charles river

Historical Control Data in Rats

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TABLE OF CONTENTS

Sprague Dawley and Wistar Rats

HCD [1]		Date Range	Page
Sprague Dawley Rats			
1.	Historical Control Fertility and Early Embryonic Development to Implantation Data	Jan 2015 - Jan 2020	3
2.	Historical Control Range-Finding Developmental Toxicity Data	Nov 2014 - Nov 2019	7
3.	Historical Control Developmental Toxicity Data (GD 21)	Jan 2018 - Dec 2019	9
4.	Historical Control Pre- and Postnatal Development, Including Maternal Function Data	Jan 2015 - Jan 2020	12
5.	Historical Control Two Generation Reproduction Data	Jan 2011 - May 2019	17
Wistar Rats			
1.	Historical Control Developmental Toxicity Data (GD 21)	Jan 2018 - Apr 2020	23

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[1] **Additional HCD endpoints and years are available upon request.**

Charles River Laboratories - Mattawan
Historical Control Fertility and
Early Embryonic Development to Implantation Data
Sprague Dawley Rat - Charles River Laboratories
1 Jan 2015 to 1 Jan 2020

Premating Estrous Cycling (14 Days)	Number of Control Groups	Mean	Minimum	Maximum
Mean Cycle Length (Days)	19	4.44	4.0	4.9
No. of Cycles (Count)	19	2.55	2.1	2.8

Reproductive and Fertility Parameters	Number of Control Groups	Number of Animals
No. Females on Study	26	604
No. Females Paired	26	602
No. Females Mated	26	601
No. Pregnant	26	574
No. Males on Study	21	488
No. Males Paired	21	484
No. Males Mated	21	472
No. Males Impregnating a Female	21	451
Females with Confirmed Mating Day	28	612

Reproductive and Fertility Parameters	Number of Control Groups	Mean	Minimum	Maximum
Female Mating Index	26	99.83	95.5	100.0
Female Fertility Index	26	95.38	75.0	100.0
Female Fecundity Index	26	95.55	75.0	100.0
Male Mating Index	21	97.52	84.0	100.0
Male Fertility Index	21	93.33	76.0	100.0
Male Fecundity Index	21	95.49	86.4	100.0
Mean Copulatory Interval (Days)	29	2.86	2.0	4.5

No. - Number

Charles River Laboratories - Mattawan
Historical Control Fertility and
Early Embryonic Development to Implantation Data
Sprague Dawley Rat - Charles River Laboratories
1 Jan 2015 to 1 Jan 2020

Maternal and Developmental Observations at Uterine Examination	Number of Control Groups	Number of Animals
No. Females on Study	28	651
No. Not Pregnant	28	39
No. Pregnant	28	612
No. Died Pregnant	28	0
No. Females with All Resorptions	28	1
No. Pregnant Detected by Stain	28	0
No. Females Pregnant No Mating Date	28	38
No. Females with Viable Embryos Day 13 Gestation	28	573

Maternal and Developmental Observations at Uterine Examination	Number of Control Groups	Mean	Minimum	Maximum
Corpora Lutea (Mean No. per Animal)	28	16.66	14.4	18.8
Implantation Sites (Mean No. per Animal)	28	14.68	12.7	16.2
Preimplantation Loss (Mean % Implants per Animal)	28	11.305	4.77	18.51
Viable Embryos (Mean No. per Animal)	28	13.84	12.0	15.3
Postimplantation Loss (Mean % Implants per Animal)	28	6.016	3.51	10.87
Resorptions (Mean No. per Animal)	28	0.84	0.5	1.5

Sperm Evaluation	Number of Control Groups	Mean	Minimum	Maximum
Sperm Motility (Mean % Motility)	21	86.75	77.2	98.0
Total Sperm Concentration per Cauda Epididymis x 10^8 (Mean)	21	2.8457	2.362	3.342
Sperm Concentration per gram Cauda Epididymis x 10^8 (Mean)	21	11.7783	8.152	54.807
Percent Abnormal (Mean)	20	3.662	2.07	7.83

No. - Number

Charles River Laboratories - Mattawan
Historical Control Fertility and Early Embryonic Development to Implantation Data
Sprague Dawley Rat - Charles River Laboratories
1 Jan 2015 to 1 Jan 2020

Organ Weights - Males

				Compared to Body Weight, percent		
	N	Mean	Range of Study Values (Means)	N	Mean	Range of Study Values (Means)
Body, g	21	543.3	440 - 580	NA	NA	NA
Epididymides, g	21	1.3549	1.179 - 1.437	20	0.24943	0.2292 - 0.2704
Prostate gland, g	21	1.0958	0.992 - 1.328	20	0.20179	0.1787 - 0.2339
Seminal vesicle with coagulating gland, g	21	2.3165	2.048 - 2.761	20	0.42685	0.3769 - 0.4852
Testes, g	21	3.5661	3.401 - 3.673	20	0.65700	0.6148 - 0.7784

N - Number of Control Groups
NA - Not Applicable
Page 3

Version 17.0

Charles River Laboratories - Mattawan
Historical Control Fertility and Early Embryonic Development to Implantation Data
Sprague Dawley Rat - Charles River Laboratories
1 Jan 2015 to 1 Jan 2020

