charles river

Historical Control Data in New Zealand White Rabbits

Les Oncins, Saint Germain Nuelles 69210, France • 33 474016501

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

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Historical Control Data

Rabbit NZW KBL

Maternal body weight gain (g) during gestation

Study	Year	Dams with live fetuses	Gestation days 0 to 3		Gestation days 3 to 6		Gestation days 0 to 6		Gestation days 6 to 9		Gestation days 9 to 13		Gestation days 13 to 16		Gestation days 16 to 20		Gestation days 6 to 20		Gestation days 20 to 24		Gestation days 24 to 29	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
A18	2018	8					140	60	32	43	98	71	70	64	19	69	219	125	85	40	76	70
B18	2018	5					61	91	14	163	138	69	122	68	50	50	325	161	33	94	68	39
D18	2018	19					157	90	67	29	114	49	79	53	27	113	287	182	64	83	107	75
E18	2018	5	49	56	91	39			55	34	57	30	21	94	39	37	171	75				
F18	2018	18	61	106	90	82			68	32	76	59	57	66	39	101	240	136				
G18	2018	15	50	60	55	76			19	65	110	35	98	63	16	35	243	121	71	55	94	92
H18	2018	4	-149	157	128	104			81	77	98	23	75	27	6	41	260	129				
I18	2018	6									154	67	33	38	-51	64			45	72	104	24
J18	2018	10					79	114	38	39	109	41	51	69	23	52	221	119	46	76	57	71
K18	2018	19					134	118	45	60	134	52	85	64	14	91	278	85	73	52	88	83
L18	2018	20					100	88	48	33	100	45	57	66	-8	83	198	130	86	53	122	85
M18	2018	8					118	90	44	37	100	51	82	35	-20	57	205	113	69	58	171	72
N18	2018	17	49	84	45	129			38	68	101	54	78	52	19	42	235	106	93	55	105	107
O18	2018	3					125	89	42	43	65	61	154	101	-87	94	174	255	122	25	135	136
P18	2018	4	74	103	69	63			81	39	72	35	91	38	21	51	265	123				
Q18	2018	4	3	84	49	51			9	29	39	77	62	81	-14	81	96	66	97	80		
R18	2018	5					129	33	62	10	85	52	102	70	29	92	277	26	87	12	169	83
S18	2018	20	91	73	63	43			17	65	94	71	85	36	-2	40	195	104	52	47	104	66
T18	2018	18	-17	106	69	87			59	52	73	58	91	69	19	72	241	154	49	83	97	119
UV18	2018	32					138	69					50	66	-20	61			16	70		
WX18	2018	38					125	46					39	64	-6	72			24	71		
Y18	2018	21					145	41	53	31					-31	84			16	70		
Z18	2018	20					161	44	50	20					-45	74			19	72		
Total		*319*																				
Mean			*39*		*68*		*131*		*46*		*99*		*69*		*0*		*235*		*50*		*104*	
SD				*101*		*83*		*76*		*52*		*57*		*64*		*75*		*130*		*70*		*86*
2015-2017		*402*	-	-	-	-	*128*	*94*	*42*	*51*	*87*	*60*	*66*	*66*	*2*	*69*	*210*	*136*	*53*	*73*	*99*	*91*

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Historical Control Data

Rabbit NZW KBL

Maternal food consumption (g/day) during gestation

Study	Year	Dams with live fetuses	Gestation days 0 to 3		Gestation days 3 to 6		Gestation days 0 to 6		Gestation days 6 to 9		Gestation days 9 to 13		Gestation days 13 to 16		Gestation days 16 to 20		Gestation days 6 to 20		Gestation days 20 to 24		Gestation days 24 to 29	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
A18	2018	8					146	20	166	21	162	22	128	39	147	33	151	21	122	38	98	22
B18	2018	5					129	21	130	86	144	80	163	24	178	23	155	36	137	45	116	31
D18	2018	19					141	20	179	17	174	19	152	37	156	49	165	27	136	41	114	34
E18	2018	5			173	10			169	16	153	6	100	46	125	26	143	26				
F18	2018	18					146	31	170	26	159	32	118	49	145	45	148	29				
G18	2018	15			99	28	151	24	153	32	151	25	128	38	149	37	146	27	133	23	120	24
H18	2018	4			142	32			166	16	152	14	144	11	167	21	158	12				
I18	2018	6									151	33	105	36	126	34	132	28	105	26	107	25
J18	2018	10					133	33	177	27	175	27	138	43	166	39	165	28	136	39	102	35
K18	2018	19					135	28	170	21	167	21	134	37	151	41	156	24	135	31	120	32
L18	2018	20					136	26	161	15	158	24	110	31	118	51	137	23	128	34	123	29
M18	2018	8					124	27	147	32	147	17	118	33	134	49	137	21	122	32	120	21
N18	2018	17	115	42	146	53			156	32	165	23	131	37	155	26	153	22	139	33	121	29
O18	2018	3	86	33	146	20			132	9	136	20	110	32	116	71	124	24	144	54	119	47
P18	2018	4	117	40	147	60			164	47	160	53	118	62	149	37	149	37				
Q18	2018	4	88	33	138	9			127	14	117	21	82	38	96	42	106	18	126	19		
R18	2018	5					130	12	150	11	144	25	105	48	136	17	135	21	140	18	135	17
S18	2018	20	119	27	156	19			132	31	128	32	110	39	130	24	126	27	139	18	126	16
T18	2018	18	93	41	143	42			154	45	145	45	116	50	145	51	141	42	118	32	100	34
UV18	2018	32					168	20	168	22	148	32	123	44	133	49			115	44		
WX18	2018	38					173	20	174	20	150	28	114	44	133	42			119	35		
Y18	2018	21					145	17	186	24	182	23	146	34	146	47			118	43		
Z18	2018	20					191	10	189	12	178	16	132	35	144	35			109	52		
Total		*319*																				
Mean			*108*		*141*		*153*		*165*		*157*		*125*		*141*		*146*		*125*		*116*	
SD				*38*		*41*		*29*		*31*		*31*		*41*		*43*		*29*		*37*		*29*
2015-2017		*402*	*-*	*-*	*-*	*-*	*159*	*30*	*173*	*24*	*164*	*27*	*135*	*46*	*148*	*38*	*NA*	*NA*	*131*	*36*	*117*	*32*

Studies WX18-1 and WX18-2 were recorded on gestation day 10 instead of gestation day 9

Studies Y18 and Z18 were recorded on gestation day 12 instead of gestation day 13

File name: I.3.1-RABBIT_KBL_G29_2018_OK.xls

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Historical Control Data

Rabbit NZW KBL

Caesarean data collected on day 29 of gestation

Study	Year	Number of females				Number of corpora lutea		Number of uterine implants		Pre-implantation loss %		Early resorptions per dam		Late resorptions per dam		Post-implantation loss %	
		Mated	Pregnant	Aborted	With live fetuses	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
A18	2018	9	8	0	8	10.8	1.9	10.4	2.0	3.4	6.8	0.1	0.4	0.1	0.4	2.1	4.0
B18	2018	6	6	0	5	10.3	1.8	10.0	1.8	3.4	5.4	1.8	4.0	0.2	0.4	20.9	39.3
C18	2018	22	19	0	19	10.2	2.1	9.6	2.3	5.9	8.9	0.7	1.1	0.2	0.4	9.2	13.4
D18	2018	22	19	1	19	11.6	1.9	10.5	2.1	10.1	10.7	0.2	0.4	0.1	0.2	2.7	6.6
E18	2018	5	5	0	5	10.4	1.5	9.8	2.4	7.0	11.0	0.2	0.4	0.0	0.0	2.2	5.0
F18	2018	20	18	1	18	10.6	2.7	9.8	3.2	10.0	13.6	0.1	0.5	0.6	1.0	6.0	10.2
G18	2018	20	16	0	15	10.3	2.3	9.5	3.1	9.0	14.1	0.7	2.2	0.4	0.7	11.4	24.4
H18	2018	5	4	0	4	10.3	1.5	9.8	1.3	4.6	5.3	0.5	1.0	0.0	0.0	6.3	12.5
I18	2018	6	6	0	6	9.8	1.7	9.2	1.9	6.9	8.9	0.0	0.0	0.2	0.4	2.4	5.8
J18	2018	10	10	0	10	11.1	1.7	10.8	1.8	2.7	6.1	0.5	0.7	0.2	0.4	7.4	5.9
K18	2018	22	19	1	19	10.6	2.2	9.9	2.4	6.5	9.4	0.3	0.6	0.4	0.8	5.8	8.9
L18	2018	22	20	1	20	12.1	2.9	10.9	2.9	10.1	12.6	0.4	0.6	0.6	0.8	8.2	7.5
M18	2018	9	8	0	8	10.3	1.2	10.0	1.3	2.5	4.7	0.0	0.0	0.4	0.7	3.9	8.1
N18	2018	20	17	0	17	11.6	2.2	10.1	2.3	13.0	15.5	0.3	0.6	0.4	0.6	6.4	7.9
O18	2018	4	3	0	3	9.3	0.6	9.0	0.0	3.3	5.8	0.3	0.6	0.3	0.6	7.4	12.8
P18	2018	5	4	0	4	12.0	3.5	10.8	1.3	7.4	14.7	0.3	0.5	0.0	0.0	2.1	4.2
Q18	2018	5	4	0	4	10.5	2.1	9.8	1.3	6.1	7.5	0.3	0.5	0.0	0.0	2.5	5.0
R18	2018	6	5	0	5	11.0	3.7	10.0	3.5	9.4	10.3	0.0	0.0	0.0	0.0	0.0	0.0
S18	2018	20	20	0	20	10.7	1.8	9.6	2.0	10.5	10.6	0.2	0.5	0.3	0.7	5.2	7.7
T18	2018	20	18	1	18	12.0	1.7	10.4	1.5	12.7	8.0	0.3	0.8	0.4	1.0	6.7	12.1
U18	2018	18	15	0	15	9.0	3.1	8.0	2.9	11.9	15.8	0.1	0.5	0.1	0.4	2.7	6.0
W18	2018	21	19	0	19	10.3	1.8	9.1	2.5	12.7	17.1	0.2	0.4	0.2	0.5	3.3	5.9
Y18	2018	22	21	0	21	10.0	2.3	9.5	2.6	6.0	10.9	0.1	0.3	0.1	0.4	2.4	4.4
Total		*319*	*284*	*5*	*282*												
			89%	*2%*	*88%*												
Mean						*10.7*		*9.8*		*8.7*		*0.3*		*0.3*		*5.6*	
SD							*2.3*		*0.8*		*11.7*		*0.9*		*0.6*		*11.0*
2015-2017		*412*	*379*	*2*	*371*	*10.6*	*2.1*	*9.6*	*2.5*	*9.6*	*14.2*	*0.3*	*0.6*	*0.3*	*0.7*	*6.0*	*11.6*
			92%	*0%*	*90%*												

