR) Mice  
609 Total Mice**

		<u>#Studies Included</u>	<u>Average</u>	<u>Minimum</u>	<u>Maximum</u>
<b>Estrous Cycling Observations</b>					
Mice Evaluated/Study	N	24	25.4	10	50
<b>Predosage Estrous Cycling</b>					
Estrous Stages/14 Days	Mean	22	2.7	2.2	3.0
Mice with 6 or more Consec. Days of Diestrus	N	22	2.1	0	7
Mice with 6 or more Consec. Days of Estrus	N	22	0.8	0	3
<b>Precohabitation Estrous Cycling</b>					
Estrous Stages/14 Days	Mean	22	2.8	2.1	3.5
Mice with 6 or more Consec. Days of Diestrus	N	23	2.0	0	6
Mice with 6 or more Consec. Days of Estrus	N	23	0.9	0	5
<b>Cohabitation</b>					
Mice in Cohabitation	N	27	24.5	8	50
Days in Cohabitation	Mean	27	2.6	1.9	4.2
Mice that Mated	N	27	24.4	8	50
	%	27	99.5	95.8	100.0
Mice with Confirmed Mating Dates	N	27	23.5	8	49
<b>Mice Mated by First Male</b>					
Days 1-7	N	26	22.8	8	48
	%	26	97.3	83.3	100.0
Days 8-14	N	19	0.7	0	3
	%	19	3.0	0.0	13.0
<b>Mice Mated by Second Male</b>					
Days 8-14	N	4	0.3	0	1
	%	4	1.1	0.0	4.2
Days 15-21	N	6	0.0	0	0
	%	6	0.0	0.0	0.0
Fertility Index	%	27	94.0	80.0	100.0
Mice Pregnant/Mice in Cohabitation	%	27	93.6	80.0	100.0

**Table 2: Summary of Hamilton-Thorne Sperm Evaluation Historical Control Data in Crl:CD1(ICR) Mice (mLs per gram testes)**

**294 Total Mice**

		<b><u>#Studies Included</u></b>	<b><u>Average</u></b>	<b><u>Minimum</u></b>	<b><u>Maximum</u></b>
Number Mice Included in Analysis/Study	N	12	24.3	20	25
<b>Sperm Motility</b>					
Number Motile	Mean	12	425.4	348.2	521.7
Motile Percent	Mean	12	90.9	87.8	93.8
Static Count (Nonmotile)	Mean	12	38.3	23.2	49.3
Total Count	Mean	12	463.7	375.4	563.2
<b>Sperm Count:</b>					
Sperm Count	Mean	11	76.0	55.6	103.1
Density	Mean	12	2098.03	1510.10	2858.84



**Table 3: Summary of Natural Delivery Historical Control Data in Crl:CD1(ICR) Mice  
177 Total Litters**

		<b>#Studies Included</b>	<b>Average</b>	<b>Minimum</b>	<b>Maximum</b>
<b>Mice Assigned to Natural Delivery/Study</b>	N	9	22.3	4	30
<b>Pregnant Mice/Study</b>	N	9	19.9	4	27
	%	8	90.9	83.3	100.0
<b>Delivered Litters/Study</b>	N	9	19.7	4	27
	%	8	98.9	95.4	100.0
<b>Duration of Gestation in Days/Study</b>	Mean	9	19.6	19.1	19.9
<b>Litters with Stillborn Pups/Study</b>	N	9	0.7	0	2
	%	9	3.1	0.0	7.4
<b>Litters with No Liveborn Pups/study</b>	N	9	0.1	0	1
	%	4	1.0	0.0	3.8
<b>Implantation Sites/ Delivered Litter</b>	Mean	7	12.6	11.9	13.6
<b>Gestation Index</b>	%	9	98.6	95.4	100.0
<b>Litters with All Pups Dying Days 1-4 Postpartum</b>	N	9	0.1	0	1
	%	6	0.0	0.0	0.0
<b>Litters with All Pups Dying Days 5-21 Postpartum</b>	N	8	0.1	0	1
	%	7	0.6	0.0	4.5
<b>Litters with All Pups Dying Days 5-22 Postpartum</b>	N	1	0.0	0	0
	%	1	0.0	0.0	0.0
<b>Pups Delivered/Litter</b>	Mean	9	11.8	11.3	12.4
<b>Liveborn Pups/Litter</b>	Mean	9	11.7	11.2	12.4
	%	9	99.3	97.0	100.0
<b>Stillborn Pups/Litter</b>	Mean	9	0.1	0.0	0.3
	%	9	0.5	0.0	2.3
<b>Pups with Unknown Vital Status/Litter</b>	N	7	0.7	0	2
<b>Pups Found Dead or Presumed Cannibalized/Litter</b>					
Day 1	N	9	1.2	0	7
	%	9	0.5	0.0	2.7
Days 2-4	N	9	2.0	0	4
	%	9	0.8	0.0	1.8
Days 5-7	N	9	2.2	0	5

**Table 3: Summary of Natural Delivery Historical Control Data in Crl:CD1(ICR) Mice**

		<b>#Studies Included</b>	<b>Average</b>	<b>Minimum</b>	<b>Maximum</b>
	%	9	1.0	0.0	2.3
Days 8-14	N	8	1.0	0	3
	%	8	0.4	0.0	1.0
Days 5-21	N	8	2.6	0	10
	%	8	1.0	0.0	3.7
Days 21-22	N	1	0.0	0	0
	%	1	0.0	0.0	0.0
<b>Viability Index (Day 4)</b>	%	8	98.8	96.1	100.0
<b>Viability Index (Day 7)</b>	%	1	98.3	98.3	98.3
<b>Lactation Index</b>	%	9	97.4	93.9	100.0
<b>Number of Surviving Pups/Litter</b>					
Day 1	Mean	9	11.7	11.2	12.4
Day 4	Mean	9	11.6	11.0	12.3
Day 7	Mean	9	11.5	10.8	12.2
Day 14	Mean	8	11.4	10.8	12.1
Day 21	Mean	8	11.3	10.6	12.0
Day 22	Mean	1	11.0	11.0	11.0
<b>Percent Male Pups Per Number of Pups Sexed</b>					
Day 1	Mean	9	51.4	43.9	55.4
Day 4	Mean	9	51.7	43.1	55.6
Day 7	Mean	9	51.6	42.7	55.3
Day 14	Mean	8	51.3	42.7	55.5
Day 21	Mean	8	51.6	42.8	57.0
Day 22	Mean	1	53.2	53.2	53.2
<b>Pup Weight/Litter (Grams)</b>					
Day 1	Mean	7	1.6	1.5	1.6
Day 4	Mean	8	2.5	2.3	2.7
Day 7	Mean	9	3.7	3.3	4.3
Day 14	Mean	8	6.3	5.8	6.8
Day 21	Mean	8	9.1	7.9	10.3
Day 22	Mean	1	11.1	11.1	11.1

**Table 4: Individual Study Passive Avoidance Historical Control Data Crl:CD1(ICR) Mice**

<b>STUDY CODE:</b>		<b>A</b>	<b>B</b>	<b>C</b>	<b>D</b>
<b>Passive Avoidance Learning</b>					
<u>Male Mice: Day 1</u>	N	20	21	19	21
Trials to Criterion	MEAN	4.6	3.6	4.3	3.8
	S.D.	1.8	1.1	1.3	0.9
Latency Trial 1	MEAN	6.2	14.5	6.3	15.4
	S.D.	4.3	14.1	3.8	14.7
Latency Trial 2	MEAN	36.6	48.7	43.3	46.4
	S.D.	23.9	18.5	19.8	17.4
Failed to Learn	N	0	0	0	
	%	0.0	0.0	0.0	
<b>Passive Avoidance Retention</b>					
<u>Male Mice: Day 2</u>	N	19	19	19	21
Trials to Criterion	MEAN	2.7	2.9	2.3	2.3
	S.D.	0.6	0.9	0.6	0.8
Latency Trial 1	MEAN	36.8	41.4	58.9	52.1
	S.D.	23.6	25.4	4.6	19.9
<b>Passive Avoidance Learning</b>					
<u>Female Mice: Day 1</u>	N	20	21	18	22
Trials to Criterion	MEAN	4.0	4.0	3.9	4.4
	S.D.	1.1	0.9	0.9	1.3
Latency Trial 1	MEAN	7.2	9.6	5.9	10.4
	S.D.	4.7	13.5	3.4	7.2
Latency Trial 2	MEAN	41.9	41.7	38.6	44.8
	S.D.	22.2	24.3	21.6	19.4
Failed to Learn	N	0	0	0	
	%	0.0	0.0	0.0	
<b>Passive Avoidance Retention</b>					
<u>Female Mice: Day 2</u>	N	20	20	18	22
Trials to Criterion	MEAN	2.7	2.9	2.3	2.4
	S.D.	1.0	0.8	0.7	0.7
Latency Trial 1	MEAN	41.6	44.7	59.4	54.9
	S.D.	24.0	23.0	2.4	15.1

