



**Final Report Amendment 1**

**17-DAY INTRAMUSCULAR TOXICITY STUDY OF BNT162B2 (V9) AND  
BNT162B3C IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

**Testing Facility Study Number: 20GR142**

**Alternative Test Article Identifier(s):**

PF-07302048: Generic number for COVID-19 vaccine program

BNT162b2 (V9): BNT162b2 (Version 9); RBP020.2; PF-07305885

BNT162b3c: BNT162b3; RBP020.8; PF-07315256

**TESTING FACILITY:**

Pfizer Worldwide Research & Development  
Drug Safety Research & Development  
Eastern Point Road  
Groton, CT 06340 USA

## **SIGNATURES**

The final report has been amended to clarify and correct the data and/or interpretation of the results following issuance on 13 Nov 2020.

Study Director

(b) (6)

## **Quality Assurance Statement Signature**

The signature for the following individual applies only to the Groton, CT [Quality Assurance Statement](#) contained in this study report.

(b) (6)

Regulatory Quality Assurance-Good Laboratory Practices, Pfizer, Groton CT.

For signatures see the [Document Approval Record](#) located on the last page of this report amendment.

## 1. AMENDED TEXT

### Section: GLP Compliance Statement

**Justification for revision(s):** Text is being revised based on feedback from regulatory authorities to clarify that manufacturing of the test articles was conducted non-GMP but characterization of the test articles was conducted under GMP conditions, and that serology analysis was conducted under Good Clinical Laboratory Practice (GCLP).

### Current:

This study was conducted in compliance with Good Laboratory Practice for Nonclinical Laboratory Studies regulations as set forth in the Code of Federal Regulations (21 CFR Part 58) with the exceptions of the analyses of alpha-1 acid glycoprotein (A1AGP) and alpha-2-macroglobulin (A2M), and testing performed on the test articles BNT162b2 (Version 9 [V9]) and BNT162b3c which were under non-GLP and non-GMP conditions, respectively. These parameters were conducted under non-GLP and non-GMP conditions and were performed according to fit-for-purpose methods. These exceptions did not have an impact on the integrity or data interpretation of the study.

### Amended To:

This study was conducted in compliance with Good Laboratory Practice for Nonclinical Laboratory Studies regulations as set forth in the Code of Federal Regulations (21 CFR Part 58) with the exceptions of the analyses of alpha-1 acid glycoprotein (A1AGP) and alpha-2-macroglobulin (A2M) which were under non-GLP conditions. Manufacturing of the test articles BNT162b2 (Version 9 [V9]) and BNT162b3c was conducted under non-GMP conditions, while characterization of the test articles was conducted under GMP conditions. Serology analysis was performed in accordance with Good Clinical Laboratory Practice (GCLP). All parameters that were conducted under non-GLP and non-GMP conditions were performed according to fit-for-purpose methods. These exceptions did not have an impact on the integrity or data interpretation of the study.



## Regulatory Quality Assurance

### *Quality Assurance Statement*

**Title:** 17-DAY INTRAMUSCULAR TOXICITY STUDY OF BNT162B2 (V9) AND BNT162B3C IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY

**Study:** 20GR142

In accordance with Pfizer policies and Regulatory Quality Assurance procedures for Good Laboratory Practice (GLP), the conduct of this study has been inspected and/or audited as follows. The Individual Quality Assurance Statement for study phase(s) conducted at other site(s) are contained within this report.

<b>Phase Inspected</b>	<b>Audit/Inspection Date GMT</b>	<b>Reporting Date GMT</b>
Report Amendment 1: Nonclinical Study	17-Dec-2020 to 17-Dec-2020	17-Dec-2020

In addition Routine Facility and Process audits are conducted in accordance with RQA SOPs and Site Monitoring Plans.

(b) (6)

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## Document Approval Record

<b>Document Name:</b>	Report Amendment
<b>Document Title:</b>	Study 20GR142 Report Amendment 1

<b>Signed By:</b>	<b>Date(GMT)</b>	<b>Signing Capacity</b>
(b) (6)	17-Dec-2020 21:25:01	Quality Assurance Approval
	17-Dec-2020 21:28:51	Author Approval



**17-DAY INTRAMUSCULAR TOXICITY STUDY OF BNT162B2 (V9) AND  
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**Testing Facility Study Number: 20GR142**

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Drug Safety Research & Development  
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Groton, CT 06340 USA

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## SIGNATURES

I approve the report and confirm that the study was conducted in compliance with GLP regulations with the exceptions noted (see [GLP Compliance Statement](#)). My interpretation and conclusion of the data accurately reflects the interpretation of the Contributing Scientists and Principal Investigators.

Study Director

(b) (6)

## Quality Assurance Statement Signature

The signature for the following individual applies only to the Groton, CT [Quality Assurance Statement](#) contained in this study report.

(b) (6)

Regulatory Quality Assurance-Good Laboratory Practices, Pfizer, Groton CT.

For signatures see the [Document Approval Record](#) located on the last page of this report.

**OTHER STUDY PERSONNEL**

The following personnel were involved in the conduct of this study:

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Comparative Medicine Activities:  
Ophthalmology Examinations:  
Study Technician(s):  
Study Scientist:  
Study Toxicologist:  
Test Formulations  
  Coordinator:  
  Formulator:  
Clinical Pathology Coordinator:  
Necropsy/Histology Coordinator:  
Biostatistician:  
Safety Biomarkers and Translational Sciences  
Scientist:  
Principal Investigators:  
Serum Antibody Sample Analysis:  
  
Clinical Pathologist:  
  
Anatomic Pathologist:  
  
Peer Review Pathologist

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(b) (6)





## **GLP COMPLIANCE STATEMENT**

This study was conducted in compliance with Good Laboratory Practice for Nonclinical Laboratory Studies regulations as set forth in the Code of Federal Regulations (21 CFR Part 58) with the exceptions of the analyses of alpha-1 acid glycoprotein (A1AGP) and alpha-2-macroglobulin (A2M), and testing performed on the test articles BNT162b2 (Version 9 [V9]) and BNT162b3c which were under non-GLP and non-GMP conditions, respectively. These parameters were conducted under non-GLP and non-GMP conditions and were performed according to fit-for-purpose methods. These exceptions did not have an impact on the integrity or data interpretation of the study.

## **ANIMAL WELFARE COMPLIANCE**

This study was conducted in accordance with the current guidelines for animal welfare (National Research Council Guide for the Care and Use of Laboratory Animals, 2011). The procedures used in this study were reviewed and approved by the Institutional Animal Care and Use Committee.

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## ABSTRACT

BNT162b2 (Version 9 [V9]) and BNT162b3c are candidate COVID-19 vaccines, which are based on a lipid nanoparticle (LNP)-RNA platform and express the SARS-CoV-2 spike protein or its derivatives. The objective of this study was to determine the toxicity and development of a specific immune response to the antigen in each of the vaccine candidates following intramuscular (IM) administration once weekly for a total of 3 doses to Wistar Han (CrI:WI[Han]) rats. The reversibility of effects was evaluated following a 3-week recovery phase.

IM administration of BNT162b2 (V9) and BNT162b3c at 30 µg RNA/dose once weekly for a total of 3 doses to Wistar Han rats was tolerated without evidence of systemic toxicity and produced nonadverse inflammatory changes consistent with expected immune responses to vaccines.

At the conclusion of the dosing phase, test article-related immune responses to both vaccines were evident as transient edema and erythema at the injection site after each dose, transient higher mean body temperatures compared with controls after each dose, higher white blood cell count (primarily involving neutrophils, monocytes and large unstained cells), and changes in acute phase reactants (higher [alpha-1 acid glycoprotein and alpha-2-macroglobulin and fibrinogen] and lower [lower albumin and albumin:globulin (AG) ratios] acute phase proteins. These test article-related changes were fully reversed after the recovery phase, with the exception of higher red cell distribution width, higher globulins, and lower AG ratio.

Changes secondary to inflammation included lower mean body weight, lower mean food consumption, transiently lower reticulocyte counts, and minor lower red cell mass at the conclusion of the dosing phase. These changes fully resolved in the recovery phase.

At the conclusion of the dosing phase, nonadverse test article-related microscopic findings consistent with immune activation and an inflammatory response included mixed cell inflammation and edema of the injection sites (which correlated with macroscopic observations of abnormal color, dark/pale and abnormal consistency, firm), increased cellularity of plasma cells and germinal centers of the draining and inguinal lymph nodes (which correlated with macroscopic observation of abnormal size, enlarged), increased cellularity of hematopoietic cells and germinal centers of the spleen (which correlated with macroscopic observation of abnormal size, enlarged and increased spleen weights), and increased cellularity of hematopoietic cells in the bone marrow were noted. These test article-related changes fully recovered, except for partial recovery of enlarged draining and inguinal lymph nodes and microscopic findings of inflammation at the injection sites, increased cellularity of plasma cells and germinal centers in the draining and inguinal lymph nodes and increased cellularity of the germinal centers in the spleen.

In addition, test article-related vacuolation of the periportal hepatocytes in the liver was observed, in the absence of biochemical evidence of liver injury, and may be related to hepatic clearance of PEGylated lipids that are part of the LNP formulation. At the end of the 3-week recovery phase, this finding was completely recovered.

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Administration of 3 once weekly doses of BNT162b2 (V9) or BNT162b3c elicited SARS-CoV-2 neutralizing antibody responses in both males and females at the end of the dosing and recovery phases of the study. SARS-CoV-2 neutralizing antibody responses were not observed in animals prior to vaccine administration or in saline-administered control animals.

In conclusion, BNT162b2 (V9) and BNT162b3c administered via intramuscular injection once weekly for a total of 3 doses to Wistar Han (CrI:WI[Han]) rats was tolerated without evidence of systemic toxicity, generated a SARS-CoV-2 neutralizing antibody response, and produced nonadverse changes consistent with an immune or inflammatory response at the conclusion of the dosing phase. At the end of the 3-week recovery phase, full or partial recovery of all findings was observed. Other nonadverse findings included vacuolation in the liver which may be related to hepatic clearance of PEGylated lipids and was noted at the conclusion of the dosing phase and completely recovered. The findings in this study are consistent with those typically associated with the intramuscular administration of LNP-encapsulated mRNA vaccines. Animals administered BNT162b2 (V9) or BNT162b3c elicited SARS-CoV-2 neutralizing antibody responses at the end of the dosing and recovery phases of the study.

## 1. INTRODUCTION AND OBJECTIVE

BNT162b2 (Version 9 [V9]) and BNT162b3c are candidate COVID-19 vaccines, which consist of an LNP-encapsulated RNA encoding the SARS-CoV-2 spike protein or its derivatives. The objective of this study was to determine the toxicity and development of a specific immune response to the antigens in each of the vaccine candidates following administration of intramuscular (IM) doses once weekly for a total of 3 doses to Wistar Han (CrI:WI[Han]) rats. The reversibility of effects was evaluated following a 3-week recovery phase.

## 2. STUDY RATIONALE

BNT162b2 (V9) and BNT162b3c were evaluated at the highest intended dose (doses up to 30 µg of RNA administered twice) in clinical trials. Therefore, 3 IM administrations of each vaccine at 30 µg RNA for a total of 3 doses were evaluated in the current study in rats on a more accelerated schedule (once weekly) compared to the clinic. The IM route is the clinical route of administration. The rat is a standard rodent test species for use in toxicity studies and has been shown to generate an immune response to very similar types of RNA-based vaccines.

## 3. MULTI-SITE INFORMATION

Microscopic examination was conducted at Pfizer, Pearl River. Evaluation of Clinical Laboratory parameters was conducted at Pfizer, Pearl River. The analysis for detection of neutralizing antibody titers (serology) to wild type live SARS-CoV-2 virus was conducted at VisMederi, Srl (Siena, Italy).

### 3.1. Communication Method

The Principal Investigator was responsible for informing the Study Director of any deviations to the protocol or Standard Operating Procedures (SOPs) and unexpected events as they occurred during the respective study phase. Other issues were communicated at the end of the respective study phase prior to the issuance of the report.

### 3.2. Reporting Method

Clinical Pathology and Anatomic Pathology Principal Investigator's reports are appended to the final study report. Data and interpretation are integrated into the final study report. The Serology Principal Investigator's report is integrated and appended to the final study report.

Methods for each phase are described in the SOP of the respective test site.

**4. CONTACT INFORMATION**

Pfizer Lead Quality Assurance (QA) <sup>a</sup>	(b) (6) Pfizer Regulatory Quality Assurance-Good Laboratory Practices (RQA-GLP) Eastern Point Road, (b) (6) Groton CT 06340 (b) (6)
Pfizer Test Site QA <sup>a</sup>	(b) (6) Pfizer Regulatory Quality Assurance-Good Laboratory Practices (RQA-GLP) (b) (6) 401 N. Middletown Road Pearl River NY 10965 (b) (6)
CRO Test Site <sup>b</sup>	(b) (6)

CRO = Contract Research Or

a. The Pfizer lead and test site QA monitored applicable study phases, audited the final study or Principal Investigator (PI) report(s), and issued QA statement(s) for work conducted at their respective test sites according to RQA-GLP SOPs. Lead QA was responsible for coordination to ensure appropriate overall study monitoring.

b. The CRO test site QA monitored the phase, audited the CRO Principal Investigator’s report, and issued a QA Statement according to CRO test site QA SOPs.

**5. MATERIALS AND METHODS**

For phases of the study conducted at Pfizer Worldwide Research & Development (Pfizer WRD), Groton, CT, details of methods described below are included in the Standard Operating Procedures of Pfizer WRD, Groton, CT and in the SOPs of the respective Pfizer WRD facility conducting those activities.

Minor deviations from the protocol and/or current standard operating procedures occurred and did not affect the quality, integrity or interpretations of the data or the conclusions of the study. The deviations are documented in the study records and are discussed in the appropriate section of the report.

**5.1. Study Schedule**

Study Initiation Date (date protocol signed):	23 Jun 2020
Experimental Start Date (first day of study-specific data collection):	24 Jun 2020
First Day of Dosing (Day 1):	06 Jul 2020
First Day of Recovery Phase:	23 Jul 2020
Dosing Phase Necropsy (first 10 animals/sex/group):	22 Jul 2020
Recovery Phase Necropsy (remaining animals):	13 Aug 2020
Experimental Completion Date (last day of study-specific data collection):	13 Aug 2020

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## 5.2. Test and Control Articles

### 5.2.1. Test Articles

#### 5.2.1.1. BNT162b2 (V9)

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Test Article Number:	BNT162b2 (V9)
Lot Number:	COVVAC/270320
Manufacturer:	Polymun
Composition	0.5 mg/mL RNA encoding the full SARS-CoV-2 Spike (S) P2 variant protein
Expiration Date:	27 Sep 2020
Storage Conditions:	Frozen at -80°C, protected from light
Composition:	See Certificate of Analysis in <a href="#">Appendix C</a> .

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#### 5.2.1.2. BNT162b3c

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Test Article Number:	BNT162b3c
Lot Number:	BCV/040620
Manufacturer:	Polymun
Composition	0.5 mg/mL RNA encoding Membrane-anchored, trimerized variant of the RBD of the SARS-CoV-2 S protein
Expiration Date:	04 Dec 2020
Storage Conditions:	Frozen at -80°C, protected from light
Composition:	See Certificate of Analysis in <a href="#">Appendix C</a> .

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### 5.2.2. Control Article(s)

#### 5.2.2.1. Vehicle

A solution of 0.9% sterile saline was used to dose the control animals (Group 1).

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Excipient:	0.9% sterile saline
Lot Number:	J8L247
Expiration Date:	31 Mar 2021

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### 5.2.3. Test Article Formulation and Analyses

#### Test Article Numbers: BNT162b2 (V9) and BNT162b3c

Type of Formulation:	Suspension
Method of Preparation:	Thawing of frozen formulation
Frequency of Preparation:	06 Jul 2020, 13 Jul 2020, and 20 Jul 2020
Storage:	Room temperature, protected from light
Formulation Handling at Time of Dispensing for Dosing:	Formulations were gently inverted to mix to ensure uniformity prior to dose administration
Stability:	2 hours from the time thaw was completed <sup>a</sup>
Concentration Analyses:	Not applicable; material was utilized as supplied

a. Reference: DOSAGE AND ADMINISTRATION INSTRUCTIONS FOR BNT162 (PF-07302048) VACCINE, 0.5 MG/ML (C459-INX100407124-V4.0). NOTE: Although the information in this reference document is not specific to the test articles utilized in this study, it was for the same platform of vaccines and was deemed appropriate for use.

### 5.3. Test System

Species:	Rat
Strain/Breed/Origin:	Wistar Han (CrI:WI[Han])
Animal Use Protocol (AUP) Number:	GTN-2011-00314
Source:	Charles River Laboratories Raleigh, NC
Age at Dose Initiation:	9 weeks
Weight at Dose Initiation:	Males: 243.1 grams - 291.6 grams Females: 172.9 grams - 209.5 grams

#### 5.3.1. Acclimation

Animals were acclimated to the laboratory environment for a minimum of 13 days prior to initiation of dosing.

#### 5.3.2. Identification

Animals were identified by a radio frequency identification device (RFID) implanted by the vendor (subscapular region) that was associated with a unique identification number for each animal. Each cage was labeled with a cage card for each animal in the cage.

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### 5.3.3. Allocation and Randomization

Clinically acceptable animals were allocated to study groups following the review of data collected prior to the initiation of dosing and using a computer-assisted randomization procedure based on body weights.

### 5.4. Housing and Environmental Conditions

Caging:	Housed individually in suspended cages
Bedding:	Enrich-n'Pure®, The Andersons, Inc.
Temperature:	68°F-79°F
Humidity:	30%-70%
Lighting:	Approximate 12-hour light, 12-hour dark cycle.
Water:	Municipal drinking water, further purified by reverse osmosis, was provided ad libitum.
Diet:	Certified Irradiated Rodent Diet 5002 (PMI Feeds Inc.) was provided ad libitum. Lot number(s) are included in the raw data.

There are no known contaminants in the food or water that interfered with the quality or integrity of the data.

### 5.5. Experimental Groups

Group Number	Test Article or Vehicle Dose (µg RNA/Dose Day)	Dose Volume (µL/injection site) <sup>a</sup>	Animal Numbers	
			Males	Females
1	0 <sup>b</sup>	60	1-15	46-60
2	30 <sup>c</sup>	60	16-30	61-75
3	30 <sup>d</sup>	60	31-45	76-90

a. Each animal received a single intramuscular injection on each dose day.

b. Sterile saline.

c. BNT162b2 (V9).

d. BNT162b3c.

Doses were administered by a single intramuscular injection (60 µL) on each dosing day (Days 1, 8, and 15) into the left hindlimb quadriceps muscle.

The first 10 animals/sex/group, by ascending animal order, were designated for necropsy at the end of the dosing phase. The remaining 5 animals were retained for the recovery phase.

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## 5.6. Observations and Measurements

### 5.6.1. Clinical Observations/Measurements

General (Cageside) Clinical Observations:	Days of Study	Time Points
	Prior to the Initiation of Dosing (PID)	Once daily
	Nondosing Days (Dosing Phase)	Twice daily, except on days when detailed clinical observations were performed, then only once daily
	Dosing Days (Dosing Phase)	Predose, except on days that predose detailed clinical observations were performed, 4 hours after the last animal was dosed, and at the end of the workday. On 06 Jul 2020 (Day 1), clinical signs were not conducted at the end of the workday for Animals 001-090.
	Recovery Phase Days	Twice daily
Detailed Clinical Observations:	Detailed clinical observations were performed twice prior to the initiation of dosing, twice weekly at approximately the same time body weights were performed, and on the day(s) of necropsy.	
Body Weight:	All animals were weighed twice prior to the initiation of dosing on PID Phase Days 1 and 6, predose on Dosing Phase Days 1, 8, and 15; on Dosing Phase Days 4 and 11 (nondosing), and a fasted weight was collected just prior to scheduled necropsy. Body weights were collected on Recovery Phase Days 1, 4, 8, 11, 15, 18, and 21.	
Food Consumption:	Quantitative food consumption was recorded on Dosing Phase Days 4, 8, 11, and 15 and on Recovery Phase Days 4, 8, 11, 15, 18, and 21.	
Ophthalmology:	<p>Ophthalmic examinations were performed once prior to the initiation of dosing (following randomization) on PID Phase Days 7/8 (males/females) and on Dosing Phase Days 15/16 (males/females).</p> <p>Recovery animals were not examined at the end of the recovery phase.</p> <p>See the Ophthalmology Report in <a href="#">Appendix B</a> for complete materials and methods.</p>	
Injection Site Scoring (Dermal Assessment):	<p>Injection sites were observed during the dosing phase once predose and approximately 4 and 24 hours postdose on all animals. Animals with a score of 2 or greater at 24 hours postdose had additional evaluations at 48 and 72 hours postdose. Animals with a continued score of 2 or greater at 72 hours postdose had additional evaluations at 120 and 144 hours postdose. After dosing on Day 15, a 72-hour postdose evaluation was conducted on recovery animals only. Injection site score was recorded according to a standardized rating scale (<a href="#">Draize, 1959</a>).</p> <p>On Dosing Phase Day 1 (06 Jul 2020), predose dermal assessments were collected on all animals for right-side injection sites (noninjection site), and at 4 hours postdose, dermal assessments were collected on Animals 1-7, 9 (Group 1, Males), and 46-58 (Group 1, Females) for right-side injection sites (noninjection site).</p>	
Body Temperature:	Body temperature was collected on all animals once prior to the initiation of dosing on PID Phase Day 6, predose on Dosing Phase Days 1, 8, and 15, and at approximately 4 and 24 hours postdose from all animals.	

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### 5.6.2. Clinical Laboratory Measurements

Schedule for Collection of Samples for Clinical Laboratory Measurements			
Parameter	Day of Study		
	Dosing Phase		Recovery Phase
	Day 4	Day 17 <sup>e</sup>	Day 22
Hematology	X <sup>a,c</sup>	X <sup>c</sup>	X <sup>c</sup>
Coagulation	NA	X <sup>c</sup>	X <sup>c</sup>
Clinical Chemistry (Core Chemistry)	X <sup>b,c</sup>	X <sup>c</sup>	X <sup>c</sup>
Clinical Chemistry (Other Biomarkers – Acute Phase Proteins)/Serum <sup>d</sup>	X <sup>b,c</sup>	X <sup>c</sup>	X <sup>c</sup>
Urinalysis	NA	X	X

NA = Not applicable; X = Scheduled collection.

a. First 7 animals/sex/group.

b. Last 8 animals/sex/group.

c. Blood samples were collected from animals in a fasted state, with the exception of same day redraws.

d. Assay performed using shared clinical chemistry sample.

e. Evaluated on animals scheduled for necropsy.

See the Clinical Pathology Report in [Appendix B](#) for complete materials and methods.

### 5.6.3. Antibody (Serology) Response to Vaccine Components

Sample Collection and Storage Conditions	
Groups:	1-3
Collection Intervals:	PID Phase Day 8 and Dosing Phase Day 17 <sup>a</sup> , and Recovery Phase Day 21 <sup>a</sup>
Collection Time Points:	PID Phase Day 8, Dosing Phase Day 17, and Recovery Phase Day 21: Once
Animals/Time Point:	All animals
Anticoagulant:	No anticoagulant
Collection Volume per Sample:	PID Phase Day 8: Approximately 0.7 mL Dosing Phase Day 17 and Recovery Phase Day 21: Approximately 1 mL
Sample Processing:	Samples were processed and stored as appropriate within 2 hours of collection
Sample Storage Conditions:	Approximately -60°C or lower

PID = Prior to initiation of dosing.

a. Samples collected prior to necropsy.

All samples collected were sent in one shipment after completion of the last blood sample collection.

Antibody Analysis	
Analysis of Samples from Control Animals (Group 1):	All samples were analyzed
Analysis of Samples from Animals Administered Test Article:	All samples were analyzed for a neutralizing antibody response to the antigens in BNT162b2 (V9) and BNT162b3c

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Incurred Sample Reanalysis (ISR)/Project Numbers	
Antibody (Serology) Sample Analysis was conducted under the following Qualified Method ID:	PFZ_20GR142-WO4_MN SarsCov2_V2_20200924_GL

See the Serology Report in [Appendix B](#) for complete materials and methods.

### 5.7. Postmortem Observations

Animals (10/sex/group) were euthanized on Dosing Phase Day 17 (2 days after the last dose). Remaining animals were euthanized on Recovery Phase Day 22, the last day of the Recovery Phase (surviving animals).

Necropsy, tissue collection, organ weights, macroscopic tissue evaluation, and microscopic examination were performed.

Bone marrow smears were collected from all animals.

See the Anatomic Pathology Report in [Appendix B](#) for complete materials and methods.

### 5.8. Statistical Analysis

Statistical analyses of body weight, body weight change, and food consumption data were conducted in Pristima and analyses of body temperature and injection site scores were conducted by DSRD Statistics using iStats v1.0 with the methods outlined below. All analyses were performed separately for each sex.

Descriptive statistics were generated for each parameter and group at each scheduled sampling time or each time interval. Statistical tests were conducted at the 5% and 1% significance levels.

Analyses of body weight and food consumption parameters were done on measurements collected for each animal at the scheduled sampling times or time intervals. In addition, body weight change at selected intervals was analyzed. Analysis of body temperature was based on the maximum body temperature after injection for each animal. Analysis of injection site score was based on the average irritation score after injection for each animal.

A nonparametric (rank-transform) one way analysis of variance (ANOVA) on all groups was conducted, with two-sided pairwise comparisons of Groups 2 and 3 to Group 1 using Dunnett's test. Average ranks were assigned to ties.

For statistical analysis performed for contributing scientist activities/measurements, see the corresponding report in [Appendix B](#).

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### 5.9. Data Acquisition

The following primary computer applications were used for the collection of data.

Computer Application	Data Collected/Usage
Pristima Preclinical Data Management Suite (Version 7.4.3)	In-life activities
DVMAX Research Version 3.1.2	Animal health records
Microsoft Excel	Sample tracking and antibody immunoassay result storage. Duplicate titration for each sample, provided two neutralization titers (MNt) for each sample. Information was documented according to VisMederi, Srl Standard Operating Procedures (WI-MNSARS-CoV-2) are stored in an Excel sheet (the basic format is provided in dedicated VisMederi, Srl procedure).
iStats Version 1.0	Statistical analysis

For data acquisition systems and version numbers of each of these systems used for contributing scientist/principal investigator activities/measurements, see the corresponding report in [Appendix B](#).

### 5.10. Data Management and Archives

Data	Location of Archive
Raw data, documentation, protocol and amendments, final report, and any specimens generated at the Test Facility	Pfizer, Groton, CT
Raw data and documents electronically archived	Pfizer OpenLab archive system or locked and retained in the source computerized system, as defined as per SOP.
Materials are retained in accordance with the Enterprise Records Retention Schedule.	
Raw data, working sheets and any template required by method procedure are archived as hard copies (original documents) in fireproof archives up to 25 years. Electronic format outputs are regularly backed up and archived in Microsoft cloud.	

## 6. RESULTS

### 6.1. Clinical Observations/Measurements

#### 6.1.1. Mortality

Individual animal mortality data are included in [Appendix 1](#).

There was no unscheduled euthanasia. All animals administered BNT162b2 (V9) or BNT162b3c survived to scheduled necropsy at the end of the dosing or recovery phase of the study.

#### 6.1.2. Clinical Signs

An incidence summary of clinical signs is presented in [Table 1](#). Individual animal clinical signs are included in [Appendix 2](#).

There were no test article-related clinical signs noted for animals administered BNT162b2 (V9) or BNT162b3c during the dosing or recovery phase.

### 6.1.3. Body Weight

Group mean body weight data are presented in [Table 3](#). Group mean body weight change during interval data are presented in [Table 4](#). Individual animal body weight data are included in [Appendix 4](#). Individual animal body weight change during interval data are included in [Appendix 5](#).

#### Dosing Phase

No test article-related mean body weight changes were noted for animals administered BNT162b2 (V9) during the dosing phase.

Test article-related lower mean body weight (0.93x-0.94x control) was noted in males only on Days 11 and 15 for BNT162b3c during the dosing phase.

#### Recovery Phase

Test article-related higher mean body weight (1.05-1.06x control) was noted in males only on Recovery Days 11, 15, 18 and 21 for animals administered BNT162b2 (V9).

No test article related body weight changes were noted for animals administered BNT162b3c during the recovery phase.

Other differences between test article and control group were not test article-related due to the small magnitude of the change, inconsistent direction of the difference, and/or inconsistency of the response.

### 6.1.4. Food Consumption

Group mean food consumption data are presented in [Table 5](#). Individual animal food consumption data are included in [Appendix 6](#).

#### Dosing Phase

Test article-related lower mean food consumption (0.83x-0.87x control) was noted on Days 4 and 11 for animals administered BNT162b2 (V9) during the dosing phase.

Test article-related lower mean food consumption (0.76x-0.92x control) was noted on Days 4 and 11 for animals administered BNT162b3c during the dosing phase.

#### Recovery Phase

Test article-related higher mean food consumption (1.08x-1.35x control) was noted throughout the recovery phase for male animals administered BNT162b2 (V9).

Test article-related higher mean food consumption (1.08x-1.30x control) was noted on Recovery Phase Days 4 and 11 for male animals administered BNT162b3c.



Other differences between test article and control group were not test article-related due to the small magnitude of the change, inconsistent direction of the difference, and/or inconsistency of the response.

### 6.1.5. Dermal Assessment

Group mean dermal assessment data are included in [Table 12](#). Individual dermal assessment data are included in [Appendix 12](#).

#### Dosing Phase

BNT162b2 (V9)-related injection site edema Grade 2 (slight, edges of area well defined by definite raising) or Grade 3 (moderate, raised approximately 1 mm) were noted in all animals (except Animal 17), and occurred following dosing on Days 1, 8 and/or 15 (see [Text Table 1](#)). The edema was generally observed up to 72 hours postdose, and fully resolved prior to dose administration on Days 8 and 15. Erythema was also observed at the injection site in all animals (except Animals 16-21 and 30), following each dose administration, however, it was only a Grade 1 (very slight, barely perceptible) and fully resolved prior to the next dose administration.

BNT162b3c-related injection site edema Grade 2 (slight, edges of area well defined by definite raising) or Grade 3 (moderate, raised approximately 1 mm) were noted in all animals, and occurred following dosing on Days 1, 8 and/or 15 (see [Text Table 2](#)). The edema was generally observed up to 72 hours postdose, and fully resolved prior to dose administration on Days 8 and 15. Erythema was also observed at the injection site in all animals (except Animal 39), following each dose administration, however, it was only a Grade 1 (very slight, barely perceptible) and fully resolved prior to the next dose administration.

**Text Table 1. BNT162b2 (V9) Animals with Injection Site Edema Score  $\geq$  2**

Animal	Clinical Sign	Total Number of Days (Dosing Phase Study Day of Occurrence)
16 M	Edema, Grade 2	1 (D16: 24 HPD)
18 M	Edema, Grade 2	4 (D9: 24 HPD; D10: 48 HPD; D16: 24 HPD; D17: 48 HPD)
19 M	Edema, Grade 2	4 (D9: 24 HPD; D10: 48 HPD; D16: 24 HPD; D17: 48 HPD)
20 M	Edema, Grade 2	5 (D9: 24 HPD; D10: 48 HPD; D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
21 M	Edema, Grade 2	6 (D2: 24 HPD; D9: 24 HPD; D10: 48 HPD; D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
22 M	Edema, Grade 2	5 (D2: 24 HPD; D3: 48 HPD; D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
	Edema, Grade 3	2 (D9: 24 HPD; D10: 48 HPD)
23 M	Edema, Grade 2	5 (D2: 24 HPD; D3: 48 HPD; D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
	Edema, Grade 3	2 (D9: 24 HPD; D10: 48 HPD)
24 M	Edema, Grade 2	3 (D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
	Edema, Grade 3	2 (D9: 24 HPD; D10: 48 HPD)
25 M	Edema, Grade 2	3 (D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
	Edema, Grade 3	2 (D9: 24 HPD; D10: 48 HPD)

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**Text Table 1. BNT162b2 (V9) Animals with Injection Site Edema Score ≥ 2 / Eqv**

Animal	Clinical Sign	Total Number of Days (Dosing Phase Study Day of Occurrence)
26 M	Edema, Grade 2	5 (D2: 24 HPD; D3: 48 HPD; D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
	Edema, Grade 3	2 (D9: 24 HPD; D10: 48 HPD)
27 M	Edema, Grade 2	5 (D2: 24 HPD; D3: 48 HPD; D9: 24 HPD; D10: 48 HPD; D11: 72 HPD)
	Edema, Grade 3	2 (D16: 24 HPD; D17: 48 HPD)
28 M	Edema, Grade 2	3 (D2: 24 HPD; D3: 48 HPD; D11: 72 HPD)
	Edema, Grade 3	4 (D9: 24 HPD; D10: 48 HPD; D16: 24 HPD; D17: 48 HPD)
29 M	Edema, Grade 2	1 (D11: 72 HPD)
	Edema, Grade 3	2 (D 9: 24 HPD; D10: 48 HPD)
30 M	Edema, Grade 2	5 (D9: 24 HPD; D10: 48 HPD; D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
61 F	Edema, Grade 2	5 (D9: 24 HPD; D10: 48 HPD; D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
62 F	Edema, Grade 2	5 (D2: 24 HPD; D3: 48 HPD; D4: 72 HPD; D6: 120 HPD; D7: 144 HPD)
	Edema, Grade 3	5 (D9: 24 HPD; D10: 48 HPD; D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
63 F	Edema, Grade 2	8 (D2: 24 HPD; D3: 48 HPD; D4: 72 HPD; D6: 120 HPD; D7: 144 HPD; D9: 24 HPD; D10: 48 HPD; D11: 72 HPD)
	Edema, Grade 3	2 (D16: 24 HPD; D17: 48 HPD)
64 F	Edema, Grade 2	9 (D2: 24 HPD; D3: 48 HPD; D4: 72 HPD; D6: 120 HPD; D7: 144 HPD; D9: 24 HPD; D10: 48 HPD; D11: 72 HPD; D17: 48 HPD)
	Edema, Grade 3	1 (D16: 24 HPD)
65 F	Edema, Grade 2	2 (D16: 24 HPD; D17: 48 HPD)
	Edema, Grade 3	3 (D9: 24 HPD; D10: 48 HPD; D11: 72 HPD)
66 F	Edema, Grade 2	6 (D2: 24 HPD; D3: 48 HPD; D4: 72 HPD; D6: 120 HPD; D7: 144 HPD; D11: 72 HPD)
	Edema, Grade 3	4 (D9: 24 HPD; D10: 48 HPD; D16: 24 HPD; D17: 48 HPD)
67 F	Edema, Grade 2	6 (D2: 24 HPD; D3: 48 HPD; D4: 72 HPD; D6: 120, D7: 144; D17: 48 HPD)
	Edema, Grade 3	4 (D9: 24 HPD; D10: 48 HPD; D11: 72 HPD; D16: 24 HPD)
68 F	Edema, Grade 2	2 (D16: 24 HPD; D17: 48 HPD)
	Edema, Grade 3	3 (D9: 24 HPD; D10: 48 HPD; D11: 72 HPD)
69 F	Edema, Grade 2	8 (D2: 24 HPD; D3: 48 HPD; D4: 72 HPD; D6: 120 HPD; D7: 144 HPD; D9: 24 HPD; D10: 48 HPD; D17: 48 HPD)
	Edema, Grade 3	1 (D16: 24 HPD)
70 F	Edema, Grade 2	2 (D16: 24 HPD; D17: 48 HPD)
	Edema, Grade 3	3 (D9: 24 HPD; D10: 48 HPD; D11: 72 HPD)
71 F	Edema, Grade 3	5 (D9: 24 HPD; D10: 48 HPD; D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
72 F	Edema, Grade 2	6 (D2: 24 HPD; D3: 48 HPD; D4: 72 HPD; D6: 120 HPD; D7: 144 HPD; D11: 72 HPD)
	Edema, Grade 3	4 (D9: 24 HPD; D10: 48 HPD; D16: 24 HPD; D17: 48 HPD)
73 F	Edema, Grade 2	10 (D2: 24 HPD; D3: 48 HPD; D4: 72 HPD; D6: 120 HPD; D7: 144 HPD; D9: 24 HPD; D10: 48 HPD; D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
74 F	Edema, Grade 2	7 (D2: 24 HPD; D3: 48 HPD; D4: 72 HPD; D6: 120 HPD; D7: 144 HPD; D11: 72 HPD; D16: 24 HPD)
	Edema, Grade 3	2 (D9: 24 HPD; D10: 48 HPD)

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**Text Table 1. BNT162b2 (V9) Animals with Injection Site Edema Score ≥ 2 / Eqpvf**

Animal	Clinical Sign	Total Number of Days (Dosing Phase Study Day of Occurrence)
75 F	Edema, Grade 2	8 (D2: 24 HPD; D3: 48 HPD; D4: 72 HPD; D6: 120 HPD; D7: 144 HPD; D9: 24 HPD; D10: 48 HPD; D11: 72 HPD)
	Edema, Grade 3	2 (D16: 24 HPD; D17: 48 HPD)

Note: Dosing Days = 1, 8, and 15.

D = Dosing Phase Day; F = Female; HPD = Hours postdose M = Male.

Grade 0 = No edema; 1 = Very slight edema (barely perceptible); 2 = Slight edema (edges of area well defined by definite raising); 3 = Moderate edema (raised approximately 1 millimeter); 4 = Severe edema (raised more than 1 millimeter and extends beyond the area of exposure).

**Text Table 2. BNT162b3c Animals with Injection Site Edema Score ≥ 2**

Animal	Clinical Sign	Total Number of Days (Dosing Phase Study Day of Occurrence)
31 M	Edema, Grade 2	4 (D2: 24 HPD; D3: 48 HPD; D11: 72 HPD; D16: 24 HPD)
	Edema, Grade 3	3 (D9: 24 HPD; D10: 48 HPD; D17: 48 HPD)
32 M	Edema, Grade 2	2 (D9: 24 HPD; D10: 48 HPD)
33 M	Edema, Grade 2	3 (D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
	Edema, Grade 3	2 (D9: 24 HPD; D10: 48 HPD)
34 M	Edema, Grade 2	6 (D2: 24 HPD; D3: 48 HPD; D9: 24 HPD; D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
	Edema, Grade 3	1 (D10: 48 HPD)
35 M	Edema, Grade 2	3 (D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
	Edema, Grade 3	2 (D9: 24 HPD; D10: 48 HPD)
36 M	Edema, Grade 2	5 (D9: 24 HPD; D10: 48 HPD; D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
37 M	Edema, Grade 2	7 (D2: 24 HPD; D3: 48 HPD; D4: 72 HPD; D6: 120 HPD; D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
	Edema, Grade 3	2 (D9: 24 HPD; D10: 48 HPD)
38 M	Edema, Grade 2	3 (D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
	Edema, Grade 3	2 (D9: 24 HPD; D10: 48 HPD)
39 M	Edema, Grade 2	4 (D9: 24 HPD; D10: 48 HPD; D16: 24 HPD; D17: 48 HPD)
40 M	Edema, Grade 2	3 (D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
	Edema, Grade 3	2 (D9: 24 HPD; D10: 48 HPD)
41 M	Edema, Grade 2	1 (D11: 72 HPD)
	Edema, Grade 3	4 (D9: 24 HPD; D10: 48 HPD; D16: 24 HPD; D17: 48 HPD)
42 M	Edema, Grade 2	3 (D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
	Edema, Grade 3	2 (D9: 24 HPD; D10: 48 HPD)
43 M	Edema, Grade 2	5 (D2: 24 HPD; D3: 48 HPD; D4: 72 HPD; D6: 120 HPD; D11: 72 HPD)
	Edema, Grade 3	4 (D9: 24 HPD; D10: 48 HPD; D16: 24 HPD; D17: 48 HPD)
44 M	Edema, Grade 2	5 (D2: 24 HPD; D3: 48 HPD; D4: 72 HPD; D6: 120 HPD; D11: 72 HPD)
	Edema, Grade 3	4 (D9: 24 HPD; D10: 48 HPD; D16: 24 HPD; D17: 48 HPD)
45 M	Edema, Grade 2	7 (D2: 24 HPD; D3: 48 HPD; D4: 72 HPD; D6: 120 HPD; D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
	Edema, Grade 3	2 (D9: 24 HPD; D10: 48 HPD)
76 F	Edema, Grade 3	5 (D9: 24 HPD; D10: 48 HPD; D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
77 F	Edema, Grade 2	1 (D13: 120 HPD)

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**Text Table 2. BNT162b3c Animals with Injection Site Edema Score  $\geq 2$  / Eqv)**

Animal	Clinical Sign	Total Number of Days (Dosing Phase Study Day of Occurrence)
	Edema, Grade 3	5 (D9: 24 HPD; D10: 48 HPD; D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
78 F	Edema, Grade 2	1 (D13: 120 HPD)
	Edema, Grade 3	5 (D9: 24 HPD; D10: 48 HPD; D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
79 F	Edema, Grade 2	7 (D2: 24 HPD; D3: 48 HPD; D4: 72 HPD; D6: 120 HPD; D7: 144 HPD; D11: 72 HPD; D17: 48 HPD)
	Edema, Grade 3	3 (D9: 24 HPD; D10: 48 HPD; D16: 24 HPD;)
80 F	Edema, Grade 2	6 (D2: 24 HPD; D3: 48 HPD; D4: 72 HPD; D6: 120 HPD; D7: 144 HPD; D11: 72 HPD)
	Edema, Grade 3	4 (D9: 24 HPD; D10: 48 HPD; D16: 24 HPD; D17: 48 HPD)
81 F	Edema, Grade 2	2 (D9: 24 HPD; D11: 72 HPD)
	Edema, Grade 3	3 (D10: 48 HPD; D16: 24 HPD; D17: 48 HPD)
82 F	Edema, Grade 2	2 (D11: 72 HPD; D17: 48 HPD)
	Edema, Grade 3	3 (D9: 24 HPD; D10: 48 HPD; D16: 24 HPD)
83 F	Edema, Grade 2	5 (D2: 24 HPD; D3: 48 HPD; D4: 72 HPD; D6: 120 HPD; D7: 144 HPD;)
	Edema, Grade 3	5 (D9: 24 HPD; D10: 48 HPD; D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
84 F	Edema, Grade 2	9 (D2: 24 HPD; D3: 48 HPD; D4: 72 HPD; D6: 120 HPD; D7: 144 HPD; D9: 24 HPD; D10: 48 HPD; D11: 72 HPD; D17: 48 HPD)
	Edema, Grade 3	1 (D16: 24 HPD)
85 F	Edema, Grade 2	6 (D2: 24 HPD; D3: 48 HPD; D4: 72 HPD; D6: 120 HPD; D7: 144 HPD; D16: 24 HPD)
	Edema, Grade 3	4 (D9: 24 HPD; D10: 48 HPD; D11: 72 HPD; D17: 48 HPD)
86 F	Edema, Grade 2	5 (D9: 24 HPD; D10: 48 HPD; D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
87 F	Edema, Grade 2	5 (D2: 24 HPD; D3: 48 HPD; D4: 72 HPD; D6: 120 HPD; D7: 144 HPD;)
	Edema, Grade 3	5 (D9: 24 HPD; D10: 48 HPD; D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
88 F	Edema, Grade 2	6 (D2: 24 HPD; D3: 48 HPD; D4: 72 HPD; D6: 120 HPD; D7: 144 HPD; D9: 24 HPD)
	Edema, Grade 3	4 (D10: 48 HPD; D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
89 F	Edema, Grade 2	5 (D9: 24 HPD; D10: 48 HPD; D11: 72 HPD; D16: 24 HPD; D17: 48 HPD)
90 F	Edema, Grade 2	6 (D9: 24 HPD; D10: 48 HPD; D11: 72 HPD; D13: 120 HPD; D16: 24 HPD; D17: 48 HPD)

Note: Doing Days = 1, 8, and 15.

D = Dosing Phase Day; F = Female; HPD = Hours postdose; M = Male.

Grade 0 = No edema; 1 = Very slight edema (barely perceptible); 2 = Slight edema (edges of area well defined by definite raising); 3 = Moderate edema (raised approximately 1 millimeter); 4 = Severe edema (raised more than 1 millimeter and extends beyond the area of exposure).

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## Recovery Phase

BNT162b2 (V9)-related injection site edema Grade 2 (slight, edges of area well defined by definite raising) or Grade 3 (moderate, raised approximately 1 mm) was noted in 2/5 males and 5/5 females following dosing on Day 15 (see Text Table 3). The edema was generally observed up to 72 hours postdose, and fully resolved. Erythema was also observed at the injection site in 2/5 females after the final dose administration, however, it was only Grade 1 (very slight, barely perceptible) and fully resolved.

BNT162b3c -related injection site edema Grade 2 (slight, edges of area well defined by definite raising) or Grade 3 (moderate, raised approximately 1 mm) was noted in 4/5 males and 5/5 females following dosing on Day 15 (see Text Table 4). The edema was generally observed up to 72 hours postdose, and fully resolved. Erythema was also observed at the injection site in 4/5 females after the final dose administration, however, it was only Grade 1 (very slight, barely perceptible) and fully resolved.

**Text Table 3. BNT162b2 (V9) Animals with Injection Site Edema Score  $\geq$  2**

Animal	Clinical Sign	Total Number of Days (Recovery Study Day of Occurrence)
26 M	Edema, Grade 2	1 (RPD1; 72 HPD)
30 M	Edema, Grade 2	1 (RPD1; 72 HPD)
71 F	Edema, Grade 2	1 (RPD1; 72 HPD)
72 F	Edema, Grade 3	1 (RPD1; 72 HPD)
73 F	Edema, Grade 2	1 (RPD1; 72 HPD)
74 F	Edema, Grade 2	1 (RPD1; 72 HPD)
75 F	Edema, Grade 3	1 (RPD1; 72 HPD)

F = Female; HPD = Hours post dose; M = Male; RPD = Recovery Phase Day

Grade 0 = No edema; 1 = Very slight edema (barely perceptible); 2 = Slight edema (edges of area well defined by definite raising); 3 = Moderate edema (raised approximately 1 millimeter); 4 = Severe edema (raised more than 1 millimeter and extends beyond the area of exposure).