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Historical Control Data

Rabbit NZW KBL

Caesarean data collected on day 29 of gestation

Study	Year	Number of females				Dead fetuses	Live litter size		Fetal weight (g)		Uterus weight (g)		Sex ratio
		Mated	Pregnant	Aborted	With live fetuses	Total	Mean	SD	Mean	SD	Mean	SD	% males
A18	2018	9	8	0	8	0	10.1	1.7	39.9	3.5	594	65	43.9
B18	2018	6	6	0	5	0	8.0	4.5	40.4	3.7	561	109	
C18	2018	22	19	0	19	0	8.7	2.4	41.3	5.1	512	113	54.4
D18	2018	22	19	1	19	0	10.3	2.4	40.5	3.9	591	122	56.3
E18	2018	5	5	0	5	0	9.6	2.5	43.0	9.1	577	124	
F18	2018	20	18	1	18	0	9.1	3.0	41.2	4.9	543	137	46.3
G18	2018	20	16	0	15	0	8.4	3.6	41.3	4.9	544	124	54.4
H18	2018	5	4	0	4	0	9.3	2.2	41.0	6.8	514	89	
I18	2018	6	6	0	6	0	9.0	2.2	41.9	3.6	532	98	
J18	2018	10	10	0	10	1	10.0	1.8	41.1	3.5	602	116	39.3
K18	2018	22	19	1	19	0	9.3	1.9	41.1	4.8	568	106	48.1
L18	2018	22	20	1	20	0	9.9	2.3	38.4	5.0	546	112	50.6
M18	2018	9	8	0	8	0	9.6	1.6	39.7	2.7	551	71	55.5
N18	2018	20	17	0	17	0	9.4	2.3	40.4	6.5	556	112	52.4
O18	2018	4	3	0	3	0	8.3	1.2	45.0	4.0	547	71	
P18	2018	5	4	0	4	0	10.5	1.0	39.2	3.0	592	60	
Q18	2018	5	4	0	4	0	9.5	1.3	33.5	2.3	494	81	
R18	2018	6	5	0	5	0	10.0	3.5	40.9	3.0	584	162	
S18	2018	20	20	0	20	0	9.1	2.0	40.0	5.1	524	105	53.9
T18	2018	20	18	1	18	0	9.7	1.8	39.7	4.0	562	91	55.5
U18	2018	18	15	0	15	0	7.7	2.7	43.2	7.3	495	151	43.5
W18	2018	21	19	0	19	0	8.7	2.4	42.2	6.2	560	136	46.3
Y18	2018	22	21	0	21	0	9.3	2.5	42.9	6.4	563	141	57.5
Total		*319*	*284*	*5*	*282*	*1*							
			89%	*2%*	*88%*								
Mean							*9.3*		*40.9*		*552*		*51.1*
SD								*2.4*		*5.1*		*121*	
2015-2017		*412*	*379*	*2*	*371*	*0*	*9.1*	*2.4*	*41.4*	*5.5*	*547*	*109*	*49.9*
			92%	*0%*	*90%*								

File name: I.3.1-RABBIT_KBL_G29_2018_OK.xls

Historical Control Data

Rabbit NZW KBL

Malformations (external, internal and skeletal)

Study	Number of litters examined	Number of fetuses examined	Number of litters with malformed fetuses	Litter incidence %	Number of malformed fetuses	Fetal incidence %	Type of malformation by fetus
A18	8	81	2	25.00	2	2.47	1st: Fused sternebrae 2nd: Omphalocele, multiple sternebrael and thoracic vertebrae (scoliosis) abnormalities
B18	5	48	0	0.00	0	0.00	
C18	19	166	1	5.26	1	0.60	Multiple abnormalities of thoracic vertebrae
D18	19	195	3	15.79	4	2.05	1st: Diaphragmatic hernia 2nd: Omphalocele 3rd: Narrowed aortic arch 4th: Fused sternebra
E18	5	48	0	0.00	0	0.00	
F18	18	164	2	11.11	2	1.22	1st: Multiple lumbar vertebrae abnormalities (centra fused; arch absent; scoliosis) 2nd: Multiple cervical vertebrae abnormalities (centra small and misaligned, arches small, malpositioned or fused; scoliosis)
G18	15	134	0	0.00	0	0.00	
H18	4	37	0	0.00	0	0.00	
I18	6	54	0	0.00	0	0.00	
J18	10	101	3	30.00	5	4.95	1st, 2nd and 3rd: Multiple thoracic vertebrae abnormalities 4th: Multiple sternebral abnormalities 5th: Absent diaphragm, gall bladder and azygos vein, multiple sternebral abnormalities
K18	19	176	2	10.53	3	1.70	1st: Fused sternebrae 2nd: Multiple sternebrae abnormalities 3rd: Malrotated hindlimbs

Historical Control Data

Rabbit NZW KBL

Malformations (external, internal and skeletal)

Study	Number of litters examined	Number of fetuses examined	Number of litters with malformed fetuses	Litter incidence %	Number of malformed fetuses	Fetal incidence %	Type of malformation by fetus
L18	20	197	3	15.00	3	1.52	1st: Multiple sternebral abnormalities 2nd: Paw hyperflexion, multiple sternebral abnormalities 3rd: Ventricular wall thick, small ventricle
M18	8	77	0	0.00	0	0.00	
N18	17	160	0	0.00	0	0.00	
O18	3	25	0	0.00	0	0.00	
P18	4	42	0	0.00	0	0.00	
Q18	4	38	0	0.00	0	0.00	
R18	5	50	0	0.00	0	0.00	
S18	20	181	3	15.00	3	1.66	1st: Malformed heart (small right ventricle with small auriculo-ventricular valves and large left ventricle) and great blood vessels (dilated aortic arch and narrowed pulmonary trunk) 2nd: Retroesophageal aortic arch 3rd: Multiple thoracic vertebrae abnormalities
T18	19	179	1	5.26	1	0.56	Three-chambered heart (two atria and one ventricle)
U18	15	116	1	6.67	3	2.59	1st: Ventricular septum defect 2nd: Malformed great blood vessels (dilated aortic arch, ductus arteriosus terminating in pulmonary arteries with atritic pulmonary trunk arising from right pulmonary artery) 3rd: Hindpaw hyperflexion
W18	19	166	1	5.26	1	0.60	Fused sternebrae
Y18	21	195	1	4.76	1	0.51	Multiple thoracic vertebrae abnormalities (misshapen, small or misaligned centra, large, small or absent arch, detached rib; scoliosis)
2018	*273*	*2529*	*20*	**7.33%**	*24*	**0.95%**	
2015-2017	*348*	*3182*	*43*	**12.36%**	*49*	**1.54%**	

Study nos. B18, E18, H18, I18, P18, Q18, R18 and T18: Dose Range Finding studies with external examination only.