Organ Weights - Females

	N	**Mean**	**Range of Study Values (Means)**
Body, g	23	314.0	290 - 331
Ovaries, g	24	0.1113	0.090 - 0.142
Uterus with cervix, g	23	8.6094	7.684 - 9.740

N - Number of Control Groups
NA - Not Applicable
Page 4

Version 17.0

Charles River Laboratories - Mattawan
Historical Control Range-Finding Developmental Toxicity Data
Sprague Dawley Rat - Charles River Laboratories
1 Nov 2014 to 1 Nov 2019

Pregnancy Data	Total
No. Control Groups	4
No. Females	34
No. Not Pregnant	1
No. Pregnant	33
No. Died Pregnant	0
No. Females with All Resorptions	0
No. Pregnant By Stain	0
No. Females with Viable Fetuses	33

Maternal and Developmental Observations at Uterine Examination and Fetal Body Weight Values	Mean	Minimum	Maximum
Pregnancy Index (%)	96.88	87.5	100.0
Corpora Lutea (Mean No. per Animal)	13.98	12.8	15.3
Implantation Sites (Mean No. per Animal)	12.68	12.0	13.7
Preimplantation Loss (Mean % per Animal)	8.070	4.80	11.72
Viable Fetuses (Mean No. per Animal)	11.63	10.1	12.8
Fetal Sex Ratio (Mean % Males per Animal)	49.07	43.5	53.1
Postimplantation Loss (Mean % per Animal)	8.873	3.63	16.93
Nonviable Fetuses (Mean No. per Animal)	0.00	0.0	0.0
Resorptions: Early and Late (Mean No. per Animal)	1.03	0.4	2.0
Resorptions: Early (Mean No. per Animal)	0.98	0.4	2.0
Resorptions: Late (Mean No. per Animal)	0.08	0.0	0.2
Mean Fetal Body Weight Male (grams)	4.219	4.10	4.37
Mean Fetal Body Weight Female (grams)	4.007	3.96	4.05
Mean Fetal Body Weight Males and Females (grams)	4.110	4.01	4.23

No. - Number

Charles River Laboratories - Mattawan
Historical Control Range-Finding Developmental Toxicity Data
Sprague Dawley Rat - Charles River Laboratories
1 Nov 2014 to 1 Nov 2019

Litter Data	Total
No. Litters Evaluated	33
No. External Fetuses Evaluated	383
No. Visceral Fetuses Evaluated	241
No. Skeletal Fetuses Evaluated	243

	Total Number		Maximum %	
	Fetuses	Litters	Fetuses	Litters
Visceral Malformation				
Thoracic cavity, thyroid, absent	1	1	1.0	10.0
Skeletal Malformation				
Rib(s), costal cartilage, fused	1	1	2.9	16.7
Skeletal Variation				
Cervical vertebra(e), neural arch(es), additional ossification center	2	1	3.1	10.0
Pectoral girdle, scapula, superior border irregular	1	1	2.3	14.3
Pelvic girdle, pubis, not ossified	1	1	1.6	10.0
Rib(s), bent	4	4	3.1	20.0
Rib(s), rudimentary	6	6	6.8	42.9
Rib(s), smaller than normal	3	3	3.1	20.0
Rib(s), unilateral full rib	1	1	2.9	16.7
Sacral vertebra(e), neural arch(es), incompletely ossified	1	1	1.6	10.0
Skull, hyoid, not ossified	16	10	29.4	66.7
Skull, interparietal bone, incompletely ossified	1	1	2.9	16.7
Skull, jugal, incompletely ossified	4	4	4.7	30.0
Skull, parietal bone, incompletely ossified	4	4	4.7	30.0
Skull, squamosal, incompletely ossified	4	4	6.3	40.0
Skull, supra occipital bone, incompletely ossified	4	4	3.1	20.0
Sternum, sternebra(e), misaligned	1	1	2.9	16.7
Sternum, sternebra(e), not ossified	33	14	29.7	83.3

No. - Number

Charles River Laboratories - Mattawan
Historical Control Developmental Toxicity Data
Sprague Dawley Rat (GD 21) - Charles River Laboratories
1 Jan 2018 to 1 Dec 2019

Pregnancy Data (GD 21)	Total
No. Control Groups	11
No. Females	260
No. Not Pregnant	10
No. Pregnant	250
No. Died Pregnant	0
No. Females with All Resorptions	0
No. Pregnant By Stain	0
No. Females with Viable Fetuses	250

Maternal and Developmental Observations at Uterine Examination and Fetal Body Weight Values	Mean	Minimum	Maximum
Pregnancy Index (%)	96.22	87.5	100.0
Corpora Lutea (Mean No. per Animal)	15.24	14.0	16.6
Implantation Sites (Mean No. per Animal)	13.25	12.4	14.2
Preimplantation Loss (Mean % per Animal)	12.290	10.40	13.82
Viable Fetuses (Mean No. per Animal)	12.60	11.7	13.7
Fetal Sex Ratio (Mean % Males per Animal)	51.65	43.2	57.8
Postimplantation Loss (Mean % per Animal)	5.334	3.15	10.25
Nonviable Fetuses (Mean No. per Animal)	0.00	0.0	0.0
Resorptions: Early and Late (Mean No. per Animal)	0.65	0.4	1.0
Resorptions: Early (Mean No. per Animal)	0.62	0.4	1.0
Resorptions: Late (Mean No. per Animal)	0.01	0.0	0.1
Mean Fetal Body Weight Male (grams)	6.134	5.43	6.40
Mean Fetal Body Weight Female (grams)	5.798	5.15	6.06
Mean Fetal Body Weight Males and Females (grams)	5.971	5.29	6.23

