

Reproductive Toxicology

Historical Control Data in Mice

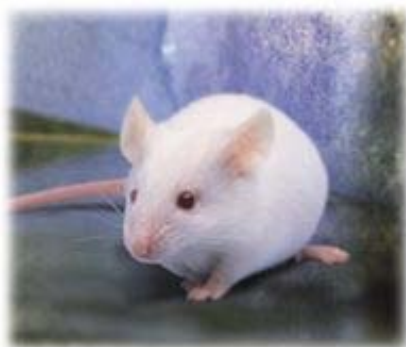


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¹ Additional HCD endpoints and years are available upon request.

HISTORICAL CONTROL DATA
MOUSE – CD-1 (CrI:CD1[ICR]), 2003 - 2018
CHARLES RIVER LABORATORIES MONTREAL
ALL ROUTES OF ADMINISTRATION

FERTILITY AND EARLY EMBRYONIC DEVELOPMENT		
GROUP PARENTAL PERFORMANCE		
Parameter	Minimum*	Maximum*
Mating Index (%)	95.0	100.0
Fertility Index (%)	81.8	100.0
Conception Rate (%)	81.8	100.0

FERTILITY AND EARLY EMBRYONIC DEVELOPMENT			
GROUP UTERINE FINDINGS			
Parameter	Average	Minimum*	Maximum*
GESTATION DAY 13 AND 15			
Total Corpora Lutea / Mouse	13.99	12.4	17.3
Total Implantation Sites / Litter	13.13	11.5	16.6
Total Live Embryos / Litter	12.27	11.1	14.6
Dead Embryos / Litter	0.04	0.0	0.1
Early Resorptions / Litter	0.85	0.3	2.0
Combined Early Resorptions + Dead / Litter	0.88	0.3	2.0
Pre-Implantation Loss (%) / Litter	6.68	2.9	11.9
Post-Implantation Loss (%) / Litter	7.39	2.8	14.4
<u>Combined Early Resorptions + Dead / Litter (%)</u>			
Dams with 1 or More	46.64	11.0	77.8
Dams with 2 or More	16.96	0.0	55.6
Dams with 3 or More	7.47	0.0	33.3
Dams with 4 or More	3.69	0.0	22.2
Dams with 5 or More	2.68	0.0	11.1
Total Resorptions / Litter	0.09	0.0	1.0

* Study ranges, based on the group incidence, group percentage or group mean

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FERTILITY AND EARLY EMBRYONIC DEVELOPMENT		
MALE REPRODUCTIVE ASSESSMENTS		
Parameter	Minimum*	Maximum*
ORGAN WEIGHTS		
Left Testis (g)	0.112	0.135
Right Testis (g)	0.120	0.141
Left Epididymis (g)	0.047	0.130
Right Epididymis (g)	0.049	0.130
EPIDIDYMAL SPERM EVALUATION		
Cauda Epididymis Weight (g)	0.015	0.023
Cauda Spermatozoa Per Gram (Millions)	477.0	1119.3
Cauda Motility (%)	29.2	92.6
CAUDA SPERMATOZOA MORPHOLOGY		
Abnormality (%)	2.7	19.9

* Study ranges, based on the group percentage or group mean

HISTORICAL CONTROL DATA
MOUSE – CD-1 (CrI:CD1[ICR]), 2003 - 2018
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PRE AND POSTNATAL STUDIES		
GROUP MATERNAL PERFORMANCE		
Parameter	Minimum*	Maximum*
Gestation Index (%)	100.0	100.0
Length of Gestation (Days)	18.6	18.9
Sex Ratio (% Males)	47.8	57.5
No. of Live Pups at Birth	11.3	13.0
No. of Dead Pups at Birth	0.0	0.3
No. of Implant Scars	12.2	14.1
Live Birth Index (%)	92.2	96.7