Historical Control Data

Rabbit NZW KBL

FETAL EXAMINATION - EXTERNAL **- page 1/1**

PERIOD	2013-2015		2016-2018	
Number of studies included	10		46	
Number of fetuses examined	1571		5480	
OBSERVATION	N	%	N	%
General : local oedema	0	0.00	3	0.05
Meningoencephalocele	0	0.00	1	0.02
Craniorachischisis	0	0.00	1	0.02
Face: malformed	0	0.00	1	0.02
Nose: small	0	0.00	1	0.02
Protruding tongue	0	0.00	1	0.02
Microphthalmia	0	0.00	1	0.02
Eye: open	0	0.00	3	0.05
Microtia	0	0.00	1	0.02
Gastroschisis	0	0.00	1	0.02
Umbilical hernia	1	0.06	0	0.00
Omphalocele	0	0.00	7	0.13
Brachydactyly	0	0.00	1	0.02
Limb: malrotated	0	0.00	2	0.04
Paw: malrotated	0	0.00	1	0.02
Paw: hyperflexion	0	0.00	7	0.13
Claw: absent	0	0.00	2	0.04

Historical Control Data

Rabbit NZW KBL

FETAL EXAMINATION - FRESH VISCERAL EXAMINATION OF BODY **- page 1/3**

PERIOD	2013-2015		2016-2018	
Number of studies included	8		29	
Number of fetuses examined	1460		4635	
OBSERVATION	N	%	N	%
General: material	0	0.00	1	0.02
Heart: multiple abnormalities	1	0.07	1	0.02
Heart: ventricular septum defect	1	0.07	2	0.04
Heart: ventricular wall thick	2	0.14	1	0.02
Heart: three-chambered	0	0.00	2	0.04
Heart: small ventricle	1	0.07	2	0.04
Carotid artery: absent common carotid trunk	479	32.81	1759	37.95
Great blood vessels: multiple abnormalities	6	0.41	5	0.11
Innominate artery : absent	3	0.21	16	0.35
Pulmonary trunk: narrowed	1	0.07	0	0.00
Aorta: malpositioned	1	0.07	0	0.00
Descending aorta: retrocaval	1	0.07	0	0.00
Aortic arch: dilated	1	0.07	0	0.00
Aortic arch: narrowed	0	0.00	1	0.02
Aortic arch: retroesophageal	1	0.07	1	0.02
Subclavian artery: malpositioned	0	0.00	1	0.02
Subclavian artery: retroesophageal	2	0.14	7	0.15
Azygos vein: absent	0	0.00	1	0.02
Azygos vein: transposed	0	0.00	17	0.37
Posterior vena cava: malpositioned	7	0.48	0	0.00
Diaphragm, Absent	0	0.00	1	0.02
Diaphragmatic hernia	1	0.07	1	0.02
Abdomen: fluid-filled	2	0.14	1	0.02
Thorax: cyst(s)	0	0.00	1	0.02
Thorax fluid-filled	1	0.07	1	0.02

Historical Control Data

Rabbit NZW KBL

FETAL EXAMINATION - FRESH VISCERAL EXAMINATION OF BODY **- page 2/3**

PERIOD	2013-2015		2016-2018	
Number of studies included	8		29	
Number of fetuses examined	1460		4635	
OBSERVATION	N	%	N	%
Thymus, Discolored	0	0.00	2	0.04
Liver: additional fissure	1	0.07	0	0.00
Liver: cyst(s)	4	0.27	17	0.37
Liver: misshapen	0	0.00	2	0.04
Liver: malpositioned	0	0.00	1	0.02
Liver: abnormal lobation	3	0.21	9	0.19
Liver: lobe absent	0	0.00	1	0.02
Liver: lobe small	1	0.07	0	0.00
Liver: fused lobes	0	0.00	1	0.02
Liver: discolored lobe	3	0.21	5	0.11
Lung: multiple abnormalities	1	0.07	0	0.00
Lung: unexpanded	0	0.00	1	0.02
Lung: discolored lobe(s)	0	0.00	1	0.02
Lung: small	1	0.07	3	0.06
Lung: lobe absent	15	1.03	68	1.47
Lung: small lobe	0	0.00	11	0.24
Lung: cyst	0	0.00	2	0.04
Stomach: malpositioned	0	0.00	1	0.02
Intestine: distended	0	0.00	1	0.02
Intestine: diverticulum	1	0.07	0	0.00
Spleen: discolored	0	0.00	2	0.04
Multiple urogenital abnormalities	0	0.00	1	0.02
Kidney: absent	0	0.00	1	0.02
Kidney: multiple abnormalities	1	0.07	0	0.00
Kidney: malpositioned	1	0.07	2	0.04
Kidney: misshapen	0	0.00	1	0.02
Renal pelvis: dilated	1	0.07	7	0.15
Renal pelvis: dilated, slight	1	0.07	0	0.00
Renal pelvis: dilated, marked	1	0.07	1	0.02

Historical Control Data

Rabbit NZW KBL

FETAL EXAMINATION - FRESH VISCERAL EXAMINATION OF BODY **- page 3/3**

PERIOD	2013-2015		2016-2018	
Number of studies included	8		29	
Number of fetuses examined	1460		4635	
OBSERVATION	N	%	N	%
Ureter: retrocaval	14	0.96	88	1.90
Ureter: fused	0	0.00	1	0.02
Ureter: convoluted	1	0.07	1	0.02
Ureter: dilated	0	0.00	1	0.02
Ureter: dilated, marked	1	0.07	0	0.00
Gallbladder: absent	0	0.00	4	0.09
Gallbladder: cyst(s)	0	0.00	1	0.02
Gallbladder: misshapen	0	0.00	1	0.02
Gallbladder: small	3	0.21	19	0.41
Gallbladder: large	0	0.00	2	0.04
Gallbladder: bilobed	2	0.14	3	0.06
Gonads: epididymis, absent	1	0.07	0	0.00
Testis: malpositioned	3	0.21	0	0.00
Testis: absent	1	0.07	0	0.00
Testis: cyst(s)	1	0.07	7	0.15
Oviduct: cyst(s)	0	0.00	1	0.02
Ovary : cyst(s)	11	0.75	32	0.69

Historical Control Data

Rabbit NZW KBL

FETAL EXAMINATION - FIXED VISCERAL EXAMINATION OF HEAD **- page 1/1**

PERIOD	2013-2015		2016-2018	
Number of studies included	8		27	
Number of fetuses examined	685		2050	
OBSERVATION	N	%	N	%
Eye: retinal fold	0	0.00	1	0.05
Eye: multiple abnormalities	0	0.00	1	0.05
Brain: misshapen	0	0.00	1	0.05

Historical Control Data

Rabbit NZW KBL

FETAL EXAMINATION - SKELETAL EXAMINATION OF BODY **- page 1/4**

PERIOD	2013-2015		2016-2018	
Number of studies included	8		28	
Number of fetuses examined	1460		4561	
OBSERVATION	N	%	N	%
Generalised incomplete ossification	0	0.00	1	0.02
General: vertebral column: multiple abnormalities	1	0.07	1	0.02
Metacarpal: unossified 1st digit	50	3.42	146	3.20
Metacarpal: unossified 2nd to 5th digits	0	0.00	2	0.04
Metacarpal: incomplete ossification of 2nd to 5th digits	0	0.00	8	0.18
Forepaws: unossified phalanx, middle	42	2.88	101	2.21
Forepaws: unossified 1st or 5th phalanx	9	0.62	0	0.00
Forepaws: unossified proximal phalanx, 2nd to 5th digits	0	0.00	4	0.09
Forepaws: incomplete ossification of phalanx, proximal	1	0.07	13	0.29
Hindpaws: unossified phalanx	9	0.62	22	0.48
Hindpaws: incomplete ossification of phalanx	1	0.07	4	0.09
Tarsal bone: unossified	15	1.03	51	1.12
Paws: claw absent	0	0.00	1	0.02
Paws : phalanx, unossified, 1st digit	8	0.55	0	0.00
Scapula: incomplete ossification	0	0.00	1	0.02
Rib: absent	1	0.07	0	0.00
Rib: incomplete ossification	8	0.55	0	0.00
Rib: fused	0	0.00	2	0.04
Rib: detached	21	1.44	122	2.67
Rib: thickened	0	0.00	1	0.02
Rib: nodulated	5	0.34	8	0.18
Rib: spatulate	1	0.07	0	0.00
Rib: short	158	10.82	438	9.60

Historical Control Data

Rabbit NZW KBL

FETAL EXAMINATION - SKELETAL EXAMINATION OF BODY **- page 2/4**

PERIOD	2013-2015		2016-2018	
Number of studies included	8		28	
Number of fetuses examined	1460		4561	
OBSERVATION	N	%	N	%
Rib: interrupted	5	0.34	13	0.29
Rib: branched	1	0.07	1	0.02
Rib: misshapen	0	0.00	1	0.02
Rib: intercostal	0	0.00	1	0.02
Rib: supernumerary cervical	1	0.07	48	1.05
Rib: supernumerary lumbar	208	14.25	673	14.76
Ribs: number of full ribs = 12/12	747	51.16	2408	52.80
Ribs: number of full ribs = 12/13	203	13.90	667	14.62
Sternebrae: minor fusion	22	1.51	29	0.64
Sternebrae: fused	2	0.14	12	0.26
Sternebrae: unossified 2nd/4th	2	0.14	1	0.02
Sternebrae: unossified 5th	212	14.52	984	21.57
Sternebrae: unossified 6th	50	3.42	142	3.11
Sternebrae: incomplete ossification of 1st/3rd	7	0.48	6	0.13
Sternebrae: incomplete ossification of 2nd/4th	24	1.64	24	0.53
Sternebrae: incomplete ossification of 6th	138	9.45	404	8.86
Sternebrae: extra ossification site	3	0.21	37	0.81
Sternebrae: multiple abnormalities	0	0.00	10	0.22
Sternebrae: asymmetric	15	1.03	25	0.55
Sternebrae: bipartite ossification	8	0.55	7	0.15
Sternebrae: misshapen	1	0.07	12	0.26
Sternebrae: misaligned	1	0.07	0	0.00
Sternebrae: hemisternebrae	1	0.07	2	0.04

