

Historical Control Data in Rats



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Contact:

Manon Beekhuijzen

**Charles River Laboratories Den Bosch B.V.
Hambakenwetering 7
5231 DD 's-Hertogenbosch
The Netherlands**

Tel: 31 73 6406700 x 831

Email: manon.beekhuijzen@crl.com

¹ Additional HCD endpoints and years are available upon request.

Historical Control Data Rat: Crl:WI(Han) (outbred, SPF-Quality)
Gestation Day 21
Study Date Range: 2016 - 2020

Endpoint	Total	Mean of Study Means						
		Mean	SD	Median	Min	Max	P5	P95
No of Studies	60							
Total No. of Animals in the Control Group	1321							
No. of Animals that Died	0							
No. of Animals that were Euthanized	0							
No. of Animals that Aborted or Delivered	3							
Percent Pregnant		98.3	2.89	100.0	90.9	100.0	90.9	100.0
No. of Animals Examined at Laparohysterectomy	1318							
No. Nongravid	23							
No. Gravid	1295							
No. with Only Resorptions	2							
No. of Dams with Live Fetuses	1293							
Mean No. Viable Fetuses/Dam		10.7	0.58	10.6	9.5	12.1	9.6	11.7
Total No. Viable Fetuses	13798							
Viable Fetuses (%/Litter)		94.8	2.11	95.6	88.4	98.5	91.0	97.9
Mean No. Postimplantation Loss/Dam		0.5	0.19	0.5	0.2	1.0	0.3	1.0
Total No. Postimplantation Losses	706							
Postimplantation Loss (%/Litter)		5.2	2.11	4.4	1.5	11.6	2.1	9.0
Dead Fetuses (%/Litter)		0.0	0.10	0.0	0.0	0.5	0.0	0.4
Early Resorptions (%/Litter)		5.0	2.11	4.3	1.5	11.6	2.1	8.7
Late Resorptions (%/Litter)		0.1	0.27	0.0	0.0	1.5	0.0	0.4
Mean No. Implantations/Dam		11.2	0.53	11.2	10.0	12.5	10.5	12.1
Mean No. Corpora Lutea/Dam		12.0	0.51	11.9	11.1	13.7	11.2	12.9
Mean No. Preimplantation Loss/Dam		0.8	0.38	0.8	0.1	1.8	0.3	1.5
Total No. Preimplantation Losses	1007							
Preimplantation Loss (%/Litter)		6.5	3.02	6.5	0.8	14.6	2.2	11.8
Total No. Male Fetuses	6774							
Total No. Female Fetuses	7024							
% Males/Litter		48.9	3.49	48.9	40.6	56.5	42.7	54.7
% Female/Litter		51.1	3.49	51.1	43.5	59.4	45.3	57.3
Mean Fetal Body Weight (g)		5.3	0.12	5.3	4.9	5.4	5.0	5.4
Mean Male Body Weight (g)		5.4	0.11	5.4	5.0	5.5	5.2	5.5
Mean Female Body Weight (g)		5.1	0.13	5.2	4.7	5.3	4.9	5.3
Male Anogenital Distance (mm)		2.8	0.20	2.8	2.6	3.3	2.6	3.3
Female Anogenital Distance (mm)		1.3	0.18	1.3	1.1	1.8	1.1	1.7
Male Placenta Weight (g) ¹		0.5	0.04	0.5	0.5	0.6	@	@
Female Placenta Weight (g) ¹		0.5	0.04	0.5	0.5	0.6	@	@

@ Insufficient number of data for calculation. ¹ Based on 3 datasets

**Historical Control Data Rat: Crl:WI(Han) (outbred. SPF-Quality)
Gestation Day 21**

No. of Studies	60	
Total No. Fetuses/Litters Examined Externally	13798	1293
Total No. Fetuses/Litters Examined Viscerally	6911	1292
Total No. Fetuses/Litters Examined Skeletally	6905	1291

	Mean of Study Means (% Per Litter Basis)							Summary Incidence (Total No. Affected)	
MALFORMATIONS	Mean	SD	Median	Min	Max	P5	P95	Fetuses	Litters
Total External Malformations								20	20
Total Visceral Malformations								28	28
Total Skeletal Malformations								74	67
Total Malformations								107	97
EXTERNAL									
Anogenital- Fissure	0.0	0.05	0.0	0.0	0.4	0.0	0.0	1	1
Anus- Atresia	0.0	0.05	0.0	0.0	0.4	0.0	0.0	1	1
Ectrodactyly	0.0	0.06	0.0	0.0	0.5	0.0	0.0	1	1
Exencephaly	0.0	0.05	0.0	0.0	0.4	0.0	0.0	1	1
Eye(s)- Bulge Absent and/or Small	0.0	0.08	0.0	0.0	0.6	0.0	0.0	1	1
Eye(s)- Open	0.0	0.05	0.0	0.0	0.4	0.0	0.0	1	1
General- Anasarca	0.0	0.08	0.0	0.0	0.5	0.0	0.0	2	2
Limb(s)- Malrotated	0.0	0.05	0.0	0.0	0.4	0.0	0.0	1	1
Lip- Cleft	0.0	0.08	0.0	0.0	0.6	0.0	0.0	1	1
Lower Jaw- Absent or small	0.0	0.09	0.0	0.0	0.5	0.0	0.3	3	3
Meningocele	0.0	0.08	0.0	0.0	0.5	0.0	0.0	2	2
Microcephaly	0.0	0.05	0.0	0.0	0.4	0.0	0.0	1	1
Palate- Cleft	0.0	0.09	0.0	0.0	0.6	0.0	0.0	2	2
Snout- Proboscis	0.0	0.05	0.0	0.0	0.4	0.0	0.0	1	1
Tail- Absent	0.0	0.05	0.0	0.0	0.4	0.0	0.0	1	1
Trunk- Omphalocele	0.0	0.15	0.0	0.0	0.6	0.0	0.5	6	6
VISCERAL									
Aorta- Overriding	0,0	0,13	0,0	0,0	1,0	0,0	0,0	1	1
Aorta- Dilated	0,0	0,13	0,0	0,0	1,0	0,0	0,0	1	1
Aortic Arch- Right-sided	0,1	0,21	0,0	0,0	0,9	0,0	0,8	5	5
Diaphragmatic Hernia	0,0	0,15	0,0	0,0	0,9	0,0	0,0	2	2

Historical Control Data Rat: Crl:WI(Han) (outbred. SPF-Quality)
Gestation Day 21

MALFORMATIONS	Mean of Study Means (% Per Litter Basis)							Summary Incidence (Total No. Affected)	
	Mean	SD	Median	Min	Max	P5	P95	Fetuses	Litters
VISCERAL (continued)									
Eye(s)- Absent and/or Small	0.1	0.71	0.0	0.0	5.3	0.0	0.9	4	4
Heart- Large	0.0	0.08	0.0	0.0	0.6	0.0	0.0	1	1
Hydrocephaly- Internal	0.0	0.15	0.0	0.0	0.9	0.0	0.0	2	2
Intestine- Absent	0.0	0.12	0.0	0.0	0.9	0.0	0.0	1	1
Lung- Abnormal Lobation	0.1	0.26	0.0	0.0	1.5	0.0	0.8	5	5
Situs Inversus	0.2	0.39	0.0	0.0	1.5	0.0	1.1	15	15
Stomach - Small	0.0	0.08	0.0	0.0	0.6	0.0	0.0	1	1
Subclavian (Left)- Retroesophageal	0.0	0.08	0.0	0.0	0.6	0.0	0.0	1	1
Ventricular Septum Defect	0.0	0.11	0.0	0.0	0.6	0.0	0.0	2	2
SKELETAL									
Brachydactyly	0.0	0.08	0.0	0.0	0.6	0.0	0.0	1	1
Costal Catilage Anomaly	0.1	0.33	0.0	0.0	1.7	0.0	0.9	6	6
Limb Bone(s)- Absent	0.0	0.20	0.0	0.0	1.3	0.0	0.0	2	2
Limb Bone(s)- Bent	0.4	0.69	0.0	0.0	2.3	0.0	2.3	15	13
Rib Anomaly	0.1	0.28	0.0	0.0	1.6	0.0	0.9	5	4
Skull Bones- Fused	0.0	0.19	0.0	0.0	1.1	0.0	0.6	3	3
Sternal Anomaly	0.0	0.13	0.0	0.0	0.7	0.0	0.0	2	2
Sternoschisis	0.1	0.24	0.0	0.0	1.1	0.0	0.8	4	4
Vertebral Anomaly With or Without Associated Rib Anomaly	0.3	0.47	0.0	0.0	1.7	0.0	1.4	20	20
Vertebral Centra Anomaly	0.1	0.23	0.0	0.0	1.3	0.0	0.8	3	3

Historical Control Data Rat: Crl:WI(Han) (outbred. SPF-Quality)

Gestation Day 21

VARIATIONS	Mean of Study Means (% Per Litter Basis)							Summary Incidence (Total No. Affected)	
	Mean	SD	Median	Min	Max	P5	P95	Fetuses	Litters
EXTERNAL									
None Observed									
VISCERAL									
Adrenal Gland- Discolored	0.0	0.12	0.0	0.0	0.9	0.0	0.0	1	1
Adrenal Gland- Displaced	0.0	0.10	0.0	0.0	0.8	0.0	0.0	1	1
Kidney(s)- Renal Papilla(e) Absent and/or Small	0.0	0.18	0.0	0.0	1.1	0.0	0.0	2	2
Liver- Discolored	0.0	0.18	0.0	0.0	0.9	0.0	0.7	3	3
Liver- Small Supernumerary Lobe(s)	3.7	2.90	3.4	0.0	9.6	0.0	8.9	253	215
Lung- Abnormal Lobation	0.0	0.10	0.0	0.0	0.8	0.0	0.0	1	1
Lung- Absent Accessory Lobe	0.0	0.10	0.0	0.0	0.8	0.0	0.0	1	1
Subclavian (Right)- Originating from the Aortic Arch	0.0	0.09	0.0	0.0	0.7	0.0	0.0	1	1
Subclavian (Right)- Retroesophageal	0.0	0.25	0.0	0.0	1.9	0.0	0.0	2	2
Thymus- Partially Undescended Horn(s)	0.0	0.22	0.0	0.0	1.5	0.0	0.0	3	3
Ureter(s)- Convoluted	0.6	1.03	0.0	0.0	5.0	0.0	2.9	36	32
Ureter(s)- Dilated	0.3	0.57	0.0	0.0	2.3	0.0	1.7	16	16
SKELETAL									
7th Cervical Rudimentary Rib(s) / Ossification Site(s)	4.4	2.45	4.1	0.0	9.9	0.0	9.0	308	244
7th Cervical Full Rib(s)	0.4	0.67	0.0	0.0	2.7	0.0	1.9	26	24
14th Full Rib(s)	6.6	3.16	6.9	0.7	12.6	0.9	11.3	462	319
14th Rudimentary Rib(s)	53.7	6.25	52.7	41.8	71.8	44.6	67.0	3691	1190
Metacarpal(s) and/or Metatarsal(s) Malpositioned	0.0	0.13	0.0	0.0	0.8	0.0	0.0	2	2
Metacarpal(s) and/or Metatarsal(s) Unossified	4.8	10.30	2.3	0.0	77.5	0.0	14.5	324	177
Pelvic Girdle- Caudal Shift	5.8	2.52	6.1	1.3	13.0	1.7	10.0	401	277
Pubis- Unossified / Reduced Ossification	0.0	0.21	0.0	0.0	1.6	0.0	0.0	1	1
Rib(s)- Bent	15.9	7.57	13.9	4.1	39.5	6.4	34.7	1056	558
Rib(s)- reduced ossification	0.0	0.12	0.0	0.0	0.9	0.0	0.0	1	1
Scapula(e)- Bent ¹	0.4	0.73	0.0	0.0	2.5	0.0	2.4	13	10
Skeleton (Entire)- General Reduced Ossification	0.0	0.10	0.0	0.0	0.8	0.0	0.0	1	1

¹ Based on 36 datasets.

**Historical Control Data Rat: Crl:WI(Han) (outbred. SPF-Quality)
Gestation Day 21**

VARIATIONS	Mean of Study Means (% Per Litter Basis)							Summary Incidence (Total No. Affected)	
	Mean	SD	Median	Min	Max	P5	P95	Fetuses	Litters
SKELETAL (continued)									
Skull Bone- Unossified Line	0.0	0.06	0.0	0.0	0.5	0.0	0.0	1	1
Skull- Reduced Ossification	12.0	12.30	9.0	2.7	95.2	4.1	23.4	846	443
Skull- Supernumerary Site	0.0	0.12	0.0	0.0	0.9	0.0	0.0	1	1
Sternebra- Supernumerary	0.0	0.23	0.0	0.0	1.8	0.0	0.0	2	1
Sternebra(e) #1, #2, #3 and/or #4 Unossified	0.0	0.21	0.0	0.0	1.6	0.0	0.0	1	1
Sternebra(e) #5 and/or #6 Unossified	0.2	0.69	0.0	0.0	3.0	0.0	2.3	16	15
Sternebra(e)- Branched	0.2	0.42	0.0	0.0	1.5	0.0	1.3	14	13
Sternebrae- Malaligned ¹	9.0	4.26	8.3	3.0	22.9	3.0	17.1	389	303
Sternebra(e) Malaligned (Severe) ²	0.0	0.17	0.0	0.0	0.8	0.0	0.6	1	1
Sternebrae- Malaligned (Slight or Moderate) ²	21.5	8.48	22.3	6.4	43.8	6.6	41.5	560	316
Sternum- Supernumerary Ossification Site	0.1	0.26	0.0	0.0	1.1	0.0	0.9	5	5
Vertebral Arches- Reduced Ossification	0.1	0.41	0.0	0.0	2.3	0.0	1.0	8	8
Vertebral Centra- Reduced Ossification	1.0	1.46	0.8	0.0	9.2	0.0	3.3	69	61
Vertebral Centra- Unossified	0.0	0.15	0.0	0.0	0.9	0.0	0.0	2	2

¹ Based on 37 datasets. ² Based on 23 datasets.

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1.1 Body Weights

1.2 Corrected Body Weight Gain Of Dams

1.3 Food Consumption

1.4 Relative Food Consumption

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**HISTORICAL DATA
FEMALES****1.1 BODY WEIGHTS (GRAM)**

DAYS	MEAN	STD.DEV.	N	P5	P95
F0-GENERATION POST COITUM					
1	222	21.0	20	193.0	260.5
2	207	17.8	1248	180.0	237.0
3	217	22.6	48	183.0	254.0
6	223	18.5	1296	194.0	254.0
9	232	18.8	1296	203.0	264.0
12	247	19.7	1296	217.0	279.0
15	261	21.0	1296	229.0	297.0
18	291	24.2	1296	253.0	331.0
21	326	28.8	1280	279.5	374.0

APPENDIX 1

**HISTORICAL DATA
FEMALES****1.2 CORRECTED BODY WEIGHT GAIN OF DAMS**

	MEAN	STD.DEV.	N	P5	P95
F0-GENERATION POST COITUM					
Corrected body weight gain (gram)	29	8.9	1278	14.9	43.4
Corrected body weight gain (%)	13	4.2	1278	6.7	20.1
Weight of uterus	75	15.6	1278	48.3	96.9

APPENDIX 1

**HISTORICAL DATA
FEMALES****1.3 FOOD CONSUMPTION (G/ANIMAL/DAY)**

DAYS	MEAN	STD.DEV.	N	P5	P95
F0-GENERATION POST COITUM					
2	19	2.7	20	13.5	23.3
4	21	3.8	1270	15.8	26.0
5	24	8.0	47	16.0	39.0
6	31	10.2	27	18.0	54.0
7	27	7.0	70	18.0	37.0
8	20	3.4	1294	14.7	25.3
9	27	7.1	48	19.0	39.0
10	26	6.4	48	19.0	35.0
11	21	3.2	1296	16.3	26.0
12	27	4.8	48	20.0	35.0
13	27	5.0	48	20.0	37.0
14	22	3.5	1293	16.7	27.3
15	28	5.5	48	21.0	37.0
16	30	9.6	48	21.0	40.0
17	23	3.3	1296	17.7	28.3
18	29	4.7	48	22.0	36.0
19	28	4.7	48	22.0	36.0
20	23	3.7	1289	18.0	28.3
21	26	4.7	48	19.0	34.0

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**HISTORICAL DATA
FEMALES****1.4 RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)**

DAYS	MEAN	STD.DEV.	N	P5	P95
F0-GENERATION POST COITUM					
2	81	10.8	20	58.2	96.7
4	93	16.8	1270	74.2	113.4
5	105	39.1	47	68.2	172.9
6	145	52.7	27	83.3	242.2
7	122	30.9	70	82.6	163.6
8	84	13.8	1294	64.8	105.8
9	118	35.6	48	85.3	174.9
10	114	30.3	48	80.6	157.0
11	84	11.7	1296	68.1	100.5
12	109	17.4	48	79.7	141.3
13	112	19.8	48	86.6	152.5
14	83	12.3	1293	67.0	101.7
15	109	21.2	48	80.8	146.6
16	115	35.6	48	76.7	151.4
17	79	10.0	1296	64.5	95.1
18	99	14.9	48	78.7	128.4
19	97	16.3	48	75.8	126.0
20	70	9.8	1279	57.9	85.2
21	79	14.3	48	61.4	104.9

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2014
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All
Selected projects	503895 509703 510049 510054 510277 510576 510626 511143 511244 511296 511312 511508 511553 511568 511810 511913 511927 512206 512218 512572 512638 512783 513531 514876 517130 517844 520541 520559 520631 520635 520636 520838 520891 520906 521063 521103 521186 521191 521198 521199 521260 521268 521322 521324 521360 521413 521465 521549 521551 521583 521601 521630 521632 521650 521681 521693 521838 521851 521887 521898 522004 522006 522107 522137 522139 522289 522499
BODY WEIGHTS (GRAM)	
Selected group	CONTROL
Selected days	1 2 3 6 9 12 15 18 21
CORRECTED BODY WEIGHT GAIN OF DAMS	
Selected group	CONTROL
Selected days	.
FOOD CONSUMPTION (G/ANIMAL/DAY)	
Selected group	CONTROL
Selected days	2 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)	
Selected group	CONTROL
Selected days	2 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21

2018-2020 historical control data OECD 414

MALES

CORRECTED ANOGENITAL DISTANCE (MM)

Mean	St.dev	N	P5	P95	Min	Max
1.61	0.180	428	1.38	1.99	1.26	2.19

FEMALES

CORRECTED ANOGENITAL DISTANCE (MM)

Mean	St.dev	N	P5	P95	Min	Max
0.77	0.164	429	0.59	1.06	0.55	1.36

Selection information

Species	Rat
Dosing type	All
Start year	2018
End year	2020

Selected projects	20140142
	20155388
	20161197
	20161205
	20161719
	20164069
	20168829
	20169529
	20172127
	20175616
	20180606
	20184659
	20185506
	20186562
	20188705
	20198563
	20198772
	20214258
	20218707
	20223627

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[1.1 Organ Weights](#)

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**HISTORICAL DATA
FEMALES****1.1 ORGAN WEIGHTS (GRAM)**

ORGAN	MEAN	STD.DEV.	N	P5	P95
ORGAN WEIGHT, END OF IN-LIFE					
Adrenals	0.081	0.0168	21	0.0550	0.1070
Body weight	324	30.8	696	274.0	374.0
Brain	2.24	0.150	22	1.914	2.423
Kidneys	1.67	0.182	131	1.422	1.971
Liver	11.42	1.971	226	8.734	15.085
Ovaries	0.173	0.0304	22	0.1210	0.2070
Pituitary	0.014	0.0024	22	0.0110	0.0160
Spleen	0.530	0.0859	44	0.4200	0.6720
Thymus	0.347	0.0990	22	0.2240	0.5130
Thyroids	0.0154	0.00415	468	0.01010	0.02260
ORGAN/BODY WEIGHT RATIOS, END OF IN-LIFE					
Adrenals	0.025	0.0042	21	0.0196	0.0311
Body weight	324	30.8	696	274.0	374.0
Brain	0.70	0.057	22	0.624	0.773
Kidneys	0.51	0.052	131	0.449	0.620
Liver	3.55	0.504	226	2.908	4.493
Ovaries	0.053	0.0077	22	0.0392	0.0655
Pituitary	0.004	0.0007	22	0.0034	0.0055
Spleen	0.166	0.0214	44	0.1373	0.2034
Thymus	0.107	0.0272	22	0.0676	0.1529
Thyroids	0.0048	0.00130	468	0.00312	0.00692

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2014
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All
Selected projects	503902 509704 510050 510056 510278 510577 510627 511144 511245 511313 511554 511570 511774 511811 511914 511928 512207 512219 512491 512573 512642 512785 515503 515716 517132 517295 517845 520542 520561 520639 520642 520839 520907 521064 521104 521130 521187 521192 521261 521269 521323 521361 521391 521414 521464 521550 521552 521584 521602 521603 521631 521633 521642 521651 521682 521694 521748 521749 521839 521850 521899 522005 522007 522108 522138 522140 522290 522500
ORGAN WEIGHTS (GRAM)	
Selected group	CONTROL
Selected parameters	ADRENALS BODYWEIG BRAIN KIDNEYS LIVER OVARIES PITUIT SPLEEN THYMUS THYROIDS UTERUS
Grouped measurements (ORGAN WEIGHTS (GRAM))	
Measurements removed	1 DAY 21 POST COITUM
END OF IN-LIFE	1 END OF TREATMENT 1 NECROPSY

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[1.1 Clinical Biochemistry](#)

APPENDIX 1

**HISTORICAL DATA
FEMALES****1.1 CLINICAL BIOCHEMISTRY**

MEASUREMENT	UNITS	MEAN	STD.DEV.	N	P5	P95
END OF TREATMENT						
ALAT	U/L	57.1	9.45	38	44.80	75.60
Albumin	g/L	27.9	2.29	38	24.50	31.60
ALP	U/L	138	52.8	38	68.0	229.0
ASAT	U/L	76.9	15.36	38	52.80	114.90
Bile Acids	umol/L	28.0	36.12	37	6.50	87.00
Total bilirubin	umol/L	2.3	0.52	38	1.30	3.10
Calcium	mmol/L	2.45	0.097	38	2.280	2.620
Cholesterol	mmol/L	1.86	0.272	38	1.410	2.370
Chloride	mmol/L	101	1.7	38	98.0	104.0
Creatinine	umol/L	38.4	2.62	38	33.30	42.90
Glucose	mmol/L	7.57	1.483	38	4.250	10.300
HDL cholesterol	mmol/L	1.13	0.205	22	0.870	1.340
Potassium	mmol/L	3.77	0.486	38	3.170	4.840
LDL Cholesterol	mmol/L	0.29	0.064	22	0.190	0.370
Sodium	mmol/L	137.7	1.68	38	135.20	140.30
Inorg.Phos	mmol/L	1.19	0.424	38	0.470	1.930
Total protein	g/L	56.8	3.85	38	50.40	63.70
Triglycerides	mmol/L	1.61	1.160	22	0.420	3.870
TSH	uIU/mL	0.353	0.2054	373	0.1270	0.6990
Total T3	ng/dL	56.6	15.29	341	20.00	80.00
Total T4	ug/dL	2.20	0.662	369	1.440	3.280
Urea	mmol/L	5.6	1.12	38	3.80	7.80

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2014
End year	2020
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All
Selected projects	503902 509704 510050 510056 510278 510577 510627 511144 511245 511313 511554 511570 511774 511811 511914 511928 512207 512219 512491 512573 512642 512785 515503 515716 517132 517295 517845 520542 520561 520639 520642 520839 520907 521064 521104 521130 521187 521192 521261 521269 521361 521391 521414 521464 521550 521552 521584 521602 521603 521631 521633 521642 521651 521682 521694 521748 521749 521850 521899 522007 522138 522290 522500
CLINICAL BIOCHEMISTRY	
Selected group	CONTROL
Selected parameters	ALAT ALB ALP ASAT BACID BILI CA CHOL CL CREA GLUC HDL HEM HEMI HEMS K LDL NA PHOS PROT TRIG TSHO TT3 TT4 UREA

2017-2021 historical control data OECD 421+422

REPRODUCTION DATA

MEASUREMENT	Mean	St.dev	N	P5	P95	Min	Max
Mating index	99	3.2	146	100	100	80	100
Fertility index	95	7.1	146	80	100	78	100
Conception index	97	6.7	19	ND ^a	ND ^a	80	100
Gestation index	98	4.4	145	89	100	78	100

