

# **Reproductive Toxicology**

## **Historical Control Data in Rabbits**



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<sup>1</sup> Date range from 2016 to 2020. Additional HCD endpoints and years are available upon request.

<sup>2</sup> Date range from 2016 to 2020, with the exception of Female Mating and Fertility (2011-2020) and Natural Delivery and Litter Parameters (2012-2020). Additional HCD endpoints and years are available upon request.

REPRODUCTIVE INDICES  
NEW ZEALAND WHITE [CrI:KBL(NZW)BR] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION

PERIOD: 2016 THROUGH 2020

|                                  | FULL STUDIES     |            |            | DOSE RANGE STUDIES |            |            |
|----------------------------------|------------------|------------|------------|--------------------|------------|------------|
| NO. OF STUDIES INCLUDED          | 44               |            |            | 54                 |            |            |
| NO. OF RABBITS TESTED            | 910              |            |            | 311                |            |            |
| NO. OF RABBITS PREGNANT          | 853              |            |            | 296                |            |            |
| NO. FOUND DEAD                   | 4                |            |            | 3                  |            |            |
| NO. ABORTED                      | 23               |            |            | 10                 |            |            |
| NO. UNSCHEDULED EUTHANASIA       | 18               |            |            | 6                  |            |            |
| NO. DELIVERED PREMATURELY        | 3                |            |            | 2                  |            |            |
| NO. CAESAREAN-SECTIONED ON GD 29 | 828              |            |            | 282                |            |            |
|                                  | <u>MEAN or %</u> | <u>MIN</u> | <u>MAX</u> | <u>MEAN or %</u>   | <u>MIN</u> | <u>MAX</u> |
| % PREGNANT                       | 93.9             | 78.6       | 100.0      | 95.2               | 66.7       | 100.0      |
| CORPORA LUTEA                    | 11.6             | 9.2        | 13.4       | 11.2               | 8.3        | 13.6       |
| IMPLANTATIONS                    | 10.7             | 7.8        | 12.1       | 10.5               | 8.3        | 13.0       |
| PREIMPLANTATION LOSS (%)         | 7.8              | 0.0        | 24.2       | 6.1                | 0.0        | 20.7       |
| LITTER SIZES                     |                  |            |            |                    |            |            |
| LIVE FETUSES                     | 10.0             | 4.3        | 11.4       | 9.8                | 7.3        | 11.8       |
| DEAD FETUSES                     | 0.0              | 0.0        | 0.1        | 0.0                | 0.0        | 0.2        |
| TOTAL RESORPTIONS                | 0.6              | 0.2        | 1.7        | 0.7                | 0.0        | 3.8        |
| EARLY RESORPTIONS                | 0.4              | 0.0        | 1.3        | 0.3                | 0.0        | 1.5        |
| LATE RESORPTIONS                 | 0.3              | 0.1        | 0.9        | 0.5                | 0.0        | 3.5        |
| POSTIMPLANTATION LOSS (%)        | 5.8              | 1.6        | 13.0       | 6.4                | 0.0        | 30.0       |
| DOES WITH ANY RESORPTIONS (%)    | 37.1             | 15.0       | 83.3       | 40.6               | 0.0        | 100.0      |

REPRODUCTIVE INDICES  
NEW ZEALAND WHITE [CrI:KBL(NZW)BR] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION

PERIOD: 2016 THROUGH 2020

| NO. OF STUDIES INCLUDED                     | FULL<br>STUDIES<br>44 |            |            | DOSE RANGE<br>STUDIES<br>54 |            |            |
|---------------------------------------------|-----------------------|------------|------------|-----------------------------|------------|------------|
|                                             | <u>MEAN or %</u>      | <u>MIN</u> | <u>MAX</u> | <u>MEAN or %</u>            | <u>MIN</u> | <u>MAX</u> |
| DOES WITH ALL CONCEPTUSES<br>RESORBED (%)   | 0.98                  | 0.0        | 10.0       | 2.2                         | 0.0        | 33.0       |
| DOES WITH ONE OR MORE<br>VIABLE FETUSES (%) | 96.0                  | 70.0       | 100.0      | 98.2                        | 60.0       | 100.0      |
| SEX RATIO (% MALES/LITTER)                  | 49.3                  | 40.5       | 64.5       | 47.8                        | 26.3       | 68.9       |
| LIVE FETAL BODY WEIGHTS<br>GRAMS/LITTER     | 39.8                  | 36.7       | 44.1       | 39.8                        | 31.2       | 45.2       |
| MALE FETUSES                                | 40.3                  | 36.6       | 43.4       | 40.2                        | 24.6       | 45.7       |
| FEMALE FETUSES                              | 39.3                  | 36.1       | 44.1       | 39.0                        | 31.8       | 44.1       |

FETAL EXTERNAL ABNORMALITIES  
NEW ZEALAND WHITE [CrI:KBL(NZW)BR] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
DOSE RANGE FINDING STUDIES

PERIOD: 2016 THROUGH 2020

NO. OF STUDIES INCLUDED 11

NO. LITTERS EXAMINED 57

NO. LIVE FETUSES EXAMINED 565

|                                |                                       | ABNORMALITIES |   | RANGE/STUDY |          |  |
|--------------------------------|---------------------------------------|---------------|---|-------------|----------|--|
|                                |                                       |               | N | N           | %        |  |
| FACE                           |                                       |               |   |             |          |  |
|                                | : Snout, short                        | L             | 2 | 0-1         | (0-20.0) |  |
| GENERAL                        |                                       | F             | 2 | 0-1         | (0-1.8)  |  |
|                                |                                       |               |   |             |          |  |
|                                | : Skin, discolored                    | L             | 1 | 0-1         | (0-16.7) |  |
|                                |                                       | F             | 1 | 0-1         | (0-1.4)  |  |
|                                | : Skin, thin                          | L             | 1 | 0-1         | (0-16.7) |  |
|                                |                                       | F             | 1 | 0-1         | (0-1.4)  |  |
|                                | : Entire body, multiple malformations | L             | 1 | 0-1         | (0-25.0) |  |
|                                |                                       | F             | 1 | 0-1         | (0-2.1)  |  |
|                                |                                       |               |   |             |          |  |
|                                |                                       |               |   |             |          |  |
|                                |                                       |               |   |             |          |  |
|                                |                                       |               |   |             |          |  |
| MOUTH                          |                                       |               |   |             |          |  |
|                                | : Palate, cleft palate                | L             | 1 | 0-1         | (0-20.0) |  |
|                                |                                       | F             | 1 | 0-1         | (0-1.5)  |  |
|                                | : Tongue, protruding                  | L             | 1 | 0-1         | (0-20.0) |  |
| TRUNK                          |                                       | F             | 1 | 0-1         | (0-1.8)  |  |
|                                |                                       |               |   |             |          |  |
|                                | : Abdomen, distended                  | L             | 2 | 0-1         | (0-20.0) |  |
|                                |                                       | F             | 2 | 0-1         | (0-1.9)  |  |
|                                | : Umbilicus, herniated                | L             | 1 | 0-1         | (0-20.0) |  |
|                                |                                       | F             | 1 | 0-1         | (0-2.2)  |  |
| FORELIMB(S) AND/OR HINDLIMB(S) |                                       |               |   |             |          |  |
|                                |                                       |               |   |             |          |  |
|                                | : Forelimb, hyperextension            | L             | 1 | 0-1         | (0-16.7) |  |
|                                |                                       | F             | 2 | 0-2         | (0-3.3)  |  |
|                                | : Forelimb, malrotated                | L             | 1 | 0-1         | (0-20.0) |  |
|                                |                                       | F             | 1 | 0-1         | (0-1.8)  |  |
|                                |                                       |               |   |             |          |  |
| PAW/DIGIT(S)                   |                                       |               |   |             |          |  |
|                                | : Forepaw, brachydactyly              | L             | 1 | 0-1         | (0-20.0) |  |
|                                | (previously Forepaw, short)           | F             | 1 | 0-1         | (0-2.0)  |  |
|                                | : Hindpaw, brachydactyly              | L             | 1 | 0-1         | (0-20.0) |  |
|                                | (previously Hindpaw, short)           | F             | 1 | 0-1         | (0-2.0)  |  |
|                                | : Forepaw, hyperextension             | L             | 2 | 0-1         | (0-25.0) |  |
|                                |                                       | F             | 2 | 0-1         | (0-2.5)  |  |
|                                | : Forepaw, hyperflexion               | L             | 3 | 0-1         | (0-20.0) |  |
|                                |                                       | F             | 3 | 0-1         | (0-2.1)  |  |
|                                | : Hindpaw, malrotated                 | L             | 1 | 0-1         | (0-20.0) |  |
|                                |                                       | F             | 1 | 0-1         | (0-1.8)  |  |
|                                | : Forepaw, polydactyly                | L             | 1 | 0-1         | (0-20.0) |  |
|                                | (previously Forepaw, supernumerary)   | F             | 1 | 0-1         | (0-1.8)  |  |
|                                | TAIL                                  |               |   |             |          |  |
| : Tail, kinked                 |                                       | L             | 1 | 0-1         | (0-20.0) |  |
|                                |                                       | F             | 1 | 0-1         | (0-1.8)  |  |
|                                |                                       |               |   |             |          |  |

L: LITTER INCIDENCE

F: FETAL INCIDENCE

Note: All summary values are based on studies with fetal findings.

FETAL EXTERNAL ABNORMALITIES  
NEW ZEALAND WHITE [CrI:KBL(NZW)BR] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

PERIOD: 2016 THROUGH 2020

NO. STUDIES INCLUDED 26

NO. LITTERS EXAMINED 495

NO. LIVE FETUSES EXAMINED 5017

|           | ABNORMALITIES                  | RANGE/STUDY |     |         |
|-----------|--------------------------------|-------------|-----|---------|
|           |                                | N           | N   | %       |
| HEAD/NECK | : Head, absent                 | L 1         | 0-1 | (0-6.7) |
|           |                                | F 1         | 0-1 | (0-0.4) |
|           | : Head, domed                  | L 8         | 0-1 | (0-6.7) |
|           |                                | F 10        | 0-2 | (0-1.4) |
|           | : Head/Neck, exencephaly       | L 1         | 0-1 | (0-5.3) |
|           |                                | F 1         | 0-1 | (0-0.5) |
| FACE      | : Eye, open eye                | L 2         | 0-1 | (0-5.3) |
|           | (previously Eye, lids open)    | F 2         | 0-1 | (0-0.5) |
|           | : Eye bulge, depression        | L 2         | 0-1 | (0-5.3) |
|           |                                | F 2         | 0-1 | (0-0.7) |
|           | : Eye, cyclopia                | L 1         | 0-1 | (0-5.0) |
|           |                                | F 1         | 0-1 | (0-0.5) |
|           | : Snout, short                 | L 1         | 0-1 | (0-5.3) |
|           |                                | F 1         | 0-1 | (0-0.6) |
|           | : Snout, misshapen             | L 1         | 0-1 | (0-5.3) |
|           |                                | F 1         | 0-1 | (0-0.7) |
|           | : Mouth, misshapen             | L 1         | 0-1 | (0-5.3) |
|           |                                | F 1         | 0-1 | (0-0.7) |
|           | : Mouth, small                 | L 1         | 0-1 | (0-5.3) |
|           |                                | F 1         | 0-1 | (0-0.7) |
|           | : Naris, absent                | L 1         | 0-1 | (0-5.3) |
|           |                                | F 1         | 0-1 | (0-0.7) |
|           | : Jaw, lower (mandible), small | L 1         | 0-1 | (0-5.3) |
|           | (previously micrognathia)      | F 1         | 0-1 | (0-0.6) |
|           | : Face, proboscis              | L 1         | 0-1 | (0-5.0) |
|           |                                | F 1         | 0-1 | (0-0.5) |
| MOUTH     | : Palate, cleft palate         | L 2         | 0-1 | (0-5.6) |
|           |                                | F 2         | 0-1 | (0-0.5) |
|           | : Tooth, absent                | L 1         | 0-1 | (0-5.0) |
|           |                                | F 1         | 0-1 | (0-0.5) |
|           | : Tongue, protruding           | L 1         | 0-1 | (0-5.3) |
|           |                                | F 1         | 0-1 | (0-0.6) |

L: LITTER INCIDENCE

F: FETAL INCIDENCE

Note: All summary values are based on studies with fetal findings.

Updated June 2021

FETAL EXTERNAL ABNORMALITIES  
NEW ZEALAND WHITE [CrI:KBL(NZW)BR] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

| ABNORMALITIES                  |                                                         |   | RANGE/STUDY |         |          |
|--------------------------------|---------------------------------------------------------|---|-------------|---------|----------|
|                                |                                                         | N | N           | %       |          |
| TRUNK                          |                                                         |   |             |         |          |
|                                | : Abdomen, distended                                    | L | 8           | 0-2     | (0-11.1) |
|                                |                                                         | F | 8           | 0-2     | (0-1.3)  |
|                                | : Umbilicus, herniated                                  | L | 3           | 0-1     | (0-6.7)  |
|                                |                                                         | F | 3           | 0-1     | (0-0.5)  |
|                                | : Trunk, gastroschisis                                  | L | 2           | 0-1     | (0-5.6)  |
|                                | F                                                       | 2 | 0-1         | (0-0.7) |          |
| GENERAL                        |                                                         |   |             |         |          |
|                                | : Skin, thin                                            | L | 2           | 0-1     | (0-6.7)  |
|                                |                                                         | F | 2           | 0-1     | (0-0.7)  |
|                                | : Skin, skin tag                                        | L | 1           | 0-1     | (0-5.3)  |
|                                |                                                         | F | 1           | 0-1     | (0-0.7)  |
|                                | : Localized subcutis, edema                             | L | 2           | 0-1     | (0-5.3)  |
|                                | F                                                       | 2 | 0-1         | (0-0.6) |          |
| FORELIMB(S) AND/OR HINDLIMB(S) |                                                         |   |             |         |          |
|                                |                                                         |   |             |         |          |
|                                | : Limb(s), flexed                                       | L | 1           | 0-1     | (0-4.2)  |
|                                |                                                         | F | 1           | 0-1     | (0-0.5)  |
|                                | : Forelimb, hyperflexion                                | L | 1           | 0-1     | (0-5.3)  |
|                                |                                                         | F | 1           | 0-1     | (0-0.6)  |
|                                | : Hindlimb, malrotated                                  | L | 1           | 0-1     | (0-6.7)  |
|                                |                                                         | F | 1           | 0-1     | (0-0.4)  |
|                                | : Forelimb, short                                       | L | 1           | 0-1     | (0-6.7)  |
|                                |                                                         | F | 1           | 0-1     | (0-0.4)  |
| PAW/DIGIT(S)                   |                                                         |   |             |         |          |
|                                | : Forepaw, hyperextension                               | L | 9           | 0-2     | (0-11.1) |
|                                |                                                         | F | 10          | 0-3     | (0-1.5)  |
|                                | : Forepaw, hyperflexion                                 | L | 10          | 0-2     | (0-10.0) |
|                                |                                                         | F | 12          | 0-4     | (0-1.9)  |
|                                | : Forepaw, malrotated                                   | L | 2           | 0-1     | (0-5.0)  |
|                                |                                                         | F | 3           | 0-2     | (0-1.0)  |
|                                | : Forepaw, brachydactyly<br>(previously Forepaw, short) | L | 1           | 0-1     | (0-6.7)  |
|                                |                                                         | F | 1           | 0-1     | (0-0.4)  |
|                                | : Hindpaw, brachydactyly<br>(previously Hindpaw, short) | L | 1           | 0-1     | (0-6.7)  |
|                                | F                                                       | 1 | 0-1         | (0-0.4) |          |
| TAIL                           |                                                         |   |             |         |          |
|                                | : Tail, misshapen                                       | L | 1           | 0-1     | (0-6.7)  |
|                                |                                                         | F | 1           | 0-1     | (0-0.4)  |
|                                | : Tail, short                                           | L | 3           | 0-1     | (0-5.6)  |
|                                |                                                         | F | 3           | 0-1     | (0-0.7)  |
|                                | : Tail, absent                                          | L | 1           | 0-1     | (0-5.3)  |
|                                |                                                         | F | 1           | 0-1     | (0-0.7)  |
|                                | : Tail, bent                                            | L | 1           | 0-1     | (0-5.3)  |
|                                | F                                                       | 1 | 0-1         | (0-1.3) |          |

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F: FETAL INCIDENCE

Note: All summary values are based on studies with fetal findings.

Updated June 2021

FETAL SOFT TISSUE ABNORMALITIES  
NEW ZEALAND WHITE [CrI:KBL(NZW)BR] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
DOSE RANGE FINDING STUDIES

PERIOD: 2016 THROUGH 2020

NO. OF STUDIES INCLUDED 7

NO. LITTERS EXAMINED 44

NO. FETUSES EXAMINED 416

|                       | ABNORMALITIES                                      | RANGE/STUDY |     |          |
|-----------------------|----------------------------------------------------|-------------|-----|----------|
|                       |                                                    | N           | N   | %        |
| LIVER                 |                                                    |             |     |          |
|                       | : Liver, large                                     | L 1         | 0-1 | (0-20.0) |
|                       |                                                    | F 1         | 0-1 | (0-1.8)  |
| HEART                 |                                                    |             |     |          |
|                       | : Ventricular septal defect                        | L 3         | 0-1 | (0-20.0) |
|                       | <i>(previously interventricular septal defect)</i> | F 3         | 0-1 | (0-1.8)  |
|                       | : Muscular ventricular septal defect               | L 2         | 0-2 | (0-22.2) |
|                       |                                                    | F 2         | 0-2 | (0-1.9)  |
|                       | : Membranous ventricular septal defect             | L 2         | 0-2 | (0-22.2) |
|                       |                                                    | F 3         | 0-3 | (0-2.7)  |
| VESSELS               |                                                    |             |     |          |
|                       | : Truncus arteriosus, persistent                   | L 4         | 0-2 | (0-22.2) |
|                       | <i>(previously Persistent truncus arteriosus)</i>  | F 5         | 0-3 | (0-2.7)  |
|                       | : Aortic arch, dilatation                          | L 2         | 0-1 | (0-20.0) |
|                       |                                                    | F 2         | 0-1 | (0-1.8)  |
|                       | : Pulmonary trunk, narrow                          | L 1         | 0-1 | (0-20.0) |
|                       |                                                    | F 1         | 0-1 | (0-1.8)  |
|                       | : Innominate artery, absent                        | L 2         | 0-1 | (0-20.0) |
|                       |                                                    | F 3         | 0-2 | (0-6.7)  |
|                       | : Subclavian artery, right, retroesophageal        | L 2         | 0-1 | (0-20.0) |
|                       |                                                    | F 3         | 0-2 | (0-6.7)  |
|                       | : Subclavian artery origin, right, malpositioned   | L 1         | 0-1 | (0-11.1) |
|                       |                                                    | F 1         | 0-1 | (0-1.1)  |
|                       | : Subclavian artery, right, malpositioned          | L 1         | 0-1 | (0-20.0) |
|                       |                                                    | F 2         | 0-2 | (0-6.7)  |
| SPLEEN                |                                                    |             |     |          |
|                       | : Spleen, absent                                   | L 1         | 0-1 | (0-12.5) |
|                       |                                                    | F 1         | 0-1 | (0-1.2)  |
| GALLBLADDER/BILE DUCT |                                                    |             |     |          |
|                       | : Gallbladder, absent                              | L 3         | 0-1 | (0-20.0) |
|                       |                                                    | F 3         | 0-1 | (0-1.7)  |

L: LITTER INCIDENCE

F: FETAL INCIDENCE

Note: All summary values are based on studies with fetal findings.

Updated June 2021



FETAL SOFT TISSUE ABNORMALITIES  
NEW ZEALAND WHITE [CrI:KBL(NZW)BR] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

PERIOD: 2016 THROUGH 2020

NO. OF STUDIES INCLUDED 33

NO. LITTERS EXAMINED 614

NO. FETUSES EXAMINED 6199

| EYE(S)        | ABNORMALITIES                                      | RANGE/STUDY |     |          |
|---------------|----------------------------------------------------|-------------|-----|----------|
|               |                                                    | N           | N   | %        |
|               | : Eye, absent                                      | L 1         | 0-1 | (0-6.7)  |
|               |                                                    | F 1         | 0-1 | (0-0.4)  |
|               | : Eye, circumcorneal hemorrhage                    | L 3         | 0-1 | (0-6.7)  |
|               |                                                    | F 3         | 0-1 | (0-0.6)  |
|               | : Cornea, opacity                                  | L 3         | 0-1 | (0-6.7)  |
|               |                                                    | F 3         | 0-1 | (0-0.6)  |
|               | : Eye, small                                       | L 1         | 0-1 | (0-4.3)  |
|               | (previously microphthalmia)                        | F 1         | 0-1 | (0-0.4)  |
|               | : Eye, both, small                                 | L 1         | 0-1 | (0-5.3)  |
|               |                                                    | F 1         | 0-1 | (0-1.3)  |
|               | : Eye, left, small                                 | L 3         | 0-2 | (0-10.5) |
|               |                                                    | F 3         | 0-2 | (0-0.9)  |
|               | : Eye, right, small                                | L 2         | 0-1 | (0-5.3)  |
|               |                                                    | F 2         | 0-1 | (0-0.5)  |
|               | : Eye, misshapen                                   | L 1         | 0-1 | (0-5.3)  |
|               |                                                    | F 1         | 0-1 | (0-0.7)  |
|               | : Eye, malpositioned                               | L 1         | 0-1 | (0-5.0)  |
|               |                                                    | F 1         | 0-1 | (0-0.5)  |
| ADRENAL GLAND |                                                    |             |     |          |
|               | : Adrenal gland, malpositioned                     | L 2         | 0-1 | (0-5.3)  |
|               |                                                    | F 2         | 0-1 | (0-1.1)  |
| BRAIN         |                                                    |             |     |          |
|               | : Brain, absent                                    | L 1         | 0-1 | (0-6.7)  |
|               |                                                    | F 1         | 0-1 | (0-0.4)  |
|               | : Lateral ventricles, dilatation, slight           | L 2         | 0-1 | (0-5.9)  |
|               |                                                    | F 2         | 0-1 | (0-1.1)  |
|               | : Lateral ventricles, dilatation, moderate         | L 4         | 0-1 | (0-5.9)  |
|               |                                                    | F 5         | 0-2 | (0-1.5)  |
|               | : Lateral ventricles, dilatation, severe           | L 7         | 0-1 | (0-6.7)  |
|               | (previously lateral ventricles, dilation, extreme) | F 8         | 0-2 | (0-1.4)  |
|               | : Third ventricle, dilatation, moderate            | L 2         | 0-1 | (0-5.9)  |
|               |                                                    | F 3         | 0-2 | (0-1.5)  |
|               | : Third ventricle, dilatation, severe              | L 5         | 0-1 | (0-5.9)  |
|               |                                                    | F 6         | 0-2 | (0-1.4)  |
|               | : Fourth ventricle, dilatation, severe             | L 1         | 0-1 | (0-5.6)  |
|               |                                                    | F 1         | 0-1 | (0-1.4)  |
|               | : Brain, misshapen                                 | L 1         | 0-1 | (0-5.0)  |
|               |                                                    | F 1         | 0-1 | (0-0.5)  |
|               | : Brain, small                                     | L 1         | 0-1 | (0-5.0)  |
|               |                                                    | F 1         | 0-1 | (0-0.5)  |
| LUNGS         |                                                    |             |     |          |
|               | : Lobe, absent                                     | L 3         | 0-2 | (0-11.1) |
|               |                                                    | F 4         | 0-3 | (0-2.0)  |
|               | : Lung, small                                      | L 2         | 0-1 | (0-5.6)  |
|               |                                                    | F 2         | 0-1 | (0-0.5)  |