Historical Control Data

Rabbit NZW KBL

FETAL EXAMINATION - SKELETAL EXAMINATION OF BODY **- page 3/4**

PERIOD	2013-2015		2016-2018	
Number of studies included	8		28	
Number of fetuses examined	1460		4561	
OBSERVATION	N	%	N	%
Vertebrae, cervical: multiple abnormalities	0	0.00	1	0.02
Vertebrae, cervical: small	0	0.00	3	0.07
Vertebrae, cervical: small arch	0	0.00	1	0.02
Vertebrae, cervical: small centrum	0	0.00	1	0.02
Vertebrae, cervical: malpositioned centrum	1	0.07	0	0.00
Vertebrae, cervical: supernumerary site	3	0.21	0	0.00
Vertebrae, cervical: incomplete ossification of centrum	3	0.21	6	0.13
Vertebrae, cervical: extra ossification	3	0.21	5	0.11
Vertebrae, cervical: misshapen centrum	0	0.00	1	0.02
Vertebrae, cervical: hemicentric centrum	2	0.14	2	0.04
Vertebrae, cervical: odontoïd process unossified	0	0.00	10	0.22
Vertebrae, lumbar: multiple abnormalities	1	0.07	2	0.04
Vertebrae, lumbar: misshapen arch	1	0.07	0	0.00
Vertebrae, lumbar: bipartite ossification of centrum	1	0.07	0	0.00
Vertebrae, lumbar: number = 5	1	0.07	0	0.00
Vertebrae, lumbar: number = 6	309	21.16	1267	27.78
Vertebrae, lumbar: number = 7	2	0.14	0	0.00
Vertebrae, lumbar: number = 8	24	1.64	83	1.82
Vertebrae, lumbar: fused centrum	0	0.00	1	0.02
Vertebrae, thoracic: multiple abnormalities	2	0.14	15	0.33
Vertebrae, thoracic: incomplete ossification of 1st-9th centrum	1	0.07	9	0.20
Vertebrae, thoracic: small centrum	1	0.07	1	0.02
Vertebrae, thoracic: hemicentric centrum	1	0.07	1	0.02
Vertebrae, thoracic: misaligned centrum	0	0.00	2	0.04
Vertebrae, thoracic: number = 12	682	46.71	2322	50.91

Historical Control Data

Rabbit NZW KBL

FETAL EXAMINATION - SKELETAL EXAMINATION OF BODY **- page 4/4**

PERIOD	2013-2015		2016-2018	
Number of studies included	8		28	
Number of fetuses examined	1460		4561	
OBSERVATION	N	%	N	%
Vertebrae, sacral: misshapen centrum	1	0.07	1	0.02
Vertebrae, caudal: malpositioned	9	0.62	26	0.57
Vertebrae, caudal: bipartite ossification	1	0.07	1	0.02
Vertebrae, caudal: small	0	0.00	1	0.02
Vertebrae, caudal: number < 14	1	0.07	5	0.11
Vertebrae, caudal: absent arch	1	0.07	1	0.02
Pelvis: incomplete ossification of pubis	16	1.10	45	0.99
Pelvis: unossified pubis	6	0.41	21	0.46
Pelvis girdle: malpositioned	21	1.44	100	2.19

Historical Control Data

Rabbit NZW KBL

FETAL EXAMINATION - SKELETAL EXAMINATION OF HEAD **- page 1/1**

PERIOD	2013-2015		2016-2018	
Number of studies included	8		28	
Number of fetuses examined	775		2453	
OBSERVATION	N	%	N	%
Generalised incomplete ossification	0	0.00	3	0.12
Skull: multiple abnormalities	0	0.00	3	0.12
Cranium: sutural bone	6	0.77	27	1.10
Cranium: extra ossification site	0	0.00	1	0.04
Fontanelle: small	10	1.29	20	0.82
Fontanelle: large	0	0.00	2	0.08
Fontanelle: fontanellar bone	1	0.13	0	0.00
Nasal: unossified line	0	0.00	14	0.57
Frontals: fused	1	0.13	0	0.00
Frontals: incomplete ossification	0	0.00	1	0.04
Frontals: unossified area	0	0.00	1	0.04
Parietal: unossified area	3	0.39	3	0.12
Parietal: unossified line	3	0.39	11	0.45
Parietal: incomplete ossification	0	0.00	2	0.08
Interparietal: incomplete ossification	0	0.00	3	0.12
Interparietal: absent	0	0.00	1	0.04
Interparietal: misshapen	0	0.00	2	0.08
Interparietal: supernumerary site	0	0.00	1	0.04
Interparietal: unossified line	0	0.00	2	0.08
Supraoccipital: misshapen	0	0.00	1	0.04
Hyoid: incomplete ossification	14	1.81	32	1.30
Hyoid: misshapen	0	0.00	5	0.20
Hyoid: bent	0	0.00	2	0.08
Presphenoid: incomplete ossification	1	0.13	4	0.16
Mandible: Incomplete ossification	0	0.00	1	0.04

Historical Control Data

Rabbit NZW KBL

Maternal body weight gain (g) during lactation

Study	Year	Dams with litters	Lactation days													
			4 to 7		7 to 11		11 to 14		14 to 17		17 to 21		21 to 28		28 to 35	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
V18	2018	16	35	80	73	47	17	72	24	77	-27	74	-37	119	15	89
X18	2018	19	33	59	36	72	28	112	21	66	-40	117	-70	120	27	78
Z18	2018	20	41	52	45	56	0	77	14	73	24	90	-105	132	13	109
O17	2017	25	55	70	14	88	51	83	55	63	-53	65	-85	76		
Q17	2017	27	31	112	45	109	27	73	9	79	-45	124	-26	77	-111	154
B15	2015	21	2	61	-11	53	-2	69	15	55	-21	66	-39	119	-22	83
E15	2015	21	-17	68	53	65	-1	74	-12	69	10	65	38	86		
D14	2014	27	28	64	52	56	4	75	1	70	-6	90	34	116	1	111
B13	2013	28	28	148	21	89	-6	72	45	87	-34	60	0	78	60	75
D13	2013	26	57	109	41	93	8	70	4	79	-40	70	-74	107		
F13	2013	24	91	87	20	83	-4	80	9	92	-22	85	-41	99	90	75
Total		*254*														
Mean			*35.7*		*34.4*		*11.1*		*17.2*		*-24.2*		*-34.8*		*7.8*	
SD				*92.6*		*79.5*		*78.5*		*75.7*		*86.1*		*109.8*		*116.4*
2008-2012		*244*	*39.9*	*71.3*	*33.1*	*72.2*	*13.7*	*76.9*	*17.4*	*77.3*	*7.8*	*67.9*	*6.6*	*79.9*	*6.4*	*93.5*

Historical Control Data

Rabbit NZW KBL

Maternal food consumption (g/animal/day) during lactation

Study	Year	Dams with litters	Lactation days															
			0 to 4		4 to 7		7 to 11		11 to 14		14 to 17		17 to 21		21 to 28		28 to 35	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
V18	2018	16	220	42	281	51	309	55	320	57	334	55	347	53	514	91	722	140
X18	2018	19	217	42	290	48	311	43	325	48	327	50	336	36	527	44	784	35
Z18	2018	20	248	41	327	34	341	40	343	43	344	42	372	42	531	57	872	75
O17	2017	25	241	28	302	42	314	53	314	38	324	44	329	31	507	78		
Q17	2017	27	227	52	306	44	325	51	339	41	344	44	353	68	534	66	770	57
B15	2015	21	227	21	304	38	309	40	315	46	324	46	327	42	447	64	686	66
E15	2015	21	223	21	275	25	306	48	309	39	308	38	321	38	466	65		
D14	2014	27	236	34	307	38	330	44	349	39	341	43	354	38	492	59	686	86
B13	2013	28	213	50	294	48	320	48	311	71	329	56	336	41	431	59	649	100
D13	2013	26	218	29	320	45	335	43	333	47	332	49	326	46	430	80		
F13	2013	25	204	37	315	41	331	37	332	47	322	55	328	48	401	72	621	133
Total		*255*																
Mean			*224.7*		*302.9*		*321.8*		*326.9*		*330.3*		*338.8*		*477.5*		*718.0*	
SD				*39.0*		*43.5*		*46.3*		*48.9*		*48.0*		*46.6*		*80.4*		*117.5*
2008-2012		*247*	*225.0*	*39.0*	*290.6*	*44.1*	*319.0*	*42.0*	*324.0*	*45.9*	*333.0*	*51.4*	*341.3*	*55.3*	*466.2*	*72.4*	*672.0*	*104.7*