**Table 5: Summary of Passive Avoidance Historical Control Data In CRL:CD1(ICR) Mice**

		<u>#Studies Included</u>	<u>Average</u>	<u>Minimum</u>	<u>Maximum</u>
<b>Passive Avoidance Learning</b>					
<u>Male Mice: Day 1</u>	N	4	20.3	19	21
Trials to Criterion	Mean	4	4.1	3.6	4.6
Latency Trial 1	Mean	4	10.6	6.2	15.4
Latency Trial 2	Mean	4	43.8	36.6	48.7
Failed to Learn	N	3	0.0	0	0
	%	3	0.0	0.0	0.0
<b>Passive Avoidance Retention</b>					
<u>Male Mice: Day 2</u>	N	4	19.5	19	21
Trials to Criterion	Mean	4	2.6	2.3	2.9
Latency Trial 1	Mean	4	47.3	36.8	58.9
<b>Passive Avoidance Learning</b>					
<u>Female Mice: Day 1</u>	N	4	20.3	18	22
Trials to Criterion	Mean	4	4.1	3.9	4.4
Latency Trial 1	Mean	4	8.3	5.9	10.4
Latency Trial 2	Mean	4	41.8	38.6	44.8
Failed to Learn	N	3	0.0	0	0
	%	3	0.0	0.0	0.0
<b>Passive Avoidance Retention</b>					
<u>Female Mice: Day 2</u>	N	4	20.0	18	22
Trials to Criterion	Mean	4	2.6	2.3	2.9
Latency Trial 1	Mean	4	50.2	41.6	59.4

**Table 6: Individual Study Functional Observational Battery Historical Control Data Crl:CD1(ICR) Male Mice**

STUDY CODE:		A	B	B	B	B	B	B	C	C	C	C	C	C	
TESTING PERIOD:				2 Hrs	8 Hrs	1 Day	7 Days	14		30	4 Hrs	1 Day	7 Days	14	
		PD45	Pre-dose	Post-dose	Post-dose	Post-dose	Post-dose	Days Post-dose	Pre-dose	min. Post-dose	Post-dose	Post-dose	Post-dose	Days Post-dose	
<b>MICE TESTED:</b>	N	19	10	10	10	10	10	10	10	10	10	10	10	10	
<b>HOME CAGE BEHAVIOR</b>															
(1) Sleeping	N		0	0	0	0	0	0	2	0	3	3	2	1	
(2) Awake, immobile	N		8	7	9	6	7	4	6	8	6	6	3	6	
(3) Normal movement	N		2	3	1	4	3	6	2	2	1	1	5	3	
(4) Unusual posture	N		0	0	0	0	0	0	0	0	0	0	0	0	
(5) Unusual behavior	N		0	0	0	0	0	0	0	0	0	0	0	0	
<b>ALTERATIONS (HOME CAGE)</b>															
(1) None	N		10	10	10	10	10	10	10	10	10	10	10	10	
(2) Stereotyped behavior	N		0	0	0	0	0	0	0	0	0	0	0	0	
(3) Bizarre behavior	N		0	0	0	0	0	0	0	0	0	0	0	0	
(4) Limb twitches/tremor	N		0	0	0	0	0	0	0	0	0	0	0	0	
(5) Whole body tremor/spasm	N		0	0	0	0	0	0	0	0	0	0	0	0	
(6) Unusual posture	N		0	0	0	0	0	0	0	0	0	0	0	0	
(7) Tonic-clonic seizure	N		0	0	0	0	0	0	0	0	0	0	0	0	
<b>REACTION TO REMOVAL</b>															
(1) Sits quietly	N		10	10	10	10	9	10	9	10	10	10	10	9	
(2) Vocalization	N		0	0	0	0	1	0	1	0	0	0	0	1	
(3) Runs or freezes	N		0	0	0	0	0	0	0	0	0	0	0	0	
(4) Tail or throat rattles	N		0	0	0	0	0	0	0	0	0	0	0	0	
	MEAN		1.0	1.0	1.0	1.0	1.1	1.0	1.1	1.0	1.0	1.0	1.0	1.1	
<b>REACTION TO HANDLING</b>															
(1) Quiet, no resistance	N		10	10	10	9	10	9	10	10	10	10	10	10	
(2) Vocalization, no resistance	N		0	0	0	1	0	1	0	0	0	0	0	0	
(3) Tense	N		0	0	0	0	0	0	0	0	0	0	0	0	
(4) Squirming	N		0	0	0	0	0	0	0	0	0	0	0	0	
	MEAN		1.0	1.0	1.0	1.1	1.0	1.1	1.0	1.0	1.0	1.0	1.0	1.0	
<b>REARS IN OPEN FIELD</b>	MEAN	7.6	9.5	9.5	7.7	6.7	8.1	9.1	6.1	17.5	8.3	6.4	8.6	10.6	

**Table 6: Individual Study Functional Observational Battery Historical Control Data Crl:CD1(ICR) Male Mice**

<b>STUDY CODE:</b>		<b>A</b>	<b>B</b>	<b>B</b>	<b>B</b>	<b>B</b>	<b>B</b>	<b>B</b>	<b>C</b>	<b>C</b>	<b>C</b>	<b>C</b>	<b>C</b>	<b>C</b>
<b>TESTING PERIOD:</b>		<b>PD45</b>	<b>Pre-dose</b>	<b>2 Hrs Post-dose</b>	<b>8 Hrs Post-dose</b>	<b>1 Day Post-dose</b>	<b>7 Days Post-dose</b>	<b>14 Days Post-dose</b>	<b>Pre-dose</b>	<b>30 min. Post-dose</b>	<b>4 Hrs Post-dose</b>	<b>1 Day Post-dose</b>	<b>7 Days Post-dose</b>	<b>14 Days Post-dose</b>
<b>DEFECATION IN OPEN FIELD</b>														
(1) None	N	10	4	3	8	2	2	3	4	6	2	5	2	2
(2) Feces normal	N	9	6	7	2	8	8	6	6	4	8	5	8	8
(3) Soft or liquid feces	N	0	0	0	0	0	0	1	0	0	0	0	0	0
<b>URINATION IN OPEN FIELD</b>														
(1) None	N	11	10	5	10	8	6	8	9	5	10	10	8	5
(2) Normal urination	N	8	0	5	0	2	4	2	1	5	0	0	2	5
(3) Excess urination	N	0	0	0	0	0	0	0	0	0	0	0	0	0
	MEAN	1.4	1.0	1.5	1.0	1.2	1.4	1.2	1.1	1.5	1.0	1.0	1.2	1.5
<b>LEVEL OF AROUSAL</b>														
(1) Stuporous	N	0	0	0	0	0	0	0	0	0	0	0	0	0
(2) Sluggish	N	0	0	0	0	0	0	0	0	0	0	0	0	0
(3) Apparently normal	N	19	10	10	10	10	10	10	10	10	10	10	10	10
(4) Sudden darting	N	0	0	0	0	0	0	0	0	0	0	0	0	0
(5) Freezing, vocalization	N	0	0	0	0	0	0	0	0	0	0	0	0	0
	MEAN	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
<b>ALTERATIONS (OPEN FIELD)</b>														
(1) None	N	19	10	10	10	10	10	10	10	10	10	10	10	10
(2) Stereotyped behavior	N	0	0	0	0	0	0	0	0	0	0	0	0	0
(3) Bizarre behavior	N	0	0	0	0	0	0	0	0	0	0	0	0	0
(4) Limb twitches / tremor	N	0	0	0	0	0	0	0	0	0	0	0	0	0
(5) Whole body tremor / spasm	N	0	0	0	0	0	0	0	0	0	0	0	0	0
(6) Unusual posture	N	0	0	0	0	0	0	0	0	0	0	0	0	0
(7) Tonic-clonic seizure	N	0	0	0	0	0	0	0	0	0	0	0	0	0
<b>GAIT PATTERN</b>														
(1) Apparently normal	N	19	10	10	10	10	10	10	10	10	10	10	10	10
(2) Ataxic	N	0	0	0	0	0	0	0	0	0	0	0	0	0
(3) Limbs splay or drag	N	0	0	0	0	0	0	0	0	0	0	0	0	0
(4) Spastic, tip-toe	N	0	0	0	0	0	0	0	0	0	0	0	0	0
(5) Duck-walk	N	0	0	0	0	0	0	0	0	0	0	0	0	0
(6) Scissors gait	N	0	0	0	0	0	0	0	0	0	0	0	0	0

**Table 6: Individual Study Functional Observational Battery Historical Control Data Crl:CD1(ICR) Male Mice**

<b>STUDY CODE:</b>		<b>A</b>	<b>B</b>	<b>B</b>	<b>B</b>	<b>B</b>	<b>B</b>	<b>B</b>	<b>C</b>	<b>C</b>	<b>C</b>	<b>C</b>	<b>C</b>	<b>C</b>	
<b>TESTING PERIOD:</b>			<b>Pre-dose</b>	<b>2 Hrs Post-dose</b>	<b>8 Hrs Post-dose</b>	<b>1 Day Post-dose</b>	<b>7 Days Post-dose</b>	<b>14 Days Post-dose</b>	<b>Pre-dose</b>	<b>30 min. Post-dose</b>	<b>4 Hrs Post-dose</b>	<b>1 Day Post-dose</b>	<b>7 Days Post-dose</b>	<b>14 Days Post-dose</b>	
		<b>PD45</b>													
<b>GAIT ABNORMALITY, SEVERITY</b>															
(1) Normal gait	N	19	10	10	10	10	10	10	10	10	10	10	10	10	10
(2) Slight	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0
(3) Moderate	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0
(4) Extreme	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	MEAN	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
<b>PALPEBRAL CLOSURE</b>															
(1) Wide open	N	19	10	10	10	10	10	10	10	10	10	10	10	10	10
(2) Slightly drooping	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0
(3) Half-closed	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0
(4) Completely shut	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	MEAN	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
<b>PROMINENCE OF THE EYE</b>															
(1) Normal	N	19	10	10	10	10	10	10	10	10	10	10	10	10	10
(2) Exophthalmos	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0
(3) Enophthalmos	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0
<b>LACRIMATION</b>															
(1) No excess	N	19	10	10	10	10	10	10	10	10	10	10	10	10	10
(2) Excess at eyelid margin	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0
(3) Margin persistently damp	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0
(4) Extends beyond margin	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	MEAN	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
<b>SALIVATION</b>															
(1) No excess	N	18	10	10	10	10	10	10	10	10	10	10	10	10	10
(2) Margin of mouth wet	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0
(3) 1/4 to 1/2 submandibular	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0
(4) Entire submandibular	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	MEAN	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
<b>PILOERECTION</b>	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0
<b>ABNORMAL RESPIRATION</b>	N	1	0	0	0	0	0	0	0	0	0	0	0	0	0