No. - Number

Charles River Laboratories - Mattawan
Historical Control Developmental Toxicity Data
Sprague Dawley Rat (GD 21) - Charles River Laboratories
1 Jan 2018 to 1 Dec 2019

Litter Data	Total
No. Litters Evaluated	250
No. External Fetuses Evaluated	3153
No. Visceral Fetuses Evaluated	2184
No. Skeletal Fetuses Evaluated	2206

	Total Number		Maximum %	
	Fetuses	Litters	Fetuses	Litters
External Malformation				
Body, dorsal surface, spina bifida	1	1	0.3	4.0
Head, eye(s), microphthalmia	1	1	0.3	4.0
Head, palate, cleft palate	1	1	0.4	5.0
Hind limb(s), entire, malrotated	4	4	0.7	8.7
External Pathological				
Placenta, entire, larger than normal	6	2	1.1	4.8
External Variation				
Body, skin, dermal hypoplasia	1	1	0.3	4.2
Visceral Malformation				
Abdominal cavity, abdomen, situs inversus complete	1	1	0.8	5.0
Abdominal cavity, kidney, misshapen	1	1	0.3	4.2
Head, retina, folded retina	7	6	2.8	13.0
Thoracic cavity, aortic arch, dilated	1	1	0.8	5.0
Thoracic cavity, situs inversus complete	1	1	0.8	5.0
Visceral Pathological				
Abdominal cavity, adrenal, discolored	17	12	3.4	25.0
Thoracic cavity, thyroid, discolored	2	2	0.6	8.3
Visceral Variation				
Abdominal cavity, ureter, dilated	2	2	0.6	8.3
Mouth, palate, rugae irregular	4	4	2.0	12.0
Thoracic cavity, esophagus, malpositioned	1	1	0.7	4.2
Skeletal Malformation				
Lumbar vertebra(e), neural arch(es), misshapen	1	1	0.7	4.0
Pelvic girdle, pubis, bent	1	1	0.3	4.2
Rib(s), fused	1	1	0.7	4.3
Sternum, sternebra(e), fused	2	2	1.4	8.7
Skeletal Variation				
Cervical vertebra(e), neural arch(es), additional ossification center	18	15	2.0	16.7

No. - Number

Charles River Laboratories - Mattawan
Historical Control Developmental Toxicity Data
Sprague Dawley Rat (GD 21) - Charles River Laboratories
1 Jan 2018 to 1 Dec 2019

	Total Number		Maximum %	
	Fetuses	**Litters**	**Fetuses**	**Litters**
Forelimb(s), humerus, irregular ossification	1	1	0.4	4.8
Lumbar vertebra(e), neural arch(es), not ossified	1	1	0.3	4.2
Pectoral girdle, scapula, superior border irregular	44	34	4.8	20.8
Pelvic girdle, ischium, incompletely ossified	1	1	0.3	4.2
Pelvic girdle, ischium, not ossified	1	1	0.3	4.2
Pelvic girdle, pubis, not ossified	1	1	0.3	4.2
Rib(s), bent	5	4	0.8	5.0
Rib(s), rudimentary	261	116	16.4	58.3
Rib(s), smaller than normal	8	8	0.7	9.5
Rib(s), unilateral full rib	1	1	0.7	4.3
Sacral vertebra(e), neural arch(es), not ossified	1	1	0.3	4.2
Skull, frontal bone, additional ossification center	2	2	0.8	5.0
Skull, hyoid, not ossified	36	19	7.8	37.5
Skull, interparietal bone, additional ossification center	1	1	0.8	5.0
Skull, interparietal bone, incompletely ossified	1	1	0.8	5.0
Skull, jugal, incompletely ossified	9	5	1.5	5.0
Skull, parietal bone, incompletely ossified	4	4	0.7	8.3
Skull, squamosal, incompletely ossified	5	4	0.6	8.3
Skull, supra occipital bone, incompletely ossified	1	1	0.3	4.2
Sternum, sternebra(e), extra	1	1	0.7	4.3
Sternum, sternebra(e), misaligned	5	5	0.8	5.0
Sternum, sternebra(e), not ossified	32	17	6.9	29.2

Charles River Laboratories - Mattawan
Historical Control Pre- and Postnatal Development, Including Maternal Function Data
Sprague Dawley Rat - Charles River Laboratories
1 Jan 2015 to 1 Jan 2020

P Natural Delivery and Litter Data	Total
No. of Control Groups	16
No. of Females on Study	387
No. of Females Pregnant	379
Females Delivering Litters	377
Females With at Least One, But Not all Stillborn Pups	25
Females With All Stillborn	0