**Text Table 4. BNT162b3c Animals with Injection Site Edema Score  $\geq$  2**

Animal	Clinical Sign	Total Number of Days (Recovery Study Day of Occurrence)
41 M	Edema, Grade 2	1 (RPD1; 72 HPD)
43 M	Edema, Grade 2	1 (RPD1; 72 HPD)
44 M	Edema, Grade 2	1 (RPD1; 72 HPD)
45 M	Edema, Grade 2	1 (RPD1; 72 HPD)
86 F	Edema, Grade 2	1 (RPD1; 72 HPD)
87 F	Edema, Grade 3	1 (RPD1; 72 HPD)
88 F	Edema, Grade 3	1 (RPD1; 72 HPD)
89 F	Edema, Grade 3	1 (RPD1; 72 HPD)
90 F	Edema, Grade 2	1 (RPD1; 72 HPD)

F = Female; HPD = Hours post dose; M = Males; RPD = Recovery Phase Day.

Grade 0 = No edema; 1 = Very slight edema (barely perceptible); 2 = Slight edema (edges of area well defined by definite raising); 3 = Moderate edema (raised approximately 1 millimeter); 4 = Severe edema (raised more than 1 millimeter and extends beyond the area of exposure).

### 6.1.6. Body Temperature

Group mean body temperature data are included in [Table 13](#). Individual body temperature data are included in [Appendix 13](#).

Test article-related higher mean body temperature differences from control were noted on Days 1 (+0.42°C-0.54°C), 8 (+0.66°C-0.98°C), and 15 (+0.13°C-1.03°C) following dose administration of BNT162b2 (V9).

Test article-related higher mean body temperature differences from control were noted on Days 1 (+0.50°C-0.71°C), 8 (+0.92°C-1.26°C) and 15 (+0.33°C-1.09°C) following dose administration of BNT162b3c.

Additional body temperature evaluations were not needed at 48 and 72 hours postdose as individual animal body temperatures were  $\leq 40^{\circ}\text{C}$  at 24 hours postdose.

### 6.1.7. Ophthalmology

The complete Ophthalmology Report is included in [Appendix B](#) and a summary of the results is included below.

There were no test article-related ophthalmic findings noted at the conclusion of the dosing phase. Recovery phase examinations were not performed due to no findings observed at the conclusion of the dosing phase.

## 6.2. Clinical Laboratory Measurements

The complete Clinical Pathology Report is included in [Appendix B](#) and a summary of the results is included below.

### Dosing Phase

Test article-related hematology and coagulation findings were similar in rats administered either BNT162b2(V9) or BNT162b3c and included higher mean white blood cell (WBC) counts and fibrinogen concentrations, lower (Day 4) and higher (Day 17) reticulocyte counts, and lower red blood cell mass (red blood cell count, hemoglobin and hematocrit ) as compared with controls.

Higher WBC primarily involved higher neutrophils, monocytes and large unstained cells , but also eosinophils and basophils. They were present on Days 4 and 17, with higher counts on Day 17 than Day 4. On Day 17, there were also test article-related higher fibrinogen concentrations in both sexes. Hypersegmented neutrophils were present on peripheral blood smears of test article-dosed animals.

In addition, there were test article-related transiently lower reticulocyte counts on Day 4, and higher reticulocytes on Day 17 (females only) with attendant expected changes in RBC indices (higher mean cell hemoglobin concentration; males on Day 4; lower mean cell hemoglobin [MCH] and higher red cell distribution width on Day 17; both sexes). These

were associated with lower RBC mass on Days 4 and 17 (comparable on both days or slightly lower on Day 17).

Test article-related clinical chemistry findings were similar in rats administered either BNT162b2(V9) or BNT162b3c and included higher mean alpha-1 acid glycoprotein and alpha-2-macroglobulin and lower AG ratios (primarily due to lower albumin with slight contribution from higher globulins) on Days 4 and 17 in both sexes.

### **Recovery Phase**

All test article-related hematology and coagulation changes noted in the dosing phase were fully reversed after a 3-week recovery phase, with the exception of higher red cell distribution width.

All test article-related clinical chemistry changes noted in the dosing phase were fully reversed after a 3-week recovery phase, with the exception of higher globulins in males administered BNT162b2(V9) and females administered BNT162b2(V9) and BNT162b3c and lower AG ratio in females administered BNT162b2(V9).

There were no test article-related findings noted in urinalysis parameters in the dosing or recovery phase.

#### **6.2.1. Bone Marrow Assessment**

The complete Clinical Pathology Report is included in [Appendix B](#) and a summary of the results is included below.

Bone marrow smears were prepared for all animals and were not examined.

#### **6.3. Antibody (Serology) Analysis**

The complete Serology Report is included in [Appendix B](#) and a summary of the results is included below.

Administration of 3 once weekly doses of BNT162b2 (V9) or BNT162b3c elicited SARS-CoV-2 neutralizing antibody responses in males and females at the end of the dosing (Day 17) and recovery phases (Day 21) of the study. SARS-CoV-2 neutralizing antibody responses were not observed in animals prior to vaccine administration or in saline-administered control animals.

#### **6.4. Postmortem Observations**

The complete Anatomic Pathology Report is included in [Appendix B](#) and a summary of the results is included below.

### **Dosing Phase**

Test article-related organ weight differences included higher absolute and relative (to body and brain weight) spleen weights in males and females administered BNT162b2 (V9) or BNT162b3c.

Test article-related macroscopic findings included large draining lymph nodes (abnormal size, enlarged) and dark/pale and/or firm injection sites (abnormal color, dark/pale and/or abnormal consistency, firm) in animals administered BNT162b2 (V9) or BNT162b3c, and large spleen and inguinal lymph nodes (abnormal size, enlarged) in animals administered BNT162b3c.

Organs with test article-related microscopic findings included the injection site (mixed cell inflammation and edema), draining and inguinal lymph nodes (increased cellularity, plasma cells and germinal centers), liver (hepatocellular vacuolation), spleen (increased cellularity, hematopoietic cells and germinal centers), and bone marrow (increased cellularity, hematopoietic cells) in both males and females administered BNT162b2 (V9) or BNT162b3c.

### **Recovery Phase**

No test article-related organ weight changes were noted at the end of the recovery phase.

Test article-related macroscopic findings observed at the end of the recovery phase were limited to large draining lymph nodes (abnormal size, enlarged) in 1 male administered BNT162b2 (V9) and 1 female administered BNT162b3c and large inguinal lymph nodes (abnormal size, enlarged) in 1 female administered BNT162b3c, indicating a partial recovery of these findings. Pale/dark and/or firm injection sites and enlarged spleen were not observed at the end of recovery phase in BNT162b2 (V9) or BNT162b3c administered males and females, indicating a complete recovery of these findings.

Test article-related microscopic findings noted at the end of the dosing phase including edema at the injection site, hepatocellular vacuolation in the liver, and increased cellularity of hematopoietic cells in the spleen and bone marrow were not observed at the end of recovery phase in BNT162b2 (V9) or BNT162b3c administered males and females, indicating a complete recovery of these findings. Inflammation at the injection site was characterized by mostly lymphocytes and plasma cells with few neutrophils (indicating partial recovery) and no edema (full recovery). However, increased cellularity of the germinal centers in the spleen partially recovered, as the incidence and/or severity of these findings were lower in recovery phase animals as compared with dosing phase animals in both males and females administered BNT162b2 (V9) or BNT162b3c. At the end of recovery phase, mature plasma cells had replaced the plasmablasts identified in the inguinal and draining lymph nodes in the dosing phase animals. In recovery phase animals, infiltration of macrophages was observed in the draining lymph nodes (minimal to mild) in both sexes administered BNT162b2 (V9) or BNT162b3c and in the inguinal lymph nodes (minimal) in both sexes administered BNT162b2 (V9). This finding was considered indicative of a reparative process (consequence of phagocytosis), which can be seen following inflammatory reactions at the injection sites.

## **7. INTEGRATED SUMMARY AND DISCUSSION OF RESULTS**

Intramuscular administration of BNT162b2 (V9) and BNT162b3c at 30 µg RNA/dose day once weekly for a total of 3 doses to Wistar Han rats was tolerated during the dosing phase without evidence of systemic toxicity, generated a SARS-CoV-2 neutralizing antibody



response, and produced nonadverse changes consistent with inflammatory and immune responses to vaccine administration.

At the conclusion of the dosing phase, test article-related responses to both vaccines were evident as transient edema (very slight to moderate) and erythema (very slight) at the injection site after each dose of BNT162b2 (V9) and BNT162b3c. Test article-related erythema and edema fully resolved prior to subsequent dose administration on Days 8 and 15 with findings generally resolved by 72 hours after the final dose administration (Recovery Phase Day 1). Transiently higher body temperature differences compared with concurrent controls were noted on Days 1 (up to +0.71°C), 8 (up to +1.26°C) and 15 (up to +1.09°C) post administration of BNT162b3c and on Days 1 (up to +0.54°C), 8 (up to +0.98°C), and 15 (up to +1.03°C) after administration of BNT162b2 (V9). Additional body temperature evaluations were not needed at 48 and 72 hours postdose as individual animal body temperatures were  $\leq 40^{\circ}\text{C}$  at 24 hours postdose.

Changes secondary to inflammation included lower mean body weight (0.93x-0.94x control on Days 11 and 15) in male animals administered BNT162b3c and lower mean food consumption (0.83x-0.87x control on Days 4 and 11) for animals administered BNT162b2 (V9) and BNT162b3c (0.76x-0.92x control on Days 4 and 11) during the dosing phase. These changes fully resolved in the recovery phase as higher mean body weight (1.05-1.06x control) was noted in males only administered BNT162b2 (V9). Additionally, higher mean food consumption (1.08x-1.35x control) was noted throughout the recovery phase for male animals administered BNT162b2 (V9) and BNT162b3c (1.08x-1.30x control).

At the conclusion of the dosing phase, all clinical pathology findings (type and magnitude) were generally similar between rats administered BNT162b2 (V9) or BNT162b3c, and consistent with expected immune responses to vaccines or secondary to inflammation. The main findings were present in both sexes on Days 4 and/or 17 and included higher acute phase proteins (alpha-1 acid glycoprotein; 7.0x-42x controls], alpha-2-macroglobulin (3.3x-128x] and fibrinogen [2.4x-2.6x]) and white blood cell count (1.28x-2.95x; primarily involving neutrophils, monocytes and large unstained cells, which typically represent large mononuclear cells) and lower albumin:globulin (0.90x-0.82x). Hypersegmented neutrophils present on peripheral blood smears were considered to be secondary to the robust increases in neutrophil counts and likely related to mobilization of bone marrow storage neutrophils and prolonged neutrophil lifespan in circulation (Ulich et al, 1988). Collectively, these findings were consistent with immune responses to vaccines. Microscopic correlates included minimally increased cellularity of hematopoietic cells (primarily myeloid) in the bone marrow and the spleen, minimal to moderate mixed cell inflammation at the injection site and increased cellularity in germinal centers of lymphoid organs. In addition, there were transiently lower reticulocyte counts on Day 4 (0.44x-0.27x), and higher reticulocytes on Day 17 (1.20x-1.31x; females only), with minor lower red cell mass on Days 4 and 17 (HCT; 0.93x-0.89x). Lower reticulocytes were interpreted to be a transient effect of innate immune responses (Abreu et al, 2018; Brooks et al, 2017; Kim et al, 2014; Wrighting & Andrews, 2006).

All test article-related clinical pathology parameter changes were fully reversed after a 3-week recovery phase, with the exception of higher red cell distribution width in males and

females administered BNT162b2(V9) (1.13x and 1.21x, respectively) and BNT162b3c (1.12x and 1.23x, respectively), higher globulins in males administered BNT162b2(V9) (1.08x) and females administered BNT162b2(V9) (1.06x) and BNT162b3c (1.07x) and lower AG ratio in females administered BNT162b2(V9) (0.91x).

Test article-related microscopic pathology findings were observed at the injection site and in the lymph nodes, spleen, bone marrow, and liver for both vaccine candidates. All microscopic findings were nonadverse, as there was no evidence of systemic toxicity or clinical signs of illness or lameness.

At the end of the dosing phase, test article-related mixed cell inflammation (mild to moderate) and edema (mild to moderate) at the injection site were consistent with findings typically associated with the IM administration of lipid nanoparticle (LNP)-encapsulated mRNA vaccines (Hassett et al, 2019). These findings correlated with macroscopic observations of abnormal color (dark/pale) and consistency (firm). At the end of the 3-week recovery phase, full recovery occurred for macroscopic findings of pale/dark and firm injection sites and the microscopic finding of edema, whereas partial recovery occurred for inflammation at the injection sites.

At the end of the dosing phase, test article-related findings in the lymph nodes (increased cellularity of plasma cells [minimal to moderate] and germinal centers [minimal to mild]), spleen (increased cellularity of hematopoietic cells [minimal] and germinal centers [minimal]), and the bone marrow (minimal increased cellularity of hematopoietic cells) were secondary to immune activation and/or inflammation at the injection site. The presence of plasma cells (interpreted as plasmablasts) in the draining and inguinal lymph nodes was interpreted to reflect a robust immunological response to the vaccines. These observations correlated with macroscopic observations of abnormal size (enlarged) in the lymph nodes and spleen and increased spleen weights. At the end of the 3-week recovery phase, full recovery occurred for higher spleen weights, macroscopic finding of enlarged spleen, and microscopic findings of increased cellularity of hematopoietic cells in the spleen and bone marrow, whereas partial recovery occurred for macroscopic findings of enlarged draining and inguinal lymph nodes, microscopic findings of increased cellularity of plasma cells and germinal centers in the draining and inguinal lymph nodes, and increased cellularity of the germinal centers in the spleen.

At the end of the dosing phase, test article-related microscopic finding of minimal portal hepatocyte vacuolation was not associated with hepatic tissue damage or liver enzyme alterations. This change may be related to hepatic clearance of the pegylated lipid in the LNP (Ivens et al, 2015). At the end of 3-week recovery phase, this finding was completely recovered.

Administration of 3 once weekly doses of BNT162b2 (V9) or BNT162b3c elicited SARS-CoV-2 neutralizing antibody responses in both males and females at the end of the dosing (Day 17) and recovery phases (Day 21) of the study. SARS-CoV-2 neutralizing antibody responses were not observed in animals prior to vaccine administration or in saline-administered control animals.

There were no other test article-related effects in the study.

## 8. CONCLUSIONS

In conclusion, BNT162b2 (V9) and BNT162b3c administered via intramuscular injection once weekly for a total of 3 doses to Wistar Han (CrI:WI[Han]) rats was tolerated without evidence of systemic toxicity, generated a SARS-CoV-2 neutralizing antibody response, and produced nonadverse changes consistent with an immune or inflammatory response at the conclusion of the dosing phase. At the end of the 3-week recovery phase, full or partial recovery of all findings was observed. Other nonadverse findings included vacuolation in the liver which may be related to hepatic clearance of PEGylated lipids and was noted at the conclusion of the dosing phase and completely recovered. The findings in this study are consistent with those typically associated with the intramuscular administration of LNP-encapsulated mRNA vaccines. Animals administered BNT162b2 (V9) or BNT162b3c elicited SARS-CoV-2 neutralizing antibody responses at the end of the dosing and recovery phases of the study.

## 9. REFERENCES

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**Table 1**  
**Clinical Signs - Daily Summary Report by Interval**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

**Footnotes**

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Note: Animals were considered normal (data not displayed in table) unless indicated otherwise.

PID = Prior to Initiation of Dosing

- = Value not applicable.

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**Table 1**  
**Clinical Signs - Daily Summary Report by Interval**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**  
**Males (PID)**

	Group Number: 1		2		3	
	Dose: 0 µg/day		30 µg/day		30 µg /day	
<b>Number of animals:</b>	15		15		15	
<b>Number Examined:</b>	15		15		15	
<b>Number Normal:</b>	15		14		15	
<b>Observations</b>	a	b	a	b	a	b
Tail Crooked	0	0	1	12	0	0

Note: a = Number of animals with Observation  
 b = Number of days Observation seen

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**Table 1**  
**Clinical Signs - Daily Summary Report by Interval**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**  
**Males (Dosing)**

	Group Number: 1		2		3	
	Dose: 0 µg/day		30 µg/day		30 µg /day	
<b>Number of animals:</b>	15		15		15	
<b>Number Examined:</b>	15		15		15	
<b>Number Normal:</b>	14		13		15	
<b>Observations</b>	a	b	a	b	a	b
Tail Crooked	0	0	1	17	0	0
Thin Appearance	1	1	0	0	0	0
Hair Loss	0	0	1	2	0	0

Note: a = Number of animals with Observation  
 b = Number of days Observation seen

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**Table 1**  
**Clinical Signs - Daily Summary Report by Interval**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**  
**Males (Recovery)**

	Group Number: 1		2		3	
	Dose: 0 µg/day		30 µg/day		30 µg /day	
<b>Number of animals:</b>	15		15		15	
<b>Number Examined:</b>	5		5		5	
<b>Number Normal:</b>	5		4		5	
<b>Observations</b>	a	b	a	b	a	b
Tail Crooked	0	0	1	22	0	0

Note: a = Number of animals with Observation  
 b = Number of days Observation seen

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**Table 1**  
**Clinical Signs - Daily Summary Report by Interval**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**  
**Females (Dosing)**

	Group Number: 1		2		3	
	Dose: 0 µg/day		30 µg/day		30 µg /day	
<b>Number of animals:</b>	15		15		15	
<b>Number Examined:</b>	15		15		15	
<b>Number Normal:</b>	15		14		14	
<b>Observations</b>	a	b	a	b	a	b
Lesion	0	0	0	0	1	1
Hair Loss	0	0	1	1	0	0

Note: a = Number of animals with Observation  
 b = Number of days Observation seen

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**Table 2**  
**Ocular Exam Summary Report by Interval**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

**Footnotes**

---

Note: Animals were considered normal (data not displayed in table) unless indicated otherwise.

PID = Prior to Initiation of Dosing

- = Value not applicable.

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**Table 2**  
**Ocular Exam Summary Report by Interval**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**  
**Males (PID)**

	Group Number: 1		2		3	
	Dose: 0 µg/day		30 µg/day		30 µg /day	
	Number of animals:		15		15	
	Number Examined:		15		15	
	Number Normal:		0		0	
<b>Observations</b>	a	b	a	b	a	b
Keratic Precipitates	1	1	0	0	1	1
No Ocular Abnormality	11	1	15	1	14	1
Retina, Tortuous Vessels	1	1	0	0	0	0
Vitreous, Hemorrhage	1	1	0	0	0	0
Vitreous, Hyaloid Remnant	1	1	0	0	0	0

Note: a = Number of animals with Observation  
 b = Number of days Observation seen

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**Ocular Exam Summary Report by Interval**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**  
**Males (Dosing)**

	Group Number: 1		2		3	
	Dose: 0 µg/day		30 µg/day		30 µg /day	
	Number of animals:		15		15	
	Number Examined:		15		15	
	Number Normal:		0		0	
<b>Observations</b>	a	b	a	b	a	b
Keratic Precipitates	1	1	0	0	1	1
No Ocular Abnormality	11	1	15	1	14	1
Retina, Tortuous Vessels	1	1	0	0	0	0
Vitreous, Hemorrhage	1	1	0	0	0	0
Vitreous, Hyaloid Remnant	1	1	0	0	0	0

Note: a = Number of animals with Observation  
 b = Number of days Observation seen

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**  
**Females (PID)**

	Group Number: 1		2		3	
	Dose: 0 µg/day		30 µg/day		30 µg /day	
<b>Number of animals:</b>	15		15		15	
<b>Number Examined:</b>	15		15		15	
<b>Number Normal:</b>	0		0		0	
<b>Observations</b>	a	b	a	b	a	b
No Ocular Abnormality	15	1	15	1	15	2

Note: a = Number of animals with Observation  
 b = Number of days Observation seen

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**Table 2**  
**Ocular Exam Summary Report by Interval**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**  
**Females (Dosing)**

	Group Number: 1		2		3	
	Dose: 0 µg/day		30 µg/day		30 µg /day	
	Number of animals:		15		15	
	Number Examined:		15		15	
	Number Normal:		0		0	
<b>Observations</b>	a	b	a	b	a	b
Keratic Precipitates	1	1	0	0	0	0
No Ocular Abnormality	14	1	15	1	15	1

Note: a = Number of animals with Observation  
 b = Number of days Observation seen

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**Table 3**  
**Body Weight (g)**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

**Footnotes**

---

N = Sample Size; SD = Standard Deviation; - = Value not applicable;  
@ = Number examined reduced due to excluded data; e = Group mean excluded from statistics;  
REF = Denotes group used as reference in the statistical tests;  
\* = Statistically significant pairwise comparison at 0.05 level;  
† = Statistically significant pairwise comparison at 0.01 level;  
‡ = Statistically significant trend at 0.05 level;  
§ = Statistically significant trend at 0.01 level.  
+ = Ascending trend sign;  
- = Descending trend sign;

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**Table 3**  
**Body Weight (g)**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Male										
Group Number:		REF			2			3		
Dose:		0 µg/day			30 µg/day			30 µg/day		
Phase	Day	N	Mean	SD	N	Mean	SD	N	Mean	SD
PID	1	15	187.71	8.56	15	188.41	7.75	15	188.03	6.62
	6	15	225.28	9.66	15	226.59	8.47	15	225.85	8.67
Dosing	1	15	264.80	11.89	15	267.18	8.15	15	263.46	12.10
	4	15	252.16	10.99	15	247.61	10.02	15	242.54	13.20
	8	15	280.60	25.91	15	283.61	12.16	15	276.29	15.86
	11	15	295.83	17.57	15	283.71	13.88	15	274.58	18.39 †
	15	15	311.47	17.82	15	302.53	15.32	15	293.29	17.38 *
Recovery	1	5	307.70	21.74	5	308.50	12.01	5	295.92	9.49
	4	5	316.08	25.11	5	320.72	13.14	5	306.16	9.09
	8	5	326.54	29.34	5	332.88	15.20	5	320.72	10.07
	11	5	330.74	30.51	5	346.54	14.64	5	327.60	8.95
	15	5	333.60	32.63	5	354.64	18.28	5	334.80	12.51
	18	5	341.42	35.91	5	359.48	16.87	5	344.14	12.32
	21	5	347.88	39.32	5	369.60	21.74	5	354.24	11.39

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**Table 3**  
**Body Weight (g)**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Group Number:		REF		Female				2		3	
Dose:		0 µg/day		30 µg/day				30 µg/day		30 µg/day	
Phase	Day	N	Mean	SD	N	Mean	SD	N	Mean	SD	
PID	1	15	158.37	7.52	15	159.83	7.42	15	159.57	6.72	
	6	15	176.36	7.52	15	176.31	7.51	15	175.61	9.68	
Dosing	1	15	194.79	8.63	15	191.53	8.38	15	192.68	9.71	
	4	15	183.19	8.90	15	177.31	6.25	15	176.93	7.46	
	8	15	206.53	11.91	15	202.51	7.98	15	198.91	12.14	
	11	15	210.23	12.88	15	203.88	8.25	15	202.83	11.29	
	15	15	214.29	11.95	15	214.02	11.69	15	213.93	14.12	
Recovery	1	5	215.08	14.40	5	207.22	4.75	5	211.92	22.04	
	4	5	217.14	16.97	5	213.00	7.23	5	214.38	17.62	
	8	5	224.02	20.44	5	220.14	7.28	5	219.88	17.62	
	11	5	224.02	17.73	5	221.50	7.28	5	218.22	15.76	
	15	5	224.24	13.98	5	220.58	5.81	5	217.30	19.01	
	18	5	225.54	15.89	5	224.56	7.07	5	225.18	20.90	
	21	5	228.86	14.34	5	231.32	10.43	5	224.46	18.18	

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**Table 4**  
**Body Weight Change During Interval (g)**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

**Footnotes**

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N = Sample Size; SD = Standard Deviation; - = Value not applicable;  
@= Number examined reduced due to excluded data; e= Group mean excluded from statistics;  
REF = Denotes group used as reference in the statistical tests;  
\* = Statistically significant pairwise comparison at 0.05 level;  
† = Statistically significant pairwise comparison at 0.01 level;  
‡ = Statistically significant trend at 0.05 level;  
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+ = Ascending trend sign;  
- = Descending trend sign;

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**Table 4**  
**Body Weight Change During Interval (g)**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**  
**Male**

Phase	Group Number:		REF		2			3		
	Days	N	0 µg/day		30 µg/day			30 µg/day		
PID	Days	N	Mean	SD	N	Mean	SD	N	Mean	SD
Dosing	1-6	15	37.57	5.03	15	38.17	3.68	15	37.81	5.25
	1-4	15	-12.64	6.48	15	-19.57	4.15 †	15	-20.92	5.13 †
	4-8	15	28.44	20.74	15	36.01	5.43	15	33.75	6.25
	8-11	15	15.23	13.92	15	0.10	4.24 †	15	-1.71	4.92 †
	11-15	15	15.64	6.06	15	18.82	3.78 *	15	18.71	3.81
Recovery	1-15	15	46.67	11.76	15	35.35	9.13 †	15	29.83	7.68 †
	1-4	5	8.38	6.59	5	12.22	3.59	5	10.24	1.50
	4-8	5	10.46	5.99	5	12.16	3.36	5	14.56	2.43
	8-11	5	4.20	2.25	5	13.66	5.19 †	5	6.88	2.09
	11-15	5	2.86	5.01	5	8.10	4.39	5	7.20	4.36
	15-18	5	7.82	4.23	5	4.84	2.74	5	9.34	1.78
	18-21	5	6.46	3.71	5	10.12	5.61	5	10.10	4.17
	1-21	5	40.18	23.53	5	61.10	11.09	5	58.32	2.92

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**Table 4**  
**Body Weight Change During Interval (g)**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

		Female								
Group Number:		REF			2			3		
Dose:		0 µg/day			30 µg/day			30 µg/day		
Phase	Days	N	Mean	SD	N	Mean	SD	N	Mean	SD
<b>PID</b>	1-6	15	17.99	2.73	15	16.48	4.42	15	16.03	5.51
<b>Dosing</b>	1-4	15	-11.61	4.28	15	-14.21	4.68	15	-15.75	4.41
	4-8	15	23.34	6.05	15	25.19	3.75	15	21.98	6.34
	8-11	15	3.71	6.72	15	1.37	5.88	15	3.92	6.86
	11-15	15	4.06	2.94	15	10.14	5.89 †	15	11.09	7.60 †
<b>Recovery</b>	1-15	15	19.50	10.28	15	22.49	7.98	15	21.25	9.62
	1-4	5	2.06	4.97	5	5.78	7.47	5	2.46	8.25
	4-8	5	6.88	5.44	5	7.14	3.16	5	5.50	2.38
	8-11	5	0.00	6.15	5	1.36	4.33	5	-1.66	4.65
	11-15	5	0.22	5.29	5	-0.92	3.88	5	-0.92	7.60
	15-18	5	1.30	3.45	5	3.98	3.54	5	7.88	2.12 †
	18-21	5	3.32	6.18	5	6.76	7.21	5	-0.72	6.12
	1-21	5	13.78	7.24	5	24.10	9.09	5	12.54	9.04

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**Table 5**  
**Food Consumption - Empty Feeder During Interval (g)**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

**Footnotes**

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N = Sample Size; SD = Standard Deviation; -= Value not applicable;  
@= Number examined reduced due to excluded data; e= Group mean excluded from statistics;  
REF = Denotes group used as reference in the statistical tree;  
\* = Statistically significant pairwise comparison at 0.05 level;  
† = Statistically significant pairwise comparison at 0.01 level;  
‡ = Statistically significant trend at 0.05 level;  
§ = Statistically significant trend at 0.01 level;  
+ = Ascending trend sign;  
- = Descending trend sign;

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**Table 5**  
**Food Consumption - Empty Feeder During Interval (g)**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

		Male										
Group Number:		REF			2			3				
Dose:		0 µg/day			30 µg/day			30 µg/day				
Phase	Days	N	Mean	SD	N	Mean	SD		N	Mean	SD	
Dosing	1-4	15	50.88	4.05	15	42.59	4.28	†	15	38.69	5.13	†
	4-8	15	90.87	21.27	15	96.75	8.55		15	91.37	11.71	
	8-11	15	64.77	5.09	15	54.02	6.13	†	15	50.45	7.45	†
	11-15	15	89.35	5.58	15	92.22	8.57		15	88.80	8.32	
	1-15	15	295.87	26.49	15	285.59	25.00		15	269.31	27.34	*
Recovery	1-4	5	48.02	6.41	5	64.74	3.38	†	5	62.26	4.67	†
	4-8	5	82.12	11.18	5	92.92	7.90		5	86.64	6.45	
	8-11	5	58.12	6.67	5	68.00	5.18	*	5	62.70	4.15	
	11-15	5	76.42	9.49	5	84.72	7.87		5	79.20	6.20	
	15-18	5	59.70	8.18	5	64.46	3.81		5	62.60	5.08	
	18-21	5	59.28	9.02	5	66.44	4.09		5	62.14	7.53	
	1-21	5	383.66	49.21	5	441.28	29.93		5	415.54	31.74	

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**Table 5**  
**Food Consumption - Empty Feeder During Interval (g)**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Female											
Group Number:		REF			2			3			
Dose:		0 µg/day			30 µg/day			30 µg /day			
Phase	Days	N	Mean	SD	N	Mean	SD	N	Mean	SD	
<b>Dosing</b>	1-4	15	37.79	4.28	15	33.02	3.62 †	15	34.63	12.73 †	
	4-8	15	74.46	8.29	15	70.83	4.58	15	71.73	6.76	
	8-11	15	48.27	6.64	15	41.85	2.97 †	15	40.42	6.17 †	
	11-15	15	65.27	7.36	15	66.59	6.62	15	68.50	8.71	
	1-15	15	225.80	24.33	15	212.29	13.55	15	215.28	24.59	
<b>Recovery</b>	1-4	5	47.60	5.58	5	49.72	4.93	5	49.02	5.33	
	4-8	5	63.32	7.66	5	66.68	2.93	5	66.88	9.55	
	8-11	5	46.32	4.38	5	46.70	3.76	5	42.72	6.58	
	11-15	5	59.08	7.68	5	60.98	4.18	5	57.88	11.68	
	15-18	5	42.44	5.72	5	43.64	5.88	5	44.76	7.31	
	18-21	5	45.00	4.09	5	46.80	4.13	5	44.76	6.43	
	1-21	5	303.76	32.65	5	314.52	18.16	5	306.02	44.46	

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**Table 6**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Parameter	Description
RBC	Red Blood Cells
HGB	Hemoglobin
HCT	Hematocrit
MCV	Mean Cell Volume
MCH	Mean Cell Hemoglobin
MCHC	Mean Cell Hemoglobin Conc
RDW	Red Cell Distribution Width
RETIC	Reticulocyte, Absolute
PLT	Platelets
MPV	Mean Platelet Volume
WBC	White Blood Cells
NEUT	Neutrophil, Absolute
LYM	Lymphocyte, Absolute
MONO	Monocyte, Absolute
EO	Eosinophil, Absolute
BASO	Basophil, Absolute
LUC	Large Unstained Cells, Absolute
PT_Rat	Prothrombin Time, Rat
APTT	Activated Partial Thromboplastin Time
FIB	Fibrinogen

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**Table 6**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

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**Footnotes**

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Note: Sample size is displayed in ( ) before the mean value.  
SD = Standard Deviation; - = Value not applicable;  
Units are displayed in the ( ) under each parameter name;  
HPD = Hours Post Dose; U = Unscheduled;  
e = Group mean excluded from statistics;  
REF = Denotes group used as reference in the statistical test;  
\* = Statistically significant pairwise comparison at 0.05 level;  
† = Statistically significant pairwise comparison at 0.01 level;  
‡ = Statistically significant trend at 0.05 level;  
§ = Statistically significant trend at 0.01 level.  
+ = Ascending trend sign;  
- = Descending trend sign;  
# = Individual parameter values reported as less than or greater than limit of quantitation are set equal to the limit to calculate the average.

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**Table 6**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male												
	Phase	Day	HPD	Group Number:		REF	2		3			
				Dose :	0 µg/day	30 µg/day	30 µg /day					
RBC (10 <sup>6</sup> /uL)	Dosing	4	--	Mean	(7)	8.117	(7)	7.774	*	(7)	7.596	†
				SD		0.265		0.292		0.273		
	17	-	Mean	(9)	7.584	(10)	7.169		(10)	7.113		
			SD		0.512		0.292		0.326			
	Recovery	22	-	Mean	(5)	7.950	(5)	8.064		(5)	7.886	
				SD		0.480		0.261		0.427		
HGB (g/dL)	Dosing	4	--	Mean	(7)	15.01	(7)	14.16	*	(7)	14.01	†
				SD		0.57		0.62		0.38		
	17	-	Mean	(9)	13.82	(10)	12.53	†	(10)	12.81	†	
			SD		0.72		0.63		0.49			
	Recovery	22	-	Mean	(5)	14.36	(5)	14.38		(5)	14.00	
				SD		1.02		0.41		0.45		
HCT (%)	Dosing	4	--	Mean	(7)	48.04	(7)	43.37	†	(7)	43.79	†
				SD		1.33		1.69		1.16		
	17	-	Mean	(9)	42.61	(10)	38.40	†	(10)	39.29	*	
			SD		2.44		1.64		1.49			

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**Table 6**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male											
	Phase	Day	HPD	Group Number:		REF	2		3		
				Dose :	0 µg/day	30 µg/day	30 µg /day				
HCT (%)	Recovery	22	-	Mean	(5)	42.78	(5)	43.72	(5)	42.98	
				SD		3.12		1.44		2.00	
MCV (fL)	Dosing	4	--	Mean	(7)	59.19	(7)	55.81 †	(7)	57.69	
				SD		1.21		1.28		1.52	
	Recovery	17	-	Mean	(9)	56.24	(10)	53.58 †	(9)	54.99	
				SD		1.37		1.36		1.35	
	Recovery	22	-	Mean	(4)	53.80	(4)	54.00	(4)	54.30	
				SD		1.15		1.03		1.25	
MCH (pg)	Dosing	4	--	Mean	(7)	18.51	(7)	18.20	(7)	18.50	
				SD		0.48		0.49		0.47	
	Recovery	17	-	Mean	(9)	18.27	(10)	17.48 †	(10)	18.01	
				SD		0.42		0.51		0.60	
	Recovery	22	-	Mean	(5)	18.06	(5)	17.84	(5)	17.80	
				SD		0.43		0.64		0.66	
MCHC (g/dL)	Dosing	4	--	Mean	(7)	31.24	(7)	32.64 †	(7)	32.04 †	
				SD		0.57		0.40		0.26	

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**Table 6**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male												
Phase	Day	HPD	Dose :	Group Number:		REF		2		3		
						0 µg/day		30 µg/day		30 µg /day		
MCHC (g/dL)	Dosing	17	-	Mean	(9)	32.46	(10)	32.65	(10)	32.61		
				SD		0.36		0.53		0.64		
	Recovery	22	-	Mean	(5)	33.60	(5)	32.90	(5)	32.60	*	
				SD		0.71		0.74		0.63		
RDW (%)	Dosing	4	--	Mean	(7)	12.27	(7)	12.83	(7)	12.44		
				SD		0.47		0.70		0.49		
		17	-	Mean	(9)	11.63	(10)	14.12	†	(9)	13.73	†
				SD		0.39		0.73		0.46		
	Recovery	22	-	Mean	(4)	11.93	(4)	13.48	†	(4)	13.33	*
				SD		0.42		0.29		0.46		
RETIC (10 <sup>3</sup> /uL)	Dosing	4	--	Mean	(7)	392.1	(7)	107.4	†	(7)	104.6	†
				SD		51.5		46.9		27.3		
		17	-	Mean	(9)	178.8	(10)	185.4		(10)	194.0	
				SD		24.1		25.9		12.4		
	Recovery	22	-	Mean	(5)	180.8	(5)	190.8		(5)	186.6	
				SD		28.9		30.4		25.4		

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**Table 6**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male												
	Phase	Day	HPD	Dose :	Group Number:							
					REF	2	3	0 µg/day	30 µg/day	30 µg /day		
PLT (10 <sup>3</sup> /uL)	Dosing	4	--	Mean	(7)	1012.7	(7)	1039.7	(7)	945.1		
				SD		169.9		94.7		132.1		
		17	-	Mean	(9)	881.3	(10)	801.3	(10)	739.0	*	
				SD		69.0		119.9		133.1		
	Recovery	22	-	Mean	(5)	847.8	(5)	904.4	(5)	837.6		
				SD		40.0		115.4		115.3		
MPV (fL)	Dosing	4	--	Mean	(7)	8.87	(7)	9.14	(7)	9.70	†	
				SD		0.35		0.71		0.37		
		17	-	Mean	(9)	9.12	(10)	9.55	(10)	9.93	†	
				SD		0.36		0.47		0.51		
	Recovery	22	-	Mean	(5)	9.00	(5)	8.84	(5)	8.88		
				SD		0.23		0.24		0.26		
WBC (10e3/uL)	Dosing	4	--	Mean	(7)	7.60	(7)	10.70	*	(7)	9.70	
				SD		1.08		3.01		1.64		
		17	-	Mean	(9)	3.84	(10)	8.83	†	(10)	8.60	†
				SD		1.67		3.62		1.15		

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**Table 6**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male										
	Phase	Day	HPD	Group Number:		REF	2		3	
				Dose :	0 µg/day	30 µg/day	30 µg /day			
WBC (10e3/uL)	Recovery	22	-	Mean	(5)	5.26	(5)	5.98	(5)	4.90
				SD		2.64		1.16		1.18
NEUT (10^3/uL)	Dosing	4	--	Mean	(7)	1.083	(7)	2.470 †	(7)	2.161 *
				SD		0.420		0.834		0.521
	Recovery	17	-	Mean	(9)	0.674	(10)	4.449 †	(10)	4.351 †
				SD		0.387		1.890		0.696
	Recovery	22	-	Mean	(5)	0.898	(5)	1.070	(5)	1.276
				SD		0.372		0.215		0.329
LYM (10^3/uL)	Dosing	4	--	Mean	(7)	6.284	(7)	7.727	(7)	7.030
				SD		1.048		2.157		1.150
	Recovery	17	-	Mean	(9)	3.009	(10)	3.792	(10)	3.547
				SD		1.282		1.624		0.574
	Recovery	22	-	Mean	(5)	4.158	(5)	4.672	(5)	3.408
				SD		2.205		1.107		0.839
MONO (10^3/uL)	Dosing	4	--	Mean	(7)	0.109	(7)	0.199 *	(7)	0.214 †
				SD		0.021		0.079		0.022

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**Table 6**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male												
Phase	Day	HPD	Dose :	Group Number:			2			3		
				REF	0 µg/day	30 µg/day	30 µg/day	30 µg/day				
MONO (10 <sup>3</sup> /uL)	Dosing	17	-	Mean	(9)	0.071	(10)	0.234	†	(10)	0.254	†
				SD		0.042		0.121		0.077		
	Recovery	22	-	Mean	(5)	0.074	(5)	0.106		(5)	0.104	
				SD		0.031		0.021		0.021		
EO (10 <sup>3</sup> /uL)	Dosing	4	--	Mean	(7)	0.081	(7)	0.086		(7)	0.091	
				SD		0.059		0.054		0.034		
		17	-	Mean	(9)	0.056	(10)	0.141	†	(10)	0.122	†
				SD		0.024		0.053		0.061		
	Recovery	22	-	Mean	(5)	0.068	(5)	0.074		(5)	0.074	
				SD		0.042		0.024		0.038		
BASO (10 <sup>3</sup> /uL)	Dosing	4	--	Mean	(7)	0.016	(7)	0.030	*	(7)	0.037	†
				SD		0.005		0.014		0.014		
		17	-	Mean	(9)	0.003	(10)	0.017	†	(10)	0.019	†
				SD		0.005		0.013		0.007		
	Recovery	22	-	Mean	(5)	0.008	(5)	0.008		(5)	0.008	
				SD		0.013		0.004		0.004		

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**Table 6**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male												
	Phase	Day	HPD	Group Number:		REF	2		3			
				Dose :	0 µg/day	30 µg/day	30 µg /day					
LUC (10 <sup>3</sup> /uL)	Dosing	4	--	Mean	(7)	0.046	(7)	0.187	†	(7)	0.183	†
				SD		0.011		0.139			0.104	
		17	-	Mean	(9)	0.026	(10)	0.209	†	(10)	0.323	†
				SD		0.013		0.145			0.118	
	Recovery	22	-	Mean	(5)	0.034	(5)	0.048		(5)	0.026	
				SD		0.027		0.011			0.009	
PT_Rat (sec)	Dosing	17	-	Mean	(8)	14.64	(9)	15.63	*	(10)	16.35	†
				SD		0.76		1.20			0.71	
	Recovery	22	-	Mean	(5)	15.34	(5)	16.64		(5)	18.68	*
				SD		1.30		1.51			1.78	
	Dosing	17	-	Mean	(8)	14.41	(9)	16.50	*	(10)	16.78	*
				SD		1.81		2.65			1.78	
Recovery	22	-	Mean	(5)	16.44	(5)	17.76	*	(5)	18.12	†	
			SD		0.50		0.79			0.67		
FIB (mg/dL)	Dosing	17	-	Mean	(8)	253.1	(9)	596.7	†	(10)	606.1	†
				SD		14.3		39.6			53.9	

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**Table 6**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male										
				Group Number:		REF	2	3		
Phase		Day	HPD	Dose :		0 µg/day	30 µg/day	30 µg /day		
FIB (mg/dL)		Recovery	22	-	<b>Mean</b>	(5) 264.8	(5) 266.6	(5) 264.0		
					<b>SD</b>	30.7	21.9	10.8		

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**Table 6**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female												
	Phase	Day	HPD	Group Number:		REF	2		3			
				Dose :	0 µg/day	30 µg/day	30 µg /day					
RBC (10 <sup>6</sup> /uL)	Dosing	4	--	Mean	(7)	7.903	(7)	7.381	*	(7)	7.470	*
				SD		0.370		0.190		0.206		
	17	-	Mean	(10)	7.423	(9)	6.872	†	(7)	6.836	†	
			SD		0.183		0.195		0.343			
	Recovery	22	-	Mean	(5)	7.262	(5)	7.838	†	(5)	7.704	*
				SD		0.267		0.256		0.208		
HGB (g/dL)	Dosing	4	--	Mean	(7)	14.53	(7)	13.56	*	(7)	13.56	*
				SD		0.59		0.62		0.58		
	17	-	Mean	(10)	13.83	(9)	12.38	†	(7)	12.24	†	
			SD		0.31		0.34		0.68			
	Recovery	22	-	Mean	(5)	13.64	(5)	13.92		(5)	14.14	
				SD		0.67		0.37		0.57		
HCT (%)	Dosing	4	--	Mean	(7)	44.91	(7)	41.79	*	(7)	41.81	*
				SD		1.91		1.79		1.29		
	17	-	Mean	(10)	41.67	(9)	38.09	†	(7)	37.21	†	
			SD		0.70		0.98		1.75			

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**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female												
				Group Number:		REF	2		3			
	Phase	Day	HPD	Dose :	0 µg/day		30 µg/day		30 µg /day			
HCT (%)	Recovery	22	-	<b>Mean</b>	(5)	40.78	(5)	42.46	(5)	42.98		
				<b>SD</b>		1.82		0.93		1.99		
MCV (fL)	Dosing	4	--	<b>Mean</b>	(7)	56.84	(7)	56.59	(7)	56.03		
				<b>SD</b>		0.87		1.75		1.91		
	Recovery	17	-	<b>Mean</b>	(10)	56.16	(9)	55.43	(6)	54.40		
				<b>SD</b>		1.19		1.71		1.97		
MCH (pg)	Recovery	22	-	<b>Mean</b>	(4)	55.80	(5)	54.22	(5)	55.78		
				<b>SD</b>		2.62		1.55		2.21		
MCHC (g/dL)	Dosing	4	--	<b>Mean</b>	(7)	18.37	(7)	18.39	(7)	18.16		
				<b>SD</b>		0.22		0.67		0.75		
	Recovery	17	-	<b>Mean</b>	(10)	18.62	(9)	17.99 †	(7)	17.89 †		
				<b>SD</b>		0.35		0.49		0.60		
Recovery	22	-	<b>Mean</b>	(5)	18.78	(5)	17.76	(5)	18.38			
			<b>SD</b>		0.97		0.38		0.82			
MCHC (g/dL)	Dosing	4	--	<b>Mean</b>	(7)	32.34	(7)	32.49	(7)	32.41		
				<b>SD</b>		0.30		0.78		0.63		

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**Table 6**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female												
	Phase	Day	HPD	Group Number:		REF	2		3			
				Dose :	0 µg/day	30 µg/day	30 µg /day					
MCHC (g/dL)	Dosing	17	-	Mean	(10)	33.18	(9)	32.50	†	(7)	32.84	
				SD		0.32		0.41			0.59	
	Recovery	22	-	Mean	(5)	33.46	(5)	32.78		(5)	32.96	
				SD		0.56		0.33			0.75	
RDW (%)	Dosing	4	--	Mean	(7)	11.11	(7)	11.39		(7)	11.97	†
				SD		0.29		0.40			0.68	
		17	-	Mean	(10)	11.33	(9)	13.34	†	(6)	13.38	†
				SD		0.43		1.04			0.64	
	Recovery	22	-	Mean	(4)	10.80	(5)	13.04	†	(5)	13.32	†
				SD		0.33		0.23			0.50	
RETIC (10 <sup>3</sup> /uL)	Dosing	4	--	Mean	(7)	301.7	(7)	129.7	†	(7)	133.6	†
				SD		39.4		35.7			39.1	
		17	-	Mean	(10)	168.9	(9)	222.1	*	(7)	203.3	
				SD		34.7		54.7			45.8	
	Recovery	22	-	Mean	(5)	153.2	(5)	155.0		(5)	136.2	
				SD		36.2		16.0			49.9	