L: LITTER INCIDENCE

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Updated June 2021

FETAL SOFT TISSUE ABNORMALITIES  
NEW ZEALAND WHITE [CrI:KBL(NZW)BR] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

|         | ABNORMALITIES                                      | RANGE/STUDY |     |          |
|---------|----------------------------------------------------|-------------|-----|----------|
|         |                                                    | N           | N   | %        |
| HEART   | : Ventricular septal defect                        | L 20        | 0-3 | (0-15.8) |
|         | <i>(previously interventricular septal defect)</i> | F 22        | 0-3 | (0-1.7)  |
|         | : Muscular ventricular septal defect               | L 6         | 0-1 | (0-6.7)  |
|         |                                                    | F 7         | 0-2 | (0-1.1)  |
|         | : Membranous ventricular septal defect             | L 10        | 0-3 | (0-15.8) |
|         |                                                    | F 13        | 0-4 | (0-1.5)  |
|         | : Heart, large                                     | L 4         | 0-1 | (0-5.6)  |
|         |                                                    | F 4         | 0-1 | (0-0.6)  |
|         | : Heart, misshapen                                 | L 1         | 0-1 | (0-5.3)  |
|         |                                                    | F 1         | 0-1 | (0-1.1)  |
| LIVER   | : Liver, large                                     | L 3         | 0-1 | (0-5.3)  |
|         |                                                    | F 3         | 0-1 | (0-1.3)  |
|         | : Liver, malpositioned                             | L 2         | 0-1 | (0-5.6)  |
|         |                                                    | F 2         | 0-1 | (0-0.7)  |
|         | : Liver, abnormal texture                          | L 1         | 0-1 | (0-5.0)  |
|         |                                                    | F 1         | 0-1 | (0-0.5)  |
|         | : Liver, discolored                                | L 1         | 0-1 | (0-5.0)  |
|         |                                                    | F 1         | 0-1 | (0-0.5)  |
|         | : Liver, misshapen                                 | L 1         | 0-1 | (0-5.0)  |
|         |                                                    | F 1         | 0-1 | (0-0.5)  |
|         | : Lobe, malpositioned                              | L 2         | 0-1 | (0-5.6)  |
|         |                                                    | F 2         | 0-1 | (0-0.6)  |
|         | : Lobe, discolored                                 | L 1         | 0-1 | (0-7.1)  |
|         |                                                    | F 1         | 0-1 | (0-0.7)  |
|         | : Lobe, misshapen                                  | L 3         | 0-1 | (0-7.1)  |
|         |                                                    | F 3         | 0-1 | (0-0.7)  |
| VESSELS | : Truncus arteriosus, persistent                   | L 18        | 0-3 | (0-15.8) |
|         | <i>(previously Persistent truncus arteriosus)</i>  | F 21        | 0-4 | (0-1.5)  |
|         | : Innominate artery, absent                        | L 14        | 0-2 | (0-12.5) |
|         |                                                    | F 16        | 0-3 | (0-1.9)  |
|         | : Subclavian artery, retroesophageal               | L 14        | 0-2 | (0-12.5) |
|         |                                                    | F 16        | 0-3 | (0-1.9)  |
|         | : Subclavian artery origin, malpositioned          | L 13        | 0-2 | (0-12.5) |
|         |                                                    | F 15        | 0-3 | (0-1.9)  |
|         | : Subclavian artery, right, malpositioned          | L 1         | 0-1 | (0-5.3)  |
|         |                                                    | F 1         | 0-1 | (0-1.1)  |
|         | : Subclavian artery, absent                        | L 1         | 0-1 | (0-6.7)  |
|         |                                                    | F 1         | 0-1 | (0-0.4)  |
|         | : Aortic arch, dilatation                          | L 13        | 0-2 | (0-12.5) |
|         |                                                    | F 15        | 0-3 | (0-1.6)  |
|         | : Aortic arch, interrupted                         | L 1         | 0-1 | (0-6.7)  |
|         |                                                    | F 1         | 0-1 | (0-0.7)  |
|         | : Aortic arch, malpositioned                       | L 1         | 0-1 | (0-6.7)  |
|         |                                                    | F 1         | 0-1 | (0-0.4)  |
|         | : Aorta, dilatation                                | L 4         | 0-1 | (0-6.7)  |
|         |                                                    | F 4         | 0-1 | (0-0.8)  |
|         | : Carotid, absent                                  | L 1         | 0-1 | (0-6.7)  |
|         |                                                    | F 1         | 0-1 | (0-0.4)  |
|         | : Pulmonary trunk, narrow                          | L 13        | 0-2 | (0-11.1) |
|         |                                                    | F 14        | 0-3 | (0-1.6)  |
|         | : Pulmonary trunk, dilatation                      | L 2         | 0-1 | (0-6.7)  |
|         |                                                    | F 2         | 0-1 | (0-0.7)  |
|         | : Ductus arteriosus, patent                        | L 2         | 0-1 | (0-6.7)  |
|         |                                                    | F 2         | 0-1 | (0-0.7)  |

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Updated June 2021

FETAL SOFT TISSUE ABNORMALITIES  
NEW ZEALAND WHITE [CrI:KBL(NZW)BR] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

|                       | ABNORMALITIES                | RANGE/STUDY |     |          |
|-----------------------|------------------------------|-------------|-----|----------|
|                       |                              | N           | N   | %        |
| GENERAL               | : Abdomen, fluid-filled      | L 7         | 0-2 | (0-11.1) |
|                       |                              | F 7         | 0-2 | (0-1.1)  |
|                       | : Thorax, fluid-filled       | L 3         | 0-1 | (0-5.3)  |
|                       |                              | F 3         | 0-1 | (0-0.6)  |
| KIDNEY(S)             | : Kidney, malpositioned      | L 3         | 0-1 | (0-5.6)  |
|                       |                              | F 3         | 0-1 | (0-0.7)  |
|                       | : Renal papilla, absent      | L 1         | 0-1 | (0-6.3)  |
|                       |                              | F 1         | 0-1 | (0-0.5)  |
|                       | : Kidney, both, fused        | L 1         | 0-1 | (0-5.6)  |
|                       |                              | F 1         | 0-1 | (0-0.4)  |
| SPLEEN                | : Spleen, malpositioned      | L 1         | 0-1 | (0-5.3)  |
|                       |                              | F 1         | 0-1 | (0-0.7)  |
|                       | : Spleen, small              | L 1         | 0-1 | (0-5.0)  |
|                       |                              | F 1         | 0-1 | (0-0.5)  |
|                       | : Spleen, misshapen          | L 1         | 0-1 | (0-5.6)  |
|                       |                              | F 1         | 0-1 | (0-0.5)  |
| URETER                | : Ureter, dilated, minimal   | L 1         | 0-1 | (0-5.3)  |
|                       |                              | F 1         | 0-1 | (0-0.7)  |
|                       | : Ureter, dilated, moderate  | L 1         | 0-1 | (0-6.3)  |
|                       |                              | F 1         | 0-1 | (0-0.5)  |
| GALLBLADDER/BILE DUCT | : Gallbladder, malpositioned | L 1         | 0-1 | (0-5.3)  |
|                       |                              | F 1         | 0-1 | (0-0.7)  |
|                       | : Gallbladder, absent        | L 1         | 0-1 | (0-5.3)  |
|                       |                              | F 1         | 0-1 | (0-0.6)  |
| STOMACH               | : Stomach, malpositioned     | L 2         | 0-1 | (0-5.6)  |
|                       |                              | F 2         | 0-1 | (0-0.7)  |
| PANCREAS              | : Pancreas, malpositioned    | L 1         | 0-1 | (0-5.3)  |
|                       |                              | F 1         | 0-1 | (0-0.7)  |
| INTESTINE             | : Intestine, malpositioned   | L 2         | 0-1 | (0-6.7)  |
|                       |                              | F 2         | 0-1 | (0-0.7)  |
| DIAPHRAGM             | : Diaphragm, hernia          | L 3         | 0-1 | (0-5.6)  |
|                       |                              | F 3         | 0-1 | (0-0.7)  |

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Updated June 2021

FETAL SKELETAL ABNORMALITIES  
NEW ZEALAND WHITE [CrI:KBL(NZW)BR] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
DOSE RANGE FINDING STUDIES

PERIOD: 2016 THROUGH 2020

NO. OF STUDIES INCLUDED 4

NO. LITTERS EXAMINED 25

NO. FETUSES EXAMINED 259

| ABNORMALITIES |                                    | RANGE/STUDY |    |     |          |
|---------------|------------------------------------|-------------|----|-----|----------|
|               |                                    | N           | N  | %   |          |
| SKULL         |                                    |             |    |     |          |
| Parietal      | : Hole, right                      | L           | 1  | 0-1 | (0-11.1) |
|               |                                    | F           | 1  | 0-1 | (0-0.8)  |
| Suture bone   | : Supernumerary Site               | L           | 1  | 0-1 | (0-11.1) |
|               |                                    | F           | 1  | 0-1 | (0-0.8)  |
| VERTEBRAE     |                                    |             |    |     |          |
| Cervical      | : Centrum, unilateral ossification | L           | 1  | 0-1 | (0-20.0) |
|               |                                    | F           | 1  | 0-1 | (0-2.1)  |
| Thoracic      | : Centrum, incomplete ossification | L           | 1  | 0-1 | (0-20.0) |
|               |                                    | F           | 1  | 0-1 | (0-2.1)  |
|               | : Centrum, unilateral ossification | L           | 1  | 0-1 | (0-20.0) |
|               |                                    | F           | 1  | 0-1 | (0-2.1)  |
|               | : Hemivertebra                     | L           | 1  | 0-1 | (0-11.1) |
|               |                                    | F           | 1  | 0-1 | (0-0.9)  |
| Caudal        | : Misaligned                       | L           | 2  | 0-1 | (0-20.0) |
|               |                                    | F           | 2  | 0-1 | (0-2.1)  |
| STERNEBRA     |                                    |             |    |     |          |
|               | : Asymmetric                       | L           | 1  | 0-1 | (0-20.0) |
|               |                                    | F           | 1  | 0-1 | (0-1.8)  |
|               | : Fused                            | L           | 4  | 0-2 | (0-40.0) |
|               |                                    | F           | 4  | 0-2 | (0-3.6)  |
|               | : Incomplete ossification          | L           | 3  | 0-2 | (0-22.2) |
|               |                                    | F           | 10 | 0-9 | (0-7.7)  |
| PELVIC GIRDLE |                                    |             |    |     |          |
| Pubis         | : Unossified                       | L           | 2  | 0-1 | (0-20.0) |
|               |                                    | F           | 2  | 0-1 | (0-1.8)  |
| RIBS          |                                    |             |    |     |          |
|               | : Malpositioned                    | L           | 1  | 0-1 | (0-20.0) |
|               |                                    | F           | 1  | 0-1 | (0-2.1)  |
|               | : Misshapen                        | L           | 1  | 0-1 | (0-20.0) |
|               |                                    | F           | 1  | 0-1 | (0-2.1)  |
|               | : Branched                         | L           | 1  | 0-1 | (0-11.1) |
|               |                                    | F           | 1  | 0-1 | (0-0.9)  |

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FETAL SKELETAL ABNORMALITIES  
NEW ZEALAND WHITE [CrI:KBL(NZW)BR] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

PERIOD: 2016 THROUGH 2020

NO. OF STUDIES INCLUDED 43

NO. LITTERS EXAMINED 799

NO. FETUSES EXAMINED 8073

|                | ABNORMALITIES                            |   | RANGE/STUDY |     |          |
|----------------|------------------------------------------|---|-------------|-----|----------|
|                |                                          |   | N           | N   | %        |
| SKULL          |                                          |   |             |     |          |
|                | : Suture bone, supernumerary site        | L | 2           | 0-1 | (0-5.6)  |
|                | <i>(previously Suture bone, present)</i> | F | 2           | 0-1 | (0-0.7)  |
| Zygomatic arch |                                          |   |             |     |          |
|                | : Absent                                 | L | 2           | 0-1 | (0-6.7)  |
|                |                                          | F | 2           | 0-1 | (0-0.7)  |
| Basisphenoid   |                                          |   |             |     |          |
|                | : Absent                                 | L | 1           | 0-1 | (0-6.7)  |
|                |                                          | F | 1           | 0-1 | (0-0.4)  |
| Exoccipitals   |                                          |   |             |     |          |
|                | : Absent                                 | L | 1           | 0-1 | (0-6.7)  |
|                |                                          | F | 1           | 0-1 | (0-0.4)  |
|                | : Misshapen                              | L | 1           | 0-1 | (0-6.7)  |
|                |                                          | F | 1           | 0-1 | (0-0.4)  |
| Frontals       |                                          |   |             |     |          |
|                | : Contains a hole                        | L | 1           | 0-1 | (0-5.9)  |
|                |                                          | F | 1           | 0-1 | (0-0.5)  |
|                | : Incomplete ossification                | L | 7           | 0-2 | (0-11.8) |
|                |                                          | F | 8           | 0-2 | (0-1.9)  |
|                | : Fused                                  | L | 1           | 0-1 | (0-6.3)  |
|                |                                          | F | 1           | 0-1 | (0-0.6)  |
|                | : Absent                                 | L | 1           | 0-1 | (0-6.7)  |
|                |                                          | F | 1           | 0-1 | (0-0.4)  |
| Mandible       |                                          |   |             |     |          |
|                | : Absent                                 | L | 1           | 0-1 | (0-6.7)  |
|                |                                          | F | 1           | 0-1 | (0-0.4)  |
|                | : Misshapen                              | L | 1           | 0-1 | (0-5.3)  |
|                |                                          | F | 1           | 0-1 | (0-0.7)  |
| Maxilla        |                                          |   |             |     |          |
|                | : Absent                                 | L | 2           | 0-1 | (0-6.7)  |
|                |                                          | F | 2           | 0-1 | (0-0.5)  |
|                | : Misshapen                              | L | 1           | 0-1 | (0-5.3)  |
|                |                                          | F | 1           | 0-1 | (0-0.7)  |
|                | : Fused                                  | L | 1           | 0-1 | (0-5.3)  |
|                |                                          | F | 1           | 0-1 | (0-0.7)  |

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FETAL SKELETAL ABNORMALITIES  
NEW ZEALAND WHITE [CrI:KBL(NZW)BR] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

| SKULL (CONT'D) | ABNORMALITIES                | RANGE/STUDY |     |          |
|----------------|------------------------------|-------------|-----|----------|
|                |                              | N           | N   | %        |
| SKULL (CONT'D) | Nasal                        |             |     |          |
|                | : Absent                     | L 1         | 0-1 | (0-6.7)  |
|                |                              | F 1         | 0-1 | (0-0.4)  |
|                | : Intranasals                | L 1         | 0-1 | (0-5.3)  |
|                |                              | F 1         | 0-1 | (0-0.5)  |
|                | : Isolated ossification site | L 3         | 0-1 | (0-5.6)  |
|                |                              | F 3         | 0-1 | (0-0.7)  |
|                | : Misshapen                  | L 2         | 0-1 | (0-5.3)  |
|                |                              | F 2         | 0-1 | (0-0.7)  |
|                | : Fused                      | L 1         | 0-1 | (0-5.0)  |
|                |                              | F 1         | 0-1 | (0-0.5)  |
|                | : Malpositioned              | L 1         | 0-1 | (0-5.0)  |
|                |                              | F 1         | 0-1 | (0-0.5)  |
|                | Palatine                     |             |     |          |
|                | : Absent                     | L 1         | 0-1 | (0-6.7)  |
|                |                              | F 1         | 0-1 | (0-0.4)  |
|                | : Incomplete ossification    | L 1         | 0-1 | (0-5.6)  |
|                |                              | F 1         | 0-1 | (0-0.4)  |
|                | : Split                      | L 2         | 0-1 | (0-5.3)  |
|                | (previously cleft)           | F 2         | 0-1 | (0-0.7)  |
|                | Parietal                     |             |     |          |
|                | : Absent                     | L 1         | 0-1 | (0-6.7)  |
|                |                              | F 1         | 0-1 | (0-0.4)  |
|                | : Contains a hole            | L 17        | 0-2 | (0-13.3) |
|                |                              | F 19        | 0-3 | (0-1.6)  |
|                | : Incomplete ossification    | L 8         | 0-2 | (0-11.1) |
|                |                              | F 9         | 0-2 | (0-1.9)  |
|                | Premaxilla                   |             |     |          |
|                | : Absent                     | L 2         | 0-1 | (0-6.7)  |
|                |                              | F 2         | 0-1 | (0-0.4)  |
|                | Pterygoid Processes          |             |     |          |
|                | : Absent                     | L 1         | 0-1 | (0-6.7)  |
|                |                              | F 1         | 0-1 | (0-0.4)  |
|                | Interparietal                |             |     |          |
|                | : Incomplete ossification    | L 2         | 0-1 | (0-5.9)  |
|                |                              | F 2         | 0-1 | (0-0.7)  |
|                | : Absent                     | L 1         | 0-1 | (0-6.7)  |
|                |                              | F 1         | 0-1 | (0-0.4)  |

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FETAL SKELETAL ABNORMALITIES  
NEW ZEALAND WHITE [CrI:KBL(NZW)BR] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

|                | ABNORMALITIES    |                                  | N | RANGE/STUDY |              |
|----------------|------------------|----------------------------------|---|-------------|--------------|
|                |                  |                                  |   | N           | %            |
| SKULL (CONT'D) | Fontanelle       | : Anterior, large, moderate      | L | 5           | 0-3 (0-15.8) |
|                |                  |                                  | F | 6           | 0-3 (0-1.5)  |
|                |                  | : Posterior, large, moderate     | L | 3           | 0-3 (0-15.8) |
|                |                  |                                  | F | 3           | 0-3 (0-1.5)  |
|                | Squamosal        | : Absent                         | L | 2           | 0-1 (0-6.7)  |
|                |                  |                                  | F | 2           | 0-1 (0-0.7)  |
|                | Supraoccipital   | : Absent                         | L | 1           | 0-1 (0-6.7)  |
|                |                  |                                  | F | 1           | 0-1 (0-0.4)  |
|                | Tympanic annulus | : Absent                         | L | 1           | 0-1 (0-6.7)  |
|                |                  |                                  | F | 1           | 0-1 (0-0.4)  |
|                | Basioccipital    | : Absent                         | L | 1           | 0-1 (0-6.7)  |
|                |                  |                                  | F | 1           | 0-1 (0-0.4)  |
| HYOID          | Ala(e)           | : Absent                         | L | 1           | 0-1 (0-6.7)  |
|                |                  |                                  | F | 1           | 0-1 (0-0.4)  |
|                |                  | : Bent<br>(previously angulated) | L | 18          | 0-2 (0-14.3) |
|                |                  |                                  | F | 20          | 0-3 (0-2.2)  |
|                |                  | : Unossified                     | L | 2           | 0-1 (0-6.3)  |
|                |                  |                                  | F | 2           | 0-1 (0-0.7)  |
|                |                  | : Short                          | L | 3           | 0-2 (0-11.1) |
|                |                  |                                  | F | 3           | 0-2 (0-1.4)  |
|                | Body             | : Unossified                     | L | 8           | 0-5 (0-27.8) |
|                |                  |                                  | F | 11          | 0-7 (0-3.9)  |
|                |                  | : Absent                         | L | 1           | 0-1 (0-6.7)  |
|                |                  |                                  | F | 1           | 0-1 (0-0.4)  |

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FETAL SKELETAL ABNORMALITIES  
NEW ZEALAND WHITE [CrI:KBL(NZW)BR] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

| VERTEBRAE | ABNORMALITIES |                                      | RANGE/STUDY |     |          |
|-----------|---------------|--------------------------------------|-------------|-----|----------|
|           |               |                                      | N           | N   | %        |
| VERTEBRAE | Cervical      | : Absent                             | L 1         | 0-1 | (0-5.0)  |
|           |               |                                      | F 1         | 0-1 | (0-0.5)  |
|           |               | : Arch, misshapen                    | L 1         | 0-1 | (0-6.7)  |
|           |               |                                      | F 1         | 0-1 | (0-0.4)  |
|           |               | : Centrum, unilateral ossification   | L 1         | 0-1 | (0-5.6)  |
|           |               |                                      | F 1         | 0-1 | (0-0.6)  |
|           |               | : Centrum, incomplete ossification   | L 7         | 0-1 | (0-9.1)  |
|           |               |                                      | F 7         | 0-1 | (0-1.0)  |
|           |               | : Centrum, unossified                | L 3         | 0-1 | (0-6.7)  |
|           |               |                                      | F 3         | 0-1 | (0-0.6)  |
|           |               | : Centrum, misshapen                 | L 1         | 0-1 | (0-5.6)  |
|           |               |                                      | F 1         | 0-1 | (0-0.6)  |
|           |               | : Supernumerary rib, cervical, full  | L 7         | 0-2 | (0-11.1) |
|           |               |                                      | F 8         | 0-2 | (0-1.1)  |
|           |               | : Supernumerary rib, cervical, short | L 50        | 0-4 | (0-20.0) |
|           |               |                                      | F 66        | 0-6 | (0-2.7)  |
|           | Thoracic      | : Hemivertebra                       | L 6         | 0-2 | (0-9.5)  |
|           |               |                                      | F 6         | 0-2 | (0-0.9)  |
|           |               | : Arch, absent                       | L 1         | 0-1 | (0-5.3)  |
|           |               |                                      | F 1         | 0-1 | (0-0.7)  |
|           |               | : Arch, fused                        | L 5         | 0-2 | (0-10.5) |
|           |               |                                      | F 5         | 0-2 | (0-1.2)  |
|           |               | : Arch, misshapen                    | L 1         | 0-1 | (0-4.8)  |
|           |               |                                      | F 1         | 0-1 | (0-0.4)  |
|           |               | : Centrum, fused                     | L 5         | 0-2 | (0-10.5) |
|           |               |                                      | F 5         | 0-2 | (0-1.2)  |
|           |               | : Centrum, misshapen                 | L 2         | 0-1 | (0-5.3)  |
|           |               |                                      | F 2         | 0-1 | (0-0.5)  |
|           |               | : Centrum, small                     | L 1         | 0-1 | (0-4.8)  |
|           |               |                                      | F 1         | 0-1 | (0-0.5)  |
|           |               | : Centrum, unossified                | L 1         | 0-1 | (0-6.7)  |
|           |               |                                      | F 1         | 0-1 | (0-0.4)  |
|           |               | : Centrum, incomplete ossification   | L 2         | 0-1 | (0-5.6)  |
|           |               |                                      | F 2         | 0-1 | (0-0.6)  |
|           |               | : Centrum, bipartite ossification    | L 2         | 0-1 | (0-6.7)  |
|           |               |                                      | F 2         | 0-1 | (0-0.7)  |
|           |               | : Centrum, unilateral ossification   | L 5         | 0-2 | (0-10.5) |
|           |               |                                      | F 5         | 0-2 | (0-1.1)  |

