

**FINAL REPORT**

**Test Facility Study No. 20256434**

**Sponsor Reference No. RN9391R58**

**A Combined Fertility and Developmental Study (Including Teratogenicity  
and Postnatal Investigations) of BNT162b1, BNT162b2 and BNT162b3 by  
Intramuscular Administration in the Wistar Rat**

**GLP Study**

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**TEST FACILITY:**

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### QUALITY ASSURANCE STATEMENT

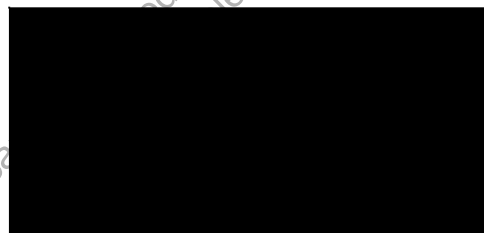
This study has been audited by Quality Assurance in accordance with the applicable Good Laboratory Practice regulations. Reports were submitted in accordance with Standard Operating Procedures as follows:

#### QA INSPECTION DATES

Date(s) of Audit	Phase(s) Audited	Dates Findings Submitted to:	
		Study Director	Study Director Management
29-Jun-2020 – 30-Jun-2020	Final Study Plan	30-Jun-2020	30-Jun-2020
23-Jul-2020	Study Plan Amendment 01	23-Jul-2020	23-Jul-2020
02-Oct-2020	Study Plan Amendment 02	02-Oct-2020	02-Oct-2020
14-Sep-2020	Physical development	14-Sep-2020	14-Sep-2020
23-Nov-2020 – 04-Dec-2020	Report Tables	04-Dec-2020	04-Dec-2020
23-Nov-2020 – 04-Dec-2020	Report – Materials and Methods	04-Dec-2020	04-Dec-2020
23-Nov-2020 – 04-Dec-2020	Data Review – Formulations	04-Dec-2020	04-Dec-2020
23-Nov-2020 – 04-Dec-2020	Data Review – Technical Operations	04-Dec-2020	04-Dec-2020
23-Nov-2020 – 04-Dec-2020	Data Review – Clinical Pathology	04-Dec-2020	04-Dec-2020
23-Nov-2020 – 04-Dec-2020	Data Review – Necropsy	04-Dec-2020	04-Dec-2020
23-Nov-2020 – 04-Dec-2020	Report	04-Dec-2020	04-Dec-2020
07-Dec-2020 - 10-Dec-2020	Report - Results	10-Dec-2020	10-Dec-2020

In addition to the above-mentioned audits, process-based and routine facility inspections were also conducted during the course of this study. Inspection findings, if any, specific to this study were reported by Quality Assurance to the Study Director and Management and listed as a Phase Audit on this Quality Assurance Statement.

The Final Report has been reviewed to assure that it accurately describes the materials and methods, and that the reported results accurately reflect the raw data.



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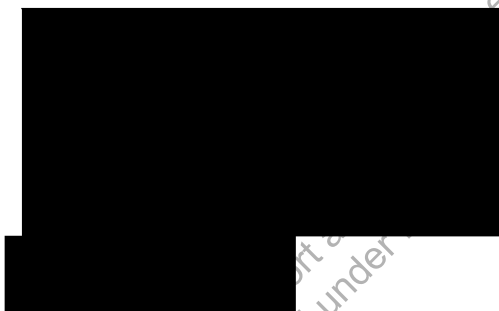
### GLP COMPLIANCE STATEMENT AND REPORT APPROVAL

The study was performed in accordance with OECD Principles of Good Laboratory Practice as required in Directive 2004/10/EC of the European Parliament and of the Council of 11 February 2004, Bonnes Pratiques de Laboratoire, Ministère de l'Emploi et de la Solidarité Française, No. 2000/5bis, arrêté du 14/03/2000.

OECD Principles of Good Laboratory Practice are accepted by Regulatory Authorities throughout the European Union, United States of America (FDA and EPA), and Japan (MHLW, MAFF, and METI) and other countries that are signatories to the OECD Mutual Acceptance of Data Agreement.

Exceptions from the above regulations are listed below.

- Antibody analysis (Appendix 26) was not conducted in compliance with GLP but in accordance with the Good Clinical Laboratory Practice (GCLP). This Test site was selected by the Sponsor because it has the most appropriate experience concerning the measurement of neutralizing antibody titres against the SARS-CoV-2 live virus by Microneutralization CPE-based method. The delegated phase for antibody analysis was fit for purpose, performed in adherence to the facilities SOPs and working instructions, by a research facility with proper expertise, and adequate history and by individuals specially trained in this technique (according to VisMederi management of personnel procedure). This exception did not adversely affect the outcome or interpretation of this study because the methods included appropriate controls to provide reliable data and analyses according to data integrity principles and local QA Report review will ensure compliance to internal procedures.



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# 1. RESPONSIBLE PERSONNEL

Role/Phase	QAU	Name	Contact Information
Study Director	Charles River	[REDACTED]	Address as cited for Test Facility
Test Facility Management	Charles River	[REDACTED]	Address as cited for Test Facility
Test Facility QAU	Charles River	[REDACTED]	Address as cited for Test Facility
Principal Investigator (PI)			
Role/Phase	GLP Compliance	Name	Contact Information
Serum Antibody Analysis <sup>a</sup>	No (compliance with the GCLP)	[REDACTED]	VisMederi Srl Strada del Petriccio e Belriguardo, 35 53100 Siena, Italy

<sup>a</sup>: Test Site selected by the Study Sponsor in agreement with the Study Director.

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## 2. ABSTRACT

The objective of this study was to assess the potential effects of BNT162b1, BNT162b2 and BNT162b3, vaccine development candidates to prevent Covid-19, and the concomitant immune response, on fertility and pre and postnatal development in the female Wistar (CRL:WI[Han]) rat.

BNT162b1, BNT162b2 and BNT162b3 were administered intramuscularly (IM) to F0 female Wistar rats 21 and 14 days before the start of mating (M-21 and M-14, respectively) and then on Gestation Day (GD) 9 and GD20, for a total of 4 dose days. A separate control group was administered saline by the same route and regimen. Each dose group consisted of 44 F0 females, 22 rats assigned to the caesarean subgroup, and 22 rats assigned to the littering subgroup. Each dose consisted of 30 µg mRNA /dosing day (■ mL/dose) IM injection in alternating quadriceps muscles.

Following completion of a mating phase with untreated males, 22 rats per group (nominally) underwent caesarean section on GD21 and were submitted to routine embryo-fetal development evaluations (caesarean subgroup). The remaining 22 rats per group (nominally) were allowed to litter and development of the offspring was observed up to weaning on Postnatal Day (PND) 21 (littering subgroup).

The following parameters and end points were evaluated in all F0 animals: Survival, clinical signs, body weights, body weight gains, food consumption, estrous cycles, mating performance, fertility and macroscopic observations. F0 females assigned to the caesarean subgroup were further examined for ovarian and uterine contents, gravid uterine weights and fetuses were evaluated for viability, sex, body weights, and external, visceral, and skeletal morphology. F0 females assigned to the littering subgroup were allowed to deliver naturally, and were further assessed for parturition, lactation, and maternal behavior, and were monitored to the day of euthanasia on Lactation Day (LD) 21. F1 offspring were assessed for survival, clinical signs, body weights, physical development (pinna unfolding and eye opening), preweaning auditory and visual function tests to screen for normal neurodevelopment, and macroscopic observations.

Blood samples were collected before administration of the first dose (baseline) and on the first day of cohabitation for each F0 female (both subgroups), on GD21 (caesarean subgroup), and on LD21 (littering subgroup females). Blood samples were also collected on GD21 from viable fetuses in each available litter (caesarean subgroup) and on PND21 from pups from each available litter (littering subgroup). Blood samples were evaluated for neutralizing antibody titres against SARS-CoV-2 live virus.

There were no deaths throughout the study related to any of the 3 vaccine candidates.

Intramuscular administration of BNT162b1, BNT162b2 and BNT162b3, before and during gestation to female Wistar rats resulted in non-adverse clinical signs and macroscopic findings localized to the injection site as well as transient, non-adverse body weight and food consumption effects after each dose administration. These maternal findings are all consistent with administration of a vaccine and an inflammatory/immune response.

There were no effects on estrous cycles, pre-coital interval, mating, fertility and pregnancy index, or on any ovarian, uterine, or litter parameters, including F1 pre and postnatal survival, growth, external, visceral, and skeletal morphology, or effects on pre-weaning physical and functional development of the F1 pups related to any of the 3 vaccine candidates.

Administration of 4 doses (2 prior to mating and 2 during gestation) of BNT162b1, BNT162b2, or BNT162b3 elicited SARS-CoV-2 neutralizing antibody responses in the majority of females just prior to mating (M0), at the end of gestation (GD21), and at the end of lactation (LD21). SARS-CoV-2 neutralizing titers were detected in most offspring (fetuses on GD21 and pups on PND21). SARS-CoV-2 neutralizing antibody titers were not observed in animals prior to vaccine administration or in saline-administered control animals.

In conclusion, intramuscular administration of BNT162b1, BNT162b2 and BNT162b3 before and during gestation to female Wistar (CRL:WI[Han]) rats was associated with non-adverse effects (body weight, food consumption and effects localized to the injection site) after each dose administration. There were no effects of any of the 3 vaccine candidates on mating performance or fertility in F0 female rats or on embryo-fetal or postnatal survival, growth, or development of the F1 offspring. An immune response was confirmed in F0 female rats following administration of each vaccine candidate and these responses were also detectable in the F1 offspring (fetuses and pups).

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### 3. INTRODUCTION

The objective of this study was to assess the potential effects of BNT162b1, BNT162b2 and BNT162b3, vaccine development candidates to prevent Covid-19, and the concomitant immune response, on fertility and pre and postnatal development in the female Wistar (CRL:WI[Han]) rat.

The design of this study was based on Guidelines from the International Conference on Harmonization, S5(R3) Detection of Reproductive and Developmental Toxicity for Human Pharmaceuticals; Department of Health and Human Services, Food and Drug Administration (FDA), 2006 Guidance on Developmental Toxicity Studies in Vaccines for Infectious Disease Indications; WHO guidelines on nonclinical evaluation of vaccines.

The Study Plan, the last Study Plan amendment, and deviations are presented in Appendix 1.

Study Initiation Date

(Study Plan signed by the Study Director): 26 Jun 2020.

Experimental Starting Date

(First date of study-specific

data collection): 29 Jun 2020.

Postnatal Development - Littering Subgroup:

Animal Arrivals: Females: 29 Jun 2020.

Males: 10 Aug 2020.

Initiation of Predose Estrous Cycle

Monitoring: 13 Jul 2020.

First Injection (Day 1 = M-21): 27 Jul 2020.

Start of Mating (M1): From 17 Aug 2020.

Littering (LD0): From 09 Sep 2020.

Necropsy of Dams and Pups  
(LD21/PND21): From 30 Sep 2020.

Embryo-Fetal Development - Caesarean Subgroup:

Animal Arrivals: Females: 13 Jul 2020.

Males: 10 Aug 2020.

Initiation of Predose Estrous Cycle

Monitoring: 27 Jul 2020.

First Injection (Day 1 = M-21) 10 Aug 2020.

Start of Mating (M1): From 31 Aug 2020.

Caesarean Sections (GD21): From 22 Sep 2020.

Experimental Completion Date

(Last necropsy): 12 Oct 2020.

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## 4. MATERIALS AND METHODS

### 4.1. Test Materials

#### 4.1.1. Test Items Characterization

The Sponsor provided to the Test Facility documentation of the identity, strength, purity, composition, and stability for the test items. Certificates of analysis were provided to the Test Facility and are presented in Appendix 2.

The characterization of the test items was conducted in a GMP environment (information provided by the Study Sponsor on 30 Nov 2020).

The Sponsor has appropriate documentation on file concerning the method of synthesis, fabrication or derivation of the test items, and this information is available to the appropriate regulatory agencies should it be requested.

#### 4.1.2. Test Material Identification

Text Table 1  
Test Item Identification

	Test Item 1	Test Item 2	Test Item 3
<b>Identification:</b>	BNT162b1	BNT162b2	BNT162b3
<b>Alternate Identification:</b>	CoVVAC	CoVVAC	CorVac BNT162b3c
<b>Batch No.:</b>	RBP020.3 LNP	RBP020.2 LNP	RBP020.8 LNP
<b>Lot No.:</b>	CoVVAC/100320	CoVVAC/270320	BCV/040620
<b>Physical Description:</b>	White to off-white suspension	White to off-white suspension	White to off-white suspension
<b>Expiry Date:</b>	10 Jan 2021	27 Nov 2020	04 Dec 2020
<b>Correction Factor:</b>	None	None	None
<b>Concentration (RNA Content):</b>	508 µg/mL	508 µg/mL	■ µg/mL
<b>Storage Conditions:</b>	Temperature set to maintain -80°C		
<b>Provided by:</b>	Sponsor		

Text Table 2  
Control Item Identification

	Control Item
<b>Identification:</b>	Sterile physiological saline (0.9% NaCl)
<b>Alternate Identification:</b>	N/A
<b>Batch/Lot Nos.:</b>	905098 and 912642
<b>Expiry Dates:</b>	30 Apr 2022 and 30 Nov 2022 respectively
<b>Storage Conditions:</b>	Ambient temperature
<b>Provided by:</b>	Test Facility

N/A: Not Applicable.

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#### 4.2. Reserve Samples

For each batch (lot) of test items supplied by the Sponsor, a reserve sample (1 unit) was collected and maintained under the appropriate storage conditions by the Test Facility.

#### 4.3. Test Items Inventory and Disposition

The test materials (e.g., test items) were received by the Test Facility for distribution as needed. Records of the receipt, distribution, storage, and disposition of test materials are maintained. All unused Sponsor supplied bulk test materials, with the exception of the reserve samples, were returned to the Sponsor after the in-life period.

#### 4.4. Dose Dispensing and Analysis

##### 4.4.1. Preparation of Formulations

The test items and control item were supplied as a ready-to-use formulations and were dispensed as needed to the animal facility.

Text Table 3  
Formulation Frequency of Preparation

Dose Formulation	Administration Dose Form	Frequency of Preparation	Storage Conditions
Control item	Solution	On each day of administration	Immediately dispensed at ambient temperature
Test item	Suspension	On each day of administration	Immediately dispensed at ambient temperature

Any residual volumes from each dosing occasion were discarded. Fresh vials were thawed for each administration.

##### 4.4.2. Sample Collection and Analysis

The test items were used as received from the Sponsor; therefore, samples for dose formulation analysis were not collected by the Test Facility.

##### 4.4.2.1. Stability and Homogeneity

The Sponsor has provided data that demonstrate that the test items formulations are stable and homogenous when stored under the same conditions as those used in the present study, as follows:

- Stable at a concentration of 0.5 mg/mL for 12 weeks at -80°C.
- Stable at a concentration of 0.5 mg/mL for at least 1 month at room temperature (information provided by the Study Sponsor on 03 Dec 2020).
- Homogenous for at least 6 hours following gentle inversion.

Homogeneity data provided by the Sponsor are retained in the study records (Study No. VR-VTR-10681). The Homogeneity Report is presented in Appendix 3.

#### **4.5. Test System**

##### **4.5.1. Receipt**

On 29 Jun 2020 and 13 Jul 2020 (females) and 10 Aug 2020 (males), Wistar rats CRL:WI(Han) were received from Charles River Laboratories France, 329 Impasse du Domaine Rozier, Les Oncins, 69210 Saint-Germain-Nuelles, France. Virgin females were 11 weeks old and weighed between 179.3 and 265.4 g at the initiation of dosing and virgin males (untreated) were 11 weeks old and weighed between 328.4 g and 415.9 g at arrival.

##### **4.5.2. Justification for Test System and Number of Animals**

At this time, studies in laboratory animals provide the best available basis for extrapolation to humans and are required to support regulatory submissions. Acceptable models which do not use live animals currently do not exist.

The rat was chosen as the animal model for this study as it is an accepted rodent species for preclinical toxicity testing by regulatory agencies. It mounts an immune response to the vaccines tested that is similar to the expected human response after vaccination.

The total number of animals to be used in this study is considered to be the minimum required to properly characterize the effects of the test item and its immune response. This study has been designed such that it does not require an unnecessary number of animals to accomplish its objectives.

##### **4.5.3. Animal Identification (F0 Males and F0 Females)**

Subcutaneously implanted electronic identification chip.

##### **4.5.4. Environmental Acclimation**

All animals received a clinical inspection for ill-health on arrival. Acclimation period was 28 days before the start of dosing for females and 7 days before the start of mating for males.

##### **4.5.5. Selection, Assignment, Replacement, and Disposition of Animals**

After arrival, animals were randomly assigned to groups.

The disposition of all animals was documented in the study records.



#### 4.5.6. Husbandry

##### 4.5.6.1. Housing

Housing: Single or group housed.

Caging: Plastic cages containing appropriate bedding.

The animals were caged as follows (see Appendix 1):

Phase	Number of Animals per Cage	
	Males	Females
Pre-mating	up to 4	up to 5
Mating	1 male + 1 female housed together	
Gestation of F0 generation	up to 4	1
Lactation of F0 generation	-	1 + litter

∴ Not applicable.

Cage Identification: Color-coded cage card indicating study, group, animal number(s), and sex.

Animals were separated during designated procedures/activities or were separated as required for monitoring and/or health purposes, as deemed appropriate by Study Director and/or clinical veterinarian. Cages were arranged on the racks in group order. Where possible, control group animals were housed on a separate rack from the test item-treated animals.

##### 4.5.6.2. Animal Enrichment

For environmental enrichment, animals were provided with items such as a wooden gnaw block and shredded paper, except when interrupted by study procedures/activities. It is considered that there are no known contaminants in the enrichment that could interfere with the outcome of the study.

##### 4.5.6.3. Environmental Conditions

The targeted conditions for animal room environment were as follows:

Temperature: 19°C to 25°C.

Humidity: ≥ 35%.

Light Cycle: 12 hours light and 12 hours dark (except during any designated procedures).

Dimmed lighting appeared 15 minutes before the lights were switched on and disappeared 15 minutes after the lights were switched off.

Ventilation: 10 or more air changes per hour.

Environmental conditions were within the targets throughout the study.

#### 4.5.6.4. Food

**Diet:** Complete rodent diet (Reference No. A04C-10, Safe), sterilized by irradiation.

**Type:** Pellets.

**Frequency:** *Ad libitum*, except during designated procedures.

**Analysis:** Each batch of diet is supplied with a certificate of analysis which is verified and authorized for release by a veterinarian. Certificates of analysis are maintained in the archives of the Test Facility. It is considered that there are no known contaminants in the feed that would interfere with the objectives of the study.

#### 4.5.6.5. Water

**Type:** Softened and filtered (0.2 µm) municipal drinking water.

**Frequency/Ration:** Freely available to each animal (except during designated procedures) (see Appendix 1).

**Analysis:** Analysed at least twice a year for chemical and bacterial contaminants by Laboratoire Santé Environnement Hygiène de Lyon, France. Certificates of analysis for the drinking water are maintained in the archives of the Test Facility. It is considered that there are no known contaminants in the water that could interfere with the outcome of the study.

#### 4.5.6.6. Veterinary Care

Veterinary care was available throughout the course of the study, and animals were examined by the veterinary staff as warranted by clinical signs or other changes. All veterinary examinations were documented in the study records and reviewed by the Study Director (details are kept in the raw data).

### 4.6. Experimental Design

Text Table 4  
Experimental Design of the F0 Generation

Group No.	Test Material	Dose (µg mRNA)	Dose Volume (mL)	Dose Concentration (mg/mL)	Number and Identification of Animals	
					Caesarean Subgroup	Littering Subgroup
1	Control item	0	0.06	0	22 (1 to 22)	22 (201 to 222)
2	BNT162b1	30	0.06	0.5	22 (23 to 44)	22 (223 to 244)
3	BNT162b2	30	0.06	0.5	22 (45 to 66)	22 (245 to 266)
4	BNT162b3	30 <sup>a</sup>	████	████	22 (67 to 88)	22 (267 to 288)

<sup>a</sup>: 30 µg RNA/dosing day was the targeted dose level. However, based on the actual RNA concentration, this group received █████ µg RNA/dosing day.  
Identification of untreated males: 301 to 388.

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#### 4.6.1. Administration of Test Materials

Only F0 females were treated, males were not treated.

Dose Route: Intramuscular injection into the quadriceps alternating on each dosing occasion.

Frequency (4 occasions): 21 days (M-21) and 14 days (M-14) before the start of the mating phase, and on GD9 and GD20.

Method: The hair of the animals on the injection area was clipped prior to the first injection and then as necessary during the dosing period. The animals were temporarily restrained for dose administration. The test item was administered under light isoflurane anaesthesia. The total volume for each dose was administered at 1 injection site in the quadriceps using an appropriate syringe and needle (BD Microfine Syringes). The right and left quadriceps were used in rotation.

Each vial was gently inverted 3 times before the first dosing to ensure homogeneity according to the Study Sponsor (see Appendix 3).

#### 4.6.2. Justification of Route and Dose

The intramuscular route of exposure was selected because this is the route of human exposure. The dose administered was the highest absolute dose considered for Women of Childbearing Potential.

#### 4.7. In-Life Procedures, Observations, and Measurements

The in-life procedures, observations, and measurements listed below were performed as specified. Untreated males were weighed, observed for morbidity and mortality and any abnormal clinical observations were recorded. These data are retained in the raw data but are not reported.

##### 4.7.1. Mortality/Moribundity Checks

Throughout the study, all F0 females were observed for general health/mortality and moribundity at least twice daily, except on days of receipt and study termination where frequency was at least once daily. Animals were not removed from the cage during observation, unless necessary for identification or confirmation of possible findings.

F1 pups were counted daily during the preweaning phase.

##### 4.7.2. Clinical Observations

###### 4.7.2.1. Cage Side Observations

Cage side observations were performed at least once daily on non-dosing days for F0 females.

During the dosing period, cage side observations were performed before and at least once after dosing for F0 females. Animals were not removed from the cage during observation, unless necessary for identification or confirmation of possible findings.

