

Reproductive Toxicology

Historical Control Data In Rats



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Rats

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¹Additional HCD endpoints and years are available upon request.

**HISTORICAL CONTROL DATA
RAT (CrI:CD(SD)) 1998-2018
CHARLES RIVER, PRECLINICAL SERVICES EDINBURGH**

Fertility Studies			
<i>Parameter</i>	<i>Mean</i>	<i>Minimum</i>	<i>Maximum</i>
Male Fertility Index (%)	97.2	83.0	100.0
Female Fertility Index (%)	98.0	85.0	100.0
Pregnancy Data			
Corpora Lutea	15.6	13.3	17.0
Implants	15.1	12.6	16.8
Early Deaths	0.8	0.2	1.6
Late Deaths	0.0	0.0	0.1
Total Deaths	0.8	0.2	1.6
Live Implants	14.4	11.9	15.8
Male absolute organ weights (g)			
Testes	3.60	3.32	3.88
Epididymides	1.34	1.08	1.50
Prostate	0.73	0.60	0.90
Seminal vesicles	2.31	1.44	2.97
With adjustment for terminal body weight (g)			
Terminal body weight	520	415	638
Testes	3.58	3.26	3.85
Epididymides	1.33	1.08	1.49
Prostate	0.73	0.60	0.91
Seminal vesicles	2.30	1.43	2.99

HISTORICAL CONTROL DATA
RAT (CrI:WI(Han)) 2002-2018
CHARLES RIVER, PRECLINICAL SERVICES EDINBURGH

Fertility Studies			
<i>Parameter</i>	<i>Mean</i>	<i>Minimum</i>	<i>Maximum</i>
Male Fertility Index (%)	97.3	90.0	100.0
Female Fertility Index (%)	97.4	90.0	100.0
Pregnancy Data			
Corpora Lutea	12.4	10.3	13.3
Implants	11.8	10.3	13.1
Early Deaths	0.5	0.2	1.0
Late Deaths	0.0	0.0	0.1
Total Deaths	0.5	0.2	1.0
Live Implants	11.3	9.8	12.6
Male absolute organ weights (g)			
Testes	3.63	3.54	3.71
Epididymides	1.35	1.27	1.45
Prostate	0.50	0.45	0.60
Organ Weights relative to terminal body weight (g)			
Terminal body weight	419.0	405.0	434.0
Testes	0.87	0.84	0.92
Epididymides	0.32	0.31	0.34
Prostate	0.12	0.11	0.14

HISTORICAL CONTROL DATA
RAT (CrI:CD(SD)) 1998-2017
CHARLES RIVER, PRECLINICAL SERVICES EDINBURGH

Day 20 of Gestation

Developmental Toxicity Studies in the Rat			
<i>Parameter</i>	<i>Mean</i>	<i>Minimum</i>	<i>Maximum</i>
Pregnancy Data			
Corpora Lutea	14.2	12.8	17
Implants	13.6	9.9	16.3
Early Deaths	0.6	0.2	1.5
Late Deaths	0.0	0	0.3
Dead fetuses	0.0	0	0.1
Total Deaths	0.7	0	1.5
Live Implants	12.9	8.7	15.8
Uterus weight (g)	78.6	56	94
Mean foetal weight (g)	3.8	3.5	4.0

Foetal examination (14,911 fetuses from 1152 litters, typically 18-24 litters per study)			
<i>Parameter</i>	<i>Mean</i>	<i>Minimum</i>	<i>Maximum</i>
Major abnormality (litter incidence per study)	1.6	0.0	5.0
Major abnormality (foetus incidence per study)	1.9	0.0	7.0
Minor visceral abnormality (litter incidence per study)	17.1	11.0	23.0
Minor visceral abnormality (foetus incidence per study)	43.1	22.0	89.0
Minor skeletal abnormality (litter incidence per study)	8.1	0.0	18.0
Minor skeletal abnormality (foetus incidence per study)	13.1	0.0	41.0

Data from Provantis

Foetal examination (324 foetuses from 23 litters, 23 litters per study)			
<i>Parameter</i>	<i>Mean</i>	<i>Minimum</i>	<i>Maximum</i>
Malformation external (number of foetuses)	0.0	0.0	0.0
Malformation external (number of litters)	0.0	0.0	0.0
Variation external (number of foetuses)	0.0	0.0	0.0
Variation external (number of litters)	0.0	0.0	0.0
Foetal examination (156 foetuses from 23 litter)			
Malformation visceral (number of foetuses)	1.0	1.0	1.0
Malformation visceral (number of litters)	1.0	1.0	1.0
Variation visceral (number of foetuses)	19.0	19.0	19.0
Variation visceral (number of litters)	10.0	10.0	10.0
Foetal examination (168 foetuses from 23 litter)			
Malformation skeletal (number of foetuses)	0.0	0.0	0.0
Malformation skeletal (number of litters)	0.0	0.0	0.0
Variation skeletal (number of foetuses)	163.0	163.0	163.0
Variation skeletal (number of litters)	23.0	23.0	23.0

Data from 1 developmental toxicity study.