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Updated June 2021



FETAL SKELETAL ABNORMALITIES  
NEW ZEALAND WHITE [CrI:KBL(NZW)BR] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

|                    |        | ABNORMALITIES             |      | RANGE/STUDY |          |
|--------------------|--------|---------------------------|------|-------------|----------|
|                    |        |                           | N    | N           | %        |
| VERTEBRAE (CONT'D) |        |                           |      |             |          |
|                    | Lumbar |                           |      |             |          |
|                    |        | : Arch, misaligned        | L 2  | 0-1         | (0-5.3)  |
|                    |        |                           | F 2  | 0-1         | (0-0.5)  |
|                    |        | : Arch, fused             | L 1  | 0-1         | (0-5.3)  |
|                    |        |                           | F 1  | 0-1         | (0-0.5)  |
|                    |        | : Hemivertebra            | L 5  | 0-1         | (0-7.1)  |
|                    |        |                           | F 5  | 0-1         | (0-0.7)  |
|                    |        | : Centrum, misaligned     | L 1  | 0-1         | (0-5.3)  |
|                    |        |                           | F 1  | 0-1         | (0-0.5)  |
|                    |        | : Centrum, misshapen      | L 2  | 0-1         | (0-6.7)  |
|                    |        |                           | F 2  | 0-1         | (0-0.5)  |
|                    |        | : Centrum, unossified     | L 1  | 0-1         | (0-6.7)  |
|                    |        |                           | F 1  | 0-1         | (0-0.4)  |
|                    |        | : Absent                  | L 1  | 0-1         | (0-5.3)  |
|                    |        |                           | F 1  | 0-1         | (0-0.6)  |
|                    |        | : Centrum, fused          | L 5  | 0-2         | (0-10.5) |
|                    |        |                           | F 5  | 0-2         | (0-1.2)  |
|                    | Sacral |                           |      |             |          |
|                    |        | : Arch, misshapen         | L 1  | 0-1         | (0-6.7)  |
|                    |        |                           | F 1  | 0-1         | (0-0.4)  |
|                    |        | : Hemivertebra            | L 1  | 0-1         | (0-5.3)  |
|                    |        |                           | F 1  | 0-1         | (0-0.5)  |
|                    |        | : Centrum, misshapen      | L 1  | 0-1         | (0-5.6)  |
|                    |        |                           | F 1  | 0-1         | (0-0.6)  |
|                    |        | : Centrum, unossified     | L 1  | 0-1         | (0-6.7)  |
|                    |        |                           | F 1  | 0-1         | (0-0.4)  |
|                    | Caudal |                           |      |             |          |
|                    |        | : Arch, fused             | L 1  | 0-1         | (0-6.7)  |
|                    |        |                           | F 1  | 0-1         | (0-0.4)  |
|                    |        | : Fused                   | L 6  | 0-1         | (0-5.6)  |
|                    |        |                           | F 6  | 0-1         | (0-0.7)  |
|                    |        | : Unossified              | L 3  | 0-1         | (0-5.0)  |
|                    |        |                           | F 3  | 0-1         | (0-0.5)  |
|                    |        | : Misaligned              | L 23 | 0-2         | (0-10.5) |
|                    |        |                           | F 23 | 0-2         | (0-1.0)  |
|                    |        | : Incomplete ossification | L 5  | 0-1         | (0-6.7)  |
|                    |        |                           | F 5  | 0-1         | (0-0.7)  |
|                    |        | : Misshapen               | L 3  | 0-1         | (0-6.7)  |
|                    |        |                           | F 3  | 0-1         | (0-0.7)  |
|                    |        | : Small                   | L 1  | 0-1         | (0-5.3)  |
|                    |        |                           | F 1  | 0-1         | (0-0.5)  |

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Updated June 2021

FETAL SKELETAL ABNORMALITIES  
NEW ZEALAND WHITE [CrI:KBL(NZW)BR] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

|         |               | ABNORMALITIES                           |       | RANGE/STUDY |          |  |
|---------|---------------|-----------------------------------------|-------|-------------|----------|--|
|         |               |                                         | N     | N           | %        |  |
| SCAPULA | Ala(e)        |                                         |       |             |          |  |
|         |               | : Misshapen                             | L 2   | 0-1         | (0-6.7)  |  |
|         |               |                                         | F 2   | 0-1         | (0-0.5)  |  |
| RIBS    |               |                                         |       |             |          |  |
|         |               | : Absent                                | L 2   | 0-1         | (0-5.6)  |  |
|         |               |                                         | F 2   | 0-1         | (0-0.7)  |  |
|         |               | : Fused                                 | L 7   | 0-2         | (0-10.5) |  |
|         |               |                                         | F 7   | 0-2         | (0-1.2)  |  |
|         |               | : Branched                              | L 6   | 0-1         | (0-6.3)  |  |
|         |               | <i>(previously one or more, split)</i>  | F 6   | 0-1         | (0-0.7)  |  |
|         |               | : Nodulated                             | L 9   | 0-1         | (0-6.3)  |  |
|         |               | <i>(previously thickened or nodule)</i> | F 9   | 0-1         | (0-0.8)  |  |
|         |               | : Short                                 | L 3   | 0-1         | (0-5.6)  |  |
|         |               |                                         | F 3   | 0-1         | (0-0.5)  |  |
|         |               | : Interrupted                           | L 8   | 0-1         | (0-7.1)  |  |
|         |               |                                         | F 8   | 0-1         | (0-0.7)  |  |
|         |               | : Misshapen                             | L 4   | 0-2         | (0-10.5) |  |
|         |               |                                         | F 4   | 0-2         | (0-1.0)  |  |
|         |               | : Intercostal                           | L 1   | 0-1         | (0-4.8)  |  |
|         |               |                                         | F 1   | 0-1         | (0-0.4)  |  |
|         | Thoracolumbar |                                         |       |             |          |  |
|         |               | : Thoracolumbar, full                   | L 41  | 0-15        | (0-75.0) |  |
|         |               | <i>(previously T13, supernumerary)</i>  | F 141 | 0-50        | (0-27.9) |  |
|         |               | : Thoracolumbar, short                  | L 35  | 0-14        | (0-70.0) |  |
|         |               | <i>(previously T13, short)</i>          | F 65  | 0-27        | (0-12.3) |  |

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FETAL SKELETAL ABNORMALITIES  
NEW ZEALAND WHITE [CrI:KBL(NZW)BR] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

|               |           | ABNORMALITIES                 |       | RANGE/STUDY |          |  |
|---------------|-----------|-------------------------------|-------|-------------|----------|--|
|               |           |                               | N     | N           | %        |  |
| STERNUM       | Sternebra |                               |       |             |          |  |
|               |           | : Fused                       | L 100 | 0-8         | (0-35.3) |  |
|               |           |                               | F 137 | 0-9         | (0-5.4)  |  |
|               |           | : Asymmetric                  | L 10  | 0-1         | (0-7.1)  |  |
|               |           |                               | F 10  | 0-1         | (0-0.8)  |  |
|               |           | : Incomplete ossification     | L 45  | 0-4         | (0-25.0) |  |
|               |           |                               | F 53  | 0-4         | (0-2.5)  |  |
|               |           | : Misshapen                   | L 32  | 0-3         | (0-13.0) |  |
|               |           |                               | F 33  | 0-3         | (0-1.5)  |  |
|               |           | : Unossified                  | L 43  | 0-16        | (0-80.0) |  |
|               |           |                               | F 135 | 0-51        | (0-28.2) |  |
|               |           | : Bipartite ossification      | L 20  | 0-3         | (0-18.8) |  |
|               |           |                               | F 26  | 0-5         | (0-2.6)  |  |
|               |           | : Split                       | L 2   | 0-2         | (0-10.5) |  |
|               |           |                               | F 7   | 0-7         | (0-3.4)  |  |
|               |           | : Isolated ossification       | L 16  | 0-2         | (0-10.5) |  |
|               |           |                               | F 23  | 0-7         | (0-3.2)  |  |
|               |           | : Small                       | L 2   | 0-1         | (0-5.6)  |  |
|               |           |                               | F 3   | 0-2         | (0-1.0)  |  |
|               | Manubrium |                               |       |             |          |  |
|               |           | : Irregularly shaped          | L 4   | 0-2         | (0-11.8) |  |
|               |           |                               | F 6   | 0-4         | (0-2.0)  |  |
|               |           | : Extra point of ossification | L 1   | 0-1         | (0-4.2)  |  |
|               |           |                               | F 1   | 0-1         | (0-0.5)  |  |
| PELVIC GIRDLE | Pubis     |                               |       |             |          |  |
|               |           | : Incomplete ossification     | L 14  | 0-2         | (0-12.5) |  |
|               |           |                               | F 15  | 0-2         | (0-1.4)  |  |
|               |           | : Unossified                  | L 15  | 0-2         | (0-11.1) |  |
|               |           |                               | F 21  | 0-7         | (0-4.8)  |  |

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FETAL SKELETAL ABNORMALITIES  
NEW ZEALAND WHITE [CrI:KBL(NZW)BR] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

|             | ABNORMALITIES                   |   | N  | RANGE/STUDY |          |
|-------------|---------------------------------|---|----|-------------|----------|
|             |                                 |   |    | N           | %        |
| FORELIMB(S) |                                 |   |    |             |          |
|             | : Humerus, misshapen            | L | 1  | 0-1         | (0-6.7)  |
|             |                                 | F | 1  | 0-1         | (0-0.4)  |
|             | : Metacarpal, unossified        | L | 11 | 0-6         | (0-33.3) |
|             |                                 | F | 24 | 0-14        | (0-7.7)  |
|             | : Metacarpal, absent            | L | 1  | 0-1         | (0-6.7)  |
|             |                                 | F | 1  | 0-1         | (0-0.4)  |
|             | : Forepaw phalanges, small      | L | 2  | 0-1         | (0-5.3)  |
|             |                                 | F | 2  | 0-1         | (0-0.6)  |
|             | : Forepaw phalanges, absent     | L | 2  | 0-1         | (0-6.7)  |
|             |                                 | F | 2  | 0-1         | (0-0.5)  |
|             | : Forepaw phalanges, unossified | L | 7  | 0-4         | (0-20.0) |
|             |                                 | F | 11 | 0-7         | (0-3.1)  |
|             | : Ulna, misshapen               | L | 1  | 0-1         | (0-6.7)  |
|             |                                 | F | 1  | 0-1         | (0-0.4)  |
|             | : Radius, short                 | L | 1  | 0-1         | (0-6.7)  |
|             |                                 | F | 1  | 0-1         | (0-0.4)  |
| HINDLIMB(S) |                                 |   |    |             |          |
|             | : Hindpaw phalanges, absent     | L | 1  | 0-1         | (0-6.7)  |
|             |                                 | F | 1  | 0-1         | (0-0.4)  |
|             | : Metatarsal, absent            | L | 1  | 0-1         | (0-6.7)  |
|             |                                 | F | 1  | 0-1         | (0-0.4)  |
|             | : Talus, unossified             | L | 1  | 0-1         | (0-5.6)  |
|             |                                 | F | 1  | 0-1         | (0-0.6)  |

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*Updated June 2021*

FETAL SKELETAL OSSIFICATION SITES  
NEW ZEALAND WHITE [CrI:KBL(NZW)BR] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
DOSE RANGE FINDING STUDIES

PERIOD: 2016 THROUGH 2020

|                         |     |
|-------------------------|-----|
| NO. OF STUDIES INCLUDED | 3   |
| NO. LITTERS EXAMINED    | 20  |
| NO. FETUSES EXAMINED    | 212 |

|                       | MEAN  | MINIMUM | MAXIMUM |
|-----------------------|-------|---------|---------|
| HYOID                 | 0.98  | 0.98    | 0.99    |
| VERTEBRAE             |       |         |         |
| CERVICAL              | 7.00  | 7.00    | 7.00    |
| THORACIC              | 12.44 | 12.31   | 12.52   |
| LUMBAR                | 6.56  | 6.48    | 6.68    |
| SACRAL                | 4.00  | 4.00    | 4.00    |
| CAUDAL                | 15.46 | 15.40   | 15.56   |
| RIBS (Pairs)          | 12.40 | 12.29   | 12.47   |
| STERNUM               |       |         |         |
| MANUBRIUM             | 1.00  | 1.00    | 1.00    |
| STERNAL CENTERS       | 3.86  | 3.77    | 3.94    |
| XIPHOID               | 0.94  | 0.86    | 1.00    |
| FORELIMB <sup>a</sup> |       |         |         |
| CARPALS               | 0.00  | 0.00    | 0.00    |
| METACARPALS           | 4.95  | 4.93    | 4.96    |
| DIGITS                | 5.00  | 5.00    | 5.00    |
| PHALANGES             | 13.94 | 13.91   | 13.98   |
| HINDLIMB <sup>a</sup> |       |         |         |
| TARSALS               | 1.98  | 1.98    | 1.99    |
| METATARSALS           | 4.00  | 4.00    | 4.00    |
| DIGITS                | 4.00  | 4.00    | 4.00    |
| PHALANGES             | 11.96 | 11.91   | 12.00   |

a. Calculated as mean per limb.

FETAL SKELETAL OSSIFICATION SITES  
NEW ZEALAND WHITE [CrI:KBL(NZW)BR] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

PERIOD: 2016 THROUGH 2020

NO. OF STUDIES INCLUDED 32

NO. LITTERS EXAMINED 595

NO. FETUSES EXAMINED 5947

|                       | MEAN  | MINIMUM | MAXIMUM |
|-----------------------|-------|---------|---------|
| HYOID                 | 1.01  | 0.98    | 1.13    |
| VERTEBRAE             |       |         |         |
| CERVICAL              | 7.00  | 7.00    | 7.00    |
| THORACIC              | 12.39 | 12.23   | 12.59   |
| LUMBAR                | 6.61  | 6.41    | 6.78    |
| SACRAL                | 4.00  | 4.00    | 4.00    |
| CAUDAL                | 15.45 | 15.30   | 15.67   |
| RIBS (Pairs)          | 12.33 | 12.19   | 12.51   |
| STERNUM               |       |         |         |
| MANUBRIUM             | 1.00  | 1.00    | 1.00    |
| STERNAL CENTERS       | 3.86  | 3.75    | 4.06    |
| XIPHOID               | 0.95  | 0.86    | 1.05    |
| FORELIMB <sup>a</sup> |       |         |         |
| CARPALS               | 0.00  | 0.00    | 0.00    |
| METACARPALS           | 4.96  | 4.83    | 5.00    |
| DIGITS                | 5.00  | 5.00    | 5.00    |
| PHALANGES             | 13.97 | 13.78   | 14.00   |
| HINDLIMB <sup>a</sup> |       |         |         |
| TARSALS               | 1.99  | 1.97    | 2.00    |
| METATARSALS           | 4.00  | 3.95    | 4.00    |
| DIGITS                | 4.00  | 4.00    | 4.00    |
| PHALANGES             | 11.99 | 11.92   | 12.00   |

a. Calculated as mean per limb.

NATURAL DELIVERY AND LITTER PARAMETERS  
NEW ZEALAND WHITE [CrI:KBL(NZW)BR] RABBITS

PERIOD: 2016 THROUGH 2020

|                                    |    |
|------------------------------------|----|
| NO. OF STUDIES INCLUDED            | 3  |
| NO. ASSIGNED TO NATURAL DELIVERY   | 62 |
| NO. FOUND DEAD                     | 0  |
| NO. ABORTED                        | 0  |
| NO. PREGNANT                       | 53 |
| NO. RABBITS THAT DELIVERED LITTERS | 51 |

|                                                                         | <u>MEAN or %</u> | <u>MIN</u> | <u>MAX</u> | <u>NO. STUDIES INCLUDED</u> |
|-------------------------------------------------------------------------|------------------|------------|------------|-----------------------------|
| PREGNANT (%)                                                            | 86.0             | 80.0       | 94.7       | 3                           |
| DELIVERED LITTERS (%)                                                   | 97.8             | 93.3       | 100.0      | 3                           |
| DURATION OF GESTATION<br>IN DAYS                                        | 31.8             | 30.3       | 32.7       | 3                           |
| IMPLANTATION SITES<br>PER DELIVERED LITTER                              | 10.2             | 9.6        | 10.6       | 3                           |
| DOES WITH STILLBORN KITS (%)                                            | 9.2              | 0          | 15.8       | 3                           |
| DOES WITH NO LIVEBORN KITS (%)                                          | 0.0              | 0.0        | 0.0        | 3                           |
| GESTATION INDEX (NO. RABBITS<br>WITH LIVEBORN/NO. PREGNANT RABBITS) (%) | 97.8             | 93.3       | 100.0      | 3                           |
| POSTIMPLANTATION LOSS/LITTER (%)                                        | 10.6             | 10.6       | 10.6       | 1                           |
| DOES WITH ALL KITS DYING<br>DAYS 1-4 POSTPARTUM (%)                     | 2.7              | 0.0        | 5.3        | 2                           |
| DOES WITH ALL KITS DYING<br>DAYS 5-28 POSTPARTUM (%)                    | 0.0              | 0.0        | 0.0        | 1                           |
| DOES WITH ALL KITS DYING<br>DAYS 5-29 POSTPARTUM (%)                    | 0.0              | 0.0        | 0.0        | 1                           |

NATURAL DELIVERY AND LITTER PARAMETERS  
NEW ZEALAND WHITE [CrI:KBL(NZW)BR] RABBITS

PERIOD: 2016 THROUGH 2020

NO. OF STUDIES

3

|                                                 | <u>MEAN or %</u> | <u>MIN</u> | <u>MAX</u> | <u>NO. STUDIES INCLUDED</u> |
|-------------------------------------------------|------------------|------------|------------|-----------------------------|
| KITS DELIVERED (TOTAL)                          | 9.2              | 8.5        | 9.7        | 3                           |
| LIVEBORN                                        | 9.2              | 9.1        | 9.2        | 2                           |
| LIVEBORN (%)                                    | 96.2             | 95.2       | 97.2       | 2                           |
| STILLBORN                                       | 0.2              | 0.2        | 0.2        | 2                           |
| STILLBORN (%)                                   | 2                | 1.8        | 2.2        | 2                           |
| KITS FOUND DEAD OR<br>PRESUMED CANNIBALIZED (%) |                  |            |            |                             |
| DAYS 1-5                                        | 8.7              | 7.6        | 9.8        | 2                           |
| DAYS 6-7                                        | 2.1              | 2.1        | 2.1        | 1                           |
| DAYS 6-8                                        | 7.0              | 7.0        | 7.0        | 1                           |
| DAYS 8-10                                       | 7.0              | 7.0        | 7.0        | 1                           |
| DAYS 9-15                                       | 2.8              | 2.8        | 2.8        | 1                           |
| DAYS 11-12                                      | 3.0              | 3.0        | 3.0        | 1                           |
| DAYS 13-14                                      | 1.6              | 1.6        | 1.6        | 1                           |
| DAYS 15-18                                      | 0.0              | 0.0        | 0.0        | 1                           |
| DAYS 16-18                                      | 0.0              | 0.0        | 0.0        | 1                           |
| DAYS 19-21                                      | 1.6              | 1.6        | 1.6        | 1                           |
| DAYS 19-22                                      | 0.0              | 0.0        | 0.0        | 1                           |
| DAYS 22-23                                      | 0.0              | 0.0        | 0.0        | 1                           |
| DAYS 23-28                                      | 0.0              | 0.0        | 0.0        | 1                           |
| DAYS 24-26                                      | 0.0              | 0.0        | 0.0        | 1                           |
| DAYS 27-29                                      | 4.8              | 4.8        | 4.8        | 1                           |



NATURAL DELIVERY AND LITTER PARAMETERS  
NEW ZEALAND WHITE [CrI:KBL(NZW)BR] RABBITS

PERIOD: 2016 THROUGH 2020

|                                                                         |             |            |            |                             |
|-------------------------------------------------------------------------|-------------|------------|------------|-----------------------------|
| NO. OF STUDIES                                                          | 3           |            |            |                             |
|                                                                         | <u>MEAN</u> | <u>MIN</u> | <u>MAX</u> | <u>NO. STUDIES INCLUDED</u> |
| VIABILITY INDEX (%)<br>(No. Live kits PND 4 or 5 / No. Live kits PND 1) | 91.3        | 90.2       | 92.4       | 2                           |
| LACTATION INDEX (%)<br>(No. Live kits PND 29 / No. Live kits PND 5)     | 76.8        | 71.0       | 82.6       | 2                           |
| SURVIVING KITS/LITTER                                                   |             |            |            |                             |
| DAY 4                                                                   | 6.5         | 6.5        | 6.5        | 1                           |
| DAY 5                                                                   | 8.4         | 8.2        | 8.5        | 2                           |
| DAY 7                                                                   | 7.2         | 5.9        | 8.4        | 2                           |
| DAY 8                                                                   | 7.6         | 7.6        | 7.6        | 1                           |
| DAY 10                                                                  | 7.7         | 7.7        | 7.7        | 1                           |
| DAY 12                                                                  | 7.5         | 7.5        | 7.5        | 1                           |
| DAY 14                                                                  | 6.3         | 5.1        | 7.4        | 2                           |
| DAY 15                                                                  | 5.3         | 3.1        | 7.4        | 2                           |
| DAY 18                                                                  | 7.4         | 7.4        | 7.4        | 1                           |
| DAY 21                                                                  | 7.2         | 7.2        | 7.2        | 1                           |
| DAY 22                                                                  | 5.25        | 3.1        | 7.4        | 2                           |
| DAY 23                                                                  | 6.4         | 6.4        | 6.4        | 1                           |
| DAY 26                                                                  | 6.4         | 6.4        | 6.4        | 1                           |
| DAY 28                                                                  | 3.0         | 3.0        | 3.0        | 1                           |
| DAY 29                                                                  | 4.0         | 1.9        | 6.0        | 2                           |

NATURAL DELIVERY AND LITTER PARAMETERS  
NEW ZEALAND WHITE [CrI:KBL(NZW)BR] RABBITS

PERIOD: 2016 THROUGH 2020

NO. OF STUDIES

3

|                  | <u>MEAN</u> | <u>MIN</u> | <u>MAX</u> | <u>NO. STUDIES INCLUDED</u> |
|------------------|-------------|------------|------------|-----------------------------|
| DEAD KITS/LITTER |             |            |            |                             |
| DAYS 4-7         | 0.6         | 0.6        | 0.6        | 1                           |
| DAYS 8-14        | 1.0         | 1.0        | 1.0        | 1                           |
| DAYS 15-28       | 0.1         | 0.1        | 0.1        | 1                           |
| DAY 29           | 0.0         | 0.0        | 0.0        | 1                           |
| DAYS 4-29        | 1.4         | 1.4        | 1.4        | 1                           |