ND^a = not determined for N < 20

Selection information

Species Rat
Dosing type All
Start year 2017
End year 2021

Selected projects	505074	514646	519373	20151967	20222350
	508973	514650	519484	20151994	20218715
	508989	514656	519506	20152394	20219839
	509008	514719	519520	20153214	
	509026	515091	519645	20155387	
	509044	515328	519674	20156955	
	509918	515453	520055	20157758	
	509944	515661	520224	20161715	
	509971	515792	520288	20161722	
	510084	516037	520294	20164070	
	510414	516148	520310	20164350	
	510917	516294	520331	20168083	
	511275	516329	520403	20168842	
	511846	516345	520451	20172120	
	512019	516356	520454	20173303	
	512350	516582	520472	20179374	
	512374	516592	20133605	20183273	
	512433	516775	20134630	20183641	
	512470	516843	20134823	20186559	
	512669	516990	20134824	20188708	
	512681	517133	20136782	20191506	
	512690	517403	20139003	20191510	
	512704	517496	20140515	20191836	
	512747	517502	20141791	20191866	
	512829	517528	20142767	20195323	
	512875	517636	20144266	20195986	
	512888	517954	20144288	20197288	
	512992	517992	20144692	20197624	
	513019	518230	20145353	20197639	
	513064	518366	20146107	20208719	
	513076	518373	20148107	20208942	
	513370	518391	20148127	20210023	
	513508	518629	20148423	20210431	
	513606	518656	20149499	20212888	
	513675	518885	20149502	20218712	
	513698	518902	20150770	20218718	
	513943	518920	20150803	20218721	
	514149	519038	20151439	20218724	
	514356	519064	20151541	20219689	
	514637	519085	20151947	20220063	

2017-2021 historical control data OECD 421+422

ESTROUS CYCLE TREATMENT PERIOD

PARAMETER	Mean	St.dev	N	P5	P95	Min	Max
Regular estrous cycle (%)	97.3	6.8	129	83.75	100	60.0	100

PARAMETER	Total	Regular	Irregular	Extended di-estrous	Acyclic	Extended estrous
Cycle classification (%)	100	94.4	2.1	2.2	0.2	0.2
Cycle classification (count)	1276	1205	27	28	2	3

ESTROUS CYCLE PRETEST PERIOD

PARAMETER	Mean	St.dev	N	P5	P95	Min	Max
Regular estrous cycle (%)	99.8	2.0	125	100	100	80.0	100

PARAMETER	Total	Regular	Irregular	Extended di-estrous	Acyclic	tended estrous
Cycle classification (%)	100	99.5	0.2	0.0	0.0	0.0
Cycle classification (count)	1250	1244	3	0	0	0

Selection information

Species	Rat
Dosing type	All
Start year	2017
End year	2021

Selected projects	505074	518629	20149499	20210431
	505553	518656	20149502	20212888
	509971	518885	20150237	20218712
	512350	518902	20150770	20218718
	513675	518920	20150803	20218721
	514149	519038	20151439	20218724
	514356	519064	20151541	20219689
	514637	519085	20151947	20220063
	514646	519373	20151967	20222350
	514650	519484	20151994	20218715
	514656	519506	20152394	20219839
	514719	519520	20153214	
	515091	519645	20155387	
	515328	519674	20156955	
	515453	520055	20157758	
	515661	520224	20161715	
	515792	520288	20161722	
	516037	520294	20164070	
	516148	520310	20164350	
	516294	520331	20168083	
	516329	520403	20168842	
	516345	520451	20172120	
	516356	520454	20173303	
	516582	20133605	20179374	
	516592	20134630	20183273	
	516775	20134823	20183641	
	516843	20134824	20186559	
	516990	20136782	20188708	
	517133	20139003	20191506	
	517403	20140515	20191510	
	517496	20141791	20191836	
	517502	20142767	20191866	
	517528	20144266	20195323	
	517636	20144288	20195986	
	517954	20144692	20197288	
	517992	20145353	20197624	
	518230	20146107	20197639	
	518366	20148107	20208719	
	518373	20148127	20208942	
	518391	20148423	20210023	

APPENDIX 1

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APPENDIX 1

**HISTORICAL DATA
FEMALES****1.1 BODY WEIGHTS (GRAM)**

DAYS	MEAN	STD.DEV.	N	P5	P95
F0-GENERATION POST COITUM					
0	232	13.4	1215	210.0	254.0
4	245	13.8	1206	222.0	269.0
7	252	14.4	1216	228.0	278.0
11	266	15.6	1207	240.0	293.0
14	276	16.6	1220	249.0	304.0
17	299	18.9	1209	268.0	329.0
20	335	23.8	1216	295.0	373.0
F0-GENERATION LACTATION					
1	260	16.9	1217	234.0	289.0
4	273	16.6	1209	245.0	300.0
5	258	11.9	5	246.0	277.0
7	280	17.3	1209	251.0	309.0
10	288	17.8	19	265.0	328.0
13	293	18.6	1206	261.0	324.0
17	298	18.7	10	276.0	337.0
20	287	17.5	5	261.0	308.0
21	281	18.9	31	252.0	319.0
28	275	17.1	10	259.0	310.0

APPENDIX 1

**HISTORICAL DATA
FEMALES****1.2 BODY WEIGHT GAIN (%)**

DAYS	MEAN	STD.DEV.	N	P5	P95
F0-GENERATION POST COITUM					
0	0	0.0	1241	0.0	0.0
4	6	2.1	1205	2.3	9.1
7	9	2.6	1215	4.4	12.8
11	15	3.3	1206	9.3	20.1
14	19	3.8	1218	13.0	25.2
17	29	4.9	1207	20.6	36.3
20	44	7.4	1214	31.8	55.3
F0-GENERATION LACTATION					
1	0	0.0	1223	0.0	0.0
4	5	3.5	1205	-1.1	9.9
5	8	3.0	5	3.8	12.1
7	8	4.0	1205	0.4	13.7
10	9	5.8	19	-6.7	15.8
13	13	5.1	1202	3.9	20.5
17	13	4.6	10	5.7	18.2
20	13	5.7	5	5.7	19.2
21	8	4.7	31	0.7	15.7
28	4	2.9	10	-0.7	8.8

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**HISTORICAL DATA
FEMALES****1.3 FOOD CONSUMPTION (G/ANIMAL/DAY)**

DAYS	MEAN	STD.DEV.	N	P5	P95
F0-GENERATION POST COITUM					
1	28	10.1	80	15.0	46.0
2	19	5.7	1195	13.0	31.0
3	30	9.7	84	18.0	48.0
4	29	10.0	97	16.0	45.0
5	31	9.5	87	18.0	47.0
6	20	5.3	1199	14.3	31.0
7	28	8.0	87	19.0	45.0
8	29	8.2	87	19.0	43.0
9	21	4.6	1204	15.3	29.5
10	29	8.8	87	19.0	44.0
11	28	8.7	97	18.0	42.0
12	31	9.2	96	17.0	47.0
13	22	5.4	1205	16.3	32.0
14	30	8.4	96	19.0	45.0
15	29	7.9	96	18.0	43.0
16	22	5.1	1200	17.0	31.0
17	30	9.3	106	19.0	49.0
18	32	8.1	95	22.0	45.0
19	24	5.1	1205	18.0	33.0
20	31	8.5	96	19.0	47.0
21	30	8.3	76	18.0	45.0
22	22	8.1	73	11.0	34.0
23	19	8.2	38	11.0	44.0
24	27	5.3	4	21.0	32.0
25	25	4.2	2	22.0	28.0
26	25	2.8	2	23.0	27.0
F0-GENERATION LACTATION					
2	34	9.8	96	17.0	52.0
3	31	8.5	1201	19.7	45.0
4	53	14.5	100	29.5	77.5
5	53	13.5	101	32.0	76.0
6	41	8.8	1205	29.0	56.0
7	61	16.6	100	37.5	90.5
8	59	13.3	110	38.0	80.0
9	64	16.2	101	44.0	92.0
10	52	9.9	1193	39.3	67.0
11	70	19.1	101	46.0	99.0
12	77	24.1	109	49.0	123.0
13	78	24.1	99	48.0	126.0
14	72	25.5	41	51.0	116.0
15	79	27.7	41	55.0	135.0
17	73	13.2	26	56.1	96.9
19	68	5.0	10	62.0	79.3
25	102	6.8	10	92.3	111.7

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**HISTORICAL DATA
FEMALES****1.4 RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)**

DAYS	MEAN	STD.DEV.	N	P5	P95
F0-GENERATION POST COITUM					
1	121	42.8	80	63.2	196.0
2	78	23.7	1195	54.8	132.0
3	123	38.5	84	72.3	187.0
4	117	39.0	97	64.3	182.9
5	124	37.1	87	72.5	196.9
6	80	20.2	1199	58.6	124.0
7	111	30.6	87	75.1	166.1
8	113	30.9	87	73.9	168.0
9	78	17.5	1204	59.6	112.8
10	110	30.9	87	67.1	165.4
11	106	31.6	97	63.0	157.4
12	116	33.1	96	62.0	174.7
13	80	18.4	1205	61.2	117.9
14	109	28.5	96	64.8	148.7
15	106	27.2	96	64.3	145.3
16	75	16.1	1200	58.9	104.8
17	100	29.9	106	58.2	160.1
18	106	27.3	95	71.9	148.6
19	71	14.7	1204	55.7	102.8
20	93	24.5	96	55.7	143.3
21	91	24.5	76	51.2	132.5
22	67	24.1	73	31.5	104.9
23	58	22.7	38	30.8	116.9
24	87	10.0	4	72.4	94.1
25	92	5.8	2	88.4	96.6
26	93	0.5	2	92.4	93.1
F0-GENERATION LACTATION					
2	132	40.2	96	59.0	201.6
3	112	30.1	1201	75.0	163.3
4	193	51.9	100	109.5	282.4
5	193	49.7	101	117.3	271.7
6	145	30.4	1205	109.0	198.0
7	216	58.2	100	132.5	312.0
8	211	47.0	110	135.0	280.0
9	228	56.6	101	152.1	317.1
10	179	34.1	1192	140.5	234.3
11	241	67.6	101	152.5	335.8
12	262	82.5	109	169.9	414.7
13	268	83.2	99	160.3	423.2
14	248	87.5	41	163.5	395.9
15	273	89.1	41	192.3	487.4
17	260	48.4	26	210.6	357.5
19	238	18.6	10	209.2	268.6
25	374	33.7	10	330.9	419.4

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**HISTORICAL DATA
FEMALES****1.5 WATER CONSUMPTION (G/ANIMAL/DAY)**

DAYS	MEAN	STD.DEV.	N	P5	P95
F0-GENERATION POST COITUM					
1	25	6.2	95	16.0	37.0
2	30	7.1	94	20.0	42.0
3	31	11.2	91	21.0	45.0
4	33	7.3	89	24.0	47.0
5	29	8.0	90	18.0	46.0
6	30	7.4	95	19.0	44.0
7	30	6.9	101	21.0	43.0
8	29	7.6	104	18.0	41.0
9	28	5.9	104	19.0	38.0
10	30	8.0	98	20.0	43.0
11	35	8.2	98	23.0	53.0
12	34	7.9	96	23.0	49.0
13	34	7.6	101	23.0	47.0
14	38	7.5	102	28.0	50.0
15	35	7.8	102	24.0	48.0
16	37	8.6	97	26.0	53.0
17	42	9.7	92	29.0	59.0
18	39	8.1	90	26.0	54.0
19	38	9.4	95	25.0	54.0
20	38	9.0	97	23.0	55.0
21	33	7.7	34	20.0	48.0
22	24	8.9	20	14.0	39.0
23	25	10.0	4	16.0	39.0
24	.	.	0	.	.
25	.	.	0	.	.
26	.	.	0	.	.
27	.	.	0	.	.
F0-GENERATION LACTATION					
2	38	9.9	95	23.0	55.0
3	44	10.6	98	29.0	62.0
4	55	11.7	104	37.0	79.0
5	48	10.4	113	31.0	67.0
6	51	11.4	123	34.0	70.0
7	59	13.0	125	35.0	82.0
8	57	11.9	123	35.0	78.0
9	62	13.1	124	42.0	85.0
10	64	12.1	121	44.0	84.0
11	68	13.8	121	43.0	87.0
12	69	14.3	124	45.0	89.0
13	74	14.2	124	47.0	94.0
14	66	17.6	34	41.0	98.0
15	69	19.0	13	28.0	90.0
16	.	.	0	.	.

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**HISTORICAL DATA
FEMALES****1.6 PRECOITAL TIME**

Day of the pairing period	Number of females mated
------------------------------	----------------------------

F0-GENERATION POST COITUM; PAIRING PERIOD 1

1	414
2	316
3	297
4	214
5	5
6	4
9	1
10	1
12	6
13	19
14	19
15	1

N	1297
MEAN PRECOITAL TIME	2.7
MEDIAN PRECOITAL TIME	2.0

F0-GENERATION POST COITUM; PAIRING PERIOD 2

-1	1
1	4
2	2
3	1

N	8
MEAN PRECOITAL TIME	1.3
MEDIAN PRECOITAL TIME	1.0

APPENDIX 1

**HISTORICAL DATA
MALES****1.7 BODY WEIGHTS OF PUPS (GRAM)**

DAYS	MEAN	STD.DEV.	N	P5	P95
F0-GENERATION LACTATION					
DAY 1	6.3	0.70	6960	5.30	7.50
DAY 4	9.5	1.26	6879	7.60	11.70
DAY 7	16.0	1.85	4649	13.10	19.00
DAY 10	23.8	2.01	41	21.10	27.60
DAY 13	30.7	2.89	4611	26.00	35.30
DAY 17	41.6	2.05	41	38.90	45.00
DAY 21	52.6	4.44	124	47.00	60.50
DAY 28	92.8	5.96	41	85.00	102.00

FEMALES**1.7 BODY WEIGHTS OF PUPS (GRAM)**

DAYS	MEAN	STD.DEV.	N	P5	P95
F0-GENERATION LACTATION					
DAY 1	6.0	0.68	6965	5.00	7.20
DAY 4	9.1	1.24	6870	7.30	11.20
DAY 7	15.4	1.84	4666	12.50	18.50
DAY 10	22.4	2.13	38	18.70	26.80
DAY 13	29.8	2.91	4628	25.10	34.70
DAY 17	40.3	1.90	37	38.00	44.00
DAY 21	50.3	4.21	117	44.00	58.00
DAY 28	85.5	4.75	37	79.00	94.00

APPENDIX 1

**HISTORICAL DATA
FEMALES****1.8 DEVELOPMENTAL DATA**

Females	MEAN	STD.DEV.	N	P5	P95
F0-GENERATION LACTATION					
Duration of gestation	21.4	0.55	1228	21.00	22.00
Dead pups at first litter check	0.1	0.64	1228	0.00	1.00
Living pups at first litter check	11.4	2.85	1228	6.00	15.00
Postnatal loss	0.2	0.81	1228	0.00	1.00
Culled pups	3.5	2.19	1228	0.00	7.00
Living pups on culling day	7.6	1.36	1228	5.00	8.00
Breeding loss culling day - rearing day	0.0	0.28	1228	0.00	0.00
Living pups on rearing day	7.6	1.47	1228	4.00	8.00

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**HISTORICAL DATA
FEMALES****1.9 DEVELOPMENTAL DATA SUBSET**

Parameter	Value
F0-GENERATION LACTATION	
Litters total	1228
Dead pups at first litter check	152
Number of litters affected	84
Living pups at first litter check	13954
Live males	6976
% of living pups at first litter check	50.0
Live females	6978
% of living pups at first litter check	50.0
Postnatal loss	200
% of living pups at first litter check	1.4
Number of litters affected	131
Culled pups	4317
Living pups on culling day	9353
Breeding loss culling day - rearing day	36
% of living pups on culling day	0.4
Number of litters affected	27
Living pups on rearing day	9274
Live males	4631
% of living pups on rearing day	49.9
Live females	4643
% of living pups on rearing day	50.1
Viability index	98.6
Weaning index	99.2

APPENDIX 1

**HISTORICAL DATA
MALES****1.10 ANOGENITAL DISTANCE AND NIPPLE RETENTION**

	MEAN	STD.DEV.	N	P5	P95
F0-GENERATION LACTATION					
anogenital dist M mm	2.68	0.294	1149	2.257	3.190
anogenital dist F mm	1.03	0.185	1150	0.732	1.350
Number of nipples	0.00	0.000	1137	0.000	0.000

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2016
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All
Selected projects	505074 505553 509971 512350 513675 514149 514356 514637 514646 514650 514656 514719 515091 515328 515453 515661 515792 516148 516294 516329 516345 516356 516582 516592 516775 516843 516990 517133 517403 517496 517502 517528 517636 517954 517992 518230 518366 518373 518391 518629 518656 518885 518902 518920 519038 519064 519085 519373 519484 519506 519520 519645 519674 520055 520224 520288 520294 520310 520331 520403 520451 520454 520472 520482 520499 520504 520517 520537 520594 520638 520670 520691 520706 520717 520737 520759 520769 520807 520814 520830 520864 520893 520913 520941 520944 520982 520995 521008 521042 521100 521107 521109 521135 521140 521143 521193 521207 521262 521273 521308 521341 521416 521443 521492 521511 521525 521577 521589 521643 521666 521714 521720 521729 521789 521802 521807 521811 521936 521947 521952 521994 522037 522065 522072 522073 522077 522081 522102 522111 522116 522164
BODY WEIGHTS (GRAM)	
Selected group	CONTROL
Selected days	0 1 4 5 7 10 11 13 14 17 20 21 28
BODY WEIGHT GAIN (%)	
Selected group	CONTROL
Selected days	0 1 4 5 7 10 11 13 14 17 20 21 28
FOOD CONSUMPTION (G/ANIMAL/DAY)	
Selected group	CONTROL
Selected days	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)	
Selected group	CONTROL
Selected days	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26
WATER CONSUMPTION (G/ANIMAL/DAY)	
Selected group	CONTROL
Selected days	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27
PRECOITAL TIME	
Selected group	CONTROL
Selected group	
BODY WEIGHTS OF PUPS (GRAM)	
Selected group	CONTROL
Selected parameters	1 10 13 17 21 28 4 7
DEVELOPMENTAL DATA	
Selected group	CONTROL
Selected parameters	BREEDING LOSS CULLING DAY - REARING DAY CULLED PUPS DEAD PUPS AT FIRST LITTER CHECK DURATION OF GESTATION LIVING PUPS AT FIRST LITTER CHECK LIVING PUPS ON CULLING DAY LIVING PUPS

Selection Criteria for Historical Data

Selection information	Value
	ON REARING DAY POSTNATAL LOSS
DEVELOPMENTAL DATA SUBSET	
Selected group	CONTROL
Selected parameters	BREEDING LOSS CULLING DAY - REARING DAY CULLED PUPS DEAD PUPS AT FIRST LITTER CHECK LIVING PUPS AT FIRST LITTER CHECK LIVING PUPS ON CULLING DAY LIVING PUPS ON REARING DAY POSTNATAL LOSS VIABILITY INDEX WEANING INDEX
ANOGENITAL DISTANCE AND NIPPLE RETENTION	
Selected group	CONTROL
Selected parameters	ANOGENITAL DIST F MM ANOGENITAL DIST M MM NUMBER OF NIPPLES

APPENDIX 1

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[1.1 Implantation Sites](#)

APPENDIX 1

**HISTORICAL DATA
FEMALES****1.1 IMPLANTATION SITES**

	UNITS	MEAN	STD.DEV.	N	P5	P95
AT NECROPSY						
Implantations		12.3	2.91	777	6.00	16.00

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2017
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All
Selected projects	517134 517996 518368 518375 518397 518658 518886 518903 518925 519039 519066 519374 519486 519507 519521 519646 519679 520056 520225 520290 520296 520312 520333 520405 520411 520467 520473 520483 520501 520506 520512 520518 520538 520595 520641 520671 520692 520707 520718 520738 520762 520770 520808 520815 520831 520858 520865 520884 520895 520915 520943 520980 520987 520997 521018 521045 521102 521136 521144 521150 521194 521209 521263 521274 521309 521342 521417 521444 521493 521514 521526 521578 521590 521644 521667 521715 521721 521730 521790 521803 521808 521812 521937 521953 522038 522066 522069 522074 522078 522082 522103 522109 522113 522165
IMPLANTATION SITES	
Selected group	CONTROL
Selected parameters	IMPL
Grouped measurements (IMPLANTATION SITES)	
AT NECROPSY	1 AT LACTATION 1 AT NECROPSY 1 AT NECROSPY 2 AT NECROPSY 3 AT LACTATION 4 AT LACTATION

APPENDIX 1

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- 1.1 Body Weights
- 1.2 Body Weight Gain
- 1.3 Food Consumption
- 1.4 Relative Food Consumption
- 1.5 Haematology
- 1.6 Clinical Biochemistry
- 1.7 Urinalysis
- 1.8 Organ Weights

APPENDIX 1

**HISTORICAL DATA
MALES****1.1 BODY WEIGHTS (GRAM)**

DAYS	MEAN	STD.DEV.	N	P5	P95
1	292	26.1	1012	267.0	330.0
2	299	18.5	20	273.5	329.0
3	298	16.9	30	277.0	332.0
4	304	18.0	50	277.0	330.0
5	309	19.6	20	283.5	343.0
6	327	13.1	10	310.0	345.0
7	331	13.4	10	311.0	348.0
8	316	25.0	1007	287.0	352.0
11	331	22.5	30	294.0	360.0
12	354	20.4	10	310.0	373.0
15	336	25.3	1008	302.0	376.0
18	344	25.8	30	305.0	377.0
22	348	25.0	1007	309.0	389.0
25	354	27.5	20	314.0	399.5
29	363	26.9	995	321.0	407.0
30	340	23.9	40	301.5	382.0
33	352	16.3	10	319.0	367.0
36	347	37.6	42	304.0	423.0
37	365	27.6	28	317.0	405.0
41	381	38.7	5	337.0	437.0
43	359	32.1	53	315.0	407.0
46	389	39.9	5	349.0	450.0
50	352	27.8	25	315.0	390.0
57	361	29.2	25	324.0	406.0
64	367	30.3	20	321.5	414.0
71	377	30.2	20	331.5	422.5
78	381	30.9	20	331.0	430.5
85	389	31.6	20	338.0	438.0

FEMALES**1.1 BODY WEIGHTS (GRAM)**

DAYS	MEAN	STD.DEV.	N	P5	P95
1	220	14.8	864	201.0	240.0
2	220	8.8	20	206.5	235.5
3	222	11.1	30	205.0	243.0
4	216	13.4	50	189.0	235.0
5	222	9.9	19	206.0	248.0
6	228	8.9	9	214.0	238.0
7	228	12.9	9	205.0	252.0
8	224	14.3	864	205.0	245.0
11	222	14.4	30	199.0	243.0
12	227	9.6	10	215.0	248.0
15	230	13.9	865	209.0	250.0
18	232	19.5	4	204.0	249.0
22	240	29.3	62	180.0	271.0
29	242	34.6	38	184.0	291.0
32	.	.	0	.	.
33	.	.	0	.	.
36	248	49.7	29	184.0	345.0
43	237	31.8	22	199.0	279.0
50	234	21.9	22	204.0	269.0
52	230	13.3	5	210.0	246.0
57	220	12.0	9	205.0	240.0
60	243	17.5	5	217.0	260.0
64	224	13.6	9	206.0	244.0
67	242	18.6	5	213.0	262.0
71	227	16.2	9	208.0	251.0

APPENDIX 1

**HISTORICAL DATA
MALES****1.2 BODY WEIGHT GAIN (%)**

DAYS	MEAN	STD.DEV.	N	P5	P95
1	0	0.0	1013	0.0	0.0
2	0	0.8	20	-1.1	1.8
3	1	1.0	30	0.0	3.1
4	3	1.5	50	0.9	5.9
5	4	1.3	20	1.8	5.9
6	5	1.1	10	3.1	6.8
7	6	1.1	10	4.7	7.9
8	8	3.7	1007	4.1	12.9
11	13	2.6	30	9.2	17.7
12	13	3.2	10	9.3	18.2
15	16	6.5	1007	9.0	22.4
18	18	4.0	30	10.8	23.2
22	20	8.8	1006	11.4	27.8
25	24	5.2	20	15.9	33.0
29	25	10.4	994	14.4	35.3
30	18	7.2	40	6.7	30.8
33	23	4.8	10	14.7	29.6
36	56	38.5	42	16.9	119.9
37	25	7.3	28	11.7	36.8
41	24	5.4	5	19.1	31.6
43	57	39.2	53	20.2	132.5
46	27	5.9	5	21.3	35.5
50	95	38.3	25	27.5	146.4
57	100	39.9	25	28.6	152.6
64	123	23.1	20	92.6	162.7
71	129	22.5	20	96.4	167.3
78	131	23.1	20	95.3	168.9
85	136	24.4	20	97.3	177.9

FEMALES**1.2 BODY WEIGHT GAIN (%)**

DAYS	MEAN	STD.DEV.	N	P5	P95
1	0	0.0	868	0.0	0.0
2	0	2.1	20	-3.6	3.8
3	0	3.3	30	-4.7	5.5
4	1	2.8	50	-3.0	6.0
5	0	1.5	19	-2.3	2.8
6	1	2.4	9	-2.9	4.2
7	1	3.4	9	-6.4	4.7
8	2	3.1	862	-1.9	7.1
11	6	3.9	30	-0.5	13.1
12	3	2.0	10	-0.9	6.0
15	5	4.3	861	-0.8	10.6
18	7	1.7	4	4.8	8.3
22	16	9.9	62	6.2	39.5
29	24	13.9	38	7.9	50.0
32	.	.	0	.	.
33	.	.	0	.	.
36	32	20.6	29	8.7	61.8
43	32	23.7	22	8.2	70.1
50	32	25.3	22	7.7	73.5
52	8	2.7	5	5.1	12.5
57	64	8.7	9	54.6	79.1
60	14	4.5	5	10.7	21.5
64	67	8.5	9	56.1	79.4
67	14	3.8	5	9.2	18.2
71	68	11.5	9	53.2	87.3

APPENDIX 1

**HISTORICAL DATA
MALES****1.3 FOOD CONSUMPTION (G/ANIMAL/DAY)**

DAYS	MEAN	STD.DEV.	N (CAGE)	P5	P95
4	23	1.9	200	20.0	25.7
5	20	0.6	2	19.7	20.6
11	23	2.1	200	19.5	26.0
12	21	0.6	2	20.7	21.6
18	23	2.4	196	19.4	27.0
19	22	0.6	4	21.6	22.9
23	.	.	0	.	.
25	22	2.5	190	18.2	25.9
26	21	1.9	6	17.6	21.9
29	.	.	0	.	.
31	28	0.1	2	27.9	28.1
32	23	1.5	6	21.4	25.1
33	24	2.9	8	19.6	28.4
34	27	.	1	26.7	26.7
38	26	.	1	25.8	25.8
39	23	1.7	5	20.1	24.5
40	23	1.1	6	21.2	24.2
43	22	.	1	21.6	21.6
46	22	1.9	5	20.2	24.8
53	22	1.9	5	19.5	24.3
60	22	0.8	4	20.5	22.5
67	21	1.6	4	19.5	23.0
74	22	2.8	4	18.4	24.2
81	21	2.0	4	18.3	22.5
87	20	1.4	2	19.4	21.4
88	.	.	0	.	.