P Natural Delivery and Litter Data	Number of Control Groups	Mean	Minimum	Maximum
Mean Gestation Length (Days)	16	21.79	21.4	22.0
Mean No. of Pups at Day 0				
Total Pups Born/Litter	16	12.27	10.9	13.4
Liveborn/Litter	16	12.16	10.8	13.3
Stillborn/Litter	16	0.09	0.0	0.3
Gestation Index (%)	16	89.40	19.0	100.0
Stillborn Index (Mean %/Litter)	16	0.937	0.00	3.36
Mean Total Implantation Scars/Litter	16	12.99	11.4	14.0
Mean No. of Live Pups/Litter				
Day 4 (Preculling)	16	12.02	10.7	13.2
Day 4 (Postculling)	16	7.94	7.8	8.0
Day 7	16	7.94	7.8	8.0
Day 14	16	7.94	7.8	8.0
Day 21	16	7.86	7.6	8.0
Day 24	2	7.80	7.6	8.0
Day 28	16	7.86	7.6	8.0
Sex Ratio (% Males per Animal) (Mean %/Litter)				
Pups Day 0	16	50.226	47.69	54.20
Pups Day 4 (Preculling)	16	50.198	47.27	55.02
Pups Day 4 (Postculling)	16	50.101	47.92	54.35
Pups Day 21	14	50.157	47.32	54.35
Pups Day 24	2	48.495	48.21	48.78
Pup Survival Indices (Mean %/Litter)				
Viability Index	16	97.796	93.24	99.65
Lactation Index	16	98.793	94.50	100.00

No. - Number

Charles River Laboratories - Mattawan
Historical Control Pre- and Postnatal Development, Including Maternal Function Data
Sprague Dawley Rat - Charles River Laboratories
1 Jan 2015 to 1 Jan 2020

F1 Pup Body Weight Values, g (Mean)	Number of Control Groups	Mean	Minimum	Maximum
Day 0				
Males	16	7.154	6.50	7.50
Females	16	6.788	6.19	7.07
Males + Females	16	6.974	6.35	7.30
Day 4 Preculling				
Males	16	11.932	10.84	12.52
Females	16	11.400	10.44	11.95
Males + Females	16	11.676	10.64	12.25
Day 7				
Males	16	19.477	17.72	20.66
Females	16	18.644	16.92	19.85
Males + Females	16	19.068	17.32	20.27
Day 14				
Males	16	38.426	36.17	40.38
Females	16	37.138	34.86	39.38
Males + Females	16	37.786	35.51	39.88
Day 21				
Males	16	62.136	57.36	65.38
Females	16	59.512	55.56	62.22
Males + Females	16	60.811	56.44	63.80
Day 24				
Males	3	79.997	78.94	81.77
Females	3	75.043	73.90	76.23
Males + Females	3	77.493	76.28	79.16
Day 28				
Males	16	106.813	94.93	113.05
Females	16	97.280	86.94	102.48
Males + Females	16	102.023	90.96	107.56

F1 Physical Development	Number of Control Groups	Mean	Minimum	Maximum
Mean Static Righting Reflex (Days)	15	2.37	2.1	2.8
Mean Pinna Detachment (Days)	15	2.41	2.1	2.7
Mean Cliff Aversion (Days)	15	11.06	11.0	11.3
Mean Eye Opening (Days)	15	14.27	14.0	15.0
Mean Air Drop Righting Reflex (Days)	15	16.20	16.0	17.0
Mean Auditory Response (Percent Pups Passing/Dam)	15	100.00	100.0	100.0

F1 Sexual Maturation	Number of Control Groups	Mean	Minimum	Maximum
Mean Vaginal Opening (Days)	16	31.76	31.2	32.5
Mean Body Weight on Day Passed Vaginal Opening, g	16	121.69	109.4	131.4
Mean Preputial Separation (Days)	16	41.49	39.9	42.7
Mean Body Weight on Day Passed Preputial Separation, g	16	241.12	216.6	267.8

Charles River Laboratories - Mattawan
Historical Control Pre- and Postnatal Development, Including Maternal Function Data
Sprague Dawley Rat - Charles River Laboratories
1 Jan 2015 to 1 Jan 2020

F1 Behavioral Observations (Motor Activity) - Male Hamilton Kinder Motor Monitor System	Number of Control Groups	Mean	Minimum	Maximum
Mean Basic Movement (count)				
0 - 5 Minutes	15	1431.67	1292.0	1689.4
5 -10 Minutes	15	1103.28	959.3	1296.7
10 -15 Minutes	15	840.46	677.7	1048.0
15-20 Minutes	15	611.59	408.6	858.6
0-20 Minutes	14	4068.14	3547.3	4946.4
Mean Fine Movement (count)				
0 - 5 Minutes	15	840.88	726.0	979.0
5 -10 Minutes	15	743.97	657.3	846.8
10 -15 Minutes	15	609.80	503.5	757.1
15-20 Minutes	15	469.33	329.4	638.2
0-20 Minutes	14	2710.06	2359.0	3214.2
Mean Rearing (count)				
0 - 5 Minutes	15	40.13	30.9	57.7
5 -10 Minutes	15	28.25	19.4	51.3
10 -15 Minutes	15	18.11	12.2	40.0
15-20 Minutes	15	11.19	5.0	34.4
0-20 Minutes	14	101.98	78.2	186.4
Mean Total Distance (cm)				
0 - 5 Minutes	15	2586.55	2365.6	3018.8
5 -10 Minutes	15	1967.57	1743.0	2283.8
10 -15 Minutes	15	1522.33	1274.0	1855.8
15-20 Minutes	15	1174.53	854.0	1590.4
0-20 Minutes	14	7271.09	6495.5	8748.9