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**Table 6**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female										
	Phase	Day	HPD	Group Number:		REF	2		3	
				Dose :	0 µg/day	30 µg/day	30 µg /day			
PLT (10 <sup>3</sup> /uL)	Dosing	4	--	Mean	(7)	927.1	(7)	1003.9	(7)	973.6
				SD		116.6		70.9		168.1
		17	-	Mean	(10)	906.9	(9)	778.0 *	(7)	757.6
				SD		124.5		88.3		151.1
	Recovery	22	-	Mean	(5)	787.6	(5)	838.2	(5)	782.0
				SD		77.7		88.0		56.6
MPV (fL)	Dosing	4	--	Mean	(7)	8.67	(7)	8.91	(7)	8.99
				SD		0.91		0.25		0.81
		17	-	Mean	(10)	9.50	(9)	9.40	(7)	9.73
				SD		0.49		0.21		0.72
	Recovery	22	-	Mean	(5)	9.20	(5)	9.02	(5)	9.18
				SD		0.42		0.34		0.33
WBC (10e3/uL)	Dosing	4	--	Mean	(7)	6.01	(7)	7.84	(7)	8.57 *
				SD		2.38		1.98		0.92
		17	-	Mean	(10)	2.16	(9)	5.70 †	(7)	6.37 †
				SD		0.45		1.33		2.46

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**Table 6**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female										
	Phase	Day	HPD	Group Number:		REF	2		3	
				Dose :	0 µg/day	30 µg/day	30 µg /day			
WBC (10e3/uL)	Recovery	22	-	Mean	(5)	2.34	(5)	2.62	(5)	2.72
				SD		0.87		0.69		1.16
NEUT (10^3/uL)	Dosing	4	--	Mean	(7)	0.920	(7)	2.306	(7)	2.879 †
				SD		1.220		0.683		0.478
	Recovery	17	-	Mean	(10)	0.409	(9)	2.469 †	(7)	2.879 †
				SD		0.198		0.711		1.238
Recovery	22	-	Mean	(5)	0.252	(5)	0.482 *	(5)	0.278	
			SD		0.051		0.279		0.051	
LYM (10^3/uL)	Dosing	4	--	Mean	(7)	4.911	(7)	5.136	(7)	5.169
				SD		1.263		1.368		0.932
	Recovery	17	-	Mean	(10)	1.651	(9)	2.833 †	(7)	3.030 †
				SD		0.289		0.872		1.209
Recovery	22	-	Mean	(5)	2.016	(5)	2.050	(5)	2.316	
			SD		0.899		0.554		1.068	
MONO (10^3/uL)	Dosing	4	--	Mean	(7)	0.093	(7)	0.176	(7)	0.234 †
				SD		0.092		0.054		0.062

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**Table 6**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female												
Phase	Day	HPD	Dose :	Group Number:		REF		2		3		
						0 µg/day		30 µg/day		30 µg /day		
MONO (10 <sup>3</sup> /uL)	Dosing	17	-	Mean	(10)	0.056	(9)	0.154	†	(7)	0.176	†
				SD		0.025		0.033		0.068		
	Recovery	22	-	Mean	(5)	0.028	(5)	0.048		(5)	0.060	*
				SD		0.013		0.011		0.025		
EO (10 <sup>3</sup> /uL)	Dosing	4	--	Mean	(7)	0.057	(7)	0.087	*	(7)	0.123	†
				SD		0.011		0.023		0.039		
		17	-	Mean	(10)	0.029	(9)	0.092	†	(7)	0.097	†
				SD		0.013		0.043		0.042		
	Recovery	22	-	Mean	(5)	0.032	(5)	0.028		(5)	0.036	
				SD		0.011		0.011		0.021		
BASO (10 <sup>3</sup> /uL)	Dosing	4	--	Mean	(7)	0.009	(7)	0.017		(7)	0.024	†
				SD		0.007		0.010		0.005		
		17	-	Mean	(10)	0.001	(9)	0.008	†	(7)	0.010	†
				SD		0.003		0.004		0.006		
	Recovery	22	-	Mean	(5)	0.000	(5)	0.000		(5)	0.002	
				SD		0.000		0.000		0.004		

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**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female													
	Phase	Day	HPD	Group Number:		REF	2		3				
				Dose :	0 µg/day	30 µg/day	30 µg /day						
LUC (10 <sup>3</sup> /uL)	Dosing	4	--	Mean	(7)	0.030	(7)	0.126	†	(7)	0.133	†	
				SD		0.028		0.093		0.060			
		17	-	Mean	(10)	0.010	(9)	0.132	†	(7)	0.190	†	
				SD		0.005		0.101		0.096			
	Recovery	22	-	Mean	(5)	0.014	(5)	0.012		(5)	0.022		
				SD		0.005		0.008		0.016			
PT_Rat (sec)	Dosing	17	-	Mean	(10)	14.12	(9)	14.89		(9)	15.38	*	
				SD		0.84		1.02		0.93			
	Recovery	22	-	Mean	(5)	13.10	(5)	13.66		(5)	13.58		
				SD		0.83		0.83		0.62			
	APTT (sec)	Dosing	17	-	Mean	(10)	15.45	(9)	15.56		(9)	14.78	
					SD		0.80		1.39		3.08		
Recovery		22	-	Mean	(5)	16.82	(5)	17.26		(5)	16.96		
				SD		0.85		0.90		0.72			
Dosing		17	-	Mean	(10)	217.2	(9)	541.9	†	(9)	563.1	†	
				SD		25.0		63.4		56.7			

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**Table 6**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female										
				Group Number:		REF	2	3		
Phase		Day	HPD	Dose :		0 µg/day	30 µg/day	30 µg /day		
FIB (mg/dL)		Recovery	22	-		<b>Mean</b>	(5) 186.4	(5) 196.6	(5) 185.0	
						<b>SD</b>	17.2	18.4	16.6	

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**Table 7**  
**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

<b>Parameter</b>	<b>Description</b>	<b>Parameter</b>	<b>Description</b>
ALT	Alanine Aminotransferase	A1AGP	Alpha-1 Acid Glycoprotein
AST	Aspartate Aminotransferase		
ALP	Alkaline Phosphatase		
GGT	Gamma Glutamyl Transferase		
TBIL	Bilirubin, Total		
CHOL	Cholesterol		
TRIG	Triglycerides		
GLUC	Glucose		
TP	Protein, Total		
ALB	Albumin		
GLOB	Globulin		
AG	Albumin/Globulin Ratio		
BUN	Blood Urea Nitrogen		
CREA	Creatinine		
PHOS	Phosphorus		
CA	Calcium		
NA	Sodium		
K	Potassium		
CL	Chloride		
A2M	Alpha-2-Macroglobulin		

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**Table 7**  
**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

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**Footnotes**

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Note: Sample size is displayed in ( ) before the mean value.  
SD = Standard Deviation; - = Value not applicable;  
Units are displayed in the ( ) under each parameter name;  
HPD = Hours Post Dose; U = Unscheduled;  
e = Group mean excluded from statistics;  
REF = Denotes group used as reference in the statistical test;  
\* = Statistically significant pairwise comparison at 0.05 level;  
† = Statistically significant pairwise comparison at 0.01 level;  
‡ = Statistically significant trend at 0.05 level;  
§ = Statistically significant trend at 0.01 level.  
+ = Ascending trend sign;  
- = Descending trend sign;  
# = Individual parameter values reported as less than or greater than limit of quantitation are set equal to the limit to calculate the average.

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**Table 7**  
**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male												
	Phase	Day	HPD	Group Number:		REF	2		3			
				Dose :	0 µg/day	30 µg/day	30 µg /day					
ALT (U/L)	Dosing	4	---	Mean	(8)	29.1	(8)	33.3	(8)	28.8		
				SD		6.9		6.5		5.6		
		17	-	Mean	(10)	18.1	(10)	22.9	*	(10)	20.8	
				SD		2.4		4.7		3.0		
	Recovery	22	-	Mean	(5)	19.2	(5)	17.6		(5)	17.4	
				SD		3.3		2.5		3.0		
AST (U/L)	Dosing	4	---	Mean	(8)	94.5	(8)	103.1		(8)	97.8	
				SD		8.3		14.7		14.0		
		17	-	Mean	(10)	71.7	(10)	84.2	*	(10)	86.8	†
				SD		5.3		15.4		8.5		
	Recovery	22	-	Mean	(5)	91.8	(5)	94.0		(5)	97.0	
				SD		10.3		13.5		4.6		
ALP (U/L)	Dosing	4	---	Mean	(8)	166.6	(8)	195.4	*	(8)	188.3	
				SD		50.3		28.2		29.0		
		17	-	Mean	(10)	97.6	(10)	103.4		(10)	110.0	
				SD		25.9		18.9		22.8		

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**Clinical Chemistry**  
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**3-WEEK RECOVERY**

Male										
	Phase	Day	HPD	Group Number:		REF	2		3	
				Dose :	0 µg/day	30 µg/day	30 µg /day			
ALP (U/L)	Recovery	22	-	<b>Mean</b>	(5)	84.4	(5)	79.6	(5)	83.4
				<b>SD</b>		17.0		9.3		18.6
GGT (U/L)	Dosing	4	---	<b>Mean</b>	(8)	3.0	(8)	3.0	(8)	3.0
				<b>SD</b>	#	0.0	#	0.0	#	0.0
	Recovery	17	-	<b>Mean</b>	(10)	3.0	(10)	3.0	(10)	3.0
				<b>SD</b>	#	0.0	#	0.0	#	0.0
	Recovery	22	-	<b>Mean</b>	(5)	3.0	(5)	3.0	(5)	3.0
				<b>SD</b>	#	0.0	#	0.0	#	0.0
TBIL (mg/dL)	Dosing	4	---	<b>Mean</b>	(8)	0.10	(8)	0.10	(8)	0.10
				<b>SD</b>	#	0.00	#	0.00	#	0.00
	Recovery	17	-	<b>Mean</b>	(10)	0.10	(10)	0.10	(10)	0.10
				<b>SD</b>	#	0.00	#	0.00	#	0.00
	Recovery	22	-	<b>Mean</b>	(5)	0.10	(5)	0.10	(5)	0.10
				<b>SD</b>	#	0.00	#	0.00	#	0.00
CHOL (mg/dL)	Dosing	4	---	<b>Mean</b>	(8)	63.0	(8)	52.5	(8)	51.8
				<b>SD</b>		9.3		7.2		15.3

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**Table 7**  
**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male												
Phase	Day	HPD	Dose :	Group Number:			2			3		
				REF	0 µg/day	30 µg/day	30 µg/day	30 µg/day				
CHOL (mg/dL)	Dosing	17	-	Mean	(10)	51.7	(10)	40.2	†	(10)	37.2	†
				SD		6.7		6.1			8.6	
	Recovery	22	-	Mean	(5)	52.8	(5)	61.0	*	(5)	56.2	
				SD		7.2		5.7			4.4	
TRIG (mg/dL)	Dosing	4	---	Mean	(8)	62.0	(8)	42.8		(8)	51.9	
				SD		25.8		10.2			19.6	
	Recovery	17	-	Mean	(10)	58.8	(10)	33.6	†	(10)	35.9	†
				SD		16.6		7.2			10.3	
	Recovery	22	-	Mean	(5)	49.0	(5)	50.8		(5)	45.6	
				SD		18.4		15.1			16.0	
GLUC (mg/dL)	Dosing	4	---	Mean	(8)	111.3	(8)	98.1		(8)	100.0	
				SD		14.2		12.6			16.7	
	Recovery	17	-	Mean	(10)	131.7	(10)	117.4		(10)	122.6	
				SD		17.0		17.0			23.9	
	Recovery	22	-	Mean	(5)	137.0	(5)	121.4		(5)	119.8	
				SD		30.1		23.7			16.1	

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**Table 7**  
**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male												
Phase	Day	HPD	Dose :	Group Number:		REF		2		3		
						0 µg/day		30 µg/day		30 µg /day		
TP (g/dL)	Dosing	4	---	Mean	(8)	6.10	(8)	5.90	(8)	5.85		
				SD		0.21		0.22		0.22		
	17	-	Mean	(10)	5.39	(10)	5.51	(10)	5.41			
			SD		0.30		0.36		0.34			
	Recovery	22	-	Mean	(5)	5.82	(5)	6.08	*	(5)	5.90	
				SD		0.16		0.11		0.14		
ALB (g/dL)	Dosing	4	---	Mean	(8)	3.98	(8)	3.71	†	(8)	3.68	†
				SD		0.14		0.15		0.14		
	17	-	Mean	(10)	3.50	(10)	3.43		(10)	3.38		
			SD		0.19		0.21		0.22			
	Recovery	22	-	Mean	(5)	3.72	(5)	3.82		(5)	3.72	
				SD		0.11		0.08		0.13		
GLOB (g/dL)	Dosing	4	---	Mean	(8)	2.13	(8)	2.19		(8)	2.18	
				SD		0.09		0.10		0.10		
	17	-	Mean	(10)	1.89	(10)	2.08	*	(10)	2.03		
			SD		0.12		0.18		0.13			

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**Table 7**  
**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male												
	Phase	Day	HPD	Group Number:		REF	2		3			
				Dose :	0 µg/day	30 µg/day	30 µg /day					
GLOB (g/dL)	Recovery	22	-	Mean	(5)	2.10	(5)	2.26	†	(5)	2.18	
				SD		0.07		0.05		0.04		
AG (None)	Dosing	4	---	Mean	(8)	1.88	(8)	1.70	†	(8)	1.69	†
				SD		0.07		0.08		0.06		
	Recovery	17	-	Mean	(10)	1.85	(10)	1.65	†	(10)	1.65	†
				SD		0.05		0.08		0.05		
BUN (mg/dL)	Dosing	4	---	Mean	(8)	23.8	(8)	26.0		(8)	23.8	
				SD		5.0		4.0		2.7		
	Recovery	17	-	Mean	(10)	18.8	(10)	18.6		(10)	19.9	
				SD		3.9		3.2		2.8		
Recovery	22	-	Mean	(5)	17.0	(5)	17.2		(5)	16.4		
			SD		1.7		1.3		3.8			
CREA (mg/dL)	Dosing	4	---	Mean	(8)	0.31	(8)	0.29		(8)	0.26	*
				SD		0.04		0.04		0.05		

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**Table 7**  
**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male										
Phase	Day	HPD	Dose :	Group Number:						
				REF	2	3				
				0 µg/day	30 µg/day	30 µg /day				
CREA (mg/dL)	Dosing	17	-	Mean	(10) 0.25	(10) 0.25	(10) 0.27			
				SD	0.05	0.07	0.05			
	Recovery	22	-	Mean	(5) 0.28	(5) 0.28	(5) 0.28			
				SD	0.04	0.04	0.04			
PHOS (mg/dL)	Dosing	4	---	Mean	(8) 7.34	(8) 7.41	(8) 7.58			
				SD	0.56	0.45	0.38			
	Recovery	17	-	Mean	(10) 8.72	(10) 8.11	(10) 8.01			
				SD	0.75	0.58	0.92			
	Recovery	22	-	Mean	(5) 6.56	(5) 6.86	(5) 6.82			
				SD	1.15	0.46	0.72			
CA (mg/dL)	Dosing	4	---	Mean	(8) 9.76	(8) 9.65	(8) 9.75			
				SD	0.25	0.28	0.32			
	Recovery	17	-	Mean	(10) 9.86	(10) 9.82	(10) 9.59			
				SD	0.34	0.35	0.30			
	Recovery	22	-	Mean	(5) 9.44	(5) 9.44	(5) 9.48			
				SD	0.11	0.29	0.27			

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**Table 7**  
**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male										
	Phase	Day	HPD	Group Number:		REF	2		3	
				Dose :	0 µg/day	30 µg/day	30 µg /day			
NA (mmol/L)	Dosing	4	---	Mean	(8)	144.4	(8)	144.1	(8)	143.8
				SD		1.6		1.4		1.2
	17	-	Mean	(10)	144.0	(10)	142.3	(10)	142.7	
			SD		1.2		1.9		1.9	
	Recovery	22	-	Mean	(5)	142.4	(5)	142.6	(5)	143.4
				SD		0.5		0.9		0.9
K (mmol/L)	Dosing	4	---	Mean	(8)	4.45	(8)	4.55	(8)	4.66
				SD		0.31		0.18		0.29
	17	-	Mean	(10)	4.30	(10)	4.36	(10)	4.32	
			SD		0.16		0.31		0.19	
	Recovery	22	-	Mean	(5)	4.12	(5)	4.26	(5)	4.20
				SD		0.28		0.26		0.20
CL (mmol/L)	Dosing	4	---	Mean	(8)	102.4	(8)	102.0	(8)	101.3
				SD		2.8		0.9		1.3
	17	-	Mean	(10)	104.8	(10)	103.4	(10)	104.2	
			SD		0.9		1.8		1.3	

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**Table 7**  
**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male												
Phase	Day	HPD	Dose :	Group Number:			2			3		
				REF	0 µg/day	30 µg/day	30 µg/day	30 µg/day				
CL (mmol/L)	Recovery	22	-	Mean	(5)	105.6	(5)	106.0	(5)	106.4		
				SD		1.5		1.0		1.1		
A2M (ug/mL)	Dosing	4	---	Mean	(8)	113.4	(8)	2318.1 †	(8)	3911.6 †		
				SD		228.9		922.4		2866.1		
	Recovery	17	-	Mean	(10)	14.0	(10)	990.6 †	(10)	1794.2 †		
				SD		3.3		730.0		1234.1		
	Recovery	22	-	Mean	(5)	8.0	(5)	19.4 *	(5)	16.2 †		
				SD		1.9		14.3		2.3		
A1AGP (ug/mL)	Dosing	4	---	Mean	(8)	174.358	(8)	1642.265 †	(8)	2351.791 †		
				SD		312.769		312.914		1053.465		
	Recovery	17	-	Mean	(10)	47.672	(10)	1835.986 †	(10)	2021.083 †		
				SD		12.664		372.467		673.967		
	Recovery	22	-	Mean	(5)	54.910	(5)	75.740	(5)	62.562		
				SD		20.556		26.083		16.549		

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**Table 7**  
**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female												
	Phase	Day	HPD	Dose :	Group Number:		REF		2		3	
							0 µg/day	30 µg/day	30 µg /day			
ALT (U/L)	Dosing	4	---	Mean	(8)	20.9	(8)	24.9	(8)	23.1		
				SD		4.3		4.3		5.2		
	Recovery	17	-	Mean	(9)	11.3	(9)	13.9 †	(8)	16.5 †		
				SD		1.3		2.1		3.3		
	Recovery	22	-	Mean	(5)	11.8	(5)	14.8	(5)	13.6		
				SD		2.2		2.2		1.8		
AST (U/L)	Dosing	4	---	Mean	(8)	81.8	(8)	96.1	(8)	91.3		
				SD		11.5		14.6		10.4		
	Recovery	17	-	Mean	(9)	69.9	(9)	81.7	(8)	80.3		
				SD		18.3		15.9		18.0		
	Recovery	22	-	Mean	(5)	65.4	(5)	73.6	(5)	67.2		
				SD		8.2		10.2		4.4		
ALP (U/L)	Dosing	4	---	Mean	(8)	92.9	(8)	137.9 †	(8)	143.4 †		
				SD		21.7		21.4		31.1		
	Recovery	17	-	Mean	(9)	50.9	(9)	78.1 †	(8)	97.4 †		
				SD		10.3		17.7		18.8		

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**Table 7**  
**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female										
	Phase	Day	HPD	Group Number:		REF	2	3		
				Dose :	0 µg/day	30 µg/day	30 µg /day			
ALP (U/L)	Recovery	22	-	Mean	(5)	34.0	(5)	37.0	(5)	29.0
				SD		6.2		6.4		7.6
GGT (U/L)	Dosing	4	---	Mean	(8)	3.0	(8)	3.0	(8)	3.0
				SD #		0.0	#	0.0	#	0.0
	Recovery	17	-	Mean	(9)	3.0	(9)	3.0	(8)	3.0
				SD #		0.0	#	0.0	#	0.0
	Recovery	22	-	Mean	(5)	3.0	(5)	3.0	(5)	3.0
				SD #		0.0	#	0.0	#	0.0
TBIL (mg/dL)	Dosing	4	---	Mean	(8)	0.10	(8)	0.10	(8)	0.10
				SD #		0.00	#	0.00	#	0.00
	Recovery	17	-	Mean	(9)	0.10	(9)	0.10	(8)	0.10
				SD #		0.00	#	0.00	#	0.00
	Recovery	22	-	Mean	(5)	0.10	(5)	0.10	(5)	0.10
				SD #		0.00	#	0.00	#	0.00
CHOL (mg/dL)	Dosing	4	---	Mean	(8)	45.6	(8)	47.3	(8)	56.6
				SD		13.4		12.3		12.4

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**Table 7**  
**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female										
Phase	Day	HPD	Dose :	Group Number:						
				REF	2	3				
				0 µg/day	30 µg/day		30 µg /day			
CHOL (mg/dL)	Dosing	17	-	Mean	(9)	33.4	(9)	33.7	(8)	31.9
				SD		11.5		6.3		4.2
	Recovery	22	-	Mean	(5)	43.0	(5)	54.2	(5)	41.2
				SD		13.0		18.9		8.6
TRIG (mg/dL)	Dosing	4	---	Mean	(8)	36.8	(8)	29.4	(8)	34.5
				SD		13.0		6.8		7.8
		17	-	Mean	(9)	27.8	(9)	25.1	(8)	26.5
				SD		8.4		5.1		5.1
	Recovery	22	-	Mean	(5)	30.8	(5)	31.8	(5)	37.2
				SD		8.7		3.7		7.9
GLUC (mg/dL)	Dosing	4	---	Mean	(8)	102.5	(8)	89.1 †	(8)	87.1 †
				SD		8.4		8.2		5.9
		17	-	Mean	(9)	111.4	(9)	99.7	(8)	99.5
				SD		16.4		7.7		8.8
	Recovery	22	-	Mean	(5)	119.4	(5)	107.6	(5)	118.0
				SD		14.3		10.7		22.2

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**Table 7**  
**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female												
Phase	Day	HPD	Dose :	Group Number:		REF		2		3		
						0 µg/day		30 µg/day		30 µg /day		
TP (g/dL)	Dosing	4	---	Mean	(8)	6.26	(8)	5.65	†	(8)	5.94	
				SD		0.35		0.17		0.23		
	17	-	Mean	(9)	5.44	(9)	4.98	†	(8)	4.96	†	
			SD		0.32		0.21		0.29			
	Recovery	22	-	Mean	(5)	6.52	(5)	6.54		(5)	6.74	
				SD		0.37		0.21		0.30		
ALB (g/dL)	Dosing	4	---	Mean	(8)	4.16	(8)	3.56	†	(8)	3.73	†
				SD		0.23		0.09		0.14		
	17	-	Mean	(9)	3.60	(9)	3.07	†	(8)	3.09	†	
			SD		0.19		0.11		0.14			
	Recovery	22	-	Mean	(5)	4.26	(5)	4.14		(5)	4.32	
				SD		0.32		0.11		0.19		
GLOB (g/dL)	Dosing	4	---	Mean	(8)	2.10	(8)	2.09		(8)	2.21	
				SD		0.14		0.08		0.10		
	17	-	Mean	(9)	1.84	(9)	1.91		(8)	1.88		
			SD		0.15		0.12		0.18			

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**Table 7**  
**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female											
Phase	Day	HPD	Dose :	Group Number:		REF		2		3	
						0 µg/day		30 µg/day		30 µg /day	
GLOB (g/dL)	Recovery	22	-	Mean	(5)	2.26	(5)	2.40	(5)	2.42	
				SD		0.11		0.10		0.13	
AG (None)	Dosing	4	---	Mean	(8)	1.98	(8)	1.71 †	(8)	1.69 †	
				SD		0.07		0.04		0.04	
		17	-	Mean	(9)	1.96	(9)	1.61 †	(8)	1.66 †	
				SD		0.12		0.06		0.12	
	Recovery	22	-	Mean	(5)	1.90	(5)	1.72 *	(5)	1.80	
				SD		0.16		0.04		0.07	
BUN (mg/dL)	Dosing	4	---	Mean	(8)	16.8	(8)	18.8	(8)	18.3	
				SD		1.9		4.2		2.5	
		17	-	Mean	(9)	17.0	(9)	18.9	(8)	20.0	
				SD		3.0		3.3		1.3	
	Recovery	22	-	Mean	(5)	16.6	(5)	18.4	(5)	18.2	
				SD		3.0		2.7		1.8	
CREA (mg/dL)	Dosing	4	---	Mean	(8)	0.31	(8)	0.23 †	(8)	0.25 *	
				SD		0.04		0.05		0.05	

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**Table 7**  
**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female										
Phase	Day	HPD	Dose :	Group Number:						
				REF	2	3				
				0 µg/day	30 µg/day	30 µg /day				
CREA (mg/dL)	Dosing	17	-	Mean	(9) 0.27	(9) 0.22	(8) 0.21			
				SD	0.07	0.04	0.04			
	Recovery	22	-	Mean	(5) 0.36	(5) 0.30	(5) 0.32			
				SD	0.05	0.00	0.04			
PHOS (mg/dL)	Dosing	4	---	Mean	(8) 6.61	(8) 6.81	(8) 6.91			
				SD	0.56	0.57	0.57			
		17	-	Mean	(9) 7.37	(9) 7.38	(8) 7.73			
				SD	0.95	0.55	1.03			
	Recovery	22	-	Mean	(5) 6.48	(5) 6.30	(5) 6.76			
				SD	0.78	0.88	0.94			
CA (mg/dL)	Dosing	4	---	Mean	(8) 9.70	(8) 9.59	(8) 9.81			
				SD	0.26	0.18	0.29			
		17	-	Mean	(9) 9.52	(9) 9.53	(8) 9.65			
				SD	0.14	0.27	0.27			
	Recovery	22	-	Mean	(5) 9.76	(5) 9.80	(5) 9.82			
				SD	0.30	0.12	0.31			

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**Table 7**  
**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female												
	Phase	Day	HPD	Dose :	Group Number:		REF		2		3	
							0 µg/day	30 µg/day	30 µg /day			
NA (mmol/L)	Dosing	4	---	Mean	(8)	143.8	(8)	143.1	(8)	143.8		
				SD		0.9		1.0		1.4		
	17	-	Mean	(9)	143.6	(9)	143.0	(8)	143.1			
			SD		1.1		1.3		0.8			
	Recovery	22	-	Mean	(5)	142.2	(5)	143.2	(5)	142.8		
				SD		1.9		0.8		1.3		
K (mmol/L)	Dosing	4	---	Mean	(8)	3.85	(8)	4.33 †	(8)	4.39 †		
				SD		0.14		0.37		0.36		
	17	-	Mean	(9)	4.46	(9)	4.53	(8)	4.75			
			SD		0.28		0.18		0.24			
	Recovery	22	-	Mean	(5)	3.84	(5)	4.00	(5)	4.00		
				SD		0.32		0.16		0.22		
CL (mmol/L)	Dosing	4	---	Mean	(8)	104.1	(8)	104.5	(8)	105.1		
				SD		1.4		1.8		2.0		
	17	-	Mean	(9)	108.0	(9)	107.7	(8)	108.1			
			SD		1.0		1.8		1.2			

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**Table 7**  
**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female											
Phase	Day	HPD	Dose :	Group Number:		REF		2		3	
						0 µg/day		30 µg/day		30 µg /day	
CL (mmol/L)	Recovery	22	-	Mean	(5)	106.8	(5)	106.0	(5)	106.8	
				SD		2.3		1.2		0.8	
A2M (ug/mL)	Dosing	4	---	Mean	(8)	212.1	(8)	703.8 †	(8)	887.1 †	
				SD		241.1		396.4		352.9	
	Recovery	17	-	Mean	(10)	33.1	(9)	521.0 †	(8)	592.0 †	
				SD		49.7		260.6		243.7	
	Recovery	22	-	Mean	(5)	17.2	(5)	16.2	(5)	16.0	
				SD		8.5		5.7		4.3	
A1AGP (ug/mL)	Dosing	4	---	Mean	(8)	239.774	(8)	1906.314 †	(8)	1677.103 †	
				SD		176.264		376.234		269.796	
	Recovery	17	-	Mean	(10)	95.959	(9)	1491.849 †	(8)	1651.071 †	
				SD		82.718		326.518		404.600	
	Recovery	22	-	Mean	(5)	62.788	(5)	47.912	(5)	57.588	
				SD		18.725		12.620		19.626	

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**Table 8**  
**Urinalysis**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

<b>Parameter</b>	<b>Description</b>
pH	pH
SG	Specific Gravity
VOLUME	Total Volume

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**Table 8**  
**Urinalysis**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

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**Footnotes**

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Note: Sample size is displayed in ( ) before the mean value.  
SD = Standard Deviation; - = Value not applicable;  
Units are displayed in the ( ) under each parameter name;  
HPD = Hours Post Dose; U = Unscheduled;  
e = Group mean excluded from statistics;  
REF = Denotes group used as reference in the statistical test;  
\* = Statistically significant pairwise comparison at 0.05 level;  
† = Statistically significant pairwise comparison at 0.01 level;  
‡ = Statistically significant trend at 0.05 level;  
§ = Statistically significant trend at 0.01 level.  
+ = Ascending trend sign;  
- = Descending trend sign;  
# = Individual parameter values reported as less than or greater than limit of quantitation are set equal to the limit to calculate the average.

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**Table 8**  
**Urinalysis**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male										
Phase	Day	Group Number:	Dose :	REF	2	3				
				0 µg/day	30 µg/day	30 µg /day				
pH (None)	Dosing	17	Mean	(10) 7.10	(10) 6.75	(10) 6.60	†			
			SD	0.39	0.35	0.32				
	Recovery	22	Mean	(5) 7.30	(5) 7.20	(5) 7.00				
			SD	0.45	0.27	0.35				
SG (None)	Dosing	17	Mean	(10) 1.0322	(10) 1.0260	(10) 1.0282				
			SD	0.0205	0.0227	0.0183				
	Recovery	22	Mean	(5) 1.0556	(5) 1.0340 *	(5) 1.0440				
			SD	0.0038	0.0146	0.0234				
VOLUME (mL)	Dosing	17	Mean	(10) 14.90	(10) 17.80	(10) 11.60				
			SD	15.54	16.95	6.88				
	Recovery	22	Mean	(5) 3.70	(5) 8.20	(5) 8.00				
			SD	0.97	5.50	10.68				

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**Table 8**  
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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

		Female								
		Group Number:	REF	2			3			
Phase	Day	Dose :	0 µg/day	30 µg/day		30 µg/day		30 µg/day		
pH (None)	Dosing	17	Mean (10)	6.75	(10)	6.20 †	(10)	6.20 †		
			SD	0.26		0.26		0.35		
	Recovery	22	Mean (5)	7.00	(5)	6.60	(5)	6.50		
			SD	0.61		0.65		0.35		
SG (None)	Dosing	17	Mean (10)	1.0243	(10)	1.0288	(10)	1.0250		
			SD	0.0128		0.0164		0.0140		
	Recovery	22	Mean (5)	1.0240	(5)	1.0364	(5)	1.0276		
			SD	0.0174		0.0177		0.0198		
VOLUME (mL)	Dosing	17	Mean (10)	9.90	(10)	9.60	(10)	9.40		
			SD	7.03		9.05		6.98		
	Recovery	22	Mean (5)	11.00	(5)	6.00	(5)	9.00		
			SD	7.38		5.09		7.52		

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**Table 9**  
**Organ Weights (g) and Ratios**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

**Footnotes**

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ABS = Absolute Value; OW = Organ Weight; BWT = Body Weight; BRN = Brain Weight; OW:BW = (g/g)\*100; OW:BRN = g/g.  
- = Value not applicable; N = Sample Size; Ratio = Group Mean / Reference Group Mean; R REF = Denotes group used as reference in the ratio calculations; SD = Standard Deviation;  
REF = Denotes group used as reference in the statistical test;  
e = Group mean excluded from statistics;  
@ = Number examined reduced due to excluded data;  
\* = Statistically significant pairwise comparison at 0.05 level;  
† = Statistically significant pairwise comparison at 0.01 level;  
‡ = Statistically significant trend at 0.05 level;  
§ = Statistically significant trend at 0.01 level;  
+ = Ascending trend sign;  
- = Descending trend sign;

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**Table 9**  
**Organ Weights (g) and Ratios**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**  
**Male - Dosing - Terminal Euthanasia**

Group Number:		REF 0 µg/day				2 30 µg/day				3 30 µg /day						
Dose:		N	Mean	Ratio	SD	N	Mean	Ratio	SD	N	Mean	Ratio	SD			
BWT	ABS	10	296.06	R REF	16.40	10	271.17	0.92	17.12	†	10	262.59	0.89	18.67	†	
Brain	ABS	10	1.9061	R REF	0.0899	10	1.9159	1.01	0.1445	10	1.9082	1.00	0.0599			
	OW:BW	10	0.6449	R REF	0.0335	10	0.7087	1.10	0.0664	†	10	0.7294	1.13	0.0481	†	
	OW:BRN	10	1.0000	R REF	0.0000	10	1.0000	1.00	0.0000	10	1.0000	1.00	0.0000			
Epididymis	ABS	10	1.1647	R REF	0.1713	10	1.0626	0.91	0.1281	10	1.0508	0.90	0.0665			
	OW:BW	10	0.3936	R REF	0.0536	10	0.3922	1.00	0.0428	10	0.4026	1.02	0.0442			
	OW:BRN	10	0.6112	R REF	0.0867	10	0.5570	0.91	0.0756	10	0.5512	0.90	0.0400			
Gland, Adrenal	ABS	10	0.0697	R REF	0.0068	10	0.0727	1.04	0.0149	10	0.0706	1.01	0.0107			
	OW:BW	10	0.0236	R REF	0.0021	10	0.0267	1.13	0.0045	10	0.0270	1.14	0.0044			
	OW:BRN	10	0.0366	R REF	0.0040	10	0.0383	1.04	0.0091	10	0.0371	1.01	0.0061			
Gland, Prostate	ABS	10	0.7215	R REF	0.1036	10	0.7324	1.02	0.2129	10	0.6755	0.94	0.1088			
	OW:BW	10	0.2439	R REF	0.0328	10	0.2699	1.11	0.0726	10	0.2575	1.06	0.0401			
	OW:BRN	10	0.3781	R REF	0.0476	10	0.3808	1.01	0.0941	10	0.3539	0.94	0.0556			
Heart	ABS	10	0.9152	R REF	0.0698	10	0.9242	1.01	0.1151	10	0.8795	0.96	0.1051			
	OW:BW	10	0.3097	R REF	0.0260	10	0.3405	1.10	0.0329	*	10	0.3346	1.08	0.0278		
	OW:BRN	10	0.4807	R REF	0.0388	10	0.4852	1.01	0.0758	10	0.4614	0.96	0.0583			
Kidney	ABS	10	2.1659	R REF	0.1836	10	2.2197	1.02	0.2229	10	2.0252	0.94	0.1974			
	OW:BW	10	0.7312	R REF	0.0411	10	0.8179	1.12	0.0507	†	10	0.7710	1.05	0.0495		
	OW:BRN	10	1.1356	R REF	0.0682	10	1.1600	1.02	0.0939	10	1.0607	0.93	0.0914			
Liver	ABS	10	8.3218	R REF	0.5205	10	7.7880	0.94	0.4860	*	10	7.5872	0.91	0.5920	†	
	OW:BW	10	2.8131	R REF	0.1435	10	2.8771	1.02	0.1801	10	2.8905	1.03	0.1234			
	OW:BRN	10	4.3681	R REF	0.2325	10	4.0850	0.94	0.3960	10	3.9783	0.91	0.3168	*		
Spleen	ABS	10	0.5951	R REF	0.0613	10	0.7700	1.29	0.1038	†	10	0.7984	1.34	0.0899	†	
	OW:BW	10	0.2008	R REF	0.0147	10	0.2842	1.42	0.0352	†	10	0.3051	1.52	0.0373	†	
	OW:BRN	10	0.3120	R REF	0.0264	10	0.4019	1.29	0.0431	†	10	0.4191	1.34	0.0521	†	

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**Table 9**  
**Organ Weights (g) and Ratios**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**  
**Male - Dosing - Terminal Euthanasia**

Group Number: Dose:		REF 0 µg/day				2 30 µg/day				3 30 µg /day			
		N	Mean	Ratio	SD	N	Mean	Ratio	SD	N	Mean	Ratio	SD
Testis	ABS	10	3.2727	R REF	0.3106	10	3.4683	1.06	0.3109	10	3.2716	1.00	0.2275
	OW:BW	10	1.1090	R REF	0.1254	10	1.2803	1.15	0.1001	* 10	1.2538	1.13	0.1447
	OW:BRN	10	1.7171	R REF	0.1440	10	1.8123	1.06	0.1262	10	1.7146	1.00	0.1080
Thymus	ABS	10	0.5914	R REF	0.0676	10	0.4673	0.79	0.0934	† 10	0.4200	0.71	0.0907
	OW:BW	10	0.1999	R REF	0.0222	10	0.1718	0.86	0.0293	* 10	0.1591	0.80	0.0275
	OW:BRN	10	0.3098	R REF	0.0266	10	0.2448	0.79	0.0507	† 10	0.2199	0.71	0.0460

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**  
**Male - Recovery - Recovery Euthanasia 1**

Group Number:		REF				2				3			
Dose:		0 µg/day				30 µg/day				30 µg /day			
		N	Mean	Ratio	SD	N	Mean	Ratio	SD	N	Mean	Ratio	SD
BWT	ABS	5	331.78	R REF	39.66	5	351.50	1.06	17.44	5	334.36	1.01	13.43
Brain	ABS	5	2.1072	R REF	0.0471	5	1.9590	0.93	0.1319	* 5	1.9408	0.92	0.0143 †
	OW:BW	5	0.6419	R REF	0.0712	5	0.5582	0.87	0.0441	5	0.5813	0.91	0.0261
	OW:BRN	5	1.0000	R REF	0.0000	5	1.0000	1.00	0.0000	5	1.0000	1.00	0.0000
Epididymis	ABS	5	1.3602	R REF	0.1271	5	1.2546	0.92	0.1995	5	1.4004	1.03	0.0631
	OW:BW	5	0.4136	R REF	0.0519	5	0.3560	0.86	0.0450	* 5	0.4189	1.01	0.0134
	OW:BRN	5	0.6457	R REF	0.0612	5	0.6387	0.99	0.0765	5	0.7216	1.12	0.0323
Gland, Adrenal	ABS	5	0.0670	R REF	0.0112	5	0.0904	1.35	0.0185	5	0.0768	1.15	0.0144
	OW:BW	5	0.0202	R REF	0.0026	5	0.0258	1.28	0.0058	5	0.0231	1.14	0.0050
	OW:BRN	5	0.0318	R REF	0.0050	5	0.0458	1.44	0.0067	† 5	0.0396	1.25	0.0074
Gland, Prostate	ABS	5	1.1332	R REF	0.2539	5	1.0192	0.90	0.1756	5	1.0446	0.92	0.1737
	OW:BW	5	0.3431	R REF	0.0795	5	0.2913	0.85	0.0589	5	0.3129	0.91	0.0557
	OW:BRN	5	0.5380	R REF	0.1211	5	0.5201	0.97	0.0778	5	0.5384	1.00	0.0901
Heart	ABS	5	1.0268	R REF	0.2019	5	1.0990	1.07	0.0611	5	1.0652	1.04	0.0604
	OW:BW	5	0.3078	R REF	0.0309	5	0.3133	1.02	0.0245	5	0.3189	1.04	0.0201
	OW:BRN	5	0.4869	R REF	0.0925	5	0.5615	1.15	0.0143	5	0.5490	1.13	0.0342
Kidney	ABS	5	2.4058	R REF	0.3649	5	2.3406	0.97	0.0687	5	2.2832	0.95	0.1908
	OW:BW	5	0.7230	R REF	0.0289	5	0.6673	0.92	0.0403	5	0.6832	0.94	0.0571
	OW:BRN	5	1.1410	R REF	0.1662	5	1.1975	1.05	0.0516	5	1.1770	1.03	0.1060
Liver	ABS	5	8.5896	R REF	1.3878	5	8.9672	1.04	0.5403	5	8.7588	1.02	0.5137
	OW:BW	5	2.5818	R REF	0.1539	5	2.5516	0.99	0.1092	5	2.6186	1.01	0.0777
	OW:BRN	5	4.0739	R REF	0.6314	5	4.5995	1.13	0.4799	5	4.5142	1.11	0.2862
Spleen	ABS	5	0.6086	R REF	0.0454	5	0.7230	1.19	0.0476	* 5	0.6604	1.09	0.1194
	OW:BW	5	0.1856	R REF	0.0272	5	0.2057	1.11	0.0079	5	0.1980	1.07	0.0382
	OW:BRN	5	0.2891	R REF	0.0253	5	0.3698	1.28	0.0248	* 5	0.3401	1.18	0.0606

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**Table 9**  
**Organ Weights (g) and Ratios**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**  
**Male - Recovery - Recovery Euthanasia 1**

Group Number: Dose:		REF 0 µg/day				2 30 µg/day				3 30 µg /day			
		N	Mean	Ratio	SD	N	Mean	Ratio	SD	N	Mean	Ratio	SD
Testis	ABS	5	3.5472	R REF	0.2609	5	3.4582	0.97	0.3788	5	3.6938	1.04	0.2452
	OW:BW	5	1.0751	R REF	0.0770	5	0.9839	0.92	0.0993	5	1.1070	1.03	0.0983
	OW:BRN	5	1.6837	R REF	0.1236	5	1.7619	1.05	0.0966	5	1.9027	1.13	0.1141 *
Thymus	ABS	5	0.4938	R REF	0.0870	5	0.5536	1.12	0.0604	5	0.4270	0.86	0.0750
	OW:BW	5	0.1515	R REF	0.0380	5	0.1572	1.04	0.0103	5	0.1284	0.85	0.0268
	OW:BRN	5	0.2348	R REF	0.0438	5	0.2833	1.21	0.0326	5	0.2198	0.94	0.0371

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**  
**Female - Dosing - Terminal Euthanasia**

Group Number:		REF				2				3			
Dose:		0 µg/day				30 µg/day				30 µg /day			
		N	Mean	Ratio	SD	N	Mean	Ratio	SD	N	Mean	Ratio	SD
BWT	ABS	10	198.73	R REF	10.80	10	194.56	0.98	10.69	10	191.82	0.97	7.14
Brain	ABS	10	1.8610	R REF	0.0694	10	1.7868	0.96	0.0595	10	1.8407	0.99	0.0783
	OW:BW	10	0.9383	R REF	0.0507	10	0.9203	0.98	0.0467	10	0.9604	1.02	0.0451
	OW:BRN	10	1.0000	R REF	0.0000	10	1.0000	1.00	0.0000	10	1.0000	1.00	0.0000
Gland, Adrenal	ABS	10	0.0882	R REF	0.0162	10	0.0886	1.00	0.0156	9@	0.0907	1.03	0.0192
	OW:BW	10	0.0442	R REF	0.0068	10	0.0454	1.03	0.0065	9@	0.0471	1.07	0.0090
	OW:BRN	10	0.0474	R REF	0.0088	10	0.0496	1.05	0.0085	9@	0.0490	1.03	0.0100
Heart	ABS	10	0.7450	R REF	0.0803	10	0.7573	1.02	0.0866	10	0.7173	0.96	0.0860
	OW:BW	10	0.3749	R REF	0.0343	10	0.3893	1.04	0.0417	10	0.3736	1.00	0.0387
	OW:BRN	10	0.4004	R REF	0.0418	10	0.4248	1.06	0.0563	10	0.3903	0.97	0.0491
Kidney	ABS	10	1.5273	R REF	0.0808	10	1.6343	1.07	0.0778	* 10	1.6164	1.06	0.1416
	OW:BW	10	0.7696	R REF	0.0415	10	0.8412	1.09	0.0418	† 10	0.8417	1.09	0.0529
	OW:BRN	10	0.8216	R REF	0.0519	10	0.9153	1.11	0.0477	† 10	0.8787	1.07	0.0758
Liver	ABS	10	5.4571	R REF	0.3313	10	5.6490	1.04	0.5559	10	5.8104	1.06	0.4922
	OW:BW	10	2.7466	R REF	0.0920	10	2.9002	1.06	0.1853	* 10	3.0247	1.10	0.1541
	OW:BRN	10	2.9329	R REF	0.1468	10	3.1630	1.08	0.3132	10	3.1580	1.08	0.2526
Ovary	ABS	10	0.1167	R REF	0.0158	10	0.1053	0.90	0.0180	9@	0.1113	0.95	0.0170
	OW:BW	10	0.0588	R REF	0.0076	10	0.0542	0.92	0.0097	9@	0.0579	0.98	0.0073
	OW:BRN	10	0.0627	R REF	0.0079	10	0.0590	0.94	0.0101	9@	0.0601	0.96	0.0085
Spleen	ABS	10	0.4382	R REF	0.0669	10	0.6796	1.55	0.1031	† 10	0.6199	1.41	0.0555
	OW:BW	10	0.2202	R REF	0.0294	10	0.3492	1.59	0.0489	† 10	0.3231	1.47	0.0261
	OW:BRN	10	0.2353	R REF	0.0333	10	0.3803	1.62	0.0550	† 10	0.3374	1.43	0.0337
Thymus	ABS	10	0.4588	R REF	0.0700	10	0.3967	0.86	0.1131	10	0.3906	0.85	0.0582
	OW:BW	10	0.2310	R REF	0.0336	10	0.2031	0.88	0.0583	10	0.2036	0.88	0.0288
	OW:BRN	10	0.2469	R REF	0.0386	10	0.2221	0.90	0.0655	10	0.2127	0.86	0.0324

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**  
**Female - Recovery - Recovery Euthanasia 1**

Group Number:		REF				2				3			
Dose:		0 µg/day				30 µg/day				30 µg /day			
		N	Mean	Ratio	SD	N	Mean	Ratio	SD	N	Mean	Ratio	SD
BWT	ABS	5	213.64	R REF	15.61	5	213.36	1.00	6.07	5	210.36	0.98	19.63
Brain	ABS	5	1.8336	R REF	0.1056	5	1.8732	1.02	0.1365	5	1.8450	1.01	0.0498
	OW:BW	5	0.8609	R REF	0.0667	5	0.8788	1.02	0.0719	5	0.8846	1.03	0.1043
	OW:BRN	5	1.0000	R REF	0.0000	5	1.0000	1.00	0.0000	5	1.0000	1.00	0.0000
Gland, Adrenal	ABS	5	0.0866	R REF	0.0097	5	0.0904	1.04	0.0139	5	0.0900	1.04	0.0072
	OW:BW	5	0.0407	R REF	0.0058	5	0.0424	1.04	0.0066	5	0.0431	1.06	0.0051
	OW:BRN	5	0.0473	R REF	0.0048	5	0.0484	1.03	0.0084	5	0.0489	1.03	0.0049
Heart	ABS	5	0.7312	R REF	0.0549	5	0.8658	1.18	0.1343	5	0.8210	1.12	0.0973
	OW:BW	5	0.3423	R REF	0.0082	5	0.4050	1.18	0.0548	5	0.3911	1.14	0.0394
	OW:BRN	5	0.3994	R REF	0.0297	5	0.4670	1.17	0.0981	5	0.4454	1.12	0.0555
Kidney	ABS	5	1.5292	R REF	0.1580	5	1.6488	1.08	0.1319	5	1.7140	1.12	0.0779
	OW:BW	5	0.7153	R REF	0.0451	5	0.7724	1.08	0.0504	5	0.8195	1.15	0.0738 *
	OW:BRN	5	0.8336	R REF	0.0651	5	0.8852	1.06	0.1104	5	0.9293	1.11	0.0428
Liver	ABS	5	5.5626	R REF	0.4283	5	5.8068	1.04	0.3353	5	5.8276	1.05	0.5596
	OW:BW	5	2.6032	R REF	0.0159	5	2.7204	1.05	0.1009	5	2.7738	1.07	0.1572
	OW:BRN	5	3.0386	R REF	0.2392	5	3.1198	1.03	0.3699	5	3.1619	1.04	0.3341
Ovary	ABS	5	0.1242	R REF	0.0347	5	0.1304	1.05	0.0384	5	0.1318	1.06	0.0253
	OW:BW	5	0.0575	R REF	0.0121	5	0.0615	1.07	0.0196	5	0.0625	1.09	0.0088
	OW:BRN	5	0.0674	R REF	0.0169	5	0.0695	1.03	0.0198	5	0.0717	1.06	0.0151
Spleen	ABS	5	0.4412	R REF	0.0967	5	0.4746	1.08	0.0375	5	0.4472	1.01	0.0825
	OW:BW	5	0.2050	R REF	0.0315	5	0.2227	1.09	0.0197	5	0.2117	1.03	0.0273
	OW:BRN	5	0.2400	R REF	0.0471	5	0.2541	1.06	0.0241	5	0.2428	1.01	0.0468
Thymus	ABS	5	0.4278	R REF	0.0718	5	0.4378	1.02	0.0238	5	0.3922	0.92	0.0443
	OW:BW	5	0.2002	R REF	0.0310	5	0.2053	1.03	0.0111	5	0.1863	0.93	0.0103
	OW:BRN	5	0.2349	R REF	0.0477	5	0.2350	1.00	0.0246	5	0.2131	0.91	0.0282

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**Table 10**  
**Summary Report of Macroscopic Observations**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

**Footnotes**

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Note: Animals that were examined and found to be normal are not included in this report and the number of animals examined reflects the total number of animals examined grossly;  
- = Value not applicable.