#### 4.7.2.2. Detailed Clinical Observations

All F0 females were removed from the cage and a detailed clinical observation was performed weekly during the pre-mating period then on each weighing day during the gestation and lactation periods.

#### 4.7.3. Body Weights

Individual body weights for F0 females were recorded as follows:

- At least weekly pretest, and twice weekly during the pre-mating and mating periods (only pre-mating data are reported).
- On GD0, GD6, GD9, GD12, GD15, GD18, GD21.
- On LD1<sup>1</sup>, LD4, LD7, LD10, LD14, LD17 and LD21 (littering subgroup only).

During the lactation phase, offspring were weighed on PND1, PND4, PND7, PND10, PND14, PND17 and PND21.

#### 4.7.4. Food Consumption

Food consumption of F0 females was recorded for the periods (days):

- Once weekly from Day 1 during pre-mating period.
- From GD0 to GD6, GD6 to GD9, GD9 to GD12, GD12 to GD15, GD15 to GD18, GD18 to GD21.
- From LD1 to LD4, LD4 to LD7, LD7 to LD10, LD10 to LD14, LD14 to LD17 and LD17 to LD21 (littering subgroup only).

#### 4.7.5. Estrous Cycles

Vaginal smears were taken daily and used to determine the cycle stage for each F0 female throughout a 14-day pre-dosing period, then for 2 weeks before mating and during cohabitation until confirmation of GD0.

#### 4.7.6. Mating

Animals were paired on the basis of 1 male and 1 F0 female from the same group (not siblings) for a maximum of 14 days.

The day of mating was confirmed by the presence of sperm in a vaginal smear or a vaginal plug and was recorded as GD0.

Mated females were separated from the males once mating had been confirmed and smearing ceased or when the appearance of the female suggested pregnancy from an undetected mating.

The same untreated males were used to mate both subgroups.

<sup>1</sup>: F208 (Control, 0 µg) and F263 (BNT162b2, 30 µg) were additionally weighed on LD0.

#### **4.8. Pregnancy and Parturition (Littering Subgroup Females)**

For each littering subgroup female, the following data were recorded:

- Date of mating (GD0).
- Date of parturition (LD0).
- Duration of gestation.
- Abnormalities of nesting or nursing behaviour.
- Number of implantation sites (at necropsy after staining with ammonium sulphide solution).

#### **4.9. Litter Data (Littering Subgroup Females)**

For each littering subgroup litter, the following data were recorded pre-weaning:

- Number of pups born (live and dead).
- External abnormalities of the pups.
- Number, weight and sex of pups on PND1, PND4, PND7, PND10, PND14, PND17 and PND21.
- Physical development of the offspring, as assessed by the intra-litter onset and duration of pinna unfolding from PND1 and eye opening from PND12.
- Behavioural and functional tests in all pups as follows:
  - Pupillary reflex and auditory reflex on PND21.
- External and necropsy findings of dead pups.

On PND4, the size of each litter was adjusted (culling) to 8 pups, where possible, by eliminating extra pups by random selection to yield where possible 4 males and 4 females per litter. Extra pups were euthanized by an intraperitoneal injection of sodium pentobarbitone.

Justification of the culling procedure: The culling of litters to a standard size is given as an optional procedure in the ICH S5(R3) regulatory guideline. Scientific opinion remains divided regarding the justification of culling (see Section 11). It was therefore decided to use culling in this study in order to be consistent with the historical data compiled by the Test Facility.

#### **4.10. Antibody Evaluation**

##### **4.10.1. Antibody Sample Collection**

Samples were collected according to Text Table 5.

Text Table 5  
Antibody Sample Collection

Group Nos.	Number of Females	Predose on Days of Dosing		Necropsy (GD21 or LD21/PND21) <sup>b</sup>
		Pretest	M0 <sup>a</sup>	
1 to 4	All F0 females	X	X	X
1 to 4	Selected fetuses from all litters of caesarean subgroup	-	-	X
1 to 4	Selected pups (1 male and 1 female if possible) from all litters of the lactation subgroup	-	-	X
Unscheduled euthanasia (dams only, done in the animal facility)		X		

X: Sample collected; -: Not collected.

M0: First day of pairing; GD: Gestation Day; LD: Lactation Day; PND: Post Natal Day.

<sup>a</sup>: Sample collected just before pairing.

<sup>b</sup>: The day of necropsy (i.e., Day 43 for failed to mate F43 (BNT162b1, 30 µg) and for mistimed pregnancy F277 (BNT162b3, 30 µg); on GD26 for not pregnant F254 (BNT162b2, 30 µg); on GD27 for not pregnant F226 (BNT162b1, 30 µg); on LD1 for euthanized moribund post-partum F276 (BNT162b3, 30 µg), for total litter death F236 (BNT162b1, 30 µg) and F279 (BNT162b3, 30 µg).

<b>Method/Comments:</b>	F0 females: Jugular vein Fetuses: Small incision after anaesthesia Pups: Intracardiac
<b>Target Volume (mL):</b>	Target 0.5 mL for F0 females Target 0.3 mL pooled per litter for fetuses Targeted 0.5 mL pooled per litter from 2 pups (ideally 1 male and 1 female)
<b>Anticoagulant:</b>	None
<b>Special Requirements:</b>	None
<b>Processing</b>	Serum

#### 4.10.2. Antibody Sample Processing

Samples were processed according to Text Table 6.

Text Table 6  
Antibody Sample Processing

Centrifugation	Volume Aliquot 1	Volume Aliquot 2	Freezing	Specific Request
1800 g 10 minutes Approximately +4°C	At least 120 µL (dams and pups) or 60 µL (fetuses) of serum	Remaining (serum)	-80°C	None

The exact time of sampling with respect to dosing was recorded for each animal (details are retained in the raw data).

#### 4.10.3. Antibody Analysis by Microneutralization CPE-Based

Each serum sample was tested in duplicate for serological detection of SARS-CoV-2 specific neutralizing antibodies. The test was carried out at Vismederi, according to Vismederi Standard Operating Procedures and dedicated working instruction “Microneutralization CPE-based assay for SARS-COV-2” (WI-MNSARS-CoV-2).

The methods and results are presented in Appendix 26.

#### **4.11. Terminal Procedures**

##### **4.11.1. Unscheduled Deaths**

A moribund female showing signs of parturition difficulties and 2 females with total litter death were euthanized by carbon dioxide inhalation and exsanguination.

The female euthanized moribund due to parturition difficulties was subject to full macroscopic examination of the thoracic and abdominal cavities, including the injection sites, to confirm pregnancy status, number of corpora lutea and numbers and types of uterine implantations. Any abnormalities observed were sampled and preserved. Retained fetuses and dead pups from this female were not examined and were discarded.

The females with total litter death were euthanized and subject to full macroscopic examination of the thoracic and abdominal cavities, including the injection sites, and number of uterine implantations. Any abnormalities observed were sampled and preserved.

One dead breeder male was discarded without further examinations.

##### **4.11.2. Scheduled Euthanasia**

Surviving animals were euthanized by carbon dioxide inhalation and exsanguination (with the exception of the PND4 extra pups - see Section 4.9) and then necropsied according to the following schedule:

F0 females:

Caesarean subgroup: On GD21.

F43 that failed to mate was euthanized after the mating period (on Day 43).

Littering subgroup: On LD21, after weaning of the F1 pups.

F226 and F254 that failed to produce a viable litter by GD26 or GD27 were euthanized and necropsied; F277 with a mistimed pregnancy (mating not detected) was euthanized and necropsied after the end of the mating period on Day 43).

Culled F1 pups:

On PND4.

Euthanized F1 pups:

On PND21.

The first 30 surviving untreated males were retained at the disposal of the Test Facility and the 57 remaining untreated males were euthanized without further examinations following completion of the majority of caesarean sections.

Selected fetuses (caesarean subgroup) and pups (littering subgroup) were sampled for blood (antibody analysis) at necropsy (see Section 4.10.1).

##### **4.11.3. Necropsy**

All adult animals and pups (including those culled on PND4) were submitted to a full macroscopic examination of the abdominal and thoracic cavities including the injection sites (for F0 females). Any abnormalities observed were recorded and preserved.

#### 4.11.3.1. Subgroup 1 (Caesarean-Section)

For each female euthanized on GD21, the ovaries and uterus were removed and examined, including examination of the placentae. The following data were recorded:

Text Table 7  
Necropsy Data

Parameters	Comments
Pregnancy status	-
Gravid uterus weight	The uterus of apparently non-pregnant females was placed in ammonium sulphide solution in order to stain any previously undetected implantation sites
Number and distribution of intrauterine implantations	Classified as: Live fetuses, dead fetuses, early resorptions and late resorptions
Number of corpora lutea	-
Fetal weights	Individual weights were recorded
Fetal sex	-

:- No comment.

#### 4.11.3.2. Subgroup 2 (Natural Delivery)

The carcasses of PND21 pups were preserved for possible skeletal examinations. No further examination was performed.

For all F0 females, the number of implantation sites were recorded.

#### 4.11.4. Fetal Examination (Caesarean-Section)

Each fetus was examined for external defects and euthanized by oral administration of sodium pentobarbitone. Approximately one half of each litter was submitted to fresh visceral examination of the body (abdominal and thoracic cavities). The head was fixed in Harrison's fluid for subsequent examination by serial sectioning. The remaining carcass was retained fixed in ethanol.

The remaining half of the fetuses in each litter was eviscerated and then processed for skeletal examination. The skeletal examinations were performed following maceration of the soft tissues with aqueous potassium hydroxide, staining of the skeleton with Alizarin red then passage into glycerol.

Soft tissue and skeletal examinations were performed using a binocular microscope.

### 5. STATISTICAL ANALYSIS

All results presented in the tables of the report are calculated using non-rounded values.

All statistical analyses were performed within the respective study phase, unless otherwise noted. Numerical data collected on scheduled occasions from all animals were summarized by occasion or by litter and statistically analyzed as indicated below according to the occasion or by litter.



### 5.1. Constructed Variables

Body weight gains (F0 generation): Calculated between each scheduled interval as well as between the following intervals: Day 1 to Day 22 (both subgroups), GD0 to GD21 (both subgroups) and LD1 to LD21 (littering subgroup).

Food consumption: Calculated between each scheduled interval as well as between the following intervals: Day 1 to Day 22 (both subgroups), GD0 to GD21 (both subgroups) and LD1 to LD21 (littering subgroup).

For both subgroups combined where applicable (caesarean and littering subgroups):

Pre-coital interval (in days): 
$$\frac{\text{Sum of days until successful insemination}}{\text{Number of inseminated females}}$$

Copulation (mating) index (in %): 
$$\frac{\text{Number of inseminated females}}{\text{Number of paired animals}} \times 100$$

Pregnancy rate (in %): 
$$\frac{\text{Number of pregnant females}}{\text{Number of paired animals}} \times 100$$

Fertility index (in %): 
$$\frac{\text{Number of pregnant females}}{\text{Number of inseminated females}} \times 100$$

For the caesarean subgroup:

Pre-implantation loss (in %): 
$$\frac{\text{Number of corpora lutea} - \text{Number of implantations}}{\text{Number of corpora lutea}} \times 100$$

Post-implantation loss (in %): 
$$\frac{\text{Number of Implantations} - \text{Number of Viable Fetuses}}{\text{Number of implantations}} \times 100$$

Sex ratio (proportion of male fetuses): 
$$\frac{\text{Number of males}}{\text{Number of fetuses}} \times 100$$

% of Fetuses with Abnormalities: 
$$\frac{\text{Number of fetuses in litter with a given finding}}{\text{Number of fetuses in litter examined}} \times 100$$

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For the littering subgroup:

$$\text{Gestation index (in \%):} \quad \frac{\text{Number of pups alive at birth}}{\text{Number of pregnant females}} \times 100$$

$$\text{Live birth index (in \%):} \quad \frac{\text{Number of pups born alive}}{\text{Number of pups born}} \times 100$$

$$\text{Pre-birth loss (in \%):} \quad \frac{\text{Number of pups born}}{\text{Number of implantation sites (scars)}} \times 100$$

$$\text{Viability index (in \%):} \quad \frac{\text{Number of pups alive on PND 4}}{\text{Number of pups alive at birth}} \times 100$$

$$\text{Weaning index (in \%):} \quad \frac{\text{Number of pups alive on PND21}}{\text{Number of pups alive on PND4*}} \times 100$$

\*: Number of pups alive on Day 4 post-partum after adjustment of litter size.

$$\text{Sex ratio (proportion of male pups):} \quad \frac{\text{Number of male pups}}{\text{Number of pups}} \times 100$$

## 5.2. Descriptive Statistical Analyses

Means, standard deviations (or % coefficient of variation or standard error, when deemed appropriate), percentages, numbers, and/or incidences were reported as appropriate by dataset.

## 5.3. Inferential Statistical Methods

All statistical tests were conducted at the 5% significance level. All pairwise comparisons were conducted using two-sided tests and were reported at the 1% and 5% levels, unless otherwise noted.

The pairwise comparisons of interest are listed below:

Group 2	vs.	Group 1
Group 3	vs.	Group 1
Group 4	vs.	Group 1

Analyses were performed according to the matrix below when possible but excluded any group with less than 3 observations.

Text Table 8  
Statistical Matrix

Variables for Inferential Analysis	Statistical Method		
	Parametric/ Non-Parametric	Non-Parametric	Incidence
Body weight <sup>a</sup>	X	-	-
Body weight gains <sup>a</sup>	X	-	-
Food consumption <sup>a</sup>	X	-	-
Delivery and litter data	X	-	-
Reflex and physical development	-	-	X
Mating performance and fertility indices	-	-	X
Parental indices and mortality	-	-	X
Gravid uterine weight and corrected maternal body weights	X	-	-
Ovarian and uterine data	X	-	-
Litter observations (litter means) <sup>c</sup>	X	-	-
Litter % of fetuses with gross/external/visceral/skeletal abnormalities <sup>b</sup>	-	X	-

X: Statistical analysis performed; -: Statistical analysis not performed.

<sup>a</sup>: Excludes animals not pregnant from the gestation and lactation phases summarization and statistical analysis.

<sup>b</sup>: Presented for sexes combined; live fetuses only.

<sup>c</sup>: Presented for males, females and sexes combined; live fetuses only.

#### 5.4. Parametric/Non-Parametric

Levene's test was used to assess the homogeneity of group variances. The groups were compared using a Dunnett's test if Levene's test was not significant or Dunn's test if it was significant.

Pre-coital interval, estrous cycle and F1 offspring functional tests data were analysed using a SAS software package. Levene's test was used to test the equality of variance across groups and Shapiro-Wilk's test was used to assess the normality of the data distribution in each group. Data with homogeneous variances and normal distribution in all groups was analysed using ANOVA followed by Dunnett's test. Data showing non-homogeneous variances or a non-normal distribution in at least 1 group was analysed using Kruskal-Wallis test followed by Wilcoxon's rank sum test.

#### 5.5. Non-Parametric

Datasets were compared using a Dunn's test.

#### 5.6. Incidence

A Fisher's exact test was used to conduct pairwise group comparisons of interest.

## 6. COMPUTERIZED SYSTEMS

Critical computerized systems used in the study are listed below or presented in the appropriate Phase Report. All computerized systems used in the conduct of this study have been validated; when a particular system has not satisfied all requirements, appropriate administrative and procedural controls were implemented to assure the quality and integrity of data.

Text Table 9  
Critical Computerized Systems

System Name	Version No.	Description of Data Collected and/or Analyzed
GTC Mozart 21	3.1	Environmental data recording
Vaisala	4.1.0	Environmental data recording
Provantis®	9 and 10	Test material receipt, accountability and/or formulation activities; in-life; postmortem; statistical analysis
Devil	2.1.148	Deviation information library
STATSAS	STATSAS 2.00	Statistical analysis
Share Document Management System	1.0	Reporting
DocuSign™	11	Collection of 21 CFR Part 11 compliant signature

Microsoft Excel® (version 2003 or higher) was employed to present certain results and perform associated calculations.

## 7. RETENTION AND DISPOSITION OF RECORDS, SAMPLES, AND SPECIMENS

All study-specific raw data, electronic data, documentation, Study Plan, retained samples and specimens, and the Final Report will be archived at the Final Report issue. All materials generated by Charles River Laboratories from this study will be transferred to a Charles River Laboratories archive and kept for a period of 2 years following the date of issue of the Final Report.

Disposition of residual/retained analytical samples was as described in the table below.

Text Table 10  
Disposition of Residual/Retained Samples

Sample Type	Disposition
Serum for Antibody analysis	Discarded

Records to be maintained included, but were not limited to, documentation and data for the following:

- Study Plan, Study Plan amendments, and deviations.
- Study schedule.
- Study-related correspondence.
- Test system receipt, health, and husbandry.
- Test materials receipt, identification and preparation.
- In-life measurements and observations.
- Reserve sample.
- Antibody sample collection and evaluation.
- Gross observations and related data.
- Organ weight measurement.
- Statistical analysis results.
- Original signed Final Report.

Original signed Study Plan and amendments signed by the Sponsor (e-signed documents) are archived at the sponsor under his responsibility. The regulatory compliance to applicable regulations of electronic signature system developed and used by the Sponsor is under his responsibility.

Study deviations were archived electronically at the Charles River Laboratories facility located in Wilmington, Massachusetts.

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## 8. RESULTS

### 8.1. Serum Antibody Analysis

(Appendix 26)

Administration of 4 doses (2 prior to mating and 2 during gestation) of BNT162b1, BNT162b2, or BNT162b3 elicited SARS-CoV-2 neutralizing antibody responses in the majority of females just prior to mating (M-14), at the end of gestation (GD21), and at the end of lactation (LD21). SARS-CoV-2 neutralizing titers were detected in most offspring (fetuses on GD21 and pups on PND21). SARS-CoV-2 neutralizing antibody titers were not observed in animals prior to vaccine administration or in saline-administered control animals.

### 8.2. Mortality

(Appendix 4, Appendix 7 and Appendix 29)

There was no unscheduled death related to any of the 3 vaccine candidates.

F276 from the BNT162b3 group (littering subgroup) had parturition difficulties and was euthanized for ethical reasons on LD1. The female delivered 8 pups. On LD0, distended/blue abdomen was noted. On LD1, hunched posture, pale, marked piloerection, bleeding at the vulva/red vaginal discharge, distended/purple abdomen were noted and 4 of the delivered pups were missing/dead/cannibalized. At necropsy, the female had 13 implantations, 3 fetuses were retained in the uterus. No macroscopic findings were noted.

Such cases of parturition difficulties are present in the historical control data for the strain of rat (Study X16 in 2016), so the presence of this isolated finding in the BNT162b3 group was considered to be incidental.

F236 from the BNT162b1 group incurred total litter death of 15 pups between birth and LD1 (9 stillborn, 3 cannibalized, 1 dead and 2 missing pups).

F279 from the BNT162b3 group delivered 8 stillborn pups.

Such cases of total litter death at or shortly after birth are present in the historical control data (2 studies (A19 in 2019 and V17 in 2017) out of 18 between 2015 and 2019). The presence of the isolated case in each of the BNT162b1 and BNT162b3 groups, with no similar finding in the BNT162b2 group, suggested that they were incidental and not related to any of the 3 vaccine candidates.

### 8.3. Clinical Observations

(Table 1, Table 2, Table 3, Appendix 5, Appendix 6, Appendix 7 and Appendix 8)

There were no adverse clinical signs during the premating and gestations periods related to any of the 3 vaccine candidates.

Following administrations (M-21, M-14, GD9 and GD20), swelling (associated or not with limping and/or piloerection for 1 or 2 days after the second dose only) was noted at the injection site for animals in the BNT162b1, BNT162b2 and BNT162b3 groups. Complete recovery was noted between each of the dose administrations. The overall health of the animals was not impacted by these transient clinical signs localized to the injection site; therefore, these observations were not considered adverse.

There were no clinical signs during the lactation period related to any of the 3 vaccine candidates.

Other clinical signs such as abnormal vocalization, chromodacryorrhea, desquamation, erythema, localized hairloss, malocclusion, long or missing teeth, red vaginal discharge, red stained fur, scab(s), sore(s) noted sporadically across the groups were considered to be incidental, related to the method of dose administration or to the pregnancy status of the females.

#### **8.4. Body Weight**

(Figure 1, Figure 2, Figure 3, Table 4, Table 5, Table 6, Table 7, Table 8, Table 9, Appendix 9, Appendix 10 and Appendix 11)

There were no adverse effects on mean body weight change related to any of the 3 vaccine candidates.

Slight body weight loss or reduced body weight gain was noted after each dose administration (M-21, M-14, GD9 and GD20) in the BNT162b1, BNT162b2 and BNT162b3 groups compared with continuous body weight gain in the control group.

Complete recovery was noted between each of the dose administrations such that absolute mean body weight was comparable with the control group at the end of the pre-mating and gestation periods, therefore none of the transient differences from control were considered adverse.

Mean body weight gain was lower in the BNT162b1 and BNT162b3 groups (26 g and 30 g), compared with the control group (33 g) throughout the lactation phase. This was not considered vaccine-related, but due to an atypical high value in the control group compared with the historical control data range (from 10.9 g to 32.6 g).

#### **8.5. Food Consumption**

(Figure 4, Figure 5, Figure 6, Table 10, Table 11, Table 12, Appendix 12, Appendix 13 and Appendix 14)

There were no adverse effects on mean food consumption related to any of the 3 vaccine candidates.

Reduced mean food consumption was noted after the first 3 dose administrations (M-21, M-14 and GD9) in the BNT162b1, BNT162b2 and BNT162b3 groups compared with the control group (up to -14, -16 and -17% on GD9, respectively). Complete recovery was noted between each of the dose administrations such that mean food consumption was comparable with the control group during the pre-mating and gestation periods, therefore none of the transient differences from control were considered adverse.

There was no vaccine-related effect on mean food consumption during the lactation period.

#### **8.6. Estrous Cycle Data**

(Table 13, Appendix 15 and Appendix 29)

There were no effects on estrous cyclicity related to any of the 3 vaccine candidates.

Mean length and regularity of the estrous cycles were comparable in all groups during the acclimatization and pre-mating periods. Mean values were within the historical control range, and no effects on pre-coital interval and copulation index are consistent with normal cycling.