FEMALES**1.3 FOOD CONSUMPTION (G/ANIMAL/DAY)**

DAYS	MEAN	STD.DEV.	N (CAGE)	P5	P95
4	16	2.0	172	13.1	18.3
5	14	0.5	2	13.4	14.0
11	16	2.0	172	12.7	18.2
12	15	0.2	2	14.5	14.8
18	17	0.8	3	15.8	17.2
25	17	0.7	3	16.2	17.5
32	17	0.7	3	16.3	17.6
39	17	0.5	3	16.3	17.3
46	16	1.6	2	15.2	17.5
53	17	0.6	2	17.0	17.9
60	16	0.3	2	16.0	16.5
67	17	0.4	2	16.3	16.8

APPENDIX 1

**HISTORICAL DATA
MALES****1.4 RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)**

DAYS	MEAN	STD.DEV.	N (CAGE)	P5	P95
4	73	6.9	200	62.8	82.1
5	66	0.6	2	65.2	66.1
11	72	7.2	200	62.3	81.3
12	69	0.7	2	68.5	69.4
18	67	7.2	196	55.9	78.1
19	63	1.5	4	61.1	64.4
23	.	.	0	.	.
25	61	6.9	190	50.9	70.5
26	56	4.2	6	49.9	61.3
29	.	.	0	.	.
31	80	0.6	2	79.2	80.1
32	68	8.1	6	57.7	76.1
33	65	6.9	8	53.3	75.7
34	71	.	1	71.2	71.2
38	68	.	1	67.8	67.8
39	67	6.1	5	56.2	70.7
40	61	3.1	6	57.0	66.3
43	55	.	1	55.5	55.5
46	63	5.2	5	55.1	68.4
53	62	5.6	5	51.9	65.6
60	59	1.3	4	57.0	59.9
67	57	3.8	4	52.9	61.0
74	57	5.5	4	50.2	61.9
81	54	3.3	4	49.1	56.5
87	54	3.3	2	51.8	56.5
88	.	.	0	.	.

FEMALES**1.4 RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)**

DAYS	MEAN	STD.DEV.	N (CAGE)	P5	P95
4	71	9.2	172	59.2	81.3
5	62	4.4	2	58.4	64.7
11	71	9.1	172	57.2	83.1
12	66	3.4	2	63.4	68.3
18	86	13.9	3	69.5	94.0
25	83	11.1	3	70.3	90.5
32	81	10.3	3	68.9	87.9
39	77	7.2	3	68.5	81.8
46	73	13.6	2	63.1	82.3
53	79	4.4	2	76.4	82.6
60	72	2.5	2	70.7	74.2
67	74	2.8	2	71.9	75.9

APPENDIX 1

**HISTORICAL DATA
MALES****1.5 HAEMATOLOGY**

MEASUREMENT	UNITS	MEAN	STD.DEV.	N	P5	P95
END OF TREATMENT						
APTT	s	18.1	3.18	385	13.10	23.00
Basophils	%WBC	0.2	0.04	13	0.10	0.20
Basophils	10E9/L	0.0	0.01	389	0.00	0.02
Eosinophils	%WBC	1.1	0.38	13	0.50	1.70
Eosinophils	10E9/L	0.1	0.04	389	0.00	0.17
Haematocrit	L/L	0.475	0.0230	390	0.4390	0.5080
Haemoglobin	mmol/L	10.0	0.43	390	9.20	10.70
LUC	%WBC	0.9	0.13	5	0.80	1.10
LUC	10E9/L	0.1	0.04	103	0.02	0.12
Lymphocytes	10E9/L	6.1	1.55	104	3.72	8.66
Lymphocytes	%WBC	84.2	4.83	8	77.80	90.20
Lymphocytes	10E9/L	6.4	1.63	284	4.00	9.10
MCH	fmol	1.14	0.041	390	1.080	1.210
MCHC	mmol/L	21.03	0.617	390	20.080	22.110
MCV	fL	54.1	1.64	390	51.50	56.80
Monocytes	%WBC	1.5	0.25	13	1.00	1.80
Monocytes	10E9/L	0.1	0.06	389	0.08	0.24
Neutrophils	10E9/L	1.0	0.33	389	0.60	1.60
Platelets	10E9/L	726	93.4	389	581.0	882.0
PT	s	18.1	1.32	379	16.20	20.50
Red blood cells	10E12/L	8.80	0.420	390	8.080	9.490
RDW	%	12.1	1.34	387	10.90	13.40
RDWg	%	12.6	0.38	3	12.30	13.00
Reticulocytes	10E9/L	222.0	40.07	390	164.40	290.70
Neutrophils	%WBC	12.9	4.70	8	7.20	19.40
WBC	10E9/L	7.6	1.78	389	5.01	10.70

FEMALES**1.5 HAEMATOLOGY**

MEASUREMENT	UNITS	MEAN	STD.DEV.	N	P5	P95
END OF TREATMENT						
APTT	s	17.9	2.77	313	13.20	22.30
Basophils	%WBC	0.1	0.09	15	0.00	0.30
Basophils	10E9/L	0.0	0.00	318	0.00	0.01
Eosinophils	%WBC	1.5	0.95	15	0.00	3.90
Eosinophils	10E9/L	0.1	0.09	318	0.00	0.20
Haematocrit	L/L	0.431	0.0240	318	0.3860	0.4690
Haemoglobin	mmol/L	8.8	0.46	318	8.10	9.50
LUC	%WBC	0.9	0.48	5	0.50	1.60
LUC	10E9/L	0.0	0.01	80	0.01	0.05
Lymphocytes	10E9/L	3.5	1.04	81	2.23	5.10
Lymphocytes	%WBC	67.7	5.54	10	60.80	77.70
Lymphocytes	10E9/L	3.4	0.96	237	2.00	5.00
MCH	fmol	1.22	0.049	318	1.140	1.300
MCHC	mmol/L	20.50	0.616	318	19.550	21.460
MCV	fL	59.4	2.46	318	55.60	63.60
Monocytes	%WBC	2.3	0.76	15	1.40	4.70
Monocytes	10E9/L	0.1	0.05	318	0.03	0.20
Neutrophils	10E9/L	1.4	0.50	318	0.80	2.20
Platelets	10E9/L	758	113.1	317	555.0	931.0
PT	s	17.6	1.18	314	15.90	19.70
Red blood cells	10E12/L	7.26	0.412	318	6.600	8.050
RDW	%	12.7	1.12	314	11.10	14.70
RDWg	%	11.9	1.05	4	10.40	12.80
Reticulocytes	10E9/L	244.6	46.23	318	175.60	321.50
Neutrophils	%WBC	28.7	5.90	10	19.30	35.90
WBC	10E9/L	5.0	1.24	318	3.16	7.20

APPENDIX 1

**HISTORICAL DATA
MALES****1.6 CLINICAL BIOCHEMISTRY**

MEASUREMENT	UNITS	MEAN	STD.DEV.	N	P5	P95
END OF TREATMENT						
ALAT	U/L	50.8	13.39	420	33.00	74.45
Albumin	g/L	32.5	1.25	420	30.60	34.60
ALP	U/L	162	47.5	420	102.0	256.0
ASAT	U/L	84.3	14.05	420	65.25	108.20
Bile Acids	umol/L	25.8	15.38	413	9.50	54.00
Total bilirubin	umol/L	2.3	0.41	420	1.60	3.00
Calcium	mmol/L	2.62	0.080	420	2.495	2.745
Cholesterol	mmol/L	1.96	0.356	420	1.410	2.545
Chloride	mmol/L	102	1.8	420	100.0	105.0
Creatinine	umol/L	36.9	2.53	420	33.00	41.20
GGT	U/L	0.8	0.14	8	0.60	1.00
Glucose	mmol/L	9.07	1.819	420	6.425	12.195
Haemo (P)	score 0/6	0	0.0	5	0.0	0.0
Haemo (I)	score 0/6	0	0.0	10	0.0	0.0
Haemo (S)	score 0/6	0	0.0	5	0.0	0.0
Potassium	mmol/L	3.91	0.241	420	3.550	4.350
Sodium	mmol/L	141.4	1.61	420	138.95	144.35
Inorg.Phos	mmol/L	2.02	0.211	420	1.660	2.350
Total protein	g/L	64.1	2.32	420	60.40	67.90
Triglycerides	mmol/L	0.75	0.349	5	0.450	1.280
TSH	uIU/mL	0.138	0.1283	150	0.0320	0.3690
Total T4	ug/dL	4.63	1.055	916	3.060	6.480
Urea	mmol/L	6.8	1.50	420	4.80	9.65

FEMALES**1.6 CLINICAL BIOCHEMISTRY**

MEASUREMENT	UNITS	MEAN	STD.DEV.	N	P5	P95
END OF TREATMENT						
ALAT	U/L	106.3	26.61	330	66.30	155.40
Albumin	g/L	29.8	1.81	330	27.30	32.80
ALP	U/L	321	150.6	330	114.0	576.0
ASAT	U/L	103.0	24.87	330	79.10	132.50
Bile Acids	umol/L	21.7	20.28	330	9.00	45.70
Total bilirubin	umol/L	2.1	0.45	330	1.50	2.90
Calcium	mmol/L	2.48	0.111	330	2.280	2.670
Cholesterol	mmol/L	2.11	0.434	330	1.530	2.840
Chloride	mmol/L	102	2.2	330	98.0	105.0
Creatinine	umol/L	39.5	5.16	330	35.00	44.40
GGT	U/L	0.8	0.26	4	0.60	1.20
Glucose	mmol/L	7.57	1.405	330	5.620	10.160
Haemo (P)	score 0/6	0	0.0	5	0.0	0.0
Haemo (I)	score 0/6	0	0.0	10	0.0	0.0
Haemo (S)	score 0/6	0	0.0	5	0.0	0.0
Potassium	mmol/L	4.61	0.438	330	3.860	5.340
Sodium	mmol/L	139.1	2.05	330	136.00	142.30
Inorg.Phos	mmol/L	1.15	0.560	330	0.330	2.080
Total protein	g/L	56.8	3.16	330	52.10	62.20
Triglycerides	mmol/L	0.45	0.269	5	0.220	0.880
TSH	uIU/mL	0.246	0.1961	146	0.0640	0.6250
Total T4	ug/dL	2.81	0.737	165	1.740	4.040
Urea	mmol/L	10.1	1.19	330	8.30	11.80
PND 4 PUPS						
Total T4	ug/dL	1.43	0.283	16	1.060	1.940

APPENDIX 1

**HISTORICAL DATA
MALES****1.7 URINALYSIS**

MEASUREMENT	UNITS	MEAN	STD.DEV.	N	P5	P95
END OF TREATMENT						
Bilirubin	score 0/3	0	0.0	5	0.0	0.0
Clarity	score 1/3	1	0.4	5	1.0	2.0
Colour	score 1/5	1	0.0	5	1.0	1.0
WBC	score 0/3	0	0.0	5	0.0	0.0
Glucose	score 0/3	0	0.0	5	0.0	0.0
Blood	score 0/3	0	0.0	5	0.0	0.0
Ketones	score 0/3	1	0.5	5	0.0	1.0
Nitrite	pos/neg	0.60	0.548	5	0.000	1.000
pH		6.9	0.42	5	6.50	7.50
Protein	score 0/3	0	0.0	5	0.0	0.0
Bacteria	score 0/3	3	0.0	5	3.0	3.0
Casts	score 0/3	0	0.0	5	0.0	0.0
Crystals	score 0/3	2	0.4	5	2.0	3.0
Epithelial cells	score 0/3	1	0.5	5	1.0	2.0
Specific gravity		1.025	0.0060	5	1.0170	1.0330
Other	score 0/3	0	0.0	5	0.0	0.0
RBC-sed.	score 0/3	0	0.0	5	0.0	0.0
WBC-sed.	score 0/3	0	0.5	5	0.0	1.0
Urobilinogen	score 0/3	0	0.0	5	0.0	0.0
Volume	mL	13	2.9	5	9.0	16.0

APPENDIX 1

**HISTORICAL DATA
MALES****1.8 ORGAN WEIGHTS (GRAM)**

ORGAN	MEAN	STD.DEV.	N	P5	P95
ORGAN WEIGHT, END OF TREATMENT					
Adrenals	0.060	0.0091	384	0.0461	0.0750
Body weight	344	25.0	955	305.0	386.0
Brain	2.03	0.073	375	1.914	2.156
Epididymides	1.091	0.0922	946	0.9490	1.2490
Heart	0.956	0.0889	375	0.8240	1.1190
Kidneys	2.26	0.225	434	1.939	2.658
Liver	8.57	1.110	460	7.099	10.431
Prostate	0.823	0.1513	918	0.5940	1.0580
Seminal vesicles	1.297	0.2352	918	0.9320	1.6750
Spleen	0.574	0.0818	395	0.4510	0.7360
Testes	3.47	0.270	946	3.014	3.906
Thymus	0.362	0.0950	395	0.2350	0.5030
Thyroids	0.0167	0.00312	917	0.01220	0.02240
ORGAN/BODY WEIGHT RATIOS, END OF TREATMENT					
Adrenals	0.018	0.0026	383	0.0134	0.0223
Body weight	344	25.0	955	305.0	386.0
Brain	0.60	0.041	374	0.531	0.665
Epididymides	0.319	0.0293	945	0.2728	0.3672
Heart	0.280	0.0197	374	0.2503	0.3156
Kidneys	0.66	0.049	433	0.589	0.738
Liver	2.49	0.237	459	2.196	2.820
Prostate	0.240	0.0430	917	0.1765	0.3102
Seminal vesicles	0.379	0.0685	917	0.2657	0.4929
Spleen	0.168	0.0211	394	0.1383	0.2023
Testes	1.01	0.090	945	0.872	1.161
Thymus	0.106	0.0267	394	0.0708	0.1450
Thyroids	0.0049	0.00087	916	0.00368	0.00646

FEMALES**1.8 ORGAN WEIGHTS (GRAM)**

ORGAN	MEAN	STD.DEV.	N	P5	P95
ORGAN WEIGHT, END OF TREATMENT					
Adrenals	0.076	0.0118	330	0.0580	0.0970
Body weight	282	21.1	839	244.0	313.9
Brain	1.90	0.071	320	1.796	2.017
Heart	0.836	0.0664	320	0.7296	0.9550
Kidneys	1.93	0.170	379	1.660	2.221
Liver	11.82	1.504	404	9.187	14.084
Ovaries	0.113	0.0193	351	0.0880	0.1410
Spleen	0.495	0.0662	340	0.3960	0.6077
Thymus	0.202	0.0468	340	0.1300	0.2895
Thyroids	0.0155	0.00328	800	0.01080	0.02130
Uterus	0.368	0.0809	321	0.2800	0.5070
ORGAN/BODY WEIGHT RATIOS, END OF TREATMENT					
Adrenals	0.027	0.0039	330	0.0207	0.0336
Body weight	282	21.1	839	244.0	313.9
Brain	0.68	0.045	320	0.607	0.754
Heart	0.296	0.0190	320	0.2657	0.3289
Kidneys	0.68	0.045	379	0.609	0.758
Liver	4.17	0.376	404	3.598	4.791
Ovaries	0.040	0.0073	351	0.0314	0.0495
Spleen	0.175	0.0212	340	0.1442	0.2130
Thymus	0.071	0.0159	340	0.0468	0.1029
Thyroids	0.0055	0.00116	798	0.00385	0.00759
Uterus	0.130	0.0294	321	0.0999	0.1743

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2017
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All
Selected projects	517134 517996 518368 518375 518397 518658 518886 518903 518925 519039 519066 519086 519374 519486 519507 519521 519646 519679 520056 520225 520290 520296 520312 520333 520405 520411 520467 520473 520483 520501 520506 520512 520518 520538 520595 520641 520671 520692 520707 520718 520738 520762 520770 520808 520815 520831 520858 520865 520884 520895 520915 520943 520980 520987 520997 521018 521045 521102 521136 521144 521150 521194 521209 521263 521274 521309 521342 521417 521444 521493 521514 521526 521578 521590 521644 521667 521715 521721 521730 521790 521803 521808 521812 521937 521953 522038 522066 522069 522074 522078 522082 522103 522109 522113 522165
BODY WEIGHTS (GRAM)	
Selected group	CONTROL
Selected days	1 2 3 4 5 6 7 8 11 12 15 18 22 25 29 30 32 33 36 37 39 41 43 44 46 50 51 52 57 58 60 64 67 71 78 85 92 99 106 113
BODY WEIGHT GAIN (%)	
Selected group	CONTROL
Selected days	1 2 3 4 5 6 7 8 11 12 15 18 22 25 29 30 32 33 36 37 39 41 43 44 46 50 51 52 57 58 60 64 67 71 78 85 92 99 106 113
FOOD CONSUMPTION (G/ANIMAL/DAY)	
Selected group	CONTROL
Selected days	4 5 11 12 18 19 23 25 26 29 31 32 33 34 37 38 39 40 43 46 47 53 54 60 67 74 81 87 88
RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)	
Selected group	CONTROL
Selected days	4 5 11 12 18 19 23 25 26 29 31 32 33 34 37 38 39 40 43 46 47 53 54 60 67 74 81 87 88
HAEMATOLOGY	
Selected group	CONTROL
Selected parameters	APTT BA BASOA1 EO EOSA1 HCT HGB LUC LUCA LUCA1 LYMPHA1 LYMPHO LYMPHOA1 MCH MCHC MCV MO MONOA1 NEUTA1 PLT PT RBC RDW RDWG RETI RETICA1 SEG WBC
CLINICAL BIOCHEMISTRY	
Selected group	CONTROL
Selected parameters	ALAT ALB ALP ASAT BACID BILI CA CHOL CL CREA GGT GLUC HEM HEMI HEMS K NA PHOS PROT TRIG TSHO TT4 UREA
URINALYSIS	
Selected group	CONTROL
Selected parameters	BILI CLA COL DILK GLU HAEM KET NIT PH PRO SBAC SCAS SCRY SEPI SG SOTH SRBC SWBC URB VOL
ORGAN WEIGHTS (GRAM)	
Selected group	CONTROL

Selection Criteria for Historical Data

Selection information	Value
Selected parameters	ADRENALS BODYWEIG BRAIN EPIDIDYM HEART KIDNEYS LIVER OVARIES PROSTATE SEMINALV SPLEEN TESTES THYMUS THYROIDS UTERUS
Grouped measurements (HAEMATOLOGY)	
Measurements removed	2 END OF RECOVERY
Grouped measurements (CLINICAL BIOCHEMISTRY)	
Measurements removed	2 END OF RECOVERY 2 PND13
PND 4 PUPS	2 PND 4 2 PND4 2 PUPS (PND 4)
Grouped measurements (URINALYSIS)	
Measurements removed	2 END OF RECOVERY
Grouped measurements (ORGAN WEIGHTS (GRAM))	
Measurements removed	2 DUMMY 2 END OF RECOVERY 3 DUMMY

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[1.1 Clinical Biochemistry](#)

APPENDIX 1

**HISTORICAL DATA
MALES****1.1 CLINICAL BIOCHEMISTRY**

MEASUREMENT	UNITS	MEAN	STD.DEV.	N	P5	P95
PUPS PND 13-16						
TSH	uIU/mL	0.154	0.0842	80	0.0625	0.2930
Total T4	ug/dL	5.98	1.194	1157	4.230	8.160
PUPS PND 21-23						
Total T4	ug/dL	4.28	0.759	21	3.380	5.330

FEMALES**1.1 CLINICAL BIOCHEMISTRY**

MEASUREMENT	UNITS	MEAN	STD.DEV.	N	P5	P95
PUPS PND 13-16						
TSH	uIU/mL	0.141	0.0858	80	0.0570	0.3340
Total T4	ug/dL	5.57	1.075	1149	3.940	7.500
PUPS PND 21-23						
Total T4	ug/dL	4.17	0.819	21	3.140	5.450

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2016
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All

Selected projects

512354 513679 514151 514639 514649 514652
 514658 514722 515329 515455 515664 515794 516053
 516064 516150 516295 516330 516347 516358 516595
 516624 516778 516847 516993 517035 517068 517135
 517407 517499 517506 517532 517638 517957 517998
 518104 518232 518369 518376 518398 518632 518660
 518888 518904 518927 519042 519068 519088 519376
 519488 519509 519523 519648 519681 520058 520227
 520292 520298 520314 520335 520407 520468 520474
 520484 520503 520508 520513 520520 520540 520597
 520640 520673 520694 520709 520720 520740 520764
 520771 520810 520817 520832 520860 520867 520981
 520989 520999 521021 521047 521101 521138 521146
 521195 521210 521276 521289 521311 521344 521419
 521494 521515 521528 521580 521592 521645 521668
 521717 521723 521732 521791 521796 521806 521809
 521814 521938 521950 521954 521967 522040 522068
 522071 522076 522080 522084 522105 522115 522167

CLINICAL BIOCHEMISTRY

Selected group	CONTROL
Selected parameters	HEMI TSHO TT4

Grouped measurements (CLINICAL BIOCHEMISTRY)**PUPS PND 13-16**

1 PND 13-15
 1 PND 13-15 PUPS
 1 PND 13-15 pups
 1 PND 14-16
 1 PND 14-16 PUPS
 1 PND14-16
 1 PUPS (PND 13-15)
 1 PUPS (PND 14-16)
 1 PUPS (PND 15)
 1 PUPS (PND13-15)
 1 PUPS (PND14-16)
 1 PUPS PND 14-16
 2 PUPS (PND 14-16)