F1 Behavioral Observations (Motor Activity) - Female Hamilton Kinder Motor Monitor System	Number of Control Groups	Mean	Minimum	Maximum
Mean Basic Movement (count)				
0 - 5 Minutes	15	1559.21	1370.8	1902.0
5 -10 Minutes	15	1219.65	985.9	1551.5
10 -15 Minutes	15	917.70	719.7	1216.0
15-20 Minutes	15	688.61	466.1	1086.0
0-20 Minutes	14	4449.04	3815.3	5790.1
Mean Fine Movement (count)				
0 - 5 Minutes	15	903.47	775.5	1104.4
5 -10 Minutes	15	792.97	667.1	982.4
10 -15 Minutes	15	642.31	530.4	818.4
15-20 Minutes	15	501.08	349.0	771.8
0-20 Minutes	14	2873.51	2517.5	3696.9
Mean Rearing (count)				
0 - 5 Minutes	15	43.65	33.0	58.6
5 -10 Minutes	15	32.67	25.0	49.7
10 -15 Minutes	15	21.25	14.6	39.1
15-20 Minutes	15	14.02	7.1	32.8
0-20 Minutes	14	115.54	87.0	176.9
Mean Total Distance (cm)				
0-5 Minutes	15	2784.20	2468.0	3353.5
5 -10 Minutes	15	2155.27	1747.6	2704.4
10 -15 Minutes	15	1650.42	1325.1	2141.7
15-20 Minutes	15	1301.40	1037.0	1925.4
0-20 Minutes	14	7895.74	6785.4	10125.0

Charles River Laboratories - Mattawan
Historical Control Pre- and Postnatal Development, Including Maternal Function Data
Sprague Dawley Rat - Charles River Laboratories
1 Jan 2015 to 1 Jan 2020

F1 Behavioral Observations (Passive Avoidance) - Male	Total
No. of Control Groups	14
No. of Animals Tested	327
Non-Responsive Animals	0

F1 Behavioral Observations (Passive Avoidance) - Male	No. of Control Groups	Mean	Minimum	Maximum
Non-Responsive Animals (%)	14	0.00	0.0	0.0
Passive (%)	14	80.46	44.0	100.0
Non-Passive (%)	14	19.54	0.0	56.0
No. of Trials (Passive Animal Only) (%)				
3	14	46.01	10.0	90.0
4	14	37.56	10.0	80.0
5	14	16.44	0.0	54.5

F1 Behavioral Observations (Passive Avoidance) - Female	Total
No. of Control Groups	14
No. of Animals Tested	328
Non-Responsive Animals	0

F1 Behavioral Observations (Passive Avoidance) - Female	No. of Control Groups	Mean	Minimum	Maximum
Non-Responsive Animals	14	0.00	0.0	0.0
Passive	14	74.30	36.0	95.0
Non-Passive (%)	14	25.71	5.0	64.0
No. of Trials (Passive Animal Only) (%)				
3	14	28.57	0.0	52.4
4	14	52.67	31.8	81.8
5	14	18.75	5.6	33.3

No. - Number

Charles River Laboratories - Mattawan
Historical Control Pre- and Postnatal Development, Including Maternal Function Data
Sprague Dawley Rat - Charles River Laboratories
1 Jan 2015 to 1 Jan 2020

F1 Reproductive and Fertility Parameters	Total
No. of Control Groups	15
No. of Females on Study	362
No. of Males on Study	362

F1 Reproductive and Fertility Parameters	Number of Control Groups	Mean	Minimum	Maximum
Female Mating Index	16	97.83	90.0	100.0
Female Fertility Index	16	92.95	80.0	100.0
Female Fecundity Index	16	95.03	80.0	100.0
Male Mating Index	16	97.21	80.0	100.0
Male Fertility Index	16	92.31	75.0	100.0
Male Fecundity Index	16	94.97	80.0	100.0
Mean Copulatory Interval (Days)	16	3.23	2.3	5.0

F1 Maternal and Developmental Observations at Gestation Day 13 Uterine Examination	Total
No. of Control Groups	15
No. of Females on Study	362
No. Not Pregnant	23
No. Pregnant	339
No. Died Pregnant	0
No. of Females with All Resorptions	0
No. of Females Pregnant by Stain	0
No. of Females with Viable Embryos Day 13 Gestation	318
No. of Females Pregnant with No Confirmed Mating Date	21