## 8.7. Maternal Mating Performance and Fertility

(Table 14 and Appendix 16)

There were no effects on mating performance or fertility related to any of the 3 vaccine candidates.

In total (caesarean and littering subgroups combined), 44, 43, 44 and 44 (out of 44) females mated in the control, BNT162b1, BNT162b2 and BNT162b3 groups, respectively (including F277, from the BNT162b3 group, not detected at the time of mating) after completion of the 14-day cohabitation period.

The copulation index was therefore 100, 97.7, 100 and 100% in the control, BNT162b1, BNT162b2 and BNT162b3 groups, respectively.

The majority of mated females were inseminated within the first 4 days of pairing (approximate duration of a normal estrous cycle). The mean pre-coital interval was consequently 3.0, 3.0, 2.8 and 2.7 days in the control, BNT162b1, BNT162b2 and BNT162b3 groups, respectively.

In total, there were 43, 41, 42 and 44 pregnant females out of 44 per group paired in the control, BNT162b1, BNT162b2 and BNT162b3 groups, respectively. The pregnancy rate was therefore 98%, 93%, 95% and 100% in the control, BNT162b1, BNT162b2 and BNT162b3 groups, respectively.

In total, there were 43/44, 41/43, 42/44 and 44/44 pregnant/mated females in control, BNT162b1, BNT162b2 and BNT162b3 groups, respectively. The fertility index was therefore 98%, 95%, 95% and 100% in the control, BNT162b1, BNT162b2 and BNT162b3 groups, respectively.

## 8.8. Caesarean Data

### 8.8.1. Gravid Uterus Weight

(Table 15 and Appendix 17)

There were no effects on mean gravid uterus weight related to any of the 3 vaccine candidates.

### 8.8.2. Pregnancy Incidence

(Table 16 and Appendix 18)

There were no effects on pregnancy incidence related to any of the 3 vaccine candidates.

There were 21/22, 20/21, 21/22, and 22/22 pregnant/mated females in the control, BNT162b1, BNT162b2 and BNT162b3 groups, respectively, at the terminal caesarean examinations, all of which had viable fetuses.



### 8.8.3. Pre-Implantation Data

(Table 16, Appendix 18 and Appendix 29)

There were no effects on the pre-implantation data related to any of the 3 vaccine candidates.

The mean numbers of corpora lutea and implantation sites were comparable in all groups.

The mean percentage pre-implantation loss was higher in the BNT162b2 and BNT162b3 groups (9.77% and 7.96%, respectively) compared with the control group (4.09%). However, the differences were not biologically meaningful and the values remained within the historical control data range (5.1% to 11.5%) for pivotal studies (see Explanation Page), so the difference was considered to be incidental.

### 8.8.4. Post-Implantation Data

(Table 16, Appendix 18 and Appendix 29)

There were no effects on embryo-fetal survival related to any of the 3 vaccine candidates.

The mean percentage post-implantation loss and the mean live litter size were comparable in all groups and consistent with the historical control data.

### 8.8.5. Fetal Data

(Table 16, Appendix 18 and Appendix 29)

There were no effects on mean fetal weight or fetal sex ratio related to any of the 3 vaccine candidates.

## 8.9. Fetal Examinations

The numbers of fetuses (litters) submitted to the different examinations were as follows:

Group No.	1	2	3	4
External examination	277 (21)	282 (20)	276 (21)	275 (22)
Internal (visceral) examination (body)	133 (21)	135 (20)	132 (21)	132 (22)
Fixed head examination	133 (21)	135 (20)	132 (21)	132 (22)
Skeletal examination (head and body)	144 (21)	147 (20)	144 (21)	143 (22)

There were no effects on fetal morphology related to any of the 3 vaccine candidates. This is consistent with no corresponding malformations in pups described in Sections 8.10.4 and 8.10.7.

### 8.9.1. External Observations

(Table 17, Appendix 20 and Appendix 29)

There were no effects on fetal external morphology related to any of the 3 vaccine candidates.

From the BNT162b1 group, Fetus 17 (F35) had exencephaly, open eye and spina bifida in the cervical region. Exencephaly and open eye are part of the background data for this strain of rat (CRL:WI(Han)). Although not present in the Test Facility Historical Control Data (HCD), neural tube defects such as spina bifida are part of the background of spontaneous abnormalities found in the rat (present in the HCD for the Sprague Dawley strain as well as other published HCD (Ku wagata, 2018)). These malformations noted for a single fetus were therefore considered incidental in view of the isolated incidence.

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In the BNT162b2 group, there was Fetus 14 (F58) had gastroschisis and Fetus 14 (F64) had a small mouth and agnathia. These malformations are part of the background data for this strain of rat (CRL:WI(Han)) and were considered incidental in view of their isolated and sporadic nature.

### 8.9.2. Visceral Observations

(Table 17, Appendix 21 and Appendix 29)

There were no effects on fetal soft tissue morphology related to any of the 3 vaccine candidates.

Fetus 13 (F24) was observed with a narrowed ductus arteriosus from the BNT162b1 group. This finding is part of the normal process of postnatal respiratory development. This finding was considered incidental in view of its isolated incidence.

Fetus 9 (F38) from the BNT162b1 group had a retinal fold. This finding is part of the background of changes for this strain of rat (CRL:WI(Han)) and was considered incidental in view of its isolated incidence.

Fetus 6 (F53) from the BNT162b2 group was observed with a right-sided aortic arch and Fetus 8 (F68) from the BNT162b3 group was observed with a ventricular septum defect. These findings are also part of the background of findings for this strain of rat (CRL:WI(Han)) and were considered incidental in view of their isolated incidences.

The other less severe soft tissue anomalies and variations are part of the background data for this strain of rat and were also incidental.

### 8.9.3. Skeletal Observations

(Table 17 and Appendix 22)

There were no effects on fetal skeletal morphology related to any of the 3 vaccine candidates.

Associated with the malformations noted externally (see Section 8.9.1), Fetus 17 (F35) from the BNT162b1 group had acrania and multiple abnormalities of thoracic and cervical vertebrae and the Fetus 14 (F64) from the BNT162b2 group had short and fused mandibles. These malformations associated with the abnormalities noted externally were considered incidental in view of their isolated incidences.

The other less severe skeletal anomalies and variations, such as supernumerary lumbar ribs, 7 lumbar vertebrae or incomplete ossification of thoracic centrum are part of the background data for this strain of rat and/or were also incidental.

## 8.10. Delivery and Litter Data

### 8.10.1. Parturition and Gestation Length

(Table 18, Appendix 23 and Appendix 29)

There were no effects on parturition and gestation length related to any of the 3 vaccine candidates.

There were 22, 21, 21 and 20 females in the control, BNT162b1, BNT162b2 and BNT162b3 groups that completed delivery and had liveborn pups giving a gestation index of 100%, 100%, 100% and 95%, respectively. This was consistent with the background data for this strain of rat.

The mean duration of gestation (approximately 22 days) was comparable in all groups. F276 from the BNT162b3 group that was euthanized due to clinical signs associated with parturition difficulties (described in Section 8.2) did not affect the overall gestation length for that group.

#### 8.10.2. Pre-Birth Loss

(Table 18, Appendix 23 and Appendix 29)

There was no effect on pre-birth loss related to any of the 3 vaccine candidates.

The mean percentage pre-birth loss was higher in the BNT162b1 (12.2%) and BNT162b3 (13.8%) groups compared with the concurrent control group (6.8%), but the differences were not biologically meaningful and the value remained consistent with the historical control data range (from 5.1% to 13.6%) for pivotal studies, so the difference was considered to be incidental.

Consequently, the mean number of pups delivered was marginally lower in the BNT162b1 and BNT162b3 groups (11.9 and 11.4, respectively) compared with the control group (13.3). However, the values remained consistent with the historical control data range (from 9.9 to 11.8) for pivotal studies.

#### 8.10.3. Pup Viability and Litter Sizes

(Table 18, Appendix 23 and Appendix 29)

There were no effects on pup viability and litter size related to any of the 3 vaccine candidates.

The live birth index was marginally lower in the BNT162b1 and BNT162b3 groups (93.2 and 94.7%, respectively) compared with control group (98%) with 17 and 12 stillborn/dead pups from 4 litters in each group, compared with 6 from 3 litters in the control group. This was due to 1 female in each of the BNT162b1 and BNT162b3 groups (F236 and F279, respectively) that incurred total litter death.

F236 from the BNT162b1 group incurred total litter death of 15 pups between birth and Lactation Day 1 (9 stillborn, 3 cannibalized, 1 dead and 2 missing pups). F279 from the BNT162b3 group delivered 8 stillborn pups. Such cases of total litter death at or shortly after birth are present in the historical control data (2 studies A19 and V17 in the HCD). The presence of the isolated case in each of the BNT162b1 and BNT162b3 groups, with no similar finding in the BNT162b2 group, suggested that they were incidental and not related to the vaccines.

Consequently, the mean live litter size was marginally lower in the BNT162b1 and BNT162b3 groups (11.0 and 11.3, respectively) compared with concurrent control group (13.0). However, the values were consistent with the background data for this strain of rat (from 9.8 to 11.6).

The viability index (PND0 through to PND4) and weaning index (PND4 through to PND21) were comparable in all groups and consistent with the historical control data.

#### 8.10.4. Pup Clinical Observations

(Table 3 and Appendix 7)

There was no pattern in the incidence or type of pup clinical observations or external abnormalities that suggested a relationship to any of the 3 vaccine candidates.

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#### **8.10.5. Pup Weights**

(Figure 7a, Figure 7b, Table 19 and Appendix 24)

There was no effect on mean pup weight throughout the pre-weaning period related to any of the 3 vaccine candidates.

#### **8.10.6. Pup Physical and Functional Development**

(Table 20 and Appendix 25)

There were no effects on pre-weaning physical (pinna unfolding and eye opening) and functional (pupil and auditory reflexes) development related to any of the 3 vaccine candidates.

#### **8.10.7. Pup Necropsy Findings**

(Appendix 28)

There was no pattern in the incidence or type of pup macroscopic observations or malformations that suggested a relationship to any of the 3 vaccine candidates.

#### **8.11. Necropsy Findings of Adult Females**

(Table 21 and Appendix 27)

There were no adverse maternal macroscopic findings related to any of the 3 vaccine candidates.

Macroscopic findings were noted at the injection sites (firm area, enlarged, edematous area and/or pale) in the BNT162b1, BNT162b2 and BNT162b3 groups. These findings were considered non-adverse as they had no impact on the overall health of the animals and are consistent with administration of a vaccine and an inflammatory/immune response localized to the injection site.

Abnormalities of the liver (diaphragmatic hernia, mottled surface, abnormal shape or adherent mass) were occasionally noted for isolated females across all groups (including controls) and were considered incidental.

Alopecia and/or sores/crusts were also noted for isolated females across the groups (including controls) and were incidental (related to the pregnancy status of the females).

## 9. INTEGRATED SUMMARY AND DISCUSSION OF RESULTS

The purpose of this study was to assess the potential effects of BNT162b1, BNT162b2 and BNT162b3, vaccine development candidates to prevent Covid-19, and the concomitant immune response, on fertility and pre and postnatal development in the pregnant and lactating female Wistar (CRL:WI[Han]) rat and on the in utero and postnatal development of their offspring.

There were no deaths throughout the study related to any of the vaccine candidates. Intramuscular administration of BNT162b1, BNT162b2 and BNT162b3, before and during gestation to female Wistar rats resulted in non-adverse clinical signs and macroscopic findings localized to the injection site as well as transient, non-adverse body weight and food consumption effects after each dose administration. These maternal effects were considered non-adverse as they had no impact on the overall health of the animals. These maternal findings are all consistent with administration of a vaccine and an inflammatory/immune response.

There were no effects on estrous cycles, pre-coital interval, mating, fertility and pregnancy index, or on any ovarian, uterine, or litter parameters, including F1 survival, growth, external, visceral, and skeletal morphology, or effects on pre-weaning physical and functional development of the F1 pups related to any of the 3 vaccine candidates.

Administration of 4 doses (2 prior to mating and 2 during gestation) of BNT162b1, BNT162b2, or BNT162b3 elicited SARS-CoV-2 neutralizing antibody responses in the majority of females just prior to mating (M0), at the end of gestation (GD21), and at the end of lactation (LD21). SARS-CoV-2 neutralizing titers were detected in most offspring (fetuses on GD21 and pups on PND21). SARS-CoV-2 neutralizing antibody titers were not observed in animals prior to vaccine administration or in saline-administered control animals.

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## 10. CONCLUSION

Intramuscular administration of BNT162b1, BNT162b2 and BNT162b3 before and during gestation to female Wistar (CRL:WI[Han]) rats was associated with non-adverse effects (body weight, food consumption and effects localized to the injection site) after each dose administration. There were no effects of any of the 3 vaccine candidates on mating performance or fertility in F0 female rats or on embryo-fetal or postnatal survival, growth, or development of the F1 offspring.

An immune response was confirmed in F0 female rats following administration of each vaccine candidate and these responses were also detectable in the F1 offspring (fetuses and pups).

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## 11. REFERENCES

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2. Agnish ND and Keller KA. The rationale for culling of rodent litters. Fundam. Appl. Toxicol. 1997 38, 2-6.
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## EXPLANATION PAGE

All day(s) referenced throughout the outputs generated are study days beginning with Study Day 1, the first day of dosing.

Abbreviations consistent throughout the Summary and Individual Tables.

Note: All of the abbreviations listed on these pages may not be applicable to this report.

The footnote "\*" = result to left has an associated comment or marker" was printed on the following table without values marked with an asterisk due to data acquisition constraints.

Statistical significances arise from automatic comparisons with the principal control.

Principal Control Group: 1.

\*: 5% significance level

\*\*: 1% significance level

\*\*\*: 0.1% significance level

Statistical significance is represented by "x", "xx" or "xxx", where "x" is a letter indicating which statistical test has been performed and where "x" corresponds to 0.05, "xx" corresponds to 0.01 and "xxx" corresponds to "0.001". On some occasions, the statistical significance does not appear on the tables due to system constraints.

## GENERAL

Abbreviation	Description
< or >	Out of range
% Diff	% Difference from control group
DC	Died post-coitum
DP or MDPP	Moribund/died post-partum
EP	Euthanized preterminally
FM	Failed to mate
FME	Failed to mate excluded
G or GD	Gestation day
LD	Lactation day
mcg	µg
Mean	Arithmetic mean
m or M, f or F	Male, Female
MT, MTP	Mistimed pregnancy
N	Number of values included in analysis
NA	Not applicable
NC	Not calculable
NF, NVF	No viable fetuses
No.	Animal number
no.	Number
NP	Not pregnant
NPE	Not pregnant excluded
NV	No viable embryos/fetuses
P	Pregnant
RC	Result comment
S.D. or SD	Standard deviation
SpCMSD	Mean SD
tCtrl	Mean treated group versus control group ratio
TD or Total LDeath	Total litter death
TR	Total resorption
UD	Unable to deliver, sacrificed
Wx	Week x

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## MORTALITY

Abbreviation	Description	Abbreviation	Description
ACCD	Accidental death	REL	Released
AD	Accidental death	TTP2	Pup transfer
AI	Interim euthanasia	TE	Terminal euthanasia
AM SIR	Mortality recorded in the morning	TERM	Terminal euthanasia
FD	Found dead	TLD	Total litter death
FL	Failed to litter	TS	Terminal euthanasia
HS	Moribund euthanasia	UE	Unscheduled euthanasia
INTM	Interim euthanasia	UNSC	Unscheduled euthanasia
PUE	Pup unscheduled euthanasia	UT	Unplanned terminal euthanasia
REC	Recovery euthanasia	VE	Removed from study alive

## CLINICAL OBSERVATIONS

Abbreviation	Description	Abbreviation	Description
xM	Clinical observations performed x minutes postdosing. Target times are presented. Actual times are kept in the raw data.	P2DS	Observation performed before the second dosing
xH or x	Clinical observations performed x hour(s) postdosing. Target times are presented. Actual times are kept in the raw data.	Part	Particulates
+xh	Clinical observations performed x hour(s) postdosing. Target times are presented. Actual times are kept in the raw data.	PM_S	Observation performed in the afternoon
AM_S	Observation performed in the morning	PR	Observation predosing
BEF	Before dosing	PT	Permanent
Daily x	Clinical observations on days without dosing	Rx	Observation during dosing
DuRx	Observation during dosing	Sev Not App	Severity not applicable
DT	Observation during dosing	UDu	Unscheduled observation during dosing
EOD	Observation performed at the end of day	Un	Unscheduled observation
no TT area	Non treated area	Unsc or NS	Unscheduled observation
OTHR	Other	VET or Veto x	Veterinary observation
P	Observation postdosing	w/	With

### Notes:

Injection site 1: left quadriceps

Injection site 2: right quadriceps

Clinical signs from all females with mating date (including not pregnant females) were presented in table "Summary Gestation Clinical Observations" and appendix "Individual Gestation Clinical Observations".

Only mistimed pregnancy female and failed to mate female were presented in appendix "Individual Clinical Observations of Excluded Females".

On 05 September 2020, sore on right forelimb was recorded for several females from littering subgroup. The females number was not recorded.

On GD18, teeth were cut from F202 (Control group). Information "lower teeth" or "upper teeth" were not recorded.

On several occasions on non-dosing days during lactation period, detailed clinical observations were recorded on timeslot BEF (before dosing).

Only animals and occasions with findings are presented.

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### BODY WEIGHT/BODY WEIGHT GAIN

Notes:

Pre-mating body weights on Days -26, -25, -21 and -20 were not represented in Figure 2 as only half animals were weighed.

F245 (BNT162b2 group) delivered on GD20, the body weight recorded on GD21 corresponds to LD1 due to system constraints.

F208 (Control group) and F263 (BNT162b2 group) were additionally weighed on LD0.

### FOOD CONSUMPTION

Note:

The quantity of remaining food was not weighed on GD21 for F245 (BNT162b2 group) because this female littered on GD20. Therefore, no food consumption was calculated for GD18 to 21 and GD0 to GD21.

### ESTROUS CYCLE

Note:

For each female, the day after which a last stage of cycle was recorded corresponds to the day where it was declared positive for the presence of sperm. This day was determined as the mating day and was recorded as Gestation Day (GD0). No mating day was determined for any female with a stage of cycle recorded on Day 36.

### GRAVID UTERINE WEIGHTS AND MATERNAL BODY WEIGHT CHANGE

Abbreviation	Description	Abbreviation	Description
0-TBW	Weight calculation from G0 to terminal body weight (corrected)	Day X	Day X of gestation
6-TBW	Weight calculation from G6 to terminal body weight (corrected)	G	Gestation day
BW	Body weight	NRQ	Not required
BWC	Body weight change	NSCH	Not scheduled to be performed
BWG	Body weight gain	TBW	Terminal body weight
		Wt	Weight

Note:

Due to the technical error, gravid uterus weight from F72 (BNT162b3 group) was not recorded.

### CAESAREAN SECTION DATA

Abbreviation	Description	Abbreviation	Description
Post-Implant Loss	Post-Implantation Loss	Pre-Implant Loss or Pre-Impl.	Pre-Implant Loss
(B)	Both (males and females)	P-Implants	Post-implantation loss
both	Both (males and females)	Post-Implant Loss	Post-implantation loss
N+ve	Number positive	Wt	Weight

### FETAL DATA AND OBSERVATIONS

Abbreviation	Description	Abbreviation	Description
!	Preparation artefact	L	Left
(%)	Mean % of litters with the abnormality	Litters(%) N	Group litter incidence
A	Anomalie	L or LF	Live fetus
A	Alive	LR	Late resorption
Abbr	Abbreviation	M	Malformation
DE	Dead embryo	PLWT	Placental weight
DF	Dead fetus – not examined	R	Right
DFE	Dead fetus - examined	S	Scar
EI	Empty implantation site	SkeletalBody	Skeletal examination of body
E or ER	Early resorption	SkeletalHead	Skeletal examination of head
FPOS	Fetal position	TR	Total resorption
FreshVisBody	Visceral examination of body on fresh tissue	U	Unsexed
FreshVisEye	Visceral examination of eye on fresh tissue	V	Variation
H	Hermaphrodite	VisBody	Visceral body
Implant ID	Implantation identification	VisHead	Visceral head
		Wt	Weight

### DELIVERY AND LITTER DATA

Abbreviation	Description	Abbreviation	Description
Cannib.	Cannibalized	N+ve	Number of positive
Implantat	Implantation	PND	Postnatal day
Miss.	Missing		

### PUP BODY WEIGHT

Abbreviation	Description	Abbreviation	Description
BW	Body weight	P4pr	Postnatal Day 4 preculling
dX	Postnatal day x	P4po	Postnatal Day 4 postculling
Meas.	Measurement	Px or PND	Postnatal Day x

### INDIVIDUAL PHYSICAL AND FUNCTIONAL DEVELOPMENT

#### Notes:

Due to culling on PND4, observation of pinna unfolding for one unselected pup (weak pup) from F251 (BNT162b2 group) was not recorded on PND5.

Due to the technical error, observation of eyes opening for three pups from F244 (BNT162b1 group) was not observed on PND15 and PND16.

Due to the technical error, observation of eyes opening for pups from F264 (BNT162b2 group) was recorded "0" on PND14. It was considered that number positive pups on PND15 was the same as PND14 for % calculation.

### MACROSCOPIC OBSERVATION

Abbreviation	Description	Abbreviation	Description
?	Questionable	M	Mass
Animal Ref.	Animal number	ML	Macroscopic lesion (impossible to weight)
C	Clinical observation	MPF	Major pathological finding
E	Excluded	NBF	Neutral buffered formalin
G	Gross pathology	TGL	Trackable gross lesion
H	Histopathology		

#### Notes:

In the summary table, if no abnormality was detected for a given removal reason, no data are presented.

Only pups and occasions with findings are presented.

### HISTORICAL CONTROL DATA

Abbreviation	Description
GD	Gestation day

#### Notes:

Values compiled from undosed and control Wistar and Sprague Dawley rats in previous studies.

Pivotal studies include those with a comparable group size as in the present study.

The historical control data presented in the Appendix are not subject to Quality Assurance audit.