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**Table 10**  
**Summary Report of Macroscopic Observations**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**  
**Study Phase: Dosing, Necropsy Status: Terminal Euthanasia**

Group Number: Dose:	Male			Female		
	1 0 µg/day	2 30 µg/day	3 30 µg /day	1 0 µg/day	2 30 µg/day	3 30 µg /day
<b>Animals Examined:</b>	<b>10</b>	<b>10</b>	<b>10</b>	<b>10</b>	<b>10</b>	<b>10</b>
<b>LIVER</b> Abnormal surface	-	1	-	-	-	-
<b>LUNG</b> Abnormal color	1	1	-	-	-	-
<b>LYMPH NODE, DRAINING</b> Abnormal size	-	1	-	-	1	4
<b>LYMPH NODE, INGUINAL</b> Abnormal size	1	-	-	-	-	2
<b>SITE, INJECTION</b> Abnormal color	-	2	1	1	3	-
Abnormal consistency	-	2	2	-	4	7
<b>SPLEEN</b> Abnormal size	-	-	-	-	-	1

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**Table 10**  
**Summary Report of Macroscopic Observations**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**  
**Study Phase: Recovery, Necropsy Status: Recovery Euthanasia 1**

Group Number: Dose:	Male			Female		
	1 0 µg/day	2 30 µg/day	3 30 µg /day	1 0 µg/day	2 30 µg/day	3 30 µg /day
<b>Animals Examined:</b>	5	5	5	5	5	5
<b>LYMPH NODE, DRAINING</b> Abnormal size	-	1	-	-	-	1
<b>LYMPH NODE, INGUINAL</b> Abnormal size	-	-	-	-	-	1
<b>ADIPOSE TISSUE</b> Abnormal color	1	-	-	-	1	-
Abnormal consistency	1	-	-	-	-	-

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**Table 11**  
**Summary Report of Microscopic Observations**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

**Footnotes**

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NOS= Not otherwise specified; - = Value not applicable.

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**Table 11**

**Summary Report of Microscopic Observations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Study Phase: Dosing, Necropsy Status: Terminal Euthanasia

		Male			Female		
Group Number:	Dose:	1	2	3	1	2	3
		0 µg/day	30 µg/day	30 µg/day	0 µg/day	30 µg/day	30 µg/day
No. Animals Per Dose Group:		10	10	10	10	10	10
ARTERY, AORTA	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	10	10	10	10
BONE MARROW, STERNUM	Number Examined	10	10	10	10	10	10
	Unremarkable	10	0	0	10	0	0
	Increased cellularity	-	10	10	-	10	10
	Minimal	-	10	10	-	10	10
BONE, STERNUM	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	10	10	10	10
BRAIN	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	10	10	10	10
CERVIX	Number Examined	-	-	-	10	10	10
	Unremarkable	-	-	-	10	10	10
EPIDIDYMIS	Number Examined	10	10	10	-	-	-
	Unremarkable	10	10	10	-	-	-
ESOPHAGUS	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	10	10	10	10

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**Table 11**

**Summary Report of Microscopic Observations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Study Phase: Dosing, Necropsy Status: Terminal Euthanasia

		Male			Female		
Group Number:		1	2	3	1	2	3
Dose:		0 µg/day	30 µg/day	30 µg/day	0 µg/day	30 µg/day	30 µg/day
No. Animals Per Dose Group:		10	10	10	10	10	10
<b>EYE</b>	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	10	9	9	8
	Mineralization, Cornea	-	-	-	-	1	-
	Minimal	-	-	-	-	1	-
Rosettes retina	Minimal	-	-	-	1	-	2
	Minimal	-	-	-	1	-	2
<b>GLAND, ADRENAL</b>	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	10	10	10	9
	Hypertrophy, Cortex	-	-	-	-	-	1
	Present	-	-	-	-	-	1
<b>GLAND, HARDERIAN</b>	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	10	6	9	7
	Degeneration/Necrosis	-	-	-	2	-	2
	Minimal	-	-	-	2	-	2
Infiltration mononuclear cell	Minimal	-	-	-	3	1	1
	Minimal	-	-	-	3	1	1
<b>GLAND, LACRIMAL, EXTRAORBITAL</b>	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	10	10	10	10
<b>GLAND, MAMMARY</b>	Number Examined	10	9	10	10	9	10
	Unremarkable	10	9	10	10	9	10

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**Summary Report of Microscopic Observations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Study Phase: Dosing, Necropsy Status: Terminal Euthanasia

		Male			Female		
Group Number:		1	2	3	1	2	3
Dose:		0 µg/day	30 µg/day	30 µg/day	0 µg/day	30 µg/day	30 µg/day
No. Animals Per Dose Group:		10	10	10	10	10	10
<b>GLAND, PARATHYROID</b>	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	10	10	10	10
<b>GLAND, PITUITARY</b>	Number Examined	10	10	10	10	10	10
	Unremarkable	10	9	8	9	10	8
	Cyst	-	1	2	1	-	2
	Minimal	-	1	2	1	-	2
<b>GLAND, PROSTATE</b>	Number Examined	10	10	10	-	-	-
	Unremarkable	10	10	9	-	-	-
	Infiltration mononuclear cell	-	-	1	-	-	-
	Minimal	-	-	1	-	-	
<b>GLAND, SALIVARY</b>	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	10	9	10	10
	Hypertrophy	-	-	-	1	-	-
	Minimal	-	-	-	1	-	
<b>GLAND, SEMINAL VESICLE</b>	Number Examined	10	10	10	-	-	-
	Unremarkable	10	10	10	-	-	-
<b>GLAND, THYROID</b>	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	10	10	10	10

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Study Phase: Dosing, Necropsy Status: Terminal Euthanasia

		Male			Female		
Group Number:		1	2	3	1	2	3
Dose:		0 µg/day	30 µg/day	30 µg/day	0 µg/day	30 µg/day	30 µg/day
No. Animals Per Dose Group:		10	10	10	10	10	10
<b>GUT-ASSOCIATED LYMPHOID TISSUE</b>	Number Examined	10	10	10	8	10	10
	Unremarkable	10	10	10	8	9	10
	Mineralization, Germinal center	-	-	-	-	1	-
	Minimal	-	-	-	-	1	-
<b>HEART</b>	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	10	10	10	10
<b>JOINT</b>	Number Examined	10	10	10	10	10	10
	Unremarkable	10	7	10	9	8	7
	Inflammation, Extra-capsular	-	3	-	-	2	3
	Minimal	-	3	-	-	2	3
Physeal dysplasia		-	-	-	1	-	-
	Minimal	-	-	-	1	-	-
<b>KIDNEY</b>	Number Examined	10	10	10	10	10	10
	Unremarkable	9	9	9	8	6	10
	Tubular basophilia	-	1	-	-	1	-
	Minimal	-	1	-	-	1	-
Infiltration mononuclear cell		-	-	1	2	3	-
	Minimal	-	-	1	2	3	-
Dilatation, Pelvis		1	-	-	-	-	-
	Minimal	1	-	-	-	-	-

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Study Phase: Dosing, Necropsy Status: Terminal Euthanasia

		Male			Female		
Group Number:		1	2	3	1	2	3
Dose:		0 µg/day	30 µg/day	30 µg/day	0 µg/day	30 µg/day	30 µg/day
No. Animals Per Dose Group:		10	10	10	10	10	10
<b>LARGE INTESTINE, CECUM</b>	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	10	10	10	10
<b>LARGE INTESTINE, COLON</b>	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	10	10	10	9
	Infiltration mixed cell, Mucosa	-	-	-	-	-	1
	Minimal	-	-	-	-	-	1
<b>LIVER</b>	Number Examined	10	10	10	10	10	10
	Unremarkable	10	5	3	10	0	3
	Vacuolation, Hepatocyte; Periportal	-	5	7	-	10	7
	Minimal	-	5	7	-	10	7
<b>LUNG</b>	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	10	9	9	10
	Infiltration mixed cell	-	-	-	1	1	-
	Minimal	-	-	-	1	1	-

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**Summary Report of Microscopic Observations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Study Phase: Dosing, Necropsy Status: Terminal Euthanasia

		Male			Female		
Group Number:		1	2	3	1	2	3
Dose:		0 µg/day	30 µg/day	30 µg/day	0 µg/day	30 µg/day	30 µg/day
No. Animals Per Dose Group:		10	10	10	10	10	10
LYMPH NODE, DRAINING	Number Examined	10	9	10	10	10	10
	Unremarkable	8	1	1	8	1	1
	Increased cellularity, Plasma cell	-	7	8	-	9	7
	Minimal	-	1	4	-	1	1
	Mild	-	4	3	-	1	5
	Moderate	-	2	1	-	7	1
	Increased cellularity, Germinal center	2	6	8	2	5	6
Minimal	1	2	2	1	3	4	
Mild	1	4	6	1	2	2	
LYMPH NODE, INGUINAL	Number Examined	9	10	10	10	10	10
	Unremarkable	8	5	4	9	4	1
	Increased cellularity, Germinal center	1	5	6	1	6	9
	Minimal	-	1	1	1	3	6
	Mild	1	4	5	-	3	3
Increased cellularity, Plasma cell		-	1	1	-	2	4
	Minimal	-	1	1	-	2	4
LYMPH NODE, MESENTERIC	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	10	10	10	10
MUSCLE, SKELETAL	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	10	10	10	10

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**Table 11**

**Summary Report of Microscopic Observations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Study Phase: Dosing, Necropsy Status: Terminal Euthanasia

	Group Number:	Male			Female		
		1	2	3	1	2	3
	Dose:	0 µg/day	30 µg/day	30 µg/day	0 µg/day	30 µg/day	30 µg/day
	No. Animals Per Dose Group:	10	10	10	10	10	10
NERVE, OPTIC	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	10	10	10	10
NERVE, PERIPHERAL	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	10	10	10	10
OVARY	Number Examined	-	-	-	10	10	10
	Unremarkable	-	-	-	10	10	10
OVIDUCT	Number Examined	-	-	-	10	10	10
	Unremarkable	-	-	-	10	10	10
PANCREAS	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	10	10	6	10
Atrophy, Acinar cell		-	-	-	-	4	-
	Minimal	-	-	-	-	4	-
Infiltration mononuclear cell, Interstitium		-	-	-	-	1	-
	Minimal	-	-	-	-	1	-

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Study Phase: Dosing, Necropsy Status: Terminal Euthanasia

		Male			Female		
Group Number:		1	2	3	1	2	3
Dose:		0 µg/day	30 µg/day	30 µg/day	0 µg/day	30 µg/day	30 µg/day
No. Animals Per Dose Group:		10	10	10	10	10	10
SITE, INJECTION	Number Examined	10	10	10	10	10	10
	Unremarkable	6	0	0	5	0	0
Inflammation		4	10	10	5	10	10
	Minimal	4	-	-	5	-	-
	Mild	-	7	5	-	7	9
	Moderate	-	3	5	-	3	1
Edema		-	9	9	-	10	10
	Mild	-	8	8	-	9	9
	Moderate	-	1	1	-	1	1
SKIN	Number Examined	10	10	10	10	9	10
	Unremarkable	10	10	10	10	9	10
SMALL INTESTINE, DUODENUM	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	10	10	10	10
SMALL INTESTINE, ILEUM	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	10	10	10	10
SMALL INTESTINE, JEJUNUM	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	10	10	10	10
SPINAL CORD	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	10	10	10	10

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**Summary Report of Microscopic Observations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Study Phase: Dosing, Necropsy Status: Terminal Euthanasia

	Group Number:	Male			Female		
		1	2	3	1	2	3
	Dose:	0 µg/day	30 µg/day	30 µg/day	0 µg/day	30 µg/day	30 µg/day
	No. Animals Per Dose Group:	10	10	10	10	10	10
<b>SPLEEN</b>	Number Examined	10	10	10	10	10	10
	Unremarkable	10	0	0	10	0	0
	Increased cellularity, Germinal center	-	5	5	-	6	5
	Minimal	-	5	5	-	6	5
Increased cellularity, Hematopoietic cell	Minimal	-	10	10	-	9	10
	Minimal	-	10	10	-	9	10
<b>STOMACH</b>	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	9	10	9	10
	Infiltration mononuclear cell, Serosa	-	-	-	-	1	-
	Minimal	-	-	-	-	1	-
Erosion	Minimal	-	-	1	-	-	-
	Minimal	-	-	1	-	-	-
<b>TESTIS</b>	Number Examined	10	10	10	-	-	-
	Unremarkable	10	10	10	-	-	-
<b>THYMUS</b>	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	10	10	10	10
<b>TONGUE</b>	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	10	10	10	10

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Study Phase: Dosing, Necropsy Status: Terminal Euthanasia

	Group Number:	Male			Female		
		1	2	3	1	2	3
	Dose:	0 µg/day	30 µg/day	30 µg/day	0 µg/day	30 µg/day	30 µg/day
	No. Animals Per Dose Group:	10	10	10	10	10	10
TRACHEA	Number Examined	10	10	10	10	10	10
	Unremarkable	10	10	10	10	10	10
URETER	Number Examined	10	9	10	10	10	10
	Unremarkable	10	9	10	10	10	10
URINARY BLADDER	Number Examined	10	10	10	9	10	10
	Unremarkable	10	10	10	9	10	10
UTERUS	Number Examined	-	-	-	10	10	10
	Unremarkable	-	-	-	10	10	10
VAGINA	Number Examined	-	-	-	10	10	10
	Unremarkable	-	-	-	10	10	10
ADIPOSE TISSUE	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-

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**Table 11**

**Summary Report of Microscopic Observations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Study Phase: Recovery, Necropsy Status: Recovery Euthanasia 1

		Male			Female		
	Group Number:	1	2	3	1	2	3
	Dose:	0 µg/day	30 µg/day	30 µg/day	0 µg/day	30 µg/day	30 µg/day
No. Animals Per Dose Group:		5	5	5	5	5	5
ARTERY, AORTA	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
BONE MARROW, STERNUM	Number Examined	5	5	5	5	5	5
	Unremarkable	5	5	5	5	5	5
BONE, STERNUM	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
BRAIN	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
CERVIX	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
EPIDIDYMIS	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
ESOPHAGUS	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
EYE	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Study Phase: Recovery, Necropsy Status: Recovery Euthanasia 1

		Male			Female		
Group Number:		1	2	3	1	2	3
Dose:		0 µg/day	30 µg/day	30 µg/day	0 µg/day	30 µg/day	30 µg/day
No. Animals Per Dose Group:		5	5	5	5	5	5
GLAND, ADRENAL	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
GLAND, HARDERIAN	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
GLAND, LACRIMAL, EXTRAORBITAL	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
GLAND, MAMMARY	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
GLAND, PARATHYROID	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
GLAND, PITUITARY	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
GLAND, PROSTATE	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
GLAND, SALIVARY	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-

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**Table 11**

**Summary Report of Microscopic Observations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Study Phase: Recovery, Necropsy Status: Recovery Euthanasia 1

		Male			Female		
		1	2	3	1	2	3
	Group Number:	1	2	3	1	2	3
	Dose:	0 µg/day	30 µg/day	30 µg/day	0 µg/day	30 µg/day	30 µg/day
	No. Animals Per Dose Group:	5	5	5	5	5	5
GLAND, SEMINAL VESICLE	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
GLAND, THYROID	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
GUT-ASSOCIATED LYMPHOID TISSUE	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
HEART	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
JOINT	Number Examined	5	5	5	5	5	5
	Unremarkable	5	5	5	5	4	4
Physeal dysplasia		-	-	-	-	1	1
	Minimal	-	-	-	-	1	1
KIDNEY	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
LARGE INTESTINE, CECUM	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
LARGE INTESTINE, COLON	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-

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**Table 11**

**Summary Report of Microscopic Observations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Study Phase: Recovery, Necropsy Status: Recovery Euthanasia 1

		Male			Female		
Group Number:		1	2	3	1	2	3
Dose:		0 µg/day	30 µg/day	30 µg/day	0 µg/day	30 µg/day	30 µg/day
No. Animals Per Dose Group:		5	5	5	5	5	5
LIVER	Number Examined	5	5	5	5	5	5
	Unremarkable	5	5	5	5	5	5
LUNG	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
LYMPH NODE, DRAINING	Number Examined	4	5	5	5	5	5
	Unremarkable	4	0	0	4	0	0
Increased cellularity, Plasma cell		-	4	5	-	4	3
	Minimal	-	4	5	-	4	3
Increased cellularity, Germinal center		-	4	4	1	3	5
	Minimal	-	3	2	1	2	4
Infiltration, Macrophage	Mild	-	1	2	-	1	1
	Minimal	-	3	4	-	3	4
	Minimal	-	2	2	-	1	1
	Mild	-	1	2	-	2	3

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**Summary Report of Microscopic Observations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Study Phase: Recovery, Necropsy Status: Recovery Euthanasia 1

		Male			Female		
Group Number:		1	2	3	1	2	3
Dose:		0 µg/day	30 µg/day	30 µg/day	0 µg/day	30 µg/day	30 µg/day
No. Animals Per Dose Group:		5	5	5	5	5	5
LYMPH NODE, INGUINAL	Number Examined	5	5	5	5	5	5
	Unremarkable	3	2	3	3	4	2
	Increased cellularity, Germinal center	2	3	2	2	1	3
	Minimal	2	3	2	2	1	3
	Increased cellularity, Plasma cell	-	-	-	-	-	1
	Minimal	-	-	-	-	-	1
LYMPH NODE, MESENTERIC	Infiltration, Macrophage	-	-	1	-	-	1
	Minimal	-	-	1	-	-	1
	Number Examined	-	-	-	-	-	-
MUSCLE, SKELETAL	Unremarkable	-	-	-	-	-	-
	Number Examined	-	-	-	-	-	-
NERVE, OPTIC	Unremarkable	-	-	-	-	-	-
	Number Examined	-	-	-	-	-	-
NERVE, PERIPHERAL	Unremarkable	-	-	-	-	-	-
	Number Examined	-	-	-	-	-	-
OVARY	Unremarkable	-	-	-	-	-	-
	Number Examined	-	-	-	-	-	-

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**Table 11**

**Summary Report of Microscopic Observations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Study Phase: Recovery, Necropsy Status: Recovery Euthanasia 1

		Male			Female		
		1	2	3	1	2	3
	Group Number:	1	2	3	1	2	3
	Dose:	0 µg/day	30 µg/day	30 µg/day	0 µg/day	30 µg/day	30 µg/day
	No. Animals Per Dose Group:	5	5	5	5	5	5
OVIDUCT	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
PANCREAS	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
SITE, INJECTION	Number Examined	5	5	5	5	5	5
	Unremarkable	5	0	0	5	0	0
Inflammation		-	5	5	-	5	5
	Minimal	-	5	5	-	5	5
SKIN	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
SMALL INTESTINE, DUODENUM	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
SMALL INTESTINE, ILEUM	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
SMALL INTESTINE, JEJUNUM	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
SPINAL CORD	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-

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**Table 11**

**Summary Report of Microscopic Observations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Study Phase: Recovery, Necropsy Status: Recovery Euthanasia 1

	Group Number:	Male			Female		
		1	2	3	1	2	3
	Dose:	0 µg/day	30 µg/day	30 µg/day	0 µg/day	30 µg/day	30 µg/day
	No. Animals Per Dose Group:	5	5	5	5	5	5
SPLEEN	Number Examined	5	5	5	5	5	5
	Unremarkable	5	4	4	5	3	3
	Increased cellularity, Germinal center	-	1	1	-	2	2
	Minimal	-	1	1	-	2	2
STOMACH	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
TESTIS	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
THYMUS	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
TONGUE	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
TRACHEA	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
URETER	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
URINARY BLADDER	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-

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**Table 11**

**Summary Report of Microscopic Observations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Study Phase: Recovery, Necropsy Status: Recovery Euthanasia 1

		Male			Female		
Group Number:		1	2	3	1	2	3
Dose:		0 µg/day	30 µg/day	30 µg/day	0 µg/day	30 µg/day	30 µg/day
No. Animals Per Dose Group:		5	5	5	5	5	5
UTERUS	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
VAGINA	Number Examined	-	-	-	-	-	-
	Unremarkable	-	-	-	-	-	-
ADIPOSE TISSUE	Number Examined	1	-	-	-	1	-
	Unremarkable	0	-	-	-	0	-
Inflammation		1	-	-	-	-	-
	Mild	1	-	-	-	-	-
Fibrosis		1	-	-	-	-	-
	Minimal	1	-	-	-	-	-
Infiltration mononuclear cell		-	-	-	-	1	-
	Mild	-	-	-	-	1	-

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Injection Site Score

20GR142: 17-DAY INTRAMUSCULAR TOXICITY STUDY OF BNT162B2 (V9) AND BNT162B3C IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY

Male

Parameter	Phase	Day	Group	N	Mean	Standard Deviation	Pairwise p-value
Edema - Left	Dosing	1	1: Saline	15	0.00	0.00	REF
			2: BNT162b2 (V9)	15	0.63	0.51	0.001 **
			3: BNT162b3c	15	0.80	0.55	0.001 **
	Dosing	8	1: Saline	15	0.00	0.00	REF
			2: BNT162b2 (V9)	15	1.19	0.51	0.001 **
			3: BNT162b3c	15	1.43	0.12	0.001 **
	Dosing	15	1: Saline	15	0.00	0.00	REF
			2: BNT162b2 (V9)	15	1.33	0.45	0.001 **
			3: BNT162b3c	15	1.54	0.46	0.001 **

REF: Denotes group used as reference in the statistical tests.

\* Statistically significant at 0.05 level

\*\* Statistically significant at 0.01 level

Injection Site Score

20GR142: 17-DAY INTRAMUSCULAR TOXICITY STUDY OF BNT162B2 (V9) AND BNT162B3C IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY

Male

Parameter	Phase	Day	Group	N	Mean	Standard Deviation	Pairwise p-value
Erythema - Left	Dosing	1	1: Saline	15	0.00	0.00	REF
			2: BNT162b2 (V9)	15	0.03	0.13	0.682
			3: BNT162b3c	15	0.04	0.13	0.270
	Dosing	8	1: Saline	15	0.00	0.00	REF
			2: BNT162b2 (V9)	15	0.23	0.27	0.001 **
			3: BNT162b3c	15	0.41	0.17	0.001 **
	Dosing	15	1: Saline	15	0.00	0.00	REF
			2: BNT162b2 (V9)	15	0.00	0.00	0.999
			3: BNT162b3c	15	0.09	0.20	0.050 *

REF: Denotes group used as reference in the statistical tests.

\* Statistically significant at 0.05 level

\*\* Statistically significant at 0.01 level

Injection Site Score

20GR142: 17-DAY INTRAMUSCULAR TOXICITY STUDY OF BNT162B2 (V9) AND BNT162B3C IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY

Female

Parameter	Phase	Day	Group	N	Mean	Standard Deviation	Pairwise p-value
Edema - Left	Dosing	1	1: Saline	15	0.00	0.00	REF
			2: BNT162b2 (V9)	15	1.28	0.57	0.001 **
			3: BNT162b3c	15	1.08	0.58	0.001 **
	Dosing	8	1: Saline	15	0.00	0.00	REF
			2: BNT162b2 (V9)	15	1.44	0.23	0.001 **
			3: BNT162b3c	15	1.47	0.28	0.001 **
	Dosing	15	1: Saline	15	0.00	0.00	REF
			2: BNT162b2 (V9)	15	1.64	0.34	0.001 **
			3: BNT162b3c	15	1.78	0.27	0.001 **

REF: Denotes group used as reference in the statistical tests.

\* Statistically significant at 0.05 level

\*\* Statistically significant at 0.01 level

Injection Site Score

20GR142: 17-DAY INTRAMUSCULAR TOXICITY STUDY OF BNT162B2 (V9) AND BNT162B3C IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY

Female

Parameter	Phase	Day	Group	N	Mean	Standard Deviation	Pairwise p-value
Erythema - Left	Dosing	1	1: Saline	15	0.00	0.00	REF
			2: BNT162b2 (V9)	15	0.56	0.38	0.001 **
			3: BNT162b3c	15	0.66	0.17	0.001 **
	Dosing	8	1: Saline	15	0.00	0.00	REF
			2: BNT162b2 (V9)	15	0.50	0.09	0.001 **
			3: BNT162b3c	15	0.58	0.11	0.001 **
	Dosing	15	1: Saline	15	0.00	0.00	REF
			2: BNT162b2 (V9)	15	0.33	0.22	0.001 **
			3: BNT162b3c	15	0.60	0.14	0.001 **

REF: Denotes group used as reference in the statistical tests.

\* Statistically significant at 0.05 level

\*\* Statistically significant at 0.01 level



Injection Site Score

20GR142: 17-DAY INTRAMUSCULAR TOXICITY STUDY OF BNT162B2 (V9) AND BNT162B3C IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY

Male

Parameter	Phase	Group	N	Mean	Standard Deviation
Edema - Left	Recovery	2: BNT162b2 (V9)	4	1.08	0.17
		3: BNT162b3c	5	0.80	0.18
Erythema - Left	Recovery	2: BNT162b2 (V9)	4	0.00	0.00
		3: BNT162b3c	5	0.00	0.00

REF: Denotes group used as reference in the statistical tests.

\* Statistically significant at 0.05 level

\*\* Statistically significant at 0.01 level

Injection Site Score

20GR142: 17-DAY INTRAMUSCULAR TOXICITY STUDY OF BNT162B2 (V9) AND BNT162B3C IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY

Female

Parameter	Phase	Group	N	Mean	Standard Deviation
Edema - Left	Recovery	2: BNT162b2 (V9)	5	1.07	0.15
		3: BNT162b3c	5	1.13	0.18
Erythema - Left	Recovery	2: BNT162b2 (V9)	5	0.13	0.18
		3: BNT162b3c	5	0.33	0.24

REF: Denotes group used as reference in the statistical tests.

\* Statistically significant at 0.05 level

\*\* Statistically significant at 0.01 level

Body Temperature (Deg C)

20GR142: 17-DAY INTRAMUSCULAR TOXICITY STUDY OF BNT162B2 (V9) AND BNT162B3C IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY

Male

Phase	Day	Group	N	Mean	Standard Deviation	Pairwise p-value
Dosing	1	1: Saline	15	38.31	0.35	REF
		2: BNT162b2 (V9)	15	38.85	0.36	0.001 **
		3: BNT162b3c	15	39.02	0.40	0.001 **
Dosing	8	1: Saline	15	37.07	0.37	REF
		2: BNT162b2 (V9)	15	38.05	0.62	0.001 **
		3: BNT162b3c	15	38.33	0.43	0.001 **
Dosing	15	1: Saline	15	37.34	0.35	REF
		2: BNT162b2 (V9)	15	38.37	0.42	0.001 **
		3: BNT162b3c	15	38.43	0.36	0.001 **

REF: Denotes group used as reference in the statistical tests.

\* Statistically significant at 0.05 level

\*\* Statistically significant at 0.01 level

Body Temperature (Deg C)

20GR142: 17-DAY INTRAMUSCULAR TOXICITY STUDY OF BNT162B2 (V9) AND BNT162B3C IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY

Female

Phase	Day	Group	N	Mean	Standard Deviation	Pairwise p-value
Dosing	1	1: Saline	15	38.08	0.44	REF
		2: BNT162b2 (V9)	15	38.50	0.53	0.044 *
		3: BNT162b3c	15	38.58	0.36	0.009 **
Dosing	8	1: Saline	15	37.81	0.38	REF
		2: BNT162b2 (V9)	15	38.47	0.44	0.001 **
		3: BNT162b3c	15	38.73	0.40	0.001 **
Dosing	15	1: Saline	15	38.02	0.74	REF
		2: BNT162b2 (V9)	15	38.15	0.54	0.963
		3: BNT162b3c	15	38.35	0.31	0.174

REF: Denotes group used as reference in the statistical tests.

\* Statistically significant at 0.05 level

\*\* Statistically significant at 0.01 level

Dead Animal Status Report

Pfizer

Study: 20GR142

StudyTitle: 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY

Test Article: BNT162b2(V9), BNT162b3c

Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

Animal #	Sex	Group	User #	Date/Time Entered	Phase Name	Day of Phase	Date/Time of Death	Approx	
001	M	1	1677	22 Jul 2020 08:53:06 AM	Dosing	17	22 Jul 2020 08:53:07 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
002	M	1	1787	22 Jul 2020 08:50:04 AM	Dosing	17	22 Jul 2020 08:50:05 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
003	M	1	727	22 Jul 2020 08:57:39 AM	Dosing	17	22 Jul 2020 08:57:40 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
004	M	1	598	22 Jul 2020 09:02:59 AM	Dosing	17	22 Jul 2020 09:02:59 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
005	M	1	727	22 Jul 2020 09:37:05 AM	Dosing	17	22 Jul 2020 09:37:06 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
006	M	1	1687	22 Jul 2020 09:46:22 AM	Dosing	17	22 Jul 2020 09:46:22 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
007	M	1	807	22 Jul 2020 09:58:31 AM	Dosing	17	22 Jul 2020 09:58:32 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
008	M	1	727	22 Jul 2020 10:17:27 AM	Dosing	17	22 Jul 2020 10:17:28 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
009	M	1	808	22 Jul 2020 10:30:03 AM	Dosing	17	22 Jul 2020 10:30:04 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
010	M	1	1777	22 Jul 2020 10:41:36 AM	Dosing	17	22 Jul 2020 10:41:36 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
011	M	1	1057	13 Aug 2020 07:32:04 AM	Recovery	22	13 Aug 2020 07:32:05 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				

(b) (6)

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**Dead Animal Status Report**

Pfizer

**Study:** 20GR142

**StudyTitle:** 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY

**Test Article:** BNT162b2(V9), BNT162b3c

Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

Animal #	Sex	Group	User #	Date/Time Entered	Phase Name	Day of Phase	Date/Time of Death	Approx	
012	M	1	232	13 Aug 2020 08:15:17 AM	Recovery	22	13 Aug 2020 08:15:18 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				
013	M	1	1307	13 Aug 2020 08:29:36 AM	Recovery	22	13 Aug 2020 08:29:37 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				
014	M	1	1777	13 Aug 2020 09:02:02 AM	Recovery	22	13 Aug 2020 09:02:03 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				
015	M	1	232	13 Aug 2020 09:23:27 AM	Recovery	22	13 Aug 2020 09:23:28 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				
016	M	2	1057	22 Jul 2020 08:42:46 AM	Dosing	17	22 Jul 2020 08:42:47 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
017	M	2	1777	22 Jul 2020 08:48:01 AM	Dosing	17	22 Jul 2020 08:48:01 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
018	M	2	1307	22 Jul 2020 09:01:59 AM	Dosing	17	22 Jul 2020 09:01:59 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
019	M	2	807	22 Jul 2020 09:08:39 AM	Dosing	17	22 Jul 2020 09:08:39 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
020	M	2	1677	22 Jul 2020 09:41:57 AM	Dosing	17	22 Jul 2020 09:41:57 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
021	M	2	1308	22 Jul 2020 09:53:57 AM	Dosing	17	22 Jul 2020 09:53:58 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
022	M	2	598	22 Jul 2020 09:59:56 AM	Dosing	17	22 Jul 2020 09:59:56 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				

(b) (6)

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**Dead Animal Status Report**

Pfizer

**Study:** 20GR142

**StudyTitle:** 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY

**Test Article:** BNT162b2(V9), BNT162b3c

Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

Animal #	Sex	Group	User #	Date/Time Entered	Phase Name	Day of Phase	Date/Time of Death	Approx	
023	M	2	1787	22 Jul 2020 10:29:38 AM	Dosing	17	22 Jul 2020 10:29:38 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
024	M	2	1307	22 Jul 2020 10:38:09 AM	Dosing	17	22 Jul 2020 10:38:10 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
025	M	2	807	22 Jul 2020 10:44:39 AM	Dosing	17	22 Jul 2020 10:44:40 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
026	M	2	1777	13 Aug 2020 07:36:45 AM	Recovery	22	13 Aug 2020 07:36:46 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				
027	M	2	598	13 Aug 2020 08:25:28 AM	Recovery	22	13 Aug 2020 08:25:29 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				
028	M	2	807	13 Aug 2020 08:44:11 AM	Recovery	22	13 Aug 2020 08:44:12 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				
029	M	2	1057	13 Aug 2020 09:12:59 AM	Recovery	22	13 Aug 2020 09:13:00 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				
030	M	2	598	13 Aug 2020 09:25:22 AM	Recovery	22	13 Aug 2020 09:25:24 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				
031	M	3	1308	22 Jul 2020 08:47:19 AM	Dosing	17	22 Jul 2020 08:47:19 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
032	M	3	1687	22 Jul 2020 08:55:08 AM	Dosing	17	22 Jul 2020 08:55:08 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
033	M	3	808	22 Jul 2020 09:03:00 AM	Dosing	17	22 Jul 2020 09:03:01 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				

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Dead Animal Status Report

Pfizer

Study: 20GR142

StudyTitle: 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY

Test Article: BNT162b2(V9), BNT162b3c

Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

Animal #	Sex	Group	User #	Date/Time Entered	Phase Name	Day of Phase	Date/Time of Death	Approx	
034	M	3	1057	22 Jul 2020 09:25:56 AM	Dosing	17	22 Jul 2020 09:25:56 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
035	M	3	808	22 Jul 2020 09:45:48 AM	Dosing	17	22 Jul 2020 09:45:49 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
036	M	3	1307	22 Jul 2020 09:56:54 AM	Dosing	17	22 Jul 2020 09:56:55 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
037	M	3	1057	22 Jul 2020 10:14:20 AM	Dosing	17	22 Jul 2020 10:14:21 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
038	M	3	1677	22 Jul 2020 10:27:35 AM	Dosing	17	22 Jul 2020 10:27:36 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
039	M	3	1687	22 Jul 2020 10:38:42 AM	Dosing	17	22 Jul 2020 10:38:43 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
040	M	3	598	22 Jul 2020 10:52:34 AM	Dosing	17	22 Jul 2020 10:52:35 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
041	M	3	808	13 Aug 2020 08:12:59 AM	Recovery	22	13 Aug 2020 08:13:00 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				
042	M	3	1057	13 Aug 2020 08:26:36 AM	Recovery	22	13 Aug 2020 08:26:36 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				
043	M	3	808	13 Aug 2020 08:59:12 AM	Recovery	22	13 Aug 2020 08:59:13 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				
044	M	3	1307	13 Aug 2020 09:10:48 AM	Recovery	22	13 Aug 2020 09:10:49 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				

(b) (6)

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Dead Animal Status Report

Pfizer

Study: 20GR142

StudyTitle: 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY

Test Article: BNT162b2(V9), BNT162b3c

Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

Animal #	Sex	Group	User #	Date/Time Entered	Phase Name	Day of Phase	Date/Time of Death	Approx	
045	M	3	807	13 Aug 2020 09:30:28 AM	Recovery	22	13 Aug 2020 09:30:29 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				
046	F	1	727	22 Jul 2020 10:55:54 AM	Dosing	17	22 Jul 2020 10:55:55 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
047	F	1	808	22 Jul 2020 11:13:53 AM	Dosing	17	22 Jul 2020 11:13:53 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
048	F	1	1307	22 Jul 2020 11:32:53 AM	Dosing	17	22 Jul 2020 11:32:54 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
049	F	1	1777	22 Jul 2020 11:53:48 AM	Dosing	17	22 Jul 2020 11:53:48 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
050	F	1	1307	22 Jul 2020 12:09:56 PM	Dosing	17	22 Jul 2020 12:09:57 PM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
051	F	1	807	22 Jul 2020 12:17:24 PM	Dosing	17	22 Jul 2020 12:17:24 PM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
052	F	1	1677	22 Jul 2020 12:29:39 PM	Dosing	17	22 Jul 2020 12:29:39 PM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
053	F	1	1057	22 Jul 2020 12:41:24 PM	Dosing	17	22 Jul 2020 12:41:24 PM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
054	F	1	1308	22 Jul 2020 01:06:59 PM	Dosing	17	22 Jul 2020 01:06:59 PM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
055	F	1	1677	22 Jul 2020 01:13:05 PM	Dosing	17	22 Jul 2020 01:13:06 PM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				

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Dead Animal Status Report

Pfizer

Study: 20GR142

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Test Article: BNT162b2(V9), BNT162b3c

Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

Animal #	Sex	Group	User #	Date/Time Entered	Phase Name	Day of Phase	Date/Time of Death	Approx	
056	F	1	808	13 Aug 2020 09:40:42 AM	Recovery	22	13 Aug 2020 09:40:43 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				
057	F	1	1777	13 Aug 2020 10:06:54 AM	Recovery	22	13 Aug 2020 10:06:55 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				
058	F	1	808	13 Aug 2020 10:24:39 AM	Recovery	22	13 Aug 2020 10:24:40 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				
059	F	1	1307	13 Aug 2020 10:37:40 AM	Recovery	22	13 Aug 2020 10:37:41 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				
060	F	1	598	13 Aug 2020 11:11:42 AM	Recovery	22	13 Aug 2020 11:11:43 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				
061	F	2	1057	22 Jul 2020 10:59:29 AM	Dosing	17	22 Jul 2020 10:59:30 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
062	F	2	1687	22 Jul 2020 11:28:12 AM	Dosing	17	22 Jul 2020 11:28:13 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
063	F	2	807	22 Jul 2020 11:34:48 AM	Dosing	17	22 Jul 2020 11:34:48 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
064	F	2	808	22 Jul 2020 12:02:00 PM	Dosing	17	22 Jul 2020 12:02:01 PM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
065	F	2	1308	22 Jul 2020 12:10:34 PM	Dosing	17	22 Jul 2020 12:10:35 PM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
066	F	2	598	22 Jul 2020 12:26:23 PM	Dosing	17	22 Jul 2020 12:26:24 PM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				

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Dead Animal Status Report

Pfizer

Study: 20GR142

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Test Article: BNT162b2(V9), BNT162b3c

Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

Animal #	Sex	Group	User #	Date/Time Entered	Phase Name	Day of Phase	Date/Time of Death	Approx	
067	F	2	808	22 Jul 2020 12:39:45 PM	Dosing	17	22 Jul 2020 12:39:46 PM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
068	F	2	1307	22 Jul 2020 12:48:19 PM	Dosing	17	22 Jul 2020 12:48:20 PM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
069	F	2	1687	22 Jul 2020 01:10:04 PM	Dosing	17	22 Jul 2020 01:10:05 PM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
070	F	2	598	22 Jul 2020 01:20:52 PM	Dosing	17	22 Jul 2020 01:20:53 PM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
071	F	2	1307	13 Aug 2020 09:45:17 AM	Recovery	22	13 Aug 2020 09:45:18 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				
072	F	2	807	13 Aug 2020 10:10:49 AM	Recovery	22	13 Aug 2020 10:10:51 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				
073	F	2	232	13 Aug 2020 10:31:30 AM	Recovery	22	13 Aug 2020 10:31:32 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				
074	F	2	807	13 Aug 2020 10:57:42 AM	Recovery	22	13 Aug 2020 10:57:44 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				
075	F	2	1057	13 Aug 2020 11:14:34 AM	Recovery	22	13 Aug 2020 11:14:35 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				
076	F	3	1308	22 Jul 2020 11:01:58 AM	Dosing	17	22 Jul 2020 11:01:59 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
077	F	3	727	22 Jul 2020 11:34:04 AM	Dosing	17	22 Jul 2020 11:34:04 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				

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Dead Animal Status Report

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Study: 20GR142

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Test Article: BNT162b2(V9), BNT162b3c

Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

Animal #	Sex	Group	User #	Date/Time Entered	Phase Name	Day of Phase	Date/Time of Death	Approx	
078	F	3	1057	22 Jul 2020 11:39:37 AM	Dosing	17	22 Jul 2020 11:39:38 AM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
079	F	3	727	22 Jul 2020 12:04:24 PM	Dosing	17	22 Jul 2020 12:04:26 PM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
080	F	3	1787	22 Jul 2020 12:15:12 PM	Dosing	17	22 Jul 2020 12:15:13 PM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
081	F	3	1687	22 Jul 2020 12:23:21 PM	Dosing	17	22 Jul 2020 12:23:22 PM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
082	F	3	727	22 Jul 2020 12:40:34 PM	Dosing	17	22 Jul 2020 12:40:35 PM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
083	F	3	807	22 Jul 2020 01:00:12 PM	Dosing	17	22 Jul 2020 01:00:12 PM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
084	F	3	1777	22 Jul 2020 01:15:45 PM	Dosing	17	22 Jul 2020 01:15:45 PM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
085	F	3	727	22 Jul 2020 01:18:09 PM	Dosing	17	22 Jul 2020 01:18:10 PM	Y	
<b>Death Status:</b> Terminal Euthanasia					<b>Death Type:</b> Scheduled				
086	F	3	1057	13 Aug 2020 09:54:23 AM	Recovery	22	13 Aug 2020 09:54:24 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				
087	F	3	598	13 Aug 2020 10:20:29 AM	Recovery	22	13 Aug 2020 10:20:29 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				
088	F	3	1057	13 Aug 2020 10:34:13 AM	Recovery	22	13 Aug 2020 10:34:14 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				

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Dead Animal Status Report

Pfizer

Study: 20GR142

StudyTitle: 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY

Test Article: BNT162b2(V9), BNT162b3c

Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

Animal #	Sex	Group	User #	Date/Time Entered	Phase Name	Day of Phase	Date/Time of Death	Approx	
089	F	3	1777	13 Aug 2020 11:07:56 AM	Recovery	22	13 Aug 2020 11:07:57 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				
090	F	3	808	13 Aug 2020 11:19:57 AM	Recovery	22	13 Aug 2020 11:19:58 AM	Y	
<b>Death Status:</b> Recovery Euthanasia 1					<b>Death Type:</b> Scheduled				
P-054#	F	-	1077	01 Jul 2020 01:57:34 PM	PID	8	01 Jul 2020 01:57:15 PM	Y	
<b>Death Status:</b> Found Dead					<b>Death Type:</b> Unscheduled Death				
<b>Comment:</b> Died after blood collection									

# = Pretest

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**Dead Animal Status Report Audit Trail**

Pfizer

**Study:** 20GR142

**StudyTitle:** 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY

**Test Article:** BNT162b2(V9), BNT162b3c

Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

No Audit Trail

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**Appendix 2**  
**Clinical Signs - Daily**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

**Footnotes**

---

Note: Animals were considered normal (data not displayed in table) unless indicated otherwise.

Note: Each interval will be concatenated with the phase name abbreviation.