PERCENT MALE KITS PER NUMBER  
OF KITS SEXED

|           |       |      |      |   |
|-----------|-------|------|------|---|
| DAY 5     | 47.55 | 43.9 | 51.2 | 2 |
| DAY 7     | 43.5  | 43.5 | 43.5 | 1 |
| DAY 8     | 50.1  | 50.1 | 50.1 | 1 |
| DAY 10    | 42.1  | 42.1 | 42.1 | 1 |
| DAY 12    | 41.2  | 41.2 | 41.2 | 1 |
| DAY 14    | 40.9  | 40.9 | 40.9 | 1 |
| DAY 15    | 49.4  | 49.4 | 49.4 | 1 |
| DAY 18    | 40.9  | 40.9 | 40.9 | 1 |
| DAY 21    | 41.0  | 41.0 | 41.0 | 1 |
| DAY 22    | 49.4  | 49.4 | 49.4 | 1 |
| DAY 23    | 41.6  | 41.6 | 41.6 | 1 |
| DAY 26    | 41.6  | 41.6 | 41.6 | 1 |
| DAY 29    | 42.3  | 42.3 | 42.3 | 1 |
| DAYS 0-29 | 38.2  | 38.2 | 38.2 | 1 |

NATURAL DELIVERY AND LITTER PARAMETERS  
NEW ZEALAND WHITE [CrI:KBL(NZW)BR] RABBITS

PERIOD: 2016 THROUGH 2020

NO. OF STUDIES

3

|                              | <u>MEAN</u> | <u>MIN</u> | <u>MAX</u> | <u>NO. STUDIES<br/>INCLUDED</u> |
|------------------------------|-------------|------------|------------|---------------------------------|
| LIVE LITTER SIZE AT WEIGHING |             |            |            |                                 |
| DAY 5                        | 8.6         | 8.5        | 8.7        | 2                               |
| DAY 7                        | 8.4         | 8.4        | 8.4        | 1                               |
| DAY 8                        | 8.0         | 8.0        | 8.0        | 1                               |
| DAY 10                       | 7.7         | 7.7        | 7.7        | 1                               |
| DAY 12                       | 7.5         | 7.5        | 7.5        | 1                               |
| DAY 14                       | 7.4         | 7.4        | 7.4        | 1                               |
| DAY 15                       | 7.8         | 7.8        | 7.8        | 1                               |
| DAY 18                       | 7.4         | 7.4        | 7.4        | 1                               |
| DAY 21                       | 7.2         | 7.2        | 7.2        | 1                               |
| DAY 22                       | 7.8         | 7.8        | 7.8        | 1                               |
| DAY 23                       | 6.4         | 6.4        | 6.4        | 1                               |
| DAY 26                       | 6.4         | 6.4        | 6.4        | 1                               |
| DAY 29                       | 6.4         | 6.4        | 6.4        | 1                               |

NATURAL DELIVERY AND LITTER PARAMETERS  
NEW ZEALAND WHITE [CrI:KBL(NZW)BR] RABBITS

PERIOD: 2016 THROUGH 2020

NO. OF STUDIES

3

|                           | <u>MEAN</u> | <u>MIN</u> | <u>MAX</u> | <u>NO. STUDIES<br/>INCLUDED</u> |
|---------------------------|-------------|------------|------------|---------------------------------|
| KIT WEIGHT/LITTER (GRAMS) |             |            |            |                                 |
| DAY 4                     | 75.8        | 75.8       | 75.8       | 1                               |
| DAY 5                     | 85.1        | 84.0       | 86.1       | 2                               |
| DAY 7                     | 106.5       | 104.5      | 108.6      | 2                               |
| DAY 8                     | 120.0       | 120.0      | 120.0      | 1                               |
| DAY 10                    | 142.6       | 136.7      | 148.5      | 2                               |
| DAY 12                    | 177.3       | 177.3      | 177.3      | 1                               |
| DAY 14                    | 203.1       | 196.2      | 209.9      | 2                               |
| DAY 15                    | 204.3       | 204.3      | 204.3      | 1                               |
| DAY 18                    | 283.3       | 244.9      | 321.6      | 2                               |
| DAY 21                    | 328.9       | 283.2      | 374.5      | 2                               |
| DAY 22                    | 339.5       | 284.1      | 394.9      | 2                               |
| DAY 23                    | 370.9       | 324.5      | 417.3      | 2                               |
| DAY 26                    | 463.7       | 407.5      | 519.9      | 2                               |
| DAY 28                    | 636.1       | 636.1      | 636.1      | 1                               |
| DAY 29                    | 555.8       | 503.0      | 608.6      | 2                               |

REPRODUCTIVE INDICES  
NEW ZEALAND WHITE [Hra:(NZW)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION

PERIOD: 2016 THROUGH 2020

|                                                | FULL<br>STUDIES | DOSE RANGE<br>STUDIES |
|------------------------------------------------|-----------------|-----------------------|
| NO. OF STUDIES INCLUDED                        | 36              | 31                    |
| NO. OF RABBITS TESTED                          | 756             | 182                   |
| NO. OF RABBITS PREGNANT                        | 735             | 178                   |
| NO. FOUND DEAD                                 | 3               | 1                     |
| NO. UNSCHEDULED DEATHS                         | 3               | 1                     |
| NO. ABORTED                                    | 3               | 0                     |
| NO. DELIVERED                                  | 2               | 1                     |
| CAESAREAN-SECTIONED ON GD 29                   | 723             | 174                   |
| NO. OF RABBITS WITH SINGLE<br>CONCEPTUS LITTER |                 |                       |
| LIVE:                                          | 1               | 0                     |
| RESORBED:                                      | 0               | 0                     |
| ABORTED:                                       | 0               | 0                     |

|                                            | <u>MEAN OR %</u> | <u>MIN</u> | <u>MAX</u> | <u>MEAN OR %</u> | <u>MIN</u> | <u>MAX</u> |
|--------------------------------------------|------------------|------------|------------|------------------|------------|------------|
| % PREGNANT                                 | 97.3             | 86.4       | 100.0      | 97.7             | 75.0       | 100.0      |
| CORPORA LUTEA                              | 10.0             | 9.2        | 11.1       | 10.3             | 8.2        | 12.0       |
| IMPLANTATIONS                              | 9.4              | 8.1        | 10.6       | 9.3              | 7.6        | 11.3       |
| PREIMPLANTATION LOSS (%)                   | 6.3              | 1.8        | 14.7       | 9.1              | 0.0        | 29.2       |
| LITTER SIZES                               |                  |            |            |                  |            |            |
| LIVE FETUSES                               | 9.1              | 8.0        | 10.1       | 9.1              | 7.5        | 10.7       |
| DEAD FETUSES                               | 0.0              | 0.0        | 0.1        | 0.0              | 0.0        | 0.0        |
| TOTAL RESORPTIONS                          | 0.3              | 0.1        | 1.1        | 0.3              | 0.0        | 1.0        |
| EARLY RESORPTIONS                          | 0.2              | 0.0        | 0.5        | 0.2              | 0.0        | 1.0        |
| LATE RESORPTIONS                           | 0.1              | 0.0        | 0.8        | 0.1              | 0.0        | 0.7        |
| POSTIMPLANTATION LOSS (%)                  | 3.2              | 0.9        | 9.3        | 2.6              | 0.0        | 10.0       |
| DOES WITH ANY RESORPTIONS (%)              | 24.1             | 5.0        | 55.0       | 18.4             | 0.0        | 67.0       |
| DOES WITH ALL CONCEPTUSES<br>RESORBED (%)  | 0.4              | 0.0        | 5.0        | 0.0              | 0.0        | 0.0        |
| DOES WITH ONE OR MORE<br>VIALE FETUSES (%) | 98.5             | 82.0       | 100.0      | 98.3             | 80.0       | 100.0      |

REPRODUCTIVE INDICES  
NEW ZEALAND WHITE [Hra:(NZW)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION

PERIOD: 2016 THROUGH 2020

| NO. OF STUDIES INCLUDED                  | FULL<br>STUDIES<br>36 |            |            | DOSE RANGE<br>STUDIES<br>31 |            |            |
|------------------------------------------|-----------------------|------------|------------|-----------------------------|------------|------------|
|                                          | <u>MEAN OR %</u>      | <u>MIN</u> | <u>MAX</u> | <u>MEAN OR %</u>            | <u>MIN</u> | <u>MAX</u> |
| DOES WITH NORMAL<br>PLACENTAE (%)        | 98.2                  | 82.0       | 100.0      | 100.0                       | 100.0      | 100.0      |
| SEX RATIO (% MALES/LITTER)               | 49.2                  | 40.7       | 57.3       | 50.6                        | 34.4       | 71.0       |
| LIVE FETAL BODY WEIGHTS<br>GRAMS/LITTER: | 41.4                  | 38.6       | 43.4       | 41.0                        | 37.4       | 45.2       |
| MALE FETUSES:                            | 41.7                  | 38.9       | 44.3       | 41.6                        | 38.6       | 45.8       |
| FEMALE FETUSES:                          | 40.7                  | 38.0       | 42.9       | 40.9                        | 36.1       | 44.8       |

FETAL EXTERNAL ABNORMALITIES  
NEW ZEALAND WHITE [Hra:(NZW)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
DOSE RANGE FINDING STUDIES

PERIOD: 2016 THROUGH 2020

|                           |     |
|---------------------------|-----|
| NO. STUDIES INCLUDED      | 5   |
| NO. LITTERS EXAMINED      | 22  |
| NO. LIVE FETUSES EXAMINED | 199 |

|                         |         | ABNORMALITIES               |   | N | RANGE/STUDY |          |
|-------------------------|---------|-----------------------------|---|---|-------------|----------|
|                         |         |                             |   |   | N           | %        |
| FACE                    | Snout   | : Short                     | L | 1 | 0-1         | (0-33.3) |
|                         |         |                             | F | 1 | 0-1         | (0-3.1)  |
| MOUTH                   | Tooth   | : Absent                    | L | 1 | 0-1         | (0-33.3) |
|                         |         |                             | F | 1 | 0-1         | (0-3.1)  |
| TRUNK                   |         | : Umbilicus, hernia         | L | 1 | 0-1         | (0-14.3) |
|                         |         |                             | F | 1 | 0-1         | (0-1.3)  |
|                         |         | : Gastroschisis             | L | 1 | 0-1         | (0-16.7) |
|                         |         |                             | F | 1 | 0-1         | (0-2.0)  |
|                         |         | : Localized subcutis, edema | L | 1 | 0-1         | (0-14.3) |
|                         |         |                             | F | 1 | 0-1         | (0-1.2)  |
|                         |         | : Abdomen, distended        | L | 1 | 0-1         | (0-14.3) |
|                         |         |                             | F | 1 | 0-1         | (0-1.2)  |
| FORE AND/OR HINDLIMB(S) | Forepaw | : Hyperflexion              | L | 1 | 0-1         | (0-16.7) |
|                         |         |                             | F | 1 | 0-1         | (0-1.4)  |

L: LITTER INCIDENCE

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Note: All summary values are based on studies with fetal findings.

FETAL EXTERNAL ABNORMALITIES  
NEW ZEALAND WHITE [Hra:(NZW)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

PERIOD: 2016 THROUGH 2020

NO. STUDIES INCLUDED 14

NO. LITTERS EXAMINED 278

NO. LIVE FETUSES EXAMINED 2517

|           |        | ABNORMALITIES             | RANGE/STUDY |   |             |
|-----------|--------|---------------------------|-------------|---|-------------|
|           |        |                           | N           | N | %           |
| FACE      | Eye    | : Open eye                | L           | 1 | 0-1 (0-5.0) |
|           |        |                           | F           | 1 | 0-1 (0-0.6) |
|           |        | : Bulge, absent           | L           | 2 | 0-1 (0-5.0) |
|           |        |                           | F           | 2 | 0-1 (0-0.6) |
|           |        | : Bulge, depression       | L           | 1 | 0-1 (0-5.0) |
|           |        |                           | F           | 1 | 0-1 (0-0.5) |
|           | Naris  | : Absent                  | L           | 1 | 0-1 (0-5.0) |
|           |        |                           | F           | 1 | 0-1 (0-0.5) |
| HEAD/NECK | Head   | : Acephalostomia          | L           | 1 | 0-1 (0-5.0) |
|           |        |                           | F           | 1 | 0-1 (0-0.5) |
|           |        | : Misshapen               | L           | 1 | 0-1 (0-5.0) |
|           |        |                           | F           | 1 | 0-1 (0-0.6) |
|           |        | : Meningocele             | L           | 1 | 0-1 (0-5.0) |
|           |        |                           | F           | 1 | 0-1 (0-0.6) |
|           |        | : Exencephaly             | L           | 1 | 0-1 (0-4.8) |
|           |        |                           | F           | 1 | 0-1 (0-0.6) |
| MOUTH     | Tongue | : Fused to floor of mouth | L           | 1 | 0-1 (0-5.0) |
|           |        |                           | F           | 1 | 0-1 (0-0.5) |
| EAR       | Pinna  | : Small                   | L           | 1 | 0-1 (0-5.0) |
|           |        |                           | F           | 1 | 0-1 (0-0.5) |

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Updated June 2021



FETAL EXTERNAL ABNORMALITIES  
NEW ZEALAND WHITE [Hra:(NZW)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

|                         | ABNORMALITIES            |   | RANGE/STUDY |     |          |
|-------------------------|--------------------------|---|-------------|-----|----------|
|                         |                          |   | N           | N   | %        |
| TRUNK                   | : Umbilicus, hernia      | L | 4           | 0-2 | (0-10.5) |
|                         |                          | F | 4           | 0-2 | (0-1.3)  |
|                         | : Gastroschisis          | L | 2           | 0-1 | (0-5.3)  |
|                         |                          | F | 2           | 0-1 | (0-0.7)  |
|                         | : Thoracogastroschisis   | L | 1           | 0-1 | (0-5.0)  |
|                         |                          | F | 1           | 0-1 | (0-0.5)  |
|                         | : Meningocele            | L | 1           | 0-1 | (0-4.5)  |
|                         |                          | F | 1           | 0-1 | (0-0.5)  |
|                         | : Abdomen, distended     | L | 2           | 0-1 | (0-9.1)  |
|                         |                          | F | 2           | 0-2 | (0-0.8)  |
|                         | Anus                     |   |             |     |          |
|                         | : Absent                 | L | 1           | 0-1 | (0-4.8)  |
|                         |                          | F | 1           | 0-1 | (0-0.8)  |
| FORE AND/OR HINDLIMB(S) | Forepaw(s)               |   |             |     |          |
|                         |                          |   |             |     |          |
|                         | : Hyperextension         | L | 2           | 0-1 | (0-5.3)  |
|                         |                          | F | 2           | 0-1 | (0-0.6)  |
|                         | : Malrotated             | L | 1           | 0-1 | (0-4.5)  |
|                         |                          | F | 1           | 0-1 | (0-0.5)  |
|                         | : Hyperflexion           | L | 4           | 0-1 | (0-6.7)  |
|                         |                          | F | 4           | 0-1 | (0-0.7)  |
|                         | Hindpaw(s)               |   |             |     |          |
|                         |                          |   |             |     |          |
|                         | : Hyperextension         | L | 4           | 0-2 | (0-10.0) |
|                         |                          | F | 4           | 0-2 | (0-1.1)  |
|                         | : Malrotated             | L | 1           | 0-1 | (0-4.5)  |
|                         |                          | F | 1           | 0-1 | (0-0.5)  |
|                         | Paw/digit                |   |             |     |          |
|                         |                          |   |             |     |          |
|                         | : Forepaw, absent        | L | 3           | 0-1 | (0-5.3)  |
|                         |                          | F | 3           | 0-1 | (0-0.6)  |
|                         | : Hindpaw, brachydactyly | L | 1           | 0-1 | (0-4.8)  |
|                         |                          | F | 1           | 0-1 | (0-0.8)  |
|                         | Claw/nail                |   |             |     |          |
|                         |                          |   |             |     |          |
|                         | : Small                  | L | 1           | 0-1 | (0-4.8)  |
|                         |                          | F | 1           | 0-1 | (0-0.8)  |
|                         | Hindlimb(s)              |   |             |     |          |
|                         |                          |   |             |     |          |
|                         | : Malrotated             | L | 4           | 0-2 | (0-10.0) |
|                         |                          | F | 4           | 0-2 | (0-1.1)  |
| TAIL                    | : Short                  | L | 1           | 0-1 | (0-4.8)  |
|                         |                          | F | 1           | 0-1 | (0-0.6)  |

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Note: All summary values are based on studies with fetal findings.

Updated June 2021

FETAL SOFT TISSUE ABNORMALITIES  
NEW ZEALAND WHITE [Hra:(NZW)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
DOSE RANGE FINDING STUDIES

PERIOD: 2016 THROUGH 2020

NO. OF STUDIES INCLUDED 10

NO. LITTERS EXAMINED 51

NO. FETUSES EXAMINED 566

| ABNORMALITIES                                    | RANGE/STUDY |     |          |
|--------------------------------------------------|-------------|-----|----------|
|                                                  | N           | N   | %        |
| <b>HEART</b>                                     |             |     |          |
| : Ventricular septum defect                      | L 1         | 0-1 | (0-11.1) |
| (previously, Interventricular septal defect)     | F 1         | 0-1 | (0-1.3)  |
| : Membranous ventricular septal defect           | L 3         | 0-2 | (0-28.6) |
|                                                  | F 3         | 0-2 | (0-2.8)  |
| : Ventricle, small                               | L 1         | 0-1 | (0-11.1) |
|                                                  | F 1         | 0-1 | (0-1.3)  |
| : Large                                          | L 2         | 0-1 | (0-14.3) |
|                                                  | F 2         | 0-1 | (0-1.6)  |
| : Misshapen                                      | L 1         | 0-1 | (0-14.3) |
|                                                  | F 1         | 0-1 | (0-1.6)  |
| : Atrium, misshapen                              | L 1         | 0-1 | (0-14.3) |
|                                                  | F 1         | 0-1 | (0-1.6)  |
| : Left A-V valve, absent                         | L 1         | 0-1 | (0-14.3) |
|                                                  | F 1         | 0-1 | (0-1.6)  |
| <b>VESSELS</b>                                   |             |     |          |
| : Innominate artery, absent                      | L 2         | 0-1 | (0-12.5) |
|                                                  | F 2         | 0-1 | (0-1.3)  |
| : Aorta, distended                               | L 1         | 0-1 | (0-14.3) |
|                                                  | F 1         | 0-1 | (0-1.6)  |
| : Aortic arch, interrupted                       | L 1         | 0-1 | (0-11.1) |
|                                                  | F 1         | 0-1 | (0-1.3)  |
| : Subclavian artery, right, retroesophageal      | L 1         | 0-1 | (0-12.5) |
|                                                  | F 1         | 0-1 | (0-1.3)  |
| : Subclavian artery origin, right, malpositioned | L 1         | 0-1 | (0-12.5) |
|                                                  | F 1         | 0-1 | (0-1.3)  |
| <b>LUNGS</b>                                     |             |     |          |
| : Lobe, absent                                   | L 8         | 0-3 | (0-42.9) |
|                                                  | F 12        | 0-7 | (0-12.8) |
| <b>KIDNEY(S)</b>                                 |             |     |          |
| : Absent                                         | L 3         | 0-1 | (0-14.3) |
|                                                  | F 3         | 0-1 | (0-1.8)  |
| : Malpositioned                                  | L 2         | 0-1 | (0-25.0) |
|                                                  | F 2         | 0-1 | (0-2.8)  |
| <b>BRAIN</b>                                     |             |     |          |
| : Lateral ventricle, dilatation, minimal         | L 1         | 0-1 | (0-14.3) |
|                                                  | F 1         | 0-1 | (0-1.6)  |

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Note: All summary values are based on studies with fetal findings.

Updated June 2021

FETAL SOFT TISSUE ABNORMALITIES  
NEW ZEALAND WHITE [Hra:(NZW)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
DOSE RANGE FINDING STUDIES

|             | ABNORMALITIES           | RANGE/STUDY |     |          |
|-------------|-------------------------|-------------|-----|----------|
|             |                         | N           | N   | %        |
| GENERAL     | : Abdomen, fluid-filled | L 2         | 0-1 | (0-14.3) |
|             |                         | F 2         | 0-1 | (0-1.6)  |
| GALLBLADDER | : Small                 | L 1         | 0-1 | (0-14.3) |
|             |                         | F 1         | 0-1 | (0-1.3)  |
| LIVER       | : Lobe, misshapen       | L 2         | 0-1 | (0-14.3) |
|             |                         | F 2         | 0-1 | (0-1.8)  |
|             | : Lobe, discolored      | L 1         | 0-1 | (0-14.3) |
|             |                         | F 1         | 0-1 | (0-1.8)  |
| URETER      | : Absent                | L 2         | 0-1 | (0-14.3) |
|             |                         | F 2         | 0-1 | (0-1.8)  |

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Note: All summary values are based on studies with fetal findings.