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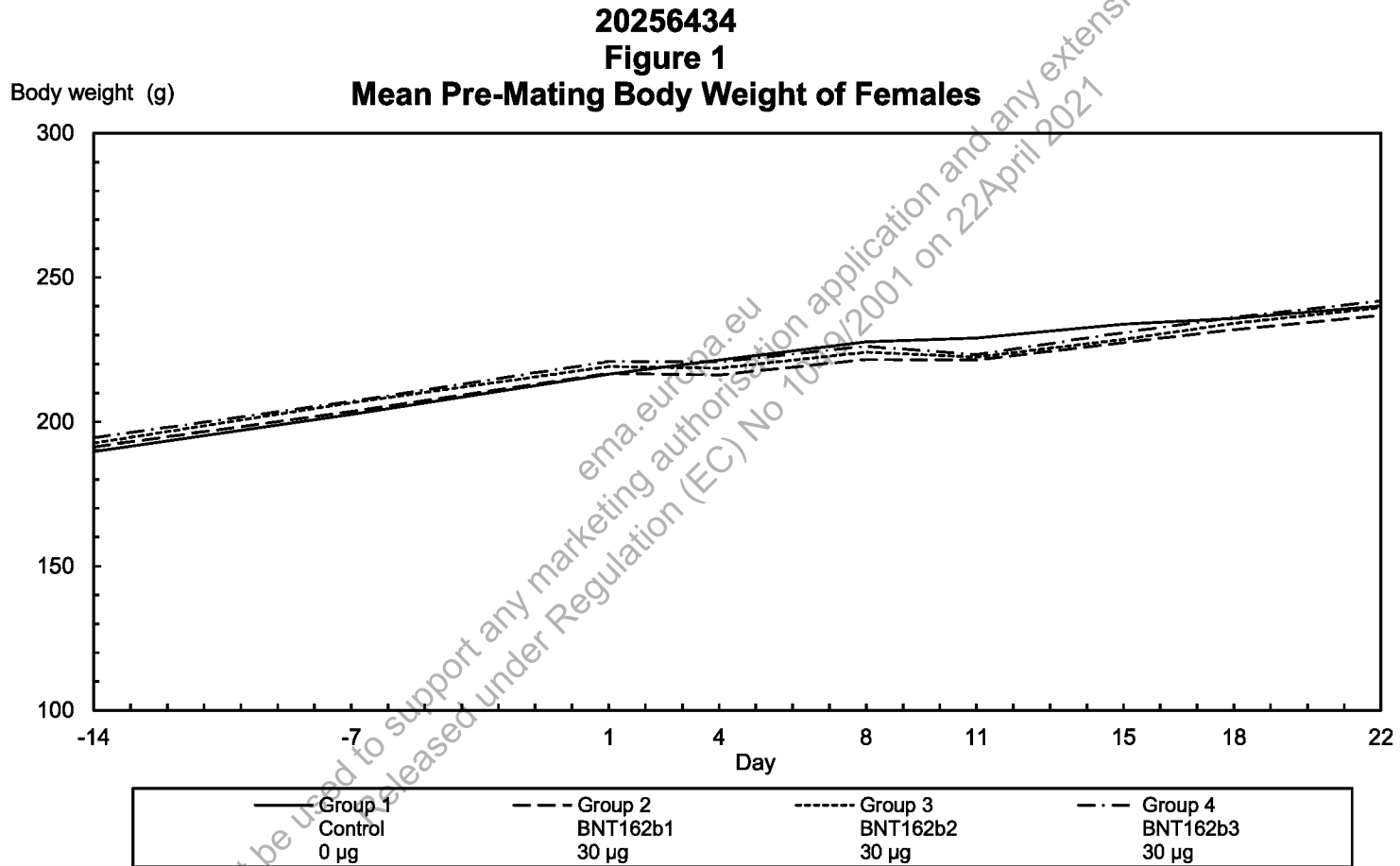
## FIGURES

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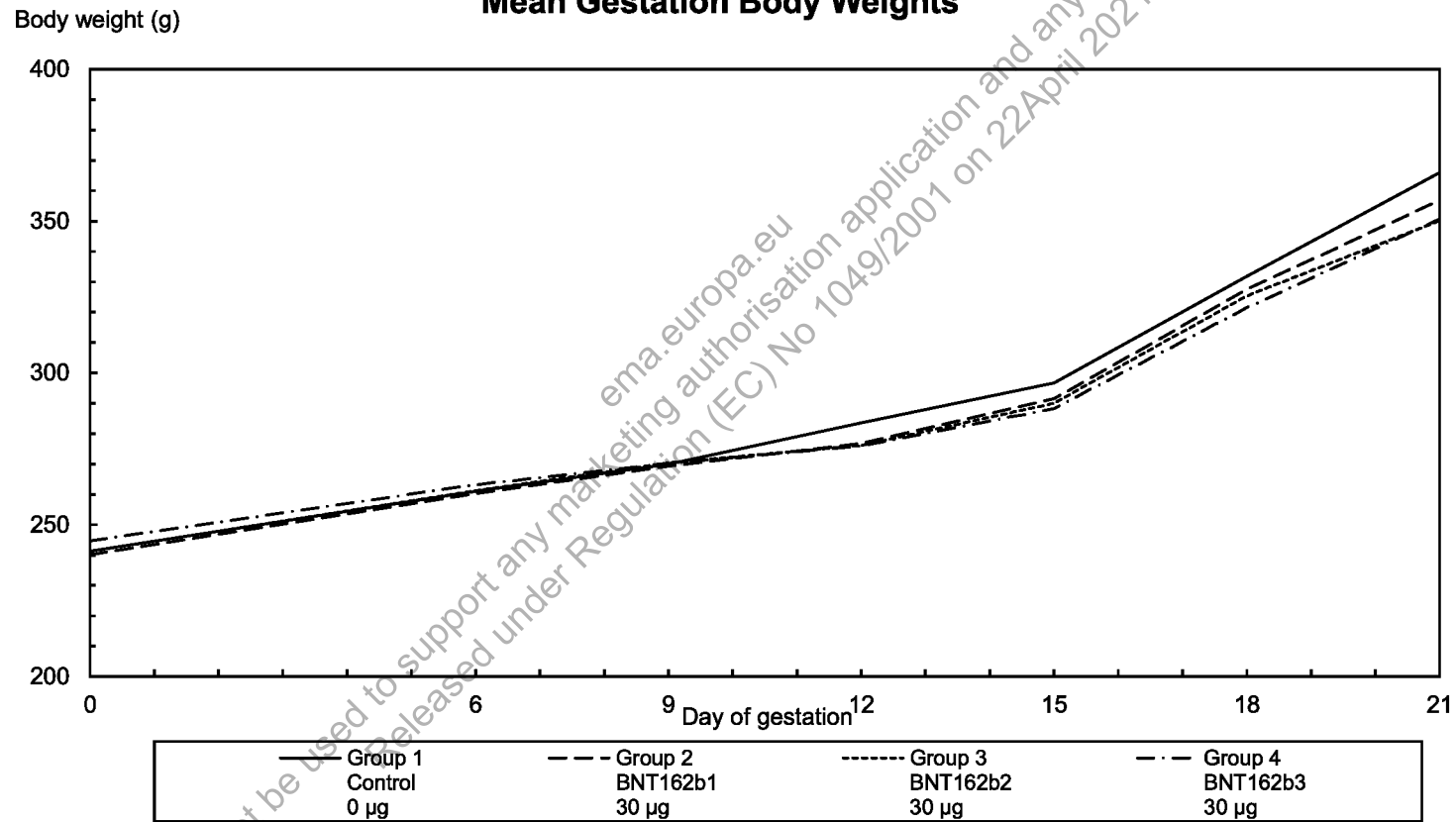
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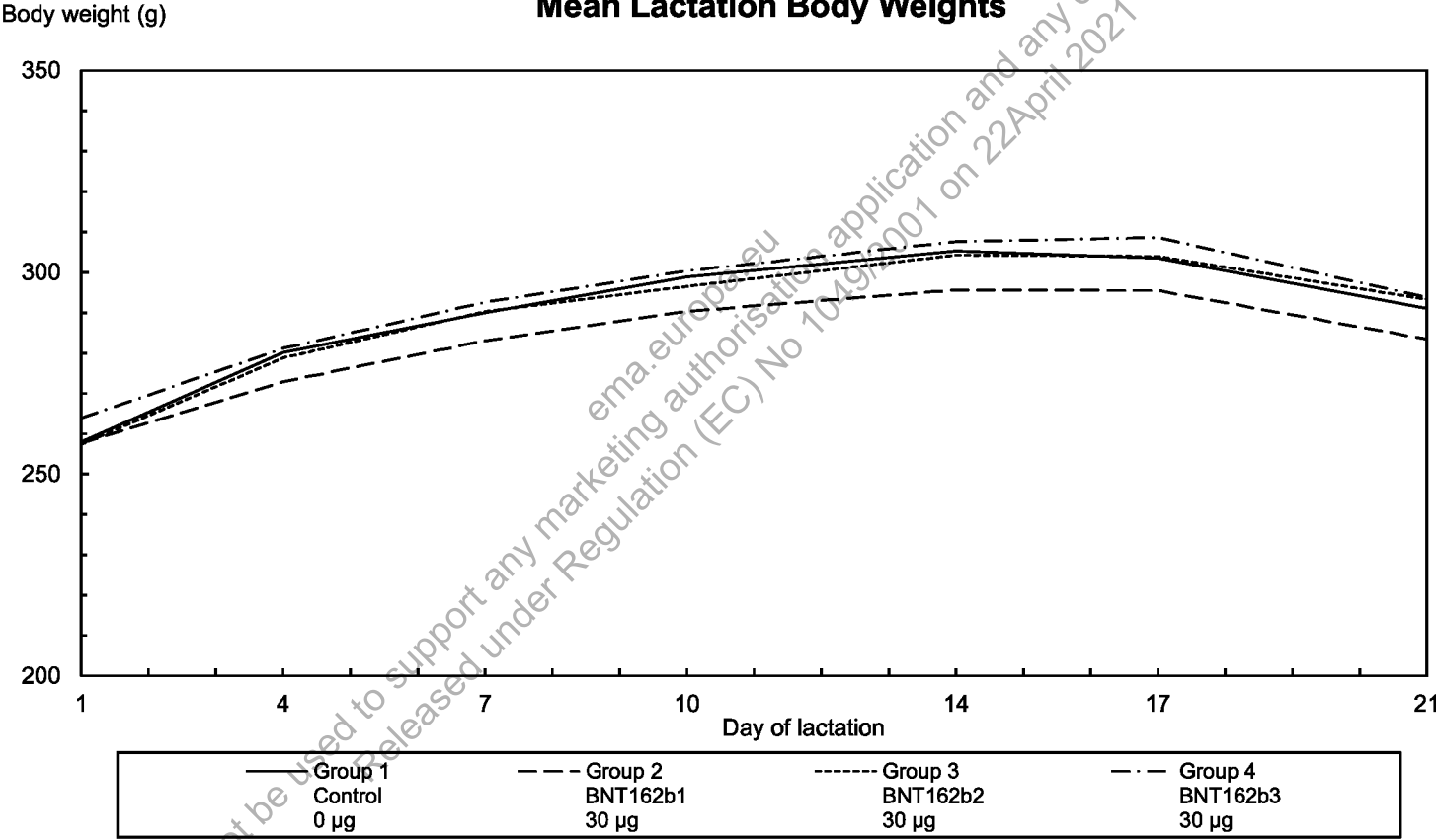
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**20256434**  
**Figure 2**  
**Mean Gestation Body Weights**



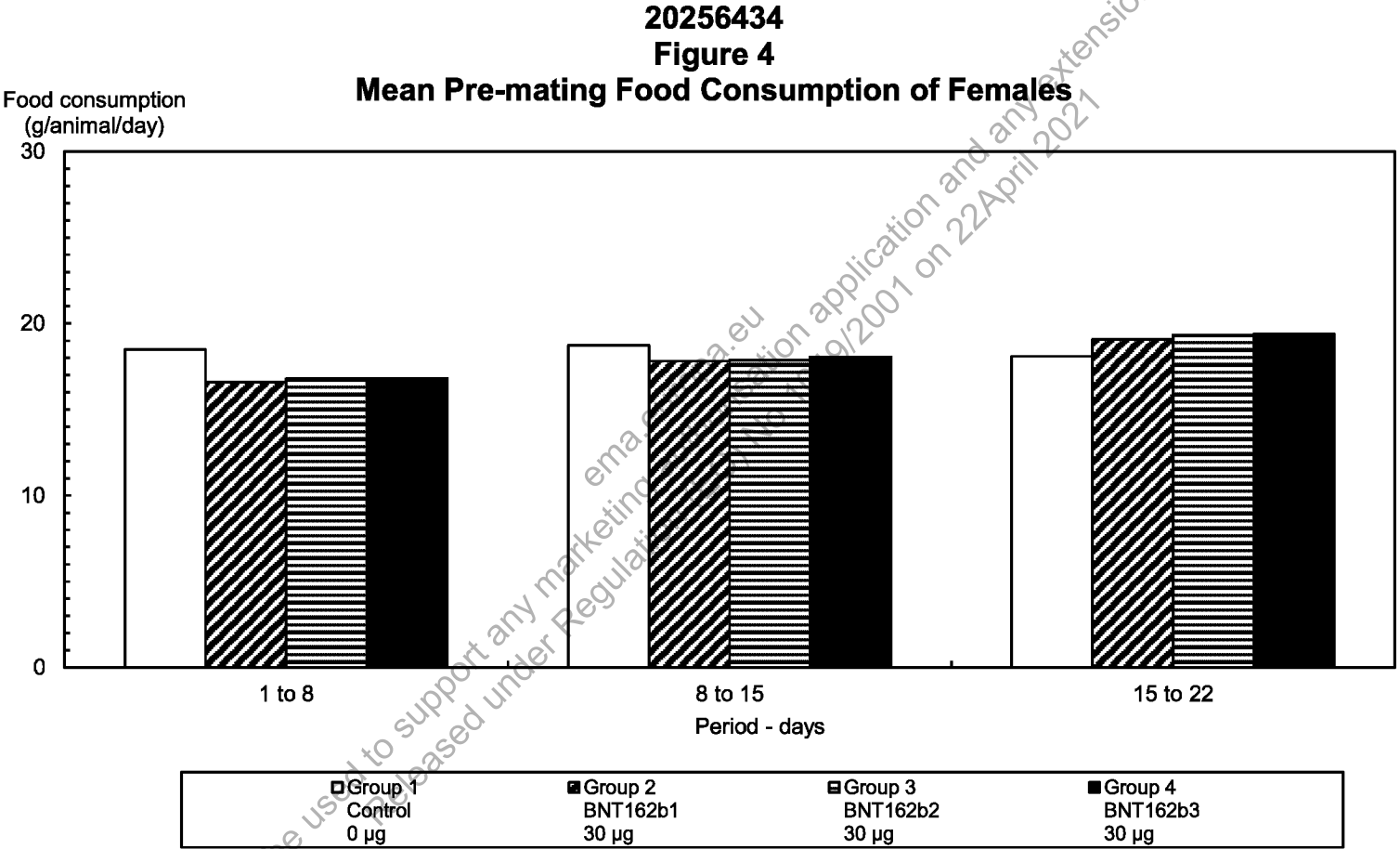
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**20256434**  
**Figure 3**  
**Mean Lactation Body Weights**



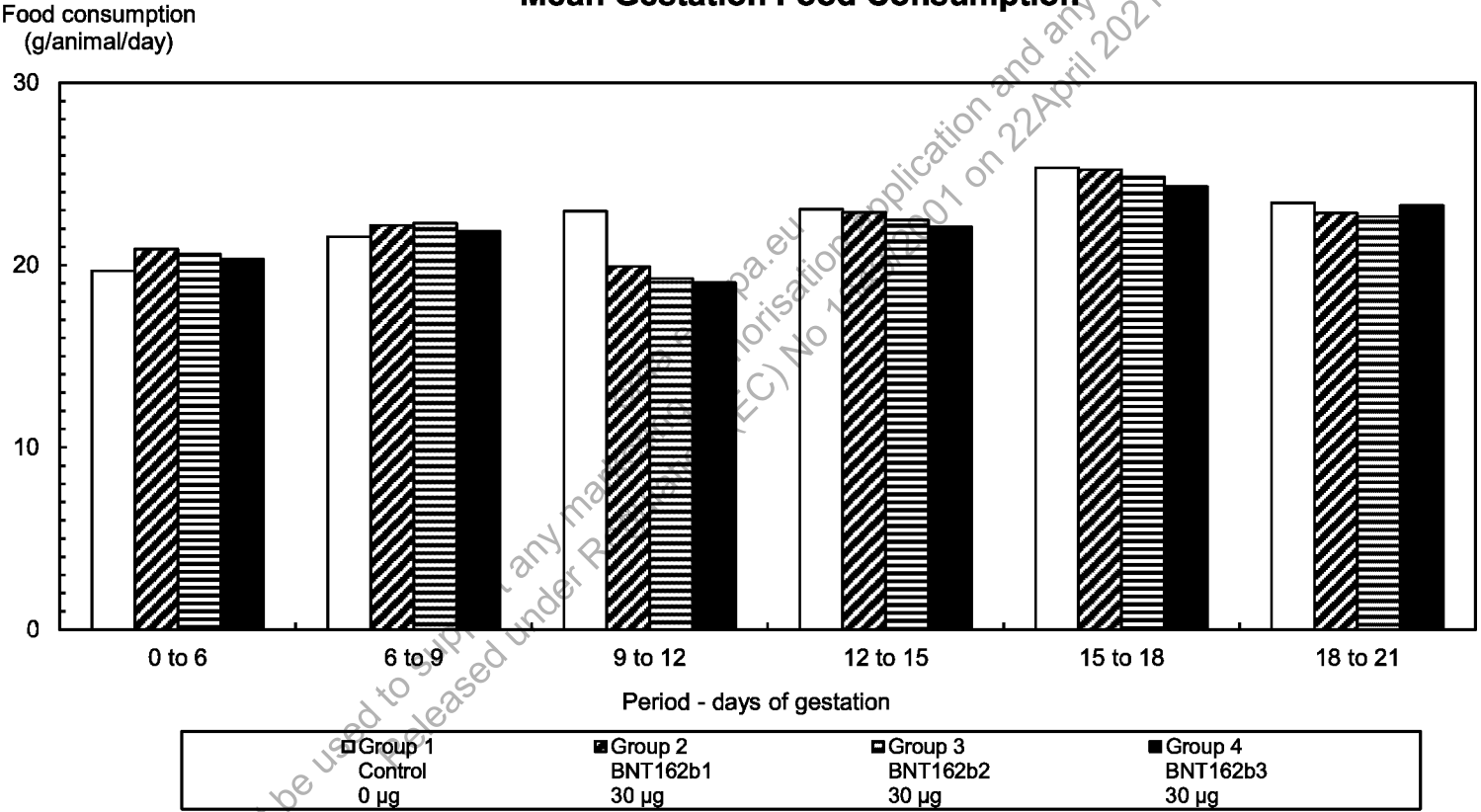
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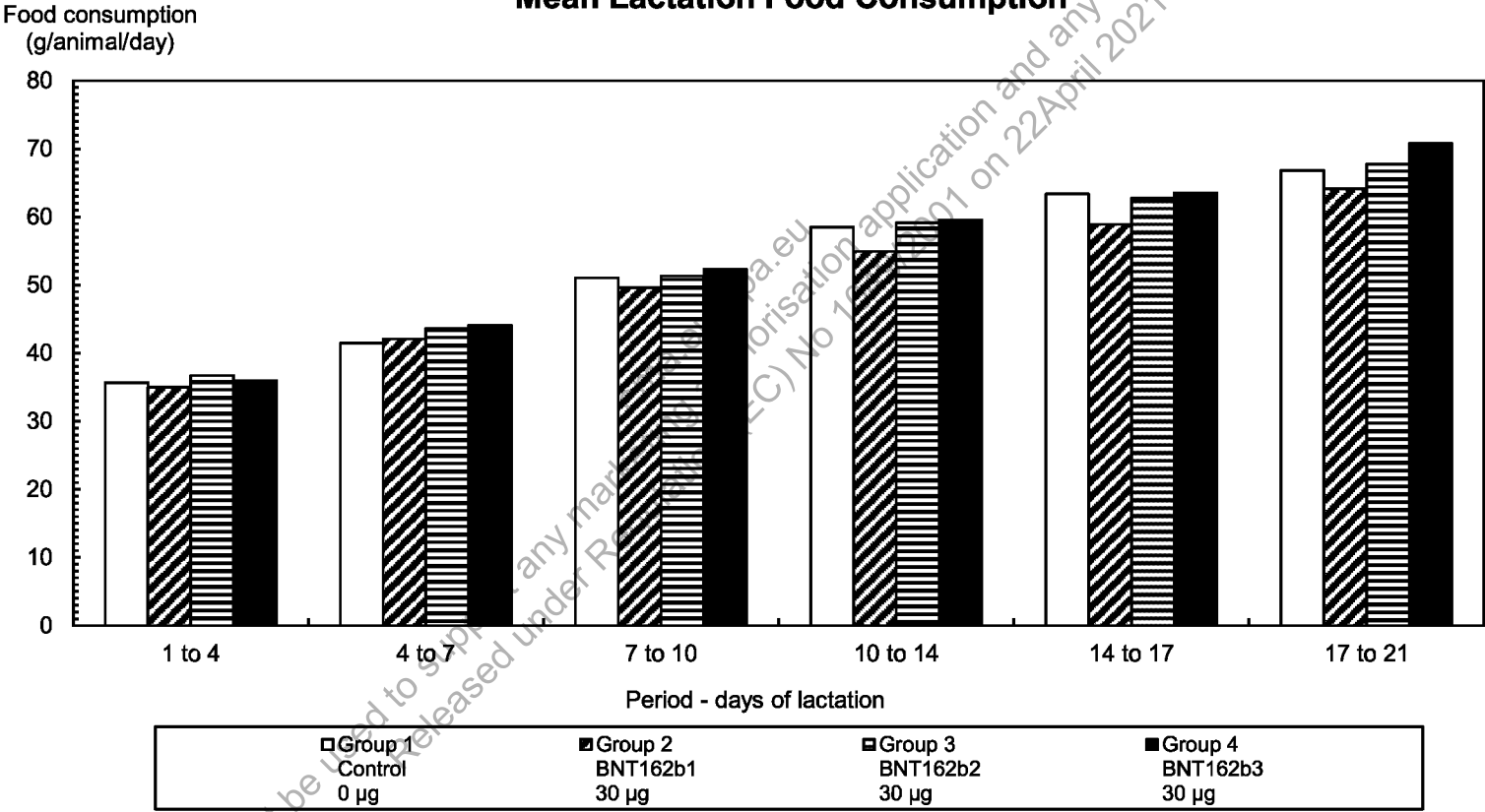
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Figure 5  
Mean Gestation Food Consumption