PUPS PND 21-23

1 PUPS (PND 21-23)
 1 PUPS (PND21-23)

DEVELOPMENTAL DATA

MEASUREMENT	Mean	St.dev	N	P5	P95	Min	Max
Total number of offspring born	107	15	132	82	132	72	136
Total number of uterine implantation sites	117	14	130	92	138	80	142
Number of live offspring on Day 1 after littering	106	15	132	80	130	72	136
Number of live offspring on Day 4 (before culling)	104	15	132	80	129	72	136
Number of live offspring on Day 4 (after culling)	71	8	131	56	80	54	88
Number of live offspring on Day 13 after littering	71	8	128	56	80	52	88
Post-implantation survival index (%)	91	4	133	83	97	77	100
Live birth index (%)	99	2	136	95	100	89	100
Viability index (%)	99	2	136	95	100	87	100
Lactation index (%)	100	1	135	98	100	88	100

Selection information

Species	Rat
Dosing type	All
Start year	2017
End year	2020

Selected projects

505074	516843	520288	20151439	20197624
509971	516990	520294	20151541	20197639
512350	517133	520310	20151947	20208719
513370	517403	520331	20151967	20208942
513508	517496	520403	20151994	20210023
513606	517502	520451	20152394	20210431
513675	517528	520454	20153214	20212888
513698	517636	520472	20155387	20218712
513943	517954	20133605	20156955	20218715
514149	517992	20134630	20157758	20218718
514356	518230	20134823	20161715	20218721
514637	518366	20134824	20161722	20218724
514646	518373	20136782	20164070	20219689
514650	518391	20139003	20164350	20219839
514656	518629	20140515	20168083	20220063
514719	518656	20141791	20168842	20222350
515091	518885	20142767	20172120	
515328	518902	20144266	20173303	
515453	518920	20144288	20179374	
515661	519038	20144692	20183273	
515792	519064	20145353	20183641	
516037	519085	20146107	20186559	
516148	519373	20148107	20188708	
516294	519484	20148127	20191506	
516329	519506	20148423	20191510	
516345	519520	20149499	20191836	
516356	519645	20149502	20191866	
516582	519674	20150237	20195323	
516592	520055	20150770	20195986	
516775	520224	20150803	20197288	

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[1.1 Corrected Anogenital Distance](#)

APPENDIX 1

**HISTORICAL DATA
FEMALES****1.1 CORRECTED ANOGENITAL DISTANCE**

	UNITS	MEAN	STD.DEV.	N	P5	P95
PND1						
norm anog dist F	mm	0.57	0.101	711	0.400	0.740
norm anog dist M	mm	1.45	0.143	708	1.240	1.680

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2017
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All

Selected projects

517134 517996 518368 518375 518397 518658
 518886 518903 518925 519039 519066 519374 519486
 519507 519521 519646 519679 520056 520225 520290
 520296 520312 520333 520405 520411 520467 520473
 520483 520501 520506 520512 520518 520538 520595
 520641 520671 520692 520707 520718 520738 520762
 520770 520808 520815 520831 520858 520865 520884
 520895 520915 520943 520980 520987 520997 521018
 521045 521102 521136 521144 521150 521194 521209
 521263 521274 521309 521342 521417 521444 521493
 521514 521526 521578 521590 521644 521667 521715
 521721 521730 521790 521803 521808 521812 521937
 521953 522038 522066 522069 522074 522078 522082
 522103 522109 522113 522165

CORRECTED ANOGENITAL DISTANCE

Selected group	CONTROL
Selected parameters	CORAGDF CORAGDM

Grouped measurements (CORRECTED ANOGENITAL DISTANCE)

PND1	1 PND 1
	2 PND 1
	2 PND1
	3 PND1 CROSS-FOSTERED
	4 PND1

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[1.1 Functional Observations](#)

APPENDIX 1

**HISTORICAL DATA
MALES****1.1 FUNCTIONAL OBSERVATIONS**

	UNITS	MEAN	STD.DEV.	N	P5	P95
TREATMENT PERIOD						
GRIP FORE	GRAM	1252	250.9	415	806.0	1643.0
GRIP HIND	GRAM	611	157.2	415	367.0	877.0
HEARING	SCORE 0/1	0	0.0	415	0.0	0.0
PUPIL L	SCORE 0/1	0	0.0	415	0.0	0.0
PUPIL R	SCORE 0/1	0	0.0	415	0.0	0.0
STATIC R	SCORE 0/1	0	0.0	415	0.0	0.0

FEMALES**1.1 FUNCTIONAL OBSERVATIONS**

	UNITS	MEAN	STD.DEV.	N	P5	P95
TREATMENT PERIOD						
GRIP FORE	GRAM	1056	232.3	310	699.0	1451.0
GRIP HIND	GRAM	567	133.5	310	365.0	793.0
HEARING	SCORE 0/1	0	0.0	310	0.0	0.0
PUPIL L	SCORE 0/1	0	0.0	310	0.0	0.0
PUPIL R	SCORE 0/1	0	0.0	310	0.0	0.0
STATIC R	SCORE 0/1	0	0.0	310	0.0	0.0

Selection Criteria for Historical Data

Selection information	Value
-----------------------	-------

Species	RAT
Dosing type	All
Start year	2017
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All

Selected projects

517134 517996 518368 518375 518397 518658
 518886 518903 518925 519039 519066 519374 519486
 519507 519521 519646 519679 520056 520225 520290
 520296 520312 520333 520405 520411 520467 520473
 520483 520501 520506 520512 520518 520538 520595
 520641 520671 520692 520707 520718 520738 520762
 520770 520808 520815 520831 520858 520865 520884
 520895 520915 520943 520980 520987 520997 521018
 521045 521102 521136 521144 521150 521194 521209
 521263 521274 521309 521342 521417 521444 521493
 521514 521526 521578 521590 521644 521667 521715
 521721 521730 521790 521803 521808 521812 521937
 521953 522038 522066 522069 522074 522078 522082
 522103 522109 522113 522165

FUNCTIONAL OBSERVATIONS

Selected group	CONTROL
Selected parameters	GRIPF GRIPH HEARING PUPILL PUPILR STRIGHT

Grouped measurements (FUNCTIONAL OBSERVATIONS)

Measurements removed

TREATMENT PERIOD

3 PRE TEST

1 AT LACTATION
 1 AT NECROPSY
 1 AT WEEK 4
 3 AT LACTATION
 3 AT WEEK 4
 3 AT WEEK4
 3 END OF TREATMEND
 3 END OF TREATMENT
 3 END TRAETMENT
 3 ENDOFTREATMENT
 3 WEEK 10
 3 WEEK 4
 4 AT LACTATION
 4 END OF TREATMENT
 4 LACTATION
 5 END OF TREATMENT

2017-2021 historical control data OECD 422

MALES

MOTOR ACTIVITY AND MOVEMENTS

MEASUREMENT	Mean	St.dev	N	P5	P95
Total movements	3599	1085	575	1918	5500
Ambulations	752	274	575	323	1262

FEMALES

MOTOR ACTIVITY AND MOVEMENTS

MEASUREMENT	Mean	St.dev	N	P5	P95
Total movements	3404	1221	506	1653	5639
Ambulations	818	337	506	342	1466

Selection information

Species	Rat
Dosing type	All
Start year	2017
End year	2021

Selected projects	505074	519038	20161722
	505553	519064	20164350
	509971	519085	20168083
	512019	519373	20168842
	512350	519484	20172120
	512433	519506	20179374
	512470	519520	20183273
	512681	519645	20183641
	512747	519674	20191506
	512829	520055	20191510
	512992	520224	20191836
	513508	520288	20191866
	513675	520294	20195323
	514149	520310	20197624
	514356	520331	20197639
	515091	520403	20208719
	515328	520451	20210431
	515453	520454	20218712
	515792	20133605	20218718
	516037	20134630	20218721
	516148	20134823	20218724
	516294	20134824	20219689
	516329	20136782	20222350
	516345	20141791	20218715
	516356	20142767	20219839
	516582	20144266	
	516592	20144288	
	516843	20144692	
	516990	20145353	
	517403	20148107	
	517636	20148127	
	517954	20149499	
	517992	20149502	
	518366	20151967	
	518373	20151994	
	518391	20152394	
	518629	20153214	
	518656	20156955	
	518885	20157758	
	518920	20161715	

2017-2021 historical control data EOGRTS

Developmental DATA

MEASUREMENT	Mean	St.dev	N	P5	P95
Post-implantation survival index (%)	93	2.4	12	ND ^a	ND ^a
Live birth index (%)	99	0.5	12	ND ^a	ND ^a
Viability index (%)	99	1.1	12	ND ^a	ND ^a
Weaning index (%)	100	0.9	12	ND ^a	ND ^a

ND^a = not determined for N < 20

Selection information

Species	Rat
Dosing type	All
Start year	2017
End year	2021

Selected projects	518906
	519713
	20137078
	20144696
	20146521
	20147222
	20151567
	20153892
	20161729
	20168827
	20169540
	20173295

2017-2021 historical control data EOGRTS (F0-generation)

ESTROUS CYCLE F0, PER STUDY

PARAMETER	Mean	St.dev	N	P5	P95	Min	Max
Regular estrous cycle (%)	94.7	9.4	12	ND	ND	68.0	100.0

ESTROUS CYCLE F0

PARAMETER	Total	Regular	Irregular	Extended di-estrous	Acyclic	Extended estrous
Cycle classification (%)	100	95.1	3.3	0.0	0.3	0.0
Cycle classification (count)	304	289	10	0	1	0

ND: not determined for N < 20

Selection information

Species	Rat
Dosing type	All
Start year	2017
End year	2021

Selected projects

F0 generation	518906
	519713
	20137078
	20146521
	20147222
	20144696
	20151567
	20153892
	20168827
	20161729
	20169540
	20173295

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[1.1 Precoital Time](#)

APPENDIX 1

**HISTORICAL DATA
FEMALES****1.1 PRECOITAL TIME**

Day of the pairing period	Number of females mated
F0-GENERATION POST COITUM; PAIRING PERIOD 1	
1	99
2	82
3	73
4	41
5	1
12	1
13	3
14	3
N	303
MEAN PRECOITAL TIME	2.5
MEDIAN PRECOITAL TIME	2.0

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2017
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All

Selected projects

518906 519713 520590 520741 520781 520856
 520945 521065 521216 521314 521365 521439

PRECOITAL TIME

Selected group	CONTROL
Selected group	

2017-2021 historical control data EOGRTS**REPRODUCTION DATA**

MEASUREMENT	Mean	St.dev	N	P5	P95
Mating index	99.0	1.8	12	ND ^a	ND ^a
Fertility index	94.9	5.7	12	ND ^a	ND ^a
Gestation index	99.0	1.8	12	ND ^a	ND ^a

ND^a = not determined for N < 20

Selection information

Species	Rat
Dosing type	All
Start year	2017
End year	2021

Selected projects	518906
	519713
	20137078
	20144696
	20146521
	20147222
	20151567
	20153892
	20168827
	20161729
	20169540
	20173295

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[1.1 Body Weights](#)

[1.2 Body Weight Gain](#)

[1.3 Food Consumption](#)

[1.4 Relative Food Consumption](#)

APPENDIX 1

**HISTORICAL DATA
FEMALES****1.1 BODY WEIGHTS (GRAM)**

DAYS	MEAN	STD.DEV.	N	P5	P95
F0-GENERATION POST COITUM					
0	229	15.2	281	205.0	254.0
4	241	15.8	282	217.0	267.0
7	248	16.0	278	222.0	276.0
11	263	17.3	283	236.0	291.0
14	271	18.1	283	245.0	301.0
17	295	20.3	283	264.0	328.0
20	332	23.8	283	297.0	370.0
30	.	.	0	.	.
F0-GENERATION LACTATION					
1	255	17.3	287	228.0	283.0
4	268	18.6	283	238.0	297.0
7	276	18.5	283	248.0	305.0
14	289	19.8	283	259.0	319.0
21	281	18.2	279	253.0	311.0

APPENDIX 1

**HISTORICAL DATA
FEMALES****1.2 BODY WEIGHT GAIN (%)**

DAYS	MEAN	STD.DEV.	N	P5	P95
F0-GENERATION POST COITUM					
0	0	0.0	288	0.0	0.0
4	6	2.2	281	2.1	9.3
7	8	2.7	277	4.3	13.0
11	15	3.3	281	9.4	20.5
14	19	3.8	281	12.7	24.8
17	29	4.6	281	21.7	36.0
20	45	6.3	281	35.3	55.1
30	.	.	0	.	.
F0-GENERATION LACTATION					
1	0	0.0	287	0.0	0.0
4	5	3.5	283	-0.7	10.5
7	8	4.0	283	1.9	15.1
14	13	5.3	283	4.5	21.5
21	10	4.9	279	1.9	18.0

APPENDIX 1

**HISTORICAL DATA
FEMALES****1.3 FOOD CONSUMPTION (G/ANIMAL/DAY)**

DAYS	MEAN	STD.DEV.	N	P5	P95
F0-GENERATION POST COITUM					
1	35	10.5	21	24.0	58.0
2	18	6.6	280	11.9	30.0
3	38	12.8	21	21.0	63.0
4	36	7.7	21	26.0	54.0
5	42	9.8	22	30.0	65.0
6	20	5.9	278	14.3	32.0
7	37	10.6	22	22.0	57.0
8	33	8.4	22	20.0	48.0
9	20	5.6	278	14.5	31.0
10	36	9.1	22	23.0	51.0
11	36	9.1	22	18.0	44.0
12	35	7.9	22	27.0	48.0
13	21	5.5	283	16.0	32.3
14	35	6.4	22	24.0	43.0
15	33	6.9	22	24.0	46.0
16	22	5.3	283	16.0	30.0
17	35	6.5	22	24.0	45.0
18	36	8.0	22	26.0	49.0
19	24	5.0	283	17.7	33.0
20	37	8.4	22	25.0	47.0
21	35	6.3	22	25.0	44.0
22	26	10.0	22	15.0	42.0
23	26	8.1	7	15.0	37.0
F0-GENERATION LACTATION					
2	40	11.1	23	24.0	53.0
3	33	8.9	281	22.3	50.3
4	59	13.5	23	42.0	86.0
5	61	14.8	23	41.0	84.0
6	41	9.6	282	31.3	60.0
7	68	13.7	23	54.0	97.0
8	64	16.2	23	45.0	86.0
9	58	16.6	50	42.0	94.0
10	77	22.5	23	46.0	118.0
11	55	12.2	255	43.4	70.0
12	69	27.8	50	43.5	141.0
13	95	30.1	23	61.0	145.0
14	100	24.6	23	71.0	135.0
15	97	24.4	23	59.0	128.0
16	79	29.3	50	46.7	130.0
17	107	29.1	23	70.0	146.0
18	67	18.1	248	52.7	102.0
19	90	35.1	49	56.8	156.0
20	109	28.4	23	67.0	149.0
21	109	27.7	23	70.0	150.0
22	78	24.5	23	51.0	129.0
23	59	27.4	22	27.0	106.0
24	48	14.6	5	38.0	73.0

APPENDIX 1

**HISTORICAL DATA
FEMALES****1.4 RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)**

DAYS	MEAN	STD.DEV.	N	P5	P95
F0-GENERATION POST COITUM					
1	151	43.6	21	100.4	225.7
2	76	28.8	280	50.9	124.7
3	155	59.5	21	84.0	264.7
4	146	30.2	21	106.6	196.4
5	172	46.1	22	120.0	273.1
6	81	23.0	278	59.0	127.0
7	148	44.5	22	84.9	248.9
8	131	36.5	22	79.1	200.8
9	77	21.9	278	56.6	119.0
10	134	35.7	22	86.5	192.6
11	132	35.5	22	67.7	177.7
12	132	30.5	22	102.1	177.6
13	79	19.2	283	60.7	120.7
14	124	24.7	22	84.2	163.3
15	119	27.9	22	87.0	187.8
16	74	17.1	283	56.9	107.8
17	116	23.5	22	80.8	149.5
18	122	30.0	22	84.4	182.5
19	71	14.1	283	56.2	94.4
20	111	25.4	22	76.5	150.0
21	102	18.8	22	75.8	136.6
22	78	29.8	22	43.3	114.2
23	75	26.4	7	43.4	115.6
F0-GENERATION LACTATION					
2	154	44.9	23	86.0	197.8
3	124	32.1	281	85.9	193.8
4	216	50.0	23	144.8	311.8
5	221	55.2	23	152.8	311.1
6	149	31.4	282	117.9	209.1
7	240	53.1	23	180.0	335.6
8	224	58.4	23	154.4	309.2
9	209	58.1	50	151.1	375.0
10	271	85.4	23	160.3	409.6
11	189	39.9	255	149.8	243.0
12	240	92.4	50	157.8	512.3
13	322	103.8	23	196.4	485.4
14	339	82.4	23	239.1	478.4
15	329	91.2	23	198.0	467.2
16	275	94.3	50	171.1	474.5
17	365	106.3	23	234.9	525.5
18	236	59.6	247	189.0	333.3
19	318	121.5	48	205.9	563.2
20	376	108.2	22	219.7	513.7
21	372	107.9	22	229.5	539.9
22	272	91.6	22	171.7	453.3
23	205	99.6	21	87.1	371.9
24	168	50.8	5	124.6	252.6

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2017
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All
Selected projects	518906 519713 520590 520741 520781 520856 520945 521065 521216 521314 521365 521439
BODY WEIGHTS (GRAM)	
Selected group	CONTROL
Selected days	0 1 4 7 11 14 17 20 21 30
BODY WEIGHT GAIN (%)	
Selected group	CONTROL
Selected days	0 1 4 7 11 14 17 20 21 30
FOOD CONSUMPTION (G/ANIMAL/DAY)	
Selected group	CONTROL
Selected days	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 34
RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)	
Selected group	CONTROL
Selected days	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 34

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[1.1 Water Consumption](#)

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**HISTORICAL DATA
FEMALES****1.1 WATER CONSUMPTION (G/ANIMAL/DAY)**

DAYS	MEAN	STD.DEV.	N	P5	P95
F0-GENERATION POST COITUM					
1	26	5.5	43	18.0	34.0
2	29	5.5	43	22.0	38.0
3	32	6.4	43	24.0	45.0
4	35	6.6	43	27.0	45.0
5	33	7.3	43	22.0	47.0
6	31	6.8	43	22.0	44.0
7	32	6.6	43	24.0	43.0
8	33	8.7	43	22.0	44.0
9	31	5.8	43	22.0	39.0
10	35	8.9	44	23.0	50.0
11	40	9.5	44	27.0	59.0
12	39	8.2	44	28.0	55.0
13	38	8.0	44	28.0	52.0
14	39	7.9	44	29.0	55.0
15	39	8.1	44	31.0	54.0
16	42	8.5	44	32.0	59.0
17	47	9.4	44	35.0	64.0
18	45	9.1	44	31.0	59.0
19	42	7.9	44	32.0	57.0
20	40	8.2	44	29.0	59.0
21	35	6.9	44	26.0	48.0
22	22	7.5	44	12.0	35.0
23	24	6.2	13	9.0	32.0
24	.	.	0	.	.
25	.	.	0	.	.
26	.	.	0	.	.
27	.	.	0	.	.
F0-GENERATION LACTATION					
2	40	8.6	45	26.0	53.0
3	48	7.1	47	37.0	59.0
4	56	9.6	47	41.0	71.0
5	54	9.3	47	39.0	69.0
6	57	9.5	47	42.0	72.0
7	65	9.1	47	51.0	78.0
8	65	10.1	47	50.0	82.0
9	67	9.9	47	53.0	84.0
10	69	9.9	47	53.0	85.0
11	73	9.3	47	60.0	86.0
12	77	10.6	47	63.0	98.0
13	80	10.7	47	61.0	99.0
14	81	11.6	47	61.0	101.0
15	79	12.4	47	59.0	95.0
16	83	10.5	47	66.0	99.0
17	86	12.3	47	68.0	110.0
18	87	12.8	47	68.0	108.0
19	91	17.1	47	68.0	122.0
20	99	13.3	47	78.0	118.0
21	116	15.8	47	93.0	142.0
22	74	26.2	47	48.0	137.0
23	63	31.7	38	31.0	139.0
24	68	31.4	24	39.0	146.0
25	39	9.2	2	32.0	45.0

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2017
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All

Selected projects

518906 519713 520590 520741 520781 520856
 520945 521065 521216 521314 521365 521439

WATER CONSUMPTION (G/ANIMAL/DAY)

Selected group CONTROL
 Selected days 1 2 3 4 5 6 7 8 9 10 11 12 13 14
 15 16 17 18 19 20 21 22 23 24 25 26 27

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- 1.1 Body Weights
- 1.2 Body Weight Gain
- 1.3 Food Consumption
- 1.4 Relative Food Consumption
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- 1.7 Implantation Sites
- 1.8 Haematology
- 1.9 Clinical Biochemistry
- 1.10 Urinalysis
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**HISTORICAL DATA
MALES****1.1 BODY WEIGHTS (GRAM)**

DAYS	MEAN	STD.DEV.	N	P5	P95
-6	156	7.2	25	146.0	165.0
1	178	44.6	306	142.0	307.0
8	223	39.3	278	185.0	331.0
9	205	11.4	28	188.0	221.0
15	261	33.6	306	222.0	347.0
22	290	30.6	306	250.0	355.0
29	316	29.6	306	276.0	372.0
36	335	30.1	306	293.0	388.0
43	352	29.7	305	308.0	400.0
50	365	31.4	305	315.0	418.0
57	377	32.6	305	327.0	434.0
64	388	33.9	305	336.0	445.0
71	396	34.8	305	344.0	451.0
78	400	34.3	286	343.0	452.0
85	401	36.3	125	342.0	455.0
92	411	36.7	38	312.0	451.0
99	422	39.8	25	348.0	460.0
106	430	41.3	25	354.0	472.0
113	436	42.5	25	356.0	483.0
119	438	42.3	25	360.0	484.0

FEMALES**1.1 BODY WEIGHTS (GRAM)**

DAYS	MEAN	STD.DEV.	N	P5	P95
-6	141	7.8	25	126.0	152.0
1	139	24.9	306	116.0	206.0
8	159	23.2	278	135.0	221.0
9	148	8.2	28	131.0	158.0
15	175	20.3	306	152.0	222.0
22	182	12.3	279	163.0	202.0
29	194	12.4	278	173.0	213.0
36	202	13.0	278	180.0	223.0
43	210	13.4	278	187.0	231.0
50	215	13.5	278	191.0	238.0
57	221	14.1	278	197.0	243.0
64	225	14.1	278	201.0	247.0
71	228	14.5	278	205.0	252.0
78	249	15.9	9	227.0	270.0
85	254	19.0	4	231.0	276.0
92	240	19.0	3	222.0	260.0
99	247	26.1	3	222.0	274.0
106	235	13.4	2	225.0	244.0
109	.	.	0	.	.

APPENDIX 1

**HISTORICAL DATA
MALES****1.2 BODY WEIGHT GAIN (%)**

DAYS	MEAN	STD.DEV.	N	P5	P95
-6	0	0.0	25	0.0	0.0
1	2	7.0	306	0.0	24.9
8	28	10.9	278	6.3	53.4
9	34	4.3	28	29.3	42.0
15	52	15.8	306	13.3	76.9
22	70	21.2	306	17.0	97.8
29	86	25.0	306	22.1	117.4
36	98	28.3	306	26.2	132.9
43	108	31.6	305	27.9	147.2
50	116	33.0	305	32.6	156.3
57	123	35.1	305	34.4	166.0
64	130	36.9	305	36.3	175.7
71	135	38.1	305	38.8	183.2
78	139	37.9	286	40.7	187.6
85	157	24.8	125	118.6	196.7
92	166	22.8	38	124.2	202.8
99	177	24.5	25	127.5	208.3
106	182	25.2	25	131.4	212.5
113	186	25.7	25	132.7	217.4
119	187	25.6	25	135.3	220.8

FEMALES**1.2 BODY WEIGHT GAIN (%)**

DAYS	MEAN	STD.DEV.	N	P5	P95
-6	0	0.0	25	0.0	0.0
1	1	3.5	306	0.0	11.3
8	15	5.5	278	5.9	25.2
9	21	4.1	28	14.7	28.9
15	28	8.7	306	10.0	40.2
22	40	8.5	279	26.4	54.6
29	49	9.8	278	34.6	65.2
36	55	10.4	278	39.1	72.7
43	61	11.5	278	42.4	80.8
50	66	12.5	278	45.7	87.2
57	70	12.7	278	50.0	90.9
64	73	12.9	278	52.0	92.6
71	76	13.3	278	54.3	99.0
78	92	16.3	9	70.1	114.6
85	92	14.1	4	79.1	111.4
92	78	5.5	3	72.1	83.1
99	82	10.4	3	72.1	93.0
106	78	5.4	2	74.4	82.1
109	.	.	0	.	.