PRE AND POSTNATAL STUDIES		
VIABILITY (%)		
Parameter	Minimum*	Maximum*
Viability Index (%) - Day 4 Post Partum	97.1	100.0
Survival Index (%) - Day 7 Post Partum	100.0	100.0
Survival Index (%) - Day 14 Post Partum	100.0	100.0
Lactation Index (%) - Day 21 Post Partum	100.0	100.0

PRE AND POSTNATAL STUDIES		
SEXUAL MATURATION		
Parameter	Minimum*	Maximum*
Vaginal Opening (Days)	24.8	28.5
Preputial Separation (Days)	25.2	27.3

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PRE AND POSTNATAL STUDIES			
PUP BODY WEIGHTS (G)			
Parameter	Average	Minimum*	Maximum*
<u>BODY WEIGHTS:</u>			
Day 0 Post Partum			
Males	1.642	1.61	1.71
Females	1.577	1.54	1.61
Total	1.605	1.58	1.65
Day 4 Post Partum			
Males	2.973	2.87	3.16
Females	2.865	2.77	2.99
Total	2.916	2.82	3.06
Day 7 Post Partum			
Males	4.973	4.82	5.07
Females	4.876	4.69	4.99
Total	4.921	4.75	5.02
Day 14 Post Partum			
Males	8.389	7.87	8.77
Females	8.308	7.67	8.68
Total	8.345	7.77	8.72
Day 21 Post Partum			
Males	13.054	12.43	13.44
Females	12.425	11.71	12.79
Total	12.736	12.07	13.07

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HISTORICAL CONTROL DATA
MOUSE – CD-1 (CrI:CD1[ICR]), 2003 - 2018
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EMBRYO-FETAL DEVELOPMENT STUDIES			
GROUP MATERNAL, OVARIAN AND UTERINE FINDINGS			
Parameter	Total	Minimum *	Maximum *
No. of Mice Mated	213	22	25
No. of Mice Pregnant	184	17	24
No. of Mice Pregnant by Ammonium Sulfide Staining	2	0	1
No. of Mice Dying or Unscheduled Euthanasia on Study	1	0	1
No. of Mice with Total Resorption	2	0	1
No. of Mice Littering Prior to Scheduled Cesarean	7	0	2
Pregnancy Rate (%)	-	68.0	96.0
Total Corpora Lutea / Mouse	-	13.5	15.3
Total Implantation Sites / Litter	-	12.2	13.8
Sex Ratio (% Males)	-	44.2	57.9
Total Live Fetuses / Litter	-	10.9	13.3
Dead Fetuses / Litter	-	0.0	0.1
Early Resorptions / Litter	-	0.2	1.1
Middle Resorptions / Litter [#]	-	0.0	0.1
Late Resorptions / Litter	-	0.0	0.3
Total Resorptions / Litter	-	0.3	1.3
Pre-Implantation Loss (%) / Litter	-	5.4	12.8
Post-Implantation Loss (%) / Litter	-	3.1	9.8

* Study ranges, based on the group incidence, group percentage or group mean

Parameter recorded from 2003 to 2008

HISTORICAL CONTROL DATA
MOUSE – CD-1 (CrI:CD1[ICR]), 2003 - 2018
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EMBRYO-FETAL DEVELOPMENT STUDIES		
FETAL FINDINGS - SUMMARY DATA		
Parameter	Minimum *	Maximum *
Fetal Weight (g) - Males	1.32	1.50
Fetal Weight (g) - Females	1.28	1.46
Fetal Weight (g) - Total	1.31	1.49
Malformations - Litters Affected (%)	0.0	22.2
Malformations - Fetuses Affected (%)	0.0	2.8
External and Visceral Variants - Litters Affected (%)	0.0	15.0
External and Visceral Variants - Fetuses Affected (%)	0.0	1.9
Skeletal Variants - Litters Affected (%)	65.2	96.3
Skeletal Variants - Fetuses Affected (%)	20.3	78.0
Thoracic centrum variants (unossified/incomplete/ semi-bipartite/bipartite)	0.0	1.8
Sternebrae 1 to 4 (unossified/incomplete/ semi-bipartite/bipartite) - Fetuses Affected (%) #	0.0	2.9
Sternebrae 5 and Xiphisternum (unossified/incomplete/ semi-bipartite/bipartite) - Fetuses Affected (%)*	16.4	28.4
Sternebrae 1 to 6 (unossified/incomplete/ semi-bipartite/bipartite) - Fetuses Affected (%)	7.5	27.6
Ribs - Total 14th/extra/rudimentary/contralateral (unilateral and bilateral) - Fetuses Affected (%)	21.5	48.5