- Value not applicable

Day(s) Observed - PID = Prior to Initiation of Dosing, D = Dosing, R = Recovery

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**Appendix 2**  
**Clinical Signs - Daily**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Male

Group Number	Dose	Animal Number	Observations	Modifier	Day(s) Observed	Total Days Seen
1	0 µg/day	012	Thin Appearance		D8	1
2	30 µg/day	024	Hair Loss	Abdomen, Thinning	D8, 15	2
		029	Tail Crooked		PID1-12, D1-17, R1-22	51

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**Appendix 2**  
**Clinical Signs - Daily**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Female

Group Number	Dose	Animal Number	Observations	Modifier	Day(s) Observed	Total Days Seen
2	30 µg/day	067	Hair Loss	Forelimb, Bilateral, Thinning	D15	1
3	30 µg /day	083	Lesion	Lumbar, Dorsal	D1	1

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**Appendix 3**  
**Ocular Exam**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

**Footnotes**

---

Note: Animals were considered normal (data not displayed in table) unless indicated otherwise.

Note: Each interval will be concatenated with the phase name abbreviation.

- Value not applicable

Day(s) Observed - PID = Prior to Initiation of Dosing, D = Dosing, R = Recovery

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**Appendix 3  
Ocular Exam**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

**Male**

<b>Group Number</b>	<b>Dose</b>	<b>Animal Number</b>	<b>Observations</b>	<b>Modifier</b>	<b>Day(s) Observed</b>	<b>Total Days Seen</b>
1	0 µg/day	001	No Ocular Abnormality	Bilateral	PID7, D15	2
		002	No Ocular Abnormality	Bilateral	PID7, D15	2
		003	No Ocular Abnormality	Bilateral	PID7, D15	2
		004	No Ocular Abnormality	Bilateral	PID7, D15	2
		005	No Ocular Abnormality	Bilateral	PID7, D15	2
		006	No Ocular Abnormality	Bilateral	PID7, D15	2
		007	No Ocular Abnormality	Bilateral	PID7, D15	2
		008	Vitreous, Hemorrhage	Mild, Left, Temporal, Ventral	PID7, D15	2
		009	No Ocular Abnormality	Bilateral	PID7, D15	2
		010	Retina, Tortuous Vessels	Minimal, Left, Generalized, Multifocal	PID7, D15	2
		011	Vitreous, Hyaloid Remnant	Minimal, Right, Central, Central	PID7, D15	2
		012	No Ocular Abnormality	Bilateral	PID7, D15	2
		013	No Ocular Abnormality	Bilateral	PID7, D15	2
		014	Keratic Precipitates	Mild, Left, Equatorial	PID7, D15	2
		015	No Ocular Abnormality	Bilateral	PID7, D15	2
2	30 µg/day	016	No Ocular Abnormality	Bilateral	PID7, D15	2
		017	No Ocular Abnormality	Bilateral	PID7, D15	2
		018	No Ocular Abnormality	Bilateral	PID7, D15	2

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**Appendix 3**

**Ocular Exam**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

**Male**

<b>Group Number</b>	<b>Dose</b>	<b>Animal Number</b>	<b>Observations</b>	<b>Modifier</b>	<b>Day(s) Observed</b>	<b>Total Days Seen</b>
2	30 µg/day	019	No Ocular Abnormality	Bilateral	PID7, D15	2
		020	No Ocular Abnormality	Bilateral	PID7, D15	2
		021	No Ocular Abnormality	Bilateral	PID7, D15	2
		022	No Ocular Abnormality	Bilateral	PID7, D15	2
		023	No Ocular Abnormality	Bilateral	PID7, D15	2
		024	No Ocular Abnormality	Bilateral	PID7, D15	2
		025	No Ocular Abnormality	Bilateral	PID7, D15	2
		026	No Ocular Abnormality	Bilateral	PID7, D15	2
		027	No Ocular Abnormality	Bilateral	PID7, D15	2
		028	No Ocular Abnormality	Bilateral	PID7, D15	2
		029	No Ocular Abnormality	Bilateral	PID7, D15	2
3	30 µg /day	030	No Ocular Abnormality	Bilateral	PID7, D15	2
		031	No Ocular Abnormality	Bilateral	PID7, D15	2
		032	No Ocular Abnormality	Bilateral	PID7, D15	2
		033	No Ocular Abnormality	Bilateral	PID7, D15	2
		034	No Ocular Abnormality	Bilateral	PID7, D15	2
		035	No Ocular Abnormality	Bilateral	PID7, D15	2
		036	No Ocular Abnormality	Bilateral	PID7, D15	2
		037	No Ocular Abnormality	Bilateral	PID7, D15	2

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**Appendix 3  
Ocular Exam**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Male

Group Number	Dose	Animal Number	Observations	Modifier	Day(s) Observed	Total Days Seen
3	30 µg /day	038	No Ocular Abnormality	Bilateral	PID7, D15	2
		039	No Ocular Abnormality	Bilateral	PID7, D15	2
		040	No Ocular Abnormality	Bilateral	PID7, D15	2
		041	Keratic Precipitates	Mild, Right, Equatorial	PID7, D15	2
		042	No Ocular Abnormality	Bilateral	PID7, D15	2
		043	No Ocular Abnormality	Bilateral	PID7, D15	2
		044	No Ocular Abnormality	Bilateral	PID7, D15	2
		045	No Ocular Abnormality	Bilateral	PID7, D15	2

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**Appendix 3**

**Ocular Exam**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Female

Group Number	Dose	Animal Number	Observations	Modifier	Day(s) Observed	Total Days Seen
1	0 µg/day	046	No Ocular Abnormality	Bilateral	PID8, D16	2
		047	No Ocular Abnormality	Bilateral	PID8, D16	2
		048	No Ocular Abnormality	Bilateral	PID8, D16	2
		049	Keratic Precipitates	Mild, Left, Equatorial	D16	1
			No Ocular Abnormality	Bilateral	PID8	1
		050	No Ocular Abnormality	Bilateral	PID8, D16	2
		051	No Ocular Abnormality	Bilateral	PID8, D16	2
		052	No Ocular Abnormality	Bilateral	PID8, D16	2
		053	No Ocular Abnormality	Bilateral	PID8, D16	2
		054	No Ocular Abnormality	Bilateral	PID8, D16	2
		055	No Ocular Abnormality	Bilateral	PID8, D16	2
		056	No Ocular Abnormality	Bilateral	PID8, D16	2
		057	No Ocular Abnormality	Bilateral	PID8, D16	2
		058	No Ocular Abnormality	Bilateral	PID8, D16	2
		059	No Ocular Abnormality	Bilateral	PID8, D16	2
060	No Ocular Abnormality	Bilateral	PID8, D16	2		
2	30 µg/day	061	No Ocular Abnormality	Bilateral	PID8, D16	2
		062	No Ocular Abnormality	Bilateral	PID8, D16	2
		063	No Ocular Abnormality	Bilateral	PID8, D16	2

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**Appendix 3**

**Ocular Exam**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Female

Group Number	Dose	Animal Number	Observations	Modifier	Day(s) Observed	Total Days Seen
2	30 µg/day	064	No Ocular Abnormality	Bilateral	PID8, D16	2
		065	No Ocular Abnormality	Bilateral	PID8, D16	2
		066	No Ocular Abnormality	Bilateral	PID8, D16	2
		067	No Ocular Abnormality	Bilateral	PID8, D16	2
		068	No Ocular Abnormality	Bilateral	PID8, D16	2
		069	No Ocular Abnormality	Bilateral	PID8, D16	2
		070	No Ocular Abnormality	Bilateral	PID8, D16	2
		071	No Ocular Abnormality	Bilateral	PID8, D16	2
		072	No Ocular Abnormality	Bilateral	PID8, D16	2
		073	No Ocular Abnormality	Bilateral	PID8, D16	2
		074	No Ocular Abnormality	Bilateral	PID8, D16	2
3	30 µg /day	075	No Ocular Abnormality	Bilateral	PID8, D16	2
		076	No Ocular Abnormality	Bilateral	PID8, D16	2
		077	No Ocular Abnormality	Bilateral	PID8, D16	2
		078	No Ocular Abnormality	Bilateral	PID8, D16	2
		079	No Ocular Abnormality	Bilateral	PID8, D16	2
		080	No Ocular Abnormality	Bilateral	PID8, D16	2
		081	No Ocular Abnormality	Bilateral	PID8, D16	2
		082	No Ocular Abnormality	Bilateral	PID8, D16	2

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**Appendix 3  
Ocular Exam**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Female

Group Number	Dose	Animal Number	Observations	Modifier	Day(s) Observed	Total Days Seen
3	30 µg /day	083	No Ocular Abnormality	Bilateral	PID8, D16	2
		084	No Ocular Abnormality	Bilateral	PID8, D16	2
		085	No Ocular Abnormality	Bilateral	PID8, D16	2
		086	No Ocular Abnormality	Bilateral	PID8, D16	2
		087	No Ocular Abnormality	Bilateral	PID8, D16	2
		088	No Ocular Abnormality	Bilateral	PID9, D16	2
		089	No Ocular Abnormality	Bilateral	PID8, D16	2
		090	No Ocular Abnormality	Bilateral	PID8, D16	2

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**Appendix 4**  
**Body Weight (g)**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

**Footnotes**

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Grp Num = Group Number; Animal Num= Animal Number; - = Value not applicable; NW = Not Weighed; e = Excluded.  
PID = Prior to the Initiation of Dosing.

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**Appendix 4  
Body Weight (g)**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Male

Grp Num	Dose	Animal Num	Phase Day:	PID		Dosing					Recovery
				1	6	1	4	8	11	15	1
1	0 µg/day	001		178.3	217.8	252.9	239.1	270.5	284.3	290.1	-
		002		198.5	242.8	283.8	271.6	307.6	321.9	339.6	-
		003		180.0	226.4	270.2	259.1	291.0	306.8	318.6	-
		004		183.2	217.4	265.1	258.3	303.8	312.2	333.9	-
		005		185.6	223.1	263.8	254.0	286.4	301.4	315.8	-
		006		179.9	221.6	266.5	256.3	293.7	305.5	321.7	-
		007		195.6	232.1	270.8	259.9	295.6	310.2	321.8	-
		008		201.9	233.3	271.0	257.5	289.2	298.7	311.9	-
		009		178.5	210.0	248.2	240.6	267.4	276.0	293.1	-
		010		185.8	225.4	262.5	248.3	281.7	292.1	309.1	-
		011		195.6	227.8	264.1	257.1	291.2	296.8	310.2	313.8
		012		200.1	239.3	280.0	245.9	200.9	264.6	296.6	307.4
		013		183.6	213.9	243.1	233.1	262.7	268.5	283.4	287.6
		014		178.6	214.6	251.1	237.2	268.9	281.5	290.2	288.9
		015		190.5	233.7	278.9	264.4	298.4	317.0	336.1	340.8
2	30 µg/day	016		199.1	231.5	262.6	237.4	274.1	270.5	289.2	-
		017		182.0	218.3	266.9	249.5	291.2	292.1	307.0	-
		018		186.8	227.1	267.1	253.9	283.3	283.7	298.2	-
		019		193.4	233.0	269.3	258.6	287.4	292.6	309.8	-
		020		178.1	216.7	253.1	230.2	265.7	261.6	276.3	-
		021		185.4	228.6	269.4	248.9	279.2	276.5	296.0	-
		022		193.3	235.0	265.8	243.9	276.6	276.2	298.3	-
		023		184.6	222.6	259.9	241.4	273.0	281.2	296.1	-
		024		175.1	213.4	257.4	234.4	267.7	261.0	275.4	-
		025		200.1	239.9	284.6	268.0	311.6	307.9	325.5	-
		026		192.2	231.0	274.9	249.7	293.8	298.6	317.7	310.9
		027		186.8	222.2	265.8	243.4	286.4	284.0	306.3	306.0
		028		194.4	224.6	262.6	244.2	276.7	275.1	299.5	290.0
		029		195.7	239.4	280.0	259.6	295.1	297.4	320.4	312.8

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**Appendix 4**  
**Body Weight (g)**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Male

Grp Num	Dose	Animal Num	Phase Day:	PID		Dosing					Recovery
				1	6	1	4	8	11	15	1
2	30 µg/day	030		179.2	215.5	268.3	251.0	292.4	297.3	322.3	322.8
3	30 µg/day	031		191.0	216.0	244.2	224.5	250.4	250.3	268.7	-
		032		178.1	210.7	254.6	234.7	264.1	258.3	274.4	-
		033		194.1	236.2	291.6	269.8	310.8	315.8	330.5	-
		034		187.5	222.4	259.6	233.8	267.7	264.5	280.4	-
		035		188.1	227.2	256.5	227.2	259.4	245.6	267.8	-
		036		195.0	239.8	274.1	254.1	288.9	287.8	308.0	-
		037		192.8	235.5	275.8	249.6	293.7	290.9	313.1	-
		038		187.6	223.9	256.2	236.1	267.4	268.3	285.9	-
		039		187.9	224.4	264.2	239.6	281.4	274.0	292.6	-
		040		177.5	216.5	255.9	240.4	271.1	268.0	293.1	-
		041		197.7	231.3	270.2	262.3	290.2	290.9	303.5	300.9
		042		187.4	228.6	259.5	243.0	269.5	273.4	290.9	289.7
		043		195.2	232.1	273.3	252.9	280.3	285.3	306.7	302.6
		044		183.6	229.0	266.9	243.7	287.0	285.6	299.3	304.1
045		177.0	214.1	249.3	226.4	262.5	260.0	284.4	282.3		

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**Appendix 4**  
**Body Weight (g)**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Male

Grp Num	Dose	Animal Num	Phase Day:	Recovery							
				4	8	11	15	18	21		
1	0 µg/day	001		-	-	-	-	-	-		
		002		-	-	-	-	-	-		
		003		-	-	-	-	-	-		
		004		-	-	-	-	-	-		
		005		-	-	-	-	-	-		
		006		-	-	-	-	-	-		
		007		-	-	-	-	-	-		
		008		-	-	-	-	-	-		
		009		-	-	-	-	-	-		
		010		-	-	-	-	-	-		
		011				320.0	328.2	331.7	328.6	333.4	341.3
		012				326.5	346.5	349.9	359.0	373.6	381.6
		013				291.7	297.5	303.2	308.8	314.5	317.1
		014				291.5	297.3	298.6	297.3	302.0	304.7
		015				350.7	363.2	370.3	374.3	383.6	394.7
2	30 µg/day	016		-	-	-	-	-	-		
		017		-	-	-	-	-	-		
		018		-	-	-	-	-	-		
		019		-	-	-	-	-	-		
		020		-	-	-	-	-	-		
		021		-	-	-	-	-	-		
		022		-	-	-	-	-	-		
		023		-	-	-	-	-	-		
		024		-	-	-	-	-	-		
		025		-	-	-	-	-	-		
		026				326.6	336.1	345.8	354.4	362.2	369.9
		027				312.9	327.4	335.6	344.3	347.4	359.0
		028				303.3	310.9	331.8	335.2	341.1	344.1
		029				323.2	337.7	350.5	355.5	361.9	371.9

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**Appendix 4**  
**Body Weight (g)**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Male

Grp Num	Dose	Animal Num	Phase Day:	Recovery						
				4	8	11	15	18	21	
2	30 µg/day	030		337.6	352.3	369.0	383.8	384.8	403.1	
3	30 µg/day	031		-	-	-	-	-	-	
		032		-	-	-	-	-	-	
		033		-	-	-	-	-	-	
		034		-	-	-	-	-	-	
		035		-	-	-	-	-	-	
		036		-	-	-	-	-	-	
		037		-	-	-	-	-	-	
		038		-	-	-	-	-	-	
		039		-	-	-	-	-	-	
		040		-	-	-	-	-	-	
		041			312.3	327.1	331.7	340.8	351.0	357.8
		042			299.5	311.4	320.1	328.4	336.8	344.2
		043			313.6	331.7	336.5	344.4	355.5	362.5
		044			311.9	324.6	333.6	344.6	351.3	366.3
		045			293.5	308.8	316.1	315.8	326.1	340.4

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**Appendix 4  
Body Weight (g)**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Female

Grp Num	Dose	Animal Num	Phase Day:	PID		Dosing					Recovery
				1	6	1	4	8	11	15	1
1	0 µg/day	046		151.3	169.9	188.5	177.4	192.7	202.2	206.7	-
		047		164.8	183.0	195.7	194.1	227.9	235.3	233.7	-
		048		156.5	170.4	185.8	172.6	195.1	187.6	190.0	-
		049		155.4	173.4	192.9	179.6	204.3	201.8	208.1	-
		050		149.6	174.8	185.3	182.4	218.0	227.9	227.0	-
		051		167.5	185.7	201.8	191.8	214.4	206.7	209.3	-
		052		158.8	176.0	206.3	190.6	213.7	213.3	220.6	-
		053		157.6	177.5	199.6	187.7	207.1	212.2	215.4	-
		054		166.0	186.8	203.7	193.6	211.0	225.7	230.7	-
		055		155.8	174.8	191.2	178.0	203.0	206.4	211.2	-
		056		166.8	181.7	203.6	188.4	211.9	210.5	219.0	224.3
		057		149.4	164.5	184.1	168.4	187.6	197.3	199.7	199.4
		058		151.7	169.0	187.0	172.2	186.8	197.4	204.0	204.8
		059		151.3	168.4	186.9	176.3	205.7	208.1	215.4	212.2
060		173.1	189.5	209.5	194.7	218.7	221.1	223.6	234.7		
2	30 µg/day	061		163.9	180.5	202.1	181.3	209.9	210.3	229.7	-
		062		157.5	172.7	183.1	174.6	203.0	205.8	208.9	-
		063		160.0	171.0	186.2	178.0	197.2	195.8	201.9	-
		064		162.7	184.5	198.0	187.2	215.7	208.9	216.1	-
		065		157.2	182.6	188.7	173.3	199.0	207.9	219.0	-
		066		171.4	186.7	203.9	187.0	215.0	215.8	219.6	-
		067		156.8	168.5	192.0	182.3	207.4	208.7	217.5	-
		068		152.0	169.9	187.6	169.0	190.5	187.7	196.9	-
		069		163.9	181.5	197.2	177.4	200.3	213.1	232.7	-
		070		174.1	188.9	202.5	185.8	206.0	211.6	227.2	-
		071		167.1	175.4	180.3	171.3	195.0	202.6	212.3	205.5
		072		153.5	174.3	196.8	177.1	207.9	198.7	213.4	206.6
		073		146.6	163.7	176.7	168.0	190.9	195.5	198.3	203.7
		074		154.4	168.3	186.3	173.0	195.0	192.4	196.3	204.8

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**Appendix 4  
Body Weight (g)**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Female

Grp Num	Dose	Animal Num	Phase Day:	PID		Dosing					Recovery
				1	6	1	4	8	11	15	1
2	30 µg/day	075		156.4	176.2	191.5	174.4	204.8	203.4	220.5	215.5
3	30 µg/day	076		169.2	176.6	204.0	186.9	204.0	209.1	215.5	-
		077		155.0	167.5	181.6	171.1	184.4	194.2	213.2	-
		078		158.2	182.3	207.2	181.9	217.2	208.4	231.7	-
		079		159.0	175.8	194.7	175.2	191.4	206.9	227.1	-
		080		159.3	181.9	195.2	184.6	216.0	220.7	223.6	-
		081		158.6	168.4	192.4	178.0	194.7	201.5	208.6	-
		082		148.7	162.1	187.5	177.1	196.6	192.1	204.4	-
		083		154.1	166.2	187.3	175.1	197.5	204.6	207.0	-
		084		165.1	188.8	200.6	184.3	213.6	210.8	217.8	-
		085		159.2	174.0	189.3	168.8	187.3	193.9	199.1	-
		086		154.4	173.5	180.3	166.1	183.6	192.9	207.6	213.3
		087		162.2	180.8	198.4	182.2	204.0	215.8	241.3	242.5
		088		150.5	159.0	172.9	161.5	180.3	176.1	182.5	180.6
089		170.6	185.8	204.4	184.1	211.3	209.9	218.4	208.1		
090		169.5	191.4	194.4	177.1	201.8	205.6	211.1	215.1		

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**Appendix 4  
Body Weight (g)**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Female

Grp Num	Dose	Animal Num	Phase Day:	Recovery							
				4	8	11	15	18	21		
1	0 µg/day	046		-	-	-	-	-	-		
		047		-	-	-	-	-	-		
		048		-	-	-	-	-	-		
		049		-	-	-	-	-	-		
		050		-	-	-	-	-	-		
		051		-	-	-	-	-	-		
		052		-	-	-	-	-	-		
		053		-	-	-	-	-	-		
		054		-	-	-	-	-	-		
		055		-	-	-	-	-	-		
		056				234.4	243.0	241.5	238.7	238.8	246.9
		057				198.4	207.9	212.2	211.5	210.8	218.3
		058				207.6	210.0	204.5	213.9	211.2	219.1
		059				209.4	209.7	218.0	217.0	221.5	218.0
		060				235.9	249.5	243.9	240.1	245.4	242.0
2	30 µg/day	061		-	-	-	-	-	-		
		062		-	-	-	-	-	-		
		063		-	-	-	-	-	-		
		064		-	-	-	-	-	-		
		065		-	-	-	-	-	-		
		066		-	-	-	-	-	-		
		067		-	-	-	-	-	-		
		068		-	-	-	-	-	-		
		069		-	-	-	-	-	-		
		070		-	-	-	-	-	-		
		071				212.7	221.2	226.2	218.8	225.0	235.6
		072				217.4	227.3	224.6	225.6	224.6	242.1
		073				200.9	207.9	210.8	213.6	215.3	215.5
		074				219.4	221.2	217.4	217.4	222.8	226.7

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**Appendix 4**  
**Body Weight (g)**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Grp Num	Dose	Animal Num	Phase Day:	Female Recovery							
				4	8	11	15	18	21		
2	30 µg/day	075		214.6	223.1	228.5	227.5	235.1	236.7		
3	30 µg/day	076		-	-	-	-	-	-		
		077		-	-	-	-	-	-		
		078		-	-	-	-	-	-		
		079		-	-	-	-	-	-		
		080		-	-	-	-	-	-		
		081		-	-	-	-	-	-		
		082		-	-	-	-	-	-		
		083		-	-	-	-	-	-		
		084		-	-	-	-	-	-		
		085		-	-	-	-	-	-		
		086				207.2	209.8	215.1	221.0	228.4	220.1
		087				235.5	239.1	233.2	241.0	252.5	246.1
		088				188.7	194.7	192.5	188.4	194.3	197.3
089				217.4	225.8	226.0	222.2	229.6	234.3		
090				223.1	230.0	224.3	213.9	221.1	224.5		

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**Appendix 5**  
**Body Weight Change During Interval (g)**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

**Footnotes**

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Grp Num = Group Number; Animal Num = Animal Number; - = Value not applicable; NW = Not Weighed; e = Excluded.

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**Appendix 5**

**Body Weight Change During Interval (g)**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

**Male**

Grp Num	Dose	Animal Num	Phase Days:	PID 1-6	Dosing					Recovery	
					1-4	4-8	8-11	11-15	1-15	1-4	4-8
1	0 µg/day	001		39.5	-13.8	31.4	13.8	5.8	37.2	-	-
		002		44.3	-12.2	36.0	14.3	17.7	55.8	-	-
		003		46.4	-11.1	31.9	15.8	11.8	48.4	-	-
		004		34.2	-6.8	45.5	8.4	21.7	68.8	-	-
		005		37.5	-9.8	32.4	15.0	14.4	52.0	-	-
		006		41.7	-10.2	37.4	11.8	16.2	55.2	-	-
		007		36.5	-10.9	35.7	14.6	11.6	51.0	-	-
		008		31.4	-13.5	31.7	9.5	13.2	40.9	-	-
		009		31.5	-7.6	26.8	8.6	17.1	44.9	-	-
		010		39.6	-14.2	33.4	10.4	17.0	46.6	-	-
		011		32.2	-7.0	34.1	5.6	13.4	46.1	6.2	8.2
		012		39.2	-34.1	-45.0	63.7	32.0	16.6	19.1	20.0
		013		30.3	-10.0	29.6	5.8	14.9	40.3	4.1	5.8
		014		36.0	-13.9	31.7	12.6	8.7	39.1	2.6	5.8
		015		43.2	-14.5	34.0	18.6	19.1	57.2	9.9	12.5
2	30 µg/day	016		32.4	-25.2	36.7	-3.6	18.7	26.6	-	-
		017		36.3	-17.4	41.7	0.9	14.9	40.1	-	-
		018		40.3	-13.2	29.4	0.4	14.5	31.1	-	-
		019		39.6	-10.7	28.8	5.2	17.2	40.5	-	-
		020		38.6	-22.9	35.5	-4.1	14.7	23.2	-	-
		021		43.2	-20.5	30.3	-2.7	19.5	26.6	-	-
		022		41.7	-21.9	32.7	-0.4	22.1	32.5	-	-
		023		38.0	-18.5	31.6	8.2	14.9	36.2	-	-
		024		38.3	-23.0	33.3	-6.7	14.4	18.0	-	-
		025		39.8	-16.6	43.6	-3.7	17.6	40.9	-	-
		026		38.8	-25.2	44.1	4.8	19.1	42.8	15.7	9.5
		027		35.4	-22.4	43.0	-2.4	22.3	40.5	6.9	14.5
		028		30.2	-18.4	32.5	-1.6	24.4	36.9	13.3	7.6

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**Appendix 5**

**Body Weight Change During Interval (g)**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

**Male**

Grp Num	Dose	Animal Num	Phase Days:	PID 1-6	Dosing					Recovery	
					1-4	4-8	8-11	11-15	1-15	1-4	4-8
2	30 µg/day	029		43.7	-20.4	35.5	2.3	23.0	40.4	10.4	14.5
		030		36.3	-17.3	41.4	4.9	25.0	54.0	14.8	14.7
3	30 µg /day	031		25.0	-19.7	25.9	-0.1	18.4	24.5	-	-
		032		32.6	-19.9	29.4	-5.8	16.1	19.8	-	-
		033		42.1	-21.8	41.0	5.0	14.7	38.9	-	-
		034		34.9	-25.8	33.9	-3.2	15.9	20.8	-	-
		035		39.1	-29.3	32.2	-13.8	22.2	11.3	-	-
		036		44.8	-20.0	34.8	-1.1	20.2	33.9	-	-
		037		42.7	-26.2	44.1	-2.8	22.2	37.3	-	-
		038		36.3	-20.1	31.3	0.9	17.6	29.7	-	-
		039		36.5	-24.6	41.8	-7.4	18.6	28.4	-	-
		040		39.0	-15.5	30.7	-3.1	25.1	37.2	-	-
		041		33.6	-7.9	27.9	0.7	12.6	33.3	11.4	14.8
		042		41.2	-16.5	26.5	3.9	17.5	31.4	9.8	11.9
		043		36.9	-20.4	27.4	5.0	21.4	33.4	11.0	18.1
		044		45.4	-23.2	43.3	-1.4	13.7	32.4	7.8	12.7
		045		37.1	-22.9	36.1	-2.5	24.4	35.1	11.2	15.3

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Appendix 5

Body Weight Change During Interval (g)

20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY

Male

Grp Num	Dose	Animal Num	Phase Days:	Recovery					
				8-11	11-15	15-18	18-21	1-21	
1	0 µg/day	001		-	-	-	-	-	
		002		-	-	-	-	-	
		003		-	-	-	-	-	
		004		-	-	-	-	-	
		005		-	-	-	-	-	
		006		-	-	-	-	-	
		007		-	-	-	-	-	
		008		-	-	-	-	-	
		009		-	-	-	-	-	
		010		-	-	-	-	-	
		011			3.5	-3.1	4.8	7.9	27.5
		012			3.4	9.1	14.6	8.0	74.2
		013			5.7	5.6	5.7	2.6	29.5
		014			1.3	-1.3	4.7	2.7	15.8
		015			7.1	4.0	9.3	11.1	53.9
2	30 µg/day	016		-	-	-	-	-	
		017		-	-	-	-	-	
		018		-	-	-	-	-	
		019		-	-	-	-	-	
		020		-	-	-	-	-	
		021		-	-	-	-	-	
		022		-	-	-	-	-	
		023		-	-	-	-	-	
		024		-	-	-	-	-	
		025		-	-	-	-	-	
		026			9.7	8.6	7.8	7.7	59.0
		027			8.2	8.7	3.1	11.6	53.0
		028			20.9	3.4	5.9	3.0	54.1

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**Appendix 5**

**Body Weight Change During Interval (g)**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

**Male**

Grp Num	Dose	Animal Num	Phase Days:	Recovery						
				8-11	11-15	15-18	18-21	1-21		
2	30 µg/day	029		12.8	5.0	6.4	10.0	59.1		
		030		16.7	14.8	1.0	18.3	80.3		
3	30 µg /day	031		-	-	-	-	-		
		032		-	-	-	-	-		
		033		-	-	-	-	-		
		034		-	-	-	-	-		
		035		-	-	-	-	-		
		036		-	-	-	-	-		
		037		-	-	-	-	-		
		038		-	-	-	-	-		
		039		-	-	-	-	-		
		040		-	-	-	-	-		
		041				4.6	9.1	10.2	6.8	56.9
		042				8.7	8.3	8.4	7.4	54.5
		043				4.8	7.9	11.1	7.0	59.9
044				9.0	11.0	6.7	15.0	62.2		
045				7.3	-0.3	10.3	14.3	58.1		

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**Appendix 5**

**Body Weight Change During Interval (g)**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

**Female**

Grp Num	Dose	Animal Num	Phase Days:	PID 1-6	Dosing					Recovery	
					1-4	4-8	8-11	11-15	1-15	1-4	4-8
1	0 µg/day	046		18.6	-11.1	15.3	9.5	4.5	18.2	-	-
		047		18.2	-1.6	33.8	7.4	-1.6	38.0	-	-
		048		13.9	-13.2	22.5	-7.5	2.4	4.2	-	-
		049		18.0	-13.3	24.7	-2.5	6.3	15.2	-	-
		050		25.2	-2.9	35.6	9.9	-0.9	41.7	-	-
		051		18.2	-10.0	22.6	-7.7	2.6	7.5	-	-
		052		17.2	-15.7	23.1	-0.4	7.3	14.3	-	-
		053		19.9	-11.9	19.4	5.1	3.2	15.8	-	-
		054		20.8	-10.1	17.4	14.7	5.0	27.0	-	-
		055		19.0	-13.2	25.0	3.4	4.8	20.0	-	-
		056		14.9	-15.2	23.5	-1.4	8.5	15.4	10.1	8.6
		057		15.1	-15.7	19.2	9.7	2.4	15.6	-1.0	9.5
		058		17.3	-14.8	14.6	10.6	6.6	17.0	2.8	2.4
		059		17.1	-10.6	29.4	2.4	7.3	28.5	-2.8	0.3
060		16.4	-14.8	24.0	2.4	2.5	14.1	1.2	13.6		
2	30 µg/day	061		16.6	-20.8	28.6	0.4	19.4	27.6	-	-
		062		15.2	-8.5	28.4	2.8	3.1	25.8	-	-
		063		11.0	-8.2	19.2	-1.4	6.1	15.7	-	-
		064		21.8	-10.8	28.5	-6.8	7.2	18.1	-	-
		065		25.4	-15.4	25.7	8.9	11.1	30.3	-	-
		066		15.3	-16.9	28.0	0.8	3.8	15.7	-	-
		067		11.7	-9.7	25.1	1.3	8.8	25.5	-	-
		068		17.9	-18.6	21.5	-2.8	9.2	9.3	-	-
		069		17.6	-19.8	22.9	12.8	19.6	35.5	-	-
		070		14.8	-16.7	20.2	5.6	15.6	24.7	-	-
		071		8.3	-9.0	23.7	7.6	9.7	32.0	7.2	8.5
		072		20.8	-19.7	30.8	-9.2	14.7	16.6	10.8	9.9
		073		17.1	-8.7	22.9	4.6	2.8	21.6	-2.8	7.0

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**Appendix 5**

**Body Weight Change During Interval (g)**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

**Female**

Grp Num	Dose	Animal Num	Phase Days:	PID 1-6	Dosing					Recovery	
					1-4	4-8	8-11	11-15	1-15	1-4	4-8
2	30 µg/day	074		13.9	-13.3	22.0	-2.6	3.9	10.0	14.6	1.8
		075		19.8	-17.1	30.4	-1.4	17.1	29.0	-0.9	8.5
3	30 µg /day	076		7.4	-17.1	17.1	5.1	6.4	11.5	-	-
		077		12.5	-10.5	13.3	9.8	19.0	31.6	-	-
		078		24.1	-25.3	35.3	-8.8	23.3	24.5	-	-
		079		16.8	-19.5	16.2	15.5	20.2	32.4	-	-
		080		22.6	-10.6	31.4	4.7	2.9	28.4	-	-
		081		9.8	-14.4	16.7	6.8	7.1	16.2	-	-
		082		13.4	-10.4	19.5	-4.5	12.3	16.9	-	-
		083		12.1	-12.2	22.4	7.1	2.4	19.7	-	-
		084		23.7	-16.3	29.3	-2.8	7.0	17.2	-	-
		085		14.8	-20.5	18.5	6.6	5.2	9.8	-	-
		086		19.1	-14.2	17.5	9.3	14.7	27.3	-6.1	2.6
		087		18.6	-16.2	21.8	11.8	25.5	42.9	-7.0	3.6
088		8.5	-11.4	18.8	-4.2	6.4	9.6	8.1	6.0		
089		15.2	-20.3	27.2	-1.4	8.5	14.0	9.3	8.4		
090		21.9	-17.3	24.7	3.8	5.5	16.7	8.0	6.9		

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**Appendix 5**  
**Body Weight Change During Interval (g)**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Grp Num	Dose	Animal Num	Phase Days:	Recovery				
				8-11	11-15	15-18	18-21	1-21
1	0 µg/day	046		-	-	-	-	-
		047		-	-	-	-	-
		048		-	-	-	-	-
		049		-	-	-	-	-
		050		-	-	-	-	-
		051		-	-	-	-	-
		052		-	-	-	-	-
		053		-	-	-	-	-
		054		-	-	-	-	-
		055		-	-	-	-	-
		056		-1.5	-2.8	0.1	8.1	22.6
		057		4.3	-0.7	-0.7	7.5	18.9
		058		-5.5	9.4	-2.7	7.9	14.3
		059		8.3	-1.0	4.5	-3.5	5.8
060		-5.6	-3.8	5.3	-3.4	7.3		
2	30 µg/day	061		-	-	-	-	-
		062		-	-	-	-	-
		063		-	-	-	-	-
		064		-	-	-	-	-
		065		-	-	-	-	-
		066		-	-	-	-	-
		067		-	-	-	-	-
		068		-	-	-	-	-
		069		-	-	-	-	-
		070		-	-	-	-	-
		071		5.0	-7.4	6.2	10.6	30.1
		072		-2.7	1.0	-1.0	17.5	35.5
		073		2.9	2.8	1.7	0.2	11.8

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**Appendix 5**

**Body Weight Change During Interval (g)**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

**Female**

Grp Num	Dose	Animal Num	Phase Days:	Recovery						
				8-11	11-15	15-18	18-21	1-21		
2	30 µg/day	074		-3.8	0.0	5.4	3.9	21.9		
		075		5.4	-1.0	7.6	1.6	21.2		
3	30 µg /day	076		-	-	-	-	-		
		077		-	-	-	-	-		
		078		-	-	-	-	-		
		079		-	-	-	-	-		
		080		-	-	-	-	-		
		081		-	-	-	-	-		
		082		-	-	-	-	-		
		083		-	-	-	-	-		
		084		-	-	-	-	-		
		085		-	-	-	-	-		
		086				5.3	5.9	7.4	-8.3	6.8
		087				-5.9	7.8	11.5	-6.4	3.6
		088				-2.2	-4.1	5.9	3.0	16.7
089				0.2	-3.8	7.4	4.7	26.2		
090				-5.7	-10.4	7.2	3.4	9.4		

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**Appendix 6**

**Food Consumption - Empty Feeder During Interval (g)**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

**Footnotes**

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Num = Number; - = Value not applicable; NW = Not Weighed; e = Excluded; SP = Spilled.

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**Appendix 6**

**Food Consumption - Empty Feeder During Interval (g)**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Male

Grp Num	Dose	Animal Num	Phase: Days:	Dosing					Recovery		
				1-4	4-8	8-11	11-15	1-15	1-4	4-8	8-11
1	0 µg/day	001		53.4	92.3	66.2	87.0	298.9	-	-	-
		002		53.5	100.9	66.5	92.1	313.0	-	-	-
		003		53.6	92.7	70.2	85.0	301.5	-	-	-
		004		51.8	106.3	66.5	96.8	321.4	-	-	-
		005		50.4	95.2	67.9	87.4	300.9	-	-	-
		006		54.3	100.3	62.6	95.1	312.3	-	-	-
		007		54.4	106.8	70.4	92.3	323.9	-	-	-
		008		45.3	89.9	64.8	84.1	284.1	-	-	-
		009		50.5	86.2	58.9	87.2	282.8	-	-	-
		010		46.8	88.5	67.6	87.4	290.3	-	-	-
		011		51.5	97.4	59.9	85.1	293.9	48.2	74.0	55.8
		012		39.7	18.5	58.5	101.2	217.9	56.2	97.1	63.2
		013		51.9	85.1	53.2	81.5	271.7	39.6	72.9	52.6
		014		53.3	95.8	69.8	84.2	303.1	44.4	75.5	52.0
		015		52.8	107.1	68.5	93.9	322.3	51.7	91.1	67.0
2	30 µg/day	016		35.5	85.3	47.2	81.5	249.5	-	-	-
		017		43.1	95.9	53.2	97.7	289.9	-	-	-
		018		46.1	101.9	57.4	88.9	294.3	-	-	-
		019		45.0	92.8	49.2	86.1	273.1	-	-	-
		020		40.7	91.7	47.0	84.9	264.3	-	-	-
		021		34.4	89.8	46.4	91.1	261.7	-	-	-

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**Appendix 6**

**Food Consumption - Empty Feeder During Interval (g)**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Male

Grp Num	Dose	Animal Num	Phase: Days:	Dosing					Recovery		
				1-4	4-8	8-11	11-15	1-15	1-4	4-8	8-11
2	30 µg/day	022		41.2	90.7	49.3	84.6	265.8	-	-	-
		023		42.2	89.0	54.1	84.2	269.5	-	-	-
		024		38.6	90.5	51.2	86.2	266.5	-	-	-
		025		51.1	114.3	61.9	104.3	331.6	-	-	-
		026		43.6	101.5	65.9	101.9	312.9	63.9	94.9	65.3
		027		46.4	101.0	57.0	90.9	295.3	62.8	89.6	63.3
		028		41.9	90.8	50.7	92.3	275.7	61.3	84.0	66.5
		029		45.7	107.5	57.2	97.8	308.2	65.6	90.9	68.2
		030		43.4	108.6	62.6	110.9	325.5	70.1	105.2	76.7
		3	30 µg/day	031		33.4	75.7	45.2	74.5	228.8	-
032				40.9	85.0	41.1	86.8	253.8	-	-	-
033				36.3	116.5	63.6	100.2	316.6	-	-	-
034				36.3	84.9	47.1	80.6	248.9	-	-	-
035				33.4	80.0	35.7	80.5	229.6	-	-	-
036				42.4	87.4	55.1	89.2	274.1	-	-	-
037				39.4	105.8	56.7	103.3	305.2	-	-	-
038				39.2	79.7	52.5	82.9	254.3	-	-	-
039				33.8	97.4	49.6	87.1	267.9	-	-	-
040				38.6	95.1	44.6	101.0	279.3	-	-	-
041				53.9	105.4	61.5	93.1	313.9	70.0	94.5	67.3
042				34.0	91.5	46.9	82.2	254.6	59.8	79.8	56.9

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**Appendix 6**

**Food Consumption - Empty Feeder During Interval (g)**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

**Male**

Grp Num	Dose	Animal Num	Phase: Days:	Dosing					Recovery		
				1-4	4-8	8-11	11-15	1-15	1-4	4-8	8-11
3	30 µg /day	043		39.6	78.2	50.6	86.5	254.9	58.4	83.2	61.6
		044		38.7	98.2	55.6	94.1	286.6	63.2	92.5	61.6
		045		40.4	89.8	50.9	90.0	271.1	59.9	83.2	66.1

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**Appendix 6**

**Food Consumption - Empty Feeder During Interval (g)**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Male

Grp Num	Dose	Animal Num	Phase: Days:	Recovery				
				11-15	15-18	18-21	1-21	
1	0 µg/day	001		-	-	-	-	
		002		-	-	-	-	
		003		-	-	-	-	
		004		-	-	-	-	
		005		-	-	-	-	
		006		-	-	-	-	
		007		-	-	-	-	
		008		-	-	-	-	
		009		-	-	-	-	
		010		-	-	-	-	
		011			69.1	53.3	50.5	350.9
		012			87.6	68.2	66.9	439.2
		013			68.6	54.3	51.6	339.6
		014			70.9	53.6	56.9	353.3
		015			85.9	69.1	70.5	435.3
2	30 µg/day	016		-	-	-	-	
		017		-	-	-	-	
		018		-	-	-	-	
		019		-	-	-	-	
		020		-	-	-	-	
		021		-	-	-	-	

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**Appendix 6**

**Food Consumption - Empty Feeder During Interval (g)**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Male

Grp Num	Dose	Animal Num	Phase: Days:	Recovery			
				11-15	15-18	18-21	1-21
2	30 µg/day	022		-	-	-	-
		023		-	-	-	-
		024		-	-	-	-
		025		-	-	-	-
		026		87.1	68.5	67.9	447.6
		027		82.1	64.7	64.1	426.6
		028		75.1	59.3	63.9	410.1
		029		82.8	62.2	63.3	433.0
		030		96.5	67.6	73.0	489.1
		3	30 µg/day	031		-	-
032				-	-	-	-
033				-	-	-	-
034				-	-	-	-
035				-	-	-	-
036				-	-	-	-
037				-	-	-	-
038				-	-	-	-
039				-	-	-	-
040				-	-	-	-
041				85.4	70.3	70.0	457.5
042				71.6	58.4	53.6	380.1

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**Appendix 6**

**Food Consumption - Empty Feeder During Interval (g)**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

**Male**

Grp Num	Dose	Animal Num	Phase: Days:	Recovery			
				11-15	15-18	18-21	1-21
3	30 µg /day	043		76.1	58.4	56.5	394.2
		044		85.8	65.0	69.8	437.9
		045		77.1	60.9	60.8	408.0

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**Appendix 6**

**Food Consumption - Empty Feeder During Interval (g)**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Female

Grp Num	Dose	Animal Num	Phase: Days:	Dosing					Recovery		
				1-4	4-8	8-11	11-15	1-15	1-4	4-8	8-11
1	0 µg/day	046		32.9	61.5	47.7	54.5	196.6	-	-	-
		047		41.0	87.3	61.3	77.0	266.6	-	-	-
		048		35.6	72.7	44.7	64.2	217.2	-	-	-
		049		36.3	72.0	43.4	63.5	215.2	-	-	-
		050		42.8	83.1	59.2	69.6	254.7	-	-	-
		051		37.5	67.9	42.3	67.2	214.9	-	-	-
		052		43.8	79.3	46.3	64.0	233.4	-	-	-
		053		39.1	74.0	47.1	61.9	222.1	-	-	-
		054		41.8	84.0	58.1	77.5	261.4	-	-	-
		055		35.1	68.4	46.2	59.1	208.8	-	-	-
		056		35.8	75.7	47.3	72.5	231.3	54.1	70.3	51.0
		057		28.2	64.0	39.5	55.0	186.7	43.2	62.4	45.0
		058		34.8	63.2	42.7	56.1	196.8	42.4	55.2	40.0
		059		40.2	81.0	44.7	65.8	231.7	45.2	56.7	45.7
060		42.0	82.8	53.6	71.2	249.6	53.1	72.0	49.9		
2	30 µg/day	061		30.3	74.3	44.2	80.6	229.4	-	-	-
		062		34.0	65.9	40.3	61.5	201.7	-	-	-
		063		36.7	70.6	38.7	66.5	212.5	-	-	-
		064		36.6	77.5	46.5	71.6	232.2	-	-	-
		065		23.9	72.6	42.7	66.2	205.4	-	-	-
		066		29.5	71.5	41.1	56.8	198.9	-	-	-

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**Appendix 6**

**Food Consumption - Empty Feeder During Interval (g)**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Female

Grp Num	Dose	Animal Num	Phase: Days:	Dosing					Recovery		
				1-4	4-8	8-11	11-15	1-15	1-4	4-8	8-11
2	30 µg/day	067		37.3	78.2	45.8	68.4	229.7	-	-	-
		068		30.0	59.8	37.7	56.7	184.2	-	-	-
		069		34.0	71.0	44.2	72.5	221.7	-	-	-
		070		32.9	70.8	41.7	71.7	217.1	-	-	-
		071		37.4	72.6	40.4	66.9	217.3	55.6	67.9	51.2
		072		34.0	71.0	38.4	66.1	209.5	47.7	68.7	47.1
		073		32.9	72.4	39.6	63.5	208.4	44.2	63.3	44.1
		074		31.4	67.3	40.0	58.1	196.8	54.2	63.8	41.9
		075		34.4	66.9	46.5	71.7	219.5	46.9	69.7	49.2
3	30 µg/day	076		38.5	76.7	50.1	70.3	235.6	-	-	-
		077		34.2	71.1	40.5	77.0	222.8	-	-	-
		078		25.5	74.6	36.2	72.1	208.4	-	-	-
		079		30.1	67.5	43.8	76.3	217.7	-	-	-
		080		37.3	82.4	55.1	74.3	249.1	-	-	-
		081		31.8	64.5	34.7	65.3	196.3	-	-	-
		082		31.7	66.9	37.4	62.8	198.8	-	-	-
		083		33.3	71.5	45.0	66.8	216.6	-	-	-
		084		78.1	75.9	39.0	62.1	255.1	-	-	-
		085		29.8	66.7	39.3	66.7	202.5	-	-	-
		086		27.3	64.9	36.4	62.6	191.2	47.8	60.3	42.8
		087		38.6	85.4	43.6	90.6	258.2	57.6	82.6	53.6

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**Appendix 6**

**Food Consumption - Empty Feeder During Interval (g)**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Female

Grp Num	Dose	Animal Num	Phase: Days:	Dosing					Recovery		
				1-4	4-8	8-11	11-15	1-15	1-4	4-8	8-11
3	30 µg /day	088		26.7	65.5	31.8	54.8	178.8	45.4	62.4	38.3
		089		28.5	64.7	37.4	60.1	190.7	44.1	59.9	42.1
		090		28.1	77.6	36.0	65.7	207.4	50.2	69.2	36.8