APPENDIX 1

**HISTORICAL DATA
MALES****1.3 FOOD CONSUMPTION (G/ANIMAL/DAY)**

DAYS	MEAN	STD.DEV.	N (CAGE)	P5	P95
-3	21	0.8	5	19.7	21.6
3	18	0.7	7	16.9	18.8
4	21	1.7	57	18.3	24.6
8	20	0.7	7	18.5	20.6
11	22	2.2	57	19.4	25.8
13	21	0.7	7	19.8	21.7
18	23	2.6	64	19.7	26.1
25	24	2.5	64	20.4	26.2
32	23	2.2	64	19.8	25.8
39	23	2.6	64	19.6	25.7
46	22	2.3	64	18.7	25.1
53	22	2.2	64	18.5	25.0
60	21	2.4	64	18.0	25.0
67	21	2.5	64	17.3	24.8
74	21	2.7	60	17.1	26.0
81	22	4.8	30	16.3	31.5
88	21	1.3	7	19.2	22.9
92	.	.	0	.	.
95	20	0.9	5	18.8	21.0
102	20	1.1	5	18.6	21.3
109	20	1.1	5	18.3	21.1
116	20	0.9	5	18.6	21.0

FEMALES**1.3 FOOD CONSUMPTION (G/ANIMAL/DAY)**

DAYS	MEAN	STD.DEV.	N (CAGE)	P5	P95
-3	16	0.8	5	15.3	17.0
3	14	0.5	7	13.2	14.3
4	15	1.3	57	13.3	17.9
8	14	0.7	7	13.3	15.5
11	15	1.3	57	13.4	17.6
13	15	0.6	7	13.9	16.0
18	15	1.3	57	13.0	17.6
25	15	1.6	57	13.6	17.1
32	16	1.0	57	13.7	17.3
39	16	1.4	57	13.3	17.9
46	15	1.4	57	13.2	18.0
53	15	1.4	57	13.0	17.7
60	15	1.3	56	12.4	17.0
67	15	1.5	57	11.8	17.0
74	.	.	0	.	.

APPENDIX 1

**HISTORICAL DATA
MALES****1.4 RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)**

DAYS	MEAN	STD.DEV.	N (CAGE)	P5	P95
-3	132	3.5	5	127.3	135.1
3	116	7.8	7	107.6	130.2
4	95	11.3	57	73.8	115.7
8	95	3.5	7	90.3	100.5
11	87	12.7	57	67.6	107.9
13	88	2.5	7	83.4	90.2
18	81	11.0	64	62.3	95.1
25	76	10.4	64	63.6	92.1
32	69	7.7	64	58.6	80.8
39	64	7.6	64	55.5	75.0
46	61	6.8	64	51.5	71.0
53	58	5.9	64	49.6	67.0
60	55	6.0	64	45.7	64.6
67	54	6.3	64	44.7	63.8
74	53	7.0	60	42.9	65.9
81	55	13.3	30	40.4	89.6
88	51	4.2	7	46.8	59.3
92	.	.	0	.	.
95	47	1.8	5	45.1	49.4
102	46	2.2	5	43.5	49.3
109	46	2.0	5	42.4	47.6
116	45	1.9	5	42.6	47.9

FEMALES**1.4 RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)**

DAYS	MEAN	STD.DEV.	N (CAGE)	P5	P95
-3	115	2.9	5	111.8	119.3
3	112	3.5	7	107.9	116.6
4	94	9.1	57	77.7	107.0
8	97	3.9	7	90.6	102.9
11	88	9.5	57	74.5	103.9
13	91	2.6	7	87.3	95.5
18	85	7.2	57	72.3	97.1
25	80	8.2	57	70.9	89.6
32	77	5.6	57	67.4	84.5
39	75	6.7	57	63.8	83.5
46	72	6.3	57	62.0	80.9
53	69	5.9	57	59.9	79.5
60	66	5.8	56	55.2	74.6
67	65	6.9	57	53.0	76.4
74	.	.	0	.	.

APPENDIX 1

**HISTORICAL DATA
MALES****1.5 WATER CONSUMPTION (G/ANIMAL/DAY)**

DAYS	MEAN	STD.DEV.	N (CAGE)	P5	P95
4	28	2.1	10	25.1	32.9
10	29	1.8	10	26.7	32.3
16	32	1.8	10	30.0	36.1
22	32	1.9	10	29.4	35.6
28	31	2.6	10	28.7	35.9
34	32	2.6	10	28.8	36.0
40	32	2.5	10	28.5	35.4
46	30	2.0	10	27.2	33.4
52	29	1.5	10	27.6	32.5
58	29	2.0	10	26.7	32.2
64	29	1.7	10	26.9	32.1
69	28	1.3	10	26.2	30.7
74	25	5.7	5	17.2	29.9
75	27	1.4	5	26.2	29.6
79	31	2.7	3	29.4	34.1
81	20	6.8	5	12.1	26.9
85	.	.	0	.	.
86	.	.	0	.	.

FEMALES**1.5 WATER CONSUMPTION (G/ANIMAL/DAY)**

DAYS	MEAN	STD.DEV.	N (CAGE)	P5	P95
4	22	1.9	10	19.3	26.8
10	22	1.4	10	20.4	25.6
16	22	2.0	10	20.4	27.2
22	23	1.6	10	20.1	25.6
28	23	1.8	10	19.8	24.8
34	24	2.6	10	21.3	28.6
40	25	2.5	10	21.5	28.5
46	24	2.6	10	20.5	28.3
52	23	2.6	10	19.5	28.1
58	24	2.6	10	20.7	28.5
64	24	2.4	10	21.7	28.7
69	24	3.0	10	20.5	29.2

APPENDIX 1

**HISTORICAL DATA
MALES****1.6 SPERM MOTILITY, CONCENTRATION AND MORPHOLOGY**

	UNITS	MEAN	STD.DEV.	N	P5	P95
END OF IN-LIFE						
SPERM COUNT EPI	10E6/gram	419.6	137.95	297	149.70	635.50
Normal morph	No of cells	175	17.2	301	136.0	194.0
Other tail	No of cells	2	2.6	301	0.0	6.0
Combined	No of cells	0	0.4	301	0.0	1.0
Detached head	No of cells	3	3.1	301	0.0	8.0
Abnormal head	No of cells	1	1.5	301	0.0	4.0
Abnormal neck	No of cells	1	1.7	301	0.0	4.0
Coiled tail	No of cells	18	16.0	301	2.0	51.0
NR OF CELLS EXAM		309	124.6	75	200.0	621.0
MOTILE SPERM	%	65	21.3	304	22.0	91.0
PROGRESSIV.SPERM	%	27	11.9	304	6.0	44.0

APPENDIX 1

**HISTORICAL DATA
FEMALES****1.7 IMPLANTATION SITES**

	UNITS	MEAN	STD.DEV.	N	P5	P95
END OF IN-LIFE Implantations		12.2	2.45	288	8.00	16.00

APPENDIX 1

**HISTORICAL DATA
MALES****1.8 HAEMATOLOGY**

MEASUREMENT	UNITS	MEAN	STD.DEV.	N	P5	P95
END OF TREATMENT						
APTT	s	19.1	3.60	117	13.90	24.40
Basophils	10E9/L	0.0	0.01	116	0.00	0.02
Eosinophils	10E9/L	0.1	0.04	116	0.00	0.17
Haematocrit	L/L	0.462	0.0237	116	0.4220	0.4980
Haemoglobin	mmol/L	9.6	0.47	116	8.60	10.30
LUC	10E9/L	0.0	0.03	40	0.01	0.11
Lymphocytes	10E9/L	5.6	1.59	40	3.79	8.42
Lymphocytes	10E9/L	4.5	1.05	76	3.10	6.46
MCH	fmol	1.11	0.043	116	1.050	1.180
MCHC	mmol/L	20.78	0.783	116	19.690	22.320
MCV	fL	53.2	1.53	116	50.90	55.80
Monocytes	10E9/L	0.2	0.06	116	0.09	0.28
Neutrophils	10E9/L	1.2	0.38	116	0.69	1.71
Platelets	10E9/L	698	86.1	115	551.0	841.0
PT	s	17.5	1.04	118	15.50	19.30
Red blood cells	10E12/L	8.69	0.463	116	7.910	9.350
RDW	%	12.6	1.20	116	11.50	14.00
Reticulocytes	10E9/L	201.7	30.67	116	142.30	249.60
WBC	10E9/L	6.3	1.49	116	4.30	9.37

FEMALES**1.8 HAEMATOLOGY**

MEASUREMENT	UNITS	MEAN	STD.DEV.	N	P5	P95
END OF TREATMENT						
APTT	s	18.3	3.25	114	13.50	23.50
Basophils	10E9/L	0.0	0.01	110	0.00	0.02
Eosinophils	10E9/L	0.1	0.06	110	0.02	0.18
Haematocrit	L/L	0.500	0.0309	110	0.4420	0.5510
Haemoglobin	mmol/L	10.4	0.55	110	9.40	11.30
LUC	10E9/L	0.0	0.02	33	0.02	0.08
Lymphocytes	10E9/L	3.0	0.78	33	1.63	4.51
Lymphocytes	10E9/L	3.2	1.05	77	1.70	4.90
MCH	fmol	1.20	0.048	110	1.130	1.290
MCHC	mmol/L	20.81	0.599	110	20.020	21.940
MCV	fL	57.8	1.88	110	55.00	61.00
Monocytes	10E9/L	0.2	0.09	110	0.07	0.35
Neutrophils	10E9/L	1.5	0.95	110	0.57	3.59
Platelets	10E9/L	868	137.4	110	649.0	1069.0
PT	s	17.8	1.15	113	15.90	19.90
Red blood cells	10E12/L	8.66	0.518	110	7.810	9.460
RDW	%	12.2	1.07	110	10.80	13.60
Reticulocytes	10E9/L	195.8	57.95	110	104.00	285.50
WBC	10E9/L	4.9	1.72	110	2.60	8.31

APPENDIX 1

**HISTORICAL DATA
MALES****1.9 CLINICAL BIOCHEMISTRY**

MEASUREMENT	UNITS	MEAN	STD.DEV.	N	P5	P95
END OF TREATMENT						
ALAT	U/L	34.3	11.48	120	24.40	47.75
Albumin	g/L	32.6	1.17	120	30.85	34.65
ALP	U/L	99	25.8	120	62.5	148.5
ASAT	U/L	82.0	15.34	120	64.95	108.30
Bile Acids	umol/L	16.6	9.74	119	6.20	37.60
Total bilirubin	umol/L	2.3	0.50	120	1.50	3.25
Calcium	mmol/L	2.58	0.081	120	2.460	2.715
Cholesterol	mmol/L	1.87	0.373	120	1.345	2.515
Chloride	mmol/L	103	1.5	120	100.5	105.0
Creatinine	umol/L	37.3	2.44	120	33.90	41.60
Glucose	mmol/L	8.57	1.260	120	6.785	10.625
Potassium	mmol/L	3.85	0.248	120	3.475	4.255
Sodium	mmol/L	141.4	1.21	120	138.95	143.25
Inorg.Phos	mmol/L	1.94	0.226	120	1.590	2.360
Total protein	g/L	63.3	2.41	120	59.75	67.25
TSH	uIU/mL	0.174	0.1796	120	0.0295	0.5140
Total T4	ug/dL	5.92	1.127	120	4.195	7.920
Urea	mmol/L	4.7	0.82	120	3.40	6.20

FEMALES**1.9 CLINICAL BIOCHEMISTRY**

MEASUREMENT	UNITS	MEAN	STD.DEV.	N	P5	P95
END OF TREATMENT						
ALAT	U/L	35.0	8.98	121	23.30	51.80
Albumin	g/L	34.8	1.50	121	32.40	36.90
ALP	U/L	85	38.2	121	43.0	136.0
ASAT	U/L	96.2	22.19	121	68.30	132.40
Bile Acids	umol/L	32.4	21.48	120	10.90	69.35
Total bilirubin	umol/L	2.3	0.56	121	1.70	3.20
Calcium	mmol/L	2.62	0.110	121	2.460	2.840
Cholesterol	mmol/L	2.27	0.528	121	1.580	3.270
Chloride	mmol/L	100	2.9	121	95.0	104.0
Creatinine	umol/L	40.6	3.01	121	35.70	46.10
Glucose	mmol/L	8.26	1.204	121	6.650	10.250
Potassium	mmol/L	3.43	0.358	121	2.920	3.970
Sodium	mmol/L	139.1	1.73	121	136.20	141.70
Inorg.Phos	mmol/L	2.15	0.431	121	1.450	2.840
Total protein	g/L	64.8	2.92	121	60.20	69.90
TSH	uIU/mL	0.204	0.1763	116	0.0300	0.6260
Total T4	ug/dL	4.66	1.364	118	2.620	7.430
Urea	mmol/L	8.9	1.32	121	7.10	11.00
PND 4 PUPS; END OF IN-LIFE						
Total T4	ug/dL	1.45	0.414	204	0.500	2.070

APPENDIX 1

**HISTORICAL DATA
MALES****1.10 URINALYSIS**

MEASUREMENT	UNITS	MEAN	STD.DEV.	N	P5	P95
END OF TREATMENT						
Bilirubin	score 0/3	0	0.1	120	0.0	0.0
Clarity	score 1/3	1	0.6	120	1.0	3.0
Colour	score 1/5	1	0.3	120	1.0	2.0
WBC	score 0/3	0	0.0	120	0.0	0.0
Glucose	score 0/3	0	0.0	120	0.0	0.0
Blood	score 0/3	0	0.4	120	0.0	1.0
Ketones	score 0/3	1	0.5	120	0.0	1.0
Nitrite	pos/neg	0.06	0.235	120	0.000	1.000
pH		6.9	0.39	120	6.50	7.50
Protein	score 0/3	0	0.5	120	0.0	1.0
Bacteria	score 0/3	3	0.4	120	2.0	3.0
Casts	score 0/3	0	0.0	120	0.0	0.0
Crystals	score 0/3	3	0.8	120	1.0	3.0
Epithelial cells	score 0/3	1	0.6	120	1.0	2.5
Specific gravity		1.031	0.0131	120	1.0155	1.0575
Other	score 0/3	0	0.1	120	0.0	0.0
RBC-sed.	score 0/3	0	0.5	120	0.0	1.0
WBC-sed.	score 0/3	0	0.5	120	0.0	1.0
Urobilinogen	score 0/3	0	0.0	120	0.0	0.0
Volume	mL	9	3.3	120	4.0	15.0

FEMALES**1.10 URINALYSIS**

MEASUREMENT	UNITS	MEAN	STD.DEV.	N	P5	P95
END OF TREATMENT						
Bilirubin	score 0/3	0	0.0	120	0.0	0.0
Clarity	score 1/3	1	0.4	120	1.0	2.0
Colour	score 1/5	1	0.2	120	1.0	1.5
WBC	score 0/3	0	0.0	120	0.0	0.0
Glucose	score 0/3	0	0.1	120	0.0	0.0
Blood	score 0/3	0	0.2	120	0.0	0.0
Ketones	score 0/3	0	0.1	120	0.0	0.0
Nitrite	pos/neg	0.10	0.301	120	0.000	1.000
pH		6.3	0.38	120	6.00	7.00
Protein	score 0/3	0	0.0	120	0.0	0.0
Bacteria	score 0/3	3	0.4	120	2.0	3.0
Casts	score 0/3	0	0.0	120	0.0	0.0
Crystals	score 0/3	1	1.2	120	0.0	3.0
Epithelial cells	score 0/3	1	0.5	120	1.0	2.0
Specific gravity		1.025	0.0078	120	1.0160	1.0385
Other	score 0/3	0	0.0	120	0.0	0.0
RBC-sed.	score 0/3	0	0.3	120	0.0	1.0
WBC-sed.	score 0/3	0	0.5	120	0.0	1.0
Urobilinogen	score 0/3	0	0.0	120	0.0	0.0
Volume	mL	15	5.8	120	7.0	25.0

APPENDIX 1

**HISTORICAL DATA
MALES****1.11 ORGAN WEIGHTS (GRAM)**

ORGAN	MEAN	STD.DEV.	N	P5	P95
ORGAN WEIGHT, END OF TREATMENT					
Adrenals	0.053	0.0077	304	0.0421	0.0660
Body weight	388	36.0	304	329.0	440.2
Brain	2.06	0.080	302	1.927	2.189
Epididymides	1.198	0.1277	300	1.0051	1.4225
Heart	1.040	0.1031	304	0.8920	1.1990
Kidneys	2.42	0.262	304	2.018	2.848
Liver	9.21	1.258	304	7.378	11.010
Pituitary	0.009	0.0013	304	0.0077	0.0116
Prostate	0.892	0.1668	304	0.6360	1.2040
Seminal vesicles	1.473	0.2651	304	1.0530	1.9160
Spleen	0.592	0.0907	304	0.4520	0.7510
Testes	3.63	0.302	300	3.132	4.096
Thymus	0.297	0.0745	304	0.2000	0.4130
Thyroids	0.0183	0.00372	302	0.01310	0.02550
ORGAN/BODY WEIGHT RATIOS, END OF TREATMENT					
Adrenals	0.014	0.0020	304	0.0109	0.0176
Body weight	388	36.0	304	329.0	440.2
Brain	0.53	0.045	302	0.463	0.610
Epididymides	0.311	0.0367	300	0.2546	0.3810
Heart	0.269	0.0198	304	0.2414	0.3029
Kidneys	0.62	0.047	304	0.555	0.710
Liver	2.37	0.204	304	2.116	2.676
Pituitary	0.002	0.0003	304	0.0020	0.0030
Prostate	0.231	0.0423	304	0.1683	0.3083
Seminal vesicles	0.381	0.0687	304	0.2775	0.4864
Spleen	0.153	0.0181	304	0.1262	0.1837
Testes	0.94	0.096	300	0.781	1.097
Thymus	0.077	0.0196	304	0.0503	0.1079
Thyroids	0.0047	0.00096	302	0.00337	0.00634

FEMALES**1.11 ORGAN WEIGHTS (GRAM)**

ORGAN	MEAN	STD.DEV.	N	P5	P95
ORGAN WEIGHT, END OF TREATMENT					
Adrenals	0.070	0.0103	301	0.0558	0.0890
Body weight	237	16.6	295	211.0	266.0
Brain	1.90	0.066	300	1.795	2.008
Heart	0.866	0.0768	301	0.7390	0.9990
Kidneys	1.90	0.156	300	1.661	2.148
Liver	8.90	1.210	299	6.684	10.898
Ovaries	0.142	0.0212	300	0.1100	0.1770
Pituitary	0.012	0.0018	300	0.0092	0.0147
Spleen	0.514	0.0718	301	0.4120	0.6260
Thymus	0.212	0.0535	301	0.1350	0.3168
Thyroids	0.0158	0.00347	301	0.01120	0.02090
Uterus	0.689	0.2624	301	0.4110	1.1500
ORGAN/BODY WEIGHT RATIOS, END OF TREATMENT					
Adrenals	0.030	0.0041	295	0.0231	0.0367
Body weight	237	16.6	295	211.0	266.0
Brain	0.80	0.057	294	0.710	0.899
Heart	0.366	0.0287	295	0.3208	0.4186
Kidneys	0.80	0.057	294	0.713	0.903
Liver	3.75	0.411	293	2.942	4.327
Ovaries	0.060	0.0093	294	0.0463	0.0750
Pituitary	0.005	0.0007	294	0.0039	0.0062
Spleen	0.217	0.0256	295	0.1777	0.2603

APPENDIX 1

**HISTORICAL DATA
FEMALES****1.11 ORGAN WEIGHTS (GRAM)**

ORGAN	MEAN	STD.DEV.	N	P5	P95
ORGAN/BODY WEIGHT RATIOS, END OF TREATMENT					
Thymus	0.089	0.0219	295	0.0586	0.1271
Thyroids	0.0067	0.00147	295	0.00466	0.00909
Uterus	0.293	0.1108	295	0.1708	0.5204

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2017
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All
Selected projects	518901 519714 520643 520790 520797 520946 521201 521217 521279 521315 521363 521437
BODY WEIGHTS (GRAM)	
Selected group	CONTROL
Selected days	-6 1 8 9 15 22 29 36 43 50 57 64 71 78 85 92 99 106 109 113 119
BODY WEIGHT GAIN (%)	
Selected group	CONTROL
Selected days	-6 1 8 9 15 22 29 36 43 50 57 64 71 78 85 92 99 106 109 113 119
FOOD CONSUMPTION (G/ANIMAL/DAY)	
Selected group	CONTROL
Selected days	-3 3 4 8 11 13 18 25 32 39 46 53 60 67 74 81 88 92 95 102 109 116
RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)	
Selected group	CONTROL
Selected days	-3 3 4 8 11 13 18 25 32 39 46 53 60 67 74 81 88 92 95 102 109 116
WATER CONSUMPTION (G/ANIMAL/DAY)	
Selected group	CONTROL
Selected days	4 10 16 22 28 34 40 46 52 58 64 69 74 75 79 81 85 86
SPERM MOTILITY, CONCETRATION AND MORPHOLGY	
Selected group	CONTROL
Selected parameters	COUNTEPI M1 M10 M11 M2 M3 M4 M5 M6 SPERMCEL SPERMMOT SPERMPRO
IMPLANTATION SITES	
Selected group	CONTROL
Selected parameters	IMPL
HAEMATOLOGY	
Selected group	CONTROL
Selected parameters	APTT BA BASOA1 EO EOSA1 HCT HGB LUC LUCA1 LYMPHA1 LYMPHO LYMPHOA1 MCH MCHC MCV MO MONOA1 NEUTA1 PLT PT RBC RDW RETI RETICA1 WBC
CLINICAL BIOCHEMISTRY	
Selected group	CONTROL
Selected parameters	ALAT ALB ALP ASAT BACID BILI CA CHOL CL CREA GLUC HEM HEMI HEMS K NA PHOS PROT TSH TSHO TT4 UREA
URINALYSIS	
Selected group	CONTROL
Selected parameters	BILI CLA COL DILK GLU HAEM KET NIT PH PRO SBAC SCAS SCRY SEPI SG SOTH SRBC SWBC URB VOL

Selection Criteria for Historical Data

Selection information	Value
-----------------------	-------

ORGAN WEIGHTS (GRAM)

Selected group

CONTROL

Selected parameters

ADRENALS BODYWEIG BRAIN EPIDIDYM HEART
 KIDNEYS LIVER OVARIES PITUIT PROSTATE SEMINALV
 SPLEEN TESTES THYMUS THYROIDS UTERUS

Grouped measurements (SPERM MOTILITY, CONCETRATION AND MORPHOLGY)

Measurements removed

1 PND 1
 2 PND 1
 2 PND1
 3 PND 1
 4 AT WEEK 10
 4 PND 1

END OF IN-LIFE

1 AT NECROPSY
 1 NECROPSY
 1 SPERM ANALYSIS
 2 AT NECROPSY
 2 END OF TREATMENT
 2 NECROPSY
 3 AT NECROPSY
 3 END OF TREATMENT
 3 SPERM ANALYSIS

Grouped measurements (IMPLANTATION SITES)

Measurements removed

1 PND 1
 1 SPERM ANALYSIS
 2 PND 1
 2 PND1
 3 PND 1
 3 SPERM ANALYSIS
 4 AT WEEK 10
 4 PND 1

END OF IN-LIFE

1 AT NECROPSY
 1 NECROPSY
 2 AT NECROPSY
 2 END OF TREATMENT
 2 NECROPSY
 3 AT NECROPSY
 3 END OF TREATMENT

Grouped measurements (CLINICAL BIOCHEMISTRY)

PND 4 PUPS; END OF IN-LIFE

2 PND 4
 2 PND 4 (PUPS)
 2 PND 4 PUPS
 2 PND 4 PUPS; END OF IN-LIFE
 2 PND4

APPENDIX 1

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[1.1 Body Weights Of Pups](#)