**Table 6: Individual Study Functional Observational Battery Historical Control Data Crl:CD1(ICR) Male Mice**

STUDY CODE:		A	B	B	B	B	B	B	C	C	C	C	C	C
TESTING PERIOD:		PD45	Pre-dose	2 Hrs Post-dose	8 Hrs Post-dose	1 Day Post-dose	7 Days Post-dose	14 Days Post-dose	Pre-dose	30 min. Post-dose	4 Hrs Post-dose	1 Day Post-dose	7 Days Post-dose	14 Days Post-dose
<b>APPEARANCE</b>														
(1) Clean and groomed	N	17	10	10	10	10	10	10	10	10	10	10	10	10
(2) Unkempt	N	2	0	0	0	0	0	0	0	0	0	0	0	0
(3) Urine and/or fecal stain	N	0	0	0	0	0	0	0	0	0	0	0	0	0
	MEAN	1.1	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
<b>VISUAL REACTION</b>														
(1) None	N	1	0	0	0	0	0	0	0	0	0	0	0	0
(2) Orienting	N	18	10	10	10	10	10	10	10	10	10	10	10	10
(3) Startle	N	0	0	0	0	0	0	0	0	0	0	0	0	0
(4) More energetic reaction	N	0	0	0	0	0	0	0	0	0	0	0	0	0
(5) Attacks	N	0	0	0	0	0	0	0	0	0	0	0	0	0
	MEAN	1.9	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
<b>TACTILE REACTION</b>														
(1) None	N	1	0	0	0	0	0	0	0	0	0	0	0	0
(2) Orienting	N	6	10	10	9	9	9	8	10	8	9	9	10	9
(3) Startle	N	12	0	0	1	1	1	2	0	2	1	1	0	1
(4) More energetic reaction	N	0	0	0	0	0	0	0	0	0	0	0	0	0
(5) Attacks	N	0	0	0	0	0	0	0	0	0	0	0	0	0
	MEAN	2.6	2.0	2.0	2.1	2.1	2.1	2.2	2.0	2.2	2.1	2.1	2.0	2.1
<b>AUDITORY STARTLE</b>														
(1) None	N	2	0	0	0	0	0	0	0	0	0	0	0	0
(2) Orienting	N	0	8	10	9	9	9	9	10	4	3	1	1	6
(3) Startle	N	17	2	0	1	1	1	1	0	6	7	9	9	4
(4) More energetic reaction	N	0	0	0	0	0	0	0	0	0	0	0	0	0
(5) Intense vocalization	N	0	0	0	0	0	0	0	0	0	0	0	0	0
	MEAN	2.8	2.2	2.0	2.1	2.1	2.1	2.1	3.0	2.6	2.7	2.9	2.9	2.4
<b>TAIL-PINCH REACTION</b>														
(1) None	N	0	0	0	0	0	0	0	0	0	0	0	0	0
(2) Orienting	N	6	3	5	3	8	8	5	5	8	8	9	8	9
(3) Startle	N	13	7	5	7	2	2	5	5	2	2	1	2	1



**Table 6: Individual Study Functional Observational Battery Historical Control Data Crl:CD1(ICR) Male Mice**

<b>STUDY CODE:</b>		<b>A</b>	<b>B</b>	<b>B</b>	<b>B</b>	<b>B</b>	<b>B</b>	<b>B</b>	<b>C</b>	<b>C</b>	<b>C</b>	<b>C</b>	<b>C</b>	
<b>TESTING PERIOD:</b>				<b>2 Hrs Post-dose</b>	<b>8 Hrs Post-dose</b>	<b>1 Day Post-dose</b>	<b>7 Days Post-dose</b>	<b>14 Days Post-dose</b>		<b>30 min. Post-dose</b>	<b>4 Hrs Post-dose</b>	<b>1 Day Post-dose</b>	<b>7 Days Post-dose</b>	<b>14 Days Post-dose</b>
		<b>PD45</b>	<b>Pre-dose</b>						<b>Pre-dose</b>					
(4) More energetic reaction	N	0	0	0	0	0	0	0	0	0	0	0	0	0
(5) Attacks	N	0	0	0	0	0	0	0	0	0	0	0	0	0
	MEAN	2.7	2.7	2.5	2.7	2.2	2.2	2.5	2.5	2.2	2.2	2.1	2.2	2.1
<b>VISUAL PLACING RESPONSE</b>														
(1) Early extension	N	19	10	10	10	10	10	10	10	10	10	10	10	10
(2) Extension after contact	N	0	0	0	0	0	0	0	0	0	0	0	0	0
(3) No extension	N	0	0	0	0	0	0	0	0	0	0	0	0	0
	MEAN	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
<b>AIR RIGHTING RESPONSE</b>														
(1) All feet land on ground	N	19	10	10	10	10	10	10	10	10	10	10	10	10
(2) Lands on side	N	0	0	0	0	0	0	0	0	0	0	0	0	0
(3) Lands on back	N	0	0	0	0	0	0	0	0	0	0	0	0	0
	MEAN	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
<b>PUPIL RESPONSE TO LIGHT</b>	N	18	10	10	10	10	10	10	10	10	10	10	10	10
<b>GRIP-STRENGTH FORELIMB (G)</b>														
Maximum	MEAN		60.0	61.5	57.5	49.5	62.5	56.0	73.0	80.0	68.0	70.0	68.5	74.5
Average	MEAN		52.0	55.5	48.5	42.8	54.5	50.5	66.2	67.5	60.5	60.2	56.2	62.8
<b>GRIP-STRENGTH HINDLIMB (G)</b>														
Maximum	MEAN		50.5	53.0	52.0	60.5	61.0	53.5	92.5	83.5	90.5	95.0	94.0	87.5
Average	MEAN		43.2	49.0	45.8	50.0	52.0	49.0	83.8	74.5	78.8	87.0	86.0	82.5
<b>LANDING FOOT SPLAY AVERAGE (CM)</b>	MEAN		4.16	3.46	3.52	3.52	3.29	3.24	3.72	3.48	3.50	3.26	3.29	3.20
<b>BODY TEMPERATURE (°C)</b>	MEAN		37.7	37.9	37.8	37.6	37.8	38.4	37.2	38.0	37.7	37.1	37.5	38.0
<b>BODY WEIGHT (Grams)</b>	MEAN	28.6	30.1	32.0	32.0	31.0	31.4	32.8	33.9	35.8			34.6	35.4

**Table 7: Individual Study Functional Observational Battery Historical Control Data Crl:CD1(ICR) Female Mice**

STUDY CODE:		A	B	B	B	B	B	B	C	C	C	C	C	C
TESTING PERIOD:				2 Hrs	8 Hrs	1 Day	7 Days	14		30	4 Hrs	1 Day	7 Days	14
		PD45	Pre-dose	Post-dose	Post-dose	Post-dose	Post-dose	Days Post-dose	Pre-dose	min. Post-dose	Post-dose	Post-dose	Post-dose	Days Post-dose
<b>MICE TESTED:</b>	N	18	10	10	10	10	10	10	10	10	10	10	10	10
<b>HOME CAGE BEHAVIOR</b>														
(1) Sleeping	N		0	1	1	0	1	1	0	0	1	1	1	2
(2) Awake, immobile	N		6	5	6	5	7	1	7	3	8	9	7	4
(3) Normal movement	N		4	4	3	5	2	8	3	7	1	0	2	4
(4) Unusual posture	N		0	0	0	0	0	0	0	0	0	0	0	0
(5) Unusual behavior	N		0	0	0	0	0	0	0	0	0	0	0	0
<b>ALTERATIONS (HOME CAGE)</b>														
(1) None	N		10	10	10	10	10	10	10	10	10	10	10	10
(2) Stereotyped behavior	N		0	0	0	0	0	0	0	0	0	0	0	0
(3) Bizarre behavior	N		0	0	0	0	0	0	0	0	0	0	0	0
(4) Limb twitches/tremor	N		0	0	0	0	0	0	0	0	0	0	0	0
(5) Whole body tremor/spasm	N		0	0	0	0	0	0	0	0	0	0	0	0
(6) Unusual posture	N		0	0	0	0	0	0	0	0	0	0	0	0
(7) Tonic-clonic seizure	N		0	0	0	0	0	0	0	0	0	0	0	0
<b>REACTION TO REMOVAL</b>														
(1) Sits quietly	N		9	9	10	9	10	9	7	9	10	9	7	7
(2) Vocalization	N		1	1	0	1	0	1	2	1	0	1	3	3
(3) Runs or freezes	N		0	0	0	0	0	0	1	0	0	0	0	0
(4) Tail or throat rattles	N		0	0	0	0	0	0	0	0	0	0	0	0
	MEAN		1.1	1.1	1.0	1.1	1.0	1.1	1.4	1.1	1.0	1.1	1.3	1.3
<b>REACTION TO HANDLING</b>														
(1) Quiet, no resistance	N		10	10	10	10	10	10	10	10	10	10	10	10
(2) Vocalization, no resistance	N		0	0	0	0	0	0	0	0	0	0	0	0