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**Appendix 6**

**Food Consumption - Empty Feeder During Interval (g)**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Female

Grp Num	Dose	Animal Num	Phase: Days:	Recovery				
				11-15	15-18	18-21	1-21	
1	0 µg/day	046		-	-	-	-	
		047		-	-	-	-	
		048		-	-	-	-	
		049		-	-	-	-	
		050		-	-	-	-	
		051		-	-	-	-	
		052		-	-	-	-	
		053		-	-	-	-	
		054		-	-	-	-	
		055		-	-	-	-	
		056			67.1	47.3	50.0	339.8
		057			56.2	39.3	46.0	292.1
		058			52.0	38.9	45.2	273.7
		059			52.6	36.9	38.6	275.7
060			67.5	49.8	45.2	337.5		
2	30 µg/day	061		-	-	-	-	
		062		-	-	-	-	
		063		-	-	-	-	
		064		-	-	-	-	
		065		-	-	-	-	
		066		-	-	-	-	

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**Food Consumption - Empty Feeder During Interval (g)**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Female

Grp Num	Dose	Animal Num	Phase: Days:	Recovery			
				11-15	15-18	18-21	1-21
2	30 µg/day	067		-	-	-	-
		068		-	-	-	-
		069		-	-	-	-
		070		-	-	-	-
		071		58.4	46.1	48.6	327.8
		072		63.9	36.2	48.1	311.7
		073		55.4	40.2	41.1	288.3
		074		61.4	44.0	44.4	309.7
		075		65.8	51.7	51.8	335.1
3	30 µg /day	076		-	-	-	-
		077		-	-	-	-
		078		-	-	-	-
		079		-	-	-	-
		080		-	-	-	-
		081		-	-	-	-
		082		-	-	-	-
		083		-	-	-	-
		084		-	-	-	-
		085		-	-	-	-
		086		60.1	44.2	41.1	296.3
		087		77.3	57.0	55.9	384.0

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**Appendix 6**

**Food Consumption - Empty Feeder During Interval (g)**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

**Female**

Grp Num	Dose	Animal Num	Phase: Days:	Recovery			
				11-15	15-18	18-21	1-21
3	30 µg /day	088		50.3	37.6	40.0	274.0
		089		52.8	41.5	42.6	283.0
		090		48.9	43.5	44.2	292.8

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**Appendix 7**

**Hematology and Coagulation**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Parameter</b>	<b>Description</b>	<b>Parameter</b>	<b>Description</b>
RBC	Red Blood Cells	BASO	Basophil, Absolute
HGB	Hemoglobin	BASO_P	Basophil
HCT	Hematocrit	LUC	Large Unstained Cells, Absolute
MCV	Mean Cell Volume	LUC_P	Large Unstained Cells
MCH	Mean Cell Hemoglobin	MORPH	Morphology
MCHC	Mean Cell Hemoglobin Conc	POIK	Poikilocytosis
RDW	Red Cell Distribution Width	BURR	Burr Cells
RETIC_P	Reticulocyte	SCHISTO	Schistocytes
RETIC	Reticulocyte, Absolute	SPHERO	Spherocytes
PLT	Platelets	SIDERO	Siderocyte-like Inclusions
MPV	Mean Platelet Volume	TARGET	Target Cells
WBC	White Blood Cells	TEAR	Tear Drop Cells
NEUT	Neutrophil, Absolute	B_STIP	Basophilic Stippling
NEUT_P	Neutrophil	HJ	Howell-Jolly Bodies
LYM	Lymphocyte, Absolute	AGGL	Agglutination
LYM_P	Lymphocyte	CLPLT	Clumped Platelets
MONO	Monocyte, Absolute	HGB_CRYS	Hemoglobin Crystals
MONO_P	Monocyte	BASOPH	Basophilia
EO	Eosinophil, Absolute	ACANTH	Acanthocytes
EO_P	Eosinophil	STOM	Stomatocytes

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**Appendix 7**

**Hematology and Coagulation**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Parameter</b>	<b>Description</b>
OTHERM	Other Morphology
DOHLE	Dohle Bodies
HYSEG	Hypersegmented Neutrophils
TOXIC_G	Toxic Granulation
TOXIC_V	Toxic Vacuolation
VACLYM	Vacuolated Lymphocytes
PT_Rat	Prothrombin Time, Rat
APTT	Activated Partial Thromboplastin Time
FIB	Fibrinogen

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**Appendix 7**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

<b>Comment</b>	<b>Description</b>
CE	Critical result for Subject # RatWis042 ; Time point R022 transmitted electronically to clinically responsible personnel.
CE	Critical result for Subject # RatWis044 ; Time point R022 transmitted electronically to clinically responsible personnel.
CL	Clotted
FT	Subject# Ratwis031; Timepoint D004; Lymphocytes
NS	No Sample
QN	Quantity Not Sufficient
RP	Clumped platelets on original result; sample redrawn and reported.
RR	Result repeated
RW	RDW and MCV not reportable due to abnormal cytogram
SR	Slide Reviewed

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**Appendix 7**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

**Footnotes**

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- Value not applicable;

Note: Each interval/day will be concatenated with the phase name abbreviation

HPD = Hours Post Dose; U = Unscheduled

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**Appendix 7**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	RBC 10 <sup>6</sup> /uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %		
1	0 µg/day	001	4D	--	8.64	15.9	50.0	57.8	18.4	31.7	11.6		
			17D	-	8.38	14.9	46.2	55.2	17.8	32.2	11.1		
		002	4D	--	8.07	15.7	48.7	60.4	19.4	32.2	12.1		
			17D	-	7.33	13.8	42.8	58.3	18.8	32.2	11.7		
		003	4D	--	8.11	15.0	49.2	60.6	18.5	30.5	12.1		
			17D	-	-	CL	-	CL	-	CL	-	CL	-
		004	4D	--	8.17	14.8	48.0	58.8	18.2	30.9	13.0		
			17D	-	7.63	14.0	42.6	55.8	18.4	32.9	11.8		
		005	4D	--	8.02	14.4	46.4	57.8	18.0	31.1	12.7		
			17D	-	7.06	12.7	38.8	55.0	18.0	32.8	12.3		
		006	4D	--	8.05	14.6	47.3	58.7	18.2	30.9	12.4		
			17D	-	7.95	14.2	44.4	55.8	17.9	32.0	12.0		
		007	4D	--	7.76	14.7	46.7	60.2	18.9	31.4	12.0		
			17D	-	7.43	13.7	42.3	57.0	18.4	32.3	11.7		
		008	17D	-	8.10	14.5	45.1	55.7	18.0	32.2	11.6		
		009	17D	-	6.75	12.8	39.4	58.5	19.0	32.5	11.4		
		010	17D	-	7.63	13.8	41.9	54.9	18.1	33.0	11.1		

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	RBC 10 <sup>6</sup> /uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %		
1	0 µg/day	011	22R	-	7.29	12.8	37.9	52.1	17.6	33.8	12.2		
		012	22R	-	8.02	14.2	43.8	54.6	17.7	32.5	12.1		
		013	22R	-	8.61	15.5	46.4	-	RW	18.0	33.4	-	RW
		014	22R	-	8.06	15.0	43.6	54.2	18.6	34.4	11.3		
		015	22R	-	7.77	14.3	42.2	54.3	18.4	33.9	12.1		
2	30 µg/day	016	4D	--	8.30	15.0	46.2	55.7	18.1	32.5	11.9		
			17D	-	7.03	12.2	36.9	52.5	17.3	33.0	13.3		
		017	4D	--	7.60	13.4	41.4	54.5	17.6	32.3	13.1		
			17D	-	6.76	11.3	35.1	51.9	16.8	32.4	14.0		
		018	4D	--	7.71	13.9	42.0	54.5	18.0	33.1	13.8		
			17D	-	7.52	13.0	38.9	51.8	17.3	33.4	15.5		
		019	4D	--	7.56	14.1	43.4	57.4	18.7	32.6	12.4		
			17D	-	7.20	12.9	39.5	54.9	17.9	32.6	13.5		
		020	4D	--	7.92	14.0	43.3	54.7	17.7	32.4	12.9		
			17D	-	7.57	12.9	39.7	52.4	17.0	32.5	13.4		
	021	4D	--	7.43	13.7	42.4	57.0	18.4	32.3	13.5			
		17D	-	6.66	11.7	36.5	54.8	17.6	32.2	14.8			

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**Appendix 7**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	RBC 10 <sup>6</sup> /uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %		
2	30 µg/day	022	4D	--	7.90	15.0	44.9	56.9	18.9	33.3	12.2		
			17D	-	7.21	13.1	39.5	54.7	18.2	33.3	14.1		
		023	17D	-	7.35	12.4	39.0	53.1	16.9	31.7	14.3		
			17D	-	7.16	12.6	39.0	54.5	17.6	32.4	14.8		
		025	17D	-	7.23	13.2	39.9	55.2	18.2	33.0	13.5		
			22R	-	8.26	14.0	43.6	52.8	17.0	32.2	13.5		
		027	22R	-	8.35	15.0	46.0	55.2	17.9	32.5	13.5		
			22R	-	8.11	14.1	43.5	53.6	17.4	32.4	13.1		
		029	22R	-	7.87	14.6	43.5	-	RW	18.5	33.6	-	RW
		030	22R	-	7.73	14.2	42.0	54.4	18.4	33.8	13.8		
3	30 µg /day	031	4D	--	7.62	13.5	42.3	55.6	17.8	32.0	11.8		
			17D	-	6.93	11.9	36.9	53.2	17.2	32.3	12.9		
		032	4D	--	7.23	13.8	42.9	59.4	19.1	32.2	13.3		
			17D	-	7.02	12.6	39.6	56.5	17.9	31.8	14.1		
		033	4D	--	7.41	13.8	43.6	58.9	18.7	31.7	12.7		
			17D	-	7.40	13.3	41.9	56.6	17.9	31.7	13.9		
034	4D	--	7.79	14.1	43.6	56.0	18.1	32.3	12.1				

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**Appendix 7**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	RBC 10 <sup>6</sup> /uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %		
3	30 µg /day	034	17D	-	7.42	13.0	39.7	53.5	17.5	32.8	13.6		
		035	4D	--	7.85	14.4	45.4	57.7	18.3	31.7	12.2		
			17D	-	7.34	13.2	40.1	54.7	18.0	33.0	13.9		
		036	4D	--	7.93	14.6	45.3	57.1	18.5	32.3	12.4		
			17D	-	7.46	13.3	40.6	54.4	17.8	32.6	13.2		
		037	4D	--	7.34	13.9	43.4	59.1	19.0	32.1	12.6		
			17D	-	6.88	12.5	38.8	56.5	18.1	32.1	13.6		
		038	17D	-	6.77	12.3	37.7	55.6	18.2	32.8	14.0		
		039	17D	-	7.37	13.3	39.7	53.9	18.0	33.4	14.4		
		040	17D	-	6.54	12.7	37.9	-	RW	19.5	33.6	-	RW
		041	22R	-	8.36	14.7	45.9	55.0	17.6	32.1	14.0		
		042	22R	-	7.62	13.8	42.5	55.7	18.1	32.5	13.1		
		043	22R	-	7.91	13.6	41.9	53.1	17.2	32.4	13.2		
		044	22R	-	8.22	14.2	43.9	53.4	17.3	32.3	13.0		
		045	22R	-	7.32	13.7	40.7	-	RW	18.8	33.7	-	RW

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**Appendix 7**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	RETIC_P %	RETIC 10 <sup>3</sup> /uL	PLT 10 <sup>3</sup> /uL	MPV fL	WBC 10e3/uL	NEUT 10 <sup>3</sup> /uL	NEUT_P %		
1	0 µg/day	001	4D	--	4.6	397	1132	8.3	7.5	0.92	12.2		
			17D	-	2.4	201	870	8.3	3.7	0.75	20.3		
		002	4D	--	4.8	387	963	8.9	5.6	0.97	17.3		
			17D	-	2.5	183	873	9.1	3.9	0.70	17.9		
		003	4D	--	5.1	414	1154	9.1	7.4	0.58	7.8		
			17D	-	-	CL	-	CL	-	CL	-	CL	-
		004	4D	--	5.5	449	1099	8.9	8.4	1.43	16.9		
			17D	-	2.5	191	958	9.3	5.4	1.29	24.1		
		005	4D	--	5.3	425	1069	8.5	8.8	0.68	7.7		
			17D	-	2.7	191	927	9.1	1.9	0.18	9.4		
		006	4D	--	4.8	386	1014	9.2	7.1	1.24	17.3		
			17D	-	2.0	159	905	9.5	5.4	1.08	19.8		
		007	4D	--	3.7	287	658	9.2	8.4	1.76	21.0		
			17D	-	1.7	126	918	8.9	6.3	0.99	15.7		
		008	17D	-	2.4	194	794	9.5	4.1	0.43	10.3		
		009	17D	-	2.9	196	750	9.2	1.5	0.29	19.6		
		010	17D	-	2.2	168	937	9.2	2.4	0.36	15.2		

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	RETIC_P %	RETIC 10 <sup>3</sup> /uL	PLT 10 <sup>3</sup> /uL	MPV fL	WBC 10e3/uL	NEUT 10 <sup>3</sup> /uL	NEUT_P %
1	0 µg/day	011	22R	-	2.5	182	909	9.2	2.2	0.60	27.6
		012	22R	-	2.8	225	834	9.2	4.9	0.93	19.1
		013	22R	-	2.1	181	865	8.8	9.5	1.49	15.7
		014	22R	-	1.8	145	809	8.7	4.6	0.56	12.1
		015	22R	-	2.2	171	822	9.1	5.1	0.91	17.9
2	30 µg/day	016	4D	--	1.3	108	910	9.9	13.0	2.97	22.8
			17D	-	2.9	204	564	10.6	6.4	3.27	50.8
		017	4D	--	0.7	53	1143	9.2	12.6	2.90	23.1
			17D	-	2.7	183	927	9.4	8.8	4.96	56.1
		018	4D	--	0.8	62	1044	9.5	14.3	2.83	19.8
			17D	-	2.0	150	815	9.4	14.5	6.56	45.1
		019	4D	--	2.4	181	1004	9.2	7.3	1.67	22.9
			17D	-	2.5	180	855	9.3	7.4	3.76	51.1
		020	4D	--	1.0	79	1177	8.9	12.0	3.24	27.0
			17D	-	2.2	167	880	9.0	12.8	7.32	57.0
	021	4D	--	1.6	119	1039	9.6	6.6	0.95	14.3	
		17D	-	2.3	153	655	9.7	3.5	1.45	41.3	

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	RETIC_P %	RETIC 10 <sup>3</sup> /uL	PLT 10 <sup>3</sup> /uL		MPV fL		WBC 10e3/uL	NEUT 10 <sup>3</sup> /uL	NEUT_P %
2	30 µg/day	022	4D	--	1.9	150	961	RP	7.7	RP	9.1	2.73	30.1
			17D	-	2.5	180	926		9.8		9.4	4.80	50.8
		023	17D	-	2.6	191	872		9.3		4.0	1.86	46.9
			17D	-	3.0	215	724		9.9		9.6	4.94	51.5
		025	17D	-	3.2	231	795		9.1		11.9	5.57	46.7
			22R	-	2.7	223	816		8.7		4.3	1.19	27.7
		027	22R	-	2.2	184	910		8.9		6.4	1.14	17.8
			22R	-	2.7	219	769		9.1		5.5	0.69	12.5
		029	22R	-	1.9	150	1054		9.0		6.3	1.20	19.0
		030	22R	-	2.3	178	973		8.5		7.4	1.13	15.3
3	30 µg /day	031	4D	--	1.5	114	898		9.6		7.6	1.38	18.0
			17D	-	2.8	194	534	SR	10.1		6.7	3.36	49.9
		032	4D	--	1.5	108	937		10.3		11.1	2.60	23.5
			17D	-	2.9	204	807		10.1		10.5	5.08	48.3
		033	4D	--	1.0	74	1187		9.6		12.3	2.89	23.5
			17D	-	2.4	178	974		9.3		9.2	5.03	54.6
		034	4D	--	1.3	101	843		10.1		9.2	2.07	22.4

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**Appendix 7**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	RETIC_P %	RETIC 10 <sup>3</sup> /uL	PLT 10 <sup>3</sup> /uL	MPV fL	WBC 10e3/uL	NEUT 10 <sup>3</sup> /uL	NEUT_P %
3	30 µg /day	034	17D	-	2.6	193	708	10.3	8.0	4.24	52.9
		035	4D	--	1.6	126	780	9.6	8.1	1.66	20.6
			17D	-	2.8	206	594	SR 10.5	7.8	3.76	48.2
		036	4D	--	1.8	143	1024	9.3	10.0	2.34	23.3
			17D	-	2.7	201	908	9.8	10.1	5.34	52.8
		037	4D	--	0.9	66	947	9.4	9.6	2.19	22.7
			17D	-	2.5	172	667	9.6	8.0	3.82	47.6
		038	17D	-	3.0	203	702	10.8	9.1	4.57	50.2
		039	17D	-	2.8	206	759	9.4	8.6	4.72	54.9
		040	17D	-	2.8	183	737	9.4	8.0	3.59	44.7
		041	22R	-	2.4	201	789	9.2	4.9	1.36	27.7
		042	22R	-	2.6	198	689	9.1	2.9	0.70	23.9
		043	22R	-	2.1	166	822	8.7	5.9	1.37	23.3
		044	22R	-	2.6	214	890	8.8	5.2	1.53	29.6
		045	22R	-	2.1	154	998	8.6	5.6	1.42	25.4

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**Appendix 7**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	LYM 10 <sup>3</sup> /uL	LYM_P %	MONO 10 <sup>3</sup> /uL	MONO_P %	EO 10 <sup>3</sup> /uL	EO_P %	BASO 10 <sup>3</sup> /uL		
1	0 µg/day	001	4D	--	6.35	84.4	0.12	1.5	0.07	0.9	0.02		
			17D	-	2.80	75.4	0.03	0.9	0.09	2.6	0.00		
		002	4D	--	4.46	79.1	0.12	2.2	0.03	0.6	0.01		
			17D	-	3.00	76.9	0.13	3.2	0.04	1.0	0.00		
		003	4D	--	6.60	89.3	0.11	1.5	0.06	0.8	0.01		
			17D	-	-	CL	-	CL	-	CL	-	CL	-
		004	4D	--	6.80	80.6	0.09	1.0	0.06	0.7	0.01		
			17D	-	3.85	71.8	0.12	2.3	0.06	1.1	0.01		
		005	4D	--	7.86	89.2	0.12	1.4	0.08	0.9	0.02		
			17D	-	1.66	87.1	0.03	1.5	0.03	1.3	0.00		
		006	4D	--	5.64	79.2	0.13	1.8	0.06	0.8	0.02		
			17D	-	4.12	75.6	0.11	2.1	0.09	1.7	0.01		
		007	4D	--	6.28	74.9	0.07	0.8	0.21	2.5	0.02		
			17D	-	5.09	81.2	0.08	1.2	0.06	1.0	0.01		
		008	17D	-	3.53	85.4	0.08	2.0	0.06	1.5	0.00		
		009	17D	-	1.14	77.0	0.03	2.2	0.02	1.1	0.00		
		010	17D	-	1.89	80.7	0.03	1.4	0.05	1.9	0.00		

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	LYM 10 <sup>3</sup> /uL	LYM_P %	MONO 10 <sup>3</sup> /uL	MONO_P %	EO 10 <sup>3</sup> /uL	EO_P %	BASO 10 <sup>3</sup> /uL
1	0 µg/day	011	22R	-	1.47	67.8	0.04	1.9	0.05	2.2	0.00
		012	22R	-	3.77	77.5	0.08	1.7	0.06	1.2	0.00
		013	22R	-	7.62	80.3	0.12	1.3	0.14	1.4	0.03
		014	22R	-	3.91	85.1	0.05	1.2	0.03	0.7	0.00
		015	22R	-	4.02	78.7	0.08	1.5	0.06	1.2	0.01
2	30 µg/day	016	4D	--	9.19	70.5	0.28	2.2	0.13	1.0	0.04
			17D	-	2.49	38.7	0.19	3.0	0.13	2.0	0.01
		017	4D	--	9.00	71.6	0.28	2.3	0.04	0.3	0.04
			17D	-	3.34	37.8	0.21	2.3	0.10	1.1	0.02
		018	4D	--	10.85	75.9	0.26	1.8	0.10	0.7	0.04
			17D	-	6.78	46.6	0.45	3.1	0.17	1.1	0.05
		019	4D	--	5.39	74.1	0.11	1.5	0.03	0.4	0.01
			17D	-	3.18	43.2	0.15	2.1	0.15	2.1	0.01
		020	4D	--	8.33	69.4	0.17	1.4	0.07	0.5	0.03
			17D	-	4.88	38.1	0.37	2.9	0.11	0.9	0.02
	021	4D	--	5.47	82.5	0.09	1.3	0.05	0.7	0.01	
		17D	-	1.72	49.2	0.06	1.8	0.13	3.7	0.00	

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	LYM 10 <sup>3</sup> /uL	LYM_P %	MONO 10 <sup>3</sup> /uL	MONO_P %	EO 10 <sup>3</sup> /uL	EO_P %	BASO 10 <sup>3</sup> /uL
2	30 µg/day	022	4D	--	5.86	64.7	0.20	2.2	0.18	2.0	0.04
			17D	-	4.11	43.5	0.25	2.7	0.17	1.8	0.02
		023	17D	-	1.84	46.5	0.14	3.5	0.06	1.4	0.01
			17D	-	4.03	42.0	0.17	1.8	0.26	2.7	0.01
		025	17D	-	5.55	46.5	0.35	2.9	0.13	1.0	0.02
			22R	-	2.93	68.5	0.09	2.2	0.04	1.0	0.00
		027	22R	-	4.98	78.0	0.11	1.7	0.09	1.5	0.01
			22R	-	4.61	83.7	0.08	1.5	0.06	1.2	0.01
		029	22R	-	4.85	76.9	0.12	1.9	0.08	1.3	0.01
		030	22R	-	5.99	80.6	0.13	1.8	0.10	1.4	0.01
3	30 µg /day	031	4D	--	5.57	72.9	0.19	2.5	0.07	0.9	0.03
			17D	-	2.82	41.9	0.11	1.6	0.12	1.7	0.01
		032	4D	--	8.07	72.9	0.22	2.0	0.05	0.4	0.04
			17D	-	4.68	44.5	0.33	3.2	0.14	1.3	0.02
		033	4D	--	8.85	72.0	0.24	1.9	0.07	0.5	0.05
			17D	-	3.41	36.9	0.29	3.2	0.09	1.0	0.02
		034	4D	--	6.69	72.3	0.21	2.3	0.09	1.0	0.03

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	LYM 10 <sup>3</sup> /uL	LYM_P %	MONO 10 <sup>3</sup> /uL	MONO_P %	EO 10 <sup>3</sup> /uL	EO_P %	BASO 10 <sup>3</sup> /uL
3	30 µg /day	034	17D	-	2.74	34.2	0.37	4.6	0.09	1.1	0.02
		035	4D	--	5.91	73.2	0.18	2.2	0.15	1.9	0.02
			17D	-	3.27	41.9	0.19	2.4	0.17	2.1	0.01
		036	4D	--	7.20	71.7	0.23	2.3	0.12	1.2	0.06
			17D	-	4.11	40.6	0.33	3.3	0.07	0.7	0.03
		037	4D	--	6.92	71.9	0.23	2.4	0.09	0.9	0.03
			17D	-	3.63	45.2	0.24	3.0	0.11	1.3	0.02
		038	17D	-	3.64	40.0	0.22	2.4	0.27	2.9	0.02
		039	17D	-	3.40	39.5	0.23	2.7	0.10	1.1	0.01
		040	17D	-	3.77	47.0	0.23	2.9	0.06	0.8	0.03
		041	22R	-	3.34	68.0	0.09	1.8	0.09	1.9	0.01
		042	22R	-	2.10	71.6	0.08	2.7	0.03	1.2	0.00
		043	22R	-	4.29	72.8	0.12	2.1	0.07	1.2	0.01
		044	22R	-	3.34	64.7	0.13	2.6	0.13	2.4	0.01
		045	22R	-	3.97	71.0	0.10	1.8	0.05	0.9	0.01

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	BASO_P %	LUC 10 <sup>3</sup> /uL	LUC_P %	MORPH none	POIK none	BURR none	SCHISTO none
1	0 µg/day	001	4D	--	0.3	0.06	0.7	-	-	-	-
			17D	-	0.1	0.03	0.7	Reported	-	-	-
		002	4D	--	0.1	0.04	0.7	-	-	-	-
			17D	-	0.0	0.03	0.8	Normal	-	-	-
		003	4D	--	0.1	0.03	0.4	-	-	-	-
			17D	-	-	CL	-	CL	-	CL	-
		004	4D	--	0.2	0.05	0.6	-	-	-	-
			17D	-	0.1	0.04	0.7	Normal	-	-	-
		005	4D	--	0.3	0.06	0.7	-	-	-	-
			17D	-	0.0	0.01	0.6	Normal	-	-	-
		006	4D	--	0.3	0.04	0.6	-	-	-	-
			17D	-	0.2	0.03	0.5	Normal	-	-	-
		007	4D	--	0.3	0.04	0.5	-	-	-	-
			17D	-	0.2	0.04	0.7	-	-	-	-
		008	17D	-	0.0	0.03	0.7	-	-	-	-
		009	17D	-	0.1	0.00	0.1	-	-	-	-
		010	17D	-	0.1	0.02	0.6	-	-	-	-

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**Appendix 7**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	BASO_P %	LUC 10 <sup>3</sup> /uL	LUC_P %	MORPH none	POIK none	BURR none	SCHISTO none	
1	0 µg/day	011	22R	-	0.2	0.01	0.3	Reported	-	Present	-	
		012	22R	-	0.1	0.02	0.4	Reported	-	Present	-	
		013	22R	-	0.3	0.08	0.9	Reported	-	Present	-	
		014	22R	-	0.1	0.03	0.7	Normal	-	-	-	
		015	22R	-	0.1	0.03	0.5	Normal	-	-	-	
2	30 µg/day	016	4D	--	0.3	0.43	3.3	-	-	-	-	
			17D	-	0.2	0.34	5.3	SR	Reported	-	-	-
		017	4D	--	0.4	0.30	2.4	-	-	-	-	
			17D	-	0.2	0.22	2.5	Reported	-	-	-	
		018	4D	--	0.3	0.21	1.5	-	-	-	-	
			17D	-	0.3	0.53	3.7	Normal	-	-	-	
		019	4D	--	0.2	0.07	0.9	-	-	-	-	
			17D	-	0.2	0.10	1.3	Reported	-	-	-	
		020	4D	--	0.3	0.17	1.4	-	-	-	-	
			17D	-	0.2	0.13	1.0	Reported	-	-	-	
	021	4D	--	0.2	0.07	1.1	-	-	-	-		
		17D	-	0.1	0.13	3.8	-	-	-	-		

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	BASO_P %	LUC 10 <sup>3</sup> /uL	LUC_P %	MORPH none	POIK none	BURR none	SCHISTO none
2	30 µg/day	022	4D	--	0.4	0.06	0.6	-	-	-	-
			17D	-	0.2	0.10	1.1	-	-	-	-
		023	17D	-	0.1	0.06	1.6	-	-	-	-
			17D	-	0.1	0.17	1.8	-	-	-	-
		025	17D	-	0.2	0.31	2.6	-	-	-	-
			22R	-	0.1	0.03	0.7	Reported	-	Present	-
		227	22R	-	0.2	0.05	0.7	Reported	-	Present	-
		228	22R	-	0.2	0.05	0.9	Reported	-	Present	-
		229	22R	-	0.2	0.05	0.8	Normal	-	-	-
		230	22R	-	0.2	0.06	0.8	Normal	-	-	-
3	30 µg /day	031	4D	--	0.4	0.40	5.3	FT	-	-	-
			17D	-	0.2	0.31	4.7	Normal	-	-	-
		032	4D	--	0.4	0.09	0.8	-	-	-	-
			17D	-	0.2	0.25	2.4	Reported	-	-	-
		033	4D	--	0.4	0.20	1.7	-	-	-	-
			17D	-	0.2	0.38	4.1	-	-	-	-
		034	4D	--	0.3	0.16	1.7	-	-	-	-

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	BASO_P %	LUC 10 <sup>3</sup> /uL	LUC_P %	MORPH none	POIK none	BURR none	SCHISTO none	
3	30 µg /day	034	17D	-	0.2	0.56	7.0	SR	Reported	-	-	-
		035	4D	--	0.3	0.15	1.8		-	-	-	-
			17D	-	0.1	0.41	5.3	SR	Reported	-	-	-
		036	4D	--	0.6	0.10	0.9		-	-	-	-
			17D	-	0.3	0.24	2.3		-	-	-	-
		037	4D	--	0.3	0.18	1.8		-	-	-	-
			17D	-	0.3	0.21	2.6		-	-	-	-
		038	17D	-	0.2	0.38	4.2		-	-	-	-
		039	17D	-	0.1	0.15	1.7		-	-	-	-
		040	17D	-	0.3	0.34	4.3		Reported	-	Present	-
		041	22R	-	0.1	0.02	0.5		Reported	-	-	-
		042	22R	-	0.0	0.02	0.6		Reported	-	Present	-
		043	22R	-	0.1	0.02	0.4		Normal	-	-	-
		044	22R	-	0.1	0.03	0.6		Normal	-	-	-
		045	22R	-	0.1	0.04	0.7		Normal	-	-	-

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	SPHERO none	SIDERO none	TARGET none	TEAR none	B_STIP none	HJ none	AGGL none	
1	0 µg/day	001	4D	--	-	-	-	-	-	-	-	
			17D	-	-	-	-	-	-	-	-	
		002	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
		003	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
		004	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
		005	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
		006	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
		007	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
		008	17D	-	-	-	-	-	-	-	-	-
		009	17D	-	-	-	-	-	-	-	-	-
		010	17D	-	-	-	-	-	-	-	-	-

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	SPHERO none	SIDERO none	TARGET none	TEAR none	B_STIP none	HJ none	AGGL none
1	0 µg/day	011	22R	-	-	-	-	-	-	-	-
		012	22R	-	-	-	-	-	-	-	-
		013	22R	-	-	-	-	-	-	-	-
		014	22R	-	-	-	-	-	-	-	-
		015	22R	-	-	-	-	-	-	-	-
2	30 µg/day	016	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-
		017	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-
		018	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-
		019	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-
		020	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-
	021	4D	--	-	-	-	-	-	-	-	
		17D	-	-	-	-	-	-	-	-	

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**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	SPHERO none	SIDERO none	TARGET none	TEAR none	B_STIP none	HJ none	AGGL none	
2	30 µg/day	022	4D	--	-	-	-	-	-	-	-	
			17D	-	-	-	-	-	-	-	-	
		023	17D	-	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
			22R	-	-	-	-	-	-	-	-	-
			22R	-	-	-	-	-	-	-	-	-
			22R	-	-	-	-	-	-	-	-	-
			22R	-	-	-	-	-	-	-	-	-
3	30 µg /day	031	4D	--	-	-	-	-	-	-	-	
			17D	-	-	-	-	-	-	-	-	
		032	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
			4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
			4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
034	4D	--	-	-	-	-	-	-	-	-		

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**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	SPHERO none	SIDERO none	TARGET none	TEAR none	B_STIP none	HJ none	AGGL none
3	30 µg /day	034	17D	-	-	-	-	-	-	-	-
		035	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-
		036	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-
		037	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-
		038	17D	-	-	-	-	-	-	-	-
		039	17D	-	-	-	-	-	-	-	-
		040	17D	-	-	-	-	-	-	-	-
		041	22R	-	-	-	-	-	-	-	-
		042	22R	-	-	-	-	-	-	-	-
		043	22R	-	-	-	-	-	-	-	-
		044	22R	-	-	-	-	-	-	-	-
		045	22R	-	-	-	-	-	-	-	-

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	CLPLT none	HGB_CR YS none	BASOPH none	ACANTH none	STOM none	OTHERM none	DOHLE none	
1	0 µg/day	001	4D	--	-	-	-	-	-	-	-	
			17D	-	Present	-	-	-	-	-	-	
		002	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
		003	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
		004	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
		005	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
		006	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
		007	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
		008	17D	-	-	-	-	-	-	-	-	-
		009	17D	-	-	-	-	-	-	-	-	-
		010	17D	-	-	-	-	-	-	-	-	-

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**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	CLPLT none	HGB_CR YS none	BASOPH none	ACANTH none	STOM none	OTHERM none	DOHLE none
1	0 µg/day	011	22R	-	-	-	-	-	-	-	-
		012	22R	-	-	-	-	-	-	-	-
		013	22R	-	-	-	-	-	-	-	-
		014	22R	-	-	-	-	-	-	-	-
		015	22R	-	-	-	-	-	-	-	-
2	30 µg/day	016	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-
		017	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-
		018	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-
		019	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-
		020	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-
	021	4D	--	-	-	-	-	-	-	-	
		17D	-	-	-	-	-	-	-	-	

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**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	CLPLT none	HGB_CR YS none	BASOPH none	ACANTH none	STOM none	OTHERM none	DOHLE none	
2	30 µg/day	022	4D	--	-	-	-	-	-	-	-	
			17D	-	-	-	-	-	-	-	-	
		023	17D	-	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
			22R	-	-	-	-	-	-	-	-	-
			22R	-	-	-	-	-	-	-	-	-
			22R	-	-	-	-	-	-	-	-	-
			22R	-	-	-	-	-	-	-	-	-
3	30 µg /day	031	4D	--	-	-	-	-	-	-	-	
			17D	-	-	-	-	-	-	-	-	
		032	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
		033	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
		034	4D	--	-	-	-	-	-	-	-	-

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**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	CLPLT none	HGB_CR YS none	BASOPH none	ACANTH none	STOM none	OTHERM none	DOHLE none
3	30 µg /day	034	17D	-	-	-	-	-	-	-	-
		035	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-
		036	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-
		037	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-
		038	17D	-	-	-	-	-	-	-	-
		039	17D	-	-	-	-	-	-	-	-
		040	17D	-	-	-	-	-	-	-	-
		041	22R	-	-	-	-	-	-	-	-
		042	22R	-	-	-	-	-	-	-	-
		043	22R	-	-	-	-	-	-	-	-
		044	22R	-	-	-	-	-	-	-	-
		045	22R	-	-	-	-	-	-	-	-

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	HYSEG none	TOXIC_G none	TOXIC_V none	VACLYM none	PT_Rat sec	APTT sec	FIB mg/dL			
1	0 µg/day	001	4D	--	-	-	-	-	-	-	-			
			17D	-	-	-	-	-	-	CL	-	CL	-	CL
		002	4D	--	-	-	-	-	-	-	-	-	-	
			17D	-	-	-	-	-	-	14.0	14.8	273		
		003	4D	--	-	-	-	-	-	-	-	-		
			17D	-	-	-	-	-	-	-	QN	-	QN	-
		004	4D	--	-	-	-	-	-	-	-	-	-	
			17D	-	-	-	-	-	-	14.8	14.9	249		
		005	4D	--	-	-	-	-	-	-	-	-	-	
			17D	-	-	-	-	-	-	14.4	14.7	239		
		006	4D	--	-	-	-	-	-	-	-	-	-	
			17D	-	-	-	-	-	-	14.6	13.3	275		
		007	4D	--	-	-	-	-	-	-	-	-	-	
			17D	-	-	-	-	-	-	14.9	10.5	RR	240	
		008	17D	-	-	-	-	-	-	14.2	15.1	259		
		009	17D	-	-	-	-	-	-	16.3	16.5	247		
		010	17D	-	-	-	-	-	-	13.9	15.5	243		

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**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	HYSEG none	TOXIC_G none	TOXIC_V none	VACLYM none	PT_Rat sec	APTT sec	FIB mg/dL	
1	0 µg/day	011	22R	-	-	-	-	-	16.2	16.0	307	
		012	22R	-	-	-	-	-	15.8	17.0	250	
		013	22R	-	-	-	-	-	16.7	16.9	278	
		014	22R	-	-	-	-	-	14.4	15.9	225	
		015	22R	-	-	-	-	-	13.6	16.4	264	
2	30 µg/day	016	4D	--	-	-	-	-	-	-	-	
			17D	-	Present	-	-	-	15.4	16.8	618 RR	
		017	4D	--	-	-	-	-	-	-	-	
			17D	-	Present	-	-	-	16.3	16.0	589	
		018	4D	--	-	-	-	-	-	-	-	
			17D	-	-	-	-	-	13.6	16.1	575	
		019	4D	--	-	-	-	-	-	-	-	
			17D	-	Present	-	-	-	-	QN	-	QN
		020	4D	--	-	-	-	-	-	-	-	-
			17D	-	Present	-	-	-	17.7	19.0	520	
021	4D	--	-	-	-	-	-	-	-	-		
	17D	-	-	-	-	-	15.1	10.4	RR	611 RR		

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**Appendix 7**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	HYSEG none	TOXIC_G none	TOXIC_V none	VACLYM none	PT_Rat sec	APTT sec	FIB mg/dL
2	30 µg/day	022	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	16.9	19.3	651 RR
		023	17D	-	-	-	-	-	15.1	15.8	626 RR
			17D	-	-	-	-	-	15.6	18.5	618 RR
		025	17D	-	-	-	-	-	15.0	16.6	562
			22R	-	-	-	-	-	14.9	17.1	276
		027	22R	-	-	-	-	-	18.5	18.4	264
			22R	-	-	-	-	-	17.5	17.9	255
		029	22R	-	-	-	-	-	17.0	18.6	240
			22R	-	-	-	-	-	15.3	16.8	298
3	30 µg /day	031	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	15.5	14.5	678 RR
		032	4D	--	-	-	-	-	-	-	-
			17D	-	Present	-	-	-	15.3	12.8	611 RR
		033	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	16.3	18.2	589
		034	4D	--	-	-	-	-	-	-	-

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	HYSEG none	TOXIC_G none	TOXIC_V none	VACLYM none	PT_Rat sec	APTT sec	FIB mg/dL	
3	30 µg /day	034	17D	-	Present	-	-	-	17.2	16.9	596	
		035	4D	--	-	-	-	-	-	-	-	
			17D	-	Present	-	-	-	16.2	18.1	678 RR	
		036	4D	--	-	-	-	-	-	-	-	
			17D	-	-	-	-	-	16.5	18.2	582	
		037	4D	--	-	-	-	-	-	-	-	
			17D	-	-	-	-	-	17.5	18.0	618 RR	
		038	17D	-	-	-	-	-	16.5	17.3	651 RR	
		039	17D	-	-	-	-	-	16.8	17.0	549	
		040	17D	-	Present	-	-	-	15.7	16.8	509	
		041	22R	-	Present	-	-	-	18.5	18.2	266	
		042	22R	-	-	-	-	-	20.2	CE	17.9	258
		043	22R	-	-	-	-	-	18.8		17.4	256
		044	22R	-	-	-	-	-	20.1	CE	19.2	258
		045	22R	-	-	-	-	-	15.8		17.9	282

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	RBC 10 <sup>6</sup> /uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %
1	0 µg/day	046	4D	--	7.21	13.4	41.0	56.8	18.5	32.6	10.6
			17D	-	7.08	13.4	41.1	58.1	19.0	32.7	11.7
		047	4D	--	8.01	14.5	44.9	56.0	18.0	32.2	11.5
			17D	-	7.61	14.2	42.7	56.1	18.7	33.3	11.5
		048	4D	--	7.69	14.3	45.0	58.5	18.6	31.9	11.3
			17D	-	7.32	13.8	41.4	56.6	18.8	33.2	11.7
		049	4D	--	8.38	15.3	47.3	56.4	18.2	32.3	11.0
			17D	-	7.62	13.7	41.6	54.7	18.0	33.0	10.9
		050	4D	--	7.94	14.7	45.2	57.0	18.6	32.6	11.2
			17D	-	7.32	13.5	41.2	56.3	18.4	32.7	11.0
		051	4D	--	7.96	14.6	45.5	57.2	18.4	32.1	11.0
			17D	-	7.31	13.8	41.6	56.9	18.8	33.1	10.8
		052	4D	--	8.13	14.9	45.5	56.0	18.3	32.7	11.2
			17D	-	7.69	14.3	42.4	55.2	18.5	33.6	10.8
		053	17D	-	7.42	13.6	40.5	54.5	18.3	33.6	11.3
		054	17D	-	7.47	13.8	41.6	55.6	18.5	33.3	12.0
		055	17D	-	7.39	14.2	42.6	57.6	19.2	33.3	11.6

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**Appendix 7**  
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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	RBC 10 <sup>6</sup> /uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %		
1	0 µg/day	056	22R	-	7.39	12.9	39.2	53.1	17.4	32.9	11.2		
		057	22R	-	7.06	14.0	40.7	-	RW	19.8	34.3	-	RW
		058	22R	-	6.97	13.5	41.0	58.8	19.4	33.0	10.8		
		059	22R	-	7.25	13.2	39.3	54.2	18.2	33.6	10.8		
		060	22R	-	7.64	14.6	43.7	57.1	19.1	33.5	10.4		
2	30 µg/day	061	4D	--	7.59	14.4	44.4	58.5	19.0	32.5	10.9		
			17D	-	6.73	12.5	38.2	56.8	18.5	32.6	12.3		
		062	4D	--	7.09	13.6	41.0	57.8	19.2	33.2	11.3		
			17D	-	6.70	12.1	38.1	56.8	18.1	31.9	13.5		
		063	4D	--	7.22	12.7	41.1	56.9	17.6	31.0	12.1		
			17D	-	6.81	11.9	37.2	54.6	17.5	32.1	13.0		
		064	4D	--	7.49	14.0	42.9	57.3	18.7	32.6	11.3		
			17D	-	7.09	12.9	39.5	55.7	18.1	32.6	12.6		
		065	4D	--	7.30	12.8	38.7	53.1	17.6	33.1	11.6		
			17D	-	6.75	12.1	36.7	54.3	17.9	33.0	15.8		
		066	4D	--	7.39	13.8	41.9	56.6	18.7	33.0	11.0		
	17D	-	6.88	12.6	37.9	55.1	18.2	33.1	12.6				

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**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	RBC 10 <sup>6</sup> /uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %	
2	30 µg/day	067	4D	--	7.59	13.6	42.5	55.9	17.9	32.0	11.5	
			17D	-	-	NS	-	NS	-	NS	-	NS
		068	17D	-	7.03	12.1	37.1	52.8	17.3	32.7	13.0	
			17D	-	6.65	12.5	38.9	58.5	18.8	32.2	13.5	
			17D	-	7.21	12.7	39.2	54.3	17.5	32.3	13.8	
			22R	-	7.72	13.8	42.2	54.6	17.9	32.8	13.4	
			22R	-	8.03	13.8	41.6	51.8	17.1	33.1	13.1	
			22R	-	7.73	14.0	43.0	55.7	18.1	32.5	13.0	
			22R	-	7.54	13.5	41.7	55.3	17.9	32.4	12.8	
			22R	-	8.17	14.5	43.8	53.7	17.8	33.1	12.9	
3	30 µg /day	076	4D	--	7.49	13.7	42.0	56.0	18.2	32.5	11.5	
			17D	-	6.65	11.7	35.7	53.7	17.6	32.7	13.1	
		077	4D	--	7.07	13.3	41.3	58.3	18.8	32.2	11.5	
			17D	-	-	CL	-	CL	-	CL	-	CL
		078	4D	--	7.67	14.4	42.8	56.2	18.8	33.6	13.4	
			17D	-	7.11	13.2	39.0	-	RW	18.5	33.8	-
		079	4D	--	7.48	13.9	43.3	57.9	18.5	32.0	11.5	

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	RBC 10 <sup>6</sup> /uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %			
3	30 µg /day	079	17D	-	6.43	11.9	37.1	57.6	18.4	32.0	13.8			
		080	4D	--	7.70	13.2	41.8	54.3	17.2	31.7	12.2			
			17D	-	6.89	12.4	37.1	53.9	18.0	33.3	14.5			
		081	4D	--	7.43	12.6	39.3	52.9	17.0	32.1	11.9			
			17D	-	6.84	11.5	35.4	51.7	16.8	32.5	13.0			
		082	4D	--	7.45	13.8	42.2	56.6	18.6	32.8	11.8			
			17D	-	6.52	11.9	36.1	55.4	18.3	33.0	12.9			
		083	17D	-	7.41	13.1	40.1	54.1	17.6	32.6	13.0			
		084	17D	-	-	CL	-	CL	-	CL	-	CL	-	CL
		085	17D	-	-	QN	-	QN	-	QN	-	QN	-	QN
		086	22R	-	7.57	14.0	43.0	56.8	18.5	32.6	12.9			
		087	22R	-	7.68	13.2	40.1	52.2	17.2	32.9	14.0			
		088	22R	-	7.86	14.4	43.3	55.1	18.4	33.3	13.1			
		089	22R	-	7.96	14.6	45.7	57.4	18.3	32.0	13.7			
		090	22R	-	7.45	14.5	42.8	57.4	19.5	34.0	12.9			

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**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	RETIC_P %	RETIC 10 <sup>3</sup> /uL	PLT 10 <sup>3</sup> /uL	MPV fL	WBC 10e3/uL	NEUT 10 <sup>3</sup> /uL	NEUT_P %
1	0 µg/day	046	4D	--	3.7	267	880	7.0	11.0	3.68	33.3
			17D	-	2.8	198	974	9.3	2.9	0.85	29.3
		047	4D	--	4.0	320	704	10.0	5.1	0.46	9.0
			17D	-	2.3	175	712	10.4	2.3	0.48	20.5
		048	4D	--	3.4	261	938	8.8	6.1	0.42	6.8
			17D	-	1.7	124	998	9.3	1.6	0.27	16.5
		049	4D	--	4.0	335	1014	8.3	5.2	0.62	12.0
			17D	-	2.2	168	980	8.9	2.9	0.51	17.5
		050	4D	--	4.6	365	1073	8.8	6.5	0.43	6.6
			17D	-	2.3	168	1050	9.2	2.2	0.55	24.3
		051	4D	--	3.4	271	953	9.2	4.2	0.37	8.8
			17D	-	2.1	154	882	SR	10.1	2.1	0.38
		052	4D	--	3.6	293	928	8.6	4.0	0.46	11.7
			17D	-	1.4	108	1019	9.2	2.0	0.28	14.2
		053	17D	-	2.4	178	929	10.0	1.7	0.36	21.5
		054	17D	-	2.5	187	701	9.5	2.1	0.23	11.3
		055	17D	-	3.1	229	824	9.1	1.8	0.18	10.1