HISTORICAL CONTROL DATA
RAT (CrI:CD(SD)) 2012-2018
CHARLES RIVER, PRECLINICAL SERVICES EDINBURGH

Day 21 of Gestation

Developmental Toxicity Studies in the Rat			
<i>Parameter</i>	<i>Mean</i>	<i>Minimum</i>	<i>Maximum</i>
Pregnancy Data			
Corpora Lutea	14.8	13.6	15.7
Implants	14.3	13.6	15.0
Early Deaths	0.7	0.3	1.2
Late Deaths	0.0	0.0	0.1
Dead fetuses	0.0	0.0	0.0
Total Deaths	0.7	0.3	1.2
Live Implants	13.7	12.6	14.5
Uterus weight (g)	103.9	96.0	109.0
Mean foetal weight (g)	5.6	5.1	5.9

Foetal examination (839 fetuses from 60 litters, typically 18-24 litters per study)			
<i>Parameter</i>	<i>Mean</i>	<i>Minimum</i>	<i>Maximum</i>
Major abnormality (litter incidence per study)	1.0	0.0	2.0
Major abnormality (foetus incidence per study)	1.3	0.0	3.0
Minor visceral abnormality (litter incidence per study)	15.7	14.0	19.0
Minor visceral abnormality (foetus incidence per study)	29.7	24.0	38.0
Minor skeletal abnormality (litter incidence per study)	11.3	9.0	14.0
Minor skeletal abnormality (foetus incidence per study)	20.3	19.0	21.0

Data from Provantis

Foetal examination (1154 fetuses from 83 litters, typically 19-22 litters per study)			
<i>Parameter</i>	<i>Mean</i>	<i>Minimum</i>	<i>Maximum</i>
Malformation external (number of fetuses)	0.8	0.0	1.0
Malformation external (number of litters)	0.8	0.0	1.0
Variation external (number of fetuses)	2.0	0.0	8.0
Variation external (number of litters)	0.3	0.0	1.0
Foetal examination (556 fetuses from 83 litters)			
Malformation visceral fixed head (number of fetuses)	0.0	0.0	0.0
Malformation visceral fixed head (number of litters)	0.0	0.0	0.0
Variation visceral fixed head (number of fetuses)	1.8	0.0	5.0
Variation visceral fixed head (number of litters)	1.0	0.0	3.0
Malformation visceral body (number of fetuses)	0.5	0.0	2.0
Malformation visceral body (number of litters)	0.5	0.0	2.0
Variation visceral body (number of fetuses)	13.8	13.0	14.0
Variation visceral body (number of litters)	10.3	8.0	12.0
Foetal examination (589 fetuses from 83 litters)			
Malformation skeletal (number of fetuses)	1.0	0.0	2.0
Malformation skeletal (number of litters)	1.0	0.0	2.0
Variation skeletal (number of fetuses)	143.3	139.0	149.0
Variation skeletal (number of litters)	20.8	19.0	22.0

HISTORICAL CONTROL DATA
RAT (CrI:WI(Han)) 2012-2016
CHARLES RIVER, PRECLINICAL SERVICES EDINBURGH

Day 20 of Gestation

Developmental Toxicity Studies in the Rat			
<i>Parameter</i>	<i>Mean</i>	<i>Minimum</i>	<i>Maximum</i>
Pregnancy Data			
Corpora Lutea	12.0	11.1	12.7
Implants	11.4	10.9	12.3
Early Deaths	0.4	0.0	0.9
Late Deaths	0.1	0.0	0.3
Dead fetuses	0.0	0.0	0.0
Total Deaths	0.5	0.0	1.1
Live Implants	10.9	9.8	11.9
Uterus weight (g)	66.0	59.0	70.0
Mean foetal weight (g)	3.8	3.7	4.0

Foetal examination (957 fetuses from 91 litters, typically 8-24 litters per study)			
<i>Parameter</i>	<i>Mean</i>	<i>Minimum</i>	<i>Maximum</i>
Major abnormality (litter incidence per study)	0.6	0.0	1.0
Major abnormality (foetus incidence per study)	0.6	0.0	1.0
Minor visceral abnormality (litter incidence per study)	13.0	4.0	23.0
Minor visceral abnormality (foetus incidence per study)	50.7	9.0	135.0
Minor skeletal abnormality (litter incidence per study)	9.8	4.0	14.0
Minor skeletal abnormality (foetus incidence per study)	15.8	8.0	21.0