**Table 7: Individual Study Functional Observational Battery Historical Control Data Crl:CD1(ICR) Female Mice**

STUDY CODE:		A	B	B	B	B	B	B	C	C	C	C	C	C	
TESTING PERIOD:			Pre-dose	2 Hrs Post-dose	8 Hrs Post-dose	1 Day Post-dose	7 Days Post-dose	14 Days Post-dose	Pre-dose	30 min. Post-dose	4 Hrs Post-dose	1 Day Post-dose	7 Days Post-dose	14 Days Post-dose	
		PD45													
(3) Tense	N		0	0	0	0	0	0	0	0	0	0	0	0	
(4) Squirming	N		0	0	0	0	0	0	0	0	0	0	0	0	
	MEAN		1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	
<b>REARS IN OPEN FIELD</b>	MEAN	10.0	12.7	14.8	9.8	7.4	9.4	15.7	8.1	18.2	9.6	8.1	9.3	11.0	
<b>DEFECATION IN OPEN FIELD</b>															
(1) None	N	9	5	5	3	2	2	2	9	6	7	2	6	3	
(2) Feces normal	N	9	5	5	7	8	8	8	1	4	3	8	4	7	
(3) Soft or liquid feces	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
<b>URINATION IN OPEN FIELD</b>															
(1) None	N	15	8	10	10	8	8	9	10	8	10	10	9	8	
(2) Normal urination	N	3	2	0	0	2	2	1	0	2	0	0	1	2	
(3) Excess urination	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
	MEAN	1.2	1.2	1.0	1.0	1.2	1.2	1.1	1.0	1.2	1.0	1.0	1.1	1.2	
<b>LEVEL OF AROUSAL</b>															
(1) Stuporous	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(2) Sluggish	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(3) Apparently normal	N	18	10	10	10	10	10	9	10	10	10	10	10	10	
(4) Sudden darting	N	0	0	0	0	0	0	1	0	0	0	0	0	0	
(5) Freezing, vocalization	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
	MEAN	3.0	3.0	3.0	3.0	3.0	3.0	3.1	3.0	3.0	3.0	3.0	3.0	3.0	
<b>ALTERATIONS (OPEN FIELD)</b>															
(1) None	N	18	10	10	10	10	10	10	10	10	10	10	10	10	
(2) Stereotyped behavior	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(3) Bizarre behavior	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(4) Limb twitches / tremor	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(5) Whole body tremor / spasm	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(6) Unusual posture	N	0	0	0	0	0	0	0	0	0	0	0	0	0	

**Table 7: Individual Study Functional Observational Battery Historical Control Data Crl:CD1(ICR) Female Mice**

STUDY CODE:		A	B	B	B	B	B	B	C	C	C	C	C	C	
TESTING PERIOD:				2 Hrs	8 Hrs	1 Day	7 Days	14		30	4 Hrs	1 Day	7 Days	14	
		PD45	Pre-dose	Post-dose	Post-dose	Post-dose	Post-dose	Days Post-dose	Pre-dose	min. Post-dose	Post-dose	Post-dose	Post-dose	Days Post-dose	
(7) Tonic-clonic seizure	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
<b>GAIT PATTERN</b>															
(1) Apparently normal	N	18	10	10	10	10	10	10	10	10	10	10	10	10	
(2) Ataxic	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(3) Limbs splay or drag	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(4) Spastic, tip-toe	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(5) Duck-walk	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(6) Scissors gait	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
<b>GAIT ABNORMALITY, SEVERITY</b>															
(1) Normal gait	N	18	10	10	10	10	10	10	10	10	10	10	10	10	
(2) Slight	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(3) Moderate	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(4) Extreme	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
	MEAN	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	
<b>PALPEBRAL CLOSURE</b>															
(1) Wide open	N	18	10	10	10	10	10	10	10	10	10	10	10	10	
(2) Slightly drooping	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(3) Half-closed	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(4) Completely shut	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
	MEAN	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	
<b>PROMINENCE OF THE EYE</b>															
(1) Normal	N	18	10	10	10	10	10	10	10	10	10	10	10	10	
(2) Exophthalmos	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(3) Enophthalmos	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
<b>LACRIMATION</b>															
(1) No excess	N	18	10	10	10	10	10	10	10	10	10	10	10	10	

**Table 7: Individual Study Functional Observational Battery Historical Control Data Crl:CD1(ICR) Female Mice**

STUDY CODE:		A	B	B	B	B	B	B	C	C	C	C	C	C	
TESTING PERIOD:		PD45	Pre-dose	2 Hrs Post-dose	8 Hrs Post-dose	1 Day Post-dose	7 Days Post-dose	14 Days Post-dose	Pre-dose	30 min. Post-dose	4 Hrs Post-dose	1 Day Post-dose	7 Days Post-dose	14 Days Post-dose	
(2) Excess at eyelid margin	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(3) Margin persistently damp	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(4) Extends beyond margin	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
	MEAN	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	
<b>SALIVATION</b>															
(1) No excess	N	18	10	10	10	10	10	10	10	10	10	10	10	10	
(2) Margin of mouth wet	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(3) 1/4 to 1/2 submandibular	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(4) Entire submandibular	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
	MEAN	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	
<b>PILOERECTION</b>	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
<b>ABNORMAL RESPIRATION</b>	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
<b>APPEARANCE</b>															
(1) Clean and groomed	N	18	10	10	10	10	10	10	10	10	10	10	10	10	
(2) Unkempt	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(3) Urine and/or fecal stain	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
	MEAN	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	
<b>VISUAL REACTION</b>															
(1) None	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(2) Orienting	N	18	10	10	10	9	8	9	10	10	10	10	10	10	
(3) Startle	N	0	0	0	0	1	2	1	0	0	0	0	0	0	
(4) More energetic reaction	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(5) Attacks	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
	MEAN	2.0	2.0	2.0	2.0	2.1	2.2	2.1	2.0	2.0	2.0	2.0	2.0	2.0	
<b>TACTILE REACTION</b>															
(1) None	N	0	0	0	0	0	0	0	0	0	0	0	0	0	

**Table 7: Individual Study Functional Observational Battery Historical Control Data Crl:CD1(ICR) Female Mice**

STUDY CODE:		A	B	B	B	B	B	B	C	C	C	C	C	C	
TESTING PERIOD:		PD45	Pre-dose	2 Hrs Post-dose	8 Hrs Post-dose	1 Day Post-dose	7 Days Post-dose	14 Days Post-dose	Pre-dose	30 min. Post-dose	4 Hrs Post-dose	1 Day Post-dose	7 Days Post-dose	14 Days Post-dose	
(2) Orienting	N	16	10	7	9	7	5	6	10	8	10	10	9	10	
(3) Startle	N	2	0	3	1	3	5	4	0	2	0	0	1	0	
(4) More energetic reaction	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(5) Attacks	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
	MEAN	2.1	2.0	2.3	2.1	2.3	2.5	2.4	2.0	2.2	2.0	2.0	2.1	2.0	
<b>AUDITORY STARTLE</b>															
(1) None	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(2) Orienting	N	7	8	7	8	7	8	7	3	3	1	2	1	6	
(3) Startle	N	10	2	3	2	3	2	3	7	7	9	8	9	4	
(4) More energetic reaction	N	1	0	0	0	0	0	0	0	0	0	0	0	0	
(5) Intense vocalization	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
	MEAN	2.7	2.2	2.3	2.2	2.3	2.2	2.3	2.7	2.7	2.9	2.8	2.9	2.4	
<b>TAIL-PINCH REACTION</b>															
(1) None	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(2) Orienting	N	13	1	0	0	0	3	0	7	8	10	8	9	9	
(3) Startle	N	5	9	10	10	10	7	10	3	2	0	2	1	1	
(4) More energetic reaction	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(5) Attacks	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
	MEAN	2.3	2.9	3.0	3.0	3.0	2.7	3.0	2.3	2.2	2.0	2.2	2.1	2.1	
<b>VISUAL PLACING RESPONSE</b>															
(1) Early extension	N	18	10	10	10	10	10	10	10	10	10	10	10	10	
(2) Extension after contact	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(3) No extension	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
	MEAN	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	
<b>AIR RIGHTING RESPONSE</b>															
(1) All feet land on ground	N	18	10	10	10	10	10	10	10	10	10	10	10	10	
(2) Lands on side	N	0	0	0	0	0	0	0	0	0	0	0	0	0	
(3) Lands on back	N	0	0	0	0	0	0	0	0	0	0	0	0	0	