* Study ranges, based on the group incidence, group percentage or group mean

Alternate tabulation for sternebral variants

HISTORICAL CONTROL DATA
MOUSE – CD-1 (CrI:CD1[ICR]), 2003 - 2018
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EMBRYO-FETAL DEVELOPMENT STUDIES				
GROUP INCIDENCE OF FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS MALFORMATIONS AND VARIANTS				
EXTERNAL (EXT) VISCERAL (VIS) SKELETAL (SKE) TECHNIQUE OF WILSON (WT)	Litters examined			
	203	Total no. of studies used		
	203	10		
	203			
MALFORMATIONS (TOTAL)	Litters affected			
	SUM 15	AVERAGE % 7.39	MIN % * 0.00	MAX % * 22.22
Cranium: Cleft palate (EXT,WT)	7	3.45	0.00	14.81
Cranium: Encephalocele (EXT)	1	0.49	0.00	4.35
Eye(s): Exophthalmia (EXT,WT)	1	0.49	0.00	5.88
Eye(s): Open (EXT,WT)	5	2.46	0.00	7.41
Eye(s): Retinal folding (WT)	1	0.49	0.00	5.88
Eye(s): Aphakia (WT)	1	0.49	0.00	5.88
Eye(s): Eyelid(s) fissure (WT)	1	0.49	0.00	5.88
Face: Mandibular micrognathia (EXT)	1	0.49	0.00	5.88
Gallbladder: Gallbladdet absent (VIS)	1	0.49	0.00	5.88
Limb(s): Brachydactyly (EXT)	1	0.49	0.00	5.88
Limb(s): Abnormal flexure of hindlimb(s) (EXT)	2	0.99	0.00	4.17
Forelimb(s): Bent radius (SKE)	1	0.49	0.00	5.88
Forelimb(s): Wavy radius (SKE)	1	0.49	0.00	5.88
Hindlimb(s): Bent (EXT)	1	0.49	0.00	5.88
Hindlimb(s): Bent tibia (SKE)	1	0.49	0.00	5.88
Hindlimb(s): Bent fibula (SKE)	1	0.49	0.00	5.88
Tibia\fibula short (SKE)	1	0.49	0.00	5.88
EXTERNAL AND VISCERAL VARIANTS (TOTAL)	6	2.96	0.00	15.00
Eye(s): Subcutaneous edema (EXT)	1	0.49	0.00	6.67
Liver: Vestigial lobe (VIS)	1	0.49	0.00	5.00
Kidney(s): Renal papilla(e) absent (VIS)	1	0.49	0.00	5.00
Kidney(s): Small/reduced (VIS)	1	0.49	0.00	5.00
Hindpaw(s): Malpositioned digit(s) (EXT)	1	0.49	0.00	5.88
Tail: Kinked (EXT)	1	0.49	0.00	5.88