F1 Maternal and Developmental Observations at Gestation Day 13 Uterine Examination	Number of Control Groups	Mean	Minimum	Maximum
Corpora Lutea (Mean No. per Animal)	15	17.75	16.5	19.3
Implantation Sites (Mean No. per Animal)	15	15.60	13.0	16.4
Preimplantation Loss (Mean % per Animal)	15	11.788	5.78	21.73
Viable Embryos (Mean No. per Animal)	15	14.71	12.3	15.7
Postimplantation Loss (Mean% Implants per Animal)	15	5.531	2.72	8.39
Resorptions (Mean No. per Animal)	15	0.87	0.4	1.4

No. - Number

Charles River Laboratories - Mattawan
Historical Control Two Generation Reproduction Data
Sprague Dawley Rat - Charles River Laboratories
1/1/2011 to 5/1/2019

Study Details	Total
No. Of Studies	**2**
P Generation Study Details	
No. Females	54
No. Females Pregnant	53
F1 Generation Study Details	
No. Females	52
No. Females Pregnant	51

Reproductive and Fertility Parameters	Number of Control Groups	Mean	Minimum	Maximum
P Generation				
Female Mating Index (%)	2	100.00	100.0	100.0
Female Fertility Index (%)	2	98.10	96.2	100.0
Female Fecundity Index (%)	2	98.10	96.2	100.0
Male Mating Index (%)	2	100.00	100.0	100.0
Male Fertility Index (%)	2	98.10	96.2	100.0
Male Fecundity Index (%)	2	98.10	96.2	100.0
Mean Copulatory Interval (days)	2	3.30	3.0	3.6
F1 Generation				
Female Mating Index (%)	2	100.00	100.0	100.0
Female Fertility Index (%)	2	98.10	96.2	100.0
Female Fecundity Index (%)	2	98.10	96.2	100.0
Male Mating Index (%)	2	100.00	100.0	100.0
Male Fertility Index (%)	2	98.10	96.2	100.0
Male Fecundity Index (%)	2	98.10	96.2	100.0
Mean Copulatory Interval (days)	2	3.00	2.8	3.2

Premating Estrous Cycling	Number of Control Groups	Mean	Minimum	Maximum
P Generation				
Mean Cycle Length (Days)	2	5.30	5.2	5.4
No. of Cycles (Count) Mean	2	3.50	3.5	3.5
F1 Generation				
Mean Cycle Length (Days)	2	4.90	4.4	5.4
No. of Cycles (Count) Mean	2	4.00	3.8	4.2
Mean Primordial Follicle Count per Animal	2	183.50	127.3	239.7

Charles River Laboratories - Mattawan
Historical Control Two Generation Reproduction Data
Sprague Dawley Rat - Charles River Laboratories
1/1/2011 to 5/1/2019

Natural Delivery and Litter Data	Number of Control Groups	Mean	Minimum	Maximum
P Generation				
Mean Gestation Length (days)	2	22.05	21.9	22.2
Gestation Index (%)	2	98.00	96.0	100.0
Stillborn Index (Mean %/Litter)	2	2.80	0.9	4.7
Mean Implantation Scars/Litter	2	15.10	15.1	15.1
No. of Females that Failed to Deliver	2	0.00	0.0	0.0
P Generation Mean Number of Live Pups/Litter				
Day 0	2	13.85	13.2	14.5
Day 4 (preculling)	2	13.20	12.9	13.5
Day 7	2	7.85	7.8	7.9
Day 14	2	7.65	7.5	7.8
Day 21	2	7.60	7.4	7.8
P Generation Pup Survival Indices				
Viability Index (Mean %/Litter)	2	94.300	93.76	94.84
Lactation Index (Mean %/Litter)	2	95.580	92.50	98.66
P Generation Pup Sex Ratio (% Males per Animal)				
Day 0 (Mean %/Litter)	2	51.82	49.2	54.5
Day 21 (Mean %/Litter)	2	51.16	50.3	52.0
F1 Generation				
Mean Gestation Length (days)	2	22.00	21.9	22.1
Gestation Index (%)	2	100.00	100.0	100.0
Stillborn Index (Mean %/Litter)	2	1.32	0.2	2.4
Mean Implantation Scars/Litter	2	15.05	15.0	15.1
No. of Females that Failed to Deliver	2	0.00	0.0	0.0
F1 Generation Mean Number of Live Pups/Litter				
Day 0	2	13.85	13.7	14.0
Day 4 (preculling)	2	13.55	13.3	13.8
Day 7	2	7.90	7.8	8.0
Day 14	2	7.90	7.8	8.0
Day 21	2	7.90	7.8	8.0
F1 Generation Pup Survival Indices				
Viability Index (Mean %/Litter)	2	97.580	97.03	98.13
Lactation Index (Mean %/Litter)	2	100.000	100.00	100.00
F1 Generation Pup Sex Ratio (% Males per Animal)				
Day 0 (Mean %/Litter)	2	47.90	47.4	48.4
Day 21 (Mean %/Litter)	2	50.10	49.5	50.7

Charles River Laboratories - Mattawan
Historical Control Two Generation Reproduction Data
Sprague Dawley Rat - Charles River Laboratories
1/1/2011 to 5/1/2019