HISTORICAL CONTROL DATA
RAT (CrI:WI(Han)) 2012-2018
CHARLES RIVER, PRECLINICAL SERVICES EDINBURGH

Day 21 of Gestation

Developmental Toxicity Studies in the Rat			
<i>Parameter</i>	<i>Mean</i>	<i>Minimum</i>	<i>Maximum</i>
Pregnancy Data			
Corpora Lutea	11.8	10.3	13.4
Implants	11.2	9.5	12.7
Early Deaths	0.4	0.0	0.9
Late Deaths	0.0	0.0	0.2
Dead fetuses	0.0	0.0	0.0
Total Deaths	0.4	0.0	0.8
Live Implants	10.8	9.3	12.4
Uterus weight (g)	78.0	70.0	87.0
Mean foetal weight (g)	5.3	4.6	5.9

Foetal examination (1280 fetuses from 115 litters, typically 18-24 litters per study)			
<i>Parameter</i>	<i>Mean</i>	<i>Minimum</i>	<i>Maximum</i>
Major abnormality (litter incidence per study)	1.5	0.0	4.0
Major abnormality (foetus incidence per study)	2.0	0.0	7.0
Minor visceral abnormality (litter incidence per study)	15.0	4.0	18.0
Minor visceral abnormality (foetus incidence per study)	37.7	5.0	60.0
Minor skeletal abnormality (litter incidence per study)	14.5	6.0	18.0
Minor skeletal abnormality (foetus incidence per study)	32.8	14.0	53.0

Data from Provantis

Foetal examination (1035 fetuses from 98 litters, typically 6-22 litters per study)			
<i>Parameter</i>	<i>Mean</i>	<i>Minimum</i>	<i>Maximum</i>
Malformation external (number of fetuses)	0.3	0.0	2.0
Malformation external (number of litters)	0.3	0.0	2.0
Variation external (number of fetuses)	2.0	0.0	18.0
Variation external (number of litters)	1.0	0.0	9.0
Foetal examination (202 fetuses from 61 litters)			
Malformation visceral (number of fetuses)	0.0	0.0	0.0
Malformation visceral (number of litters)	0.0	0.0	0.0
Variation visceral (number of fetuses)	8.0	0.0	22.0
Variation visceral (number of litters)	5.0	0.0	16.0
Foetal examination (386 fetuses from 81 litters)			
Malformation skeletal (number of fetuses)	0.4	0.0	2.0
Malformation skeletal (number of litters)	0.2	0.0	1.0
Variation skeletal (number of fetuses)	72.8	0.0	115.0
Variation skeletal (number of litters)	13.8	0.0	22.0

HISTORICAL CONTROL DATA
RAT (CrI:CD(SD)) 1998-2017
CHARLES RIVER, PRECLINICAL SERVICES EDINBURGH

Pre and Post Natal Studies (Typically from group sizes of 8-32)			
<i>Parameter</i>	<i>Mean</i>	<i>Minimum</i>	<i>Maximum</i>
Pregnancy rate (%)	93.7	75.0	100
Litters where all pups died	1.1	0.0	6.0
Duration of gestation (days)	21.6	21.1	22.0
Litter mean values (F0 generation)			
Implants	13.9	12.2	16.5
Live pups Day 0	12.9	10.9	15.8
Live pups Day 4	12.4	10.8	15.3
Live pups Day 21	12.3	10.8	15.2
Birth Index (%)	92.8	87.0	98.0
Live Birth Index (%)	98.4	95.0	100
Viability Index (%)	92.0	73.0	100
Lactation Index (%)	99.3	95.0	100
Male pup weight Day 1 (g)	6.7	6.3	7.4
Male pup weight Day 4 (g)	9.9	8.5	11.0
Male pup weight Day 21 (g)	47.1	42.2	53.6
Female pup weight Day 1 (g)	6.4	5.6	7.0
Female pup weight Day 4 (g)	9.4	8.0	10.4
Female pup weight Day 21 (g)	45.3	40.2	52.5

HISTORICAL CONTROL DATA
RAT (CrI:CD(SD)) 1998-2017
CHARLES RIVER, PRECLINICAL SERVICES EDINBURGH

Pre and Post Natal Studies (continued)			
<i>Parameter</i>	<i>Mean</i>	<i>Minimum</i>	<i>Maximum</i>
Pinna detachment (days)			
All males	3.9	3.2	5.5
Median males	3.4	2.6	4.3
All females	3.9	3.1	5.6
Median females	3.4	2.7	4.4
Incisor eruption (days)			
All males	13.0	11.2	14.5
Median males	12.2	10.3	13.7
All females	13.0	11.0	14.4
Median females	12.2	10.6	13.7
Eye opening (days)			
All males	15.3	14.5	16.2
Median males	14.8	14.4	15.5
All females	15.2	14.6	15.9
Median females	14.7	14.1	15.3
Vaginal opening			
Age (days)	39.8	33.4	36.1
Weight (g)	119.6	114.0	126.0
Preputial separation			
Age (days)	43.1	40.4	47.6
Weight (g)	210.4	191.0	224.0
F1 Male Fertility Index (%)	97.2	90	100
F1 Female Fertility Index (%)	97.9	90	100
F1 females: mean number of implants	15.7	14.5	16.5
F1 females: mean number of live pups	19.6	13.6	15.8