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	RETIC_P %	RETIC 10 <sup>3</sup> /uL	PLT 10 <sup>3</sup> /uL	MPV fL	WBC 10e3/uL	NEUT 10 <sup>3</sup> /uL	NEUT_P %		
1	0 µg/day	056	22R	-	2.6	192	843	9.0	1.7	0.25	14.6		
		057	22R	-	2.0	141	651	9.1	2.1	0.23	10.9		
		058	22R	-	2.7	188	803	9.2	2.4	0.33	14.0		
		059	22R	-	1.9	138	824	9.9	1.7	0.26	15.6		
		060	22R	-	1.4	107	817	8.8	3.8	0.19	4.9	SR	
2	30 µg/day	061	4D	--	1.8	137	1130	8.7	8.5	2.66	31.2		
			17D	-	4.0	269	730	9.0	3.8	1.82	48.4		
		062	4D	--	1.6	113	966	8.9	8.0	2.43	30.5		
			17D	-	3.2	214	662	SR	9.5	6.2	SR	3.22	52.4
		063	4D	--	2.3	166	910	9.1	5.2	1.24	23.9		
			17D	-	3.0	204	759	9.7	4.0	1.85	46.0		
		064	4D	--	2.5	187	1019	9.2	6.0	1.47	24.4		
			17D	-	2.9	206	699	9.5	4.9	1.74	35.4		
		065	4D	--	1.2	88	956	8.7	7.7	2.84	37.0		
			17D	-	2.8	189	871	9.3	5.6	3.12	56.2		
	066	4D	--	1.4	103	1042	9.2	11.4	3.02	26.5			
		17D	-	2.3	158	827	9.4	8.0	3.58	44.7			

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	RETIC_P %	RETIC 10 <sup>3</sup> /uL	PLT 10 <sup>3</sup> /uL	MPV fL	WBC 10e3/uL	NEUT 10 <sup>3</sup> /uL	NEUT_P %	
2	30 µg/day	067	4D	--	1.5	114	1004	8.6	8.1	2.48	30.5	
			17D	-	-	NS	-	NS	-	NS	-	NS
		068	17D	-	-	3.0	211	882	9.5	6.6	2.06	31.4
				-	-	5.2	346	881	9.5	6.5	2.81	43.0
		070	17D	-	-	2.8	202	691	9.2	5.7	2.02	35.6
				-	-	2.2	170	738	9.5	2.5	0.33	13.3
		072	22R	-	-	2.0	161	953	8.6	1.7	0.25	14.6
				-	-	1.7	131	797	9.1	3.2	0.96	29.8
		074	22R	-	-	2.2	166	905	9.1	3.4	0.47	13.8
				-	-	1.8	147	798	8.8	2.3	0.40	17.7
3	30 µg /day	076	4D	--	1.3	97	849	9.5	7.6	2.67	35.4	
			17D	-	3.0	200	714	9.8	6.1	3.08	50.6	
		077	4D	--	--	2.6	184	1066	9.0	8.0	3.30	41.4
				-	-	-	CL	-	CL	-	CL	-
		078	4D	--	--	0.9	69	913	9.3	9.8	2.66	27.0
				-	-	2.5	178	682	10.2	9.0	4.07	45.0
		079	4D	--	--	2.1	157	1160	8.9	7.9	2.58	32.7

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	RETIC_P %	RETIC 10 <sup>3</sup> /uL	PLT 10 <sup>3</sup> /uL	MPV fL	WBC 10e3/uL	NEUT 10 <sup>3</sup> /uL	NEUT_P %			
3	30 µg /day	079	17D	-	4.6	296	799	9.9	2.5	1.08	43.4			
		080	4D	--	1.7	131	1102	RP	7.5	RP	9.4	2.56	27.2	
			17D	-	2.4	165	944	9.9	6.1	2.78	45.3			
		081	4D	--	1.9	141	1044	8.6	7.9	2.59	32.8			
			17D	-	2.6	178	907	8.5	4.6	2.25	48.7			
		082	4D	--	2.1	156	681	10.1	9.4	3.79	40.3			
			17D	-	3.5	228	492	10.7	9.7	4.76	49.0			
		083	17D	-	2.4	178	765	9.1	6.6	2.13	32.0			
		084	17D	-	-	CL	-	CL	-	CL	-	CL	-	CL
		085	17D	-	-	QN	-	QN	-	QN	-	QN	-	QN
		086	22R	-	1.7	129	729	9.0	1.4	0.30	21.7			
		087	22R	-	1.6	123	744	8.8	3.2	0.33	10.3			
		088	22R	-	1.3	102	872	9.2	1.7	0.21	12.5			
		089	22R	-	2.8	223	767	9.7	4.2	0.31	7.5			
		090	22R	-	1.4	104	798	9.2	3.1	0.24	7.8			

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	LYM 10 <sup>3</sup> /uL	LYM_P %	MONO 10 <sup>3</sup> /uL	MONO_P %	EO 10 <sup>3</sup> /uL	EO_P %	BASO 10 <sup>3</sup> /uL
1	0 µg/day	046	4D	--	6.89	62.4	0.30	2.7	0.06	0.5	0.02
			17D	-	1.91	66.3	0.07	2.5	0.04	1.5	0.00
		047	4D	--	4.48	88.0	0.05	1.0	0.07	1.3	0.01
			17D	-	1.79	76.9	0.03	1.1	0.02	1.0	0.00
		048	4D	--	5.56	91.0	0.05	0.8	0.05	0.8	0.01
			17D	-	1.31	80.0	0.03	2.1	0.02	1.2	0.00
		049	4D	--	4.41	84.7	0.07	1.3	0.06	1.2	0.01
			17D	-	2.22	76.0	0.10	3.6	0.05	1.9	0.01
		050	4D	--	5.93	91.1	0.06	1.0	0.05	0.8	0.01
			17D	-	1.60	71.2	0.05	2.0	0.04	1.9	0.00
		051	4D	--	3.75	88.8	0.05	1.1	0.04	1.0	0.00
			17D	-	1.56	75.4	0.08	3.8	0.04	1.8	0.00
		052	4D	--	3.36	84.6	0.07	1.7	0.07	1.6	0.00
			17D	-	1.66	83.2	0.03	1.4	0.01	0.7	0.00
		053	17D	-	1.22	73.6	0.05	2.7	0.02	1.4	0.00
		054	17D	-	1.74	84.7	0.04	1.9	0.03	1.7	0.00
		055	17D	-	1.50	83.7	0.08	4.3	0.02	1.1	0.00

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**Appendix 7**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	LYM 10 <sup>3</sup> /uL	LYM_P %	MONO 10 <sup>3</sup> /uL	MONO_P %	EO 10 <sup>3</sup> /uL	EO_P %	BASO 10 <sup>3</sup> /uL
1	0 µg/day	056	22R	-	1.40	81.2	0.03	1.7	0.03	1.8	0.00
		057	22R	-	1.77	85.3	0.04	2.0	0.02	1.1	0.00
		058	22R	-	1.97	82.5	0.04	1.8	0.03	1.1	0.00
		059	22R	-	1.38	81.5	0.01	0.8	0.03	1.6	0.00
		060	22R	-	3.56	92.8	0.02	0.6	0.05	1.2	0.00
2	30 µg/day	061	4D	--	5.47	64.1	0.16	1.9	0.10	1.2	0.02
			17D	-	1.72	45.7	0.12	3.2	0.05	1.4	0.00
		062	4D	--	4.92	61.6	0.19	2.4	0.11	1.4	0.02
			17D	-	2.30	37.4	0.19	3.0	0.19	3.1	0.01
		063	4D	--	3.74	71.7	0.10	2.0	0.07	1.3	0.01
			17D	-	1.92	47.6	0.11	2.6	0.11	2.7	0.01
		064	4D	--	4.25	70.8	0.14	2.3	0.06	1.0	0.00
			17D	-	2.86	58.2	0.15	3.0	0.07	1.5	0.01
		065	4D	--	4.33	56.5	0.27	3.5	0.10	1.3	0.02
			17D	-	2.14	38.6	0.13	2.4	0.08	1.5	0.00
	066	4D	--	7.90	69.2	0.21	1.9	0.11	1.0	0.03	
		17D	-	4.00	50.0	0.20	2.5	0.11	1.3	0.01	

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**Appendix 7**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	LYM 10 <sup>3</sup> /uL	LYM_P %	MONO 10 <sup>3</sup> /uL	MONO_P %	EO 10 <sup>3</sup> /uL	EO_P %	BASO 10 <sup>3</sup> /uL				
2	30 µg/day	067	4D	--	5.34	65.8	0.16	1.9	0.06	0.8	0.02				
			17D	-	-	NS	-	NS	-	NS	-	NS			
		068	17D	068	17D	-	4.04	61.5	0.19	3.0	0.10	1.4	0.01		
					17D	-	3.43	52.6	0.16	2.5	0.05	0.7	0.01		
					17D	-	3.09	54.4	0.14	2.5	0.07	1.3	0.01		
					22R	-	2.07	83.4	0.04	1.6	0.03	1.3	0.00		
					22R	-	1.39	81.0	0.04	2.3	0.03	1.7	0.00		
					22R	-	2.16	67.1	0.06	2.0	0.01	0.4	0.00		
					22R	-	2.88	83.5	0.04	1.1	0.03	0.8	0.00		
					22R	-	1.75	77.5	0.06	2.6	0.04	1.6	0.00		
3	30 µg /day	076	4D	--	4.38	57.9	0.25	3.3	0.12	1.6	0.02				
			17D	-	2.61	43.0	0.12	2.0	0.10	1.7	0.01				
		077	4D	077	4D	--	4.31	54.1	0.15	1.9	0.12	1.5	0.02		
					17D	-	-	CL	-	CL	-	CL	-	CL	
		078	4D	078	4D	--	6.60	67.1	0.20	2.1	0.20	2.1	0.03		
					17D	-	4.29	47.5	0.18	2.0	0.11	1.3	0.01		
					4D	079	4D	--	4.89	62.0	0.18	2.3	0.10	1.3	0.02

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**Appendix 7**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	LYM 10 <sup>3</sup> /uL	LYM_P %	MONO 10 <sup>3</sup> /uL	MONO_P %	EO 10 <sup>3</sup> /uL	EO_P %	BASO 10 <sup>3</sup> /uL			
3	30 µg /day	079	17D	-	1.14	45.8	0.09	3.7	0.03	1.4	0.00			
		080	4D	--	6.35	67.6	0.25	2.7	0.09	1.0	0.03			
			17D	-	2.91	47.5	0.21	3.4	0.14	2.3	0.01			
		081	4D	--	4.61	58.3	0.33	4.2	0.09	1.1	0.03			
			17D	-	2.03	43.9	0.12	2.6	0.08	1.7	0.01			
		082	4D	--	5.04	53.7	0.28	3.0	0.14	1.5	0.02			
			17D	-	4.29	44.2	0.26	2.7	0.15	1.5	0.02			
		083	17D	-	3.94	59.3	0.25	3.7	0.07	1.1	0.01			
		084	17D	-	-	CL	-	CL	-	CL	-	CL	-	CL
		085	17D	-	-	QN	-	QN	-	QN	-	QN	-	QN
		086	22R	-	1.03	73.8	0.03	2.3	0.02	1.8	0.00			
		087	22R	-	2.79	86.4	0.06	1.8	0.02	0.7	0.00			
		088	22R	-	1.42	82.5	0.05	2.8	0.03	1.5	0.00			
		089	22R	-	3.63	87.2	0.10	2.5	0.07	1.6	0.01			
		090	22R	-	2.71	87.8	0.06	2.1	0.04	1.4	0.00			

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**Appendix 7**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	BASO_P %	LUC 10 <sup>3</sup> /uL	LUC_P %	MORPH none	POIK none	BURR none	SCHISTO none
1	0 µg/day	046	4D	--	0.2	0.09	0.8	-	-	-	-
			17D	-	0.0	0.01	0.5	Normal	-	-	-
		047	4D	--	0.2	0.02	0.4	-	-	-	-
			17D	-	0.1	0.01	0.4	Normal	-	-	-
		048	4D	--	0.2	0.03	0.5	-	-	-	-
			17D	-	0.0	0.00	0.2	Normal	-	-	-
		049	4D	--	0.1	0.03	0.6	-	-	-	-
			17D	-	0.2	0.02	0.8	Normal	-	-	-
		050	4D	--	0.1	0.02	0.4	-	-	-	-
			17D	-	0.0	0.01	0.4	-	-	-	-
		051	4D	--	0.1	0.01	0.3	-	-	-	-
			17D	-	0.0	0.01	0.7	Normal	-	-	-
		052	4D	--	0.1	0.01	0.4	-	-	-	-
			17D	-	0.0	0.01	0.3	-	-	-	-
		053	17D	-	0.1	0.01	0.6	-	-	-	-
		054	17D	-	0.0	0.01	0.4	-	-	-	-
		055	17D	-	0.1	0.01	0.7	-	-	-	-

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**Appendix 7**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	BASO_P %	LUC 10 <sup>3</sup> /uL	LUC_P %	MORPH none	POIK none	BURR none	SCHISTO none
1	0 µg/day	056	22R	-	0.2	0.01	0.5	Normal	-	-	-
		057	22R	-	0.1	0.01	0.6	Normal	-	-	-
		058	22R	-	0.0	0.02	0.7	Normal	-	-	-
		059	22R	-	0.0	0.01	0.6	Normal	-	-	-
		060	22R	-	0.1	0.02	0.5	Reported	-	Present	-
2	30 µg/day	061	4D	--	0.2	0.13	1.5	-	-	-	-
			17D	-	0.0	0.05	1.3	Reported	-	-	-
		062	4D	--	0.2	0.32	4.0	-	-	-	-
			17D	-	0.2	0.24	3.9	Reported	-	-	-
		063	4D	--	0.2	0.05	1.0	-	-	-	-
			17D	-	0.1	0.04	0.9	Reported	-	-	-
		064	4D	--	0.1	0.08	1.3	-	-	-	-
			17D	-	0.1	0.09	1.8	Reported	-	Present	-
		065	4D	--	0.3	0.11	1.4	-	-	-	-
			17D	-	0.1	0.07	1.2	-	-	-	-
		066	4D	--	0.2	0.14	1.2	-	-	-	-
	17D	-	0.1	0.12	1.5	-	-	-	-		

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	BASO_P %	LUC 10 <sup>3</sup> /uL	LUC_P %	MORPH none	POIK none	BURR none	SCHISTO none
2	30 µg/day	067	4D	--	0.2	0.05	0.7	-	-	-	-
			17D	-	-	NS	-	NS	-	NS	-
		068	17D	-	0.2	0.17	2.5	-	-	-	-
			069	17D	-	0.1	0.07	1.1	-	-	-
		070	17D	-	0.2	0.34	6.0	SR	Reported	-	-
			071	22R	-	0.1	0.00	0.1	Normal	-	-
		072	22R	-	0.0	0.01	0.5	Normal	-	-	-
			073	22R	-	0.0	0.02	0.7	Normal	-	-
		074	22R	-	0.1	0.02	0.6	Reported	-	Present	-
			075	22R	-	0.2	0.01	0.5	Reported	-	Present
3	30 µg /day	076	4D	--	0.3	0.12	1.6	-	-	-	-
			17D	-	0.2	0.15	2.4	Reported	-	-	
		077	4D	--	0.3	0.07	0.9	-	-	-	-
			17D	-	-	CL	-	CL	-	CL	-
		078	4D	--	0.3	0.14	1.4	-	-	-	-
			17D	-	0.2	0.37	4.1	Reported	-	-	-
		079	4D	--	0.2	0.11	1.4	-	-	-	-

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**Appendix 7**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	BASO_P %	LUC 10 <sup>3</sup> /uL	LUC_P %	MORPH none	POIK none	BURR none	SCHISTO none			
3	30 µg /day	079	17D	-	0.2	0.14	5.6	SR	Reported	-	-	-		
		080	4D	--	0.3	0.11	1.2	-	-	-	-	-		
			17D	-	0.2	0.08	1.3	Reported	-	Present	-	-		
		081	4D	--	0.3	0.26	3.3	-	-	-	-	-		
			17D	-	0.2	0.13	2.8	-	-	-	-	-		
		082	4D	--	0.2	0.12	1.3	-	-	-	-	-		
			17D	-	0.2	0.22	2.3	Reported	-	Present	-	-		
		083	17D	-	0.2	0.24	3.7	-	-	-	-	-		
		084	17D	-	-	CL	-	CL	-	CL	-	CL	-	CL
		085	17D	-	-	QN	-	QN	-	QN	-	QN	-	QN
		086	22R	-	0.1	0.00	0.3	Normal	-	-	-	-		
		087	22R	-	0.0	0.03	0.9	Normal	-	-	-	-		
		088	22R	-	0.3	0.01	0.4	Normal	-	-	-	-		
		089	22R	-	0.2	0.04	0.9	Reported	-	Present	-	-		
		090	22R	-	0.1	0.03	0.9	Reported	-	Present	-	-		

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**Appendix 7**  
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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	SPHERO none	SIDERO none	TARGET none	TEAR none	B_STIP none	HJ none	AGGL none	
1	0 µg/day	046	4D	--	-	-	-	-	-	-	-	
			17D	-	-	-	-	-	-	-	-	
		047	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
		048	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
		049	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
		050	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
		051	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
		052	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
		053	17D	-	-	-	-	-	-	-	-	-
		054	17D	-	-	-	-	-	-	-	-	-
		055	17D	-	-	-	-	-	-	-	-	-

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	SPHERO none	SIDERO none	TARGET none	TEAR none	B_STIP none	HJ none	AGGL none
1	0 µg/day	056	22R	-	-	-	-	-	-	-	-
		057	22R	-	-	-	-	-	-	-	-
		058	22R	-	-	-	-	-	-	-	-
		059	22R	-	-	-	-	-	-	-	-
		060	22R	-	-	-	-	-	-	-	-
2	30 µg/day	061	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-
		062	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-
		063	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-
		064	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-
		065	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-
	066	4D	--	-	-	-	-	-	-	-	
		17D	-	-	-	-	-	-	-	-	

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	SPHERO none	SIDERO none	TARGET none	TEAR none	B_STIP none	HJ none	AGGL none	
2	30 µg/day	067	4D	--	-	-	-	-	-	-	-	
			17D	-	-	NS	-	NS	-	NS	-	NS
		068	17D	-	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
			22R	-	-	-	-	-	-	-	-	-
			22R	-	-	-	-	-	-	-	-	-
			22R	-	-	-	-	-	-	-	-	-
			22R	-	-	-	-	-	-	-	-	-
3	30 µg /day	076	4D	--	-	-	-	-	-	-	-	
			17D	-	-	-	-	-	-	-	-	
		077	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	CL	-	CL	-	CL	-	CL
			4D	--	-	-	-	-	-	-	-	-
		078	4D	-	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
			4D	--	-	-	-	-	-	-	-	-
			4D	--	-	-	-	-	-	-	-	-

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**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	SPHERO none	SIDERO none	TARGET none	TEAR none	B_STIP none	HJ none	AGGL none	
3	30 µg /day	079	17D	-	-	-	-	-	-	-	-	
		080	4D	--	-	-	-	-	-	-	-	
			17D	-	-	-	-	-	-	-	-	
		081	4D	--	-	-	-	-	-	-	-	
			17D	-	-	-	-	-	-	-	-	
		082	4D	--	-	-	-	-	-	-	-	
			17D	-	-	-	-	-	-	-	-	
		083	17D	-	-	-	-	-	-	-	-	
		084	17D	-	-	CL	-	CL	-	CL	-	CL
		085	17D	-	-	QN	-	QN	-	QN	-	QN
		086	22R	-	-	-	-	-	-	-	-	-
		087	22R	-	-	-	-	-	-	-	-	-
		088	22R	-	-	-	-	-	-	-	-	-
		089	22R	-	-	-	-	-	-	-	-	-
		090	22R	-	-	-	-	-	-	-	-	-

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**Appendix 7**  
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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	CLPLT none	HGB_CR YS none	BASOPH none	ACANTH none	STOM none	OTHERM none	DOHLE none	
1	0 µg/day	046	4D	--	-	-	-	-	-	-	-	
			17D	-	-	-	-	-	-	-	-	
		047	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
		048	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
		049	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
		050	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
		051	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
		052	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-	-
		053	17D	-	-	-	-	-	-	-	-	-
		054	17D	-	-	-	-	-	-	-	-	-
		055	17D	-	-	-	-	-	-	-	-	-

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**Appendix 7**  
**Hematology and Coagulation**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	CLPLT none	HGB_CR YS none	BASOPH none	ACANTH none	STOM none	OTHERM none	DOHLE none
1	0 µg/day	056	22R	-	-	-	-	-	-	-	-
		057	22R	-	-	-	-	-	-	-	-
		058	22R	-	-	-	-	-	-	-	-
		059	22R	-	-	-	-	-	-	-	-
		060	22R	-	-	-	-	-	-	-	-
2	30 µg/day	061	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-
		062	4D	--	-	-	-	-	-	-	-
			17D	-	Present	-	-	-	-	-	-
		063	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-
		064	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-
		065	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	-	-
	066	4D	--	-	-	-	-	-	-	-	
	17D	-	-	-	-	-	-	-	-	-	

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**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	CLPLT none	HGB_CR YS none	BASOPH none	ACANTH none	STOM none	OTHERM none	DOHLE none		
2	30 µg/day	067	4D	--	-	-	-	-	-	-	-		
			17D	-	-	NS	-	NS	-	NS	-	NS	
		068	17D	17D	-	-	-	-	-	-	-	-	-
				17D	-	-	-	-	-	-	-	-	-
				17D	-	-	-	-	-	-	-	-	-
				17D	-	-	-	-	-	-	-	-	-
				22R	-	-	-	-	-	-	-	-	-
				22R	-	-	-	-	-	-	-	-	-
				22R	-	-	-	-	-	-	-	-	-
				22R	-	-	-	-	-	-	-	-	-
3	30 µg /day	076	4D	--	-	-	-	-	-	-	-		
			17D	-	-	-	-	-	-	-	-		
		077	4D	4D	--	-	-	-	-	-	-	-	-
				17D	-	-	CL	-	CL	-	CL	-	CL
				4D	--	-	-	-	-	-	-	-	-
				17D	-	-	-	-	-	-	-	-	-
				4D	--	-	-	-	-	-	-	-	-
				17D	-	-	-	-	-	-	-	-	-
079	4D	4D	--	-	-	-	-	-	-	-	-		

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**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	CLPLT none	HGB_CR YS none	BASOPH none	ACANTH none	STOM none	OTHERM none	DOHLE none	
3	30 µg /day	079	17D	-	-	-	-	-	-	-	-	
		080	4D	--	-	-	-	-	-	-	-	
			17D	-	-	-	-	-	-	-	-	
		081	4D	--	-	-	-	-	-	-	-	
			17D	-	-	-	-	-	-	-	-	
		082	4D	--	-	-	-	-	-	-	-	
			17D	-	-	-	-	-	-	-	-	
		083	17D	-	-	-	-	-	-	-	-	
		084	17D	-	-	CL	-	CL	-	CL	-	CL
		085	17D	-	-	QN	-	QN	-	QN	-	QN
		086	22R	-	-	-	-	-	-	-	-	-
		087	22R	-	-	-	-	-	-	-	-	-
		088	22R	-	-	-	-	-	-	-	-	-
		089	22R	-	-	-	-	-	-	-	-	-
		090	22R	-	-	-	-	-	-	-	-	-

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	HYSEG none	TOXIC_G none	TOXIC_V none	VACLYM none	PT_Rat sec	APTT sec	FIB mg/dL	
1	0 µg/day	046	4D	--	-	-	-	-	-	-	-	
			17D	-	-	-	-	-	14.4	15.6	215	
		047	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	15.1	16.4	219
		048	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	14.7	16.3	201
		049	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	13.5	15.9	235
		050	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	13.4	14.2	263
		051	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	13.5	15.0	204
		052	4D	--	-	-	-	-	-	-	-	-
			17D	-	-	-	-	-	-	14.6	16.0	220
		053	17D	-	-	-	-	-	-	14.6	15.9	188
		054	17D	-	-	-	-	-	-	14.9	14.9	183
		055	17D	-	-	-	-	-	-	12.5	14.3	244

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	HYSEG none	TOXIC_G none	TOXIC_V none	VACLYM none	PT_Rat sec	APTT sec	FIB mg/dL
1	0 µg/day	056	22R	-	-	-	-	-	14.3	16.2	189
		057	22R	-	-	-	-	-	12.0	15.7	185
		058	22R	-	-	-	-	-	13.3	17.3	173
		059	22R	-	-	-	-	-	13.0	17.8	171
		060	22R	-	-	-	-	-	12.9	17.1	214
2	30 µg/day	061	4D	--	-	-	-	-	-	-	-
			17D	-	Present	-	-	-	15.2	12.7	520
		062	4D	--	-	-	-	-	-	-	-
			17D	-	Present	-	-	-	13.7	15.2	549
		063	4D	--	-	-	-	-	-	-	-
			17D	-	Present	-	-	-	14.2	16.1	462
		064	4D	--	-	-	-	-	-	-	-
			17D	-	Present	-	-	-	17.0	14.3	509
		065	4D	--	-	-	-	-	-	-	-
			17D	-	-	-	-	-	14.8	15.7	526
	066	4D	--	-	-	-	-	-	-	-	
		17D	-	-	-	-	-	14.6	17.0	526	

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	HYSEG none	TOXIC_G none	TOXIC_V none	VACLYM none	PT_Rat sec	APTT sec	FIB mg/dL		
2	30 µg/day	067	4D	--	-	-	-	-	-	-	-		
			17D	-	-	NS	-	NS	-	NS	-	QN	-
		068	17D		-	-	-	-	-	14.5	15.7	504	
					-	-	-	-	15.9	16.0	603	RR	
		070	17D		-	Present	-	-	-	14.1	17.3	678	RR
					-	-	-	-	13.8	17.0	165		
		072	22R		-	-	-	-	-	13.5	16.7	209	
					-	-	-	-	13.9	16.4	210		
		074	22R		-	-	-	-	-	14.7	17.5	197	
					-	-	-	-	12.4	18.7	202		
3	30 µg /day	076	4D	--	-	-	-	-	-	-	-		
			17D	-	Present	-	-	-	14.9	16.7	643	RR	
		077	4D		--	-	-	-	-	-	-	-	
					-	-	CL	-	CL	-	CL	-	QN
		078	4D		--	-	-	-	-	-	-	-	
					-	Present	-	-	-	15.6	16.6	603	RR
		079	4D		--	-	-	-	-	-	-	-	
					-	-	-	-	-	-	-	-	

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	HYSEG none	TOXIC_G none	TOXIC_V none	VACLYM none	PT_Rat sec	APTT sec	FIB mg/dL			
3	30 µg /day	079	17D	-	Present	-	-	-	16.3	16.6	634	RR		
		080	4D	--	-	-	-	-	-	-	-	-		
			17D	-	Present	-	-	-	14.3	16.2	531			
		081	4D	--	-	-	-	-	-	-	-	-		
			17D	-	-	-	-	-	15.2	15.2	520			
		082	4D	--	-	-	-	-	-	-	-	-		
			17D	-	Present	-	-	-	15.6	15.9	499			
		083	17D	-	-	-	-	-	15.3	16.9	603	RR		
		084	17D	-	-	CL	-	CL	-	CL	17.1	8.8	RR	515
		085	17D	-	-	QN	-	QN	-	QN	14.1	10.1	RR	520
		086	22R	-	-	-	-	-	-	12.9	16.2	188		
		087	22R	-	-	-	-	-	-	14.0	17.2	160		
		088	22R	-	-	-	-	-	-	14.0	17.7	182		
		089	22R	-	-	-	-	-	-	14.1	16.2	189		
		090	22R	-	-	-	-	-	-	12.9	17.5	206		

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

<b>Parameter</b>	<b>Description</b>	<b>Parameter</b>	<b>Description</b>
ALT	Alanine Aminotransferase	ICT_IND	Icterus Index
AST	Aspartate Aminotransferase	LIP_IND	Lipemic Index
ALP	Alkaline Phosphatase	A2M	Alpha-2-Macroglobulin
GGT	Gamma Glutamyl Transferase	A1AGP	Alpha-1 Acid Glycoprotein
TBIL	Bilirubin, Total		
CHOL	Cholesterol		
TRIG	Triglycerides		
GLUC	Glucose		
TP	Protein, Total		
ALB	Albumin		
GLOB	Globulin		
AG	Albumin/Globulin Ratio		
BUN	Blood Urea Nitrogen		
CREA	Creatinine		
PHOS	Phosphorus		
CA	Calcium		
NA	Sodium		
K	Potassium		
CL	Chloride		
HEM_IND	Hemolytic Index		

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**3-WEEK RECOVERY**

<b>Comment</b>	<b>Description</b>
NS	No Sample
QN	Quantity Not Sufficient
RR	Result repeated

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

**Footnotes**

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- Value not applicable;

Note: Each interval/day will be concatenated with the phase name abbreviation

HPD = Hours Post Dose; U = Unscheduled

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**Appendix 8**  
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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	ALT U/L	AST U/L	ALP U/L	GGT U/L	TBIL mg/dL	CHOL mg/dL	TRIG mg/dL
1	0 µg/day	001	17D	-	22	63	92	<3	<0.1	46	69
		002	17D	-	18	72	88	<3	<0.1	50	87
		003	17D	-	17	71	79	<3	0.1	62	42
		004	17D	-	20	71	85	<3	<0.1	54	64
		005	17D	-	19	70	145	<3	<0.1	54	64
		006	17D	-	17	76	86	<3	<0.1	44	56
		007	17D	-	20	75	146	<3	<0.1	46	73
		008	4D	---	34	88	130	<3	<0.1	57	35
			17D	-	15	75	74	<3	<0.1	44	30
		009	4D	---	27	99	135	<3	<0.1	60	76
			17D	-	19	80	88	<3	<0.1	57	45
		010	4D	---	32	108	179	<3	<0.1	78	103
			17D	-	14	64	93	<3	<0.1	60	58
		011	4D	---	28	84	173	<3	<0.1	54	59
			22R	-	25	108	85	<3	<0.1	49	42
		012	4D	---	16	96	171	<3	<0.1	61	33
			22R	-	17	89	93	<3	<0.1	56	80

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**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	ALT U/L	AST U/L	ALP U/L	GGT U/L	TBIL mg/dL	CHOL mg/dL	TRIG mg/dL
1	0 µg/day	013	4D	---	27	102	131	<3	<0.1	52	44
			22R	-	18	95	74	<3	<0.1	44	35
		014	4D	---	40	86	134	<3	<0.1	72	91
			22R	-	18	82	63	<3	<0.1	52	37
		015	4D	---	29	93	280	<3	<0.1	70	55
			22R	-	18	85	107	<3	<0.1	63	51
2	30 µg/day	016	17D	-	20	92	93	<3	0.1	37	44
			17D	-	25	94	126	<3	<0.1	33	38
		018	17D	-	24	84	94	<3	0.1	42	44
			17D	-	20	63	105	<3	<0.1	44	38
		020	17D	-	24	105	91	<3	<0.1	40	31
			17D	-	16	68	114	<3	<0.1	41	22
		022	17D	-	18	63	67	<3	<0.1	28	28
			4D	---	36	104	199	<3	<0.1	47	42
		024	17D	-	25	103	132	<3	<0.1	48	30
			4D	---	47	122	193	<3	<0.1	53	32
			17D	-	33	89	100	<3	<0.1	43	28

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**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	ALT U/L	AST U/L	ALP U/L	GGT U/L	TBIL mg/dL	CHOL mg/dL	TRIG mg/dL		
2	30 µg/day	025	4D	---	32	91	214	<3	<0.1	66	44		
			17D	-	24	81	112	<3	<0.1	46	33		
		026	4D	---	33	126	182	<3	<0.1	58	52		
			22R	-	17	103	81	<3	<0.1	68	77		
		027	4D	---	29	108	201	<3	<0.1	43	31		
			22R	-	22	105	75	<3	<0.1	56	46		
		028	4D	---	25	97	136	<3	<0.1	55	34		
			22R	-	16	102	71	<3	<0.1	66	40		
		029	4D	---	34	87	206	<3	<0.1	49	60		
			22R	-	17	86	76	<3	<0.1	59	42		
		030	4D	---	30	90	232	<3	<0.1	49	47		
			22R	-	16	74	95	<3	<0.1	56	49		
		3	30 µg /day	031	17D	-	18	76	97	<3	<0.1	32	29
					032	17D	-	22	72	103	<3	<0.1	30
033	17D				-	21	88	101	<3	<0.1	35	59	
034	17D				-	19	91	95	<3	<0.1	44	28	
035	17D				-	24	94	152	<3	0.1	46	38	

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**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	ALT U/L	AST U/L	ALP U/L	GGT U/L	TBIL mg/dL	CHOL mg/dL	TRIG mg/dL
3	30 µg /day	036	17D	-	19	81	80	<3	<0.1	28	28
		037	17D	-	26	88	113	<3	<0.1	32	31
		038	4D	---	24	94	206	<3	<0.1	39	27
			17D	-	20	94	146	<3	<0.1	38	24
		039	4D	---	32	110	202	<3	<0.1	78	70
			17D	-	16	99	97	<3	<0.1	55	44
		040	4D	---	29	81	216	<3	<0.1	46	61
			17D	-	23	85	116	<3	<0.1	32	40
		041	4D	---	41	82	186	<3	<0.1	58	62
			22R	-	22	93	94	<3	<0.1	54	71
		042	4D	---	27	93	177	<3	<0.1	45	71
			22R	-	16	95	68	<3	<0.1	54	48
		043	4D	---	26	123	143	<3	<0.1	41	26
			22R	-	14	105	66	<3	<0.1	54	38
		044	4D	---	24	97	153	<3	<0.1	37	33
			22R	-	18	96	79	<3	<0.1	55	28
		045	4D	---	27	102	223	<3	<0.1	70	65

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**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	ALT U/L	AST U/L	ALP U/L	GGT U/L	TBIL mg/dL	CHOL mg/dL	TRIG mg/dL
3	30 µg /day	045	22R	-	17	96	110	<3	<0.1	64	43

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**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	AG none	BUN mg/dL	CREA mg/dL
1	0 µg/day	001	17D	-	148	5.7	3.7	2.0	1.8	22	0.3
		002	17D	-	138	5.3	3.4	1.9	1.8	22	0.3
		003	17D	-	136	5.2	3.4	1.8	1.9	18	0.3
		004	17D	-	100	5.2	3.4	1.8	1.9	12	0.2
		005	17D	-	137	5.8	3.8	2.0	1.9	24	0.2
		006	17D	-	138	5.4	3.5	1.9	1.8	16	0.3
		007	17D	-	104	5.8	3.7	2.1	1.8	15	0.2
		008	4D	---	98	5.9	3.8	2.1	1.8	26	0.3
			17D	-	152	5.0	3.3	1.7	1.9	23	0.3
		009	4D	---	100	5.9	3.9	2.0	2.0	20	0.3
			17D	-	128	5.5	3.6	1.9	1.9	18	0.2
		010	4D	---	129	6.2	4.0	2.2	1.8	28	0.3
			17D	-	136	5.0	3.2	1.8	1.8	18	0.2
		011	4D	---	109	5.8	3.8	2.0	1.9	19	0.3
			22R	-	110	5.9	3.8	2.1	1.8	20	0.3
		012	4D	---	124	6.4	4.2	2.2	1.9	29	0.4
	22R	-	157	5.6	3.6	2.0	1.8	16	0.3		

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**Appendix 8**  
**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	AG none	BUN mg/dL	CREA mg/dL
1	0 µg/day	013	4D	---	90	6.1	4.0	2.1	1.9	18	0.3
			22R	-	117	5.9	3.8	2.1	1.8	17	0.3
		014	4D	---	117	6.3	4.1	2.2	1.9	20	0.3
			22R	-	121	6.0	3.8	2.2	1.7	16	0.2
		015	4D	---	123	6.2	4.0	2.2	1.8	30	0.3
			22R	-	180	5.7	3.6	2.1	1.7	16	0.3
2	30 µg/day	016	17D	-	143	5.9	3.6	2.3	1.6	23	0.4
			17D	-	100	5.8	3.6	2.2	1.6	16	0.2
		018	17D	-	142	5.3	3.4	1.9	1.8	24	0.3
		019	17D	-	129	5.9	3.7	2.2	1.7	16	0.3
		020	17D	-	102	5.0	3.1	1.9	1.6	14	0.2
		021	17D	-	114	5.7	3.4	2.3	1.5	19	0.2
		022	17D	-	125	5.1	3.2	1.9	1.7	20	0.2
		023	4D	---	100	5.6	3.6	2.0	1.8	27	0.3
			17D	-	103	5.9	3.7	2.2	1.7	18	0.3
		024	4D	---	79	6.1	3.9	2.2	1.8	24	0.3
			17D	-	118	5.2	3.3	1.9	1.7	16	0.2

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**Appendix 8**  
**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	AG none	BUN mg/dL	CREA mg/dL		
2	30 µg/day	025	4D	---	89	6.0	3.8	2.2	1.7	22	0.3		
			17D	-	98	5.3	3.3	2.0	1.6	20	0.2		
		026	4D	---	97	5.8	3.6	2.2	1.6	25	0.2		
			22R	-	149	6.2	3.9	2.3	1.7	18	0.3		
		027	4D	---	116	5.9	3.7	2.2	1.7	35	0.3		
			22R	-	138	6.1	3.8	2.3	1.7	17	0.3		
		028	4D	---	115	5.6	3.5	2.1	1.7	25	0.3		
			22R	-	98	5.9	3.7	2.2	1.7	16	0.3		
		029	4D	---	98	6.2	3.9	2.3	1.7	23	0.3		
			22R	-	96	6.1	3.9	2.2	1.8	19	0.2		
		030	4D	---	91	6.0	3.7	2.3	1.6	27	0.3		
			22R	-	126	6.1	3.8	2.3	1.7	16	0.3		
		3	30 µg /day	031	17D	-	124	5.1	3.1	2.0	1.6	25	0.3
					032	17D	-	119	5.2	3.3	1.9	1.7	19
033	17D				-	160	6.0	3.8	2.2	1.7	22	0.3	
034	17D				-	139	5.3	3.3	2.0	1.6	22	0.3	
035	17D				-	100	6.0	3.7	2.3	1.6	21	0.3	

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**Appendix 8**  
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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	AG none	BUN mg/dL	CREA mg/dL
3	30 µg /day	036	17D	-	158	5.2	3.3	1.9	1.7	17	0.2
		037	17D	-	120	5.6	3.5	2.1	1.7	18	0.3
		038	4D	---	78	5.9	3.8	2.1	1.8	22	0.2
			17D	-	98	5.3	3.3	2.0	1.6	21	0.3
		039	4D	---	91	6.1	3.8	2.3	1.7	25	0.2
			17D	-	118	5.3	3.3	2.0	1.6	18	0.2
		040	4D	---	110	5.7	3.6	2.1	1.7	22	0.3
			17D	-	90	5.1	3.2	1.9	1.7	16	0.2
		041	4D	---	101	5.9	3.7	2.2	1.7	20	0.3
			22R	-	142	6.0	3.8	2.2	1.7	20	0.3
		042	4D	---	131	6.0	3.8	2.2	1.7	25	0.3
			22R	-	124	5.8	3.7	2.1	1.8	12	0.3
		043	4D	---	85	5.4	3.4	2.0	1.7	23	0.2
			22R	-	117	5.7	3.5	2.2	1.6	17	0.2
		044	4D	---	109	5.8	3.6	2.2	1.6	29	0.3
			22R	-	119	6.0	3.8	2.2	1.7	13	0.3
		045	4D	---	95	6.0	3.7	2.3	1.6	24	0.3

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**Appendix 8**  
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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	AG none	BUN mg/dL	CREA mg/dL
3	30 µg /day	045	22R	-	97	6.0	3.8	2.2	1.7	20	0.3

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**Appendix 8**  
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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	PHOS mg/dL	CA mg/dL	NA mmol/L	K mmol/L	CL mmol/L	HEM_IND none	ICT_IND none
1	0 µg/day	001	17D	-	8.8	9.8	146	4.2	106	Negative	Negative
		002	17D	-	8.3	9.7	145	4.2	105	Slight	Negative
		003	17D	-	8.6	10.0	143	4.6	105	Negative	Negative
		004	17D	-	7.7	9.7	142	4.2	104	Negative	Negative
		005	17D	-	10.2	10.2	143	4.5	103	Negative	Negative
		006	17D	-	8.3	9.9	143	4.3	105	Negative	Negative
		007	17D	-	8.9	10.4	145	4.3	105	Negative	Negative
		008	4D	---	7.1	9.5	144	4.2	102	Negative	Negative
			17D	-	9.7	9.9	144	4.2	105	Slight	Negative
		009	4D	---	7.3	9.4	143	4.1	101	Negative	Negative
			17D	-	8.7	9.9	145	4.1	104	Negative	Negative
		010	4D	---	7.6	9.7	144	5.0	100	Negative	Negative
			17D	-	8.0	9.1	144	4.4	106	Negative	Negative
		011	4D	---	7.3	10.0	144	4.7	102	Slight	Negative
			22R	-	4.7	RR 9.4	142	4.2	106	Negative	Negative
		012	4D	---	6.8	9.9	148	4.6	109	Slight	Negative
	22R	-	6.2	9.3	142	4.4	106	Negative	Negative		

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	PHOS mg/dL	CA mg/dL	NA mmol/L	K mmol/L	CL mmol/L	HEM_IND none	ICT_IND none
1	0 µg/day	013	4D	---	6.6	9.6	144	4.3	102	Slight	Negative
			22R	-	7.2	9.5	143	4.0	106	Slight	Negative
		014	4D	---	7.6	10.1	145	4.2	102	Negative	Negative
			22R	-	7.2	9.6	143	4.3	107	Slight	Negative
		015	4D	---	8.4	9.9	143	4.5	101	Slight	Negative
			22R	-	7.5	9.4	142	3.7	103	Negative	Negative
2	30 µg/day	016	17D	-	7.2	9.8	141	4.4	102	Negative	Negative
			17D	-	8.0	10.1	142	4.4	101	Negative	Negative
		018	17D	-	7.6	9.3	138	4.1	101	Negative	Negative
		019	17D	-	7.5	10.2	144	4.4	105	Negative	Negative
		020	17D	-	8.2	9.2	141	4.4	104	Negative	Negative
		021	17D	-	8.2	9.9	142	4.5	102	Slight	Negative
		022	17D	-	8.6	9.7	143	5.0	106	Negative	Negative
		023	4D	---	7.1	9.3	145	4.4	104	Negative	Negative
			17D	-	8.2	10.2	144	4.4	105	Negative	Negative
		024	4D	---	7.7	9.8	145	4.5	102	Negative	Negative
	17D	-	9.2	9.8	144	4.2	105	Negative	Negative		

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	PHOS mg/dL	CA mg/dL	NA mmol/L	K mmol/L	CL mmol/L	HEM_IND none	ICT_IND none		
2	30 µg/day	025	4D	---	7.1	9.9	144	4.3	102	Negative	Negative		
			17D	-	8.4	10.0	144	3.8	103	Negative	Negative		
		026	4D	---	7.9	9.7	143	4.8	101	Negative	Negative		
			22R	-	6.4	9.9	142	4.4	105	Negative	Negative		
		027	4D	---	7.3	9.4	142	4.5	101	Negative	Negative		
			22R	-	6.9	9.4	142	4.6	107	Slight	Negative		
		028	4D	---	6.7	9.3	143	4.5	102	Negative	Negative		
			22R	-	7.6	9.2	143	4.0	107	Negative	Negative		
		029	4D	---	7.5	9.8	146	4.6	102	Negative	Negative		
			22R	-	6.8	9.2	144	4.3	105	Negative	Negative		
		030	4D	---	8.0	10.0	145	4.8	102	Negative	Negative		
			22R	-	6.6	9.5	142	4.0	106	Negative	Negative		
		3	30 µg /day	031	17D	-	7.6	9.2	140	4.2	105	Slight	Negative
					032	17D	-	6.5	9.4	143	4.1	106	Negative
033	17D				-	6.7	10.0	143	4.6	103	Negative	Negative	
034	17D				-	8.5	9.3	139	4.2	102	Negative	Negative	
035	17D				-	7.9	10.0	143	4.3	104	Negative	Negative	

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**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	PHOS mg/dL	CA mg/dL	NA mmol/L	K mmol/L	CL mmol/L	HEM_IND none	ICT_IND none
3	30 µg /day	036	17D	-	8.4	9.6	143	4.2	104	Negative	Negative
		037	17D	-	9.6	9.7	142	4.7	103	Slight	Negative
		038	4D	---	7.5	9.4	143	4.5	102	Negative	Negative
			17D	-	8.2	9.4	145	4.3	106	Slight	Negative
		039	4D	---	7.8	10.1	145	4.6	99	Negative	Negative
			17D	-	8.7	9.9	144	4.2	104	Negative	Negative
		040	4D	---	7.1	9.7	145	4.2	101	Negative	Negative
			17D	-	8.0	9.4	145	4.4	105	Negative	Negative
		041	4D	---	8.1	10.0	143	4.7	100	Negative	Negative
			22R	-	6.8	9.3	144	4.1	106	Negative	Negative
		042	4D	---	7.0	9.7	144	5.0	101	Negative	Negative
			22R	-	5.6	9.2	144	3.9	108	Negative	Negative
		043	4D	---	7.5	9.5	142	4.7	103	Negative	Negative
			22R	-	7.0	9.5	143	4.4	107	Slight	Negative
		044	4D	---	7.9	9.4	143	4.5	102	Negative	Negative
			22R	-	7.4	9.5	142	4.3	105	Negative	Negative
		045	4D	---	7.7	10.2	145	5.1	102	Negative	Negative