**Table 7: Individual Study Functional Observational Battery Historical Control Data Crl:CD1(ICR) Female Mice**

STUDY CODE:		A	B	B	B	B	B	B	C	C	C	C	C	C
TESTING PERIOD:			Pre-dose	2 Hrs Post-dose	8 Hrs Post-dose	1 Day Post-dose	7 Days Post-dose	14 Days Post-dose	Pre-dose	30 min. Post-dose	4 Hrs Post-dose	1 Day Post-dose	7 Days Post-dose	14 Days Post-dose
		PD45												
	MEAN	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
<b>PUPIL RESPONSE TO LIGHT</b>	N	18	10	10	10	10	10	10	10	10	10	10	10	10
<b>GRIP-STRENGTH FORELIMB (G)</b>														
Maximum	MEAN		54.5	58.0	48.5	52.5	68.0	73.0	79.5	73.0	66.5	68.0	67.5	63.0
Average	MEAN		46.5	50.2	39.5	44.0	60.8	65.5	71.2	62.0	57.5	55.8	54.8	50.5
<b>GRIP-STRENGTH HINDLIMB (G)</b>														
Maximum	MEAN		46.5	47.5	49.0	49.5	49.0	53.0	75.5	75.0	91.5	87.5	77.5	84.0
Average	MEAN		39.8	41.8	44.5	42.2	42.5	45.5	65.5	68.8	80.5	81.0	74.2	78.5
<b>LANDING FOOT SPLAY AVERAGE (CM)</b>	MEAN		3.59	3.30	3.44	3.04	3.22	3.10	3.85	3.88	3.74	3.58	3.46	3.36
<b>BODY TEMPERATURE (°C)</b>	MEAN		37.8	37.8	37.9	37.9	37.8	38.2	37.7	38.6	37.9	38.0	38.0	38.3
<b>BODY WEIGHT (Grams)</b>	MEAN	22.8	26.4	27.4		26.4	27.4	28.9	27.0	28.0			28.2	29.0

**Table 8: Summary of Functional Observational Battery Historical CONTROL DATA  
Crl:CD1(ICR) Male Mice**

		AVERAGE	MIN.	MAX.	# EVALUATIONS INCLUDED
<b>MICE TESTED:</b>	N	10.7	10	19	13
<b>HOME CAGE BEHAVIOR</b>					
(1) Sleeping	N	0.9	0	3	12
(2) Awake, immobile	N	6.3	3	9	12
(3) Normal movement	N	2.8	1	6	12
(4) Unusual posture	N	0.0	0	0	12
(5) Unusual behavior	N	0.0	0	0	12
<b>ALTERATIONS (HOME CAGE)</b>					
(1) None	N	10.0	10	10	12
(2) Stereotyped behavior	N	0.0	0	0	12
(3) Bizarre behavior	N	0.0	0	0	12
(4) Limb twitches/tremor	N	0.0	0	0	12
(5) Whole body tremor/spasm	N	0.0	0	0	12
(6) Unusual posture	N	0.0	0	0	12
(7) Tonic-clonic seizure	N	0.0	0	0	12
<b>REACTION TO REMOVAL</b>					
(1) Sits quietly	N	9.8	9	10	12
(2) Vocalization	N	0.3	0	1	12
(3) Runs or freezes	N	0.0	0	0	12
(4) Tail or throat rattles	N	0.0	0	0	12
	MEAN	1.0	1.0	1.1	12
<b>REACTION TO HANDLING</b>					
(1) Quiet, no resistance	N	9.8	9	10	12
(2) Vocalization, no resistance	N	0.2	0	1	12
(3) Tense	N	0.0	0	0	12
(4) Squirming	N	0.0	0	0	12
	MEAN	1.0	1.0	1.1	12
<b>REARS IN OPEN FIELD</b>	MEAN	8.9	6.1	17.5	13
<b>DEFECATION IN OPEN FIELD</b>					
(1) None	N	4.1	2	10	13
(2) Feces normal	N	6.5	2	9	13
(3) Soft or liquid feces	N	0.1	0	1	13
<b>URINATION IN OPEN FIELD</b>					
(1) None	N	8.1	5	11	13
(2) Normal urination	N	2.6	0	8	13
(3) Excess urination	N	0.0	0	0	13
	MEAN	1.2	1.0	1.5	13
<b>LEVEL OF AROUSAL</b>					
(1) Stuporous	N	0.0	0	0	13
(2) Sluggish	N	0.0	0	0	13
(3) Apparently normal	N	10.7	10	19	13
(4) Sudden darting	N	0.0	0	0	13
(5) Freezing, vocalization	N	0.0	0	0	13



**Table 8: Summary of Functional Observational Battery Historical Control Data  
Crl:CD1(ICR) Male Mice**

		AVERAGE	MIN.	MAX.	# EVALUATIONS INCLUDED
	MEAN	3.0	3.0	3.0	13
<b>ALTERATIONS (OPEN FIELD)</b>					
(1) None	N	10.7	10	19	13
(2) Stereotyped behavior	N	0.0	0	0	13
(3) Bizarre behavior	N	0.0	0	0	13
(4) Limb twitches / tremor	N	0.0	0	0	13
(5) Whole body tremor / spasm	N	0.0	0	0	13
(6) Unusual posture	N	0.0	0	0	13
(7) Tonic-clonic seizure	N	0.0	0	0	13
<b>GAIT PATTERN</b>					
(1) Apparently normal	N	10.7	10	19	13
(2) Ataxic	N	0.0	0	0	13
(3) Limbs splay or drag	N	0.0	0	0	13
(4) Spastic, tip-toe	N	0.0	0	0	13
(5) Duck-walk	N	0.0	0	0	13
(6) Scissors gait	N	0.0	0	0	13
<b>GAIT ABNORMALITY, SEVERITY</b>					
(1) Normal gait	N	10.7	10	19	13
(2) Slight	N	0.0	0	0	13
(3) Moderate	N	0.0	0	0	13
(4) Extreme	N	0.0	0	0	13
	MEAN	1.0	1.0	1.0	13
<b>PALPEBRAL CLOSURE</b>					
(1) Wide open	N	10.7	10	19	13
(2) Slightly drooping	N	0.0	0	0	13
(3) Half-closed	N	0.0	0	0	13
(4) Completely shut	N	0.0	0	0	13
	MEAN	1.0	1.0	1.0	13
<b>PROMINENCE OF THE EYE</b>					
(1) Normal	N	10.7	10	19	13
(2) Exophthalmos	N	0.0	0	0	13
(3) Enophthalmos	N	0.0	0	0	13
<b>LACRIMATION</b>					
(1) No excess	N	10.7	10	19	13
(2) Excess at eyelid margin	N	0.0	0	0	13
(3) Margin persistently damp	N	0.0	0	0	13
(4) Extends beyond margin	N	0.0	0	0	13
	MEAN	1.0	1.0	1.0	13
<b>SALIVATION</b>					
(1) No excess	N	10.6	10	18	13
(2) Margin of mouth wet	N	0.0	0	0	13
(3) 1/4 to 1/2 submandibular	N	0.0	0	0	13
(4) Entire submandibular	N	0.0	0	0	13
	MEAN	1.0	1.0	1.0	13
<b>PILOERECTOR</b>	N	0.0	0	0	13
<b>ABNORMAL RESPIRATION</b>	N	0.1	0	1	13

**Table 8: Summary of Functional Observational Battery Historical Control Data  
Crl:CD1(ICR) Male Mice**

		AVERAGE	MIN.	MAX.	# EVALUATIONS INCLUDED
<b>APPEARANCE</b>					
(1) Clean and groomed	N	10.5	10	17	13
(2) Unkempt	N	0.2	0	2	13
(3) Urine and/or fecal stain	N	0.0	0	0	13
	MEAN	1.0	1.0	1.1	13
<b>VISUAL REACTION</b>					
(1) None	N	0.1	0	1	13
(2) Orienting	N	10.6	10	18	13
(3) Startle	N	0.0	0	0	13
(4) More energetic reaction	N	0.0	0	0	13
(5) Attacks	N	0.0	0	0	13
	MEAN	2.0	1.9	2.0	13
<b>TACTILE REACTION</b>					
(1) None	N	0.1	0	1	13
(2) Orienting	N	8.9	6	10	13
(3) Startle	N	1.7	0	12	13
(4) More energetic reaction	N	0.0	0	0	13
(5) Attacks	N	0.0	0	0	13
	MEAN	2.1	2.0	2.6	13
<b>AUDITORY STARTLE</b>					
(1) None	N	0.2	0	2	13
(2) Orienting	N	6.1	0	10	13
(3) Startle	N	4.5	0	17	13
(4) More energetic reaction	N	0.0	0	0	13
(5) Intense vocalization	N	0.0	0	0	13
	MEAN	2.5	2.0	3.0	13
<b>TAIL-PINCH REACTION</b>					
(1) None	N	0.0	0	0	13
(2) Orienting	N	6.5	3	9	13
(3) Startle	N	4.2	1	13	13
(4) More energetic reaction	N	0.0	0	0	13
(5) Attacks	N	0.0	0	0	13
	MEAN	2.4	2.1	2.7	13
<b>VISUAL PLACING RESPONSE</b>					
(1) Early extension	N	10.7	10	19	13
(2) Extension after contact	N	0.0	0	0	13
(3) No extension	N	0.0	0	0	13
	MEAN	1.0	1.0	1.0	13
<b>AIR RIGHTING RESPONSE</b>					
(1) All feet land on ground	N	10.7	10	19	13
(2) Lands on side	N	0.0	0	0	13
(3) Lands on back	N	0.0	0	0	13
	MEAN	1.0	1.0	1.0	13
<b>PUPIL RESPONSE TO LIGHT</b>					
	N	10.6	10	18	13
<b>GRIP-STRENGTH FORELIMB (G)</b>					
Maximum	MEAN	65.08	49.5	80.0	12