APPENDIX 1

**HISTORICAL DATA
MALES****1.1 BODY WEIGHTS OF PUPS (GRAM)**

DAYS	MEAN	STD.DEV.	N	P5	P95
F0-GENERATION LACTATION					
DAY 1	6.3	0.67	1674	5.30	7.60
DAY 4	9.5	1.18	1660	7.70	11.70
DAY 6	14.6	1.43	97	12.30	16.70
DAY 7	15.9	1.73	1146	13.10	18.80
DAY 8	18.6	1.21	20	16.85	21.10
DAY 9	21.1	1.99	97	17.10	23.80
DAY 11	26.2	2.33	96	22.20	29.90
DAY 13	30.8	2.72	741	26.90	35.50
DAY 14	32.6	2.75	399	27.70	36.60
DAY 15	35.1	2.72	96	30.20	39.30
DAY 17	38.4	3.01	95	33.20	43.40
DAY 19	41.6	3.74	95	36.20	47.20
DAY 21	50.5	4.74	1120	43.00	59.00

FEMALES**1.1 BODY WEIGHTS OF PUPS (GRAM)**

DAYS	MEAN	STD.DEV.	N	P5	P95
F0-GENERATION LACTATION					
DAY 1	6.0	0.64	1598	5.10	7.20
DAY 4	9.2	1.18	1580	7.40	11.20
DAY 6	14.3	1.37	97	11.60	16.10
DAY 7	15.4	1.71	1072	12.80	18.30
DAY 8	17.9	2.07	22	13.70	20.50
DAY 9	20.7	2.07	97	16.50	23.50
DAY 11	25.6	2.60	97	20.70	29.00
DAY 13	30.0	2.78	707	26.10	34.60
DAY 14	31.9	2.74	360	27.15	35.80
DAY 15	34.3	3.23	97	29.00	39.20
DAY 17	37.6	3.38	97	32.30	42.70
DAY 19	40.7	3.76	97	34.10	46.90
DAY 21	49.0	4.38	1046	42.00	56.00

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2017
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All

Selected projects

518906 519713 520590 520741 520781 520856
 520945 521065 521216 521314 521365 521439

BODY WEIGHTS OF PUPS (GRAM)

Selected group CONTROL
 Selected parameters 1 11 13 14 15 17 19 21 4 6 7 8 9

APPENDIX 1

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[1.1 Anogenital Distance And Nipple Retention](#)

APPENDIX 1

**HISTORICAL DATA
MALES****1.1 ANOGENITAL DISTANCE AND NIPPLE RETENTION**

	MEAN	STD.DEV.	N	P5	P95
F0-GENERATION LACTATION					
anogenital dist M mm	2.72	0.314	262	2.304	3.357
anogenital dist F mm	1.07	0.161	261	0.898	1.406
Number of nipples	0.00	0.000	260	0.000	0.000

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2017
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All

Selected projects

519713 520590 520741 520781 520856 520945
 521065 521216 521314 521365 521439

ANOGENITAL DISTANCE AND NIPPLE RETENTION

Selected group CONTROL
 Selected parameters ANOGENITAL DIST F MM ANOGENITAL
 DIST M MM NUMBER OF NIPPLES

APPENDIX 1

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[1.1 Corrected Anogenital Distance](#)

APPENDIX 1

**HISTORICAL DATA
FEMALES****1.1 CORRECTED ANOGENITAL DISTANCE**

	UNITS	MEAN	STD.DEV.	N	P5	P95
PND 1						
norm anog dist F	mm	0.59	0.087	234	0.480	0.790
norm anog dist M	mm	1.47	0.160	235	1.250	1.760

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2017
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All
Selected projects	519714 520643 520790 520797 520946 521201 521217 521279 521315 521363 521437
CORRECTED ANOGENITAL DISTANCE	
Selected group	CONTROL
Selected parameters	CORAGDF CORAGDM
Grouped measurements (CORRECTED ANOGENITAL DISTANCE)	
Measurements removed	1 AT NECROPSY 1 NECROPSY 1 SPERM ANALYSIS 2 AT NECROPSY 2 END OF TREATMENT 2 NECROPSY 3 AT NECROPSY 3 END OF TREATMENT 3 SPERM ANALYSIS 4 AT WEEK 10
PND 1	1 PND 1 2 PND 1 2 PND1 3 PND 1 4 PND 1

2017-2021 historical control data EOGRTS**REPRODUCTION DATA**

MEASUREMENT	Mean	St.dev	N	P5	P95
Mating index	98.3	2.6	6	ND ^a	ND ^a
Fertility index	98.3	2.6	6	ND ^a	ND ^a
Gestation index	99.2	2.0	6	ND ^a	ND ^a

ND^a = not determined for N < 20

Selection information

Species	Rat
Dosing type	All
Start year	2017
End year	2021

Selected projects	518906
	20137078
	20147222
	20151567
	20168827
	20161729

APPENDIX 1

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[1.1 Body Weights](#)

[1.2 Body Weight Gain](#)

[1.3 Food Consumption](#)

[1.4 Relative Food Consumption](#)

APPENDIX 1

**HISTORICAL DATA
FEMALES****1.1 BODY WEIGHTS (GRAM)**

DAYS	MEAN	STD.DEV.	N	P5	P95
F1-GENERATION POST COITUM					
0	228	16.8	121	206.0	257.0
4	240	17.4	122	214.0	271.0
7	246	18.2	122	218.0	278.0
11	259	19.0	122	230.0	294.0
14	268	19.9	122	240.0	304.0
17	292	21.5	122	261.0	328.0
20	328	24.4	122	292.0	367.0
F1-GENERATION LACTATION					
1	252	18.6	124	224.0	285.0
4	267	19.9	124	240.0	301.0
7	275	20.0	124	247.0	311.0
14	285	20.5	123	259.0	321.0
21	280	18.7	123	252.0	309.0

APPENDIX 1

**HISTORICAL DATA
FEMALES****1.2 BODY WEIGHT GAIN (%)**

DAYS	MEAN	STD.DEV.	N	P5	P95
F1-GENERATION POST COITUM					
0	0	0.0	125	0.0	0.0
4	5	2.2	121	1.8	8.7
7	8	2.7	121	3.9	12.0
11	14	3.0	121	9.3	18.7
14	18	3.3	121	12.6	23.1
17	28	4.4	121	20.5	35.1
20	44	6.2	121	34.1	53.5
F1-GENERATION LACTATION					
1	0	0.0	125	0.0	0.0
4	6	3.2	124	1.6	11.4
7	9	3.9	124	3.1	15.0
14	13	5.2	123	4.6	20.5
21	11	4.6	123	4.1	18.0

APPENDIX 1

**HISTORICAL DATA
FEMALES****1.3 FOOD CONSUMPTION (G/ANIMAL/DAY)**

DAYS	MEAN	STD.DEV.	N	P5	P95
F1-GENERATION POST COITUM					
1	35	9.6	18	19.0	56.0
2	19	7.3	121	12.8	37.0
3	36	7.5	18	27.0	51.0
4	35	9.3	18	19.0	61.0
5	36	8.9	18	24.0	59.0
6	23	8.6	122	15.0	37.0
7	37	12.8	18	21.0	76.0
8	34	8.5	18	16.0	55.0
9	22	6.2	122	15.5	35.0
10	35	10.0	18	22.0	67.0
11	36	11.1	18	19.0	61.0
12	38	10.5	18	25.0	68.0
13	22	7.9	122	14.3	41.0
14	34	8.1	18	22.0	55.0
15	35	7.9	18	25.0	52.0
16	23	6.6	122	16.3	36.0
17	36	7.5	18	26.0	53.0
18	38	8.6	18	26.0	56.0
19	26	6.6	122	18.7	38.0
20	37	7.9	18	25.0	53.0
21	34	8.7	17	22.0	53.0
22	25	6.4	10	14.0	35.0
23	26	4.8	7	20.0	34.0
F1-GENERATION LACTATION					
2	44	13.7	18	29.0	90.0
3	35	10.6	124	25.3	50.0
4	68	16.2	18	43.0	98.0
5	65	19.6	18	41.0	108.0
6	44	13.5	123	33.7	72.0
7	73	23.1	18	48.0	118.0
8	77	23.7	18	51.0	123.0
9	60	19.2	43	39.0	99.0
10	87	24.0	18	64.0	136.0
11	61	19.6	98	46.9	108.0
12	71	27.4	43	48.3	129.0
13	95	28.0	18	47.0	149.0
14	104	35.3	18	48.0	155.0
15	98	34.0	18	52.0	141.0
16	76	28.6	43	51.3	150.0
17	110	31.5	18	62.4	159.0
18	73	26.3	98	55.3	143.0
19	83	35.3	43	55.0	158.0
20	110	35.0	18	53.0	158.0
21	100	36.4	16	48.0	156.0
22	101	28.3	9	59.0	139.0

APPENDIX 1

**HISTORICAL DATA
FEMALES****1.4 RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)**

DAYS	MEAN	STD.DEV.	N	P5	P95
F1-GENERATION POST COITUM					
1	148	41.3	18	78.5	221.3
2	82	31.7	121	56.8	153.5
3	148	31.2	18	107.3	201.6
4	143	36.8	18	72.8	231.9
5	144	35.4	18	92.0	238.9
6	92	33.4	122	64.0	153.4
7	149	50.6	18	79.5	305.2
8	134	34.7	18	67.5	220.9
9	85	24.7	122	64.0	134.2
10	133	38.7	18	81.2	259.7
11	134	41.1	18	75.4	236.4
12	142	40.4	18	92.3	263.6
13	84	27.9	122	56.0	149.4
14	123	27.4	18	78.0	189.7
15	128	27.7	18	86.2	184.9
16	79	21.2	122	58.4	124.6
17	119	24.4	18	83.6	173.2
18	128	27.6	18	90.6	194.4
19	78	18.4	122	60.5	110.7
20	111	23.1	18	79.4	159.6
21	101	25.4	17	61.3	156.8
22	74	18.4	10	41.2	100.9
23	77	14.1	7	57.6	94.7
F1-GENERATION LACTATION					
2	171	55.2	18	121.8	361.4
3	131	36.9	124	98.6	177.2
4	244	54.6	18	153.6	352.5
5	234	69.2	18	155.9	397.1
6	161	43.4	123	128.5	261.0
7	256	76.9	18	163.3	396.4
8	270	77.8	18	173.5	429.1
9	216	62.1	43	156.6	325.8
10	306	78.6	18	219.9	494.5
11	211	63.0	98	167.4	380.3
12	250	88.0	43	183.4	441.3
13	322	83.6	18	163.2	473.0
14	354	112.6	18	155.3	520.5
15	331	108.5	18	174.5	503.6
16	268	90.2	43	184.6	473.2
17	373	99.7	18	214.8	567.9
18	259	88.7	98	201.2	490.2
19	296	117.0	43	206.7	542.5
20	386	117.2	18	179.7	570.4
21	347	121.1	16	190.5	554.0
22	351	95.3	9	204.2	484.3

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2017
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All
Selected projects	520648 520853 520949 521320 521638 522225
BODY WEIGHTS (GRAM)	
Selected group	CONTROL
Selected days	0 1 4 7 11 14 17 20 21
BODY WEIGHT GAIN (%)	
Selected group	CONTROL
Selected days	0 1 4 7 11 14 17 20 21
FOOD CONSUMPTION (G/ANIMAL/DAY)	
Selected group	CONTROL
Selected days	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)	
Selected group	CONTROL
Selected days	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25

2017-2021 historical control data EOGRTS (F1-generation)

ESTROUS CYCLE Cohort 1A, PND 75-88, PER STUDY

PARAMETER	Mean	St.dev	N	P5	P95	Min	Max
Regular estrous cycle (%)	95.0	6.4	12	ND	ND	80.0	100.0

ESTROUS CYCLE Cohort 1A, PND 75-88

PARAMETER	Total	Regular	Irregular	Extended di-estrous	Acyclic	Extended estrous
Cycle classification (%)	100	95.0	2.1	0.0	0.0	0.4
Cycle classification (count)	239	227	5	0	0	1

ND: not determined for N < 20

Selection information

Species	Rat
Dosing type	All
Start year	2017
End year	2021

Selected projects

Cohort 1A F1 generation:

518906
519713
20137078
20144696
20146521
20147222
20151567
20153892
20161729
20168827
20169540
20173295

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[1.1 Precoital Time](#)

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**HISTORICAL DATA
FEMALES****1.1 PRECOITAL TIME**

Day of the pairing period	Number of females mated
------------------------------	----------------------------

F1-GENERATION POST COITUM; PAIRING PERIOD 1

1	29
2	35
3	31
4	27
6	2
13	2
14	1

N	127
MEAN PRECOITAL TIME	2.8
MEDIAN PRECOITAL TIME	2.0

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2017
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All

Selected projects

520648 520853 520949 521320 521638 522225

PRECOITAL TIME

Selected group	CONTROL
Selected group	

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[1.1 Water Consumption](#)

APPENDIX 1

**HISTORICAL DATA
FEMALES****1.1 WATER CONSUMPTION (G/ANIMAL/DAY)**

DAYS	MEAN	STD.DEV.	N	P5	P95
F1-GENERATION POST COITUM					
1	25	4.6	13	17.0	33.0
2	29	5.3	9	22.0	38.0
3	36	4.7	7	29.0	44.0
4	37	6.4	8	29.0	47.0
5	33	5.7	23	25.0	39.0
6	33	6.3	17	24.0	44.0
7	37	6.4	17	25.0	46.0
8	33	7.6	37	21.0	45.0
9	35	6.7	17	23.0	51.0
10	35	9.3	17	22.0	52.0
11	41	6.2	17	33.0	52.0
12	38	8.4	41	26.0	51.0
13	40	5.5	16	28.0	52.0
14	44	7.8	17	28.0	60.0
15	40	7.5	41	30.0	54.0
16	45	6.7	17	33.0	56.0
17	47	7.7	17	35.0	61.0
18	46	8.6	41	33.0	57.0
19	45	7.8	17	31.0	58.0
20	42	5.9	17	31.0	51.0
21	39	7.5	41	29.0	51.0
22	28	9.2	17	14.0	47.0
23	29	10.5	7	20.0	52.0
24	.	.	0	.	.
25	.	.	0	.	.
26	.	.	0	.	.
F1-GENERATION LACTATION					
2	42	8.6	43	29.0	58.0
3	50	8.7	19	31.0	64.0
4	61	7.8	19	42.0	77.0
5	59	31.2	43	43.0	74.0
6	59	11.2	19	31.0	77.0
7	67	10.5	19	37.0	85.0
8	66	12.9	43	47.0	89.0
9	69	9.2	18	53.0	87.0
10	73	12.9	18	52.0	95.0
11	74	8.4	18	56.0	95.0
12	82	15.9	42	59.0	106.0
13	85	12.6	18	65.0	114.0
14	86	12.9	18	60.0	111.0
15	85	20.1	41	61.0	105.0
16	85	11.4	18	60.0	103.0
17	88	13.5	18	60.0	108.0
18	92	13.3	18	62.0	113.0
19	89	12.3	18	69.0	107.0
20	100	12.8	18	84.0	129.0
21	121	16.3	16	93.0	151.0
22	125	12.5	16	105.0	152.0
23	.	.	0	.	.

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2017
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All

Selected projects

520648 520853 520949 521320 521638 522225

WATER CONSUMPTION (G/ANIMAL/DAY)

Selected group	CONTROL
Selected days	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28

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[1.1 General](#)

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**HISTORICAL DATA
MALES****1.1 GENERAL**

	UNITS	MEAN	STD.DEV.	N	P5	P95
PND (PBS)						
BPS	PND	41.5	1.81	722	39.00	45.00
BW BPS	gram	173	13.9	722	151.0	196.0

FEMALES**1.1 GENERAL**

	UNITS	MEAN	STD.DEV.	N	P5	P95
PND (VO)						
BW VO	gram	95	12.6	720	72.5	115.0
First estrus	PND	35.3	3.13	239	31.00	39.00
Time to first E	DAYS	3.5	1.64	20	1.00	5.50
Time to first E	days	3.9	2.12	219	1.00	7.00
VO	PND	31.4	2.36	722	27.00	35.00

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2017
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All
Selected projects	518905 519715 520645 520792 520852 520948 521203 521219 521281 521317 521366 521440
GENERAL	
Selected group	CONTROL
Selected parameters	BPS BWBPS BWVO FE FEL VO
Grouped measurements (GENERAL)	
PND (PBS)	2 PND (BPS) 2 PND(BPS) 6 PND (BPS)
PND (VO)	1 PND (VO + FE) 1 PND (VO) 5 PND (VO)

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[1.1 Body Weights](#)

[1.2 Body Weight Gain](#)

[1.3 Food Consumption](#)

[1.4 Relative Food Consumption](#)

[1.5 Water Consumption](#)

APPENDIX 1

**HISTORICAL DATA
MALES****1.1 BODY WEIGHTS (GRAM)**

DAYS	MEAN	STD.DEV.	N	P5	P95
1	50	4.6	736	43.0	58.0
8	75	9.1	741	60.0	90.0
14	118	11.1	60	96.5	134.0
15	118	14.0	560	98.5	139.0
16	129	11.1	120	111.0	145.0
21	167	12.5	59	143.0	186.0
22	168	15.3	680	146.0	191.0
27	205	14.3	50	184.0	225.0
29	212	18.2	660	184.0	237.5
35	260	16.9	50	232.0	283.0
36	253	21.1	570	220.0	286.0
42	287	22.8	100	253.5	319.0
43	290	23.6	460	253.5	329.0
48	298	22.2	50	256.0	334.0
49	322	27.1	90	278.0	359.0
50	315	26.0	420	274.5	358.0
56	336	27.4	100	292.0	372.5
57	335	28.9	415	292.0	381.0
58	346	34.2	40	302.5	396.5
63	355	29.8	80	302.5	397.5
64	354	31.8	420	306.0	404.5
70	371	30.7	80	315.5	414.0
71	366	31.3	328	318.0	419.0
77	382	29.3	40	329.5	420.0
78	379	33.2	185	329.0	430.0
84	390	29.8	62	340.0	426.0
85	387	32.9	95	335.0	439.0
91	393	32.4	25	351.0	439.0
92	401	33.1	85	354.0	454.0
98	403	34.4	25	358.0	458.0
99	412	32.9	40	358.5	466.5
106	413	28.7	20	372.5	472.0

FEMALES**1.1 BODY WEIGHTS (GRAM)**

DAYS	MEAN	STD.DEV.	N	P5	P95
1	49	4.3	734	42.0	56.0
8	70	7.9	737	57.0	82.0
14	104	10.0	60	86.5	118.5
15	105	10.8	559	90.0	120.0
16	111	10.6	117	91.0	125.0
21	136	10.2	50	118.0	154.0
22	134	12.1	589	117.0	151.0
27	154	11.2	50	135.0	173.0
29	154	11.7	563	136.0	173.0
35	177	12.4	50	159.0	198.0
36	171	12.8	543	152.0	191.0
42	186	14.5	99	162.0	207.0
43	186	14.0	458	165.0	209.0
48	187	13.9	49	166.0	209.0
49	202	15.0	90	178.0	226.0
50	195	14.3	418	173.0	220.0
56	206	17.1	99	178.0	235.0
57	204	15.5	413	180.0	230.0
58	212	18.5	40	181.5	244.0
63	213	17.7	79	182.0	245.0
64	212	16.2	429	187.0	240.0

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**HISTORICAL DATA
FEMALES****1.1 BODY WEIGHTS (GRAM)**

DAYS	MEAN	STD.DEV.	N	P5	P95
70	218	17.0	79	187.0	248.0
71	218	15.6	327	192.0	246.0
77	223	18.0	35	196.0	252.0
78	223	15.9	203	200.0	251.0
84	218	14.6	45	198.0	244.0
85	228	16.5	48	205.0	260.0
92	231	18.8	21	211.0	263.0
98	.	.	0	.	.
99	248	10.6	2	240.0	255.0
106	261	.	1	261.0	261.0
107	278	.	1	278.0	278.0
113	249	.	1	249.0	249.0
120	256	.	1	256.0	256.0

APPENDIX 1

**HISTORICAL DATA
MALES****1.2 BODY WEIGHT GAIN (%)**

DAYS	MEAN	STD.DEV.	N	P5	P95
1	0	0.0	920	0.0	0.0
8	51	14.8	734	26.7	75.6
14	135	22.8	60	97.4	178.1
15	138	23.2	554	103.2	180.0
16	152	19.3	120	121.3	186.3
21	233	30.7	59	189.3	287.5
22	236	27.1	674	194.8	283.3
27	311	38.2	50	263.5	373.9
29	323	35.4	654	269.4	385.4
35	420	50.0	50	350.9	508.7
36	407	43.7	565	343.5	485.0
42	485	52.3	100	410.3	574.2
43	477	51.2	456	397.9	568.4
48	522	51.2	50	456.7	597.8
49	541	58.4	88	453.6	640.9
50	526	57.9	418	435.2	632.5
56	586	63.4	100	499.1	693.2
57	565	63.4	413	470.0	691.1
58	584	53.7	38	486.8	667.4
63	626	69.3	80	523.0	755.2
64	602	66.7	416	494.7	726.1
70	659	71.9	80	546.1	791.3
71	627	70.9	324	516.1	762.5
77	687	71.3	40	557.8	804.7
78	655	75.7	181	543.1	788.9
84	672	75.9	62	564.8	809.1
85	675	78.8	93	520.0	821.7
91	660	72.3	25	561.2	770.8
92	697	79.4	83	567.2	836.4
98	679	79.1	25	564.3	814.6
99	721	78.1	38	620.3	856.5
106	726	82.8	19	567.7	958.3

FEMALES**1.2 BODY WEIGHT GAIN (%)**

DAYS	MEAN	STD.DEV.	N	P5	P95
1	0	0.0	925	0.0	0.0
8	44	12.9	730	23.0	65.9
14	115	20.6	60	75.9	150.1
15	116	18.1	553	88.1	145.7
16	125	17.8	117	100.0	148.8
21	182	29.1	50	137.3	220.4
22	176	24.1	583	141.4	211.4
27	221	35.8	50	170.6	283.3
29	218	27.0	559	176.9	262.2
35	269	41.5	50	210.7	335.7
36	252	31.0	539	207.7	300.0
42	294	40.4	99	235.4	367.6
43	281	34.1	454	231.4	335.4
48	306	35.2	49	256.3	372.5
49	318	44.2	88	255.4	388.1
50	300	37.3	416	248.1	360.5
56	337	47.7	99	270.8	418.2
57	318	40.2	411	263.5	385.7
58	333	37.5	38	272.9	391.5
63	352	49.5	79	283.3	440.9
64	335	41.7	425	276.4	397.9

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**HISTORICAL DATA
FEMALES****1.2 BODY WEIGHT GAIN (%)**

DAYS	MEAN	STD.DEV.	N	P5	P95
70	363	48.5	79	295.7	438.1
71	345	38.2	323	285.2	411.4
77	369	47.4	35	303.5	445.0
78	356	40.7	199	294.5	431.7
84	351	34.7	45	305.4	408.9
85	370	43.8	47	305.6	436.4
92	373	54.8	20	277.9	459.3
98	.	.	0	.	.
99	425	77.0	2	370.6	479.5
106	493	.	1	493.2	493.2
107	504	.	1	504.3	504.3
113	466	.	1	465.9	465.9
120	482	.	1	481.8	481.8

APPENDIX 1

**HISTORICAL DATA
MALES****1.3 FOOD CONSUMPTION (G/ANIMAL/DAY)**

DAYS	MEAN	STD.DEV.	N (CAGE)	P5	P95
4	9	0.8	148	7.3	9.9
11	14	1.2	124	11.5	15.2
12	14	1.0	24	12.9	15.8
18	18	1.1	124	16.6	19.9
19	19	1.0	24	17.4	20.4
25	21	1.1	144	19.3	22.8
32	23	1.6	124	20.6	25.9
39	24	1.9	112	21.1	27.1
45	22	0.7	10	20.1	22.8
46	24	2.0	102	20.9	27.0
52	21	0.8	10	20.1	22.3
53	24	2.1	101	20.3	26.9
59	20	1.0	8	18.7	21.6
60	23	2.0	85	19.9	26.5
61	26	1.3	8	23.9	27.3
66	20	0.8	8	18.8	21.3
67	22	2.2	77	19.1	26.1
73	19	0.8	4	17.9	19.6
74	22	2.6	47	17.3	25.2
80	20	.	1	19.8	19.8
81	22	1.9	30	17.5	24.4
87	22	1.2	9	21.1	24.5
88	22	2.4	17	18.1	25.8
94	22	0.6	5	21.5	22.9
95	24	3.4	8	19.4	30.2
102	21	4.2	4	15.8	26.1

FEMALES**1.3 FOOD CONSUMPTION (G/ANIMAL/DAY)**

DAYS	MEAN	STD.DEV.	N (CAGE)	P5	P95
4	8	1.0	148	6.5	9.9
11	12	0.8	124	10.7	13.2
12	12	1.5	24	10.5	13.7
18	14	1.0	113	13.2	16.1
19	14	2.5	19	7.7	21.7
25	15	1.1	123	13.7	17.3
32	16	1.4	119	13.7	18.7
39	16	1.5	112	13.9	18.5
45	14	0.5	10	13.2	14.9
46	16	1.5	102	13.7	18.2
52	14	0.6	10	12.9	14.8
53	16	1.4	101	13.9	18.2
59	13	0.6	8	12.4	14.5
60	16	1.7	87	13.7	19.1
61	17	0.5	8	16.4	17.9
66	13	0.4	8	12.8	13.8
67	16	1.7	78	13.2	18.5
73	13	0.3	4	12.3	13.1
74	15	1.4	50	13.1	17.6
80	13	.	1	12.6	12.6
81	15	1.4	16	11.8	16.7
87	.	.	0	.	.
88	15	0.5	4	14.5	15.7
95	.	.	0	.	.