*Updated June 2021*

FETAL SOFT TISSUE ABNORMALITIES  
NEW ZEALAND WHITE [Hra:(NZW)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

PERIOD: 2016 THROUGH 2020

NO. OF STUDIES INCLUDED 25

NO. LITTERS EVALUATED 498  
NO. FETUSES EVALUATED 4502  
NO. HEADS EVALUATED 4502  
NO. BODIES EVALUATED 4502

|       |                                                     | ABNORMALITIES |   | RANGE/STUDY |          |
|-------|-----------------------------------------------------|---------------|---|-------------|----------|
|       |                                                     |               | N | N           | %        |
| BRAIN |                                                     |               |   |             |          |
|       | : Small                                             | L             | 1 | 0-1         | (0-4.8)  |
|       |                                                     | F             | 1 | 0-1         | (0-0.6)  |
|       | : Absent                                            | L             | 2 | 0-1         | (0-5.0)  |
| EYES  |                                                     | F             | 2 | 0-1         | (0-0.6)  |
|       | : Small                                             | L             | 5 | 0-2         | (0-9.1)  |
|       |                                                     | F             | 8 | 0-3         | (0-1.5)  |
|       | : Absent                                            | L             | 1 | 0-1         | (0-5.0)  |
|       |                                                     | F             | 1 | 0-1         | (0-0.6)  |
|       | : Circumcorneal hemorrhage                          | L             | 5 | 0-1         | (0-5.3)  |
|       |                                                     | F             | 6 | 0-2         | (0-1.0)  |
|       | : Lens, opacity                                     | L             | 1 | 0-1         | (0-4.5)  |
|       |                                                     | F             | 1 | 0-1         | (0-0.5)  |
|       |                                                     |               |   |             |          |
| HEART |                                                     |               |   |             |          |
|       | : Misshapen                                         | L             | 1 | 0-1         | (0-5.0)  |
|       |                                                     | F             | 1 | 0-1         | (0-0.5)  |
|       | : Atrium, small                                     | L             | 1 | 0-1         | (0-5.3)  |
|       |                                                     | F             | 1 | 0-1         | (0-0.5)  |
|       | : Ventricular septum defect                         | L             | 2 | 0-1         | (0-5.3)  |
|       | <i>(Previously, Interventricular septal defect)</i> | F             | 2 | 0-1         | (0-0.6)  |
|       | : Membranous ventricular septal defect              | L             | 4 | 0-2         | (0-10.0) |
|       |                                                     | F             | 4 | 0-2         | (0-0.9)  |
|       | : Muscular ventricular septal defect                | L             | 2 | 0-1         | (0-6.7)  |
|       |                                                     | F             | 2 | 0-1         | (0-1.0)  |
|       | : Septum, absent                                    | L             | 2 | 0-1         | (0-5.3)  |
|       |                                                     | F             | 2 | 0-1         | (0-0.6)  |
|       | : Malpositioned                                     | L             | 1 | 0-1         | (0-5.0)  |
|       |                                                     | F             | 1 | 0-1         | (0-0.5)  |

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Updated June 2021

FETAL SOFT TISSUE ABNORMALITIES  
NEW ZEALAND WHITE [Hra:(NZW)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

| VESSELS | ABNORMALITIES                                                 |   | RANGE/STUDY |     |         |
|---------|---------------------------------------------------------------|---|-------------|-----|---------|
|         |                                                               |   | N           | N   | %       |
|         | : Innominate artery, absent                                   | L | 5           | 0-1 | (0-5.3) |
|         |                                                               | F | 5           | 0-1 | (0-0.6) |
|         | : Ductus arteriosus, absent                                   | L | 1           | 0-1 | (0-5.0) |
|         |                                                               | F | 1           | 0-1 | (0-0.5) |
|         | : Patent ductus, arteriosus                                   | L | 1           | 0-1 | (0-5.0) |
|         |                                                               | F | 1           | 0-1 | (0-0.5) |
|         | : Aortic arch, dilated                                        | L | 4           | 0-1 | (0-5.3) |
|         |                                                               | F | 4           | 0-1 | (0-0.6) |
|         | : Aortic arch, absent                                         | L | 1           | 0-1 | (0-5.0) |
|         |                                                               | F | 1           | 0-1 | (0-0.5) |
|         | : Aortic arch, right-sided                                    | L | 1           | 0-1 | (0-5.0) |
|         |                                                               | F | 1           | 0-1 | (0-0.5) |
|         | : Persistent truncus arteriosus                               | L | 3           | 0-1 | (0-6.7) |
|         |                                                               | F | 3           | 0-1 | (0-0.7) |
|         | : Interrupted aortic arch                                     | L | 3           | 0-1 | (0-5.0) |
|         |                                                               | F | 3           | 0-1 | (0-0.6) |
|         | : Pulmonary trunk, dilated                                    | L | 1           | 0-1 | (0-5.0) |
|         |                                                               | F | 1           | 0-1 | (0-0.5) |
|         | : Pulmonary trunk, narrow                                     | L | 2           | 0-1 | (0-5.3) |
|         |                                                               | F | 2           | 0-1 | (0-0.6) |
|         | : Pulmonary trunk, malpositioned                              | L | 1           | 0-1 | (0-5.0) |
|         |                                                               | F | 1           | 0-1 | (0-0.5) |
|         | : Pulmonary trunk, right-sided                                | L | 1           | 0-1 | (0-5.0) |
|         |                                                               | F | 1           | 0-1 | (0-0.6) |
|         | : Carotid, malpositioned                                      | L | 1           | 0-1 | (0-5.0) |
|         |                                                               | F | 1           | 0-1 | (0-0.6) |
|         | : Carotid origin, left, malpositioned                         | L | 1           | 0-1 | (0-5.0) |
|         |                                                               | F | 1           | 0-1 | (0-0.5) |
|         | : Carotid origin, right, malpositioned                        | L | 1           | 0-1 | (0-5.0) |
|         |                                                               | F | 1           | 0-1 | (0-0.5) |
|         | : Subclavian artery origin, malpositioned                     | L | 3           | 0-1 | (0-5.3) |
|         |                                                               | F | 3           | 0-1 | (0-0.6) |
|         | : Subclavian artery origin, left, malpositioned               | L | 1           | 0-1 | (0-5.0) |
|         |                                                               | F | 1           | 0-1 | (0-0.5) |
|         | : Subclavian artery origin, right, malpositioned              | L | 1           | 0-1 | (0-5.0) |
|         |                                                               | F | 1           | 0-1 | (0-0.5) |
|         | : Subclavian artery, retroesophageal                          | L | 2           | 0-1 | (0-5.3) |
|         |                                                               | F | 2           | 0-1 | (0-0.5) |
|         | : Subclavian artery, supernumerary                            | L | 1           | 0-1 | (0-5.6) |
|         |                                                               | F | 1           | 0-1 | (0-0.6) |
|         | : Left subclavian arises from pulmonary artery                | L | 1           | 0-1 | (0-5.0) |
|         |                                                               | F | 1           | 0-1 | (0-0.6) |
|         | : Right subclavian arises to the left of the left subclavian  | L | 1           | 0-1 | (0-5.0) |
|         |                                                               | F | 1           | 0-1 | (0-0.5) |
|         | : Right subclavian passes dorsal to the trachea and esophagus | L | 2           | 0-1 | (0-5.0) |
|         |                                                               | F | 2           | 0-1 | (0-0.6) |
|         | : Great vessels, transposition                                | L | 2           | 0-1 | (0-5.3) |
|         |                                                               | F | 2           | 0-1 | (0-0.5) |

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Updated June 2021

FETAL SOFT TISSUE ABNORMALITIES  
NEW ZEALAND WHITE [Hra:(NZW)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

| ABNORMALITIES         |                              |   | RANGE/STUDY |     |          |
|-----------------------|------------------------------|---|-------------|-----|----------|
|                       |                              |   | N           | N   | %        |
| LUNGS                 | : Small                      | L | 6           | 0-1 | (0-5.0)  |
|                       |                              | F | 6           | 0-1 | (0-0.6)  |
|                       | : Lobe, absent               | L | 25          | 0-5 | (0-22.7) |
|                       |                              | F | 33          | 0-7 | (0-3.6)  |
| DIAPHRAGM             | : Hernia                     | L | 3           | 0-1 | (0-5.0)  |
|                       |                              | F | 4           | 0-2 | (0-1.0)  |
| GENERAL               | : Abdomen, fluid filled      | L | 2           | 0-2 | (0-9.1)  |
|                       |                              | F | 2           | 0-2 | (0-0.8)  |
| LIVER                 | : Liver, malpositioned       | L | 3           | 0-2 | (0-10.0) |
|                       |                              | F | 3           | 0-2 | (0-2.2)  |
|                       | : Liver, large               | L | 2           | 0-1 | (0-5.0)  |
|                       |                              | F | 2           | 0-1 | (0-0.5)  |
|                       | : Abnormal texture           | L | 1           | 0-1 | (0-4.5)  |
|                       |                              | F | 1           | 0-1 | (0-0.4)  |
|                       | : Liver, misshapen           | L | 1           | 0-1 | (0-5.0)  |
|                       |                              | F | 1           | 0-1 | (0-0.5)  |
|                       | : Lobe, misshapen            | L | 5           | 0-1 | (0-4.8)  |
|                       |                              | F | 5           | 0-1 | (0-0.8)  |
|                       | : Lobe, malpositioned        | L | 3           | 0-1 | (0-4.8)  |
|                       |                              | F | 3           | 0-1 | (0-0.8)  |
|                       | : Lobe, discolored           | L | 1           | 0-1 | (0-5.0)  |
|                       |                              | F | 1           | 0-1 | (0-0.5)  |
| GALLBLADDER/BILE DUCT | : Gallbladder, absent        | L | 1           | 0-1 | (0-4.8)  |
|                       |                              | F | 1           | 0-1 | (0-0.8)  |
|                       | : Gallbladder, small         | L | 2           | 0-1 | (0-4.5)  |
|                       |                              | F | 4           | 0-3 | (0-0.5)  |
|                       | : Gallbladder, malpositioned | L | 1           | 0-1 | (0-5.3)  |
|                       |                              | F | 1           | 0-1 | (0-0.7)  |
| KIDNEY(S)             | : Low set                    | L | 1           | 0-1 | (0-5.0)  |
|                       |                              | F | 1           | 0-1 | (0-0.6)  |
|                       | : Renal pelvis, dilated      | L | 1           | 0-1 | (0-5.0)  |
|                       |                              | F | 1           | 0-1 | (0-0.6)  |
|                       | : Kidney, malpositioned      | L | 1           | 0-1 | (0-4.8)  |
|                       |                              | F | 1           | 0-1 | (0-0.8)  |

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FETAL SOFT TISSUE ABNORMALITIES  
NEW ZEALAND WHITE [Hra:(NZW)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

|                 | ABNORMALITIES   |   | RANGE/STUDY |     |          |
|-----------------|-----------------|---|-------------|-----|----------|
|                 |                 |   | N           | N   | %        |
| ADRENAL GLAND   | : Large         | L | 1           | 0-1 | (0-4.5)  |
|                 |                 | F | 3           | 0-1 | (0-1.5)  |
| STOMACH         | : Malpositioned | L | 2           | 0-1 | (0-4.8)  |
|                 |                 | F | 2           | 0-1 | (0-0.6)  |
| INTESTINES      | : Malpositioned | L | 4           | 0-2 | (0-10.5) |
|                 |                 | F | 5           | 0-3 | (0-2.0)  |
| THYMUS          | : Discolored    | L | 1           | 0-1 | (0-5.3)  |
|                 |                 | F | 1           | 0-1 | (0-0.5)  |
| GONAD           | : Ovary, cyst   | L | 2           | 0-1 | (0-4.8)  |
|                 |                 | F | 2           | 0-1 | (0-0.6)  |
| URINARY BLADDER | : Absent        | L | 1           | 0-1 | (0-4.8)  |
|                 |                 | F | 1           | 0-1 | (0-0.8)  |

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*Updated June 2021*

FETAL SKELETAL ABNORMALITIES  
NEW ZEALAND WHITE [Hra:(NZW)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
DOSE RANGE FINDING STUDIES

PERIOD: 2016 THROUGH 2020

NO. OF STUDIES INCLUDED 8

LITTERS EXAMINED 58

FETUSES EXAMINED 526

|           |                                    | RANGE/STUDY |    |     |          |
|-----------|------------------------------------|-------------|----|-----|----------|
|           | ABNORMALITIES                      |             | N  | N   | %        |
| SKULL     |                                    |             |    |     |          |
|           | Parietal                           |             |    |     |          |
|           | : Hole                             | L           | 1  | 0-1 | (0-11.1) |
|           |                                    | F           | 1  | 0-1 | (0-1.3)  |
| HYOID     |                                    |             |    |     |          |
|           | Ala(e)                             |             |    |     |          |
|           | : Angulated                        | L           | 1  | 0-1 | (0-16.7) |
|           |                                    | F           | 1  | 0-1 | (0-1.7)  |
|           | : Bent                             | L           | 5  | 0-2 | (0-22.2) |
|           |                                    | F           | 11 | 0-4 | (0-5.1)  |
| VERTEBRAE |                                    |             |    |     |          |
|           | Thoracic                           |             |    |     |          |
|           | : Arches and/or centra, fused      | L           | 1  | 0-1 | (0-11.1) |
|           |                                    | F           | 1  | 0-1 | (0-1.3)  |
|           | : Hemivertebra                     | L           | 1  | 0-1 | (0-11.1) |
|           |                                    | F           | 2  | 0-2 | (0-2.5)  |
|           | : Arch, misshapen                  | L           | 1  | 0-1 | (0-11.1) |
|           |                                    | F           | 1  | 0-1 | (0-1.3)  |
|           | Lumbar                             |             |    |     |          |
|           | : Centrum, fused                   | L           | 1  | 0-1 | (0-11.1) |
|           |                                    | F           | 1  | 0-1 | (0-1.3)  |
|           | : Centrum, unilateral ossification | L           | 1  | 0-1 | (0-11.1) |
|           |                                    | F           | 1  | 0-1 | (0-1.3)  |
|           | : Hemivertebra                     | L           | 2  | 0-1 | (0-11.1) |
|           |                                    | F           | 2  | 0-1 | (0-1.3)  |
|           | : Absent                           | L           | 1  | 0-1 | (0-14.3) |
|           |                                    | F           | 1  | 0-1 | (0-1.6)  |
|           | : Supernumerary                    | L           | 1  | 0-1 | (0-14.3) |
|           |                                    | F           | 1  | 0-1 | (0-3.6)  |
|           | Caudal                             |             |    |     |          |
|           | : One or more misaligned           | L           | 1  | 0-1 | (0-14.3) |
|           |                                    | F           | 1  | 0-1 | (0-1.6)  |
|           | : Incomplete ossification          | L           | 1  | 0-1 | (0-12.5) |
|           |                                    | F           | 1  | 0-1 | (0-1.0)  |
|           | Cervical                           |             |    |     |          |
|           | : Supernumerary rib, short         | L           | 3  | 0-2 | (0-22.2) |
|           |                                    | F           | 6  | 0-5 | (0-6.6)  |
|           | : Centrum, incomplete ossification | L           | 1  | 0-1 | (0-14.3) |
|           |                                    | F           | 1  | 0-1 | (0-1.6)  |

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FETAL SKELETAL ABNORMALITIES  
NEW ZEALAND WHITE [Hra:(NZW)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
DOSE RANGE FINDING STUDIES

|                                |      | RANGE/STUDY |           |
|--------------------------------|------|-------------|-----------|
| ABNORMALITIES                  | N    | N           | %         |
| <b>RIBS</b>                    |      |             |           |
| : One or more, split, branched | L 2  | 0-1         | (0-14.3)  |
|                                | F 2  | 0-1         | (0-1.6)   |
| : Short                        | L 1  | 0-1         | (0-11.1)  |
|                                | F 1  | 0-1         | (0-1.3)   |
| : Fused                        | L 2  | 0-1         | (0-25.0)  |
|                                | F 2  | 0-1         | (0-2.5)   |
| : Thoracolumbar, full          | L 13 | 0-7         | (0-100.0) |
|                                | F 42 | 0-26        | (0-41.9)  |
| : Thoracolumbar, short         | L 10 | 0-6         | (0-85.7)  |
|                                | F 20 | 0-13        | (0-21.0)  |
| <b>STERNUM</b>                 |      |             |           |
| Sternebrae                     |      |             |           |
| : Fused                        | L 9  | 0-3         | (0-33.3)  |
|                                | F 16 | 0-7         | (0-8.9)   |
| : Asymmetric                   | L 4  | 0-2         | (0-22.2)  |
|                                | F 4  | 0-2         | (0-2.5)   |
| : Bipartite ossification       | L 3  | 0-2         | (0-22.2)  |
|                                | F 3  | 0-2         | (0-2.5)   |
| : Incomplete ossification      | L 7  | 0-3         | (0-42.9)  |
|                                | F 13 | 0-9         | (0-14.5)  |
| : Isolated ossification        | L 2  | 0-1         | (0-14.3)  |
|                                | F 2  | 0-1         | (0-1.8)   |
| : Misshapen                    | L 3  | 0-2         | (0-22.2)  |
|                                | F 3  | 0-2         | (0-2.6)   |
| : Unossified                   | L 3  | 0-2         | (0-28.6)  |
|                                | F 4  | 0-2         | (0-5.2)   |
| <b>FORELIMB</b>                |      |             |           |
| Forepaw                        |      |             |           |
| : Phalanges, unossified        | L 9  | 0-5         | (0-71.4)  |
|                                | F 18 | 0-12        | (0-19.4)  |

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FETAL SKELETAL ABNORMALITIES  
NEW ZEALAND WHITE [Hra:(NZW)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

PERIOD: 2016 THROUGH 2020

|                         |      |
|-------------------------|------|
| NO. OF STUDIES INCLUDED | 36   |
| NO. LITTERS EVALUATED   | 718  |
| NO. FETUSES EVALUATED   | 6508 |
| NO. HEADS EVALUATED     | 6508 |
| NO. BODIES EVALUATED    | 6508 |

| SKULL       | ABNORMALITIES                | RANGE/STUDY |    |             |
|-------------|------------------------------|-------------|----|-------------|
|             |                              | N           | N  | %           |
| Suture bone | : Present                    | L           | 3  | 0-2 (0-9.5) |
|             |                              | F           | 3  | 0-2 (0-1.1) |
|             | : Absent                     | L           | 2  | 0-1 (0-5.6) |
|             |                              | F           | 2  | 0-1 (0-0.6) |
|             | : Incomplete ossification    | L           | 4  | 0-1 (0-6.7) |
|             |                              | F           | 12 | 0-9 (0-4.5) |
|             | : Misshapen                  | L           | 1  | 0-1 (0-4.8) |
|             |                              | F           | 1  | 0-1 (0-0.6) |
|             | : Bone present               | L           | 1  | 0-1 (0-5.0) |
|             |                              | F           | 1  | 0-1 (0-0.6) |
|             | : Large                      | L           | 1  | 0-1 (0-4.5) |
|             |                              | F           | 1  | 0-1 (0-0.5) |
|             | : Large                      | L           | 1  | 0-1 (0-4.5) |
|             |                              | F           | 1  | 0-1 (0-0.5) |
|             | : Misshapen                  | L           | 1  | 0-1 (0-5.0) |
|             |                              | F           | 1  | 0-1 (0-0.5) |
|             | : Absent                     | L           | 1  | 0-1 (0-5.0) |
|             |                              | F           | 1  | 0-1 (0-0.5) |
|             | : Misshapen                  | L           | 1  | 0-1 (0-5.0) |
|             |                              | F           | 1  | 0-1 (0-0.5) |
|             | : Contained a hole           | L           | 6  | 0-2 (0-9.1) |
|             |                              | F           | 6  | 0-2 (0-1.0) |
|             | : Isolated ossification site | L           | 3  | 0-1 (0-5.6) |
|             |                              | F           | 5  | 0-2 (0-1.1) |
|             | : Absent                     | L           | 2  | 0-1 (0-5.0) |
|             |                              | F           | 2  | 0-1 (0-0.6) |
|             | : Incomplete ossification    | L           | 3  | 0-1 (0-6.7) |
|             |                              | F           | 3  | 0-1 (0-0.7) |
|             | : Misshapen                  | L           | 2  | 0-1 (0-5.0) |
|             |                              | F           | 2  | 0-1 (0-0.6) |

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FETAL SKELETAL ABNORMALITIES  
NEW ZEALAND WHITE [Hra:(NZW)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

| SKULL (CONT.)       | ABNORMALITIES                                         | RANGE/STUDY |   |             |
|---------------------|-------------------------------------------------------|-------------|---|-------------|
|                     |                                                       | N           | N | %           |
| Presphenoid         | : Absent                                              | L           | 2 | 0-1 (0-5.6) |
|                     |                                                       | F           | 2 | 0-1 (0-0.6) |
| Pterygoid Processes | : Absent                                              | L           | 2 | 0-1 (0-5.6) |
|                     |                                                       | F           | 2 | 0-1 (0-0.6) |
| Interparietals      | : Incomplete ossification                             | L           | 4 | 0-1 (0-5.6) |
|                     |                                                       | F           | 4 | 0-1 (0-0.6) |
|                     | : Misshapen                                           | L           | 1 | 0-1 (0-4.5) |
|                     |                                                       | F           | 1 | 0-1 (0-0.5) |
|                     | : Absent                                              | L           | 3 | 0-1 (0-5.0) |
|                     |                                                       | F           | 3 | 0-1 (0-0.6) |
| Nasals              | : Suture bone<br>(previously contained an internasal) | L           | 3 | 0-2 (0-9.5) |
|                     |                                                       | F           | 3 | 0-2 (0-1.1) |
|                     | : Absent                                              | L           | 2 | 0-1 (0-5.0) |
|                     |                                                       | F           | 2 | 0-1 (0-0.6) |
|                     | : Supernumerary site                                  | L           | 1 | 0-1 (0-4.8) |
|                     |                                                       | F           | 1 | 0-1 (0-0.8) |
|                     | : Incomplete ossification                             | L           | 1 | 0-1 (0-6.7) |
|                     |                                                       | F           | 1 | 0-1 (0-0.7) |
|                     | : Isolated ossification site                          | L           | 1 | 0-1 (0-5.3) |
|                     |                                                       | F           | 1 | 0-1 (0-0.6) |
| Mandibles           | : Incomplete ossification                             | L           | 1 | 0-1 (0-6.7) |
|                     |                                                       | F           | 1 | 0-1 (0-0.7) |
| Premaxilla          | : Absent                                              | L           | 2 | 0-1 (0-5.0) |
|                     |                                                       | F           | 2 | 0-1 (0-0.6) |
|                     | : Incomplete ossification                             | L           | 1 | 0-1 (0-6.7) |
|                     |                                                       | F           | 1 | 0-1 (0-0.7) |
| Maxilla             | : Absent                                              | L           | 2 | 0-1 (0-5.0) |
|                     |                                                       | F           | 2 | 0-1 (0-0.6) |
|                     | : Incomplete ossification                             | L           | 1 | 0-1 (0-6.7) |
|                     |                                                       | F           | 1 | 0-1 (0-0.7) |
| Squamosal           | : Absent                                              | L           | 2 | 0-1 (0-5.6) |
|                     |                                                       | F           | 2 | 0-1 (0-0.6) |
|                     | : Misshapen                                           | L           | 3 | 0-1 (0-6.7) |
|                     |                                                       | F           | 3 | 0-1 (0-0.7) |
|                     | : Fused                                               | L           | 1 | 0-1 (0-5.6) |
|                     |                                                       | F           | 1 | 0-1 (0-0.6) |

L: LITTER INCIDENCE

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Updated June 2021

FETAL SKELETAL ABNORMALITIES  
NEW ZEALAND WHITE [Hra:(NZW)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

| SKULL (CONT.) | ABNORMALITIES    | RANGE/STUDY               |      |              |
|---------------|------------------|---------------------------|------|--------------|
|               |                  | N                         | N    | %            |
|               | Tympanic annulus | : Absent                  | L 2  | 0-1 (0-5.6)  |
|               |                  |                           | F 2  | 0-1 (0-0.6)  |
|               |                  | : Incomplete ossification | L 1  | 0-1 (0-6.7)  |
|               |                  |                           | F 1  | 0-1 (0-0.7)  |
|               | Zygomatics       | : Absent                  | L 2  | 0-1 (0-5.6)  |
|               |                  |                           | F 2  | 0-1 (0-0.6)  |
|               |                  | : Fused                   | L 2  | 0-1 (0-5.6)  |
|               |                  |                           | F 2  | 0-1 (0-0.6)  |
|               |                  | : Incomplete ossification | L 1  | 0-1 (0-5.6)  |
|               |                  |                           | F 1  | 0-1 (0-0.6)  |
|               |                  | : Arch, misshapen         | L 2  | 0-1 (0-5.0)  |
|               |                  |                           | F 4  | 0-3 (0-1.5)  |
|               | Palate           | : Absent                  | L 2  | 0-1 (0-5.0)  |
|               |                  |                           | F 2  | 0-1 (0-0.6)  |
|               | Supraoccipital   | : Absent                  | L 3  | 0-1 (0-5.6)  |
|               |                  |                           | F 3  | 0-1 (0-0.6)  |
|               |                  | : Misshapen               | L 1  | 0-1 (0-5.6)  |
|               |                  |                           | F 1  | 0-1 (0-0.6)  |
|               |                  | : Small                   | L 1  | 0-1 (0-5.0)  |
|               |                  |                           | F 1  | 0-1 (0-0.6)  |
| HYOID         | Ala(e)           | : Incomplete ossification | L 2  | 0-2 (0-10.0) |
|               |                  |                           | F 2  | 0-2 (0-1.0)  |
|               |                  | : Bent                    | L 64 | 0-5 (0-26.7) |
|               |                  |                           | F 74 | 0-7 (0-3.7)  |
|               |                  | : Bent, left              | L 3  | 0-2 (0-10.0) |
|               |                  |                           | F 3  | 0-2 (0-1.5)  |
|               |                  | : Bent, right             | L 4  | 0-2 (0-9.5)  |
|               |                  |                           | F 4  | 0-2 (0-1.0)  |
|               | Body             | : Incomplete ossification | L 5  | 0-1 (0-5.6)  |
|               |                  |                           | F 5  | 0-1 (0-0.6)  |
|               |                  | : Unossified              | L 3  | 0-1 (0-4.8)  |
|               |                  |                           | F 3  | 0-1 (0-0.6)  |