Preweaning Pup Body Weight Values	Number of Control Groups	Mean	Minimum	Maximum
P Generation Mean Pup Body Weights (grams)				
Day 0 Females	2	6.260	6.23	6.29
Day 4 (preculling) Females	2	9.425	9.23	9.62
Day 7 Females	2	16.105	15.91	16.30
Day 14 Females	2	34.030	33.40	34.66
Day 21 Females	2	55.900	55.79	56.01
Day 0 Males	2	6.625	6.59	6.66
Day 4 (preculling) Males	2	9.845	9.68	10.01
Day 7 Males	2	16.615	16.52	16.71
Day 14 Males	2	35.360	34.52	36.20
Day 21 Males	2	58.105	57.47	58.74
Day 0 Total	2	6.455	6.43	6.48
Day 4 (preculling) Total	2	9.660	9.50	9.82
Day 7 Total	2	16.360	16.25	16.47
Day 14 Total	2	34.680	33.90	35.46
Day 21 Total	2	56.710	55.98	57.44
F1 Generation Mean Pup Body Weights (grams)				
Day 0 Females	2	6.350	6.24	6.46
Day 4 (preculling) Females	2	10.115	10.04	10.19
Day 7 Females	2	17.155	17.14	17.17
Day 14 Females	2	35.635	35.52	35.75
Day 21 Females	2	57.990	57.48	58.50
Day 0 Males	2	6.775	6.72	6.83
Day 4 (preculling) Males	2	10.700	10.63	10.77
Day 7 Males	2	18.010	18.01	18.01
Day 14 Males	2	36.765	36.69	36.84
Day 21 Males	2	60.480	59.78	61.18
Day 0 Total	2	6.550	6.48	6.62
Day 4 (preculling) Total	2	10.395	10.35	10.44
Day 7 Total	2	17.565	17.53	17.60
Day 14 Total	2	36.175	36.04	36.31
Day 21 Total	2	59.195	58.64	59.75

Charles River Laboratories - Mattawan
Historical Control Two Generation Reproduction Data
Sprague Dawley Rat - Charles River Laboratories
1/1/2011 to 5/1/2019

Sperm Evaluation	Number of Control Groups	Mean	Minimum	Maximum
P Generation				
Sperm Motility (Mean % Motility)	2	88.45	85.8	91.1
Total Sperm Concentration per Cauda Epididymis x 10^8 (Mean)	2	2.9050	2.499	3.311
Sperm Concentration per gram Cauda Epididymis x 10^8 (Mean)	2	8.9040	7.964	9.844
Percent Abnormal (Mean)	2	7.100	4.75	9.45
F1 Generation				
Sperm Motility (Mean % Motility)	2	87.25	83.7	90.8
Total Sperm Concentration per Cauda Epididymis x 10^8 (Mean)	2	3.3195	3.285	3.354
Sperm Concentration per gram Cauda Epididymis x 10^8 (Mean)	2	10.1685	10.002	10.335
Percent Abnormal (Mean)	2	2.51	2.37	2.65

F1 Sexual Maturation	Number of Control Groups	Mean	Minimum	Maximum
Vaginal Opening (Days) Mean	2	33.00	32.5	33.5
Body Weight on Day Passed Vaginal Opening, g	2	123.50	117.2	129.8
Preputial Separation (Days) Mean	2	44.40	44.3	44.5
Body Weight on Day Passed Preputial Separation, g	2	234.20	232.6	235.8

Charles River Laboratories - Mattawan
Historical Control Two Generation Reproduction Data
Sprague Dawley Rat - Charles River Laboratories
P Generation
1/1/2011 to 5/1/2019

Organ Weights - Males

				Compared to Body Weight, percent		
	N	Mean	Range	N	Mean	Range
Body weight, g	2	592.5	585 - 600	NA	NA	NA
Cauda, epididymis, right, g	2	0.3245	0.311 - 0.338	2	0.05530	0.0539 - 0.0567
Epididymides, g	2	1.4205	1.387 - 1.454	2	0.24190	0.2402 - 0.2436
Prostate gland, g	2	0.9700	0.751 - 1.189	2	0.16545	0.1260 - 0.2049
Seminal vesicles with coagulating glands, g	2	2.2800	2.192 - 2.368	2	0.38790	0.3790 - 0.3968
Testes, g	2	3.7375	3.686 - 3.789	2	0.63735	0.6192 - 0.6555

Organ Weights - Females

				Compared to Body Weight, percent		
	N	Mean	Range	N	Mean	Range
Body weight, g	2	323.5	314 - 333	NA	NA	NA
Ovaries, g	2	0.1045	0.104 - 0.105	2	0.03245	0.0314 - 0.0335
Uterus with cervix, g	1	0.6430	0.643 - 0.643	1	0.20600	0.2060 - 0.2060
Uterus with oviducts and cervix, g	1	1.2350	1.235 - 1.235	1	0.37090	0.3709 - 0.3709

Charles River Laboratories - Mattawan
Historical Control Two Generation Reproduction Data
Sprague Dawley Rat - Charles River Laboratories
F1 Generation
1/1/2011 to 5/1/2019