**Table 8: Summary of Functional Observational Battery Historical Control Data  
Crl:CD1(ICR) Male Mice**

		<b>AVERAGE</b>	<b>MIN.</b>	<b>MAX.</b>	<b># EVALUATIONS INCLUDED</b>
Average	MEAN	56.43	42.8	67.5	12
<b>GRIP-STRENGTH HINDLIMB (G)</b>					
Maximum	MEAN	72.79	50.5	95.0	12
Average	MEAN	65.13	43.2	87.0	12
<b>LANDING FOOT SPLAY AVERAGE (CM)</b>	MEAN	3.47	3.2	4.2	12
<b>BODY TEMPERATURE (°C)</b>	MEAN	37.73	37.1	38.4	12
<b>BODY WEIGHT (Grams)</b>	MEAN	32.51	28.6	35.8	11

**Table 9: Summary of Functional Observational Battery Historical Control Data  
Crl:CD1(ICR) Female Mice**

		AVERAGE	MIN.	MAX.	# EVALUATIONS INCLUDED
<b>MICE TESTED:</b>	N	10.6	10	18	13
<b>HOME CAGE BEHAVIOR</b>					
(1) Sleeping	N	0.8	0	2	12
(2) Awake, immobile	N	5.7	1	9	12
(3) Normal movement	N	3.6	0	8	12
(4) Unusual posture	N	0.0	0	0	12
(5) Unusual behavior	N	0.0	0	0	12
<b>ALTERATIONS (HOME CAGE)</b>					
(1) None	N	10.0	10	10	12
(2) Stereotyped behavior	N	0.0	0	0	12
(3) Bizarre behavior	N	0.0	0	0	12
(4) Limb twitches/tremor	N	0.0	0	0	12
(5) Whole body tremor/spasm	N	0.0	0	0	12
(6) Unusual posture	N	0.0	0	0	12
(7) Tonic-clonic seizure	N	0.0	0	0	12
<b>REACTION TO REMOVAL</b>					
(1) Sits quietly	N	8.8	7	10	12
(2) Vocalization	N	1.2	0	3	12
(3) Runs or freezes	N	0.1	0	1	12
(4) Tail or throat rattles	N	0.0	0	0	12
	MEAN	1.1	1.0	1.4	12
<b>REACTION TO HANDLING</b>					
(1) Quiet, no resistance	N	10.0	10	10	12
(2) Vocalization, no resistance	N	0.0	0	0	12
(3) Tense	N	0.0	0	0	12
(4) Squirming	N	0.0	0	0	12
	MEAN	1.0	1.0	1.0	12
<b>REARS IN OPEN FIELD</b>	MEAN	11.1	7.4	18.2	13
<b>DEFECATION IN OPEN FIELD</b>					
(1) None	N	4.7	2	9	13
(2) Feces normal	N	5.9	1	9	13
(3) Soft or liquid feces	N	0.0	0	0	13
<b>URINATION IN OPEN FIELD</b>					
(1) None	N	9.5	8	15	13
(2) Normal urination	N	1.2	0	3	13
(3) Excess urination	N	0.0	0	0	13
	MEAN	1.1	1.0	1.2	13

**Table 9: Summary of Functional Observational Battery Historical Control Data  
Crl:CD1(ICR) Female Mice**

		AVERAGE	MIN.	MAX.	# EVALUATIONS INCLUDED
<b>LEVEL OF AROUSAL</b>					
(1) Stuporous	N	0.0	0	0	13
(2) Sluggish	N	0.0	0	0	13
(3) Apparently normal	N	10.5	9	18	13
(4) Sudden darting	N	0.1	0	1	13
(5) Freezing, vocalization	N	0.0	0	0	13
	MEAN	3.0	3.0	3.1	13
<b>ALTERATIONS (OPEN FIELD)</b>					
(1) None	N	10.6	10	18	13
(2) Stereotyped behavior	N	0.0	0	0	13
(3) Bizarre behavior	N	0.0	0	0	13
(4) Limb twitches / tremor	N	0.0	0	0	13
(5) Whole body tremor / spasm	N	0.0	0	0	13
(6) Unusual posture	N	0.0	0	0	13
(7) Tonic-clonic seizure	N	0.0	0	0	13
<b>GAIT PATTERN</b>					
(1) Apparently normal	N	10.6	10	18	13
(2) Ataxic	N	0.0	0	0	13
(3) Limbs splay or drag	N	0.0	0	0	13
(4) Spastic, tip-toe	N	0.0	0	0	13
(5) Duck-walk	N	0.0	0	0	13
(6) Scissors gait	N	0.0	0	0	13
<b>GAIT ABNORMALITY, SEVERITY</b>					
(1) Normal gait	N	10.6	10	18	13
(2) Slight	N	0.0	0	0	13
(3) Moderate	N	0.0	0	0	13
(4) Extreme	N	0.0	0	0	13
	MEAN	1.0	1.0	1.0	13
<b>PALPEBRAL CLOSURE</b>					
(1) Wide open	N	10.6	10	18	13
(2) Slightly drooping	N	0.0	0	0	13
(3) Half-closed	N	0.0	0	0	13
(4) Completely shut	N	0.0	0	0	13
	MEAN	1.0	1.0	1.0	13
<b>PROMINENCE OF THE EYE</b>					
(1) Normal	N	10.6	10	18	13
(2) Exophthalmos	N	0.0	0	0	13
(3) Enophthalmos	N	0.0	0	0	13
<b>LACRIMATION</b>					
(1) No excess	N	10.6	10	18	13
(2) Excess at eyelid margin	N	0.0	0	0	13
(3) Margin persistently damp	N	0.0	0	0	13

**Table 9: Summary of Functional Observational Battery Historical Control Data  
Crl:CD1(ICR) Female Mice**

		AVERAGE	MIN.	MAX.	# EVALUATIONS INCLUDED
(4) Extends beyond margin	N	0.0	0	0	13
	MEAN	1.0	1.0	1.0	13
<b>SALIVATION</b>					
(1) No excess	N	10.6	10	18	13
(2) Margin of mouth wet	N	0.0	0	0	13
(3) 1/4 to 1/2 submandibular	N	0.0	0	0	13
(4) Entire submandibular	N	0.0	0	0	13
	MEAN	1.0	1.0	1.0	13
<b>PILOERECTION</b>					
	N	0.0	0	0	13
<b>ABNORMAL RESPIRATION</b>					
	N	0.0	0	0	13
<b>APPEARANCE</b>					
(1) Clean and groomed	N	10.6	10	18	13
(2) Unkempt	N	0.0	0	0	13
(3) Urine and/or fecal stain	N	0.0	0	0	13
	MEAN	1.0	1.0	1.0	13
<b>VISUAL REACTION</b>					
(1) None	N	0.0	0	0	13
(2) Orienting	N	10.3	8	18	13
(3) Startle	N	0.3	0	2	13
(4) More energetic reaction	N	0.0	0	0	13
(5) Attacks	N	0.0	0	0	13
	MEAN	2.0	2.0	2.2	13
<b>TACTILE REACTION</b>					
(1) None	N	0.0	0	0	13
(2) Orienting	N	9.0	5	16	13
(3) Startle	N	1.6	0	5	13
(4) More energetic reaction	N	0.0	0	0	13
(5) Attacks	N	0.0	0	0	13
	MEAN	2.2	2.0	2.5	13
<b>AUDITORY STARTLE</b>					
(1) None	N	0.0	0	0	13
(2) Orienting	N	5.2	1	8	13
(3) Startle	N	5.3	2	10	13
(4) More energetic reaction	N	0.1	0	1	13
(5) Intense vocalization	N	0.0	0	0	13
	MEAN	2.5	2.2	2.9	13
<b>TAIL-PINCH REACTION</b>					
(1) None	N	0.0	0	0	13
(2) Orienting	N	5.2	0	13	13
(3) Startle	N	5.4	0	10	13
(4) More energetic reaction	N	0.0	0	0	13

**Table 9: Summary of Functional Observational Battery Historical Control Data  
Crl:CD1(ICR) Female Mice**

		AVERAGE	MIN.	MAX.	# EVALUATIONS INCLUDED
(5) Attacks	N	0.0	0	0	13
	MEAN	2.5	2.0	3.0	13
<b>VISUAL PLACING RESPONSE</b>					
(1) Early extension	N	10.6	10	18	13
(2) Extension after contact	N	0.0	0	0	13
(3) No extension	N	0.0	0	0	13
	MEAN	1.0	1.0	1.0	13
<b>AIR RIGHTING RESPONSE</b>					
(1) All feet land on ground	N	10.6	10	18	13
(2) Lands on side	N	0.0	0	0	13
(3) Lands on back	N	0.0	0	0	13
	MEAN	1.0	1.0	1.0	13
<b>PUPIL RESPONSE TO LIGHT</b>	N	10.6	10	18	13
<b>GRIP-STRENGTH FORELIMB (G)</b>					
Maximum	MEAN	64.33	48.5	79.5	12
Average	MEAN	54.86	39.5	71.2	12
<b>GRIP-STRENGTH HINDLIMB (G)</b>					
Maximum	MEAN	65.46	46.5	91.5	12
Average	MEAN	58.73	39.8	81.0	12
<b>LANDING FOOT SPLAY AVERAGE (CM)</b>	MEAN	3.46	3.0	3.9	12
<b>BODY TEMPERATURE (°C)</b>	MEAN	37.99	37.7	38.6	12
<b>BODY WEIGHT (Grams)</b>	MEAN	27.15	22.8	29.0	10

**Table 10: Individual Study  
Motor Activity Historical Control Data in Crl:CD1(ICR) Male Mice:  
Mean Number of Movements**