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Updated June 2021

FETAL SKELETAL ABNORMALITIES  
NEW ZEALAND WHITE [Hra:(NZW)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

| VERTEBRAE |          | ABNORMALITIES                                                    |   | RANGE/STUDY |     |          |
|-----------|----------|------------------------------------------------------------------|---|-------------|-----|----------|
|           |          |                                                                  |   | N           | N   | %        |
| VERTEBRAE | Cervical | : Arch, fused                                                    | L | 2           | 0-1 | (0-5.0)  |
|           |          |                                                                  | F | 2           | 0-1 | (0-0.6)  |
|           |          | : Arch, misshapen                                                | L | 1           | 0-1 | (0-5.0)  |
|           |          |                                                                  | F | 1           | 0-1 | (0-0.5)  |
|           |          | : Arch, incomplete ossification                                  | L | 2           | 0-1 | (0-5.9)  |
|           |          |                                                                  | F | 2           | 0-1 | (0-0.6)  |
|           |          | : Arches, large                                                  | L | 1           | 0-1 | (0-6.7)  |
|           |          |                                                                  | F | 1           | 0-1 | (0-0.7)  |
|           |          | : Centrum, fused                                                 | L | 3           | 0-1 | (0-6.7)  |
|           |          |                                                                  | F | 3           | 0-1 | (0-0.7)  |
|           |          | : Centrum, unilateral ossification                               | L | 6           | 0-2 | (0-10.5) |
|           |          |                                                                  | F | 6           | 0-2 | (0-1.1)  |
|           |          | : Centrum, incomplete ossification                               | L | 12          | 0-3 | (0-15.0) |
|           |          |                                                                  | F | 16          | 0-3 | (0-1.8)  |
|           |          | : Centrum, unossified                                            | L | 4           | 0-3 | (0-14.3) |
|           |          |                                                                  | F | 4           | 0-3 | (0-2.0)  |
|           |          | : Centrum, misaligned                                            | L | 1           | 0-1 | (0-5.0)  |
|           |          |                                                                  | F | 1           | 0-1 | (0-0.5)  |
|           |          | : Centrum, malpositioned                                         | L | 1           | 0-1 | (0-4.5)  |
|           |          |                                                                  | F | 1           | 0-1 | (0-0.5)  |
|           |          | : Centrum, bipartite ossification                                | L | 1           | 0-1 | (0-5.0)  |
|           |          |                                                                  | F | 1           | 0-1 | (0-0.6)  |
|           |          | : Centrum, isolated ossification site                            | L | 2           | 0-2 | (0-9.5)  |
|           |          |                                                                  | F | 2           | 0-2 | (0-1.1)  |
|           |          | : Hemivertebra                                                   | L | 2           | 0-1 | (0-6.7)  |
|           |          |                                                                  | F | 2           | 0-1 | (0-0.7)  |
|           |          | : Lateral ossification site<br>present at 7th cervical vertebra  | L | 1           | 0-1 | (0-4.8)  |
|           |          |                                                                  | F | 1           | 0-1 | (0-0.6)  |
|           |          | : Atlas, ventral arch, misshapen                                 | L | 1           | 0-1 | (0-5.0)  |
|           |          |                                                                  | F | 1           | 0-1 | (0-0.6)  |
|           |          | : Atlas, ventral arch, incomplete ossification                   | L | 1           | 0-1 | (0-5.6)  |
|           |          |                                                                  | F | 1           | 0-1 | (0-0.6)  |
|           |          | : Supernumerary                                                  | L | 1           | 0-1 | (0-4.8)  |
|           |          |                                                                  | F | 1           | 0-1 | (0-0.8)  |
|           |          | : Supernumerary rib, cervical, full                              | L | 8           | 0-2 | (0-13.3) |
|           |          |                                                                  | F | 11          | 0-3 | (0-2.1)  |
|           |          | : Supernumerary rib, cervical, short                             | L | 35          | 0-4 | (0-22.2) |
|           |          |                                                                  | F | 49          | 0-7 | (0-4.7)  |
|           | Thoracic | : Hemivertebra                                                   | L | 10          | 0-3 | (0-14.3) |
|           |          |                                                                  | F | 13          | 0-4 | (0-2.0)  |
|           |          | : Centrum, bipartite ossification                                | L | 1           | 0-1 | (0-5.0)  |
|           |          |                                                                  | F | 1           | 0-1 | (0-0.6)  |
|           |          | : Centrum, unilateral ossification                               | L | 6           | 0-1 | (0-5.3)  |
|           |          |                                                                  | F | 6           | 0-1 | (0-0.7)  |
|           |          | : Centrum, misshapen<br>(previously centrum, irregularly shaped) | L | 3           | 0-1 | (0-6.7)  |
|           |          |                                                                  | F | 3           | 0-1 | (0-0.8)  |
|           |          | : Centrum, misaligned                                            | L | 2           | 0-1 | (0-5.3)  |
|           |          |                                                                  | F | 2           | 0-1 | (0-0.7)  |
|           |          | : Centrum, unossified                                            | L | 2           | 0-1 | (0-6.7)  |
|           |          |                                                                  | F | 2           | 0-1 | (0-0.8)  |
|           |          | : Centrum, fused                                                 | L | 6           | 0-2 | (0-9.5)  |
|           |          |                                                                  | F | 7           | 0-2 | (0-1.4)  |
|           |          | : Centrum, incomplete ossification                               | L | 6           | 0-2 | (0-9.5)  |
|           |          |                                                                  | F | 7           | 0-3 | (0-2.0)  |

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Updated June 2021

FETAL SKELETAL ABNORMALITIES  
NEW ZEALAND WHITE [Hra:(NZW)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

| VERTEBRAE (CONT.) | ABNORMALITIES                                | RANGE/STUDY |     |          |
|-------------------|----------------------------------------------|-------------|-----|----------|
|                   |                                              | N           | N   | %        |
| Thoracic (Cont.)  | : Arch, small                                | L 8         | 0-2 | (0-13.3) |
|                   |                                              | F 8         | 0-2 | (0-1.6)  |
|                   | : Arch, incomplete ossification              | L 2         | 0-1 | (0-4.5)  |
|                   |                                              | F 2         | 0-1 | (0-0.5)  |
|                   | : Arch, misaligned                           | L 1         | 0-1 | (0-4.5)  |
|                   |                                              | F 1         | 0-1 | (0-0.5)  |
|                   | : Arch, fused                                | L 4         | 0-1 | (0-6.7)  |
|                   |                                              | F 4         | 0-1 | (0-0.8)  |
|                   | : Arch, large                                | L 1         | 0-1 | (0-4.5)  |
|                   |                                              | F 1         | 0-1 | (0-0.5)  |
|                   | : Supernumerary                              | L 1         | 0-1 | (0-4.8)  |
|                   |                                              | F 1         | 0-1 | (0-0.5)  |
| Lumbar            | : Hemivertebra                               | L 1         | 0-1 | (0-4.8)  |
|                   |                                              | F 1         | 0-1 | (0-0.5)  |
|                   | : Arch, fused                                | L 1         | 0-1 | (0-5.0)  |
|                   |                                              | F 1         | 0-1 | (0-0.6)  |
|                   | : Arch, misshapen                            | L 1         | 0-1 | (0-4.8)  |
|                   |                                              | F 1         | 0-1 | (0-0.8)  |
|                   | : Arch, misaligned                           | L 1         | 0-1 | (0-5.0)  |
|                   |                                              | F 1         | 0-1 | (0-0.6)  |
|                   | : Arch, Absent                               | L 1         | 0-1 | (0-4.5)  |
|                   |                                              | F 1         | 0-1 | (0-0.5)  |
|                   | : Arch, small                                | L 2         | 0-2 | (0-9.5)  |
|                   |                                              | F 2         | 0-2 | (0-1.3)  |
|                   | : Centrum, fused                             | L 2         | 0-1 | (0-4.8)  |
|                   |                                              | F 2         | 0-1 | (0-0.8)  |
|                   | : Centrum, unilateral ossification           | L 5         | 0-2 | (0-10.0) |
|                   |                                              | F 5         | 0-2 | (0-1.1)  |
|                   | : Centrum, small                             | L 1         | 0-1 | (0-5.0)  |
|                   |                                              | F 1         | 0-1 | (0-0.6)  |
|                   | : Centrum, misaligned                        | L 2         | 0-1 | (0-5.6)  |
|                   |                                              | F 2         | 0-1 | (0-0.6)  |
|                   | : Centrum, incomplete ossification           | L 3         | 0-2 | (0-9.5)  |
|                   |                                              | F 3         | 0-2 | (0-1.3)  |
|                   | : Centrum, unossified                        | L 1         | 0-1 | (0-5.0)  |
|                   |                                              | F 1         | 0-1 | (0-0.6)  |
|                   | : Arch, splayed (open)                       | L 1         | 0-1 | (0-4.5)  |
|                   | <i>(previously Arch, open)</i>               | F 1         | 0-1 | (0-0.5)  |
|                   | : Supernumerary                              | L 5         | 0-2 | (0-9.5)  |
|                   | <i>(previously supernumerary, 6 present)</i> | F 6         | 0-2 | (0-1.0)  |
| Sacral            | : Incomplete ossification                    | L 2         | 0-1 | (0-4.8)  |
|                   |                                              | F 2         | 0-1 | (0-0.6)  |
|                   | : Arch, fused                                | L 1         | 0-1 | (0-4.8)  |
|                   |                                              | F 1         | 0-1 | (0-0.8)  |
|                   | : Centrum, fused                             | L 1         | 0-1 | (0-4.8)  |
|                   |                                              | F 2         | 0-2 | (0-1.6)  |
|                   | : Hemivertebra                               | L 1         | 0-1 | (0-4.8)  |
|                   |                                              | F 1         | 0-1 | (0-0.8)  |

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Updated June 2021

FETAL SKELETAL ABNORMALITIES  
NEW ZEALAND WHITE [Hra:(NZW)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

| VERTEBRAE (CONT.) |  | ABNORMALITIES                          | RANGE/STUDY |      |          |
|-------------------|--|----------------------------------------|-------------|------|----------|
|                   |  |                                        | N           | N    | %        |
| Caudal            |  | : Misaligned                           | L 15        | 0-2  | (0-11.1) |
|                   |  |                                        | F 16        | 0-3  | (0-1.5)  |
|                   |  | : Fused                                | L 2         | 0-1  | (0-5.0)  |
|                   |  |                                        | F 2         | 0-1  | (0-0.8)  |
|                   |  | : Small                                | L 2         | 0-1  | (0-4.8)  |
|                   |  |                                        | F 2         | 0-1  | (0-0.8)  |
|                   |  | : Absent                               | L 1         | 0-1  | (0-4.8)  |
|                   |  |                                        | F 1         | 0-1  | (0-0.6)  |
|                   |  | : Hermivertebra                        | L 1         | 0-1  | (0-4.8)  |
|                   |  |                                        | F 1         | 0-1  | (0-0.8)  |
|                   |  | : Centrum, incomplete ossification     | L 1         | 0-1  | (0-5.0)  |
|                   |  |                                        | F 1         | 0-1  | (0-0.5)  |
|                   |  | : Incomplete ossification              | L 10        | 0-3  | (0-13.6) |
|                   |  |                                        | F 11        | 0-3  | (0-1.5)  |
|                   |  | : Unossified                           | L 1         | 0-1  | (0-4.5)  |
|                   |  |                                        | F 1         | 0-1  | (0-0.5)  |
|                   |  | : Misshapen                            | L 1         | 0-1  | (0-5.6)  |
|                   |  |                                        | F 1         | 0-1  | (0-0.6)  |
| RIBS              |  | : Fused                                | L 9         | 0-2  | (0-9.5)  |
|                   |  |                                        | F 10        | 0-2  | (0-1.4)  |
|                   |  | : Branched                             | L 6         | 0-2  | (0-10.0) |
|                   |  | <i>(previously split)</i>              | F 6         | 0-2  | (0-1.0)  |
|                   |  | : Nodulated                            | L 10        | 0-2  | (0-9.1)  |
|                   |  | <i>(previously thickened)</i>          | F 10        | 0-2  | (0-1.0)  |
|                   |  | : Flat                                 | L 2         | 0-2  | (0-9.1)  |
|                   |  |                                        | F 2         | 0-2  | (0-1.0)  |
|                   |  | : Misshapen                            | L 9         | 0-1  | (0-5.0)  |
|                   |  | <i>(previously irregularly shaped)</i> | F 9         | 0-1  | (0-0.6)  |
|                   |  | : Thick                                | L 1         | 0-1  | (0-4.5)  |
|                   |  | <i>(previously broad)</i>              | F 1         | 0-1  | (0-0.5)  |
|                   |  | : Short                                | L 5         | 0-3  | (0-14.3) |
|                   |  |                                        | F 5         | 0-3  | (0-1.8)  |
|                   |  | : Incompletely ossified                | L 3         | 0-1  | (0-5.9)  |
|                   |  |                                        | F 4         | 0-2  | (0-1.1)  |
|                   |  | : Interrupted                          | L 3         | 0-2  | (0-9.1)  |
|                   |  |                                        | F 3         | 0-2  | (0-1.0)  |
|                   |  | : Thoracolumbar, full                  | L 139       | 0-21 | (0-95.5) |
|                   |  | <i>(previously T13, supernumerary)</i> | F 529       | 0-85 | (0-46.9) |
|                   |  | : Thoracolumbar, full, minimal         | L 2         | 0-1  | (0-4.8)  |
|                   |  |                                        | F 2         | 0-1  | (0-0.6)  |
|                   |  | : Thoracolumbar, short                 | L 145       | 0-19 | (0-86.4) |
|                   |  | <i>(previously T13, short)</i>         | F 353       | 0-60 | (0-30.8) |
|                   |  | : Supernumerary                        | L 1         | 0-1  | (0-4.8)  |
|                   |  |                                        | F 1         | 0-1  | (0-0.5)  |
|                   |  | : Detached                             | L 1         | 0-1  | (0-4.8)  |
|                   |  | <i>(previously Unattached)</i>         | F 1         | 0-1  | (0-0.7)  |

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Updated June 2021

FETAL SKELETAL ABNORMALITIES  
NEW ZEALAND WHITE [Hra:(NZW)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

|               |             | ABNORMALITIES                          | RANGE/STUDY |      |          |
|---------------|-------------|----------------------------------------|-------------|------|----------|
|               |             |                                        | N           | N    | %        |
| STERNUM       | Sternebrae  |                                        |             |      |          |
|               |             | : Fused                                | L 86        | 0-7  | (0-33.3) |
|               |             |                                        | F 112       | 0-10 | (0-5.2)  |
|               |             | : Asymmetric                           | L 16        | 0-2  | (0-10.0) |
|               |             |                                        | F 16        | 0-2  | (0-1.1)  |
|               |             | : Incomplete ossification              | L 82        | 0-10 | (0-50.0) |
|               |             |                                        | F 114       | 0-14 | (0-8.7)  |
|               |             | : Misshapen                            | L 38        | 0-3  | (0-15.0) |
|               |             | <i>(previously irregularly shaped)</i> | F 42        | 0-5  | (0-3.2)  |
|               |             | : Large                                | L 1         | 0-1  | (0-5.0)  |
|               |             |                                        | F 1         | 0-1  | (0-0.5)  |
|               |             | : Small                                | L 1         | 0-1  | (0-5.3)  |
|               |             |                                        | F 1         | 0-1  | (0-0.6)  |
|               |             | : Sternoschisis                        | L 4         | 0-2  | (0-10.0) |
|               |             | <i>(previously Split)</i>              | F 5         | 0-2  | (0-1.1)  |
|               |             | : Unossified                           | L 47        | 0-9  | (0-40.9) |
|               |             |                                        | F 86        | 0-18 | (0-9.2)  |
|               |             | : Isolated ossification site           | L 46        | 0-5  | (0-26.3) |
|               |             |                                        | F 68        | 0-8  | (0-4.8)  |
|               |             | : Bipartite ossification               | L 25        | 0-3  | (0-16.7) |
|               |             |                                        | F 28        | 0-3  | (0-1.9)  |
|               |             | : Supernumerary site                   | L 4         | 0-2  | (0-10.5) |
|               |             |                                        | F 4         | 0-2  | (0-1.2)  |
| PELVIC GIRDLE | Pubis       |                                        |             |      |          |
|               |             | : Incomplete ossification              | L 8         | 0-2  | (0-9.5)  |
|               |             |                                        | F 9         | 0-2  | (0-1.1)  |
|               |             | : Unossified                           | L 5         | 0-1  | (0-6.7)  |
| FORELIMB(S)   | Phalanx     |                                        |             |      |          |
|               |             | : Absent                               | L 11        | 0-8  | (0-38.1) |
|               |             |                                        | F 21        | 0-18 | (0-9.3)  |
|               |             | : Unossified                           | L 64        | 0-13 | (0-61.9) |
|               |             |                                        | F 189       | 0-51 | (0-25.0) |
|               |             | : Small                                | L 1         | 0-1  | (0-5.6)  |
|               | Digit(s)    |                                        | F 1         | 0-1  | (0-0.6)  |
|               |             | : Absent                               | L 3         | 0-1  | (0-5.6)  |
|               | Metacarpals |                                        | F 3         | 0-1  | (0-0.6)  |
|               |             | : Absent                               | L 1         | 0-1  | (0-5.3)  |
|               |             |                                        | F 1         | 0-1  | (0-0.6)  |
| HINDLIMB(S)   | Phalanx     |                                        |             |      |          |
|               |             | : Unossified                           | L 3         | 0-2  | (0-9.1)  |
|               |             |                                        | F 4         | 0-3  | (0-1.5)  |
|               |             | : Small                                | L 1         | 0-1  | (0-5.0)  |
|               |             |                                        | F 1         | 0-1  | (0-0.6)  |
|               |             |                                        |             |      |          |

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FETAL SKELETAL OSSIFICATION SITES  
NEW ZEALAND WHITE [Hra:(NZW)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
DOSE RANGE FINDING STUDIES

PERIOD: 2016 THROUGH 2020

NO. OF STUDIES INCLUDED 5

NO. LITTERS EXAMINED 38

NO. FETUSES EXAMINED 349

|                       | MEAN  | MINIMUM | MAXIMUM |
|-----------------------|-------|---------|---------|
| HYOID                 | 1.00  | 1.00    | 1.00    |
| VERTEBRAE             |       |         |         |
| CERVICAL              | 7.00  | 7.00    | 7.00    |
| THORACIC              | 12.59 | 12.47   | 12.83   |
| LUMBAR                | 6.41  | 6.17    | 6.54    |
| SACRAL                | 4.00  | 4.00    | 4.00    |
| CAUDAL                | 15.66 | 15.41   | 15.97   |
| RIBS (Pairs)          | 12.53 | 12.39   | 12.80   |
| STERNUM               |       |         |         |
| MANUBRIUM             | 1.00  | 1.00    | 1.00    |
| STERNAL CENTERS       | 3.92  | 3.87    | 4.00    |
| XIPHOID               | 0.94  | 0.91    | 0.99    |
| FORELIMB <sup>a</sup> |       |         |         |
| CARPALS               | 0.00  | 0.00    | 0.00    |
| METACARPALS           | 4.96  | 4.90    | 5.00    |
| DIGITS                | 5.00  | 5.00    | 5.00    |
| PHALANGES             | 13.87 | 13.83   | 13.96   |
| HINDLIMB <sup>a</sup> |       |         |         |
| TARSALS               | 2.00  | 2.00    | 2.00    |
| METATARSALS           | 4.00  | 4.00    | 4.00    |
| DIGITS                | 4.00  | 4.00    | 4.00    |
| PHALANGES             | 12.00 | 12.00   | 12.00   |

a. Calculated as mean per limb

FETAL SKELETAL OSSIFICATION SITES  
NEW ZEALAND WHITE [Hra:(NZW)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

PERIOD: 2016 THROUGH 2020

NO. OF STUDIES INCLUDED 27

NO. LITTERS EXAMINED 529

NO. FETUSES EXAMINED 4819

|                       | MEAN  | MINIMUM | MAXIMUM |
|-----------------------|-------|---------|---------|
| HYOID                 | 1.01  | 0.99    | 1.18    |
| VERTEBRAE             |       |         |         |
| CERVICAL              | 7.00  | 7.00    | 7.00    |
| THORACIC              | 12.55 | 12.32   | 12.71   |
| LUMBAR                | 6.46  | 6.29    | 6.67    |
| SACRAL                | 4.00  | 4.00    | 4.00    |
| CAUDAL                | 15.68 | 15.27   | 15.90   |
| RIBS (Pairs)          | 12.49 | 12.30   | 12.63   |
| STERNUM               |       |         |         |
| MANUBRIUM             | 1.00  | 1.00    | 1.00    |
| STERNAL CENTERS       | 3.92  | 3.82    | 3.98    |
| XIPHOID               | 0.95  | 0.91    | 0.99    |
| FORELIMB <sup>a</sup> |       |         |         |
| CARPALS               | 0.00  | 0.00    | 0.00    |
| METACARPALS           | 4.96  | 4.86    | 5.00    |
| DIGITS                | 5.00  | 5.00    | 5.00    |
| PHALANGES             | 13.88 | 13.70   | 13.98   |
| HINDLIMB <sup>a</sup> |       |         |         |
| TARSALS               | 2.00  | 1.99    | 2.00    |
| METATARSALS           | 4.00  | 3.99    | 4.00    |
| DIGITS                | 4.00  | 4.00    | 4.00    |
| PHALANGES             | 11.99 | 11.90   | 12.00   |

a. Calculated as mean per limb

FEMALE MATING AND FERTILITY  
NEW ZEALAND WHITE [Hra:(NZW)SPF] RABBITS

PERIOD: 2011 THROUGH 2020

NO. OF STUDIES INCLUDED 6

SUMMARY

| TOTAL RABBITS                            |   | 227         |                |                |                 | NO. STUDIES |
|------------------------------------------|---|-------------|----------------|----------------|-----------------|-------------|
|                                          |   | <u>MEAN</u> | <u>MINIMUM</u> | <u>MAXIMUM</u> | <u>INCLUDED</u> |             |
| RABBITS IN COHABITATION                  | N | 38          | 6              | 54             | 6               |             |
| RABBITS THAT MATED                       | N | 35          | 6              | 51             | 6               |             |
|                                          | % | 92.5        | 85.2           | 100.0          | 6               |             |
| RABBITS WITH CONFIRMED MATING DATES      | N | 18          | 18             | 18             | 1               |             |
| MATING PERIOD                            |   |             |                |                |                 |             |
| 1st PAIRING                              | N | 11          | 6              | 15             | 2               |             |
|                                          | % | 91.7        | 83.3           | 100.0          | 2               |             |
| 2nd PAIRING                              | N | 0           | 0              | 0              | 2               |             |
|                                          | % | 0.0         | 0.0            | 0.0            | 2               |             |
| 3rd PAIRING                              | N | 1           | 0              | 1              | 2               |             |
|                                          | % | 2.8         | 0.0            | 5.6            | 2               |             |
| 4th PAIRING                              | N | 1           | 1              | 1              | 1               |             |
|                                          | % | 5.6         | 5.6            | 5.6            | 1               |             |
| 5th PAIRING                              | N | 0           | 0              | 0              | 1               |             |
|                                          | % | 0.0         | 0.0            | 0.0            | 1               |             |
| 6th PAIRING                              | N | 1           | 1              | 1              | 1               |             |
|                                          | % | 5.6         | 5.6            | 5.6            | 1               |             |
| FERTILITY INDEX <sup>1</sup>             | N | 32          | 6              | 48             | 6               |             |
|                                          | N | 35          | 6              | 51             | 6               |             |
|                                          | % | 92.1        | 83.3           | 100.0          | 6               |             |
| RABBITS PREGNANT/RABBITS IN COHABITATION | N | 32          | 6              | 48             | 6               |             |
|                                          | N | 38          | 6              | 54             | 6               |             |
|                                          | % | 85.3        | 71.4           | 100.0          | 6               |             |