* Study ranges, based on the group incidence

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EMBRYO-FETAL DEVELOPMENT STUDIES				
GROUP INCIDENCE OF FETAL SKELETAL FINDINGS				
SKELETAL (SKE)	Litters examined 203		Total no. of studies used 10	
	Litters affected			
SKELETAL VARIANTS (TOTAL)	SUM 164	AVERAGE % 80.79	MIN % * 65.22	MAX % * 96.30
SKULL				
Frontal bone(s): Incomplete ossification	55	27.09	0.00	94.12
Parietal bone(s): Incomplete ossification	8	3.94	0.00	29.41
Supraoccipital bone: Incomplete ossification	35	17.24	0.00	41.18
Interparietal bone: Incomplete ossification	2	0.99	0.00	5.88
Hyoid bone: Incomplete ossification	4	1.97	0.00	9.52
Hyoid bone: Unossified	3	1.48	0.00	5.88
Nasal bone: Unossified	1	0.49	0.00	5.88
Premaxilla: Incomplete ossification	1	0.49	0.00	5.88
Maxilla: Incomplete ossification	1	0.49	0.00	5.88
Mandible: Incomplete ossification	1	0.49	0.00	5.88
Zygomatic bone(s): Incomplete ossification	1	0.49	0.00	5.88
VERTEBRAL COLUMN				
Extra pre-sacral vertebra(e)	6	2.96	0.00	17.65
25 pre-sacral vertebrae	1	0.49	0.00	5.88
Ossification center on 1st lumbar vertebra or 14th thoracic vertebra	40	19.70	5.88	45.45
Sacral vertebral centrum: Semi-bipartite	1	0.49	0.00	4.76
Caudal vertebra(e): Reduced no.	61	30.05	11.76	63.64
Caudal vertebral arch(es): Fused	1	0.49	0.00	3.70
STERNEBRAL COLUMN				
Extra	26	12.81	0.00	29.41
Fused	4	1.97	0.00	11.76
Misaligned	2	0.99	0.00	11.76
RIBS				
Extra 14th rib	1	0.49	0.00	5.88
Ossification center(s) on 7th cervical vertebra(e)	36	17.73	0.00	33.33
Rib(s) on 7th cervical vertebra(e)	41	20.20	0.00	47.06
Rib(s): Incomplete ossification	1	0.49	0.00	5.88
PELVIC GIRDLE				
Pubic bone(s): Incomplete ossification	1	0.49	0.00	5.88
LIMBS				
Reduced no. of phalange(s) in forepaw(s)	17	8.37	0.00	17.65
Reduced no. of phalange(s) in hindpaw(s)	11	5.42	0.00	13.33
Reduced no. of tarsal(s)	9	4.43	0.00	52.94

* Study ranges, based on the group incidence

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EMBRYO-FETAL DEVELOPMENT STUDIES				
GROUP INCIDENCE OF FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS MALFORMATIONS AND VARIANTS				
EXTERNAL (EXT) VISCERAL (VIS) SKELETAL (SKE) TECHNIQUE OF WILSON (WT)	Fetuses examined			
	2498	Total no. of studies used		
	1250	10		
	1253			
	1250			
MALFORMATIONS (TOTAL)	Fetuses affected			
	SUM 23	AVERAGE % 0.92	MIN % * 0.00	MAX % * 2.79
Cranium: Cleft palate (EXT,WT)	14	0.56	0.00	2.23
Cranium: Encephalocele (EXT)	1	0.04	0.00	0.37
Eye(s): Exophthalmia (EXT,WT)	1	0.04	0.00	0.47
Eye(s): Open (EXT,WT)	5	0.20	0.00	0.56
Eye(s): Retinal folding (WT)	1	0.08	0.00	0.88
Eye(s): Aphakia (WT)	1	0.08	0.00	0.88
Eye(s): Eyelid(s) fissure (WT)	1	0.08	0.00	0.97
Face: Mandibular micrognathia (EXT)	4	0.16	0.00	1.87
Gallbladder: Gallbladdet absent (VIS)	2	0.16	0.00	1.94
Limb(s): Brachydactyly (EXT)	3	0.12	0.00	1.40
Limb(s): Abnormal flexure of hindlimb(s) (EXT)	2	0.08	0.00	0.32
Forelimb(s): Bent radius (SKE)	1	0.08	0.00	0.92
Forelimb(s): Wavy radius (SKE)	3	0.24	0.00	2.75
Hindlimb(s): Bent (EXT)	4	0.16	0.00	1.87
Hindlimb(s): Bent tibia (SKE)	1	0.08	0.00	0.92
Hindlimb(s): Bent fibula (SKE)	2	0.16	0.00	1.83
Tibia\fibula short (SKE)	4	0.32	0.00	3.67
EXTERNAL AND VISCERAL VARIANTS (TOTAL)	9	0.36	0.00	1.87
Eye(s): Subcutaneous edema (EXT)	1	0.04	0.00	0.57
Liver: Vestigial lobe (VIS)	1	0.08	0.00	0.83
Kidney(s): Renal papilla(e) absent (VIS)	1	0.08	0.00	0.83
Kidney(s): Small/reduced (VIS)	1	0.08	0.00	0.83
Hindpaw(s): Malpositioned digit(s) (EXT)	4	0.16	0.00	1.87
Tail: Kinked (EXT)	1	0.04	0.00	0.49