Historical Control Data

Rabbit NZW KBL

Post-partum litter data

Study	Year	Number of females mated	Number of females					Gestation length (days)		Number of uterine implants		Number of pups born		Pre-birth loss index %	Live birth index %	Pup viability index %
			Pregnant	With liveborn	With live pups											
					at L4	at L28	at L35	Mean	SD	Mean	SD	Mean	SD			
V18	2018	20	17	17	17	16	16	31.6	0.7	8.8	1.8	8.1	2.0	7.4	96.2	97.6
X18	2018	20	19	19	19	19	19	31.4	0.8	9.3	1.4	8.8	1.4	4.1	96.4	100
Z18	2018	21	21	20	20	20	20	31.6	0.6	10.5	1.4	9.8	1.6	6.7	98.0	97.9
O17	2017	29	28	25	25	25		31.4	0.5	8.8	2.3	8.3	2.2	5.2	97.6	100
Q17	2017	28	28	27	27	27	27	31.3	0.5	9.6	2.1	9.3	2.1	4.25	95.8	100
B15	2015	23	21	21	21	21	21	31.3	0.5	9.6	1.8	8.9	2.2	4.5	96.4	96.2
E15	2015	25	21	21	21	21		31.8	0.4	8.4	2.3	8.0	2.1	3.8	95.3	99.4
D14	2014	29	28	28	27	27	27	31.5	0.8	9.2	2.3	8.5	2.0	7.3	97.0	96.1
B13	2013	29	28	28	28	28	28	31.5	0.6	9.3	1.8	8.6	1.8		93.8	97.8
D13	2013	28	27	26	26	25		31.5	0.5	9.4	2.8	9.0	2.6	3.8	96.6	96.9
F13	2013	28	26	25	24	24	24	31.6	0.7	9.0	2.2	8.6	2		95.5	91.1
Total		*280*	*264*	*257*	*255*	*253*	*182*									
%			*94%*	*92%*												
Mean								*31.5*		*9.2*		*9.0*		*5.2*	*96.2*	*97.5*
SD									*0.6*		*2.2*		*1.5*			
2008-2012		*290*	*257*	*249*	*245*	*149*	*166*	*31.8*	*0.6*	*1.0*	*9.2*	*8.0*	*2.8*	*NA*	*96.1*	*95.9*
			89%	*86%*												

L = Lactation day

Historical Control Data

Rabbit NZW KBL

Post-partum litter data

Study	Year	Number of females mated	Pup weaning index % at L28	Pup weaning index % at L35	Pup sex ratio % males
V18	2018	20		93.4	56.8
X18	2018	20		94.4	57.2
Z18	2018	21		92.6	51.0
O17	2017	29	93.5		48.5
Q17	2017	28		91.6	52.8
B15	2015	23		91.9	47.2
E15	2015	25			51.6
D14	2014	29		88.2	
B13	2013	29		87.8	53.5
D13	2013	28	88.6		45.7
F13	2013	28		84.5	50.6
Total		*280*			
%					
Mean			*91.1*	*90.2*	*51.9*
SD					
2008-2012		*290*	*87.8*	*89.1*	*52.8*

L = Lactation day

Historical Control Data

Rabbit NZW KBL

Post-partum data - pup weights (g)

Study	Year	Litters with liveborn at L4	Postnatal days													
			4		7		11		14		21		28		35	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
V18	2018	17	95.4	16.9	131.7	21.3	178.8	31.8	218.4	40.3	308.2	57.6	520.1	99.2	838.8	140.4
X18	2018	19	88.7	10.0	121.9	14.5	165.0	16.6	198.3	21.2	272.7	32.8	481.8	59.4	768.5	83.0
Z18	2018	20	85.1	11.0	117.4	13.9	160.7	20.4	189.5	23.7	264.9	33.5	457.9	56.1	750.2	75.5
O17	2017	25	92.2	16.6	123.7	22.1	165.1	35.7	197.5	41.9	282.9	63.4	481.0	96.1		
Q17	2017	27	85.5	14.0	119.3	22.9	163.1	32.3	195.9	41.7	269.1	58.8	463.8	85.5	722.3	119.8
B15	2015	21	79.0	12.0	107.1	18.7	145.8	30.0	171.7	36.3	246.9	62.1	445.8	91.9	702.5	126.0
E15	2015	21	82.6	16.5	117.3	21.2	164.1	33.8	198.6	43.4	290.5	70.1	506.4	94.4		
D14	2014	27	88.0	20.9	120.3	30.3	162.7	35.8	198.6	49.9	283.9	72.3	505.2	109.4	790.7	143.9
B13	2013	28	83.0	20.5	111.7	30.6	155.4	44.7	185.4	55.0	265.9	74.7	461.9	104.4	752.9	130.8
D13	2013	26	83.0	23.7	112.0	33.8	153.3	49.4	183.4	55.7	253.7	85.9	442.4	97.8		
F13	2013	24	79.7	16.2	107.0	23.0	147.7	33.8	179.1	44.3	257.6	66.3	435.3	115.7	703.9	164.2
Total		*255*														
Mean			*85.4*		*116.8*		*159.6*		*191.7*		*271.3*		*471.3*		*750.6*	
SD				*17.4*		*24.9*		*35.5*		*44.2*		*65.6*		*96.5*		*131.6*
2008-2012		*245*	*86.6*	*20.4*	*116.9*	*29.1*	*161.7*	*39.5*	*194.4*	*48.7*	*285.6*	*74.5*	*498.5*	*112.1*	*784.8*	*147.6*

Historical Control Data

Rabbit NZW KBL

Pre-weaning development - % of pups positive

Study	Year	Number of litters	Incisor eruption	Eye opening									
			PND4	PND4	PND7	PND8	PND9	PND10	PND11	PND12	PND13	PND14	PND15	PND16
Z18	2018	20	100	0	0	0	6	43	85	100	100	100	100	100
O17	2017	25	100	0	1	1	12	49	86	95	99	100	100	100
Q17	2017	27	100	0	0	0	2	21	81	93	100	100	100	100
B15	2015	21	100	0	0	1	5	35	69	93	97	100	100	100
E15	2015	21	100	0	0	1	9	44	87	97	99	100	100	100
B13	2013	28	100	0	0	0	0	14	50	77	96	100	100	100
D13	2013	26	100	0	0	0	0	18	64	91	98	100	100	100
F13	2013	24	100	0	0	0	0	2	47	76	96	99	100	100
Total		*192*												
Mean %			*100*	*0.0*	*0.1*	*0.3*	*4.0*	*27.2*	*70.3*	*89.7*	*98.0*	*99.9*	*100*	*100*
2008-2012		*245*	*100*				*1.5*	*17.1*	*64.6*	*84.4*	*95.2*	*99.2*	*99.6*	*100*

PND = postnatal day

Historical Control Data

Rabbit NZW KBL

Pre-weaning development - % of pups positive

Study	Year	Number of litters	Fur growth		Surface righting reflex	Pupillary reflex - PND35	Auditory reflex - PND35
			PND4	PND7	PND11		
Z18	2018	20	100	100	100	100	100
O17	2017	25	76	100	100		
Q17	2017	27	100	100	100	100	100
B15	2015	21	100	100	100	100	100
E15	2015	21	100	100	100		
B13	2013	28	100	100		100	100
D13	2013	26	100	100	100	100	100
F13	2013	24	100	100	100	99	100
Total		*192*					
Mean %			*96.9*	*100*	*100*	*100*	*100*
2008-2012		*245*	*99*	*100*	*100*	*100*	*100*

PND = postnatal day

Historical Control Data

Rabbit NZW KBL

Fertility data

Study	Year	Number of females		Copulation index	Number of females		Fertility index
		Paired	Inseminated	%	Pregnant	With live litter	%
UV18	2018	44	39	89	33	32	85
WX18	2018	44	41	93	38	38	93
YZ18	2018	44	43	98	42	41	98
M17	2017	15	15	100	13	13	87
NO17	2017	54	54	100	50	49	93
PQ17	2017	55	52	95	51	50	98
AB15	2015	50	45	90	43	42	96
DE15	2015	54	52	96	46	44	88
CD14	2014	55	52	95	50	50	96
AB13	2013	55	53	96	51	49	96
CD13	2013	55	52	95	48	48	92
EF13	2013	55	52	95	49	49	94
G13	2013	6	6	100	6	6	100
Total		*586*	*556*	*95.1*	*520*	*511*	*93.7*
			95%		*94%*	*92%*	
Mean							
SD							

File name: I.3.3-RABBIT_KBL_fertility_2018_OK.xls

Historical Control Data

Rabbit NZW KBL

Maternal body weight gain (g) of females treated by continuous IV infusion during gestation

Study	Year	Volume infused	Dams with live	Gestation days 0 to 6		Gestation days 6 to 9		Gestation days 9 to 13		Gestation days 13 to 16		Gestation days 16 to 20		Gestation days 20 to 24		Gestation days 24 to 29	
		mL/kg/day	fetuses	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
A18	2018	9.6	20	-30	91	-8	57	58	74	51	54	13	47	132	55	169	73
B18	2018	10.0	8	-45	123	21	62	28	66	-1	60	-127	84	168	79	140	52
C18	2018	4.8	6	-111	101	7	76	73	114	-1	68	18	83	130	84	163	52
A17	2017	12	7			12	33	98	62	61	62	76	56	135	49	84	83
B17	2017	9.6	6	-62	146	7	56	92	43	58	27	12	51	129	57	134	75
A9	2009	12	6	-145	128	-20	54	28	47	8	27	-34	61	143	69	86	72
B9	2009	12	21	39	129	12	75	-27	81	14	88	-16	77	87	76	115	77
A7	2007	12	20	-122	183	26	70	18	62	53	60	15	76	110	88	133	58
B7	2007	12	5	-70	50	-63	40	60	41	50	45	-11	53	103	47	146	70
C7	2007	12	5	14	63	-40	148	35	71	31	25	25	47	110	50	125	39
D7	2007	12	4	-7	100	-78	116	44	66	29	79	-17	77	272	288	-25	315
A6	2006	12	5	-162	125	14	80	4	69	21	31	-14	41	89	35	140	68
B6	2006	12	6	-72	72	-37	34	23	57	88	64	-49	50	157	108	137	54
A2	2002	12	5	-51	89	-37	82	4	83	109	82	-53	70	114	47	138	36
B2	2002	12	19	-87	87	-29	40	-1	40	74	57	5	63	82	33	138	61
Total			*143*														
Mean				*-58*		*-7*		*28*		*46*		*-6*		*125*		*136*	
SD					*129*		*69*		*73*		*64*		*74*		*74*		*73*
Non-infusion studies 2018																	
			319	*131*	*76*	*46*	*52*	*99*	*57*	*69*	*64*	*0*	*75*	*50*	*70*	*104*	*86*

Studies C7 and D7 were recorded on gestation day 10.