<sup>1</sup> Number of pregnancies / number of rabbits that mated

Updated June 2021

NATURAL DELIVERY AND LITTER PARAMETERS  
NEW ZEALAND WHITE [Hra:NZW)SPF] RABBITS

PERIOD: 2012 THROUGH 2020

|                                                                  |      |                       |                |                |                             |
|------------------------------------------------------------------|------|-----------------------|----------------|----------------|-----------------------------|
| NO. OF STUDIES INCLUDED                                          | 7    | SUMMARY               |                |                |                             |
|                                                                  |      | <u>MEAN</u>           | <u>MINIMUM</u> | <u>MAXIMUM</u> | <u>NO. STUDIES INCLUDED</u> |
| RABBITS ASSIGNED TO NATURAL DELIVERY                             | N    | 175 = TOTAL RABBITS   |                |                |                             |
| FOUND DEAD                                                       | N    | 1 = TOTAL FOUND DEAD  |                |                |                             |
| ABORTED                                                          | N    | 1 = TOTAL ABORTED     |                |                |                             |
| PREGNANT                                                         | N    | 146 = TOTAL PREGNANT  |                |                |                             |
|                                                                  | %    | 83.3                  | 70.8           | 100.0          | 7                           |
| DELIVERED LITTERS                                                | N    | 144 = TOTAL DELIVERED |                |                |                             |
|                                                                  | %    | 100.0                 | 100.0          | 100.0          | 7                           |
| DURATION OF GESTATION IN DAYS                                    | MEAN | 32.3                  | 32.1           | 32.7           | 7                           |
| IMPLANTATION SITES PER DELIVERED LITTER                          | MEAN | 7.9                   | 7.2            | 8.7            | 7                           |
| DOES WITH STILLBORN KITS                                         | N    | 2.1                   | 0.0            | 6.0            | 7                           |
|                                                                  | %    | 10.5                  | 0.0            | 25.0           | 7                           |
| DOES WITH NO LIVEBORN KITS                                       | N    | 0.0                   | 0.0            | 0.0            | 7                           |
|                                                                  | %    | 0.0                   | 0.0            | 0.0            | 7                           |
| GESTATION INDEX (NO. RABBITS WITH LIVEBORN/NO. PREGNANT RABBITS) | %    | 100.0                 | 100.0          | 100.0          | 7                           |
| DOES WITH ALL KITS DYING DAYS 1-4 POSTPARTUM                     | %    | 3.7                   | 0.0            | 10.0           | 7                           |
| DAYS 5-21 POSTPARTUM                                             | N    | 0                     | 0              | 1              | 3                           |
|                                                                  | %    | 2.1                   | 0.0            | 6.2            | 3                           |
| DAYS 5-29 POSTPARTUM                                             | N    | 0                     | 0              | 0              | 1                           |
|                                                                  | %    | 0.0                   | 0.0            | 0.0            | 1                           |
| DAYS 5-35 POSTPARTUM                                             | N    | 1                     | 0              | 1              | 2                           |
|                                                                  | %    | 3.0                   | 0.0            | 5.9            | 2                           |

NATURAL DELIVERY AND LITTER PARAMETERS  
NEW ZEALAND WHITE [Hra:NZW)SPF] RABBITS

PERIOD: 2012 THROUGH 2020

|                                          |      | <u>MEAN</u> | <u>MINIMUM</u> | <u>MAXIMUM</u> | <u>NO. STUDIES INCLUDED</u> |
|------------------------------------------|------|-------------|----------------|----------------|-----------------------------|
| KITS DELIVERED (TOTAL)                   | N    | 161.7       | 113.0          | 220.0          | 7                           |
|                                          | MEAN | 7.8         | 7.1            | 8.8            | 7                           |
| LIVEBORN                                 | MEAN | 7.3         | 6.9            | 7.8            | 7                           |
|                                          | N    | 151         | 112            | 195            | 7                           |
|                                          | %    | 93.8        | 88.6           | 99.1           | 7                           |
| STILLBORN                                | MEAN | 0.2         | 0.0            | 0.8            | 7                           |
|                                          | N    | 4           | 0              | 12             | 7                           |
|                                          | %    | 2.6         | 0.0            | 9.2            | 7                           |
| UNKNOWN VITAL STATUS                     | N    | 6           | 0              | 22             | 7                           |
| KITS FOUND DEAD OR PRESUMED CANNIBALIZED |      |             |                |                |                             |
| DAYS 1-4                                 | N    | 15          | 2              | 31             | 5                           |
|                                          | N    | 148         | 112            | 185            | 5                           |
|                                          | %    | 10.6        | 1.1            | 18.8           | 5                           |
| DAYS 4-7                                 | N    | 17          | 6              | 27             | 2                           |
|                                          | N    | 157         | 126            | 187            | 2                           |
|                                          | %    | 9.6         | 4.8            | 14.4           | 2                           |
| DAYS 5-7                                 | N    | 6           | 2              | 12             | 5                           |
|                                          | N    | 132         | 95             | 183            | 5                           |
|                                          | %    | 4.3         | 1.9            | 8.5            | 5                           |
| DAYS 8-10                                | N    | 5           | 2              | 8              | 2                           |
|                                          | N    | 133         | 105            | 160            | 2                           |
|                                          | %    | 3.5         | 1.9            | 5.0            | 2                           |
| DAYS 8-11                                | N    | 7           | 7              | 7              | 1                           |
|                                          | N    | 120         | 120            | 120            | 1                           |
|                                          | %    | 5.8         | 5.8            | 5.8            | 1                           |
| DAYS 8-14                                | N    | 4           | 3              | 8              | 4                           |
|                                          | N    | 132         | 93             | 172            | 4                           |
|                                          | %    | 3.1         | 2.3            | 4.6            | 4                           |

NATURAL DELIVERY AND LITTER PARAMETERS  
NEW ZEALAND WHITE [Hra:NZW)SPF] RABBITS

PERIOD: 2012 THROUGH 2020

| KITS FOUND DEAD OR<br>PRESUMED CANNIBALIZED (CONT.) |   | <u>MEAN</u> | <u>MINIMUM</u> | <u>MAXIMUM</u> | <u>NO. STUDIES<br/>INCLUDED</u> |
|-----------------------------------------------------|---|-------------|----------------|----------------|---------------------------------|
| DAYS 11-14                                          | N | 1           | 0              | 2              | 2                               |
|                                                     | N | 128         | 103            | 152            | 2                               |
|                                                     | % | 0.7         | 0.0            | 1.3            | 2                               |
| DAYS 12-14                                          | N | 0           | 0              | 0              | 1                               |
|                                                     | N | 113         | 113            | 113            | 1                               |
|                                                     | % | 0.0         | 0.0            | 0.0            | 1                               |
| DAYS 15-17                                          | N | 0           | 0              | 0              | 1                               |
|                                                     | N | 113         | 113            | 113            | 1                               |
|                                                     | % | 0.0         | 0.0            | 0.0            | 1                               |
| DAYS 15-18                                          | N | 1           | 0              | 2              | 6                               |
|                                                     | N | 127         | 90             | 164            | 6                               |
|                                                     | % | 0.3         | 0.0            | 1.2            | 6                               |
| DAYS 18-21                                          | N | 1           | 1              | 1              | 1                               |
|                                                     | N | 113         | 113            | 113            | 1                               |
|                                                     | % | 0.9         | 0.9            | 0.9            | 1                               |
| DAYS 19-21                                          | N | 0           | 0              | 2              | 6                               |
|                                                     | N | 127         | 90             | 162            | 6                               |
|                                                     | % | 0.2         | 0.0            | 1.2            | 6                               |
| DAYS 22-24                                          | N | 0           | 0              | 0              | 1                               |
|                                                     | N | 103         | 103            | 103            | 1                               |
|                                                     | % | 0.0         | 0.0            | 0.0            | 1                               |
| DAYS 22-28                                          | N | 1           | 0              | 2              | 4                               |
|                                                     | N | 137         | 112            | 160            | 4                               |
|                                                     | % | 0.8         | 0.0            | 1.6            | 4                               |
| DAYS 25-29                                          | N | 0           | 0              | 0              | 1                               |
|                                                     | N | 103         | 103            | 103            | 1                               |
|                                                     | % | 0.0         | 0.0            | 0.0            | 1                               |
| DAYS 29-35                                          | N | 0           | 0              | 1              | 4                               |
|                                                     | N | 136         | 111            | 159            | 4                               |
|                                                     | % | 0.2         | 0.0            | 0.6            | 4                               |

NATURAL DELIVERY AND LITTER PARAMETERS  
NEW ZEALAND WHITE [Hra:NZW)SPF] RABBITS

PERIOD: 2012 THROUGH 2020

|                                        |      | <u>MEAN</u> | <u>MINIMUM</u> | <u>MAXIMUM</u> | <u>NO. STUDIES INCLUDED</u> |
|----------------------------------------|------|-------------|----------------|----------------|-----------------------------|
| VIABILITY INDEX                        | %    | 87.9        | 81.2           | 98.9           | 4                           |
| (No.Live kits PD4 / No.Live kits PD1)  | N    | 139         | 95             | 183            | 4                           |
|                                        | N    | 157         | 117            | 185            | 4                           |
| VIABILITY INDEX                        | %    | 95.5        | 95.5           | 95.5           | 1                           |
| (No.Live kits PD5 / No.Live kits PD1)  | N    | 107         | 107            | 107            | 1                           |
|                                        | N    | 112         | 112            | 112            | 1                           |
| VIABILITY INDEX                        | %    | 85.6        | 85.6           | 85.6           | 1                           |
| (No.Live kits PD7 / No.Live kits PD4)  | N    | 160         | 160            | 160            | 1                           |
|                                        | N    | 187         | 187            | 187            | 1                           |
| LACTATION INDEX                        | %    | 94.8        | 94.7           | 94.8           | 2                           |
| (No.Live kits PD21 / No.Live kits PD4) | N    | 110         | 90             | 129            | 2                           |
|                                        | N    | 116         | 95             | 136            | 2                           |
| LACTATION INDEX                        | %    | 96.3        | 96.3           | 96.3           | 1                           |
| (No.Live kits PD29 / No.Live kits PD5) | N    | 103         | 103            | 103            | 1                           |
|                                        | N    | 107         | 107            | 107            | 1                           |
| LACTATION INDEX                        | %    | 87.4        | 86.3           | 88.1           | 3                           |
| (No.Live kits PD35 / No.Live kits PD4) | N    | 131         | 111            | 158            | 3                           |
|                                        | N    | 150         | 126            | 183            | 3                           |
| LACTATION INDEX                        | %    | 93.1        | 93.1           | 93.1           | 1                           |
| (No.Live kits PD35 / No.Live kits PD7) | N    | 149         | 149            | 149            | 1                           |
|                                        | N    | 160         | 160            | 160            | 1                           |
| SURVIVING KITS/LITTER                  |      |             |                |                |                             |
| Day 4                                  | MEAN | 6.7         | 5.7            | 7.4            | 7                           |
| Day 7                                  | MEAN | 6.4         | 5.2            | 7.0            | 7                           |
| Day 10                                 | MEAN | 6.1         | 5.0            | 6.6            | 6                           |
| Day 11                                 | MEAN | 6.6         | 6.6            | 6.6            | 1                           |
| Day 14                                 | MEAN | 6.0         | 5.0            | 6.6            | 6                           |
| Day 18                                 | MEAN | 6.1         | 5.0            | 6.6            | 7                           |
| Day 21                                 | MEAN | 6.1         | 5.0            | 6.6            | 7                           |
| Day 24                                 | MEAN | 6.4         | 6.4            | 6.4            | 1                           |
| Day 28                                 | MEAN | 6.0         | 5.0            | 6.5            | 4                           |
| Day 29                                 | MEAN | 6.4         | 6.4            | 6.4            | 1                           |
| Day 35                                 | MEAN | 6.0         | 5.0            | 6.5            | 4                           |

NATURAL DELIVERY AND LITTER PARAMETERS  
NEW ZEALAND WHITE [Hra:NZW)SPF] RABBITS

PERIOD: 2012 THROUGH 2020

|                                            |      | <u>MEAN</u> | <u>MINIMUM</u> | <u>MAXIMUM</u> | <u>NO. STUDIES INCLUDED</u> |
|--------------------------------------------|------|-------------|----------------|----------------|-----------------------------|
| PERCENT MALE KITS PER NUMBER OF KITS SEXED |      |             |                |                |                             |
| Day 4                                      | MEAN | 50.3        | 43.2           | 60.0           | 7                           |
| Day 7                                      | MEAN | 51.4        | 42.9           | 59.8           | 7                           |
| Day 10                                     | MEAN | 50.7        | 42.1           | 59.8           | 7                           |
| Day 14                                     | MEAN | 50.6        | 42.1           | 59.8           | 7                           |
| Day 18                                     | MEAN | 50.7        | 42.1           | 59.8           | 7                           |
| Day 21                                     | MEAN | 50.7        | 42.1           | 59.8           | 7                           |
| Day 24                                     | MEAN | 42.1        | 42.1           | 42.1           | 1                           |
| Day 28                                     | MEAN | 50.7        | 46.4           | 54.8           | 4                           |
| Day 29                                     | MEAN | 42.1        | 42.1           | 42.1           | 1                           |
| Day 35                                     | MEAN | 50.8        | 46.4           | 54.8           | 4                           |
| LIVE LITTER SIZE AT WEIGHING               |      |             |                |                |                             |
| Day 4                                      | MEAN | 7.0         | 5.9            | 7.8            | 7                           |
| Day 7                                      | MEAN | 6.7         | 5.6            | 7.5            | 7                           |
| Day 10                                     | MEAN | 6.5         | 5.5            | 7.3            | 7                           |
| Day 14                                     | MEAN | 6.5         | 5.5            | 7.2            | 7                           |
| Day 18                                     | MEAN | 6.5         | 5.5            | 7.2            | 7                           |
| Day 21                                     | MEAN | 6.4         | 5.5            | 7.2            | 7                           |
| Day 24                                     | MEAN | 6.4         | 6.4            | 6.4            | 1                           |
| Day 28                                     | MEAN | 6.3         | 5.4            | 6.9            | 4                           |
| Day 29                                     | MEAN | 6.4         | 6.4            | 6.4            | 1                           |
| Day 35                                     | MEAN | 6.3         | 5.4            | 6.9            | 4                           |



NATURAL DELIVERY AND LITTER PARAMETERS  
NEW ZEALAND WHITE [Hra:NZW)SPF] RABBITS

PERIOD: 2012 THROUGH 2020

| KIT WEIGHT/LITTER (GRAMS) |      | <u>MEAN</u> | <u>MINIMUM</u> | <u>MAXIMUM</u> | <u>NO. STUDIES INCLUDED</u> |
|---------------------------|------|-------------|----------------|----------------|-----------------------------|
| Day 4                     | MEAN | 82.8        | 77.0           | 92.1           | 7                           |
| Day 7                     | MEAN | 118.4       | 111.7          | 132.0          | 7                           |
| Day 10                    | MEAN | 158.3       | 148.9          | 175.2          | 7                           |
| Day 14                    | MEAN | 217.4       | 202.2          | 243.9          | 7                           |
| Day 18                    | MEAN | 275.1       | 246.5          | 310.8          | 7                           |
| Day 21                    | MEAN | 317.7       | 295.5          | 357.2          | 7                           |
| Day 24                    | MEAN | 383.6       | 383.6          | 383.6          | 1                           |
| Day 28                    | MEAN | 508.5       | 444.2          | 594.2          | 4                           |
| Day 29                    | MEAN | 556.3       | 556.3          | 556.3          | 1                           |
| Day 35                    | MEAN | 760.9       | 701.8          | 863.6          | 4                           |

REPRODUCTIVE INDICES  
DUTCH BELTED [Haz:(DB)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION

PERIOD: 2016 THROUGH 2020

|                               | FULL STUDIES     |            |            | DOSE RANGE STUDIES |            |            |
|-------------------------------|------------------|------------|------------|--------------------|------------|------------|
| NO. OF STUDIES INCLUDED       | 6                |            |            | 4                  |            |            |
| NO. OF RABBITS TESTED         | 88               |            |            | 22                 |            |            |
| NO. OF RABBITS PREGNANT       | 88               |            |            | 22                 |            |            |
| NO. FOUND DEAD                | 1                |            |            | 0                  |            |            |
| NO. ABORTED                   | 0                |            |            | 2                  |            |            |
| NO. DELIVERED PREMATURELY     | 1                |            |            | 0                  |            |            |
| NO. UNSCHEDULED EUTHANASIA    | 1                |            |            | 0                  |            |            |
| CAESAREAN-SECTIONED ON GD 29  | 87               |            |            | 20                 |            |            |
|                               | <u>MEAN or %</u> | <u>MIN</u> | <u>MAX</u> | <u>MEAN or %</u>   | <u>MIN</u> | <u>MAX</u> |
| % PREGNANT                    | 99.2             | 95.0       | 100.0      | 100.0              | 100.0      | 100.0      |
| CORPORA LUTEA                 | 7.6              | 7.0        | 8.2        | 7.9                | 7.2        | 8.5        |
| IMPLANTATIONS                 | 7.1              | 6.4        | 7.5        | 7.0                | 5.8        | 8.5        |
| PREIMPLANTATION LOSS (%)      | 5.5              | 1.2        | 8.3        | 11.0               | 0.0        | 20.4       |
| LITTER SIZES                  |                  |            |            |                    |            |            |
| LIVE FETUSES                  | 6.9              | 6.4        | 7.2        | 6.4                | 3.8        | 8.5        |
| DEAD FETUSES                  | 0.0              | 0.0        | 0.0        | 0.0                | 0.0        | 0.0        |
| TOTAL RESORPTIONS             | 0.2              | 0.0        | 0.4        | 0.7                | 0.0        | 2.0        |
| EARLY RESORPTIONS             | 0.2              | 0.0        | 0.4        | 0.3                | 0.0        | 0.8        |
| LATE RESORPTIONS              | 0.0              | 0.0        | 0.1        | 0.4                | 0.0        | 1.2        |
| POSTIMPLANTATION LOSS (%)     | 2.9              | 0.0        | 5.2        | 12.8               | 0.0        | 41.6       |
| DOES WITH ANY RESORPTIONS (%) | 20.0             | 0.0        | 36.4       | 31.9               | 0.0        | 80.0       |

REPRODUCTIVE INDICES  
DUTCH BELTED [Haz:(DB)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION

PERIOD: 2016 THROUGH 2020

| NO. OF STUDIES INCLUDED                     | FULL<br>STUDIES<br>6 |            |            | DOSE RANGE<br>STUDIES<br>4 |            |            |
|---------------------------------------------|----------------------|------------|------------|----------------------------|------------|------------|
|                                             | <u>MEAN or %</u>     | <u>MIN</u> | <u>MAX</u> | <u>MEAN or %</u>           | <u>MIN</u> | <u>MAX</u> |
| DOES WITH ALL CONCEPTUSES<br>RESORBED (%)   | 0.0                  | 0.0        | 0.0        | 5.0                        | 0.0        | 20.0       |
| DOES WITH ONE OR MORE<br>VIABLE FETUSES (%) | 99.1                 | 94.7       | 100.0      | 95.0                       | 80.0       | 100.0      |
| SEX RATIO (% MALES/LITTER)                  | 49.4                 | 42.0       | 57.6       | 49.5                       | 41.5       | 55.0       |
| LIVE FETAL BODY WEIGHTS<br>GRAMS/LITTER:    | 38.2                 | 37.4       | 39.0       | 33.3                       | 30.8       | 35.8       |
| MALE FETUSES:                               | 35.8                 | 34.1       | 39.9       | 35.3                       | 33.9       | 36.9       |
| FEMALE FETUSES:                             | 35.6                 | 33.7       | 38.4       | 33.3                       | 31.6       | 34.7       |

FETAL EXTERNAL ABNORMALITIES  
DUTCH BELTED [Haz:(DB)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

PERIOD: 2016 THROUGH 2020

|                           |     |
|---------------------------|-----|
| NO. OF STUDIES INCLUDED   | 4   |
| NO. LITTERS EXAMINED      | 85  |
| NO. LIVE FETUSES EXAMINED | 591 |

|                         | ABNORMALITIES                                                                             |   | RANGE/STUDY |     |         |
|-------------------------|-------------------------------------------------------------------------------------------|---|-------------|-----|---------|
|                         |                                                                                           |   | N           | N   | %       |
| HEAD/NECK               | : Acephalostomia                                                                          | L | 1           | 0-1 | (0-5.6) |
|                         |                                                                                           | F | 1           | 0-1 | (0-0.9) |
|                         | : Cranial meningocele                                                                     | L | 1           | 0-1 | (0-5.6) |
|                         |                                                                                           | F | 1           | 0-1 | (0-0.9) |
| MOUTH                   | : Palate, cleft palate                                                                    | L | 1           | 0-1 | (0-4.5) |
|                         |                                                                                           | F | 2           | 0-2 | (0-1.3) |
| GENERAL                 | : Entire subcutis, edema<br>(previously Entire body, subcutaneous<br>edema - generalized) | L | 2           | 0-1 | (0-4.8) |
|                         |                                                                                           | F | 2           | 0-1 | (0-0.7) |
| FORE AND/OR HINDLIMB(S) | : Forelimb, hyperextension                                                                | L | 1           | 0-1 | (0-4.5) |
|                         |                                                                                           | F | 2           | 0-2 | (0-1.3) |
| PAW/DIGIT               | : Forepaw, hyperextension                                                                 | L | 1           | 0-1 | (0-4.5) |
|                         |                                                                                           | F | 2           | 0-2 | (0-1.3) |
| TAIL                    | : Short                                                                                   | L | 2           | 0-1 | (0-4.8) |
|                         |                                                                                           | F | 3           | 0-2 | (0-1.2) |