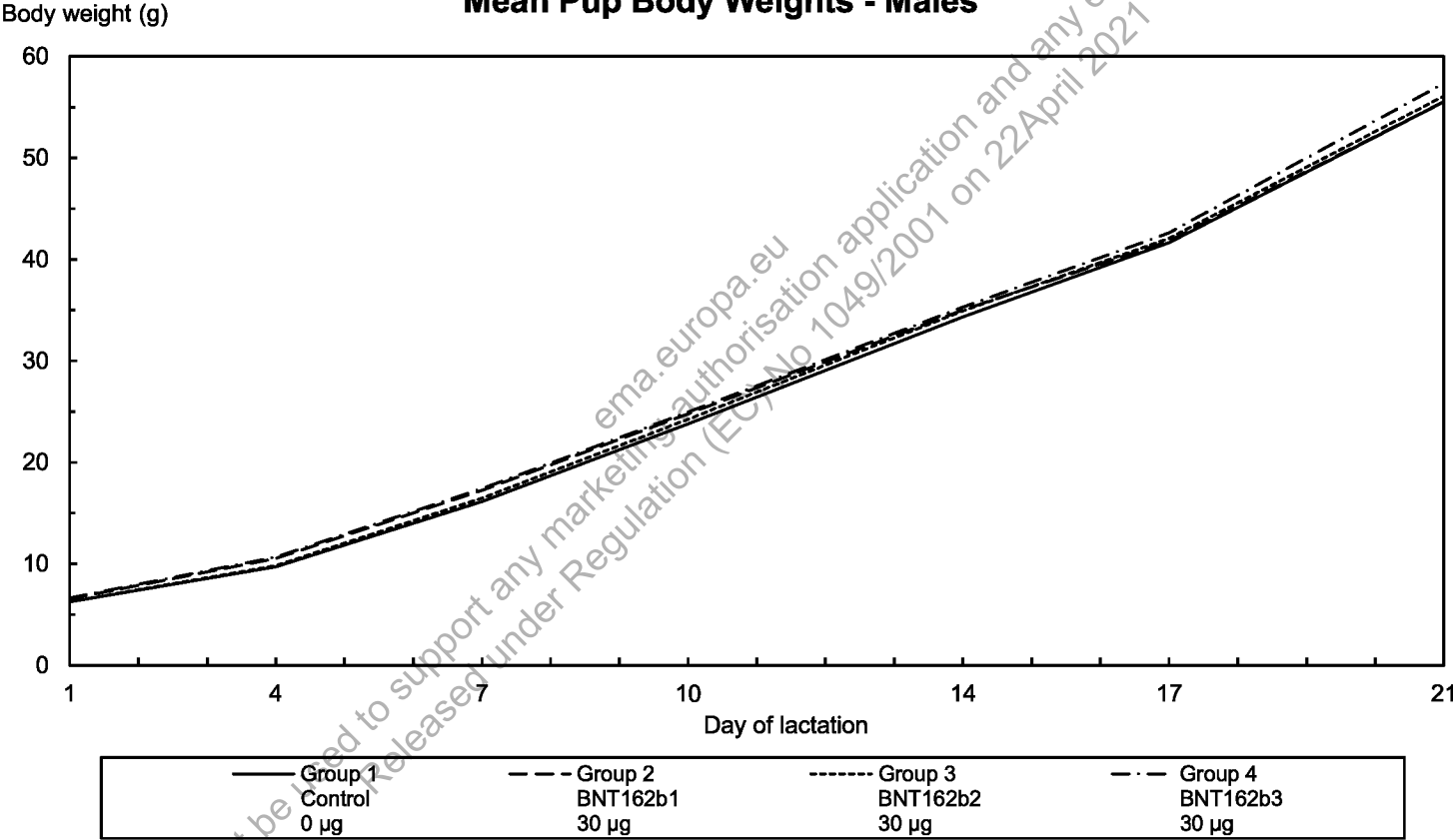
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Figure 6  
Mean Lactation Food Consumption



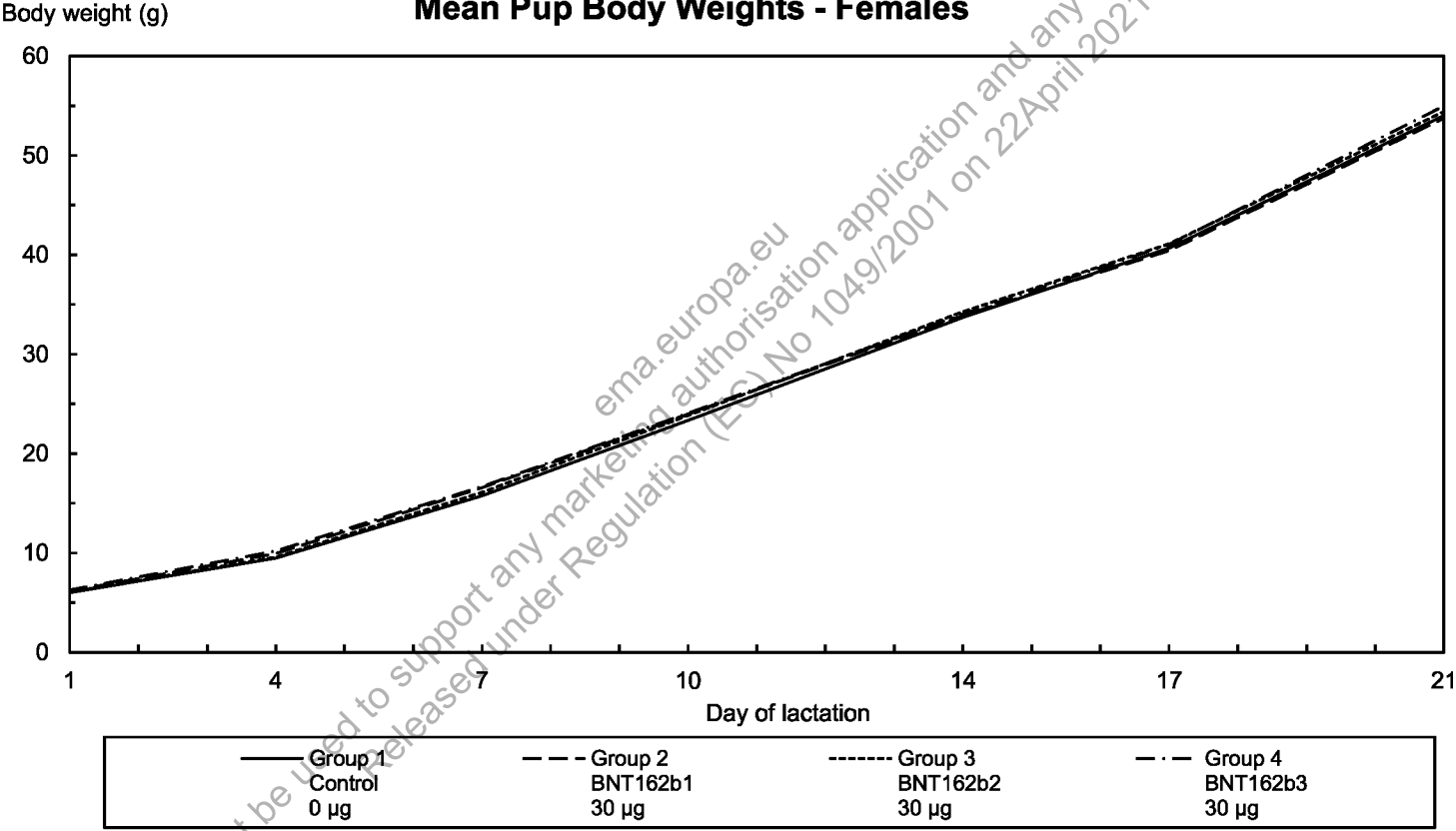
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Figure 7a  
Mean Pup Body Weights - Males



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20256434  
Figure 7b  
Mean Pup Body Weights - Females



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## TABLES

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Provantis  
Summary Pre-Mating Clinical Observations of Females  
20256434

Date: 07-Dec-2020 12:36 Page: 1

Day numbers relative to Start Date					
	Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg	
-----					
Abnormal vocalisation					
Number of Observations	.	1	.	.	
Number of Animals	.	1	.	.	
Days from - to	.	9 9	.	.	
Chromodacryorrhea					
Number of Observations	.	.	1	3	
Number of Animals	.	.	1	1	
Days from - to	.	.	17 17	-2 1	
Desquamation					
Number of Observations	7	2	1	.	
Number of Animals	5	2	1	.	
Days from - to	2 8	2 2	2 2	.	
Erythema.					
Number of Observations	5	13	6	6	
Number of Animals	3	8	3	3	
Days from - to	1 2	1 2	1 2	1 2	
Limping					
Number of Observations	.	26	26	30	
Number of Animals	.	13	13	15	
Days from - to	.	9 10	9 10	9 10	
Localised hairloss					
Number of Observations	10	17	1	20	
Number of Animals	4	6	1	5	
Days from - to	-26 15	-26 15	-25 -25	-7 15	

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Provantis  
Summary Pre-Mating Clinical Observations of Females  
20256434

Date: 07-Dec-2020 12:36 Page: 2

Day numbers relative to Start Date					
Sex: Female					
	Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg	
Missing tooth					
Number of Observations	2	.	.	.	.
Number of Animals	1	.	.	.	.
Days from - to	-3 1	.	.	.	.
Piloerection					
Number of Observations	.	1	2	7	
Number of Animals	.	1	1	6	
Days from - to	.	9 9	9 10	9 10	
Red vaginal discharge					
Number of Observations	.	1	.	.	
Number of Animals	.	1	.	.	
Days from - to	.	-13 -13	.	.	
Scab(s).					
Number of Observations	5	.	.	3	
Number of Animals	5	.	.	2	
Days from - to	-26 15	.	.	-7 9	
Swelling.					
Number of Observations	.	74	92	86	
Number of Animals	.	43	44	43	
Days from - to	.	2 9	2 15	2 9	
Teeth long					
Number of Observations	1	.	.	.	
Number of Animals	1	.	.	.	
Days from - to	15 15	.	.	.	

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Provantis  
Summary Gestation Clinical Observations  
20256434

Date: 19-Oct-2020 17:57 Page: 1

Day numbers relative to Mating Date					
Sex: Female					
	Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg	
Localised hairloss					
Number of Observations	20	32	33	28	
Number of Animals	6	9	11	9	
Days from - to	6 21	0 21	0 21	0 21	
Malocclusion					
Number of Observations	5	.	.	.	
Number of Animals	1	.	.	.	
Days from - to	9 21	.	.	.	
Piloerection					
Number of Observations	.	.	.	1	
Number of Animals	.	.	.	1	
Days from - to	.	.	.	21 21	
Red stained fur					
Number of Observations	.	3	3	.	
Number of Animals	.	1	1	.	
Days from - to	.	6 12	6 12	.	
Scab(s).					
Number of Observations	1	2	2	3	
Number of Animals	1	2	2	2	
Days from - to	0 0	21 21	9 21	15 18	
Sore(s).					
Number of Observations	1	.	.	.	
Number of Animals	1	.	.	.	
Days from - to	15 15	.	.	.	

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Provantis  
Summary Gestation Clinical Observations  
20256434

Date: 19-Oct-2020 17:57 Page: 2

Day numbers relative to Mating Date					
Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Swelling.					
	Number of Observations	.	5	12	25
	Number of Animals	.	5	10	20
	Days from - to	.	12 21	12 21	12 21
Teeth long					
	Number of Observations	1	.	.	.
	Number of Animals	1	.	.	.
	Days from - to	0 0	.	.	.
Pup(s) - Cold to touch					
	Number of Observations	.	.	1	.
	Number of Animals	.	.	1	.
	Days from - to	.	.	21 21	.

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Provantis  
Summary Lactation Clinical Observations  
20256434

Date: 19-Oct-2020 17:58 Page: 1

Day numbers relative to Litter Date				
Sex: Female	Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Bleeding				
Number of Observations	.	.	.	1
Number of Animals	.	.	.	1
Days from - to	.	.	.	1 1
Coloured skin				
Number of Observations	.	.	.	2
Number of Animals	.	.	.	1
Days from - to	.	.	.	0 1
Hunched				
Number of Observations	.	.	.	1
Number of Animals	.	.	.	1
Days from - to	.	.	.	1 1
Hunched gait				
Number of Observations	.	1	.	.
Number of Animals	.	1	.	.
Days from - to	.	1 1	.	.
Localised hairloss				
Number of Observations	26	16	18	14
Number of Animals	5	4	3	2
Days from - to	1 21	1 21	1 21	1 21
Malocclusion				
Number of Observations	7	.	.	.
Number of Animals	1	.	.	.
Days from - to	1 21	.	.	.

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Provantis  
Summary Lactation Clinical Observations  
20256434

Date: 19-Oct-2020 17:58 Page: 2

Sex: Female		Day numbers relative to Litter Date			
		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
-----					
Nodule(s).					
	Number of Observations	1	.	.	.
	Number of Animals	1	.	.	.
	Days from - to	21 21	.	.	.
Pale					
	Number of Observations	.	.	.	2
	Number of Animals	.	.	.	1
	Days from - to	.	.	.	0 1
Partly closed eye(s)					
	Number of Observations	.	1	.	.
	Number of Animals	.	1	.	.
	Days from - to	.	1 1	.	.
Piloerection					
	Number of Observations	.	1	.	2
	Number of Animals	.	1	.	2
	Days from - to	.	1 1	.	0 1
Purple area(s)					
	Number of Observations	.	.	.	1
	Number of Animals	.	.	.	1
	Days from - to	.	.	.	1 1
Red vaginal discharge					
	Number of Observations	.	.	.	1
	Number of Animals	.	.	.	1
	Days from - to	.	.	.	1 1
-----					

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Provantis  
Summary Lactation Clinical Observations  
20256434

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Day numbers relative to Litter Date									
		Control 0mcg		BNT162b1 30mcg		BNT162b2 30mcg		BNT162b3 30mcg	
-----									
Scab(s).									
Number of Observations		6		2		5		.	
Number of Animals		2		1		2		.	
Days from - to		4	21	17	21	4	21	.	
Soft distended abdomen									
Number of Observations		.		.		.		2	
Number of Animals		.		.		.		1	
Days from - to		.		.		.		0	1
Sore(s)									
Number of Observations		3		.		.		.	
Number of Animals		1		.		.		.	
Days from - to		13	20	.		.		.	
Swelling.									
Number of Observations		2		.		3		2	
Number of Animals		1		.		3		2	
Days from - to		9	10	.		1	1	1	1
Teeth cut									
Number of Observations		1		.		.		.	
Number of Animals		1		.		.		.	
Days from - to		1	1	.		.		.	
Total litter death									
Number of Observations		.		.		.		1	
Number of Animals		.		.		.		1	
Days from - to		.		.		.		1	1

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Provantis  
Summary Lactation Clinical Observations  
20256434

Date: 19-Oct-2020 17:58 Page: 4

Day numbers relative to Litter Date				
Sex: Female	Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Pup(s) - Weak				
Number of Observations	.	6	6	5
Number of Animals	.	1	2	3
Days from - to	.	0 5	0 4	1 4
Pup(s) - Thin				
Number of Observations	.	.	1	1
Number of Animals	.	.	1	1
Days from - to	.	.	3 3	0 0
Pup(s) - Pale				
Number of Observations	.	.	2	1
Number of Animals	.	.	2	1
Days from - to	.	.	0 3	0 0
Pup(s) - Cold to touch				
Number of Observations	.	.	3	4
Number of Animals	.	.	3	3
Days from - to	.	.	0 3	0 1
Pup(s) - Cyanotic				
Number of Observations	.	1	1	1
Number of Animals	.	1	1	1
Days from - to	.	0 0	3 3	0 0
Pup(s) - Incomplete hair growth				
Number of Observations	17	18	18	11
Number of Animals	2	2	2	1
Days from - to	9 20	10 19	10 21	11 21

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Provantis  
Summary Lactation Clinical Observations  
20256434

Date: 19-Oct-2020 17:58 Page: 5

Day numbers relative to Litter Date					
Sex: Female					
	Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg	
Pup(s) - Haematoma(s)					
Number of Observations	6	5	3	3	
Number of Animals	2	1	2	1	
Days from - to	1 11	0 4	0 1	1 3	
Pup(s) - Chromodacryorrhea					
Number of Observations	.	1	.	2	
Number of Animals	.	1	.	1	
Days from - to	.	21 21	.	20 21	
Pup(s) - Lacrimation					
Number of Observations	.	1	.	.	
Number of Animals	.	1	.	.	
Days from - to	.	21 21	.	.	
MORIBUND SACRIFICE					
Number of Observations	.	.	.	1	
Number of Animals	.	.	.	1	
Days from - to	.	.	.	1 1	
UNPLANNED TERMINAL SACRIFICE					
Number of Observations	.	1	.	.	
Number of Animals	.	1	.	.	
Days from - to	.	1 1	.	.	
Pup(s) - Red ocular mucous mem					
Number of Observations	.	1	.	.	
Number of Animals	.	1	.	.	
Days from - to	.	21 21	.	.	

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Mean Pre-Mating Body Weight of Females

20256434

Body Weight (g)					
Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Start Date					
-26	Mean	160.99 R <sup>1</sup>	161.48	163.60	174.20
	SD	13.11	14.55	17.64	28.03
	N	22	22	22	22
	%Diff	-	0.31	1.63	8.21
-25	Mean	163.98 L <sup>2</sup>	167.96	165.56	166.96
	SD	14.48	16.62	14.15	14.03
	N	22	22	22	22
	%Diff	-	2.43	0.97	1.82
-21	Mean	173.80 L <sup>2</sup>	172.03	176.97	179.10
	SD	13.45	15.91	17.45	17.32
	N	22	22	22	22
	%Diff	-	-1.02	1.82	3.04
-20	Mean	177.46 I <sup>3</sup>	183.25	179.14	179.91
	SD	14.57	16.26	16.54	15.07
	N	22	22	22	22
	%Diff	-	3.26	0.95	1.38

Statistical Test: Generalised Anova/Ancova Test Transformation: Automatic

1 [R - Automatic Transformation: Rank]

2 [L - Automatic Transformation: Log]

3 [I - Automatic Transformation: Identity (No Transformation)]

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Mean Pre-Mating Body Weight of Females

20256434

Body Weight (g)					
Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Start Date					
-14	Mean	189.68 L <sup>1</sup>	191.26	192.61	194.48
	SD	15.40	16.74	16.69	16.19
	N	44	44	44	44
	%Diff	-	0.83	1.55	2.53
-7	Mean	202.55 R <sup>2</sup>	203.53	206.60	207.03
	SD	16.23	17.40	16.39	16.74
	N	44	44	44	44
	%Diff	-	0.48	2.00	2.21
1	Mean	216.49 I <sup>3</sup>	216.79	219.15	220.91
	SD	17.85	18.82	17.75	17.74
	N	44	44	44	44
	%Diff	-	0.14	1.23	2.04
4	Mean	221.34 L <sup>1</sup>	216.24	218.51	220.73
	SD	17.81	19.15	18.10	18.29
	N	44	44	44	44
	%Diff	-	-2.31	-1.28	-0.27

Statistical Test: Generalised Anova/Ancova Test Transformation: Automatic

1 [L - Automatic Transformation: Log]

2 [R - Automatic Transformation: Rank]

3 [I - Automatic Transformation: Identity (No Transformation)]

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Mean Pre-Mating Body Weight of Females

20256434

Body Weight (g)					
Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Start Date					
8	Mean	227.71 L <sup>1</sup>	221.55	224.13	226.21
	SD	18.80	19.59	19.18	19.50
	N	44	44	44	44
	%Diff	-	-2.71	-1.57	-0.66
11	Mean	229.02 L <sup>1</sup>	221.35	222.45	223.24
	SD	18.42	18.93	18.60	18.99
	N	44	44	44	44
	%Diff	-	-3.35	-2.87	-2.52
15	Mean	233.81 L <sup>1</sup>	227.38	228.58	230.89
	SD	17.24	18.93	18.32	17.28
	N	44	44	44	44
	%Diff	-	-2.75	-2.23	-1.25
18	Mean	235.81 L <sup>1</sup>	231.91	234.09	236.18
	SD	16.08	19.90	18.89	17.92
	N	44	44	44	44
	%Diff	-	-1.65	-0.73	0.16

Statistical Test: Generalised Anova/Ancova Test Transformation: Automatic

1 [L - Automatic Transformation: Log]

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Provantis  
Mean Pre-Mating Body Weight of Females

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Body Weight (g)					
Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Start Date					
22	Mean	240.13 L <sup>1</sup>	236.78	239.54	241.85
	SD	18.13	19.79	19.41	18.46
	N	44	44	44	44
	%Diff	-	-1.39	-0.25	0.71

Statistical Test: Generalised Anova/Ancova Test Transformation: Automatic

1 [L - Automatic Transformation: Log]

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Provantis  
Mean Pre-Mating Body Weight Change of Females

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20256434

Body Weight Change (g)					
Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Start Date					
-26--21	Mean	12.82 R <sup>1</sup>	10.55	13.36	4.90
	SD	4.35	4.88	3.59	21.94
	N	22	22	22	22
	%Diff	.	-17.73	4.26	-61.77
-25--20	Mean	13.48 I <sup>2</sup>	15.29	13.57	12.95
	SD	5.15	4.92	4.99	3.36
	N	22	22	22	22
	%Diff	.	13.42	0.67	-3.94
-20--14	Mean	13.00 R <sup>1</sup>	12.71	13.76	14.09
	SD	5.23	5.61	6.67	3.34
	N	22	22	22	22
	%Diff	.	-2.24	5.84	8.32
-21--14	Mean	15.08 I <sup>2</sup>	14.52	15.36	15.86
	SD	3.94	3.24	4.71	4.62
	N	22	22	22	22
	%Diff	.	-3.71	1.84	5.15