STUDY CODE:		A	A	B	B	B	B	B	C	C	C	C	C
		PD22	PD61	Pre-dose	2 Hrs Post-dose	1 Day Post-dose	7 Days Post-dose	14 Days Post-dose	Pre-dose	4 Hrs. Post-dose	1 Day Post-dose	7 Days Post-dose	14 Days Post-dose
NUMBER OF MICE:		15	19	10	10	10	10	10	10	10	10	10	10
<b>NUMBER OF MOVEMENTS</b>													
BLOCK 1	MEAN	59.4	78.5	56.7	49.8	46.4	51.8	52.6	59.5	56.0	59.2	61.1	63.5
BLOCK 2	MEAN	52.7	73.6	52.6	47.3	42.7	52.0	51.9	60.6	47.2	48.3	54.8	54.9
BLOCK 3	MEAN	53.5	70.4	44.7	48.6	44.1	46.0	44.5	52.2	43.5	44.5	47.9	53.2
BLOCK 4	MEAN	56.4	69.8	50.1	45.9	43.9	40.7	41.2	42.9	38.4	41.9	40.2	56.3
BLOCK 5	MEAN	53.1	68.5	52.0	45.6	44.4	41.4	41.5	49.7	38.1	44.5	46.7	49.3
BLOCK 6	MEAN	42.7	66.6	36.7	35.3	37.9	37.8	32.3	44.4	44.8	45.5	46.0	50.9
BLOCK 7	MEAN	40.7	65.2	47.7	36.3	32.1	24.2	32.9	42.1	34.3	38.5	47.9	52.2
BLOCK 8	MEAN	40.3	65.5	30.1	34.9	28.0	19.5	31.5	38.2	30.9	38.7	39.4	47.8
BLOCK 9	MEAN	35.2	62.0	22.4	38.3	24.6	14.5	23.1	34.2	27.8	29.1	40.3	49.1
BLOCK 10	MEAN	35.8	63.2	27.8	32.0	19.8	12.1	19.4	30.5	21.3	27.5	36.5	45.0
BLOCK 11	MEAN	35.9	59.8	23.3	26.6	11.6	5.2	24.8	30.2	21.1	23.8	38.2	49.0
BLOCK 12	MEAN	38.5	60.2	25.6	19.4	15.0	6.1	19.6	26.9	27.9	17.1	33.8	39.8
BLOCK 13	MEAN	29.7	64.3	24.9	21.2	14.8	13.0	21.3	26.4	24.1	14.9	37.6	49.1
BLOCK 14	MEAN	32.7	66.0	22.8	16.3	11.3	18.6	23.0	20.2	17.6	15.2	20.9	46.0
BLOCK 15	MEAN	32.6	66.0	22.5	15.9	12.9	13.1	19.1	22.9	18.4	19.4	22.5	50.1
BLOCK 16	MEAN	31.1	57.2	14.2	22.2	13.1	10.1	14.8	21.8	14.6	20.0	20.0	35.7
BLOCK 17	MEAN	34.6	60.3	16.7	22.1	15.4	5.4	16.3	17.3	7.3	11.3	8.1	28.0
BLOCK 18	MEAN	35.1	63.3	14.3	15.5	9.2	4.1	7.4	19.4	11.1	4.8	8.9	26.3
<b>TOTAL MOVEMENTS</b>	MEAN	740.1	1180.6	585.1	573.2	467.2	415.6	517.2	639.4	524.4	544.2	650.8	846.2



**Table 11: Individual Study  
Motor Activity Historical Control Data in Crl:CD1(ICR) Female Mice:  
Mean Number of Movements**

STUDY CODE:		A	A	B	B	B	B	B	C	C	C	C	C
		PD22	PD61	Pre-dose	2 Hrs. Post-dose	1 Day Post-dose	7 Days Post-dose	14 Days Post-dose	Pre-dose	4 Hrs. Post-dose	1 Day Post-dose	7 Days Post-dose	14 Days Post-dose
NUMBER OF MICE:		17	18	10	10	10	10	10	10	10	10	10	10
NUMBER OF MOVEMENTS													
BLOCK 1	MEAN	58.7	83.2	63.5	60.8	57.0	59.5	55.8	67.2	68.4	64.4	62.7	63.9
BLOCK 2	MEAN	56.0	76.6	56.8	56.1	48.7	59.1	53.7	67.0	55.8	56.2	59.6	63.0
BLOCK 3	MEAN	44.8	77.4	49.9	54.0	44.5	49.4	59.1	57.9	55.8	53.2	59.6	51.9
BLOCK 4	MEAN	44.5	72.1	53.7	46.8	52.1	44.5	54.0	52.5	53.9	50.6	60.4	65.8
BLOCK 5	MEAN	39.2	75.5	52.5	40.6	44.5	47.8	54.6	57.0	45.7	44.1	57.4	62.1
BLOCK 6	MEAN	34.4	66.2	43.3	50.8	32.0	40.2	50.3	55.9	54.5	43.7	58.2	61.9
BLOCK 7	MEAN	29.9	69.2	43.8	52.1	32.2	35.2	49.3	49.1	43.4	37.4	53.3	60.7
BLOCK 8	MEAN	37.5	68.6	48.7	45.1	41.5	33.8	48.0	51.6	30.1	31.5	45.8	53.8
BLOCK 9	MEAN	36.7	67.7	44.3	41.9	31.4	23.4	38.1	39.8	23.1	23.6	47.0	44.1
BLOCK 10	MEAN	31.6	68.2	45.1	33.1	34.5	19.4	30.1	39.4	16.5	28.4	38.3	48.3
BLOCK 11	MEAN	34.9	60.2	35.2	32.7	15.3	13.4	31.2	42.3	20.9	26.6	29.6	47.2
BLOCK 12	MEAN	27.2	63.0	31.0	31.4	18.3	12.1	28.3	43.4	14.4	18.9	22.8	47.7
BLOCK 13	MEAN	24.6	70.5	24.7	31.3	18.0	11.9	23.1	36.2	6.1	11.0	15.6	37.6
BLOCK 14	MEAN	26.3	63.5	27.8	31.1	20.8	10.7	20.7	27.5	6.0	17.6	11.8	34.5
BLOCK 15	MEAN	23.6	63.6	21.5	17.3	15.9	9.0	14.1	29.7	9.0	17.8	12.3	33.0
BLOCK 16	MEAN	26.4	63.2	26.9	18.1	13.6	12.6	11.3	32.1	7.5	15.3	4.3	34.8
BLOCK 17	MEAN	21.4	63.7	13.0	14.4	15.5	9.3	5.2	27.2	5.6	11.0	3.5	38.9
BLOCK 18	MEAN	23.6	61.4	9.1	12.9	15.2	9.0	8.8	19.8	3.0	9.9	2.7	36.3
TOTAL MOVEMENTS	MEAN	621.3	1233.8	690.8	670.5	551.0	500.3	635.7	795.6	519.7	561.2	644.9	885.5

**Table 12: Summary of Motor Activity Historical Control Data in Crl:CD1(ICR) Male Mice:  
Mean Number of Movements**

<b>Testing Block</b>	<b>#Evaluations <u>Included</u></b>	<b><u>Average</u></b>	<b><u>Minimum</u></b>	<b><u>Maximum</u></b>
Block 1	12	57.9	46.4	78.5
Block 2	12	53.2	42.7	73.6
Block 3	12	49.4	43.5	70.4
Block 4	12	47.3	38.4	69.8
Block 5	12	47.9	38.1	68.5
Block 6	12	43.4	32.3	66.6
Block 7	12	41.2	24.2	65.2
Block 8	12	37.1	19.5	65.5
Block 9	12	33.4	14.5	62.0
Block 10	12	30.9	12.1	63.2
Block 11	12	29.1	5.2	59.8
Block 12	12	27.5	6.1	60.2
Block 13	12	28.4	13.0	64.3
Block 14	12	25.9	11.3	66.0
Block 15	12	26.3	12.9	66.0
Block 16	12	22.9	10.1	57.2
Block 17	12	20.2	5.4	60.3
Block 18	12	18.3	4.1	63.3
<b>Total Movements</b>	12	640.3	415.6	1180.6

**Table 13: Summary of Motor Activity Historical Control Data in Crl:CD1(ICR) Female Mice:  
Mean Number of Movements**

<b>Testing Block</b>	<b>#Evaluations <u>Included</u></b>	<b><u>Average</u></b>	<b><u>Minimum</u></b>	<b><u>Maximum</u></b>
Block 1	12	63.8	55.8	83.2
Block 2	12	59.1	48.7	76.6
Block 3	12	54.8	44.5	77.4
Block 4	12	54.2	44.5	72.1
Block 5	12	51.8	39.2	75.5
Block 6	12	49.3	32.0	66.2
Block 7	12	46.3	29.9	69.2
Block 8	12	44.7	30.1	68.6
Block 9	12	38.4	23.1	67.7
Block 10	12	36.1	16.5	68.2
Block 11	12	32.5	13.4	60.2
Block 12	12	29.9	12.1	63.0
Block 13	12	25.9	6.1	70.5
Block 14	12	24.9	6.0	63.5
Block 15	12	22.2	9.0	63.6
Block 16	12	22.2	4.3	63.2
Block 17	12	19.1	3.5	63.7
Block 18	12	17.6	2.7	61.4
<b>Total Movements</b>	12	692.5	500.3	1233.8

**Table 14: Individual Study, Motor Activity Historical Control Data in Crl:CD1(ICR) Male Mice:  
Time Spent in Movement (Seconds)**