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Updated June 2021

FETAL SOFT TISSUE ABNORMALITIES  
DUTCH BELTED [Haz:(DB)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
DOSE RANGE FINDING STUDIES

PERIOD: 2016 THROUGH 2020

|                         |    |
|-------------------------|----|
| NO. OF STUDIES INCLUDED | 2  |
| NO. LITTERS EXAMINED    | 11 |
| NO. FETUSES EXAMINED    | 69 |

|             | ABNORMALITIES                               |   | N | N   | %        |
|-------------|---------------------------------------------|---|---|-----|----------|
| HEART       |                                             |   |   |     |          |
|             | : Ventricular septum, defect                | L | 1 | 0-1 | (0-14.3) |
|             | (previously Interventricular septal defect) | F | 1 | 0-1 | (0-2.0)  |
| GALLBLADDER |                                             |   |   |     |          |
|             | : Bilobed                                   | L | 1 | 0-1 | (0-14.3) |
|             |                                             | F | 1 | 0-1 | (0-2.0)  |
|             | : Supernumerary                             | L | 1 | 0-1 | (0-25.0) |
|             |                                             | F | 2 | 0-2 | (0-10.5) |

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FETAL SOFT TISSUE ABNORMALITIES  
DUTCH BELTED [Haz:(DB)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

PERIOD: 2016 THROUGH 2020

|                         |     |
|-------------------------|-----|
| NO. OF STUDIES INCLUDED | 6   |
| NO. LITTERS EXAMINED    | 129 |
| NO. FETUSES EXAMINED    | 892 |

|                |                                                                             | RANGE/STUDY |     |          |
|----------------|-----------------------------------------------------------------------------|-------------|-----|----------|
|                | ABNORMALITIES                                                               | N           | N   | %        |
| BRAIN          | : Lateral ventricle, dilated, minimal                                       | L 1         | 0-1 | (0-4.5)  |
|                |                                                                             | F 1         | 0-1 | (0-0.6)  |
|                | : Lateral ventricle, dilated, moderate                                      | L 1         | 0-1 | (0-4.5)  |
|                |                                                                             | F 1         | 0-1 | (0-0.6)  |
|                | : Cerebral hemisphere, absent                                               | L 1         | 0-1 | (0-5.6)  |
|                |                                                                             | F 1         | 0-1 | (0-0.9)  |
| ADRENAL GLANDS | : Misshapen                                                                 | L 1         | 0-1 | (0-4.5)  |
|                |                                                                             | F 1         | 0-1 | (0-0.7)  |
| EYE(S)         | : Absent                                                                    | L 1         | 0-1 | (0-5.6)  |
|                |                                                                             | F 1         | 0-1 | (0-0.9)  |
| LUNGS          | : Small                                                                     | L 3         | 0-2 | (0-9.1)  |
|                |                                                                             | F 4         | 0-3 | (0-1.9)  |
| TRACHEA        | : Cartilage rings, absent                                                   | L 1         | 0-1 | (0-4.5)  |
|                |                                                                             | F 1         | 0-1 | (0-0.6)  |
| HEART          | : Ventricular septum, defect<br>(previously Interventricular septal defect) | L 9         | 0-3 | (0-14.3) |
|                |                                                                             | F 10        | 0-4 | (0-2.6)  |
|                | : Ventricle, double outlet                                                  | L 2         | 0-1 | (0-4.8)  |
|                |                                                                             | F 2         | 0-1 | (0-0.7)  |
|                | : Ventricle, small                                                          | L 1         | 0-1 | (0-4.8)  |
|                |                                                                             | F 1         | 0-1 | (0-0.7)  |
|                | : Atrium, small                                                             | L 1         | 0-1 | (0-4.8)  |
|                |                                                                             | F 1         | 0-1 | (0-0.7)  |
| VESSELS        | : Aortic arch, dilated                                                      | L 1         | 0-1 | (0-4.5)  |
|                |                                                                             | F 1         | 0-1 | (0-0.7)  |
|                | : Pulmonary trunk, narrow                                                   | L 1         | 0-1 | (0-4.8)  |
|                |                                                                             | F 1         | 0-1 | (0-0.7)  |
| GALLBLADDER    | : Bilobed                                                                   | L 7         | 0-3 | (0-13.6) |
|                |                                                                             | F 7         | 0-3 | (0-1.9)  |
|                | : Absent                                                                    | L 4         | 0-2 | (0-9.1)  |
|                |                                                                             | F 7         | 0-4 | (0-2.5)  |
|                | : Supernumerary                                                             | L 21        | 0-6 | (0-27.3) |
|                |                                                                             | F 24        | 0-8 | (0-5.1)  |
|                | : Small                                                                     | L 4         | 0-2 | (0-9.5)  |
|                |                                                                             | F 5         | 0-2 | (0-1.3)  |
| GENERAL        | : Abdomen, fluid filled                                                     | L 2         | 0-1 | (0-4.8)  |
|                |                                                                             | F 2         | 0-1 | (0-0.7)  |
|                | : Thorax, fluid filled                                                      | L 3         | 0-2 | (0-9.1)  |
|                |                                                                             | F 4         | 0-3 | (0-1.9)  |

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F: FETAL INCIDENCE

Note: All summary values are based on studies with fetal findings.

Updated June 2021

FETAL SOFT TISSUE ABNORMALITIES  
DUTCH BELTED [Haz:(DB)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

|         | ABNORMALITIES                   |   | RANGE/STUDY |              |
|---------|---------------------------------|---|-------------|--------------|
|         |                                 |   | N           | %            |
| KIDNEYS | : Absent                        | L | 4           | 0-2 (0-8.3)  |
|         |                                 | F | 5           | 0-3 (0-3.82) |
|         | : Renal pelvis, dilated, severe | L | 1           | 0-1 (0-4.5)  |
|         |                                 | F | 1           | 0-1 (0-0.7)  |
|         | : Absent                        | L | 2           | 0-1 (0-4.5)  |
|         |                                 | F | 2           | 0-1 (0-1.0)  |
|         | : Ureter, dilated, minimal      | L | 1           | 0-1 (0-4.5)  |
|         |                                 | F | 1           | 0-1 (0-0.7)  |
| GONAD   | : Ovaries, malpositioned        | L | 1           | 0-1 (0-4.5)  |
|         |                                 | F | 1           | 0-1 (0-0.7)  |

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*Updated June 2021*

FETAL SKELETAL ABNORMALITIES  
DUTCH BELTED [Haz:(DB)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
DOSE RANGE FINDING STUDIES

PERIOD: 2016 THROUGH 2020

|                         |    |
|-------------------------|----|
| NO. OF STUDIES INCLUDED | 1  |
| LITTERS EXAMINED        | 7  |
| FETUSES EXAMINED        | 50 |

|             |            | ABNORMALITIES                      |   | RANGE/STUDY |      |          |
|-------------|------------|------------------------------------|---|-------------|------|----------|
|             |            |                                    |   | N           | N    | %        |
| SKULL       | Parietals  | : Contain hole(s)                  | L | 2           | 0-2  | (0-28.6) |
|             |            |                                    | F | 2           | 0-2  | (0-4.0)  |
| VERTEBRAE   | Cervical   | : Arch, incomplete ossification    | L | 1           | 0-1  | (0-14.3) |
|             |            |                                    | F | 1           | 0-1  | (0-2.0)  |
|             |            | : Centrum, unilateral ossification | L | 1           | 0-1  | (0-14.3) |
|             |            |                                    | F | 1           | 0-1  | (0-2.0)  |
|             | Caudal     | : Misaligned                       | L | 1           | 0-1  | (0-14.3) |
|             |            |                                    | F | 1           | 0-1  | (0-2.0)  |
|             |            | : Incomplete ossification          | L | 1           | 0-1  | (0-14.3) |
|             |            |                                    | F | 1           | 0-1  | (0-2.0)  |
| RIBS        |            | : Thoracolumbar, full              | L | 4           | 0-4  | (0-57.1) |
|             |            |                                    | F | 6           | 0-6  | (0-12.0) |
|             |            | : Thoracolumbar, short             | L | 6           | 0-6  | (0-85.7) |
|             |            |                                    | F | 11          | 0-11 | (0-22.0) |
| STERNUM     | Sternebrae | : Fused                            | L | 1           | 0-1  | (0-14.3) |
|             |            |                                    | F | 1           | 0-1  | (0-2.0)  |
|             |            | : Supernumerary site               | L | 1           | 0-1  | (0-14.3) |
|             |            |                                    | F | 1           | 0-1  | (0-2.0)  |
| FORELIMB(S) | Phalanges  | : Unossified                       | L | 5           | 0-5  | (0-71.4) |
|             |            |                                    | F | 10          | 0-10 | (0-20.0) |

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FETAL SKELETAL ABNORMALITIES  
DUTCH BELTED [Haz:(DB)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

PERIOD: 2016 THROUGH 2020

|                         |     |
|-------------------------|-----|
| NO. OF STUDIES INCLUDED | 6   |
| LITTERS EXAMINED        | 129 |
| FETUSES EXAMINED        | 891 |

|       |                 | ABNORMALITIES                    |      | RANGE/STUDY |          |  |
|-------|-----------------|----------------------------------|------|-------------|----------|--|
|       |                 |                                  | N    | N           | %        |  |
| SKULL | Frontals        | : Incomplete ossification        | L 3  | 0-2         | (0-8.3)  |  |
|       |                 |                                  | F 4  | 0-4         | (0-2.8)  |  |
|       |                 | : Incomplete ossification, right | L 1  | 0-1         | (0-4.2)  |  |
|       |                 |                                  | F 1  | 0-1         | (0-1.4)  |  |
|       |                 | : Absent                         | L 1  | 0-1         | (0-5.6)  |  |
|       |                 |                                  | F 1  | 0-1         | (0-0.9)  |  |
|       | Parietals       | : Contain hole(s)                | L 34 | 0-11        | (0-50.0) |  |
|       |                 |                                  | F 66 | 0-23        | (0-14.6) |  |
|       |                 | : Hole, left                     | L 1  | 0-1         | (0-4.2)  |  |
|       |                 |                                  | F 1  | 0-1         | (0-1.4)  |  |
|       |                 | : Hole, right                    | L 3  | 0-3         | (0-12.5) |  |
|       |                 |                                  | F 3  | 0-3         | (0-3.6)  |  |
|       |                 | : Misshapen                      | L 1  | 0-1         | (0-5.6)  |  |
|       |                 |                                  | F 1  | 0-1         | (0-0.9)  |  |
|       |                 | : Isolated ossification site     | L 3  | 0-2         | (0-9.1)  |  |
|       |                 |                                  | F 3  | 0-2         | (0-1.3)  |  |
|       | Interparietals  | : Misshapen                      | L 1  | 0-1         | (0-5.6)  |  |
|       |                 |                                  | F 1  | 0-1         | (0-0.9)  |  |
|       | Nasals          | : Absent                         | L 1  | 0-1         | (0-5.6)  |  |
|       |                 |                                  | F 1  | 0-1         | (0-0.9)  |  |
|       | Palatine        | : Cleft                          | L 1  | 0-1         | (0-4.5)  |  |
|       |                 |                                  | F 2  | 0-2         | (0-1.3)  |  |
|       |                 | : Absent                         | L 1  | 0-1         | (0-5.6)  |  |
|       |                 |                                  | F 1  | 0-1         | (0-0.9)  |  |
|       | Supraoccipitals | : Misshapen                      | L 1  | 0-1         | (0-5.6)  |  |
|       |                 |                                  | F 1  | 0-1         | (0-0.9)  |  |
|       | Suture          | : Bone, present                  | L 1  | 0-1         | (0-4.5)  |  |
|       |                 |                                  | F 1  | 0-1         | (0-0.7)  |  |
|       | Zygomatic arch  | : Misshapen                      | L 1  | 0-1         | (0-5.6)  |  |
|       |                 |                                  | F 1  | 0-1         | (0-0.9)  |  |
|       | Premaxilla      | : Absent                         | L 1  | 0-1         | (0-5.6)  |  |
|       |                 |                                  | F 1  | 0-1         | (0-0.9)  |  |
|       | Maxilla         | : Misshapen                      | L 1  | 0-1         | (0-5.6)  |  |
|       |                 |                                  | F 1  | 0-1         | (0-0.9)  |  |

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Updated June 2021

FETAL SKELETAL ABNORMALITIES  
DUTCH BELTED [Haz:(DB)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

|                | ABNORMALITIES                        | RANGE/STUDY |      |          |
|----------------|--------------------------------------|-------------|------|----------|
|                |                                      | N           | N    | %        |
| SKULL (CONT'D) | Squamosal                            |             |      |          |
|                | : Absent                             | L 1         | 0-1  | (0-5.6)  |
|                |                                      | F 1         | 0-1  | (0-0.9)  |
|                | Hyoid                                |             |      |          |
|                | : Ala(e), incomplete ossification    | L 4         | 0-3  | (0-14.3) |
|                |                                      | F 4         | 0-3  | (0-2.0)  |
| VERTEBRAE      | : Ala(e), unossified                 | L 2         | 0-1  | (0-4.8)  |
|                |                                      | F 2         | 0-1  | (0-0.7)  |
|                | Cervical                             |             |      |          |
|                | : Arch, incomplete ossification      | L 6         | 0-3  | (0-14.3) |
|                |                                      | F 9         | 0-6  | (0-4.0)  |
|                | : Arch, misshapen                    | L 3         | 0-2  | (0-9.1)  |
|                |                                      | F 5         | 0-4  | (0-2.7)  |
|                | : Centrum, unilateral ossification   | L 8         | 0-3  | (0-14.3) |
|                |                                      | F 9         | 0-4  | (0-2.6)  |
|                | : Centrum, incomplete ossification   | L 4         | 0-2  | (0-9.5)  |
|                |                                      | F 5         | 0-2  | (0-1.3)  |
|                | : Supernumerary Rib, Cervical, Short | L 2         | 0-2  | (0-9.1)  |
|                |                                      | F 2         | 0-2  | (0-1.3)  |
|                | Thoracic                             |             |      |          |
|                | : Arch, large                        | L 1         | 0-1  | (0-4.5)  |
|                |                                      | F 1         | 0-1  | (0-0.7)  |
|                | : Arch, incomplete ossification      | L 1         | 0-1  | (0-4.5)  |
|                |                                      | F 1         | 0-1  | (0-0.6)  |
|                | : Centrum, incomplete ossification   | L 3         | 0-2  | (0-9.5)  |
|                |                                      | F 3         | 0-2  | (0-1.3)  |
|                | : Centrum, unilateral ossification   | L 4         | 0-3  | (0-14.3) |
|                |                                      | F 5         | 0-4  | (0-2.6)  |
|                | : Centrum, fused                     | L 1         | 0-1  | (0-4.5)  |
|                |                                      | F 1         | 0-1  | (0-0.6)  |
|                | : Hemivertebra                       | L 1         | 0-1  | (0-4.5)  |
|                |                                      | F 1         | 0-1  | (0-0.7)  |
|                | Lumbar                               |             |      |          |
|                | : Absent                             | L 3         | 0-2  | (0-9.5)  |
|                |                                      | F 3         | 0-2  | (0-1.3)  |
|                | : Supernumerary                      | L 1         | 0-1  | (0-4.8)  |
|                |                                      | F 1         | 0-1  | (0-0.7)  |
|                | : Hemivertebra                       | L 1         | 0-1  | (0-4.5)  |
|                |                                      | F 1         | 0-1  | (0-0.6)  |
|                | Caudal                               |             |      |          |
|                | : Misaligned                         | L 23        | 0-6  | (0-27.3) |
|                |                                      | F 28        | 0-9  | (0-6.0)  |
|                | : Fused                              | L 6         | 0-2  | (0-9.5)  |
|                |                                      | F 6         | 0-2  | (0-1.3)  |
|                | : Incomplete ossification            | L 20        | 0-6  | (0-27.3) |
|                |                                      | F 27        | 0-10 | (0-6.7)  |
|                | : Misshapen                          | L 2         | 0-1  | (0-4.8)  |
|                | (previously Irregularly shaped)      | F 2         | 0-1  | (0-0.7)  |
|                | : Unossified                         | L 1         | 0-1  | (0-4.5)  |
|                |                                      | F 1         | 0-1  | (0-0.7)  |

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Updated June 2021

FETAL SKELETAL ABNORMALITIES  
DUTCH BELTED [Haz:(DB)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

|               |            |               |                                           |   | RANGE/STUDY |      |          |
|---------------|------------|---------------|-------------------------------------------|---|-------------|------|----------|
|               |            |               |                                           |   | N           | N    | %        |
| RIBS          |            | ABNORMALITIES |                                           |   |             |      |          |
|               |            |               | : Long                                    | L | 1           | 0-1  | (0-4.5)  |
|               |            |               |                                           | F | 1           | 0-1  | (0-0.7)  |
|               |            |               | : Thick                                   | L | 1           | 0-1  | (0-4.5)  |
|               |            |               | <i>(previously Broad)</i>                 | F | 1           | 0-1  | (0-0.7)  |
|               |            |               | : Thin                                    | L | 1           | 0-1  | (0-4.8)  |
|               |            |               |                                           | F | 1           | 0-1  | (0-0.7)  |
|               |            |               | : Fused                                   | L | 1           | 0-1  | (0-4.5)  |
|               |            |               |                                           | F | 1           | 0-1  | (0-0.7)  |
|               |            |               | : Branched                                | L | 1           | 0-1  | (0-4.8)  |
|               |            |               | <i>(previously Split)</i>                 | F | 1           | 0-1  | (0-0.7)  |
|               |            |               | : Short                                   | L | 1           | 0-1  | (0-4.8)  |
|               |            |               |                                           | F | 1           | 0-1  | (0-0.7)  |
|               |            |               | : Centrum, unilateral ossification        | L | 2           | 0-2  | (0-9.1)  |
|               |            |               |                                           | F | 2           | 0-2  | (0-1.3)  |
|               |            |               | : Supernumerary rib, thoracolumbar, full  | L | 31          | 0-9  | (0-42.9) |
|               |            |               | <i>(previously T13, supernumerary)</i>    | F | 67          | 0-21 | (0-14.1) |
|               |            |               | : Supernumerary rib, thoracolumbar, short | L | 55          | 0-19 | (0-86.4) |
|               |            |               | <i>(previously T13, short)</i>            | F | 114         | 0-40 | (0-26.5) |
| STERNUM       | Sternebrae |               |                                           |   |             |      |          |
|               |            |               | : Fused                                   | L | 9           | 0-5  | (0-20.8) |
|               |            |               |                                           | F | 11          | 0-6  | (0-3.4)  |
|               |            |               | : Incomplete ossification                 | L | 4           | 0-1  | (0-5.6)  |
|               |            |               |                                           | F | 4           | 0-1  | (0-0.9)  |
|               |            |               | : Asymmetric                              | L | 1           | 0-1  | (0-4.5)  |
|               |            |               |                                           | F | 1           | 0-1  | (0-0.7)  |
|               |            |               | : Isolated ossification site              | L | 5           | 0-4  | (0-22.2) |
|               |            |               |                                           | F | 10          | 0-8  | (0-5.6)  |
|               |            |               | : Misshapen                               | L | 4           | 0-2  | (0-11.1) |
|               |            |               | <i>(previously Irregularly shaped)</i>    | F | 4           | 0-2  | (0-1.5)  |
|               |            |               | : Supernumerary site                      | L | 11          | 0-5  | (0-22.7) |
|               |            |               |                                           | F | 12          | 0-6  | (0-4.0)  |
|               |            |               | : Bipartite ossification                  | L | 1           | 0-1  | (0-5.6)  |
|               |            |               |                                           | F | 1           | 0-1  | (0-0.9)  |
| CLAVICULAE    |            |               |                                           |   |             |      |          |
|               |            |               | : Thickened                               | L | 1           | 0-1  | (0-4.8)  |
|               |            |               |                                           | F | 2           | 0-2  | (0-1.3)  |
|               |            |               | : Misshapen                               | L | 1           | 0-1  | (0-4.5)  |
|               |            |               |                                           | F | 1           | 0-1  | (0-0.7)  |
|               |            |               | : Incomplete ossification                 | L | 1           | 0-1  | (0-4.8)  |
|               |            |               |                                           | F | 1           | 0-1  | (0-0.7)  |
|               |            |               |                                           |   |             |      |          |
| PELVIC GIRDLE | Pubis      |               |                                           |   |             |      |          |
|               |            |               | : Incomplete ossification                 | L | 3           | 0-1  | (0-4.8)  |
|               |            |               |                                           | F | 3           | 0-1  | (0-0.7)  |
|               |            |               |                                           |   |             |      |          |
| FORELIMB(S)   | Phalanges  |               |                                           |   |             |      |          |
|               |            |               | : Unossified                              | L | 62          | 0-17 | (0-77.3) |
|               |            |               |                                           | F | 153         | 0-42 | (0-26.8) |
|               |            |               |                                           |   |             |      |          |

L: LITTER INCIDENCE

F: FETAL INCIDENCE

Note: All summary values are based on studies with fetal findings.

Updated June 2021

FETAL SKELETAL OSSIFICATION SITES  
DUTCH BELTED [Haz:(DB)SPF] RABBITS  
GESTATION DAY 29 CAESAREAN-SECTION  
FULL STUDIES

PERIOD: 2016 THROUGH 2020

NO. OF STUDIES INCLUDED 2

NO. LITTERS EXAMINED 42

NO. FETUSES EXAMINED 283

|                       | MEAN  | MINIMUM | MAXIMUM |
|-----------------------|-------|---------|---------|
| HYOID                 | 1.00  | 1.00    | 1.00    |
| VERTEBRAE             |       |         |         |
| CERVICAL              | 7.00  | 7.00    | 7.00    |
| THORACIC              | 12.18 | 12.14   | 12.22   |
| LUMBAR                | 6.82  | 6.77    | 6.86    |
| SACRAL                | 4.00  | 4.00    | 4.00    |
| CAUDAL                | 15.54 | 15.41   | 15.67   |
| RIBS (Pairs)          | 12.15 | 12.12   | 12.17   |
| STERNUM               |       |         |         |
| MANUBRIUM             | 1.00  | 1.00    | 1.00    |
| STERNAL CENTERS       | 4.02  | 4.00    | 4.04    |
| XIPHOID               | 1.00  | 1.00    | 1.00    |
| FOREPAWS <sup>a</sup> |       |         |         |
| CARPALS               | 0.00  | 0.00    | 0.00    |
| METACARPALS           | 5.00  | 5.00    | 5.00    |
| DIGITS                | 5.00  | 5.00    | 5.00    |
| PHALANGES             | 13.88 | 13.83   | 13.93   |
| HINDPAWS <sup>a</sup> |       |         |         |
| TARSALS               | 2.00  | 2.00    | 2.00    |
| METATARSALS           | 4.00  | 4.00    | 4.00    |
| DIGITS                | 4.00  | 4.00    | 4.00    |
| PHALANGES             | 12.00 | 12.00   | 12.00   |

a. Calculated as mean per limb