Organ Weights - Males

				Compared to Body Weight, percent		
	N	Mean	Range	N	Mean	Range
Body weight, g	2	625.0	618 - 632	NA	NA	NA
Cauda, epididymis, right, g	2	0.3265	0.319 - 0.334	2	0.05270	0.0510 - 0.0544
Epididymides, g	2	1.4585	1.455 - 1.462	2	0.23535	0.2336 - 0.2371
Prostate gland, g	2	0.8385	0.594 - 1.083	2	0.13445	0.0976 - 0.1713
Seminal vesicles with coagulating glands, g	2	2.2740	2.185 - 2.363	2	0.36560	0.3554 - 0.3758
Testes, g	2	3.8430	3.812 - 3.874	2	0.62035	0.6182 - 0.6225

Organ Weights - Females

				Compared to Body Weight, percent		
	N	Mean	Range	N	Mean	Range
Body weight, g	2	346.0	343 - 349	NA	NA	NA
Ovaries, g	2	0.1060	0.100 - 0.112	2	0.03070	0.0287 - 0.0327
Uterus with cervix, g	1	0.5850	0.585 - 0.585	1	0.16800	0.1680 - 0.1680
Uterus with oviducts and cervix, g	1	1.4340	1.434 - 1.434	1	0.41810	0.4181 - 0.4181

Charles River Laboratories - Mattawan
Historical Control Developmental Toxicity Data
Wistar Han Rat (GD 21) - Charles River Laboratories
1 Jan 2018 to 1 Apr 2020

Pregnancy Data (GD 21)	Total
No. Studies	4
No. Females	100
No. Not Pregnant	2
No. Pregnant	98
No. Early Deliveries	3
No. Died Pregnant	0
No. Females with All Resorptions	1
No. Pregnant By Stain	0
No. Females with Viable Fetuses	94

Maternal and Developmental Observations at Uterine Examination and Fetal Body Weight Values	Mean	Minimum	Maximum
Pregnancy Index (%)	98.00	96.0	100.0
Corpora Lutea (Mean No. per Animal)	11.85	11.3	12.1
Implantation Sites (Mean No. per Animal)	9.85	9.3	10.3
Preimplantation Loss (Mean % per Animal)	15.445	11.17	22.37
Viable Fetuses (Mean No. per Animal)	9.23	8.4	9.8
Fetal Sex Ratio (Mean % Males per Animal)	48.48	42.0	51.2
Postimplantation Loss (Mean % per Animal)	8.045	3.64	11.44
Nonviable Fetuses (Mean No. per Animal)	0.00	0.0	0.0
Resorptions: Early and Late (Mean No. per Animal)	0.65	0.4	0.9
Resorptions: Early (Mean No. per Animal)	0.63	0.3	0.9
Resorptions: Late (Mean No. per Animal)	0.00	0.0	0.0
Mean Fetal Body Weight Male (grams)	5.5615	5.401	5.633
Mean Fetal Body Weight Female (grams)	5.3073	5.155	5.415
Mean Fetal Body Weight Males and Females (grams)	5.4475	5.285	5.537

No. - Number

Charles River Laboratories - Mattawan
Historical Control Developmental Toxicity Data
Wistar Han Rat (GD 21) - Charles River Laboratories
1 Jan 2018 to 1 Apr 2020

Litter Data	Total
No. Litters Evaluated	94
No. External Fetuses Evaluated	875
No. Visceral Fetuses Evaluated	435
No. Skeletal Fetuses Evaluated	440

	Total Number		Maximum %	
	Fetuses	Litters	Fetuses	Litters
External Malformation				
Hind limb(s), entire, malrotated	8	7	1.7	12.5
Head, entire, exencephaly	1	1	0.5	4.2
External Variation				
Tail, entire, bent	1	1	0.5	4.2
Skeletal Malformation				
Cervical vertebra(e), neural arch(es), absent	1	1	0.8	4.2
Cervical vertebra(e), neural arch(es), misshapen	2	2	0.9	4.5
Pectoral girdle, scapula, bent	1	1	0.8	4.2
Skull, parietal bone, misshapen	1	1	1.0	4.3
Skeletal Variation				
Cervical vertebra(e), neural arch(es), additional ossification center	32	24	13.3	41.7
Rib(s), bent	46	28	11.7	36.4
Rib(s), rudimentary	212	80	55.0	91.7
Rib(s), unilateral full rib	7	6	2.7	8.7
Skull, interparietal bone, incompletely ossified	1	1	0.9	4.5
Skull, jugal, fused	2	2	0.9	4.2
Skull, jugal, incompletely ossified	7	7	3.3	16.7
Skull, parietal bone, incompletely ossified	25	19	6.7	25.0
Skull, squamosal, incompletely ossified	3	3	1.8	9.1
Skull, supra occipital bone, incompletely ossified	2	2	0.9	4.5
Sternum, sternebra(e), misaligned	4	3	2.8	9.1
Sternum, sternebra(e), not ossified	2	2	2.0	8.7
Rib(s), not ossified	1	1	0.9	4.2
Pectoral girdle, scapula, superior border irregular	1	1	0.8	4.2
Skull, interparietal bone, additional ossification center	2	2	0.9	4.5
Skull, interparietal bone, misshapen	1	1	1.0	4.3
Visceral Malformation				
Head, retina, folded	3	3	1.8	8.3

No. - Number