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**HISTORICAL DATA
MALES****1.4 RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)**

DAYS	MEAN	STD.DEV.	N (CAGE)	P5	P95
4	117	11.5	148	102.1	137.8
11	117	10.0	124	104.1	139.3
12	111	4.6	24	103.6	117.3
18	111	5.3	124	103.4	121.5
19	109	3.6	24	103.0	114.6
25	101	5.3	144	93.1	110.6
32	92	5.4	124	84.8	101.3
39	83	5.2	112	75.6	92.7
45	72	1.4	10	69.9	74.9
46	76	5.2	102	68.6	84.2
52	65	1.4	10	62.3	67.0
53	70	5.1	101	63.0	78.6
59	59	1.5	8	56.5	60.9
60	65	5.1	85	58.0	73.8
61	72	2.6	8	68.9	75.3
66	56	1.2	8	54.2	58.0
67	61	5.0	76	54.0	70.3
73	52	1.3	4	49.7	52.5
74	57	6.4	47	48.1	66.4
80	51	.	1	51.2	51.2
81	57	4.6	30	48.8	64.2
87	56	2.3	9	52.4	60.0
88	56	4.9	17	47.5	63.3
94	55	2.3	5	52.5	57.8
95	57	8.6	8	48.6	76.2
102	52	10.3	4	39.1	64.4

FEMALES**1.4 RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)**

DAYS	MEAN	STD.DEV.	N (CAGE)	P5	P95
4	119	14.5	148	98.4	143.3
11	116	8.8	124	106.4	135.8
12	108	10.3	24	100.5	117.8
18	109	6.2	113	100.3	119.7
19	104	11.3	18	64.6	114.6
25	100	6.5	123	89.7	110.6
32	93	6.8	119	83.0	103.9
39	86	6.6	112	76.2	97.7
45	75	1.7	10	71.6	77.4
46	81	6.2	102	72.1	90.9
52	69	2.0	10	64.5	71.8
53	77	5.4	101	68.6	85.9
59	64	2.4	8	61.0	67.7
60	74	6.6	87	65.0	84.5
61	81	2.1	8	77.7	83.7
66	63	2.0	8	59.8	66.7
67	72	6.4	77	61.8	82.9
73	60	1.1	4	58.0	60.6
74	68	6.0	50	59.1	77.4
80	60	.	1	59.8	59.8
81	65	6.2	16	54.4	76.0
87	.	.	0	.	.
88	67	2.0	4	65.1	69.2
95	.	.	0	.	.

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**HISTORICAL DATA
MALES****1.5 WATER CONSUMPTION (G/ANIMAL/DAY)**

DAYS	MEAN	STD.DEV.	N (CAGE)	P5	P95
4	12	2.8	24	7.6	15.8
10	21	1.5	24	19.0	23.7
16	26	2.7	24	23.8	31.4
22	29	1.4	24	27.1	31.7
29	32	2.0	23	29.6	35.0
35	36	2.5	8	32.8	39.7
36	33	2.2	10	29.8	36.6
41	36	3.1	8	32.0	39.9
42	36	2.7	8	31.7	40.5
44	36	2.0	5	33.0	37.8
47	36	2.8	8	32.0	39.7
48	34	2.7	8	29.0	38.3
51	36	3.3	5	31.0	39.2
53	35	2.4	8	31.6	38.7
54	34	3.4	8	27.8	39.2
58	33	2.9	5	28.7	36.5
59	34	1.8	8	30.6	36.2
60	35	3.1	8	29.0	39.3
65	33	2.6	13	29.0	36.1
66	32	2.4	8	27.0	34.9
71	30	5.8	7	17.6	34.9
72	31	4.6	12	22.5	37.2
77	32	4.2	9	23.2	36.4
78	33	3.1	5	28.0	36.4
81	.	.	0	.	.
82	28	2.7	5	25.1	31.1
84	30	1.1	4	29.1	31.6
89	29	2.0	5	26.3	31.8
90	31	0.4	4	30.1	30.9
96	33	0.4	4	33.0	34.0
100	31	.	1	30.5	30.5

FEMALES**1.5 WATER CONSUMPTION (G/ANIMAL/DAY)**

DAYS	MEAN	STD.DEV.	N (CAGE)	P5	P95
4	12	2.7	24	8.0	14.9
10	19	1.4	24	17.4	21.9
16	22	1.8	24	19.1	25.2
22	23	1.9	20	19.4	26.5
29	24	1.9	17	21.0	27.1
35	25	2.2	9	21.6	28.7
36	24	1.7	8	22.2	26.7
41	26	2.3	9	22.7	28.9
42	25	2.4	8	23.0	29.4
44	30	2.5	5	27.0	33.4
47	27	2.1	8	23.8	29.3
48	24	2.2	8	21.6	27.5
51	30	2.4	5	27.8	33.9
53	26	2.5	8	22.4	29.2
54	25	2.1	8	22.0	28.4
58	28	1.6	5	27.3	31.0
59	26	2.2	8	23.0	29.4
60	26	2.7	8	21.8	30.9
65	27	2.7	13	23.4	33.1
66	24	2.6	8	20.5	28.9
71	26	3.2	7	20.8	30.3
72	24	3.4	12	17.3	29.5

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**HISTORICAL DATA
FEMALES****1.5 WATER CONSUMPTION (G/ANIMAL/DAY)**

DAYS	MEAN	STD.DEV.	N (CAGE)	P5	P95
77	29	2.7	9	25.3	33.2
78	27	2.3	5	24.2	29.8
81	.	.	0	.	.

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2017
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All
Selected projects	518905 519715 520645 520792 520852 520948 521203 521219 521281 521317 521366 521440
BODY WEIGHTS (GRAM)	
Selected group	CONTROL
Selected days	1 8 14 15 16 21 22 27 29 35 36 42 43 48 49 50 56 57 58 63 64 70 71 77 78 84 85 91 92 98 99 105 106 107 112 113 119 120
BODY WEIGHT GAIN (%)	
Selected group	CONTROL
Selected days	1 8 14 15 16 21 22 27 29 35 36 42 43 48 49 50 56 57 58 63 64 70 71 77 78 84 85 91 92 98 99 105 106 107 112 113 119 120
FOOD CONSUMPTION (G/ANIMAL/DAY)	
Selected group	CONTROL
Selected days	4 11 12 18 19 25 32 39 45 46 52 53 59 60 61 66 67 73 74 80 81 87 88 94 95 102
RELATIVE FOOD CONSUMPTION (G/KG BODY WEIGHT/DAY)	
Selected group	CONTROL
Selected days	4 11 12 18 19 25 32 39 45 46 52 53 59 60 61 66 67 73 74 80 81 87 88 94 95 102
WATER CONSUMPTION (G/ANIMAL/DAY)	
Selected group	CONTROL
Selected days	4 10 16 22 29 35 36 41 42 44 47 48 51 53 54 58 59 60 65 66 71 72 77 78 81 82 84 89 90 96 100

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[1.1 Sperm Motility, Concentration And Morphology](#)

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**HISTORICAL DATA
MALES****1.1 SPERM MOTILITY, CONCENTRATION AND MORPHOLOGY**

	UNITS	MEAN	STD.DEV.	N	P5	P95
SPERM ANALYSIS COHORT 1B						
SPERM COUNT EPI	10E6/gram	416.5	117.59	25	158.80	555.80
MOTILE SPERM	%	68	16.7	25	31.0	89.0
PROGRESSIV. SPERM	%	27	9.3	25	14.0	39.0
END OF TREATMENT						
SPERM COUNT EPI	10E6/gram	441.4	137.58	238	209.10	634.00
Normal morph	No of cells	178	16.0	236	147.0	195.0
Other tail	No of cells	1	1.7	236	0.0	5.0
Combined	No of cells	0	0.4	236	0.0	1.0
Detached head	No of cells	3	4.1	236	0.0	8.0
Abnormal head	No of cells	1	1.3	236	0.0	3.0
Abnormal neck	No of cells	1	1.9	236	0.0	5.0
Coiled tail	No of cells	15	14.9	236	0.0	46.0
NR OF CELLS EXAM		258	78.2	40	117.0	405.0
MOTILE SPERM	%	65	20.0	240	23.5	90.0
PROGRESSIV. SPERM	%	27	14.3	240	5.0	53.0

Selection Criteria for Historical Data

Selection information	Value
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Species	RAT
Dosing type	All
Start year	2017
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All

Selected projects

518905 519715 520645 520792 520852 520948
521203 521219 521281 521317 521366 521440

SPERM MOTILITY, CONCETRATION AND MORPHOLOGY

Selected group	CONTROL
Selected parameters	COUNTEPI COUNTTES M1 M10 M11 M2 M3 M5 M6 SPERMCEL SPERMMOT SPERMPRO

Grouped measurements (SPERM MOTILITY, CONCETRATION AND MORPHOLOGY)

END OF TREATMENT	3 COHORT 1A 3 END OF TREATMENT 3 SPERM ANALYSIS 5 COHORT 1A; SPERM ANALYSIS 5 SPERM ANALYSIS 5 SPERM ANALYSIS COHORT 1A 8 COHORT 1A; END OF TREATMENT
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[1.1 Organ Weights](#)

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**HISTORICAL DATA
MALES****1.1 ORGAN WEIGHTS (GRAM)**

ORGAN	MEAN	STD.DEV.	N	P5	P95
ORGAN WEIGHT, COHORT 1A; END OF IN-LIFE					
Adrenals	0.060	0.0090	240	0.0460	0.0745
Axillary lymph node	0.07	0.031	111	0.035	0.123
Body weight	348	31.5	239	298.0	399.3
Brain	2.01	0.077	239	1.875	2.136
Epididymides	1.056	0.1031	240	0.8965	1.2085
Heart	0.976	0.0878	240	0.8377	1.1201
Kidneys	2.35	0.248	240	1.979	2.776
Liver	9.17	1.082	240	7.534	11.128
Mandibular lymph nod	0.092	0.0235	10	0.0660	0.1440
Mesenteric lymph nod	0.354	0.1886	121	0.1820	0.7800
Pituitary	0.009	0.0012	240	0.0068	0.0104
Prostate	0.642	0.1301	240	0.4420	0.8778
Seminal vesicles	1.050	0.2106	240	0.6855	1.4350
Spleen	0.585	0.0835	240	0.4540	0.7280
Testes	3.54	0.282	240	3.117	4.020
Thymus	0.412	0.0853	240	0.2875	0.5670
Thyroids	0.0165	0.00336	239	0.01120	0.02260
ORGAN WEIGHT, COHORT 1B; END OF IN-LIFE					
Adrenals	0.054	0.0083	249	0.0400	0.0680
Body weight	395	35.9	250	334.0	448.7
Epididymides	1.143	0.1086	249	0.9820	1.3200
Kidneys	2.66	0.264	25	2.265	3.093
Liver	11.92	1.147	20	9.893	13.624
Pituitary	0.009	0.0013	250	0.0067	0.0111
Prostate	0.803	0.1572	249	0.5670	1.0590
Seminal vesicles	1.370	0.2567	249	0.9470	1.7993
Testes	3.68	0.301	249	3.209	4.203
Thyroids	0.0175	0.00323	250	0.01200	0.02280
ORGAN WEIGHT, COHORT 2A; END OF IN-LIFE					
Body weight	337	30.0	70	300.0	384.0
Brain	2.28	0.107	70	2.111	2.460
ORGAN WEIGHT, COHORT 2B; END OF IN-LIFE					
Body weight	50	4.5	70	42.7	57.0
Brain	1.79	0.101	70	1.624	1.931
ORGAN WEIGHT, COHORT SURPLUS; END OF IN-LIFE					
Body weight	57	6.7	110	46.0	68.0
Brain	1.49	0.057	110	1.380	1.572
FIXED THYMUS	0.270	0.0420	10	0.2040	0.3220
Kidneys	0.68	0.096	10	0.544	0.860
Liver	2.07	0.382	10	1.465	2.564
Spleen	0.293	0.0614	110	0.2110	0.4110
Thymus	0.237	0.0453	100	0.1785	0.3085
Thyroids	0.0064	0.00192	20	0.00370	0.01000
ORGAN/BODY WEIGHT RATIOS, COHORT 1A; END OF IN-LIFE					
Adrenals	0.017	0.0025	239	0.0133	0.0216
Axillary lymph node	0.019	0.0085	111	0.0103	0.0372
Body weight	348	31.5	239	298.0	399.3
Brain	0.58	0.047	238	0.510	0.676
Epididymides	0.305	0.0325	239	0.2582	0.3633
Heart	0.281	0.0195	239	0.2513	0.3150
Kidneys	0.68	0.056	239	0.588	0.779
Liver	2.63	0.180	239	2.358	2.972
Mandibular lymph nod	0.026	0.0061	10	0.0197	0.0383
Mesenteric lymph nod	0.102	0.0526	121	0.0518	0.2207
Pituitary	0.002	0.0003	239	0.0020	0.0030
Prostate	0.185	0.0359	239	0.1265	0.2459
Seminal vesicles	0.303	0.0610	239	0.2057	0.4189
Spleen	0.168	0.0193	239	0.1371	0.2007

APPENDIX 1

**HISTORICAL DATA
MALES****1.1 ORGAN WEIGHTS (GRAM)**

ORGAN	MEAN	STD.DEV.	N	P5	P95
ORGAN/BODY WEIGHT RATIOS, COHORT 1A; END OF IN-LIFE					
Testes	1.02	0.106	239	0.859	1.208
Thymus	0.118	0.0211	239	0.0836	0.1557
Thyroids	0.0047	0.00090	238	0.00326	0.00622
ORGAN/BODY WEIGHT RATIOS, COHORT 1B; END OF IN-LIFE					
Adrenals	0.014	0.0021	249	0.0103	0.0179
Body weight	395	35.9	250	334.0	448.7
Epididymides	0.291	0.0298	249	0.2463	0.3381
Kidneys	0.65	0.040	25	0.573	0.728
Liver	3.19	0.141	20	2.932	3.388
Pituitary	0.002	0.0003	250	0.0018	0.0028
Prostate	0.203	0.0364	249	0.1452	0.2607
Seminal vesicles	0.348	0.0616	249	0.2392	0.4474
Testes	0.94	0.094	249	0.784	1.102
Thyroids	0.0044	0.00082	250	0.00306	0.00609
ORGAN/BODY WEIGHT RATIOS, COHORT 2A; END OF IN-LIFE					
Body weight	337	30.0	70	300.0	384.0
Brain	0.68	0.064	70	0.597	0.780
ORGAN/BODY WEIGHT RATIOS, COHORT 2B; END OF IN-LIFE					
Body weight	50	4.5	70	42.7	57.0
Brain	3.61	0.360	70	3.063	4.241
ORGAN/BODY WEIGHT RATIOS, COHORT SURPLUS; END OF IN-LIFE					
Body weight	57	6.7	110	46.0	68.0
Brain	2.65	0.269	110	2.261	3.106
FIXED THYMUS	0.533	0.0433	10	0.4636	0.5906
Kidneys	1.11	0.064	10	1.010	1.211
Liver	3.90	0.345	10	3.450	4.620
Spleen	0.518	0.0940	110	0.3794	0.6826
Thymus	0.413	0.0716	100	0.3338	0.4892
Thyroids	0.0121	0.00480	20	0.00676	0.02199

FEMALES**1.1 ORGAN WEIGHTS (GRAM)**

ORGAN	MEAN	STD.DEV.	N	P5	P95
ORGAN WEIGHT, COHORT 1A; END OF IN-LIFE					
Adrenals	0.068	0.0143	240	0.0496	0.0880
Axillary lymph node	0.05	0.018	109	0.027	0.086
Body weight	203	16.2	238	176.1	232.1
Brain	1.85	0.071	240	1.734	1.972
Heart	0.666	0.0582	240	0.5750	0.7645
Kidneys	1.52	0.138	240	1.308	1.785
Liver	5.59	0.587	240	4.781	6.700
Mandibular lymph nod	0.162	0.0930	10	0.0400	0.3040
Mesenteric lymph nod	0.283	0.1147	120	0.1523	0.5725
Ovaries	0.138	0.0222	240	0.1065	0.1762
Pituitary	0.010	0.0017	240	0.0080	0.0127
Spleen	0.409	0.0605	240	0.3180	0.5195
Thymus	0.352	0.0669	240	0.2552	0.4615
Thyroids	0.0136	0.00281	240	0.00960	0.01845
Uterus	0.576	0.2308	240	0.3530	1.0680
ORGAN WEIGHT, COHORT 1B; END OF IN-LIFE					
Adrenals	0.068	0.0124	245	0.0470	0.0895
Body weight	247	29.8	244	207.0	296.0
Kidneys	2.09	0.142	24	1.889	2.342

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**HISTORICAL DATA
FEMALES****1.1 ORGAN WEIGHTS (GRAM)**

ORGAN	MEAN	STD.DEV.	N	P5	P95
ORGAN WEIGHT, COHORT 1B; END OF IN-LIFE					
Liver	8.20	1.355	29	6.511	10.525
Ovaries	0.138	0.0826	246	0.1030	0.1680
Pituitary	0.011	0.0018	246	0.0084	0.0137
Thyroids	0.0147	0.00277	246	0.01050	0.01970
Uterus	0.589	0.2827	246	0.3600	1.0560
ORGAN WEIGHT, COHORT 2A; END OF IN-LIFE					
Body weight	207	17.5	69	177.7	237.8
Brain	2.11	0.109	69	1.948	2.297
ORGAN WEIGHT, COHORT 2B; END OF IN-LIFE					
Body weight	48	4.5	69	42.0	55.3
Brain	1.74	0.087	70	1.575	1.856
ORGAN WEIGHT, COHORT SURPLUS; END OF IN-LIFE					
Body weight	54	5.6	109	45.7	66.0
Brain	1.42	0.059	110	1.340	1.520
FIXED THYMUS	0.293	0.0288	10	0.2670	0.3610
Kidneys	0.60	0.056	10	0.505	0.718
Liver	2.05	0.209	10	1.745	2.468
Spleen	0.286	0.0543	110	0.2053	0.3840
Thymus	0.236	0.0455	100	0.1669	0.3270
Thyroids	0.0070	0.00272	20	0.00225	0.01225
ORGAN/BODY WEIGHT RATIOS, COHORT 1A; END OF IN-LIFE					
Adrenals	0.034	0.0066	238	0.0247	0.0427
Axillary lymph node	0.024	0.0083	108	0.0129	0.0401
Body weight	203	16.2	238	176.1	232.1
Brain	0.92	0.072	238	0.819	1.056
Heart	0.330	0.0236	238	0.2926	0.3667
Kidneys	0.75	0.058	238	0.667	0.857
Liver	2.76	0.225	238	2.444	3.132
Mandibular lymph nod	0.080	0.0463	10	0.0167	0.1528
Mesenteric lymph nod	0.139	0.0569	119	0.0733	0.2811
Ovaries	0.068	0.0107	238	0.0527	0.0861
Pituitary	0.005	0.0008	238	0.0039	0.0063
Spleen	0.202	0.0238	238	0.1644	0.2458
Thymus	0.173	0.0306	238	0.1252	0.2222
Thyroids	0.0067	0.00134	238	0.00468	0.00927
Uterus	0.287	0.1190	238	0.1705	0.5511
ORGAN/BODY WEIGHT RATIOS, COHORT 1B; END OF IN-LIFE					
Adrenals	0.028	0.0044	243	0.0208	0.0356
Body weight	247	29.8	244	207.0	296.0
Kidneys	0.76	0.058	22	0.699	0.881
Liver	3.65	0.404	29	3.142	4.266
Ovaries	0.057	0.0348	244	0.0401	0.0716
Pituitary	0.004	0.0008	244	0.0034	0.0059
Thyroids	0.0060	0.00115	244	0.00437	0.00797
Uterus	0.245	0.1316	244	0.1385	0.4705
ORGAN/BODY WEIGHT RATIOS, COHORT 2A; END OF IN-LIFE					
Body weight	207	17.5	69	177.7	237.8
Brain	1.03	0.096	69	0.873	1.205
ORGAN/BODY WEIGHT RATIOS, COHORT 2B; END OF IN-LIFE					
Body weight	48	4.5	69	42.0	55.3
Brain	3.65	0.373	69	3.165	4.325
ORGAN/BODY WEIGHT RATIOS, COHORT SURPLUS; END OF IN-LIFE					
Body weight	54	5.6	109	45.7	66.0
Brain	2.64	0.254	109	2.174	3.103
FIXED THYMUS	0.561	0.0395	10	0.5132	0.6333

APPENDIX 1

**HISTORICAL DATA
FEMALES****1.1 ORGAN WEIGHTS (GRAM)**

ORGAN	MEAN	STD.DEV.	N	P5	P95
ORGAN/BODY WEIGHT RATIOS, COHORT SURPLUS; END OF IN-LIFE					
Kidneys	1.10	0.051	10	1.023	1.195
Liver	3.88	0.246	10	3.518	4.244
Spleen	0.529	0.0958	109	0.3930	0.7065
Thymus	0.433	0.0621	99	0.3293	0.5448
Thyroids	0.0133	0.00545	20	0.00461	0.02514

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2017
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All
Selected projects	518905 519715 520645 520792 520852 520948 521203 521219 521281 521317 521366 521440
ORGAN WEIGHTS (GRAM)	
Selected group	CONTROL
Selected parameters	ADRENALS AXILLN BODYWEIG BRAIN EPIDIDYM FIXZWEZE HEART KIDNEYS LIVER MANDLN MESENTLN OVARIES PITUIT PROSTATE SEMINALV SPLEEN TESTES THYMUS THYROIDS UTERUS
Grouped measurements (ORGAN WEIGHTS (GRAM))	
Measurements removed	3 DUMMY 7 COHORT 3; END OF IN-LIFE 7 DUMMY 8 COHORT 3/POS CONTROL; POST-IMMUNIZATION 8 COHORT 3; END OF IN-LIFE
COHORT 1A; END OF IN-LIFE	1 COHORT 1A 3 COHORT 1A; END OF IN-LIFE 5 COHORT 1A; END OF IN-LIFE 6 COHORT 1A; END OF IN-LIFE 7 COHORT 1A; END OF IN-LIFE
COHORT 1B; END OF IN-LIFE	2 COHORT 1B 4 COHORT 1B; END OF IN-LIFE 6 COHORT 1B; END OF IN-LIFE
COHORT 1C; END OF IN-LIFE	2 COHORT 1C; END OF IN-LIFE 3 COHORT 1C 3 COHORT 1C; END OF IN-LIFE 4 COHORT 1C; END OF IN-LIFE 7 COHORT 1C; END OF IN-LIFE 8 COHORT 1C; END OF IN-LIFE
COHORT 2A; END OF IN-LIFE	4 COHORT 2A; END OF IN-LIFE 5 COHORT 2A; END OF IN-LIFE
COHORT 2B; END OF IN-LIFE	1 COHORT 2B; END OF IN-LIFE 2 COHORT 2B; END OF IN-LIFE
COHORT SURPLUS; END OF IN-LIFE	1 COHORT SURPLUS; END OF IN-LIFE 2 COHORT SURPLUS; END OF IN-LIFE 2 COHORT SURPLUS; END OF IN-LIFE 4 SURPLUS