Historical Control Data

Rabbit NZW KBL

Maternal food consumption (g/day) of females treated by continuous IV infusion during gestation

Study	Year	Volume infused	Dams with live	Gestation days 0 to 6		Gestation days 6 to 9		Gestation days 9 to 13		Gestation days 13 to 16		Gestation days 16 to 20		Gestation days 20 to 24		Gestation days 24 to 29	
		mL/kg/day	fetuses	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
A18	2018	9.6	20	114	26	119	35	124	41	111	46	143	30	149	31	145	25
B18	2018	10.0	8	94	30	114	23	98	26	36	34	43	36	132	25	146	21
C18	2018	4.8	6			132	24	119	42	103	48	128	42	138	26	142	15
A17	2017	12	7			152	22	146	28	134	43	162	28	177	21	147	30
B17	2017	9.6	6	125	24	152	36	137	29	143	13	153	23	148	26	137	25
A9	2009	12	6	93	45	123	40	100	34	89	48	102	31	137	34	143	45
B9	2009	12	21	134	23	130	43	117	43	95	38	124	35	134	32	129	33
A7	2007	12	20	96	38	129	27	121	25	111	34	129	23	140	19	146	18
B7	2007	12	5	94	28	121	15	116	6	109	16	120	19	136	22	137	17
C7	2007	12	5	118	22	112	38	114	32	116	18	131	6	135	10	131	10
D7	2007	12	4	112	25	115	19	99	10	77	21	113	20	129	20	126	11
A6	2006	12	5	90	23	135	14	113	40	103	34	106	18	129	19	137	19
B6	2006	12	6	115	10	124	26	124	39	115	37	132	26	148	20	149	20
A2	2002	12	5	85	23	97	36	98	25	105	25	131	15	136	21	149	22
B2	2002	12	19	109	26	125	22	117	23	110	28	124	26	137	29	137	23
Total			*143*														
Mean				*99*		*126*		*118*		*104*		*125*		*141*		*140*	
SD					*43*		*32*		*33*		*40*		*36*		*27*		*25*
Non-infusion studies 2018																	
			319	*153*	29	*165*	31	*157*	31	*125*	41	*141*	43	*125*	37	*116*	*29*

Studies C7 and D7 were recorded on gestation day 10.

Historical Control Data

Rabbit NZW KBL

Caesarean data collected on day 29 of gestation: females treated by continuous IV infusion during gestation

Stud	Year	Volume infused mL/kg/day	Number of females				Number of corpora lutea		Number of uterine implants		Pre-implantation loss %		Early resorptions per dam		Late resorptions per dam		Post-implantation loss %	
			Mated	Pregnant	Aborted	With live fetuses	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
A18	2018	9.6	22	21	0	20	10.4	1.6	9.6	2.1	7.7	12.6	0.9	1.7	0.3	0.9	13.6	24.2
B18	2018	10.0	9	9	1	8	11.0	2.0	8.9	1.1	18.0	11.6	0.3	0.5	1.1	1.7	15.9	17.9
C18	2018	4.8	6	6	0	6	9.5	1.9	8.8	1.7	6.6	7.7	0.5	0.8	0.2	0.4	7.7	8.7
A17	2017	12	8	7	0	7	9.0	1.8	7.9	2.8	15.3	16.5	0.4	0.5	0.0	0.0	6.3	9.4
B17	2017	9.6	6	6	0	6	11.2	3.7	9.8	3.9	13.1	9.8	1.3	2.3	0.0	0.0	9.2	13.7
A9	2009	12	6	6	0	6	9.8	1.9	8.3	2.9	17.4	20.2	0.7	0.8	0.3	0.5	10.1	12.4
B9	2009	12	22	22	1	21	11.6	2.2	10.1	2.4	12.6	12.6	0.5	2.2	0.5	0.7	8.0	17.3
A7	2007	12	22	20	0	20	12.1	2.3	10.1	2.4	15.8	16.1	0.6	1.0	0.2	0.5	8.8	12.7
C7	2007	12	6	5	0	5	10.8	0.5	9.5	1.7	11.8	13.9					16.3	12.5
D7	2007	12	6	5	0	4	12.0	2.6	10.7	3.1	11.3	14.0					7.7	6.8
A6	2006	12	6	6	0	5	11.3	3.7	9.5	3.4	17.7	15.1	0.5	1.2	0.2	0.4	17.9	40.3
B6	2006	12	6	6	0	6	12.2	4.0	10.8	2.8	9.9	13.1	0.8	1.6	0.7	1.2	12.3	17.0
A2	2002	12	6	5	0	5	11.0	3.1	10.2	3.3	7.3	11.9	0.2	0.4	0.6	0.9	6.9	6.7
B2	2002	12	22	19	0	19	11.1	2.1	10.1	2.4	9.7	12.7	1.1	1.7	0.2	0.4	12.0	14.3
Total			*153*	*143*	*2*	*138*												
				93%	*1%*	*90%*												
Mean							*11.1*		*9.7*		*12.2*		*0.7*		*0.3*		*10.8*	
SD								*2.4*		*2.5*		*13.5*		*1.5*		*0.8*		*16.9*
Non-infusion studies 2018																		
			319	*284*	*5*	*282*	*10.7*	*2.3*	*9.8*	*0.8*	*8.7*	*11.7*	*0.3*	*0.9*	*0.3*	*0.6*	*5.6*	*11.0*
				89%	*2%*	*88%*												

Historical Control Data

Rabbit NZW KBL

Caesarean data collected on day 29 of gestation: females treated by continuous IV infusion during gestation

Stud	Year	Volume infused mL/kg/day	Number of females				Dead fetuses	Live litter size		Fetal weight (g)		Uterus weight (g)		Placental weight (g)		Sex ratio %
			Mated	Pregnant	Aborted	With live fetuses	Total	Mean	SD	Mean	SD	Mean	SD	Mean	SD	males
A18	2018	9.6	22	21	0	20	0	8.4	2.9	41.3	4.1	532	101			44.7
B18	2018	10.0	9	9	1	8	0	7.5	2.1	38.4	5.8	450	54			55.4
C18	2018	4.8	6	6	0	6	0	8.2	1.7	42.2	4.7	487	110			
A17	2017	12	8	7	0	7	0	7.4	2.8	43.3	3.5	473	163			48.3
B17	2017	9.6	6	6	0	6	0	8.5	1.8	42.5	2.8	515	109			
A9	2009	12	6	6	0	6	0	7.3	2.4	34.9	5.1			5.1	1.1	
B9	2009	12	22	22	1	21	0	9.1	2.5	36.3	4.5			5.9	1.1	40.1
A7	2007	12	22	20	0	20	0	9.3	2.5	36.1	4.4			5.4	0.7	46.1
C7	2007	12	6	5	0	5	1	8.0	2.2	38.7	4.0					
D7	2007	12	6	5	0	4	1	10.0	3.6	37.1	1.0					
A6	2006	12	6	6	0	5	0	8.8	4.4	34.4	5.9					
B6	2006	12	6	6	0	6	0	9.3	2.7	36.9	4.3					
A2	2002	12	6	5	0	5	0	9.4	2.8	34.0	4.2					37.9
B2	2002	12	22	19	0	19	0	8.8	2.5	36.0	5.8					52.4
Total			*153*	*143*	*2*	*138*	*2*									
				93%	*1%*	*90%*										
Mean								*8.7*		*37.9*		*501*		*5.6*		*46.2*
SD									*2.6*		*5.2*		*109*		*1.0*	
Non-infusion studies 2018																
			319	*284*	*5*	*282*	*1*	*9.3*	*2.4*	*40.9*	*5.1*	*552*	*121*	*NA*	*NA*	*51.1*
				89%	*2%*	*88%*										

Historical Control Data

Rabbit NZW KBL

Malformations (external, internal and skeletal): females treated by continuous IV infusion during gestation

Study	Number of litters examined	Number of fetuses examined	Number of litters with malformed fetuses	Litter incidence %	Number of malformed fetuses	Fetal incidence %	Type of malformation by fetus
A18	20	177	0	-	0	-	
B18	8	60	1	12.5	1	1.7	1st: Malformed heart (ventricular septum defect with dilated left ventricle), Aortic arch dilated
C18	6	49	0	-	0	-	
A17	7	52	1	14.3	1	1.9	1st: Dilated aortic arch, atretic pulmonary trunk
B17	6	51	0	-	0	-	
A9	6	44	0	-	0	-	
B9	21	192	0	-	0	-	
A7	20	185	0	-	0	-	
D7	3	30	0	-	0	-	
A6	5	52	0	-	0	-	
B6	6	56	0	-	0	-	
A2	5	47	0	-	0	-	
B2	19	167	3	15.8	3	1.8	1st: Eye absent bulge 2nd: Single naris 3rd: Omphalocele
2002-2017	*132*	*1162*	*5*	**3.8%**	*5*	**0.4%**	
Non-infusion studies 2018							
	273	*2529*	*20*	*7.3%*	*24*	*0.9%*	

Study nos. A2, A6, B6, D7, A9 and B17: Dose Range Finding studies with external examination only.