Statistical Test: Generalised Anova/Ancova Test Transformation: Automatic

1 [R - Automatic Transformation: Rank]

2 [I - Automatic Transformation: Identity (No Transformation)]

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Provantis  
Mean Pre-Mating Body Weight Change of Females

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Body Weight Change (g)					
Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Start Date					
-14--7	Mean	12.88 R <sup>1</sup>	12.27	13.98	12.56
	SD	5.50	5.49	6.82	5.01
	N	44	44	44	44
	%Diff	.	-4.69	8.60	-2.49
-7-1	Mean	13.94 R <sup>1</sup>	13.26	12.55	13.88
	SD	7.32	6.20	9.13	6.88
	N	44	44	44	44
	%Diff	.	-4.89	-9.96	-0.47
1-4	Mean	4.85 <sup>2</sup>	-0.55 ddd <sup>3</sup>	-0.64 ddd <sup>3</sup>	-0.17 ddd <sup>3</sup>
	SD	4.74	4.17	4.73	4.77
	N	44	44	44	44
	%Diff	.	-111.39	-113.13	-103.56
4-8	Mean	6.37 R <sup>1</sup>	5.31	5.62	5.48
	SD	4.25	4.78	4.16	4.61
	N	44	44	44	44
	%Diff	.	-16.63	-11.81	-13.99

Statistical Test: Generalised Anova/Ancova Test Transformation: Automatic

1 [R - Automatic Transformation: Rank]  
3 [ddd - Test: Dunnett 2 Sided p < 0.001]

2 [I,aaa - Automatic Transformation: Identity (No Transformation), (All Groups) Test: Analysis of Variance p < 0.001]

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Provantis  
Mean Pre-Mating Body Weight Change of Females

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Body Weight Change (g)					
Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Start Date					
8-11	Mean	1.31 <sup>1</sup>	-0.20	-1.69	-2.97 ddd <sup>5</sup>
	SD	6.07	6.20	5.67	3.46
	N	44	44	44	44
	%Diff	.	-114.96	-229.04	-327.48
11-15	Mean	4.79 R <sup>2</sup>	6.03	6.14	7.65
	SD	6.17	7.14	5.49	6.37
	N	44	44	44	44
	%Diff	.	25.76	28.13	59.72
15-18	Mean	2.00 R, k <sup>3</sup>	4.54	5.50 dd <sup>4</sup>	5.28 d <sup>6</sup>
	SD	5.69	4.88	4.64	4.36
	N	44	44	44	44
	%Diff	.	126.82	175.11	164.09
18-22	Mean	4.32 R <sup>2</sup>	4.87	5.45	5.67
	SD	4.23	4.43	3.97	3.97
	N	44	44	44	44
	%Diff	.	12.73	26.25	31.25

Statistical Test: Generalised Anova/Ancova Test Transformation: Automatic

1 [R, kk - Automatic Transformation: Rank, (All Groups) Test: Kruskal-Wallis p < 0.01]  
3 [R, k - Automatic Transformation: Rank, (All Groups) Test: Kruskal-Wallis p < 0.05]  
5 [ddd - Test: Dunnett Non-Parametric 2 Sided p < 0.001]

2 [R - Automatic Transformation: Rank]  
4 [dd - Test: Dunnett Non-Parametric 2 Sided p < 0.01]  
6 [d - Test: Dunnett Non-Parametric 2 Sided p < 0.05]

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Provantis  
Mean Pre-Mating Body Weight Change of Females

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Body Weight Change (g)					
Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Start Date					
1-22	Mean	23.64 R <sup>1</sup>	20.00	20.39	20.94
	SD	9.93	9.15	9.45	11.19
	N	44	44	44	44
	%Diff	.	-15.40	-13.73	-11.41

Statistical Test: Generalised Anova/Ancova Test Transformation: Automatic

1 [R - Automatic Transformation: Rank]

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Provantis  
Mean Gestation Body Weight

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Body Weight (g)

Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Mating (Litter: )					
0	Mean	241.30 L <sup>1</sup>	240.13	241.23	244.67
	SD	20.73	18.71	19.34	19.37
	N	43	41	42	43
	%Diff	-	-0.48	-0.03	1.40
6	Mean	261.04 L <sup>1</sup>	260.28	261.16	263.20
	SD	22.34	19.77	18.67	19.49
	N	43	41	42	43
	%Diff	-	-0.29	0.05	0.83
9	Mean	269.97 L <sup>1</sup>	269.32	270.42	270.19
	SD	22.98	21.13	19.10	20.37
	N	43	41	42	43
	%Diff	-	-0.24	0.17	0.08
12	Mean	283.52 L <sup>1</sup>	276.80	276.13	275.92
	SD	24.24	22.43	18.87	20.30
	N	43	41	42	43
	%Diff	-	-2.37	-2.61	-2.68

Statistical Test: Generalised Anova/Ancova Test Transformation: Automatic

1 [L - Automatic Transformation: Log]

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Provantis  
Mean Gestation Body Weight

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Body Weight (g)					
Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Mating (Litter: )					
15	Mean	296.72 L <sup>1</sup>	291.58	290.04	288.22
	SD	24.44	24.02	21.19	20.47
	N	43	41	42	43
	%Diff	-	-1.73	-2.25	-2.86
18	Mean	331.88 L <sup>1</sup>	327.54	325.33	321.45
	SD	27.03	27.31	25.07	20.68
	N	43	41	42	43
	%Diff	-	-1.31	-1.97	-3.14
21	Mean	365.98 L <sup>1</sup> , a <sup>2</sup>	356.87	350.15 d <sup>3</sup>	350.69 d <sup>3</sup>
	SD	29.55	30.51	31.12	23.41
	N	43	41	42	43
	%Diff	-	-2.49	-4.32	-4.18

Statistical Test: Generalised Anova/Ancova Test Transformation: Automatic

1 [L - Automatic Transformation: Log]

3 [d - Test: Dunnett 2 Sided p < 0.05]

2 [a - Automatic Transformation: Identity (No Transformation), (All Groups) Test: Analysis of Variance p < 0

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Provantis  
Mean Gestation Body Weight Change

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Body Weight Change (g)					
Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Mating (Litter: )					
0-6	Mean	19.75 <sup>1</sup>	20.15	19.94	18.53
	SD	6.20	4.10	5.40	4.82
	N	43	41	42	43
	%Diff	.	2.03	0.95	-6.16
6-9	Mean	8.93 <sup>1,a</sup>	9.04	9.26	6.99
	SD	3.82	4.18	4.37	3.14
	N	43	41	42	43
	%Diff	.	1.30	3.71	-21.72
9-12	Mean	13.55 <sup>3</sup>	7.48 <sup>ddd5</sup>	5.70 <sup>ddd5</sup>	5.73 <sup>ddd5</sup>
	SD	3.77	4.23	4.16	3.66
	N	43	41	42	43
	%Diff	.	-44.80	-57.89	-57.67
12-15	Mean	13.20 <sup>R4</sup>	14.78	13.91	12.30
	SD	3.24	4.19	6.22	4.16
	N	43	41	42	43
	%Diff	.	11.90	5.37	-6.85

Statistical Test: Generalised Anova/Ancova Test Transformation: Automatic

1 [I - Automatic Transformation: Identity (No Transformation)]

2 [I,a - Automatic Transformation: Identity (No Transformation), (All Groups) Test: Analysis of Variance p < 0

3 [I,aaa - Automatic Transformation: Identity (No Transformation), (All Groups) Test: Analysis of Variance p < 0

5 [ddd - Test: Dunnett 2 Sided p < 0.001]

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Provantis  
Mean Gestation Body Weight Change

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20256434

Body Weight Change (g)					
Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Mating (Litter: )					
15-18	Mean	35.16 <sup>1</sup>	35.96	35.29	33.23
	SD	5.81	6.24	7.81	5.40
	N	43	41	42	43
	%Diff	.	2.28	0.38	-5.48
18-21	Mean	34.10 <sup>2</sup>	29.33 ddd <sup>3</sup>	24.82 ddd <sup>3</sup>	29.24 ddd <sup>3</sup>
	SD	5.64	6.08	22.27	5.95
	N	43	41	42	43
	%Diff	.	-13.98	-27.20	-14.25
0-21	Mean	124.68 <sup>2</sup>	116.73 <sup>d4</sup>	108.93 ddd <sup>3</sup>	106.02 ddd <sup>3</sup>
	SD	14.14	16.60	22.08	11.15
	N	43	41	42	43
	%Diff	.	-6.37	-12.64	-14.96

Statistical Test: Generalised Anova/Ancova Test Transformation: Automatic

1 [I - Automatic Transformation: Identity (No Transformation)]

3 [ddd - Test: Dunnett Non-Parametric 2 Sided p < 0.001]

2 [R, kkk - Automatic Transformation: Rank, (All Groups) Test: Kruskal-Wallis p < 0.001]

4 [d - Test: Dunnett Non-Parametric 2 Sided p < 0.05]

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Provantis  
Mean Lactation Body Weight

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20256434

Body Weight (g)					
Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Littering (Litter:					
1	Mean	257.97 R <sup>1</sup>	257.66	257.36	263.87
	SD	29.31	19.99	19.91	28.90
	N	22	21	21	19
	%Diff	-	-0.12	-0.24	2.29
4	Mean	280.10 R <sup>1</sup>	272.85	278.83	281.15
	SD	26.24	23.11	17.71	26.39
	N	22	20	21	19
	%Diff	-	-2.59	-0.45	0.38
7	Mean	289.97 L <sup>2</sup>	283.05	290.31	292.63
	SD	24.89	20.52	17.19	26.75
	N	22	20	21	19
	%Diff	-	-2.39	0.12	0.92
10	Mean	298.86 L <sup>2</sup>	290.35	296.55	300.34
	SD	23.50	21.79	17.47	27.15
	N	22	20	21	19
	%Diff	-	-2.85	-0.77	0.50

Statistical Test: Generalised Anova/Ancova Test Transformation: Automatic

1 [R - Automatic Transformation: Rank]

2 [L - Automatic Transformation: Log]

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Provantis  
Mean Lactation Body Weight

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20256434

Body Weight (g)					
Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Littering (Litter:					
14	Mean	305.30 <sup>1</sup>	295.65	304.29	307.64
	SD	23.50	19.58	18.86	24.63
	N	22	20	21	19
	%Diff	-	-3.16	-0.33	0.77
17	Mean	303.55 <sup>1</sup>	295.52	303.92	308.65
	SD	22.84	19.31	17.88	24.78
	N	22	20	21	19
	%Diff	-	-2.65	0.12	1.68
21	Mean	291.04 <sup>1</sup>	283.47	293.30	293.81
	SD	21.86	16.75	15.56	20.01
	N	22	20	21	19
	%Diff	-	-2.60	0.78	0.95

Statistical Test: Generalised Anova/Ancova Test Transformation: Automatic

1 [1 - Automatic Transformation: Identity (No Transformation)]

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Provantis  
Mean Lactation Body Weight Change

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20256434

Body Weight Change (g)					
Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Littering (Litter:					
1-4	Mean	22.13 R <sup>1</sup>	15.16	21.47	17.28
	SD	9.92	9.17	10.49	9.07
	N	22	20	21	19
	%Diff	.	-31.49	-2.99	-21.91
4-7	Mean	9.88 I <sup>2</sup>	10.20	11.48	11.48
	SD	4.27	7.15	4.88	6.16
	N	22	20	21	19
	%Diff	.	3.22	16.24	16.22
7-10	Mean	8.89 I <sup>2</sup>	7.31	6.24	7.71
	SD	5.32	5.58	6.01	5.79
	N	22	20	21	19
	%Diff	.	-17.80	-29.75	-13.23
10-14	Mean	6.44 I <sup>2</sup>	5.30	7.74	7.29
	SD	5.28	5.44	7.51	7.29
	N	22	20	21	19
	%Diff	.	-17.73	20.22	13.34

Statistical Test: Generalised Anova/Ancova Test Transformation: Automatic

1 [R - Automatic Transformation: Rank]

2 [I - Automatic Transformation: Identity (No Transformation)]

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Provantis  
Mean Lactation Body Weight Change

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20256434

Body Weight Change (g)					
Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Littering (Litter:					
14-17	Mean	-1.75 <sup>1</sup>	-0.13	-0.37	1.01
	SD	6.22	5.06	7.06	6.06
	N	22	20	21	19
	%Diff	.	-92.57	-79.05	157.74
17-21	Mean	-12.50 <sup>1</sup>	-12.05	-10.62	-14.84
	SD	7.56	6.75	6.62	7.50
	N	22	20	21	19
	%Diff	.	-3.64	-15.08	18.65
1-21	Mean	33.07 <sup>1</sup>	25.78	35.94	29.94
	SD	16.53	13.87	11.57	17.76
	N	22	20	21	19
	%Diff	.	-22.07	8.68	-9.48

Statistical Test: Generalised Anova/Ancova Test Transformation: Automatic

1 [I - Automatic Transformation: Identity (No Transformation)]

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Provantis  
Mean Pre-Mating Food Consumption of Females

06-Nov-2020 15:48:40 Page: 1

20256434FC

Sex: Female		Food Consumption (g/animal/day)			
Day(s) Relative to Start Date		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
1-8	Mean	18.49 <sup>1</sup>	16.60ddd <sup>4</sup>	16.79ddd <sup>4</sup>	16.80ddd <sup>4</sup>
	SD	1.44	1.25	1.15	0.34
	N	44	44	44	44
	%Diff	.	-10.21	-9.17	-9.12
8-15	Mean	18.73R,k <sup>2</sup>	17.82 d <sup>5</sup>	17.87 d <sup>5</sup>	18.07
	SD	1.71	0.72	1.32	1.62
	N	44	44	44	44
	%Diff	.	-4.84	-4.57	-3.51
15-22	Mean	18.09 <sup>1</sup>	19.08ddd <sup>4</sup>	19.34ddd <sup>4</sup>	19.39ddd <sup>4</sup>
	SD	1.03	0.59	0.86	1.24
	N	44	44	44	44
	%Diff	.	5.49	6.94	7.19
1-22	Mean	18.43 <sup>3</sup>	17.83ddd <sup>4</sup>	18.00	18.09
	SD	1.08	0.48	0.82	0.86
	N	44	44	44	44
	%Diff	.	-3.26	-2.34	-1.89

Statistical Test: Generalised Anova/Ancova Test Transformation: Automatic

1 [R,kkk - Automatic Transformation: Rank, (All Groups) Test: Kruskal-Wallis p < 0.001]  
3 [R,kk - Automatic Transformation: Rank, (All Groups) Test: Kruskal-Wallis p < 0.01]  
5 [d - Test: Dunnett Non-Parametric 2 Sided p < 0.05]

2 [R,k - Automatic Transformation: Rank, (All Groups) Test: Kruskal-Wallis p < 0.05]  
4 [ddd - Test: Dunnett Non-Parametric 2 Sided p < 0.001]

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Provantis  
Mean Gestation Food Consumption

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20256434

Food Consumption (g/animal/day)					
Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Mating (Litter: )					
0-6	Mean	19.69 L <sup>1</sup>	20.88	20.59	20.32
	SD	2.59	3.04	1.99	2.30
	N	43	41	42	43
	%Diff	.	6.04	4.61	3.23
6-9	Mean	21.56 I <sup>2</sup>	22.18	22.29	21.86
	SD	2.64	2.54	2.23	2.59
	N	43	41	42	43
	%Diff	.	2.86	3.38	1.39
9-12	Mean	22.95 <sup>3</sup>	19.92 ddd <sup>4</sup>	19.26 ddd <sup>4</sup>	19.03 ddd <sup>4</sup>
	SD	2.63	2.40	2.22	2.16
	N	43	41	42	43
	%Diff	.	-13.20	-16.08	-17.07
12-15	Mean	23.06 L <sup>1</sup>	22.90	22.46	22.10
	SD	2.19	2.67	2.22	2.34
	N	43	41	42	43
	%Diff	.	-0.65	-2.59	-4.13

Statistical Test: Generalised Anova/Ancova Test Transformation: Automatic

1 [L - Automatic Transformation: Log]

2 [I - Automatic Transformation: Identity (No Transformation)]

3 [I,aaa - Automatic Transformation: Identity (No Transformation), (All Groups) Test: Analysis of Variance p =

4 [ddd - Test: Dunnett 2 Sided p < 0.001]

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Provantis  
Mean Gestation Food Consumption

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20256434

Sex: Female		Food Consumption (g/animal/day)			
Day(s) Relative to Mating (Litter: )		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
15-18	Mean	25.33 R <sup>1</sup>	25.23	24.84	24.30
	SD	3.58	2.93	2.77	2.17
	N	43	41	42	43
	%Diff	.	-0.41	-1.94	-4.08
18-21	Mean	23.41 I <sup>2</sup>	22.84	22.66	23.25
	SD	2.71	2.74	2.17	2.89
	N	43	41	41	43
	%Diff	.	-2.43	-3.21	-0.69
0-21	Mean	22.24 I <sup>2</sup>	22.12	21.80	21.60
	SD	2.21	2.23	1.75	1.98
	N	43	41	41	43
	%Diff	.	-0.55	-1.98	-2.89

Statistical Test: Generalised Anova/Ancova Test Transformation: Automatic

1 [R - Automatic Transformation: Rank]

2 [I - Automatic Transformation: Identity (No Transformation)]

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Provantis  
Mean Lactation Food Consumption

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20256434

Sex: Female		Food Consumption (g/animal/day)			
Day(s) Relative to Littering (Litter:		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
1-4	Mean	35.64 <sup>1</sup>	34.99	36.72	35.99
	SD	4.25	5.34	5.72	4.96
	N	22	20	21	19
	%Diff	.	-1.82	3.02	0.99
4-7	Mean	41.48 <sup>2</sup>	42.08	43.65	44.10
	SD	3.84	4.87	4.93	5.60
	N	22	20	21	19
	%Diff	.	1.45	5.22	6.31
7-10	Mean	51.06 <sup>2</sup>	49.58	51.31	52.34
	SD	3.96	5.54	6.20	4.98
	N	22	20	21	19
	%Diff	.	-2.90	0.49	2.51
10-14	Mean	58.48 <sup>3</sup>	54.93	59.12	59.52
	SD	5.13	6.19	7.17	4.17
	N	22	20	21	19
	%Diff	.	-6.08	1.09	1.77

Statistical Test: Generalised Anova/Ancova Test Transformation: Automatic

1 [I - Automatic Transformation: Identity (No Transformation)]

3 [R, kk - Automatic Transformation: Rank, (All Groups) Test: Kruskal-Wallis p < 0.01]

2 [R - Automatic Transformation: Rank]

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Provantis  
Mean Lactation Food Consumption

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20256434

Food Consumption (g/animal/day)					
Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Littering (Litter:					
14-17	Mean	63.35 R,k <sup>1</sup>	58.90 d <sup>3</sup>	62.73	63.51
	SD	4.74	6.83	7.84	4.06
	N	22	20	21	19
	%Diff	.	-7.03	-0.97	0.25
17-21	Mean	66.81 <sup>2</sup>	64.10	67.71	70.76 d <sup>3</sup>
	SD	6.05	7.15	8.32	4.86
	N	22	20	21	19
	%Diff	.	-4.07	1.34	5.91
1-21	Mean	53.79 R,k <sup>1</sup>	51.64	54.53	55.45
	SD	4.26	5.64	6.18	3.94
	N	22	20	21	19
	%Diff	.	-4.00	1.37	3.08

Statistical Test: Generalised Anova/Ancova Test Transformation: Automatic

1 [R,k - Automatic Transformation: Rank, (All Groups) Test: Kruskal-Wallis p < 0.05]

3 [d - Test: Dunnett Non-Parametric 2 Sided p < 0.05]

2 [R,kk - Automatic Transformation: Rank, (All Groups) Test: Kruskal-Wallis p < 0.01]

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20256434  
Mean Estrous Cycle Data - Before Dosing

Parameter	Cycle length (days)	Irregularity index	Percentage of estrus days	Percentage of females acyclic or with acyclic period
Group 1, Control, 0 µg				
MEAN	4.02	0.19	26.95	
SD	0.19	0.30	6.14	0
N	44	44	44	
Group 2, BNT162b1, 30 µg				
MEAN	4.00	0.26	27.04	
SD	0.11	0.32	4.87	4.5
N	42	42	42	
Group 3, BNT162b2, 30 µg				
MEAN	4.00	0.18	26.70	
SD	0.11	0.30	5.00	4.5
N	42	42	42	
Group 4, BNT162b3, 30 µg				
MEAN	3.99	0.19	25.85	
SD	0.08	0.31	3.85	4.5
N	42	42	42	

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20256434  
Mean Estrous Cycle Data - Pre-Mating Period

Parameter	Cycle length (days)	Irregularity index	Percentage of estrus days	Percentage of females acyclic or with acyclic period
Group 1, Control, 0 µg				
MEAN	4.00	0.03	25.19	
SD	0.00	0.14	3.94	18.2
N	36	36	36	
Group 2, BNT162b1, 30 µg				
MEAN	4.08	0.07	25.16	
SD	0.20	0.14	3.32	29.5
N	31	31	31	
Group 3, BNT162b2, 30 µg				
MEAN	4.02	0.05	24.07	
SD	0.13	0.12	3.66	18.2
N	36	36	36	
Group 4, BNT162b3, 30 µg				
MEAN	4.11	0.06	25.00	
SD	0.37	0.16	3.79	27.3
N	32	32	32	

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20256434  
Summary of Cohabitation Data and Maternal Performance  
Littering and Caesarean Subsets