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[1.1 General](#)

APPENDIX 1

**HISTORICAL DATA
MALES****1.1 GENERAL**

	UNITS	MEAN	STD.DEV.	N	P5	P95
COHORT 2A						
BRAIN LENGTH	MM	26.04	1.076	10	23.510	27.040
BRAIN WIDTH	MM	15.39	0.372	10	14.760	15.880
LENGTH OF BRAIN	MM	23.93	1.782	60	20.830	26.460
WIDTH OF BRAIN	MM	15.42	0.584	60	14.315	16.320
COHORT 2B						
BRAIN LENGTH	MM	20.40	0.783	10	19.400	22.230
BRAIN WIDTH	MM	15.16	0.317	10	14.560	15.800
LENGTH OF BRAIN	MM	20.79	1.398	60	18.830	23.605
WIDTH OF BRAIN	MM	15.23	0.497	60	14.535	16.250

FEMALES**1.1 GENERAL**

	UNITS	MEAN	STD.DEV.	N	P5	P95
COHORT 2A						
BRAIN LENGTH	MM	24.17	1.104	10	22.470	26.160
BRAIN WIDTH	MM	15.17	0.409	10	14.550	15.880
LENGTH OF BRAIN	MM	22.94	1.979	59	19.940	26.400
WIDTH OF BRAIN	MM	15.10	0.596	59	14.030	16.000
COHORT 2B						
BRAIN LENGTH	MM	21.15	1.156	10	20.040	24.080
BRAIN WIDTH	MM	15.04	0.412	10	14.460	15.930
LENGTH OF BRAIN	MM	20.69	1.556	60	18.610	24.260
WIDTH OF BRAIN	MM	15.12	0.409	60	14.445	15.830

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2017
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All
Selected projects	518905 519715 520645 520792 520852 520948 521203 521219 521281 521317 521366 521440
GENERAL	
Selected group	CONTROL
Selected parameters	BRAINL BRAINW TESTESL TESTESW
Grouped measurements (GENERAL)	
COHORT 2A	4 BRAIN DIMENSIONS COHORT 2A 4 COHORT 2A; BRAIN DIMENSIONS 11 BRAIN DIMENSIONS: COHORT 2A
COHORT 2B	3 BRAIN DIMENSIONS COHORT 2B 3 COHORT 2B; BRAIN DIMENSIONS 10 BRAIN DIMENSIONS: COHORT 2B

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[1.1 Body Weights Of Pups](#)

APPENDIX 1

**HISTORICAL DATA
MALES****1.1 BODY WEIGHTS OF PUPS (GRAM)**

DAYS	MEAN	STD.DEV.	N	P5	P95
F1-GENERATION LACTATION					
DAY 1	6.3	0.62	739	5.40	7.40
DAY 4	9.6	1.05	732	8.00	11.40
DAY 7	16.2	1.68	488	13.50	18.80
DAY 13	30.9	2.53	271	26.90	35.40
DAY 14	32.7	2.69	220	28.35	37.30
DAY 21	49.7	4.81	490	42.00	58.00

FEMALES**1.1 BODY WEIGHTS OF PUPS (GRAM)**

DAYS	MEAN	STD.DEV.	N	P5	P95
F1-GENERATION LACTATION					
DAY 1	6.0	0.60	708	5.10	7.00
DAY 4	9.3	1.08	702	7.50	11.10
DAY 7	15.7	1.56	488	13.30	18.10
DAY 13	29.9	2.51	265	26.10	33.60
DAY 14	32.1	2.42	227	28.60	36.30
DAY 21	48.3	4.19	491	42.00	55.00

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2017
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All

Selected projects

520648 520853 520949 521320 521638 522225

BODY WEIGHTS OF PUPS (GRAM)

Selected group	CONTROL
Selected parameters	1 13 14 21 4 7

APPENDIX 1

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[1.1 Corpora Lutea And Follicle count](#)

**HISTORICAL DATA
FEMALES****1.1 CORPORA LUTEA**

	UNITS	MEAN	STD.DEV.	N	P5	P95
FOLLICLES / CORPORA LUTEA						
Corpora Lutea		82.5	16.59	20	61.00	117.50
Follicle Count		68.1	22.64	20	34.50	111.50

Selection Criteria for Historical Data

Selection information	Value
-----------------------	-------

Species	RAT
Dosing type	All
Start year	2017
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All

Selected projects

518905 519715 520645 520792 520852 520948
521203 521219 521281 521317 521366 521440

CORPORA LUTEA

Selected group	CONTROL
Selected parameters	CLFIXED FCFIXED

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[1.1 Implantation Sites](#)

APPENDIX 1

**HISTORICAL DATA
FEMALES****1.1 IMPLANTATION SITES**

	UNITS	MEAN	STD.DEV.	N	P5	P95
AT NECROPSY						
Implantations		12.5	1.92	125	10.00	15.00

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2017
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All

Selected projects

518905 519715 520645 520792 520852 520948
 521203 521219 521281 521317 521366 521440

IMPLANTATION SITES

Selected group	CONTROL
Selected parameters	IMPL

Grouped measurements (IMPLANTATION SITES)

AT NECROPSY	3 AT NECROPSY
	4 AT NECROPSY
	6 IMPLANTATIONS
	7 AT NECROPSY
	12 AT NECROPSY

2017-2021 historical control data EOGRTS F1**Developmental DATA**

MEASUREMENT	Mean	St.dev	N	P5	P95
Post-implantation survival index (%)	94	1.9	6	ND ^a	ND ^a
Live birth index (%)	99	1.4	6	ND ^a	ND ^a
Viability index (%)	99	0.7	6	ND ^a	ND ^a
Weaning index (%)	100	0.5	6	ND ^a	ND ^a

ND^a = not determined for N < 20

Selection information

Species	Rat
Dosing type	All
Start year	2017
End year	2021

Selected projects	518906
	20137078
	20147222
	20151567
	20161729
	20168827

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[1.1 Anogenital Distance And Nipple Retention](#)

APPENDIX 1

**HISTORICAL DATA
MALES****1.1 ANOGENITAL DISTANCE AND NIPPLE RETENTION**

	MEAN	STD.DEV.	N	P5	P95
F1-GENERATION LACTATION					
anogenital dist M mm	2.67	0.246	97	2.238	3.152
anogenital dist F mm	0.99	0.124	98	0.760	1.186
Number of nipples	0.00	0.000	104	0.000	0.000

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2017
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All

Selected projects

520648 520853 520949 521320 522225

ANOGENITAL DISTANCE AND NIPPLE RETENTION

Selected group	CONTROL
Selected parameters	ANOGENITAL DIST F MM ANOGENITAL DIST M MM NUMBER OF NIPPLES

APPENDIX 1

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[1.1 Corrected Anogenital Distance](#)

APPENDIX 1

**HISTORICAL DATA
FEMALES****1.1 CORRECTED ANOGENITAL DISTANCE**

	UNITS	MEAN	STD.DEV.	N	P5	P95
PND 1						
norm anog dist F	mm	0.55	0.066	98	0.430	0.650
norm anog dist M	mm	1.44	0.119	97	1.220	1.640

Selection Criteria for Historical Data

Selection information	Value
-----------------------	-------

Species	RAT
Dosing type	All
Start year	2017
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All

Selected projects

519715 520645 520792 520852 520948 521203
521219 521281 521317 521366 521440

CORRECTED ANOGENITAL DISTANCE

Selected group	CONTROL
Selected parameters	CORAGDF CORAGDM

Grouped measurements (CORRECTED ANOGENITAL DISTANCE)

PND 1	2 PND 1
	7 PND 1
	8 PND 1
	8 PND1
	9 COHORT 1B: PND 1

2017-2021 historical control data EOGRTS MAMS F1-rats

MALES

COHORT 2A - MOTOR ACTIVITY AND MOVEMENTS

MEASUREMENT	Mean	St.dev	N	P5	P95
Total movements	4402	1293	70	2565.3	6869.3
Ambulations	981	351	70	472.0	1604.4

FEMALES

COHORT 2A - MOTOR ACTIVITY AND MOVEMENTS

MEASUREMENT	Mean	St.dev	N	P5	P95
Total movements	5643	1748	69	2898.5	8816.0
Ambulations	1630	560	69	772.0	2631.0

Selection information

Species	Rat
Dosing type	All
Start year	2017
End year	2021

Selected projects	20146521
	20147222
	20151567
	20153892
	20161729
	20168827
	20169540

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[1.1 Haematology](#)

APPENDIX 1

**HISTORICAL DATA
MALES****1.1 HAEMATOLOGY**

MEASUREMENT	UNITS	MEAN	STD.DEV.	N	P5	P95
END OF IN-LIFE						
APTT	s	19.5	2.81	117	14.40	23.40
Basophils	10E9/L	0.0	0.01	115	0.00	0.02
Eosinophils	10E9/L	0.1	0.04	115	0.05	0.18
Haematocrit	L/L	0.462	0.0205	115	0.4230	0.4900
Haemoglobin	mmol/L	9.7	0.36	115	9.00	10.20
T-cells	%Lymphoid cells	42.6	6.53	120	32.50	53.40
T-helper cells	%Lymphoid cells	27.8	4.74	120	20.20	35.60
T-cytotoxic cell	%Lymphoid cells	13.7	3.12	120	8.80	18.50
B-cells	%Lymphoid cells	42.1	6.10	120	32.05	52.65
NK-cells	%Lymphoid cells	4.9	1.34	120	3.00	6.95
Th/Tc		2.1	0.45	120	1.38	2.89
LUC	10E9/L	0.0	0.02	38	0.02	0.10
Lymphocytes	10E9/L	5.5	1.24	38	3.28	8.04
Lymphocytes	10E9/L	5.4	1.18	77	3.40	7.09
MCH	fmol	1.12	0.041	115	1.060	1.210
MCHC	mmol/L	20.92	0.601	115	19.960	22.090
MCV	fL	53.7	1.64	115	50.90	56.30
Monocytes	10E9/L	0.2	0.06	115	0.08	0.28
Neutrophils	10E9/L	1.1	0.35	115	0.67	1.69
Platelets	10E9/L	722	79.6	115	601.0	851.0
PT	s	17.2	1.01	118	15.60	18.80
Red blood cells	10E12/L	8.61	0.389	115	7.990	9.060
RDW	%	12.1	1.02	115	10.90	13.40
Reticulocytes	10E9/L	217.4	30.28	115	163.20	267.50
WBC	10E9/L	6.8	1.45	115	4.26	9.33

FEMALES**1.1 HAEMATOLOGY**

MEASUREMENT	UNITS	MEAN	STD.DEV.	N	P5	P95
END OF IN-LIFE						
APTT	s	19.6	2.74	115	15.00	23.00
Basophils	10E9/L	0.0	0.01	114	0.00	0.01
Eosinophils	10E9/L	0.1	0.03	114	0.03	0.11
Haematocrit	L/L	0.437	0.0274	114	0.3900	0.4700
Haemoglobin	mmol/L	9.1	0.51	114	8.10	9.80
T-cells	%Lymphoid cells	41.6	6.51	120	32.85	54.05
T-helper cells	%Lymphoid cells	27.0	4.25	120	20.55	34.50
T-cytotoxic cell	%Lymphoid cells	13.5	3.38	120	9.45	20.45
B-cells	%Lymphoid cells	42.7	6.43	120	31.95	52.95
NK-cells	%Lymphoid cells	5.3	1.41	120	2.85	7.70
Th/Tc		2.1	0.48	120	1.33	2.97
LUC	10E9/L	0.0	0.02	38	0.01	0.07
Lymphocytes	10E9/L	3.8	1.08	38	1.81	6.37
Lymphocytes	10E9/L	3.2	0.90	76	1.98	4.99
MCH	fmol	1.14	0.040	114	1.080	1.210
MCHC	mmol/L	20.89	0.550	114	20.020	21.900
MCV	fL	54.7	1.73	114	52.00	57.60
Monocytes	10E9/L	0.1	0.04	114	0.04	0.17
Neutrophils	10E9/L	0.6	0.30	114	0.25	1.09
Platelets	10E9/L	728	97.6	114	563.0	907.0
PT	s	17.2	1.12	114	15.50	19.00
Red blood cells	10E12/L	7.99	0.493	114	7.160	8.750
RDW	%	10.9	0.63	114	10.10	12.00
Reticulocytes	10E9/L	204.8	31.55	114	153.10	256.00
WBC	10E9/L	4.2	1.15	114	2.39	6.47

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2017
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All
Selected projects	518905 519715 520645 520792 520852 520948 521203 521219 521281 521317 521366 521440
HAEMATOLOGY	
Selected group	CONTROL
Selected parameters	APTT BA BASOA1 EO EOSA1 HCT HGB IMMUNO01 IMMUNO02 IMMUNO03 IMMUNO04 IMMUNO05 IMMUNO12 LUC LUCA1 LYMPHA1 LYMPHO MCHC MCV MO MONOA1 NEUTA1 PLT PT RBC RDW RETI RETICA1 SEG WBC
Grouped measurements (HAEMATOLOGY)	
END OF IN-LIFE	2 COHORT 1A 2 COHORT 1A; END OF IN-LIFE 3 COHORT 1A: IMMUNO 3 COHORT 1A; END OF IN-LIFE 3 COHORT 1A; IMMUNO 3 IMMUNO 4 COHORT 1A: IMMUNO 4 COHORT 1A; IMMUNO 5 COHORT 1A; END OF IN-LIFE 6 COHORT 1A; IMMUNO

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[1.1 Clinical Biochemistry](#)

APPENDIX 1

**HISTORICAL DATA
MALES****1.1 CLINICAL BIOCHEMISTRY**

MEASUREMENT	UNITS	MEAN	STD.DEV.	N	P5	P95
COHORT 1A; END OF IN-LIFE						
ALAT	U/L	32.9	5.01	120	25.60	43.00
Albumin	g/L	33.3	1.06	120	31.45	34.95
ALP	U/L	117	27.5	120	79.0	166.0
ASAT	U/L	81.1	10.99	120	65.85	102.55
Bile Acids	umol/L	20.2	13.50	119	8.10	46.40
Total bilirubin	umol/L	2.2	0.49	120	1.60	3.15
Calcium	mmol/L	2.60	0.076	120	2.475	2.715
Cholesterol	mmol/L	1.94	0.386	120	1.310	2.570
Chloride	mmol/L	103	1.7	120	100.0	105.0
Creatinine	umol/L	36.1	2.59	120	32.20	41.50
Glucose	mmol/L	8.55	1.137	120	6.740	10.715
Potassium	mmol/L	3.76	0.220	120	3.360	4.140
Sodium	mmol/L	141.7	1.31	120	139.40	143.95
Inorg.Phos	mmol/L	2.08	0.179	120	1.790	2.380
Total protein	g/L	64.4	2.09	120	61.00	67.65
TSH	uIU/mL	0.188	0.2803	119	0.0360	0.5260
Total T4	ug/dL	6.26	1.185	119	4.200	8.190
Urea	mmol/L	4.9	0.87	120	3.65	6.55
COHORT 2B; END OF IN-LIFE						
TSH	uIU/mL	0.107	0.0775	30	0.0510	0.2610
Total T4	ug/dL	5.43	1.149	30	3.820	7.590
COHORT 3/POS CONTROL; POST-IMMUNIZATION						
a-SRBC IgM	U/mL	11958	8891.3	10	3405.4	33083.9
a-SRBC IgM	µg/mL	54	10.8	40	43.4	72.9
COHORT 3/POS CONTROL; PRE-IMMUNIZATION						
a-SRBC IgM	U/mL	464	142.3	10	283.0	702.3
a-SRBC IgM	µg/mL	43	4.8	40	35.1	50.7
COHORT SURPLUS; END OF IN-LIFE						
TSH	uIU/mL	0.081	0.0528	100	0.0245	0.2065
Total T4	ug/dL	4.64	0.913	100	2.985	6.210

FEMALES**1.1 CLINICAL BIOCHEMISTRY**

MEASUREMENT	UNITS	MEAN	STD.DEV.	N	P5	P95
COHORT 1A; END OF IN-LIFE						
ALAT	U/L	26.2	6.66	120	19.95	34.55
Albumin	g/L	35.7	1.77	120	32.95	38.65
ALP	U/L	61	20.6	120	37.0	99.5
ASAT	U/L	82.3	21.85	120	64.90	104.10
Bile Acids	umol/L	16.4	13.73	120	5.15	44.20
Total bilirubin	umol/L	2.2	0.58	120	1.40	3.40
Calcium	mmol/L	2.59	0.068	120	2.500	2.705
Cholesterol	mmol/L	1.49	0.396	120	0.830	2.220
Chloride	mmol/L	104	1.8	120	100.0	106.0
Creatinine	umol/L	40.4	3.06	120	36.00	45.70
Glucose	mmol/L	7.49	1.045	120	5.990	9.480
Potassium	mmol/L	3.32	0.247	120	2.940	3.750
Sodium	mmol/L	141.3	1.84	120	138.10	143.95
Inorg.Phos	mmol/L	1.75	0.278	120	1.305	2.200
Total protein	g/L	66.1	3.04	120	61.70	71.05
TSH	uIU/mL	0.075	0.0605	120	0.0130	0.2025
Total T4	ug/dL	3.45	1.126	120	1.850	5.955
Urea	mmol/L	6.4	1.14	120	4.70	8.10

APPENDIX 1

**HISTORICAL DATA
FEMALES****1.1 CLINICAL BIOCHEMISTRY**

MEASUREMENT	UNITS	MEAN	STD.DEV.	N	P5	P95
COHORT 1B; END OF IN-LIFE						
TSH	uIU/mL	0.197	0.2047	10	0.0410	0.6110
Total T4	ug/dL	3.96	0.499	10	2.980	4.690
COHORT 2B; END OF IN-LIFE						
TSH	uIU/mL	0.081	0.0428	30	0.0300	0.1800
Total T4	ug/dL	5.03	1.102	30	2.990	7.190
COHORT 3/POS CONTROL; POST-IMMUNIZATION						
a-SRBC IgM	U/mL	6878	3218.6	10	2973.6	13295.5
a-SRBC IgM	µg/mL	65	23.1	40	49.7	83.0
COHORT 3/POS CONTROL; PRE-IMMUNIZATION						
a-SRBC IgM	U/mL	320	99.5	10	169.2	515.4
a-SRBC IgM	µg/mL	46	4.9	40	36.8	52.5
COHORT SURPLUS; END OF IN-LIFE						
TSH	uIU/mL	0.076	0.0571	100	0.0245	0.1765
Total T4	ug/dL	4.67	0.964	100	3.225	6.570
PND 4 PUPS						
Total T4	ug/dL	1.90	0.293	21	1.530	2.280

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2017
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All
Selected projects	518905 519715 520645 520792 520852 520948 521203 521219 521281 521317 521366 521440
CLINICAL BIOCHEMISTRY	
Selected group	CONTROL
Selected parameters	ALAT ALB ALBGL ALP ASAT BACID BILI CA CHOL CL CREA GLUC HEM HEMI HEMS IMMUNO01 K NA PHOS PHOSLIP PROT TGLOB TRIG TSHO TT4 UREA
Grouped measurements (CLINICAL BIOCHEMISTRY)	
COHORT 1A; END OF IN-LIFE	2 COHORT 1A 2 COHORT 1A; END OF IN-LIFE 3 COHORT 1A; END OF IN-LIFE 5 COHORT 1A; END OF IN-LIFE
COHORT 1B; END OF IN-LIFE	5 COHORT 1B
COHORT 2B; END OF IN-LIFE	1 COHORT 2B; END OF IN-LIFE 2 COHORT 2B; END OF IN-LIFE
COHORT 3/POS CONTROL; POST-IMMUNIZATION	8 COHORT 3/POS CONTROL; POST-IMMUNIZATIO 9 COHORT 3/POS CONTROL; POST-IMMUNIZATION
COHORT 3/POS CONTROL; PRE-IMMUNIZATION	8 COHORT 3/POS CONTROL; PRE-IMMUNIZATION 9 COHORT 3/POS CONTROL; PRE-IMMUNIZATION
COHORT SURPLUS; END OF IN-LIFE	1 COHORT SUPPLUS; END OF IN-LIFE 1 COHORT SURPLUS; END OF IN-LIFE 1 SURPLUS 2 COHORT SURPLUS; END OF IN-LIFE 2 COHORT SURPLUS; END OF INLIFE
PND 4 PUPS	7 PND 4 PUPS

APPENDIX 1

CONTENTS

[1.1 Urinalysis](#)

APPENDIX 1

**HISTORICAL DATA
MALES****1.1 URINALYSIS**

MEASUREMENT	UNITS	MEAN	STD.DEV.	N	P5	P95
COHORT 1A; END OF IN-LIFE						
Bilirubin	score 0/3	0	0.3	120	0.0	1.0
Clarity	score 1/3	2	0.7	120	1.0	3.0
Colour	score 1/5	1	0.4	120	1.0	2.0
WBC	score 0/3	0	0.0	120	0.0	0.0
Glucose	score 0/3	0	0.0	120	0.0	0.0
Blood	score 0/3	0	0.4	120	0.0	1.0
Ketones	score 0/3	0	0.4	120	0.0	1.0
Nitrite	pos/neg	0.13	0.332	120	0.000	1.000
pH		6.9	0.46	120	6.50	7.50
Protein	score 0/3	0	0.5	120	0.0	1.0
Bacteria	score 0/3	3	0.3	120	2.0	3.0
Casts	score 0/3	0	0.1	120	0.0	0.0
Crystals	score 0/3	3	0.7	120	1.0	3.0
Epithelial cells	score 0/3	1	0.6	120	1.0	2.0
Specific gravity		1.029	0.0109	120	1.0135	1.0505
Other	score 0/3	0	0.0	120	0.0	0.0
RBC-sed.	score 0/3	0	0.5	120	0.0	1.0
WBC-sed.	score 0/3	0	0.5	120	0.0	1.0
Urobilinogen	score 0/3	0	0.0	120	0.0	0.0
Volume	mL	10	5.7	120	4.0	20.0

FEMALES**1.1 URINALYSIS**

MEASUREMENT	UNITS	MEAN	STD.DEV.	N	P5	P95
COHORT 1A; END OF IN-LIFE						
Bilirubin	score 0/3	0	0.2	120	0.0	0.0
Clarity	score 1/3	1	0.5	120	1.0	2.5
Colour	score 1/5	1	0.3	120	1.0	2.0
WBC	score 0/3	0	0.0	120	0.0	0.0
Glucose	score 0/3	0	0.0	120	0.0	0.0
Blood	score 0/3	0	0.1	120	0.0	0.0
Ketones	score 0/3	0	0.0	120	0.0	0.0
Nitrite	pos/neg	0.12	0.322	120	0.000	1.000
pH		6.5	0.52	120	6.00	7.00
Protein	score 0/3	0	0.2	120	0.0	0.0
Bacteria	score 0/3	3	0.5	120	2.0	3.0
Casts	score 0/3	0	0.0	120	0.0	0.0
Crystals	score 0/3	2	1.1	120	0.0	3.0
Epithelial cells	score 0/3	1	0.6	120	0.0	2.0
Specific gravity		1.025	0.0099	120	1.0110	1.0420
Other	score 0/3	0	0.0	120	0.0	0.0
RBC-sed.	score 0/3	0	0.4	120	0.0	1.0
WBC-sed.	score 0/3	0	0.5	120	0.0	1.0
Urobilinogen	score 0/3	0	0.0	120	0.0	0.0
Volume	mL	8	4.6	120	3.0	15.0

Selection Criteria for Historical Data

Selection information	Value
Species	RAT
Dosing type	All
Start year	2017
End year	All
Strains	CRL HAN WISTAR
Study description	All
Age at start of treatment	All
Selected projects	518905 519715 520645 520792 520852 520948 521203 521219 521281 521317 521366 521440
URINALYSIS	
Selected group	CONTROL
Selected parameters	BILI CLA COL DILK GLU HAEM KET NAU NIT PH PRO SBAC SCAS SCRY SEPI SG SOTH SRBC SWBC URB VOL
Grouped measurements (URINALYSIS)	
COHORT 1A; END OF IN-LIFE	2 COHORT 1A 2 COHORT 1A; END OF IN-LIFE 3 COHORT 1A; END OF IN-LIFE 5 COHORT 1A; END OF IN-LIFE