Study no. B18: Dose Range Finding studies with external and visceral examinations only.

File name: II.3.1-RABBIT_KBL_PERFUSION_2018_OK.xls

Historical Control Data

Rabbit NZW KBL **page 1/1**

FETAL EXAMINATION - EXTERNAL - Females treated by continuous IV infusion during gestation

	Continous IV infusion 2002 to 2018		**Non-infusion 2016-2018**	
Number of studies included	13		46	
Number of fetuses examined	1163		5480	
OBSERVATION	N	%	N	%
General : local oedema	0	0.00	3	0.05
Meningoencephalocele	0	0.00	1	0.02
Craniorachischisis	0	0.00	1	0.02
Eye: absent bulge	1	0.09	0	0.00
Microphthalmia	0	0.00	1	0.02
Eye: open	0	0.00	3	0.05
Microtia	0	0.00	1	0.02
Face: malformed	0	0.00	1	0.02
Nose: small	0	0.00	1	0.02
Protruding tongue	0	0.00	1	0.02
Single naris	1	0.09	0	0.00
Jaw: short	1	0.09	0	0.00
Limbs: hyperflexion	1	0.09	0	0.00
Limbs: malrotated	2	0.17	2	0.04
Paw: hyperflexion	2	0.17	7	0.13
Paw: malrotated	0	0.00	1	0.02
Brachydactyly	0	0.00	1	0.02
Claw: absent	0	0.00	2	0.04
Umbilical hernia	1	0.09	0	0.00
Gastroschisis	0	0.00	1	0.02
Omphalocele	0	0.00	7	0.13
Tail: short	1	0.09	0	0.00
Tail: bent	3	0.26	0	0.00

Historical Control Data

Rabbit NZW KBL **page 1/3**

FETAL EXAMINATION - FRESH VISCERAL EXAMINATION OF BODY - Females treated by continuous IV infusion during gestation

	Continous IV infusion 2002 to 2018		**Non-infusion 2016-2018**	
Number of studies included	6		29	
Number of fetuses examined	833		4635	
OBSERVATION	N	%	N	%
General: material	0	0.00	1	0.02
Heart: multiple abnormalities	1	0.12	1	0.02
Heart: ventricular septum defect	0	0.00	2	0.04
Heart: ventricular wall thick	0	0.00	1	0.02
Heart: three-chambered	0	0.00	2	0.04
Heart: small ventricle	0	0.00	2	0.04
Carotid artery: absent common carotid trunk	124	14.89	1759	37.95
Great blood vessels: multiple abnormalities	0	0.00	5	0.11
Innominate artery: absent	0	0.00	16	0.35
Pulmonary trunk: atresia	1	0.12	0	0.00
Aortic arch: dilated	2	0.24	0	0.00
Aortic arch: narrowed	0	0.00	1	0.02
Aortic arch: retroesophageal	0	0.00	1	0.02
Subclavian artery: malpositioned	0	0.00	1	0.02
Subclavian artery: retroesophageal	0	0.00	7	0.15
Azygos vein: absent	0	0.00	1	0.02
Azygos vein: transposed	0	0.00	17	0.37
Diaphragm: absent	0	0.00	1	0.02
Diaphragmatic hernia	0	0.00	1	0.02
Abdomen: fluid-filled	0	0.00	1	0.02
Thorax: cyst(s)	0	0.00	1	0.02
Thorax: fluid-filled	0	0.00	1	0.02
Thymus: discolored	0	0.00	2	0.04

Historical Control Data

Rabbit NZW KBL

FETAL EXAMINATION - FRESH VISCERAL EXAMINATION OF BODY - Females treated by continuous IV infusion during gestation

	Continous IV infusion 2002 to 2018		**Non-infusion 2016-2018**	
Number of studies included	6		29	
Number of fetuses examined	833		4635	
OBSERVATION	N	%	N	%
Liver: cyst(s)	0	0.00	17	0.37
Liver: misshapen	0	0.00	2	0.04
Liver: malpositioned	0	0.00	1	0.02
Liver: abnormal lobation	0	0.00	9	0.19
Liver: fused lobes	0	0.00	1	0.02
Liver: lobe absent	0	0.00	1	0.02
Liver: discolored lobe	0	0.00	5	0.11
Lung: multiple abnormalities	0	0.00	0	0.00
Lung: unexpanded	0	0.00	1	0.02
Lung: discolored lobe(s)	0	0.00	1	0.02
Lung: small	0	0.00	3	0.06
Lung: lobe absent	11	1.32	68	1.47
Lung: small lobe	1	0.12	11	0.24
Lung: cyst	0	0.00	2	0.04
Intestine: distended	0	0.00	1	0.02
Spleen: discolored	0	0.00	2	0.04
Stomach: malpositioned	0	0.00	1	0.02

Historical Control Data

Rabbit NZW KBL **page 3/3**

FETAL EXAMINATION - FRESH VISCERAL EXAMINATION OF BODY - Females treated by continuous IV infusion during gestation

	0 **0**		**0** **0**	
Number of studies included	2002 to 2018		2016-2018	
Number of fetuses examined	6		29	
OBSERVATION	N	%	N	%
Multiple urogenital abnormalities	0	0.00	1	0.02
Kidney: absent	0	0.00	1	0.02
Kidney: malpositionned	0	0.00	2	0.04
Kidney: misshapen	0	0.00	1	0.02
Renal pelvis: dilated	1	0.12	7	0.15
Renal pelvis: dilated, marked	0	0.00	1	0.02
Ureter: retrocaval	7	0.84	88	1.90
Ureter: fused	0	0.00	1	0.02
Ureter: convoluted	0	0.00	1	0.02
Ureter: dilated	0	0.00	1	0.02
Gallbladder: absent	0	0.00	4	0.09
Gallbladder: cyst(s)	0	0.00	1	0.02
Gallbladder: misshapen	0	0.00	1	0.02
Gallbladder: small	0	0.00	19	0.41
Gallbladder: large	0	0.00	2	0.04
Gallbladder: bilobed	1	0.12	3	0.06
Testis: cyst(s)	0	0.00	7	0.15
Oviducts : cyst(s)	0	0.00	1	0.02
Ovary : cyst(s)	1	0.12	32	0.69

Historical Control Data

Rabbit NZW KBL **page 1/1**

FETAL EXAMINATION - FIXED VISCERAL EXAMINATION OF HEAD - Females treated by continuous IV infusion during gestation

	Continous IV infusion 2002 to 2018		**Non-infusion 2016-2018**	
Number of studies included	4		27	
Number of fetuses examined	339		2050	
OBSERVATION	N	%	N	%
Microphthalmia	1	0.29	0	0.00
Aphakia	1	0.29	0	0.00
Eye: multiple abnormalities	0	0.00	1	0.05
Eye: retinal fold	0	0.00	1	0.05
Brain: hydrocephaly	1	0.29	0	0.00
Brain: misshapen	0	0.00	1	0.05
Brain: porencephalic cyst(s)	3	0.88	0	0.00
Brain: dilated cerebral ventricles	1	0.29	0	0.00
Brain: vacuole	1	0.29	0	0.00
Single nasal tract	1	0.29	0	0.00

Historical Control Data

Rabbit NZW KBL

FETAL EXAMINATION - SKELETAL EXAMINATION OF BODY - Females treated by continuous IV infusion during gestation

	Continous IV infusion 2002 to 2018		Non-infusion 2016-2018	
Number of studies included	5		28	
Number of fetuses examined	773		4561	
OBSERVATION	N	%	N	%
Generalised incomplete ossification	0	0.00	1	0.02
Vertebral column: multiple abnormalities	0	0.00	1	0.02
Metacarpals: unossified 1st digit	48	6.21	146	3.20
Metacarpals: unossified 2nd to 5th digit	0	0.00	2	0.04
Metacarpals: incomplete ossification 2nd to 5th digit	6	0.78	8	0.18
Forepaws: unossified phalanx	7	0.91	0	0.00
Forepaws: unossified phalanx, middle	0	0.00	101	2.21
Forepaws: unossified 1st or 5th phalanx	87	11.25	0	0.00
Forepaws: unossified proximal phalanx, 2nd to 5th digits	0	0.00	4	0.09
Forepaws: incomplete ossification of phalanx	12	1.55	0	0.00
Forepaws: incomplete ossification of phalanx, proximal	0	0.00	13	0.29
Hindpaws: unossified phalanx	10	1.29	22	0.48
Hindpaws: incomplete ossification of phalanx	14	1.81	4	0.09
Hindpaws: misshapen	1	0.13	0	0.00
Tarsal bone: incomplete ossification	8	1.03	0	0.00
Tarsal bone: unossified	3	0.39	51	1.12
Paws: claw absent	0	0.00	1	0.02
Scapula: misshapen	5	0.65	0	0.00
Scapula: incomplete ossification	0	0.00	1	0.02