GROUP	1	2	3	4
DOSING	Control 0 µg	BNT162b1 30 µg	BNT162b2 30 µg	BNT162b3 30 µg
<u>LITTERING AND CAESAREAN SUBSETS:</u>				
NUMBER OF FEMALES:				
Paired	44	44	44	44
Failed to mate	0	1C	0	0
Inseminated	44	43	44	44
Not pregnant	1C	1C+1L	1C+1L	0
Mistimed pregnancy	0	0	0	1L
Pregnant	43	41	42	44
PRE - COITAL INTERVAL - DAYS				
MEAN	3.0	3.0	2.8	2.7
SD	2.2	1.9	1.7	1.2
N	44	43	44	43 <sup>(1)</sup>
COPULATION INDEX (%)	100	98	100	100
PREGNANCY RATE (%)	98	93	95	100
FERTILITY INDEX (%)	98	95	95	100
Caesarean phase (inseminated females)				
- With viable fetuses	21	20	21	22
Lactation phase (inseminated females)				
- Females with live pups <sup>(2)</sup>	22	21	21	20
- Euthanized moribund post-partum	0	0	0	1
- Total litter death post-partum	0	1	0	1
- Reared pups to weaning	22	20	21	19
GESTATION INDEX (%)	100	100	100	95

C: Caesarean phase

L: Lactation phase

<sup>(1)</sup> mistimed pregnancy for one pair of rats

<sup>(2)</sup> including one euthanized moribund post-partum female from group 4

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Mean Gravid Uterus Weight and Maternal Body Weight Change

20256434

Day(s): G21 Relative to Mating (Litter: A)

Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Gravid Uterus (g)	Mean	86.32 R,k <sup>1</sup>	91.78 d <sup>2</sup>	87.65	82.47
	SD	7.69	15.18	13.48	11.93
	N	21	20	21	22
	%Diff	-	6.32	1.53	-4.46
Necropsy BW (g)	Mean	366.51 I,a <sup>3</sup>	368.68	351.47	352.54
	SD	24.72	28.34	26.24	19.30
	N	21	20	21	22
	%Diff	-	0.59	-4.11	-3.81
Adjusted BW (g)	Mean	280.19 L <sup>4</sup>	276.90	263.82	270.07
	SD	22.08	26.67	15.75	19.29
	N	21	20	21	22
	%Diff	-	-1.17	-5.84	-3.61
Net BWC from G6 (g)	Mean	104.25 <sup>5</sup>	103.80	93.20 dd <sup>6</sup>	91.73 ddd <sup>7</sup>
	SD	7.27	13.24	15.12	9.37
	N	21	20	21	22
	%Diff	-	-0.44	-10.61	-12.01
Net BWC - Uterine Wt (g)	Mean	17.93 <sup>8</sup>	12.02	5.55 ddd <sup>9</sup>	9.26 d <sup>0</sup>
	SD	7.54	11.37	8.56	10.16
	N	21	20	21	22
	%Diff	-	-32.98	-69.06	-48.36
Mean Foetal Wt (Both) (g)	Mean	4.89 I <sup>+</sup>	4.86	4.90	4.84
	SD	0.23	0.26	0.30	0.21
	N	21	20	21	21
	%Diff	-	-0.55	0.25	-1.05
No. Live Foetuses	Mean	13.2 R,k <sup>1</sup>	14.1	13.1	12.5
	SD	1.6	2.6	2.1	1.9
	%Diff	-	6.9	-0.4	-5.2

+ [Footnote is displayed in the Comments and Markers page]

1 [R,k - Automatic Transformation: Rank, (All Groups) Test: Kruskal-Wallis p < 0.05]

2 [d - Test: Dunnett Non-Parametric 2 Sided p < 0.05]

3 [I,a - Automatic Transformation: Identity (No Transformation), (All Groups) Test: Analysis of Variance p < 0.05]

4 [L - Automatic Transformation: Log]

5 [R,kkk - Automatic Transformation: Rank, (All Groups) Test: Kruskal-Wallis p < 0.001]

6 [dd - Test: Dunnett Non-Parametric 2 Sided p < 0.01]

7 [ddd - Test: Dunnett Non-Parametric 2 Sided p < 0.001]

8 [I,aaa - Automatic Transformation: Identity (No Transformation), (All Groups) Test: Analysis of Variance p < 0.001]

9 [ddd - Test: Dunnett 2 Sided p < 0.001]

0 [d - Test: Dunnett 2 Sided p < 0.05]

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Mean Caesarean Section Data

20256434

Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Mating (Litter: A)					
Females Pregnant [CHSQFS]	N+ve	21	20	21	22
Dams with Viable Foetuses		21	20	21	22
No. of Corpora Lutea [GEN AN]	Mean	14.7 I <sup>1</sup>	15.3	15.5	15.0
	SD	1.6	2.3	2.1	1.8
	Sum	309 I <sup>1</sup>	305	326	331
No. of Implantations [GEN AN]	Mean	14.1 R <sup>2</sup>	14.6	14.0	13.8
	SD	1.6	2.4	2.2	2.2
	Sum	296 R <sup>2</sup>	291	294	303
Pre-Implantation Loss [GEN AN]	Mean	0.6 R,k <sup>3</sup>	0.7	1.5 d <sup>4</sup>	1.3
	SD	1.0	0.9	1.3	2.2
	Sum	13 R,k <sup>3</sup>	14	32 d <sup>4</sup>	28
Pre-Implantation Loss (%) [KWLWCX]	Mean	4.09 k <sup>5</sup>	4.77	9.77 d <sup>4</sup>	7.96
	SD	6.56	6.54	8.09	12.38
	Sum	16 R <sup>2</sup>	9	14	23
Early Resorptions (%) [KWLWCX]	Mean	5.04	3.36	4.62	7.09
	SD	7.23	6.74	6.12	8.72
	Sum	16 R <sup>2</sup>	0	4	5
Late Resorptions (%) [KWLWCX]	Mean	1.05	0.00	1.23	1.56
	SD	2.66	0.00	3.27	4.47
	Sum	0 R <sup>2</sup>	0	0	0
No. of Dead Foetuses [GEN AN]	Mean	0.0 R <sup>2</sup>	0.0	0.0	0.0
	SD	0.0	0.0	0.0	0.0
	Sum	0 R <sup>2</sup>	0	0	0
Post-Implantation Loss [GEN AN]	Mean	0.9 R <sup>2</sup>	0.5	0.9	1.3
	SD	1.2	0.8	1.2	1.4
	Sum	19 R <sup>2</sup>	9	18	28

[CHSQFS] - Chi-Squared & Fisher's Exact

[GEN AN] - Generalised Anova/Ancova Test

[KWLWCX] - Kruskal Wallis & Wilcoxon

1 [I - Automatic Transformation: Identity (No Transformation)]

2 [R - Automatic Transformation: Rank]

3 [R,k - Automatic Transformation: Rank, (All Groups) Test: Kruskal-Wallis p < 0.05]

4 [d - Test: Dunnett Non-Parametric 2 Sided p < 0.05]

5 [k - (All Groups) Test: Kruskal-Wallis p < 0.05]

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Mean Caesarean Section Data

20256434

Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Mating (Litter: A)					
Post-Implantation Loss (%) [KWLWCX]	Mean	8.10	3.36	5.85	8.64
	SD	7.64	6.74	7.28	9.08
No. of Live Foetuses [GEN AN]	Mean	13.2 R,k <sup>1</sup>	14.1	13.1	12.5
	SD	1.6	2.6	2.1	1.9
	Sum	277 R,k <sup>1</sup>	282	276	275
No. of Male Foetuses [GEN AN]	Mean	6.1 I <sup>2</sup>	6.8	6.7	6.2
	SD	1.7	2.1	2.0	1.7
	Sum	129 I <sup>2</sup>	136	141	137
No. of Female Foetuses [GEN AN]	Mean	7.0 I <sup>2</sup>	7.3	6.4	6.3
	SD	2.1	2.2	1.5	1.6
	Sum	148 I <sup>2</sup>	146	135	138
Male Foetuses (%) [KWLWCX]	Mean	46.96	48.09	50.66	49.84
	SD	14.27	12.44	10.69	11.04
Total Litter Weight (g) [GEN AN]	Mean	64.23 <sup>3</sup>	68.36 <sup>d4</sup>	64.32	60.57
	SD	5.91	12.20	10.53	9.49
	N	21	20	21	21
	%Diff	.	6.43	0.14	-5.70
Mean Foetal Weight (both) (g) [GEN AN]	Mean	4.89 I <sup>2</sup>	4.86	4.90	4.84
	SD	0.23	0.26	0.30	0.21
	N	21	20	21	21
	%Diff	.	-0.55	0.25	-1.05
Mean Foetal Weight (M) (g) [GEN AN]	Mean	5.00 I <sup>2</sup>	4.97	5.02	4.96
	SD	0.21	0.30	0.30	0.25
Mean Foetal Weight (F) (g) [GEN AN]	Mean	4.79 I <sup>2</sup>	4.76	4.77	4.71
	SD	0.24	0.24	0.32	0.20

[KWLWCX] - Kruskal Wallis & Wilcoxon

[GEN AN] - Generalised Anova/Ancova Test

1 [R,k - Automatic Transformation: Rank, (All Groups) Test: Kruskal-Wallis p < 0.05]

2 [I - Automatic Transformation: Identity (No Transformation)]

3 [R,kk - Automatic Transformation: Rank, (All Groups) Test: Kruskal-Wallis p < 0.01]

4 [d - Test: Dunnett Non-Parametric 2 Sided p < 0.05]

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Provantis  
Summary of Foetal External, Visceral and Skeletal Observations

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20256434

Exam Type: External		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Number of Fetuses Examined:		277	282	276	275
Number of Litters Examined:		21	20	21	22
<b>Head/neck</b>					
Head/neck, Exencephaly - (M)	Fetuses N(%)	0(0.0)	1(0.4)	0(0.0)	0(0.0)
	Litters N(%)	0(0.0)	1(5.0)	0(0.0)	0(0.0)
<b>Eye</b>					
Eye, Open - (M)	Fetuses N(%)	0(0.0)	1(0.4)	0(0.0)	0(0.0)
	Litters N(%)	0(0.0)	1(5.0)	0(0.0)	0(0.0)
<b>Mouth/Jaw</b>					
Mouth, Misshapen - (M)	Fetuses N(%)	0(0.0)	0(0.0)	1(0.4)	0(0.0)
	Litters N(%)	0(0.0)	0(0.0)	1(4.8)	0(0.0)
Jaw, Agnathia - (M)	Fetuses N(%)	0(0.0)	0(0.0)	1(0.4)	0(0.0)
	Litters N(%)	0(0.0)	0(0.0)	1(4.8)	0(0.0)
<b>Body</b>					
Trunk, Gastroschisis - (M)	Fetuses N(%)	0(0.0)	0(0.0)	1(0.4)	0(0.0)
	Litters N(%)	0(0.0)	0(0.0)	1(4.8)	0(0.0)
Trunk, Spina bifida - (M)	Fetuses N(%)	0(0.0)	1(0.4)	0(0.0)	0(0.0)
	Litters N(%)	0(0.0)	1(5.0)	0(0.0)	0(0.0)

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Provantis  
Summary of Foetal External, Visceral and Skeletal Observations

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Exam Type: Visceral Body (Rat)		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Number of Fetuses Examined:		133	135	132	132
Number of Litters Examined:		21	20	21	22
<b>Heart</b>					
Heart, Ventricular septum defect - (M)	Fetuses N(%)	0(0.0)	0(0.0)	0(0.0)	1(0.8)
	Litters N(%)	0(0.0)	0(0.0)	0(0.0)	1(4.5)
<b>Liver</b>					
Liver, Abnormal lobation - (A)	Fetuses N(%)	1(0.8)	0(0.0)	0(0.0)	0(0.0)
	Litters N(%)	1(4.8)	0(0.0)	0(0.0)	0(0.0)
<b>Lung</b>					
Lobe, Absent - (A)	Fetuses N(%)	0(0.0)	0(0.0)	1(0.8)	1(0.8)
	Litters N(%)	0(0.0)	0(0.0)	1(4.8)	1(4.5)
Lobe, Supernumerary - (A)	Fetuses N(%)	0(0.0)	0(0.0)	0(0.0)	1(0.8)
	Litters N(%)	0(0.0)	0(0.0)	0(0.0)	1(4.5)
<b>Major blood vessel</b>					
Aortic arch, Right-sided - (M)	Fetuses N(%)	0(0.0)	0(0.0)	1(0.8)	0(0.0)
	Litters N(%)	0(0.0)	0(0.0)	1(4.8)	0(0.0)
Ductus arteriosus, Narrowed - (M)	Fetuses N(%)	0(0.0)	1(0.7)	0(0.0)	0(0.0)
	Litters N(%)	0(0.0)	1(5.0)	0(0.0)	0(0.0)
Subclavian artery, Malpositioned - (A)	Fetuses N(%)	0(0.0)	1(0.7)	0(0.0)	0(0.0)
	Litters N(%)	0(0.0)	1(5.0)	0(0.0)	0(0.0)
Umbilical artery, Transposed - (V)	Fetuses N(%)	7(5.3)	12(8.9)	13(9.8)	13(9.8)
	Litters N(%)	6(28.6)	9(45.0)	8(38.1)	9(40.9)

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Summary of Foetal External, Visceral and Skeletal Observations

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20256434					
Exam Type: Visceral Body (Rat)		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Number of Fetuses Examined:		133	135	132	132
Number of Litters Examined:		21	20	21	22
<b>Vein</b>					
Azygos vein, Transposed - (A)		Fetuses N(%)	1(0.8)	0(0.0)	0(0.0)
		Litters N(%)	1(4.8)	0(0.0)	0(0.0)

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Summary of Foetal External, Visceral and Skeletal Observations

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Exam Type: Visceral Head (Rat)		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Number of Fetuses Examined:		133	135	132	132
Number of Litters Examined:		21	20	21	22
Eye Retina, Fold - (M)	Fetuses N(%)	0(0.0)	1(0.7)	0(0.0)	0(0.0)
	Litters N(%)	0(0.0)	1(5.0)	0(0.0)	0(0.0)

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Summary of Foetal External, Visceral and Skeletal Observations

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Exam Type: Skeletal Head (Rat-G21)		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Number of Fetuses Examined:		144	147	144	143
Number of Litters Examined:		21	20	21	22
<b>Skull</b>					
Cranium, Acrania - (M)	Fetuses N(%)	0(0.0)	1(0.7)	0(0.0)	0(0.0)
	Litters N(%)	0(0.0)	1(5.0)	0(0.0)	0(0.0)
Hyoid, Incomplete ossification - (A)	Fetuses N(%)	0(0.0)	1(0.7)	1(0.7)	1(0.7)
	Litters N(%)	0(0.0)	1(5.0)	1(4.8)	1(4.5)
Interparietal, Incomplete ossification - (V)	Fetuses N(%)	3(2.1)	1(0.7)	4(2.8)	6(4.2)
	Litters N(%)	3(14.3)	1(5.0)	3(14.3)	4(18.2)
Mandible, Fused - (M)	Fetuses N(%)	0(0.0)	0(0.0)	1(0.7)	0(0.0)
	Litters N(%)	0(0.0)	0(0.0)	1(4.8)	0(0.0)
Mandible, Misshapen - (A)	Fetuses N(%)	0(0.0)	0(0.0)	1(0.7)	0(0.0)
	Litters N(%)	0(0.0)	0(0.0)	1(4.8)	0(0.0)
Mandible, Short - (M)	Fetuses N(%)	0(0.0)	0(0.0)	1(0.7)	0(0.0)
	Litters N(%)	0(0.0)	0(0.0)	1(4.8)	0(0.0)
Parietal, Incomplete ossification - (V)	Fetuses N(%)	0(0.0)	0(0.0)	3(2.1)	0(0.0)
	Litters N(%)	0(0.0)	0(0.0)	3(14.3)	0(0.0)
Presphenoid, Incomplete ossification - (A)	Fetuses N(%)	1(0.7)	0(0.0)	0(0.0)	0(0.0)
	Litters N(%)	1(4.8)	0(0.0)	0(0.0)	0(0.0)
Squamosal, Incomplete ossification - (V)	Fetuses N(%)	0(0.0)	0(0.0)	1(0.7)	0(0.0)
	Litters N(%)	0(0.0)	0(0.0)	1(4.8)	0(0.0)
Supraoccipital, Incomplete ossification - (V)	Fetuses N(%)	0(0.0)	0(0.0)	2(1.4)	0(0.0)
	Litters N(%)	0(0.0)	0(0.0)	2(9.5)	0(0.0)

1 [c - Group Factor Chi-Squared & Fisher's Exact Test: Chi-Squared p < 0.05]

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Summary of Foetal External, Visceral and Skeletal Observations

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Exam Type: Skeletal Body (Rat-G21)		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Number of Fetuses Examined:		144	147	144	143
Number of Litters Examined:		21	20	21	22
<b>General</b>					
Vertebra, Presacral vertebral arches = 27 - (A)	Fetuses N(%)	0(0.0)	2(1.4)	1(0.7)	3(2.1)
	Litters N(%)	0(0.0)	2(10.0)	1(4.8)	3(13.6)
<b>Forepaw</b>					
Phalanx, Unossified - (A)	Fetuses N(%)	9(6.3)	2(1.4)	6(4.2)	6(4.2)
	Litters N(%)	7(33.3)	1(5.0)	3(14.3)	4(18.2)
<b>Hindpaw</b>					
Metatarsal, Unossified, 1st digit - (V)	Fetuses N(%)	3(2.1)	2(1.4)	3(2.1)	1(0.7)
	Litters N(%)	3(14.3)	1(5.0)	3(14.3)	1(4.5)
Phalanx, Unossified, proximal 2nd to 5th digits - (V)	Fetuses N(%)	46(31.9)	32(21.8)	22(15.3)	25(17.5)
	Litters N(%)	11(52.4)	8(40.0)	7(33.3)	9(40.9)
<b>Ribs</b>					
Ribs, Supernumerary cervical - (A)	Fetuses N(%)	3(2.1)	1(0.7)	0(0.0)	0(0.0)
	Litters N(%)	3(14.3)	1(5.0)	0(0.0)	0(0.0)
Ribs, Supernumerary lumbar - (A)	Fetuses N(%)	3(2.1)	5(3.4)	12(8.3)	6(4.2)
	Litters N(%)	3(14.3)	3(15.0)	6(28.6)	4(18.2)
Ribs, Thick - (A)	Fetuses N(%)	2(1.4)	1(0.7)	4(2.8)	5(3.5)
	Litters N(%)	1(4.8)	1(5.0)	3(14.3)	3(13.6)
Ribs, Wavy - (A)	Fetuses N(%)	0(0.0)	1(0.7)	1(0.7)	3(2.1)
	Litters N(%)	0(0.0)	1(5.0)	1(4.8)	3(13.6)
Ribs, Supernumerary lumbar, short - (V)	Fetuses N(%)	57(39.6)	75(51.0)	71(49.3)	75(52.4)
	Litters N(%)				

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Summary of Foetal External, Visceral and Skeletal Observations

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Exam Type: Skeletal Body (Rat-G21)		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Number of Fetuses Examined:		144	147	144	143
Number of Litters Examined:		21	20	21	22
<b>Ribs (Continued...)</b>					
Ribs, Supernumerary lumbar, short - (V)	Litters N(%)	17(81.0)	19(95.0)	18(85.7)	22(100.0)
<b>Sternebra</b>					
Sternebra, Asymmetric - (A)	Fetuses N(%)	1(0.7)	1(0.7)	0(0.0)	0(0.0)
	Litters N(%)	1(4.8)	1(5.0)	0(0.0)	0(0.0)
Sternebra, Extra ossification site - (A)	Fetuses N(%)	0(0.0)	0(0.0)	0(0.0)	1(0.7)
	Litters N(%)	0(0.0)	0(0.0)	0(0.0)	1(4.5)
Sternebra, Incomplete ossification, 1st/3rd - (A)	Fetuses N(%)	1(0.7)	0(0.0)	1(0.7)	0(0.0)
	Litters N(%)	1(4.8)	0(0.0)	1(4.8)	0(0.0)
Sternebra, Incomplete ossification, 2nd/4th - (V)	Fetuses N(%)	1(0.7)	1(0.7)	2(1.4)	1(0.7)
	Litters N(%)	1(4.8)	1(5.0)	2(9.5)	1(4.5)
Sternebra, Incomplete ossification, 6th - (V)	Fetuses N(%)	0(0.0)	0(0.0)	0(0.0)	1(0.7)
	Litters N(%)	0(0.0)	0(0.0)	0(0.0)	1(4.5)
Sternebra, Minor fusion - (A)	Fetuses N(%)	1(0.7)	0(0.0)	0(0.0)	0(0.0)
	Litters N(%)	1(4.8)	0(0.0)	0(0.0)	0(0.0)
Sternebra, Misshapen - (A)	Fetuses N(%)	0(0.0)	1(0.7)	0(0.0)	0(0.0)
	Litters N(%)	0(0.0)	1(5.0)	0(0.0)	0(0.0)
Sternebra, Unossified, 5th - (A)	Fetuses N(%)	0(0.0)	1(0.7)	0(0.0)	0(0.0)
	Litters N(%)	0(0.0)	1(5.0)	0(0.0)	0(0.0)
<b>Vertebra</b>					
Caudal, Number < 5 - (A)	Fetuses N(%)	0(0.0)	0(0.0)	2(1.4)	2(1.4)

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Summary of Foetal External, Visceral and Skeletal Observations