STUDY CODE:		A	A	B	B	B	B	B	C	C	C	C	C
		PD22	PD61	Pre-dose	2 Hrs. Post-dose	1 Day Post-dose	7 Days Post-dose	14 Days Post-dose	Pre-dose	4 Hrs Post-dose	1 Day Post-dose	7 Days Post-dose	14 Days Post-dose
NUMBER OF MICE:		15	19	10	10	10	10	10	10	10	10	10	10
<b>TIME (SECONDS) SPENT IN MOVEMENT</b>													
BLOCK 1	MEAN	85.1	162.8	124.5	136.0	107.9	116.9	126.9	140.5	128.2	139.2	136.4	150.8
BLOCK 2	MEAN	70.3	155.0	120.3	113.8	91.5	95.6	107.8	115.1	98.6	110.5	119.0	120.2
BLOCK 3	MEAN	70.5	144.3	88.5	104.5	77.9	79.0	101.2	111.0	89.6	87.5	100.9	109.0
BLOCK 4	MEAN	70.0	134.2	105.6	100.0	83.6	71.4	87.8	88.6	78.5	83.9	85.5	117.5
BLOCK 5	MEAN	68.9	126.4	100.5	99.0	81.9	69.0	87.4	97.9	69.4	86.2	82.5	97.6
BLOCK 6	MEAN	54.5	125.0	72.3	80.6	64.5	75.4	59.4	91.7	91.4	91.2	91.8	101.7
BLOCK 7	MEAN	51.1	133.5	83.5	90.0	60.8	38.7	53.0	81.5	64.5	78.6	98.4	108.3
BLOCK 8	MEAN	63.1	111.7	60.7	66.1	55.0	29.1	55.1	71.7	59.3	64.7	73.0	83.0
BLOCK 9	MEAN	46.3	105.6	48.2	77.9	47.2	24.4	48.6	70.7	47.1	56.1	76.0	90.2
BLOCK 10	MEAN	47.9	110.5	49.2	56.7	38.9	15.3	34.0	62.3	43.7	53.8	70.8	83.7
BLOCK 11	MEAN	44.9	95.4	50.0	53.2	22.9	5.0	40.5	57.9	38.3	43.8	59.0	90.3
BLOCK 12	MEAN	51.9	97.0	55.4	44.0	26.4	6.4	43.0	49.4	50.3	30.8	51.9	69.2
BLOCK 13	MEAN	33.7	105.3	48.9	38.9	31.6	20.5	45.8	46.6	45.9	24.1	61.5	83.5
BLOCK 14	MEAN	39.1	106.3	40.3	34.2	15.8	29.2	49.6	43.8	33.8	26.9	35.2	71.8
BLOCK 15	MEAN	45.9	101.6	37.4	32.7	20.0	19.7	34.1	42.6	42.5	34.0	36.7	89.0
BLOCK 16	MEAN	40.0	86.6	22.4	39.0	22.4	12.7	27.6	35.8	27.4	29.0	35.5	57.8
BLOCK 17	MEAN	45.0	81.7	26.3	43.1	24.5	6.9	23.3	28.9	13.0	13.8	11.2	39.6
BLOCK 18	MEAN	42.7	97.0	24.9	27.0	16.2	5.3	11.1	35.1	22.0	9.0	12.5	45.0
<b>TOTAL TIME SPENT IN MOVEMENT</b>	MEAN	970.8	2079.8	1158.9	1236.7	889.0	720.5	1036.2	1271.1	1043.5	1063.1	1237.8	1608.2

**Table 15: Individual Study, Motor Activity Historical Control Data in Crl:CD1(ICR) Female Mice:  
Time Spent in Movement (Seconds)**

STUDY CODE:		A	A	B	B	B	B	B	C	C	C	C	C
		PD22	PD61	Pre-dose	2 Hrs. Post-dose	1 Day Post-dose	7 Days Post-dose	14 Days Post-dose	Pre-dose	4 Hrs. Post-dose	1 Day Post-dose	7 Days Post-dose	14 Days Post-dose
NUMBER OF MICE:		17	18	10	10	10	10	10	NA	NA	NA	NA	NA
<b>TIME (SECONDS) SPENT IN MOVEMENT</b>													
BLOCK 1	MEAN	92.5	162.4	128.6	143.8	121.6	120.8	133.4	159.8	147.4	122.7	142.3	153.2
BLOCK 2	MEAN	76.1	154.7	112.2	116.7	101.2	131.0	124.2	132.0	107.0	99.5	128.2	141.4
BLOCK 3	MEAN	59.5	157.3	101.0	120.4	89.8	101.7	128.2	112.2	108.9	84.8	116.9	111.5
BLOCK 4	MEAN	54.1	148.2	118.4	86.0	107.1	84.0	110.9	95.2	91.6	80.7	117.4	133.4
BLOCK 5	MEAN	48.0	150.7	89.3	88.6	88.2	99.2	98.4	105.1	88.4	73.5	113.1	120.9
BLOCK 6	MEAN	48.8	135.6	80.5	90.1	47.1	96.5	106.6	121.3	86.9	80.0	113.2	120.7
BLOCK 7	MEAN	35.5	130.6	88.8	108.1	59.9	68.4	86.4	91.0	68.2	65.7	99.1	110.3
BLOCK 8	MEAN	47.2	131.0	95.0	92.5	82.1	72.0	92.6	95.3	43.6	55.7	82.5	92.6
BLOCK 9	MEAN	39.8	126.9	85.1	91.0	47.0	38.8	63.5	74.2	36.9	34.4	85.1	77.6
BLOCK 10	MEAN	40.8	111.2	95.4	65.2	66.4	26.2	53.8	66.8	33.6	41.9	63.0	84.6
BLOCK 11	MEAN	46.7	125.3	60.7	55.9	21.8	21.5	50.5	72.8	33.0	39.6	42.1	95.2
BLOCK 12	MEAN	35.0	122.3	59.0	53.0	23.0	18.5	50.2	86.0	17.1	22.9	29.8	76.5
BLOCK 13	MEAN	29.6	117.5	35.3	65.4	23.7	20.1	30.6	73.3	2.8	14.9	16.1	60.1
BLOCK 14	MEAN	32.4	120.9	45.3	50.9	24.6	14.4	23.8	41.8	3.7	24.8	9.9	57.9
BLOCK 15	MEAN	35.0	113.8	35.6	26.4	31.8	8.8	18.3	46.0	7.1	25.3	10.4	50.5
BLOCK 16	MEAN	37.6	104.6	49.1	24.6	19.8	9.2	9.9	55.6	6.7	18.8	1.3	54.3
BLOCK 17	MEAN	31.0	124.1	16.1	12.7	23.0	10.5	3.0	34.6	5.7	14.9	1.1	71.2
BLOCK 18	MEAN	34.5	114.8	7.2	16.8	25.9	16.9	7.2	30.5	0.7	13.6	0.1	68.2
<b>TOTAL TIME SPENT IN MOVEMENT</b>	MEAN	824.2	2352.1	1302.6	1308.1	1004.0	958.5	1191.5	1493.5	889.3	913.7	1171.6	1680.1

**Table 16: Summary of Motor Activity Historical Control Data in Crl:CD1(ICR) Male Mice:  
Time Spent in Movement (Seconds)**

	<b>#Evaluations <u>Included</u></b>	<b><u>Average</u></b>	<b><u>Minimum</u></b>	<b><u>Maximum</u></b>
Block 1	12	129.6	85.1	162.8
Block 2	12	109.8	70.3	155.0
Block 3	12	97.0	70.5	144.3
Block 4	12	92.2	70.0	134.2
Block 5	12	88.9	68.9	126.4
Block 6	12	83.3	54.5	125.0
Block 7	12	78.5	38.7	133.5
Block 8	12	66.0	29.1	111.7
Block 9	12	61.5	24.4	105.6
Block 10	12	55.6	15.3	110.5
Block 11	12	50.1	5.0	95.4
Block 12	12	48.0	6.4	97.0
Block 13	12	48.9	20.5	105.3
Block 14	12	43.8	15.8	106.3
Block 15	12	44.7	19.7	101.6
Block 16	12	36.4	12.7	86.6
Block 17	12	29.8	6.9	81.7
Block 18	12	29.0	5.3	97.0
<b>Total Time Spent in Movement</b>	12	1190.3	720.5	2079.8

**Table 17: Summary of Motor Activity Historical Control Data in Crl:CD1(ICR) Female Mice:  
Time Spent in Movement (Seconds)**

	<b>#Evaluations <u>Included</u></b>	<b><u>Average</u></b>	<b><u>Minimum</u></b>	<b><u>Maximum</u></b>
Block 1	12	135.7	92.5	162.4
Block 2	12	118.7	76.1	154.7
Block 3	12	107.7	59.5	157.3
Block 4	12	102.3	54.1	148.2
Block 5	12	97.0	48.0	150.7
Block 6	12	93.9	47.1	135.6
Block 7	12	84.3	35.5	130.6
Block 8	12	81.8	43.6	131.0
Block 9	12	66.7	34.4	126.9
Block 10	12	62.4	26.2	111.2
Block 11	12	55.4	21.5	125.3
Block 12	12	49.4	17.1	122.3
Block 13	12	40.8	2.8	117.5
Block 14	12	37.5	3.7	120.9
Block 15	12	34.1	7.1	113.8
Block 16	12	32.6	1.3	104.6
Block 17	12	29.0	1.1	124.1
Block 18	12	28.0	0.1	114.8
<b>Total Time Spent in Movement</b>	12	1257.4	824.2	2352.1