Change of method of examination in 2013

Historical Control Data

Rabbit NZW KBL

FETAL EXAMINATION - SKELETAL EXAMINATION OF BODY - Females treated by continuous IV infusion during gestation

	Continous IV infusion		**Non-infusion**	
	2002 to 2018		**2016-2018**	
Number of studies included	5		28	
Number of fetuses examined	773		4561	
OBSERVATION	N	%	N	%
Rib: fused	0	0.00	2	0.04
Rib: detached	49	6.34	122	2.67
Rib: nodulated	2	0.26	8	0.18
Rib: short	143	18.50	438	9.60
Rib: interrupted	0	0.00	13	0.29
Rib: branched	0	0.00	1	0.02
Rib: misshapen	0	0.00	1	0.02
Rib: intercostal	0	0.00	1	0.02
Rib: bifid	1	0.13	0	0.00
Rib: thickened	0	0.00	1	0.02
Rib: unossified area	2	0.26	0	0.00
Rib: cervical	1	0.13	0	0.00
Rib: supernumerary cervical	3	0.39	48	1.05
Rib: supernumerary lumbar	48	6.21	673	14.76
Ribs: number of full ribs = 11/12	0	0.00	0	0.00
Ribs: number of full ribs = 12/12	270	34.93	2408	52.80
Ribs: number of full ribs = 12/13	117	15.14	667	14.62

Change of method of examination in 2013

Historical Control Data

Rabbit NZW KBL

FETAL EXAMINATION - SKELETAL EXAMINATION OF BODY - Females treated by continuous IV infusion during gestation

	Continous IV infusion 2002 to 2018		Non-infusion 2016-2018	
Number of studies included	5		28	
Number of fetuses examined	773		4561	
OBSERVATION	N	%	N	%
Sternebrae: multiple abnormalities	0	0.00	10	0.22
Sternebrae: major fusion	1	0.13	0	0.00
Sternebrae: minor fusion	11	1.42	29	0.64
Sternebrae: fused	0	0.00	12	0.26
Sternebrae: unossified 2nd/4th	0	0.00	1	0.02
Sternebrae: unossified 5th	134	17.34	984	21.57
Sternebrae: unossified 6th	33	4.27	142	3.11
Sternebrae: incomplete ossification of 1st/3rd	6	0.78	6	0.13
Sternebrae: incomplete ossification of 2nd/4th	50	6.47	24	0.53
Sternebrae: incomplete ossification of 6th	133	17.21	404	8.86
Sternebrae: extra ossification site	0	0.00	37	0.81
Sternebrae: asymmetric	10	1.29	25	0.55
Sternebrae: bipartite	6	0.78	7	0.15
Sternebrae: misshapen	1	0.13	12	0.26
Sternebra: hemisternebra	0	0.00	2	0.04
Vertebrae, cervical: multiple abnormalities	0	0.00	1	0.02
Vertebrae, cervical: small	0	0.00	3	0.07
Vertebrae, cervical: small arch	0	0.00	1	0.02
Vertebrae, cervical: small centrum	0	0.00	1	0.02
Vertebrae, cervical: incomplete ossification of centrum	11	1.42	6	0.13
Vertebrae, cervical: extra ossification	0	0.00	5	0.11
Vertebrae, cervical: hemicentric centrum	0	0.00	2	0.04

Change of method of examination in 2013

Historical Control Data

Rabbit NZW KBL

FETAL EXAMINATION - SKELETAL EXAMINATION OF BODY - Females treated by continuous IV infusion during gestation

	Continous IV infusion		**Non-infusion**	
	2002 to 2018		**2016-2018**	
Number of studies included	5		28	
Number of fetuses examined	773		4561	
OBSERVATION	N	%	N	%
Vertebrae, cervical: misshapen centrum	0	0.00	1	0.02
Vertebrae, cervical: fused centrum	1	0.13	0	0.00
Vertebrae, cervical: odontoïd process unossified	1	0.13	10	0.22
Vertebrae, lumbar: multiple abnormalities	0	0.00	2	0.04
Vertebrae, lumbar: fused centrum	0	0.00	1	0.02
Vertebrae, lumbar: number=5	2	0.26	0	0.00
Vertebrae, lumbar: number=6	56	7.24	1267	27.78
Vertebrae, lumbar: number=8	6	0.78	83	1.82
Vertebrae, thoracic: multiple abnormalities	0	0.00	15	0.33
Vertebrae, thoracic: incomplete ossification of 1-4th centrum	5	0.65	0	0.00
Vertebrae, thoracic: incomplete ossification of 1st-9th centrum	0	0.00	9	0.20
Vertebrae, thoracic: incomplete ossification of 5-8th centrum	47	6.08	0	0.00
Vertebrae, thoracic: incomplete ossification of 9-13th centrum	4	0.52	0	0.00
Vertebrae, thoracic: small centrum	0	0.00	1	0.02
Vertebrae, thoracic: hemicentric centrum	0	0.00	1	0.02
Vertebrae, thoracic: misaligned centrum	0	0.00	2	0.04
Vertebrae, thoracic: number=12	126	16.30	2322	50.91
Vertebrae, sacral: misshapen arch	1	0.13	0	0.00
Vertebrae, sacral: misshapen centrum	0	0.00	1	0.02

Change of method of examination in 2013

Historical Control Data

Rabbit NZW KBL

FETAL EXAMINATION - SKELETAL EXAMINATION OF BODY - Females treated by continuous IV infusion during gestation

	Continous IV infusion		**Non-infusion**	
	2002 to 2018		**0**	
Number of studies included	5		Non-infusion	
Number of fetuses examined	773		0	
OBSERVATION	N	%	N	%
Vertebrae, caudal: malpositionned	6	0.78	26	0.57
Vertebrae, caudal: bipartite ossification	1	0.13	1	0.02
Vertebrae, caudal: small	0	0.00	1	0.02
Vertebrae, caudal: misshapen	1	0.13	0	0.00
Vertebrae, caudal: number < 14	0	0.00	5	0.11
Vertebrae, caudal: absent arch	0	0.00	1	0.02
Vertebrae, caudal: fused	1	0.13	0	0.00
Pelvis: incomplete ossification of pubis	36	4.66	45	0.99
Pelvis: unossified pubis	4	0.52	21	0.46
Pelvic girdle: malpositioned	6	0.78	100	2.19

Change of method of examination in 2013

Historical Control Data

Rabbit NZW KBL

FETAL EXAMINATION - SKELETAL EXAMINATION OF HEAD - Females treated by continuous IV infusion during gestation

	Continous IV infusion 2002 to 2018		**Non-infusion 2016-2018**	
Number of studies included	5		28	
Number of fetuses examined	434		2453	
OBSERVATION	N	%	N	%
Generalised incomplete ossification	0	0.00	3	0.12
Skull: multiple abnormalities	0	0.00	3	0.12
Cranium: sutural bone	3	0.69	27	1.10
Cranium: extra ossification site	0	0.00	1	0.04
Fontanelle: small	23	5.30	20	0.82
Fontanelle: large	2	0.46	2	0.08
Nasal: sutural bone	2	0.46	0	0.00
Nasal: unossified bone	0	0.00	14	0.57
Frontals: fused	1	0.23	0	0.00
Frontals: incomplete ossification	0	0.00	1	0.04
Frontals: unossified area	0	0.00	1	0.04
Parietal: unossified area	2	0.46	3	0.12
Parietal: unossified line	3	0.69	11	0.45
Parietal: incomplete ossification	0	0.00	2	0.08
Parietal: sutural bone	3	0.69	0	0.00
Interparietal: incomplete ossification	6	1.38	3	0.12
Interparietal: absent	0	0.00	1	0.04
Interparietal: misshapen	0	0.00	2	0.08
Interparietal: supernumerary site	0	0.00	1	0.04
Interparietal: unossified line	0	0.00	2	0.08
Interparietal: fused	1	0.23	0	0.00
Supraoccipital: misshapen	0	0.00	1	0.04
Mandible: incomplete ossification	0	0.00	1	0.04

Historical Control Data

Rabbit NZW KBL

FETAL EXAMINATION - SKELETAL EXAMINATION OF HEAD - Females treated by continuous IV infusion during gestation

	Continous IV infusion 2002 to 2018		**Non-infusion 2016-2018**	
Number of studies included	5		28	
Number of fetuses examined	434		2453	
OBSERVATION	N	%	N	%
Palate: incomplete ossification	1	0.23	0	0.00
Hyoid: incomplete ossification	64	14.75	32	1.30
Hyoid: misshapen	0	0.00	5	0.20
Hyoid: bent	0	0.00	2	0.08
Presphenoid: incomplete ossification	3	0.69	4	0.16