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Exam Type: Skeletal Body (Rat-G21)		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Number of Fetuses Examined:		144	147	144	143
Number of Litters Examined:		21	20	21	22
<b>Vertebra (Continued...)</b>					
Caudal, Number < 5 - (A)	Litters N(%)	0(0.0)	0(0.0)	2(9.5)	2(9.1)
Cervical, Fused arch - (A)	Fetuses N(%)	0(0.0)	1(0.7)	0(0.0)	0(0.0)
	Litters N(%)	0(0.0)	1(5.0)	0(0.0)	0(0.0)
Cervical, Incomplete ossification of arch - (A)	Fetuses N(%)	0(0.0)	0(0.0)	2(1.4)	0(0.0)
	Litters N(%)	0(0.0)	0(0.0)	2(9.5)	0(0.0)
Cervical, Multiple abnormalities - (M)	Fetuses N(%)	0(0.0)	1(0.7)	0(0.0)	0(0.0)
	Litters N(%)	0(0.0)	1(5.0)	0(0.0)	0(0.0)
Cervical, Odontoid process unossified - (V)	Fetuses N(%)	9(6.3)	7(4.8)	6(4.2)	5(3.5)
	Litters N(%)	7(33.3)	4(20.0)	4(19.0)	5(22.7)
Cervical, Unossified centrum - (V)	Fetuses N(%)	3(2.1)	2(1.4)	2(1.4)	1(0.7)
	Litters N(%)	3(14.3)	2(10.0)	2(9.5)	1(4.5)
Lumbar, Number = 7 - (A)	Fetuses N(%)	1(0.7)	0(0.0)	3(2.1)	4(2.8)
	Litters N(%)	1(4.8)	0(0.0)	2(9.5)	4(18.2)
Sacral, Misshapen arch - (A)	Fetuses N(%)	0(0.0)	1(0.7)	0(0.0)	0(0.0)
	Litters N(%)	0(0.0)	1(5.0)	0(0.0)	0(0.0)
Thoracic, Bipartite ossification of centrum - (A)	Fetuses N(%)	0(0.0)	1(0.7)	0(0.0)	0(0.0)
	Litters N(%)	0(0.0)	1(5.0)	0(0.0)	0(0.0)
Thoracic, Incomplete ossification of centrum, 1st to 9th - (A)	Fetuses N(%)	1(0.7)	0(0.0)	3(2.1)	3(2.1)
	Litters N(%)	1(4.8)	0(0.0)	3(14.3)	3(13.6)
Thoracic, Incomplete ossification of centrum, 10th to 13th - (A)	Fetuses N(%)	6(4.2)	3(2.0)	9(6.3)	1(0.7)

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Summary of Foetal External, Visceral and Skeletal Observations

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Exam Type: Skeletal Body (Rat-G21)		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Number of Fetuses Examined:		144	147	144	143
Number of Litters Examined:		21	20	21	22
<b>Vertebra (Continued...)</b>					
Thoracic, Incomplete ossification of centrum, 10th to 13th. - (A)	Litters N(%)	5(23.8) c <sup>1</sup>	3(15.0)	9(42.9)	1(4.5)
Thoracic, Multiple abnormalities - (M)	Fetuses N(%)	0(0.0)	1(0.7)	0(0.0)	0(0.0)
	Litters N(%)	0(0.0)	1(5.0)	0(0.0)	0(0.0)
Thoracic, Number = 14 - (A)	Fetuses N(%)	0(0.0)	1(0.7)	0(0.0)	0(0.0)
	Litters N(%)	0(0.0)	1(5.0)	0(0.0)	0(0.0)

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Summary of Delivery and Litter Data

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Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Littering (Litter: A)					
Females Completing Delivery [CHSQFS]	N+ve	22	21	21	20
with Liveborn Pups [CHSQFS]	N+ve	22	21	21	19
with Stillborn Pups [CHSQFS]	N+ve	3	4	2	2
with all Stillborn Pups [CHSQFS]	N+ve	0	0	0	1
with all Dead PND 21 [CHSQFS]	N+ve	0	1	0	1
Gestation Length (Days) [GEN AN]	Mean	22.1 <sup>1</sup>	22.3	22.0	22.6 <sup>dd2</sup>
	SD	0.4	0.6	0.7	0.6
	N	22	21	21	20
Number of Implantation Sites [GEN AN]	Mean	14.3 <sup>13</sup>	13.4	14.2	13.2
	SD	2.2	2.4	2.2	1.5
	N	22	21	21	20
	Sum	314 <sup>13</sup>	281	298	264
Pre-Birth Loss (%) [GEN AN]	Mean	6.80 <sup>R,k4</sup>	12.22	8.22	13.76 <sup>d5</sup>
	SD	8.75	16.42	15.51	10.39
	N	22	21	21	20
Pups Delivered/Litter [GEN AN]	Mean	13.3 <sup>R,k4</sup>	11.9	13.1	11.4 <sup>d5</sup>
	SD	2.5	3.2	3.1	1.7
	N	22	21	21	20
	Sum	293 <sup>R,k4</sup>	249	276	227 <sup>d5</sup>

[CHSQFS] - Chi-Squared & Fisher's Exact

1 [R,kk - Automatic Transformation: Rank, (All Groups) Test: Kruskal-Wallis p < 0.01]

3 [I - Automatic Transformation: Identity (No Transformation)]

5 [d - Test: Dunnett Non-Parametric 2 Sided p < 0.05]

[GEN AN] - Generalised Anova/Ancova Test

2 [dd - Test: Dunnett Non-Parametric 2 Sided p < 0.01]

4 [R,k - Automatic Transformation: Rank, (All Groups) Test: Kruskal-Wallis p < 0.05]

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Summary of Delivery and Litter Data

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Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Littering (Litter: A)					
Live Pups PND 0 [GEN AN]	Mean	13.0 R,k <sup>1</sup>	11.0	13.0	11.3 d <sup>2</sup>
	SD	2.5	3.6	3.1	1.6
	N	22	21	21	19
	Sum	287 R,k <sup>1</sup>	232	274	215 d <sup>2</sup>
Live Pups PND 1 [GEN AN]	Mean	13.0 R,k <sup>1</sup>	11.4	13.0	11.2 d <sup>2</sup>
	SD	2.4	3.1	3.0	1.6
	N	22	20	21	19
	Sum	285 R,k <sup>1</sup>	228	273	213 d <sup>2</sup>
Live Pups Precull [GEN AN]	Mean	12.9 R,k <sup>1</sup>	11.4	12.9	11.2 d <sup>2</sup>
	SD	2.3	3.1	2.9	1.6
	N	22	20	21	19
	Sum	284 R,k <sup>1</sup>	228	271	213 d <sup>2</sup>
Live Pups Postcull [GEN AN]	Mean	8.0 R <sup>3</sup>	7.7	7.8	8.0
	SD	0.0	1.1	1.1	0.0
	N	22	20	21	19
	Sum	176 R <sup>3</sup>	154	163	152
Live Pups PND 7 [GEN AN]	Mean	8.0 R <sup>3</sup>	7.7	7.8	8.0
	SD	0.0	1.1	1.1	0.0
	N	22	20	21	19
	Sum	176 R <sup>3</sup>	154	163	152

[GEN AN] - Generalised Anova/Ancova Test  
2 [d - Test: Dunnett Non-Parametric 2 Sided p < 0.05]

1 [R,k - Automatic Transformation: Rank, (All Groups) Test: Kruskal-Wallis p < 0.05]  
3 [R - Automatic Transformation: Rank]  
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Summary of Delivery and Litter Data

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Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Littering (Litter: A)					
Live Pups PND 10 [GEN AN]	Mean	8.0 R <sup>1</sup>	7.7	7.8	8.0
	SD	0.0	1.1	1.1	0.0
	N	22	20	21	19
	Sum	176 R <sup>1</sup>	154	163	152
Live Pups PND 14 [GEN AN]	Mean	8.0 R <sup>1</sup>	7.7	7.8	8.0
	SD	0.0	1.1	1.1	0.0
	N	22	20	21	19
	Sum	176 R <sup>1</sup>	154	163	152
Live Pups PND 17 [GEN AN]	Mean	8.0 R <sup>1</sup>	7.7	7.8	8.0
	SD	0.0	1.1	1.1	0.0
	N	22	20	21	19
	Sum	176 R <sup>1</sup>	154	163	152
Live Pups PND 21 [GEN AN]	Mean	8.0 R <sup>1</sup>	7.7	7.8	8.0
	SD	0.2	1.1	1.1	0.0
	N	22	20	21	19
	Sum	175 R <sup>1</sup>	154	163	152
Dead, Miss., Cannib. PND 0 [CHSQFS]	Sum	6	17	2	12
Dead, Miss., Cannib. PND 1-4 [CHSQFS]	Sum	3	4	3	2
Dead, Miss., Cannib. PND 5-21 [CHSQFS]	Sum	1	0	0	0
Dead, Miss., Cannib. PND 0-21 [CHSQFS]	Sum	10	21	5	14

[GEN AN] - Generalised Anova/Ancova Test  
1 [R - Automatic Transformation: Rank]

[CHSQFS] - Chi-Squared & Fisher's Exact

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Provantis  
Summary of Delivery and Litter Data

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Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Littering (Litter: A)					
Live Birth Index (%)		98.0	93.2	99.3	94.7
Viability Index (PND 0-4) (%)		99.0	98.3	98.9	99.1
Weaning Index (PND 4-21) (%)		99.4	100.0	100.0	100.0
Sex Ratio PND 1 - % Males [CHSQFS]	Mean	51.0	47.1	48.0	49.7
Sex Ratio PND 21 - % Males [CHSQFS]	Mean	49.7	50.6	47.6	49.3

[CHSQFS] - Chi-Squared & Fisher's Exact

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Mean Pup Body Weight (grams)

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Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Littering (Litter: A)					
Mean Pup BW - Males d1 [GEN AN]	Mean	6.25 R <sup>1</sup>	6.54	6.27	6.64
	SD	0.82	0.45	0.73	0.99
	N	22	20	20	20
	%Diff	.	4.55	0.23	6.27
Mean Pup BW - Males d4 [GEN AN]	Mean	9.71 I <sup>2</sup>	10.53	9.81	10.66 w <sup>3</sup>
	SD	1.26	1.19	1.21	1.70
	N	22	20	20	19
	%Diff	.	8.41	1.00	9.75
Mean Pup BW - Males d7 [GEN AN]	Mean	16.14 R <sup>1</sup>	17.23	16.47	17.40 S <sup>4</sup>
	SD	1.76	1.61	1.74	2.01
	N	22	20	20	19
	%Diff	.	6.80	2.07	7.82
Mean Pup BW - Males d10 [GEN AN]	Mean	23.79 R <sup>1</sup>	24.79	24.24	24.96 S <sup>4</sup>
	SD	2.17	1.93	1.87	2.37
	N	22	20	20	19
	%Diff	.	4.17	1.87	4.90
Mean Pup BW - Males d14 [GEN AN]	Mean	34.35 I <sup>2</sup>	35.01	34.93	35.31
	SD	2.76	2.36	2.13	2.71
	N	22	20	20	19
	%Diff	.	1.93	1.69	2.81

[GEN AN] - Generalised Anova/Ancova Test  
2 [I - Automatic Transformation: Identity (No Transformation)]  
4 [S - Test: Shirley 2 Sided p < 0.05]

1 [R - Automatic Transformation: Rank]  
3 [w - Test: Williams 2 Sided p < 0.05]

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Provantis  
Mean Pup Body Weight (grams)

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Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Littering (Litter: A)					
Mean Pup BW - Males d17 [GEN AN]	Mean	41.64 <sup>1</sup>	41.82	42.07	42.63
	SD	3.10	2.77	2.36	2.95
	N	22	20	20	19
	%Diff	.	0.42	1.04	2.37
Mean Pup BW - Males d21 [GEN AN]	Mean	55.53 <sup>1</sup>	55.55	56.10	57.35
	SD	4.02	3.93	3.22	4.41
	N	22	20	20	19
	%Diff	.	0.04	1.03	3.28
Mean Pup BW - Males d4 Postculling [GEN AN]	Mean	9.71 <sup>1</sup>	10.51	9.78	10.66 <sup>w2</sup>
	SD	1.31	1.18	1.24	1.72
	N	22	20	20	19
	%Diff	.	8.14	0.66	9.73
Mean Pup BW - Females d1 [GEN AN]	Mean	6.00 <sup>1</sup>	6.16	6.06	6.27
	SD	0.82	0.52	0.73	0.98
	N	22	20	21	20
	%Diff	.	2.65	0.97	4.59
Mean Pup BW - Females d4 [GEN AN]	Mean	9.47 <sup>1</sup>	9.95	9.58	10.21
	SD	1.25	1.13	1.33	1.66
	N	22	20	21	19
	%Diff	.	5.10	1.25	7.87

[GEN AN] - Generalised Anova/Ancova Test  
2 [w - Test: Williams 2 Sided p < 0.05]

1 [I - Automatic Transformation: Identity (No Transformation)]

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Provantis  
Mean Pup Body Weight (grams)

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20256434

Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Littering (Litter: A)					
Mean Pup BW - Females d7 [GEN AN]	Mean	15.77 R <sup>1</sup>	16.56	16.10	16.69 S <sup>3</sup>
	SD	1.72	1.01	1.75	2.03
	N	22	20	21	19
	%Diff	.	5.00	2.14	5.83
Mean Pup BW - Females d10 [GEN AN]	Mean	23.35 R <sup>1</sup>	23.99	23.82	24.07
	SD	2.21	0.98	1.85	2.37
	N	22	20	21	19
	%Diff	.	2.73	1.99	3.05
Mean Pup BW - Females d14 [GEN AN]	Mean	33.71 I <sup>2</sup>	33.91	34.28	34.04
	SD	2.88	1.72	2.04	2.51
	N	22	20	21	19
	%Diff	.	0.59	1.70	0.98
Mean Pup BW - Females d17 [GEN AN]	Mean	40.69 I <sup>2</sup>	40.42	41.10	41.03
	SD	3.16	2.18	2.26	2.49
	N	22	20	21	19
	%Diff	.	-0.66	1.00	0.83
Mean Pup BW - Females d21 [GEN AN]	Mean	54.02 I <sup>2</sup>	53.74	54.42	54.98
	SD	4.18	3.05	2.66	3.71
	N	22	20	21	19
	%Diff	.	-0.51	0.73	1.77

[GEN AN] - Generalised Anova/Ancova Test  
2 [I - Automatic Transformation: Identity (No Transformation)]

1 [R - Automatic Transformation: Rank]  
3 [S - Test: Shirley 2 Sided p < 0.05]

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Provantis  
Mean Pup Body Weight (grams)

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20256434

Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Littering (Litter: A)					
Mean Pup BW - Females d4 Postculling [GEN AN]	Mean	9.49 <sup>1</sup>	10.07	9.59	10.24
	SD	1.25	1.08	1.37	1.68
	N	22	20	21	19
	%Diff	.	6.16	1.09	7.92
Mean Pup Body Weight d1 [GEN AN]	Mean	6.13 <sup>R<sup>2</sup></sup>	6.34	6.19	6.45
	SD	0.82	0.49	0.74	0.97
	N	22	20	21	20
	%Diff	.	3.50	1.06	5.30
Mean Pup Body Weight d4 [GEN AN]	Mean	9.60 <sup>1</sup>	10.26	9.75	10.44
	SD	1.25	1.12	1.31	1.66
	N	22	20	21	19
	%Diff	.	6.91	1.65	8.80
Mean Pup Body Weight d7 [GEN AN]	Mean	15.95 <sup>R<sup>2</sup></sup>	16.94 <sup>S<sup>3</sup></sup>	16.34 <sup>S<sup>3</sup></sup>	17.05 <sup>S<sup>3</sup></sup>
	SD	1.71	1.30	1.73	1.92
	N	22	20	21	19
	%Diff	.	6.18	2.46	6.90
Mean Pup Body Weight d10 [GEN AN]	Mean	23.57 <sup>R<sup>2</sup></sup>	24.44	24.07	24.52 <sup>S<sup>3</sup></sup>
	SD	2.15	1.53	1.81	2.27
	N	22	20	21	19
	%Diff	.	3.66	2.10	4.00

[GEN AN] - Generalised Anova/Ancova Test  
2 [R - Automatic Transformation: Rank]

1 [I - Automatic Transformation: Identity (No Transformation)]  
3 [S - Test: Shirley 2 Sided p < 0.05]

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Provantis  
Mean Pup Body Weight (grams)

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Sex: Female		Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Day(s) Relative to Littering (Litter: A)					
Mean Pup Body Weight d14 [GEN AN]	Mean	34.03 <sup>1</sup>	34.50	34.63	34.67
	SD	2.78	2.12	2.00	2.50
	N	22	20	21	19
	%Diff	.	1.39	1.77	1.90
Mean Pup Body Weight d17 [GEN AN]	Mean	41.16 <sup>1</sup>	41.17	41.59	41.83
	SD	3.11	2.54	2.19	2.59
	N	22	20	21	19
	%Diff	.	0.02	1.06	1.62
Mean Pup Body Weight d21 [GEN AN]	Mean	54.75 <sup>1</sup>	54.71	55.23	56.13
	SD	4.07	3.55	2.71	3.82
	N	22	20	21	19
	%Diff	.	0.06	0.87	2.51
Mean Pup BW d4 Postculling [GEN AN]	Mean	9.60 <sup>1</sup>	10.32	9.75	10.45
	SD	1.26	1.06	1.34	1.66
	N	22	20	21	19
	%Diff	.	7.51	1.51	8.88

[GEN AN] - Generalised Anova/Ancova Test

1 [I - Automatic Transformation: Identity (No Transformation)]

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20256434 Summary of Reflex and Physical Development				
Group	1	2	3	4
Dose level	Control 0 µg	BNT162b1 30µg	BNT162b2 30µg	BNT162b3 30µg
PINNA UNFOLDING				
- % of pups positive:				
day 1 <i>post-partum</i>	5	5	6	24***
day 2 <i>post-partum</i>	51	66	51	68*
day 3 <i>post-partum</i>	98	100 <sup>(1)</sup>	99	100
day 4 <i>post-partum</i>	100	100	100 <sup>(3)</sup>	
EYE OPENING				
- % of pups positive:				
day 12 <i>post-partum</i>	0	2	3	3
day 13 <i>post-partum</i>	19	22	9	29
day 14 <i>post-partum</i>	83	85	79	82
day 15 <i>post-partum</i>	99	99 <sup>(2)</sup>	96	99
day 16 <i>post-partum</i>	100	100 <sup>(2)</sup>	100	100
day 17 <i>post-partum</i>				
PUPILLARY REFLEX - day 21 <i>post-partum</i>				
- % of pups positive:	100	99	100	100
AUDITORY REFLEX - day 21 <i>post-partum</i>				
- % of pups positive:	100	100	100	100

<sup>(1)</sup>: 99.6%

<sup>(2)</sup>: values excluded for three pups that were not observed after PND14 in error

<sup>(3)</sup>: 99.7%, one unselected pup for culling was not observed after PND4

\*:  $p \leq 0.05$ ; \*\*\*  $p \leq 0.001$

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Provantis  
Summary of Maternal Macroscopic Observations  
20256434

Date: 13-Nov-2020 9:31 Page: 1

----- FEMALES -----				
Removal Reason: TERMINAL SACRIFICE	Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
	Number of Animals on Study : 44 (44)	41 (41)	43 (43)	41 (41)
-----				
LIVER;				
Submitted.....	(2)	(0)	(1)	(2)
No Visible Lesions.....	0	0	0	0
Hernia; diaphragm; between right and left median lobes .....	2	0	0	0
Mottled surface; all lobes .....	0	0	0	2
Abnormal shape; left median lobe .....	0	0	0	1
Small; left median lobe .....	0	0	0	1
Mass a; adherent to surrounding tissue; papillary process; solid; dark; heterogeneous .....	0	0	1	0
IDENTIFICATION;				
Submitted.....	(3)	(8)	(12)	(15)
No Visible Lesions.....	3	8	12	15
SKIN/SUBCUTIS;				
Submitted.....	(2)	(3)	(6)	(1)
No Visible Lesions.....	0	0	0	0
Alopecia; single; forelimb; right; left .....	0	1	3	0
Alopecia; single; forelimb; left .....	1	1	0	0
Alopecia; single; abdominal region; thoracic region .....	0	1	0	0
Alopecia; single; thoracic region .....	0	0	1	0
Alopecia; single; thoracic region; abdominal .....	0	0	1	0
Alopecia; right; forepaw; abdominal; left .....	0	0	0	1
Sore/crust; many; back; head .....	0	0	1	0
Sore/crust; many; forelimb; left .....	0	1	0	0
Sore/crust; single; right .....	0	1	0	0
Sore/crust; single; forelimb; right .....	0	0	1	0
Sore/crust; single; hindlimb; left .....	1	0	0	0
Sore/crust; single; abdominal region .....	2	0	0	0
NO CORRELATE;				
Submitted.....	(9)	(6)	(5)	(3)

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Provantis  
Summary of Maternal Macroscopic Observations  
20256434

Date: 13-Nov-2020 9:31 Page: 2

----- FEMALES -----				
Removal Reason: TERMINAL SACRIFICE	Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Number of Animals on Study :	44	41	43	41
Number of Animals Completed:	(44)	(41)	(43)	(41)
NO CORRELATE; (continued)				
No Visible Lesions.....	0	0	0	0
No correlate .....	9	6	6	3
INJECTION SITE 1;				
Submitted.....	(0)	(8)	(9)	(15)
No Visible Lesions.....	0	8	9	14
Pale .....	0	0	0	1
INJECTION SITE 2;				
Submitted.....	(0)	(8)	(10)	(15)
No Visible Lesions.....	0	0	0	0
Firm area .....	0	7	9	14
Enlarged .....	0	7	8	14
Oedematous area .....	0	0	1	0
Pale .....	0	2	4	10

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Provantis  
Date: 13-Nov-2020 9:31 Page: 3  
Summary of Maternal Macroscopic Observations  
20256434

----- FEMALES -----				
Removal Reason: MORIBUND SACRIFICE				
	Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Number of Animals on Study :	0	0	0	1
Number of Animals Completed:	(0)	(0)	(0)	(1)
-----				
NO CORRELATE;				
Submitted.....	(0)	(0)	(0)	(0)
No Visible Lesions.....	0	0	0	0
No correlate .....	0	0	0	1

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Provantis  
Summary of Maternal Macroscopic Observations  
20256434

Date: 13-Nov-2020 9:31 Page: 4

----- FEMALES -----				
Removal Reason: UNPLANNED TERMINAL SACRIFICE	Control 0mcg	BNT162b1 30mcg	BNT162b2 30mcg	BNT162b3 30mcg
Number of Animals on Study :	0	2	1	1
Number of Animals Completed:	(0)	(2)	(1)	(1)
LIVER;				
Submitted.....	(0)	(0)	(0)	(1)
No Visible Lesions.....	0	0	0	0
Pale; all lobes .....	0	0	0	1
SPLEEN;				
Submitted.....	(0)	(0)	(0)	(1)
No Visible Lesions.....	0	0	0	0
Enlarged .....	0	0	0	1
IDENTIFICATION;				
Submitted.....	(0)	(1)	(0)	(1)
No Visible Lesions.....	0	1	0	1
SKIN/SUBCUTIS;				
Submitted.....	(0)	(1)	(0)	(0)
No Visible Lesions.....	0	0	0	0
Alopecia; single; forelimb; abdominal region; left .....	0	1	0	0

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