* Study ranges, based on the group incidence

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EMBRYO-FETAL DEVELOPMENT STUDIES				
GROUP INCIDENCE OF FETAL EXTERNAL, VISCERAL AND SKELETAL FINDINGS MALFORMATIONS AND MINOR VARIANTS				
SKELETAL (SKE)	Fetuses examined 1253		Total no. of studies used 10	
SKELETAL VARIANTS (TOTAL)	Fetuses affected			
	SUM 502	AVERAGE % 40.06	MIN % * 20.33	MAX % * 77.98
SKULL				
Frontal bone(s): Incomplete ossification	170	13.57	0.00	65.14
Parietal bone(s): Incomplete ossification	16	1.28	0.00	9.17
Supraoccipital bone: Incomplete ossification	70	5.59	0.00	16.98
Interparietal bone: Incomplete ossification	2	0.16	0.00	0.92
Hyoid bone: Incomplete ossification	4	0.32	0.00	1.63
Hyoid bone: Unossified	3	0.24	0.00	0.92
Nasal bone: Unossified	2	0.16	0.00	1.83
Premaxilla: Incomplete ossification	2	0.16	0.00	1.83
Maxilla: Incomplete ossification	2	0.16	0.00	1.83
Mandible: Incomplete ossification	2	0.16	0.00	1.83
Zygomatic bone(s): Incomplete ossification	2	0.16	0.00	1.83
VERTEBRAL COLUMN				
Extra pre-sacral vertebra(e)	8	0.64	0.00	2.83
25 pre-sacral vertebrae	1	0.08	0.00	0.92
Ossification center on 1st lumbar vertebra or 14th thoracic vertebra	43	3.43	0.94	8.59
Sacral vertebral centrum: Semi-bipartite	1	0.08	0.00	0.81
Caudal vertebra(e): Reduced no.	116	9.26	1.92	18.75
Caudal vertebral arch(es): Fused	1	0.08	0.00	0.55
STERNEBRAL COLUMN				
Extra	44	3.51	0.00	8.24
Fused	4	0.32	0.00	1.98
Misaligned	2	0.16	0.00	1.98
RIBS				
Extra 14th rib	1	0.08	0.00	0.92
Ossification center(s) on 7th cervical vertebra(e)	46	3.67	0.00	7.69
Rib(s) on 7th cervical vertebra(e)	60	4.79	0.00	11.88
Rib(s): Incomplete ossification	1	0.08	0.00	0.92
PELVIC GIRDLE				
Pubic bone(s): Incomplete ossification	1	0.08	0.00	0.92
LIMBS				
Reduced no. of phalange(s) in forepaw(s)	26	2.08	0.00	5.50
Reduced no. of phalange(s) in hindpaw(s)	14	1.12	0.00	3.67
Reduced no. of tarsal(s)	21	1.68	0.00	19.81

* Study ranges, based on the group incidence