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	PHOS mg/dL	CA mg/dL	NA mmol/L	K mmol/L	CL mmol/L	HEM_IND none	ICT_IND none
3	30 µg /day	045	22R	-	7.3	9.9	144	4.3	106	Negative	Negative

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**Appendix 8**  
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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	LIP_IND none	A2M ug/mL	A1AGP ug/mL
1	0 µg/day	001	17D	-	Negative	12	68.67
		002	17D	-	Negative	15	52.23
		003	17D	-	Negative	19	24.30
		004	17D	-	Negative	12	34.45
		005	17D	-	Negative	11	43.22
		006	17D	-	Negative	9	60.45
		007	17D	-	Negative	15	53.83
		008	4D	---	Negative	679	948.10
			17D	-	Negative	13	47.23
		009	4D	---	Negative	53	75.58
			17D	-	Negative	19	50.35
		010	4D	---	Negative	44	63.18
			17D	-	Negative	15	41.99
		011	4D	---	Negative	37	75.39
			22R	-	Negative	10	91.41
		012	4D	---	Negative	32	61.74
	22R	-	Negative	9	43.29		

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**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	LIP_IND none	A2M ug/mL	A1AGP ug/mL
1	0 µg/day	013	4D	---	Negative	21	48.94
			22R	-	Negative	9	49.54
		014	4D	---	Negative	17	55.88
			22R	-	Negative	6	43.79
		015	4D	---	Negative	24	66.05
			22R	-	Negative	6	46.52
2	30 µg/day	016	17D	-	Negative	1801	2632.51
			17D	-	Negative	886	1974.42
		018	17D	-	Negative	576	1817.56
			17D	-	Negative	223	1176.32
		020	17D	-	Negative	783	1720.69
			17D	-	Negative	2686	2072.64
		022	17D	-	Negative	724	1782.38
			023	4D	---	Negative	1325
		17D		-	Negative	395	1845.24
		024	4D	---	Negative	2333	1571.10
17D	-		Negative	997	1794.51		

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**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	LIP_IND none	A2M ug/mL	A1AGP ug/mL	
2	30 µg/day	025	4D	---	Negative	1139	1636.32	
			17D	-	Negative	835	1543.59	
		026	4D	---	Negative	2678	2378.00	
			22R	-	Negative	9	66.75	
		027	4D	---	Negative	1679	1616.32	
			22R	-	Negative	10	69.36	
		028	4D	---	Negative	2817	1627.92	
			22R	-	Negative	16	55.29	
		029	4D	---	Negative	3963	1499.70	
			22R	-	Negative	44	65.90	
030	4D	---	Negative	2611	1452.44			
	22R	-	Negative	18	121.40			
3	30 µg /day	031	17D	-	Negative	2132	2019.27	
			032	17D	-	Negative	2439	1495.94
			033	17D	-	Negative	1104	2068.21
			034	17D	-	Negative	1496	1355.49
			035	17D	-	Negative	4973	3485.55

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	HPD	LIP_IND none	A2M ug/mL	A1AGP ug/mL
3	30 µg /day	036	17D	-	Negative	1321	1953.14
		037	17D	-	Negative	1688	2785.50
		038	4D	---	Negative	1370	1538.05
			17D	-	Negative	858	2072.35
		039	4D	---	Negative	4147	1841.85
			17D	-	Negative	1072	1311.89
		040	4D	---	Negative	3404	2437.64
			17D	-	Negative	859	1663.49
		041	4D	---	Negative	1457	1815.29
			22R	-	Negative	15	84.77
		042	4D	---	Negative	10485	4831.95
			22R	-	Negative	19	55.24
		043	4D	---	Negative	4106	2495.36
			22R	-	Negative	17	46.84
		044	4D	---	Negative	2755	1830.75
			22R	-	Negative	13	50.71
		045	4D	---	Negative	3569	2023.44

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**3-WEEK RECOVERY**

Male

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Group Number	Dose	Animal	Day	HPD	LIP_IND none	A2M ug/mL	A1AGP ug/mL
3	30 µg /day	045	22R	-	Negative	17	75.25

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**Appendix 8**  
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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	ALT U/L	AST U/L	ALP U/L	GGT U/L	TBIL mg/dL	CHOL mg/dL	TRIG mg/dL	
1	0 µg/day	046	17D	-	12	88	60	<3	<0.1	39	45	
		047	17D	-	9	66	62	<3	<0.1	28	32	
		048	17D	-	12	70	37	<3	<0.1	20	20	
		049	17D	-	11	52	56	<3	<0.1	48	29	
		050	17D	-	11	102	65	<3	<0.1	26	22	
		051	17D	-	11	46	48	<3	0.1	28	22	
		052	17D	-	-	QN	-	QN	-	QN	-	QN
		053	4D	---	26	74	65	<3	<0.1	33	29	
			17D	-	14	75	38	<3	0.1	27	19	
		054	4D	---	28	94	96	<3	<0.1	41	32	
			17D	-	11	78	48	<3	<0.1	30	34	
		055	4D	---	18	64	91	<3	<0.1	72	62	
			17D	-	11	52	44	<3	<0.1	55	27	
		056	4D	---	15	99	94	<3	<0.1	34	32	
			22R	-	10	77	36	3	<0.1	26	22	
		057	4D	---	21	87	84	<3	<0.1	43	25	
			22R	-	15	59	34	<3	0.1	56	40	

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**Appendix 8**  
**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	ALT U/L	AST U/L	ALP U/L	GGT U/L	TBIL mg/dL	CHOL mg/dL	TRIG mg/dL			
1	0 µg/day	058	4D	---	20	78	131	<3	<0.1	53	31			
			22R	-	13	61	41	<3	0.1	53	35			
		059	4D	---	21	74	113	<3	<0.1	54	52			
			22R	-	11	59	35	<3	<0.1	47	36			
		060	4D	---	18	84	69	<3	<0.1	35	31			
			22R	-	10	71	24	<3	<0.1	33	21			
2	30 µg/day	061	17D	-	14	96	73	<3	<0.1	41	30			
			062	17D	-	13	88	76	<3	<0.1	33	35		
		063	17D	-	13	71	87	<3	<0.1	34	25			
			064	17D	-	13	81	110	<3	<0.1	24	20		
		065	17D	-	15	96	89	<3	0.1	28	21			
			066	17D	-	10	57	49	<3	<0.1	32	22		
		067	17D	-	-	NS	-	NS	-	NS	-	NS	-	NS
			068	4D	---	29	110	132	<3	<0.1	32	24		
		17D		-	18	103	58	<3	<0.1	29	21			
		069	4D	---	23	90	123	<3	<0.1	47	24			
			17D	-	14	81	80	<3	0.1	42	29			

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**Appendix 8**  
**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	ALT U/L	AST U/L	ALP U/L	GGT U/L	TBIL mg/dL	CHOL mg/dL	TRIG mg/dL		
2	30 µg/day	070	4D	---	27	79	108	<3	<0.1	63	34		
			17D	-	15	62	81	<3	<0.1	40	23		
		071	4D	---	20	84	134	<3	<0.1	41	26		
			22R	-	14	62	35	<3	0.1	49	33		
		072	4D	---	30	120	182	<3	<0.1	68	43		
			22R	-	17	82	46	<3	<0.1	75	37		
		073	4D	---	20	98	144	<3	<0.1	39	33		
			22R	-	12	86	41	<3	<0.1	34	30		
		074	4D	---	21	83	135	<3	<0.1	41	24		
			22R	-	14	72	31	<3	<0.1	40	32		
		075	4D	---	29	105	145	<3	<0.1	47	27		
			22R	-	17	66	32	<3	<0.1	73	27		
		3	30 µg /day	076	17D	-	19	113	118	<3	0.1	33	28
					17D	-	-	QN	-	QN	-	QN	-
078	17D			-	15	66	123	<3	0.1	32	22		
079	17D			-	22	86	87	<3	<0.1	31	29		
080	17D			-	13	87	94	<3	<0.1	34	36		

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**Appendix 8**  
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**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	ALT U/L	AST U/L	ALP U/L	GGT U/L	TBIL mg/dL	CHOL mg/dL	TRIG mg/dL		
3	30 µg /day	081	17D	-	12	52	80	<3	<0.1	23	23		
		082	17D	-	16	71	107	<3	<0.1	30	29		
		083	4D	---	20	85	163	<3	<0.1	71	31		
			17D	-	17	85	102	<3	<0.1	36	25		
		084	4D	---	33	109	157	<3	<0.1	57	46		
			17D	-	18	82	68	<3	<0.1	36	20		
		085	4D	---	21	93	181	<3	<0.1	57	28		
			17D	-	-	NS	-	NS	-	NS	-	NS	-
		086	4D	---	29	103	163	<3	<0.1	50	31		
			22R	-	16	70	29	<3	<0.1	44	27		
		087	4D	---	18	93	157	<3	<0.1	39	28		
			22R	-	14	62	37	<3	<0.1	29	37		
		088	4D	---	21	79	125	<3	<0.1	47	28		
			22R	-	13	69	23	<3	<0.1	37	32		
		089	4D	---	23	83	110	<3	<0.1	77	38		
			22R	-	14	72	36	<3	<0.1	52	45		
		090	4D	---	20	85	91	<3	<0.1	55	46		

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**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	ALT U/L	AST U/L	ALP U/L	GGT U/L	TBIL mg/dL	CHOL mg/dL	TRIG mg/dL
3	30 µg /day	090	22R	-	11	63	20	<3	<0.1	44	45

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	AG none	BUN mg/dL	CREA mg/dL	
1	0 µg/day	046	17D	-	118	4.8	3.3	1.5	2.2	17	0.2	
		047	17D	-	128	5.5	3.7	1.8	2.1	17	0.3	
		048	17D	-	105	5.5	3.5	2.0	1.8	14	0.2	
		049	17D	-	97	5.5	3.6	1.9	1.9	23	0.3	
		050	17D	-	97	5.3	3.5	1.8	1.9	13	0.2	
		051	17D	-	127	5.6	3.7	1.9	1.9	16	0.3	
		052	17D	-	-	QN	-	QN	-	QN	-	QN
		053	4D	---	112	6.6	4.4	2.2	2.0	15	0.3	
			17D	-	83	6.0	4.0	2.0	2.0	15	0.3	
		054	4D	---	94	6.4	4.2	2.2	1.9	17	0.3	
			17D	-	122	5.3	3.5	1.8	1.9	19	0.2	
		055	4D	---	115	6.7	4.5	2.2	2.0	20	0.4	
			17D	-	126	5.5	3.6	1.9	1.9	19	0.4	
		056	4D	---	90	5.6	3.8	1.8	2.1	17	0.3	
			22R	-	108	6.2	4.0	2.2	1.8	17	0.4	
		057	4D	---	101	6.0	4.0	2.0	2.0	19	0.3	
			22R	-	130	6.5	4.4	2.1	2.1	13	0.3	

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	AG none	BUN mg/dL	CREA mg/dL			
1	0 µg/day	058	4D	---	101	6.3	4.2	2.1	2.0	15	0.3			
			22R	-	129	7.1	4.7	2.4	2.0	17	0.4			
		059	4D	---	101	6.4	4.2	2.2	1.9	15	0.3			
			22R	-	130	6.6	4.3	2.3	1.9	21	0.4			
		060	4D	---	106	6.1	4.0	2.1	1.9	16	0.3			
			22R	-	100	6.2	3.9	2.3	1.7	15	0.3			
2	30 µg/day	061	17D	-	90	5.4	3.3	2.1	1.6	20	0.2			
			062	17D	-	111	5.1	3.1	2.0	1.6	20	0.3		
		063	17D	-	98	4.9	3.1	1.8	1.7	23	0.3			
			064	17D	-	106	5.0	3.1	1.9	1.6	22	0.2		
		065	17D	-	89	5.0	3.0	2.0	1.5	16	0.2			
			066	17D	-	107	4.9	3.0	1.9	1.6	14	0.2		
		067	17D	-	-	NS	-	NS	-	NS	-	NS	-	NS
			068	4D	---	72	5.7	3.6	2.1	1.7	16	0.2		
		17D		-	94	4.9	3.0	1.9	1.6	22	0.2			
		069	4D	---	92	5.7	3.6	2.1	1.7	14	0.2			
			17D	-	102	4.6	2.9	1.7	1.7	15	0.2			

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	AG none	BUN mg/dL	CREA mg/dL		
2	30 µg/day	070	4D	---	94	5.9	3.7	2.2	1.7	25	0.3		
			17D	-	100	5.0	3.1	1.9	1.6	18	0.2		
		071	4D	---	89	5.7	3.6	2.1	1.7	16	0.2		
			22R	-	115	6.8	4.3	2.5	1.7	14	0.3		
		072	4D	---	97	5.6	3.5	2.1	1.7	20	0.2		
			22R	-	98	6.5	4.1	2.4	1.7	18	0.3		
		073	4D	---	97	5.3	3.4	1.9	1.8	17	0.2		
			22R	-	96	6.3	4.0	2.3	1.7	20	0.3		
		074	4D	---	85	5.6	3.5	2.1	1.7	25	0.2		
			22R	-	121	6.7	4.2	2.5	1.7	21	0.3		
		075	4D	---	87	5.7	3.6	2.1	1.7	17	0.3		
			22R	-	108	6.4	4.1	2.3	1.8	19	0.3		
		3	30 µg /day	076	17D	-	106	5.4	3.3	2.1	1.6	19	0.3
					17D	-	-	QN	-	QN	-	QN	-
078	17D			-	90	5.2	3.2	2.0	1.6	21	0.2		
079	17D			-	107	5.0	3.1	1.9	1.6	20	0.2		
080	17D			-	88	5.0	3.2	1.8	1.8	20	0.2		

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	AG none	BUN mg/dL	CREA mg/dL		
3	30 µg /day	081	17D	-	103	4.9	3.0	1.9	1.6	19	0.2		
		082	17D	-	89	4.4	2.9	1.5	1.9	21	0.2		
		083	4D	---	85	5.8	3.6	2.2	1.6	19	0.2		
			17D	-	105	4.9	3.0	1.9	1.6	18	0.2		
		084	4D	---	91	5.7	3.6	2.1	1.7	23	0.2		
			17D	-	108	4.9	3.0	1.9	1.6	22	0.2		
		085	4D	---	88	6.2	3.9	2.3	1.7	19	0.3		
			17D	-	-	NS	-	NS	-	NS	-	NS	-
		086	4D	---	75	5.7	3.6	2.1	1.7	14	0.2		
			22R	-	108	6.3	4.1	2.2	1.9	17	0.3		
		087	4D	---	96	5.7	3.6	2.1	1.7	17	0.3		
			22R	-	104	6.8	4.3	2.5	1.7	20	0.3		
		088	4D	---	87	6.1	3.8	2.3	1.7	19	0.3		
			22R	-	95	6.9	4.4	2.5	1.8	20	0.3		
		089	4D	---	87	6.2	3.9	2.3	1.7	18	0.3		
			22R	-	137	7.1	4.6	2.5	1.8	18	0.4		
		090	4D	---	88	6.1	3.8	2.3	1.7	17	0.2		

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	AG none	BUN mg/dL	CREA mg/dL
3	30 µg /day	090	22R	-	146	6.6	4.2	2.4	1.8	16	0.3

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	PHOS mg/dL	CA mg/dL	NA mmol/L	K mmol/L	CL mmol/L	HEM_IND none	ICT_IND none	
1	0 µg/day	046	17D	-	8.2	9.4	144	4.7	109	Negative	Negative	
		047	17D	-	8.4	9.4	143	4.0	107	Negative	Negative	
		048	17D	-	7.1	9.5	145	4.3	108	Negative	Negative	
		049	17D	-	7.2	9.4	145	4.4	108	Negative	Negative	
		050	17D	-	7.4	9.5	144	4.8	109	Negative	Negative	
		051	17D	-	6.0	9.5	142	4.3	109	Negative	Negative	
		052	17D	-	-	QN	-	QN	-	QN	-	QN
		053	4D	---	6.2	9.8	144	3.7	104	Negative	Negative	
			17D	-	5.9	9.5	144	4.2	108	Negative	Negative	
		054	4D	---	7.8	9.9	144	3.7	104	Slight	Negative	
			17D	-	8.5	9.7	143	4.6	106	Negative	Negative	
		055	4D	---	6.9	10.2	144	3.9	105	Negative	Negative	
			17D	-	7.6	9.8	142	4.8	108	Negative	Negative	
		056	4D	---	6.3	9.4	142	4.0	103	Negative	Negative	
			22R	-	6.1	9.5	143	3.6	107	Negative	Negative	
		057	4D	---	6.6	9.5	143	3.8	103	Negative	Negative	
	22R	-	7.2	10.1	142	4.0	107	Negative	Negative			

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**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	PHOS mg/dL	CA mg/dL	NA mmol/L	K mmol/L	CL mmol/L	HEM_IND none	ICT_IND none			
1	0 µg/day	058	4D	---	6.4	9.6	144	3.7	107	Slight	Negative			
			22R	-	7.0	9.9	144	3.8	108	Negative	Negative			
		059	4D	---	6.0	9.7	144	4.0	104	Negative	Negative			
			22R	-	5.3	9.4	139	3.5	103	Negative	Negative			
		060	4D	---	6.7	9.5	145	4.0	103	Slight	Negative			
			22R	-	6.8	9.9	143	4.3	109	Negative	Negative			
2	30 µg/day	061	17D	-	7.4	9.8	144	4.8	106	Negative	Negative			
			062	17D	-	8.1	9.9	144	4.3	110	Slight	Negative		
		063	17D	-	7.0	9.3	144	4.5	109	Negative	Negative			
		064	17D	-	8.3	9.6	142	4.4	106	Negative	Negative			
		065	17D	-	7.3	9.7	141	4.6	106	Negative	Negative			
		066	17D	-	6.7	9.7	143	4.3	110	Negative	Negative			
		067	17D	-	-	NS	-	NS	-	NS	-	NS	-	NS
		068	4D	---	7.0	9.5	143	4.4	104	Slight	Negative			
			17D	-	7.2	9.1	145	4.7	109	Negative	Negative			
		069	4D	---	6.0	9.4	144	3.9	107	Negative	Negative			
			17D	-	7.6	9.4	142	4.5	107	Negative	Negative			

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**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	PHOS mg/dL	CA mg/dL	NA mmol/L	K mmol/L	CL mmol/L	HEM_IND none	ICT_IND none		
2	30 µg/day	070	4D	---	6.7	9.5	143	4.6	105	Negative	Negative		
			17D	-	6.8	9.3	142	4.7	106	Negative	Negative		
		071	4D	---	7.0	9.8	142	4.2	105	Negative	Negative		
			22R	-	5.6	9.7	143	3.9	107	Negative	Negative		
		072	4D	---	7.3	9.5	142	4.6	101	Negative	Negative		
			22R	-	5.4	9.7	142	4.2	104	Slight	Negative		
		073	4D	---	5.9	9.4	143	4.2	104	Negative	Negative		
			22R	-	6.3	9.8	144	4.1	106	Negative	Negative		
		074	4D	---	7.2	9.8	143	4.9	104	Negative	Negative		
			22R	-	7.6	10.0	143	4.0	107	Negative	Negative		
		075	4D	---	7.4	9.8	145	3.8	106	Negative	Negative		
			22R	-	6.6	9.8	144	3.8	106	Negative	Negative		
		3	30 µg /day	076	17D	-	7.2	9.5	143	4.6	109	Negative	Negative
					077	17D	-	-	QN	-	QN	-	QN
078	17D				-	7.8	9.9	143	4.4	108	Negative	Negative	
079	17D				-	9.7	10.0	143	5.2	107	Negative	Negative	
080	17D				-	6.6	9.6	142	4.7	108	Negative	Negative	

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**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	PHOS mg/dL	CA mg/dL	NA mmol/L	K mmol/L	CL mmol/L	HEM_IND none	ICT_IND none		
3	30 µg /day	081	17D	-	6.9	9.6	144	4.6	110	Negative	Negative		
		082	17D	-	8.0	9.2	144	4.8	109	Negative	Negative		
		083	4D	---	6.7	10.0	142	4.4	105	Negative	Negative		
			17D	-	8.6	9.9	142	4.9	106	Slight	Negative		
		084	4D	---	6.9	10.1	144	4.8	105	Negative	Negative		
			17D	-	7.0	9.5	144	4.8	108	Slight	Negative		
		085	4D	---	6.2	9.7	146	4.2	107	Negative	Negative		
			17D	-	-	NS	-	NS	-	NS	-	NS	-
		086	4D	---	6.6	9.3	143	4.1	103	Negative	Negative		
			22R	-	7.8	9.5	144	4.0	107	Negative	Negative		
		087	4D	---	8.1	9.5	145	3.8	108	Negative	Negative		
			22R	-	7.0	9.8	144	3.7	106	Negative	Negative		
		088	4D	---	6.9	10.1	144	4.7	107	Negative	Negative		
			22R	-	6.1	9.9	143	4.1	108	Negative	Negative		
		089	4D	---	6.6	9.9	142	4.8	103	Negative	Negative		
			22R	-	7.4	10.3	142	3.9	106	Negative	Negative		
		090	4D	---	7.3	9.9	144	4.3	103	Slight	Negative		

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**Appendix 8**  
**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	PHOS mg/dL	CA mg/dL	NA mmol/L	K mmol/L	CL mmol/L	HEM_IND none	ICT_IND none
3	30 µg /day	090	22R	-	5.5	9.6	141	4.3	107	Negative	Negative

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**Appendix 8**  
**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	LIP_IND none	A2M ug/mL	A1AGP ug/mL	
1	0 µg/day	046	17D	-	Negative	33	94.42	
		047	17D	-	Negative	22	80.84	
		048	17D	-	Negative	173	328.40	
		049	17D	-	Negative	15	71.66	
		050	17D	-	Negative	10	80.68	
		051	17D	-	Negative	26	69.19	
		052	17D	-	-	QN	13	49.83
		053	4D	---	Negative	211	287.21	
			17D	-	Negative	18	54.31	
		054	4D	---	Negative	530	391.89	
			17D	-	Negative	11	67.97	
		055	4D	---	Negative	612	582.86	
			17D	-	Negative	10	62.29	
		056	4D	---	Negative	22	72.80	
			22R	-	Negative	16	84.10	
		057	4D	---	Negative	20	165.20	
			22R	-	Negative	11	54.10	

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**Appendix 8**  
**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	LIP_IND none	A2M ug/mL	A1AGP ug/mL			
1	0 µg/day	058	4D	---	Negative	255	220.09			
			22R	-	Negative	32	48.05			
		059	4D	---	Negative	29	77.14			
			22R	-	Negative	15	45.77			
		060	4D	---	Negative	18	121.00			
			22R	-	Negative	12	81.92			
2	30 µg/day	061	17D	-	Negative	948	1837.15			
			062	17D	-	Negative	599	1641.31		
		063	17D	-	Negative	249	1335.38			
		064	17D	-	Negative	796	1360.18			
		065	17D	-	Negative	405	1320.56			
		066	17D	-	Negative	260	1397.00			
		067	17D	-	-	NS	-	NS	-	NS
		068	4D	---	Negative	1214	1990.76			
			17D	-	Negative	484	1043.02			
		069	4D	---	Negative	255	1426.67			
			17D	-	Negative	231	1358.38			

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**Appendix 8**  
**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	LIP_IND none	A2M ug/mL	A1AGP ug/mL		
2	30 µg/day	070	4D	---	Negative	511	1993.04		
			17D	-	Negative	717	2133.66		
		071	4D	---	Negative	966	1716.82		
			22R	-	Negative	14	26.72		
		072	4D	---	Negative	1231	2125.32		
			22R	-	Negative	15	53.78		
		073	4D	---	Negative	289	1471.09		
			22R	-	Negative	11	46.76		
		074	4D	---	Negative	744	1933.38		
			22R	-	Negative	26	53.28		
		075	4D	---	Negative	420	2593.43		
			22R	-	Negative	15	59.02		
		3	30 µg /day	076	17D	-	Negative	989	2110.38
					077	17D	-	- QN	- QN
078	17D				-	Negative	953	1992.92	
079	17D				-	Negative	530	1837.66	
080	17D				-	Negative	399	1607.53	

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**Appendix 8**  
**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	LIP_IND none	A2M ug/mL	A1AGP ug/mL		
3	30 µg /day	081	17D	-	Negative	447	1295.34		
		082	17D	-	Negative	588	855.25		
		083	4D	---	Negative	1178	2088.91		
			17D	-	Negative	377	1754.23		
		084	4D	---	Negative	597	1882.91		
			17D	-	Negative	453	1755.26		
		085	4D	---	Negative	886	1606.16		
			17D	-	-	NS	-	NS	-
		086	4D	---	Negative	883	1965.13		
			22R	-	Negative	16	39.63		
		087	4D	---	Negative	563	1350.77		
			22R	-	Negative	22	73.06		
		088	4D	---	Negative	606	1429.46		
			22R	-	Negative	18	34.16		
		089	4D	---	Negative	1600	1484.34		
			22R	-	Negative	13	63.68		
		090	4D	---	Negative	784	1609.14		

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**Appendix 8**  
**Clinical Chemistry**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	HPD	LIP_IND none	A2M ug/mL	A1AGP ug/mL
3	30 µg /day	090	22R	-	Negative	11	77.41

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**Appendix 9**

**Urinalysis**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Parameter</b>	<b>Description</b>
COLOR	Color
CLARITY	Clarity
pH	pH
GLU	Glucose Urine
KET	Ketones
PRO	Protein
BIL	Bilirubin
BLOOD	Blood
SG	Specific Gravity
VOLUME	Total Volume
F_ELEM	Formed Elements
U_RBC	RBC, Urine
U_WBC	WBC, Urine
SQ_EPI	Epithelial Cells, Squamous
TR_PHOS	Crystal, Triple Phosphate
SPERM	Sperm

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**Appendix 9**  
**Urinalysis**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

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**Footnotes**

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- Value not applicable;

Note: Each interval/day will be concatenated with the phase name abbreviation

HPD = Hours Post Dose; U = Unscheduled

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**Appendix 9**  
**Urinalysis**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	COLOR none	CLARITY none	pH none	GLU mg/dL	KET mg/dL	PRO mg/dL	BIL none	BLOOD none
1	0 µg/day	001	17D	Dark Yellow	Clear	7.5	Negative	15	30	Negative	Negative
		002	17D	Dark Yellow	Clear	6.5	Negative	15	30	Negative	Negative
		003	17D	Dark Yellow	Cloudy	7.0	Negative	15	30	Negative	Negative
		004	17D	Yellow	Clear	7.0	Negative	Trace	Trace	Negative	Negative
		005	17D	Dark Yellow	Clear	6.5	Negative	15	30	Negative	Negative
		006	17D	Yellow	Clear	7.5	Negative	Trace	Negative	Negative	Negative
		007	17D	Yellow	Clear	7.5	Negative	Negative	Negative	Negative	Negative
		008	17D	Yellow	Clear	7.0	Negative	Negative	Negative	Negative	Negative
		009	17D	Dark Yellow	Cloudy	7.0	Negative	15	100	Negative	Negative
		010	17D	Dark Yellow	Clear	7.5	Negative	Trace	30	Negative	Negative
		011	22R	Dark Yellow	Cloudy	7.0	Negative	15	30	Negative	Negative
		012	22R	Dark Yellow	Clear	7.0	Negative	15	30	Negative	Negative
		013	22R	Dark Yellow	Clear	7.5	Negative	15	30	Negative	Negative
		014	22R	Dark Yellow	Clear	7.0	Negative	15	30	Negative	Negative
		015	22R	Dark Yellow	Clear	8.0	Negative	15	30	Negative	Negative
2	30 µg/day	016	17D	Yellow	Clear	6.5	Negative	Trace	Trace	Negative	Negative
		017	17D	Yellow	Clear	7.0	Negative	Negative	Negative	Negative	Negative
		018	17D	Dark Yellow	Cloudy	6.5	Negative	Trace	100	Negative	Negative
		019	17D	Yellow	Clear	7.0	Negative	Trace	Trace	Negative	Negative
		020	17D	Yellow	Clear	7.0	Negative	Negative	Negative	Negative	Negative

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**Appendix 9**  
**Urinalysis**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	COLOR none	CLARITY none	pH none	GLU mg/dL	KET mg/dL	PRO mg/dL	BIL none	BLOOD none
2	30 µg/day	021	17D	Yellow	Clear	7.0	Negative	Negative	Negative	Negative	Negative
		022	17D	Dark Yellow	Cloudy	6.0	Negative	15	100	Small	Negative
		023	17D	Yellow	Clear	7.0	Negative	Trace	Trace	Negative	Negative
		024	17D	Yellow	Clear	6.5	Negative	Negative	Negative	Negative	Negative
		025	17D	Yellow	Clear	7.0	Negative	Trace	Negative	Negative	Negative
		026	22R	Dark Yellow	Clear	7.0	Negative	15	30	Negative	Negative
		027	22R	Yellow	Clear	7.5	Negative	Trace	Trace	Negative	Negative
		028	22R	Yellow	Clear	7.0	Negative	Trace	Trace	Negative	Negative
		029	22R	Dark Yellow	Clear	7.5	Negative	15	30	Negative	Negative
		030	22R	Yellow	Clear	7.0	Negative	15	30	Negative	Negative
3	30 µg/day	031	17D	Dark Yellow	Clear	6.5	Negative	15	30	Negative	Negative
		032	17D	Yellow	Clear	7.0	Negative	Trace	Trace	Negative	Negative
		033	17D	Dark Yellow	Cloudy	6.0	Negative	Trace	100	Small	Negative
		034	17D	Yellow	Clear	6.5	Negative	Negative	Negative	Negative	Negative
		035	17D	Yellow	Clear	6.5	Negative	Trace	30	Negative	Negative
		036	17D	Yellow	Clear	7.0	Negative	Negative	Negative	Negative	Negative
		037	17D	Yellow	Clear	6.5	Negative	Trace	Trace	Negative	Negative
		038	17D	Dark Yellow	Clear	6.5	Negative	Trace	30	Negative	Negative
		039	17D	Yellow	Clear	6.5	Negative	Trace	Negative	Negative	Negative
		040	17D	Yellow	Clear	7.0	Negative	Negative	Negative	Negative	Negative

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**Appendix 9**  
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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	COLOR none	CLARITY none	pH none	GLU mg/dL	KET mg/dL	PRO mg/dL	BIL none	BLOOD none
3	30 µg /day	041	22R	Dark Yellow	Cloudy	7.0	Negative	15	30	Negative	Negative
		042	22R	Yellow	Clear	7.5	Negative	Negative	Negative	Negative	Negative
		043	22R	Dark Yellow	Clear	7.0	Negative	40	100	Negative	Negative
		044	22R	Dark Yellow	Clear	6.5	Negative	15	30	Negative	Negative
		045	22R	Yellow	Clear	7.0	Negative	Trace	30	Negative	Negative

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**Appendix 9**  
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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	SG none	VOLUME mL	F_ELEM none	U_RBC /HPF	U_WBC /HPF	SQ_EPI /LPF	TR_PHOS /HPF	SPERM none
1	0 µg/day	001	17D	1.035	7.0	Reported	-	-	-	Many	Present
		002	17D	1.049	5.0	Reported	-	-	0-5	-	Present
		003	17D	1.043	6.0	Reported	-	0-5	0-5	Moderate	Present
		004	17D	1.016	16.0	Reported	-	-	0-5	-	Present
		005	17D	1.047	5.0	Reported	-	-	0-5	-	Present
		006	17D	1.013	17.0	-	-	-	-	-	-
		007	17D	1.008	37.0	-	-	-	-	-	-
		008	17D	1.006	48.0	-	-	-	-	-	-
		009	17D	1.067	2.0	-	-	-	-	-	-
		010	17D	1.038	6.0	-	-	-	-	-	-
		011	22R	1.051	3.0	Reported	-	-	0-5	Moderate	Present
		012	22R	1.059	4.5	Reported	-	0-5	0-5	Few	Present
		013	22R	1.057	3.0	Reported	0-5	-	0-5	Few	Present
		014	22R	1.059	3.0	Reported	-	-	0-5	Few	Present
		015	22R	1.052	5.0	Reported	-	0-5	0-5	Moderate	Present
2	30 µg/day	016	17D	1.020	13.0	Reported	-	0-5	0-5	Few	Present
		017	17D	1.013	17.0	Reported	-	-	0-5	-	Present
		018	17D	1.063	3.0	Reported	-	-	0-5	Many	-
		019	17D	1.029	9.0	Reported	-	-	-	Few	Present
		020	17D	1.007	28.0	Reported	-	-	0-5	-	Present

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**Appendix 9**  
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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	SG none	VOLUME mL	F_ELEM none	U_RBC /HPF	U_WBC /HPF	SQ_EPI /LPF	TR_PHOS /HPF	SPERM none
2	30 µg/day	021	17D	1.005	60.0	-	-	-	-	-	-
		022	17D	1.070	2.0	-	-	-	-	-	-
		023	17D	1.025	8.0	-	-	-	-	-	-
		024	17D	1.011	23.0	-	-	-	-	-	-
		025	17D	1.017	15.0	-	-	-	-	-	-
		026	22R	1.048	4.0	Reported	0-5	-	-	Few	Present
		027	22R	1.026	10.0	Reported	-	0-5	0-5	Few	Present
		028	22R	1.013	17.0	Reported	-	0-5	0-5	-	Present
		029	22R	1.046	4.0	Reported	-	0-5	0-5	Moderate	Present
		030	22R	1.037	6.0	Reported	0-5	0-5	0-5	Few	Present
3	30 µg /day	031	17D	1.056	3.0	Reported	-	-	0-5	Few	Present
		032	17D	1.023	9.0	Reported	-	0-5	0-5	Few	Present
		033	17D	1.060	3.0	Reported	-	0-5	0-5	Few	Present
		034	17D	1.013	20.0	Reported	-	-	0-5	-	Present
		035	17D	1.022	9.0	Reported	-	-	0-5	Few	Present
		036	17D	1.016	17.0	-	-	-	-	-	-
		037	17D	1.020	13.0	-	-	-	-	-	-
		038	17D	1.045	5.0	-	-	-	-	-	-
		039	17D	1.014	15.0	-	-	-	-	-	-
		040	17D	1.013	22.0	-	-	-	-	-	-

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Male

Group Number	Dose	Animal	Day	SG none	VOLUME mL	F_ELEM none	U_RBC /HPF	U_WBC /HPF	SQ_EPI /LPF	TR_PHOS /HPF	SPERM none
3	30 µg /day	041	22R	1.057	3.0	Reported	-	0-5	0-5	Moderate	Present
		042	22R	1.011	27.0	Reported	-	0-5	0-5	-	Present
		043	22R	1.070	2.0	Reported	-	0-5	0-5	Few	Present
		044	22R	1.052	3.0	Reported	-	0-5	0-5	Moderate	Present
		045	22R	1.030	5.0	Reported	-	-	0-5	Few	Present

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**Appendix 9**  
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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	COLOR none	CLARITY none	pH none	GLU mg/dL	KET mg/dL	PRO mg/dL	BIL none	BLOOD none
1	0 µg/day	046	17D	Dark Yellow	Clear	6.5	Negative	Trace	Negative	Negative	Negative
		047	17D	Yellow	Clear	7.0	Negative	Negative	Negative	Negative	Negative
		048	17D	Dark Yellow	Clear	6.5	Negative	Negative	Trace	Negative	Negative
		049	17D	Yellow	Clear	7.0	Negative	Negative	Trace	Negative	Negative
		050	17D	Yellow	Clear	7.0	Negative	Negative	Negative	Negative	Negative
		051	17D	Yellow	Clear	7.0	Negative	Negative	Negative	Negative	Negative
		052	17D	Dark Yellow	Clear	6.5	Negative	Negative	Negative	Negative	Negative
		053	17D	Dark Yellow	Clear	6.5	Negative	Trace	Trace	Negative	Negative
		054	17D	Yellow	Clear	6.5	Negative	Negative	Negative	Negative	Negative
		055	17D	Yellow	Clear	7.0	Negative	Negative	Negative	Negative	Negative
		056	22R	Yellow	Clear	7.0	Negative	Trace	Trace	Negative	Negative
		057	22R	Yellow	Clear	7.0	Negative	Negative	Negative	Negative	Negative
		058	22R	Yellow	Clear	6.5	Negative	Negative	Negative	Negative	Negative
		059	22R	Dark Yellow	Clear	6.5	Negative	Trace	Trace	Negative	Negative
		060	22R	Yellow	Clear	8.0	Negative	Negative	Negative	Negative	Negative
2	30 µg/day	061	17D	Dark Yellow	Clear	6.0	Negative	Negative	Trace	Negative	Negative
		062	17D	Dark Yellow	Clear	6.0	Negative	Trace	Trace	Negative	Negative
		063	17D	Dark Yellow	Clear	6.0	Negative	Trace	30	Negative	Negative
		064	17D	Yellow	Clear	6.0	Negative	Negative	Negative	Negative	Negative
		065	17D	Yellow	Clear	6.5	Negative	Negative	Negative	Negative	Negative

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**Appendix 9**  
**Urinalysis**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	COLOR none	CLARITY none	pH none	GLU mg/dL	KET mg/dL	PRO mg/dL	BIL none	BLOOD none
2	30 µg/day	066	17D	Dark Yellow	Clear	6.5	Negative	Negative	Trace	Negative	Negative
		067	17D	Yellow	Clear	6.5	Negative	Negative	Negative	Negative	Negative
		068	17D	Dark Yellow	Clear	6.0	Negative	Negative	Trace	Negative	Negative
		069	17D	Yellow	Clear	6.5	Negative	Negative	Negative	Negative	Negative
		070	17D	Dark Yellow	Cloudy	6.0	Negative	Negative	Trace	Negative	Negative
		071	22R	Dark Yellow	Clear	6.5	Negative	Trace	Trace	Negative	Negative
		072	22R	Yellow	Clear	6.0	Negative	Negative	Negative	Negative	Negative
		073	22R	Dark Yellow	Clear	7.0	Negative	15	30	Negative	Negative
		074	22R	Yellow	Clear	7.5	Negative	Negative	Negative	Negative	Negative
		075	22R	Dark Yellow	Clear	6.0	Negative	Trace	Trace	Negative	Negative
3	30 µg /day	076	17D	Dark Yellow	Clear	6.5	Negative	Negative	Trace	Negative	Negative
		077	17D	Yellow	Clear	6.5	Negative	Negative	Negative	Negative	Negative
		078	17D	Dark Yellow	Clear	6.5	Negative	Trace	30	Negative	Negative
		079	17D	Yellow	Clear	6.0	Negative	Trace	Trace	Negative	Negative
		080	17D	Yellow	Clear	6.0	Negative	Negative	Negative	Negative	Negative
		081	17D	Dark Yellow	Cloudy	6.0	Negative	Trace	30	Negative	Negative
		082	17D	Yellow	Clear	6.0	Negative	Negative	Negative	Negative	Negative
		083	17D	Yellow	Clear	6.5	Negative	Negative	Negative	Negative	Negative
		084	17D	Yellow	Clear	6.5	Negative	Negative	Negative	Negative	Negative
		085	17D	Dark Yellow	Clear	5.5	Negative	Negative	30	Negative	Negative

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**Appendix 9**  
**Urinalysis**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	COLOR none	CLARITY none	pH none	GLU mg/dL	KET mg/dL	PRO mg/dL	BIL none	BLOOD none
3	30 µg /day	086	22R	Yellow	Clear	6.5	Negative	Negative	Negative	Negative	Negative
		087	22R	Yellow	Clear	6.5	Negative	Negative	Negative	Negative	Negative
		088	22R	Dark Yellow	Clear	7.0	Negative	Trace	30	Negative	Negative
		089	22R	Dark Yellow	Clear	6.0	Negative	Negative	Trace	Negative	Negative
		090	22R	Yellow	Clear	6.5	Negative	Negative	Negative	Negative	Negative

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**Appendix 9**  
**Urinalysis**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	SG none	VOLUME mL	F_ELEM none	U_RBC /HPF	U_WBC /HPF	SQ_EPI /LPF	TR_PHOS /HPF
1	0 µg/day	046	17D	1.035	5.0	Reported	-	0-5	0-5	Few
		047	17D	1.024	8.0	Reported	-	-	0-5	Few
		048	17D	1.035	4.0	Reported	-	-	0-5	-
		049	17D	1.033	5.0	Reported	-	0-5	0-5	Few
		050	17D	1.010	17.0	Reported	-	-	0-5	-
		051	17D	1.015	12.0	-	-	-	-	-
		052	17D	1.029	5.0	-	-	-	-	-
		053	17D	1.044	4.0	-	-	-	-	-
		054	17D	1.011	14.0	-	-	-	-	-
		055	17D	1.007	25.0	-	-	-	-	-
		056	22R	1.042	3.0	Reported	-	0-5	0-5	-
		057	22R	1.011	18.0	Reported	0-5	0-5	0-5	-
		058	22R	1.010	15.0	Reported	-	0-5	0-5	-
		059	22R	1.044	3.0	Reported	0-5	0-5	0-5	Few
2	30 µg/day	060	22R	1.013	16.0	Reported	-	0-5	0-5	-
		061	17D	1.046	4.0	Reported	-	-	0-5	-
		062	17D	1.037	2.0	Reported	-	0-5	0-5	-
		063	17D	1.054	2.0	Reported	-	-	0-5	Few
		064	17D	1.008	26.0	Reported	-	-	0-5	-
		065	17D	1.014	12.0	Reported	-	0-5	0-5	-

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**Appendix 9**  
**Urinalysis**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	SG none	VOLUME mL	F_ELEM none	U_RBC /HPF	U_WBC /HPF	SQ_EPI /LPF	TR_PHOS /HPF
2	30 µg/day	066	17D	1.036	4.0	-	-	-	-	-
		067	17D	1.011	17.0	-	-	-	-	-
		068	17D	1.034	4.0	-	-	-	-	-
		069	17D	1.011	22.0	-	-	-	-	-
		070	17D	1.037	3.0	-	-	-	-	-
		071	22R	1.044	3.5	Reported	0-5	0-5	0-5	-
		072	22R	1.016	14.0	Reported	-	0-5	0-5	-
		073	22R	1.059	1.5	Reported	-	0-5	0-5	Few
		074	22R	1.021	8.0	Reported	-	0-5	0-5	Few
		075	22R	1.042	3.0	Reported	-	0-5	0-5	-
3	30 µg /day	076	17D	1.033	3.0	Reported	-	-	0-5	Few
		077	17D	1.011	20.0	Reported	-	0-5	0-5	-
		078	17D	1.035	4.0	Reported	-	0-5	0-5	-
		079	17D	1.028	5.0	Reported	-	0-5	0-5	-
		080	17D	1.010	16.0	Reported	-	-	0-5	-
		081	17D	1.038	3.0	-	-	-	-	-
		082	17D	1.025	7.0	-	-	-	-	-
		083	17D	1.011	15.0	-	-	-	-	-
		084	17D	1.010	18.0	-	-	-	-	-
		085	17D	1.049	3.0	-	-	-	-	-

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**Appendix 9**  
**Urinalysis**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A**  
**3-WEEK RECOVERY**

Female

Group Number	Dose	Animal	Day	SG none	VOLUME mL	F_ELEM none	U_RBC /HPF	U_WBC /HPF	SQ_EPI /LPF	TR_PHOS /HPF
3	30 µg /day	086	22R	1.009	20.0	Reported	-	0-5	0-5	-
		087	22R	1.021	8.0	Reported	-	0-5	0-5	Few
		088	22R	1.055	1.5	Reported	-	0-5	0-5	Few
		089	22R	1.041	3.0	Reported	-	0-5	0-5	-
		090	22R	1.012	12.5	Reported	-	0-5	0-5	-

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**Appendix 10**

**Organ Weights (g) and Ratios**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

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**Footnotes**

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- = Value not applicable; NW = Not Weighed; e = Excluded.

ABS = Absolute Value; OW = Organ Weight; BW = Body Weight; BRN = Brain Weight;

OW:BW = (g/g)\*100; OW:BRN = g/g.

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**Appendix 10**

**Organ Weights (g) and Ratios**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Male													
Group Number	Dose	Animal Number	Phase-Planned Sacrifice Group	BW (g)	Brain			Epididymis			Gland, Adrenal		
					ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN
1	0 µg/day	001	Dosing-Terminal Euthanasia	269.7	1.834	0.680	1.000	1.242	0.461	0.677	0.070	0.026	0.038
		002	Dosing-Terminal Euthanasia	321.3	1.931	0.601	1.000	1.522	0.474	0.788	0.083	0.026	0.043
		003	Dosing-Terminal Euthanasia	300.0	1.951	0.650	1.000	1.275	0.425	0.654	0.077	0.026	0.039
		004	Dosing-Terminal Euthanasia	315.7	2.098	0.665	1.000	1.224	0.388	0.583	0.063	0.020	0.030
		005	Dosing-Terminal Euthanasia	294.1	1.928	0.656	1.000	1.211	0.412	0.628	0.071	0.024	0.037
		006	Dosing-Terminal Euthanasia	304.8	1.851	0.607	1.000	1.018	0.334	0.550	0.066	0.022	0.036
		007	Dosing-Terminal Euthanasia	304.1	1.894	0.623	1.000	0.907	0.298	0.479	0.073	0.024	0.039
		008	Dosing-Terminal Euthanasia	286.7	1.760	0.614	1.000	1.136	0.396	0.645	0.070	0.024	0.040
		009	Dosing-Terminal Euthanasia	276.4	1.946	0.704	1.000	1.066	0.386	0.548	0.062	0.022	0.032
		010	Dosing-Terminal Euthanasia	287.8	1.868	0.649	1.000	1.046	0.363	0.560	0.062	0.022	0.033
		011	Recovery-Recovery Euthanasia 1	329.10	2.173	0.660	1.000	1.454	0.442	0.669	0.065	0.020	0.030
		012	Recovery-Recovery Euthanasia 1	362.80	2.080	0.573	1.000	1.522	0.420	0.732	0.062	0.017	0.030
		013	Recovery-Recovery Euthanasia 1	304.00	2.098	0.690	1.000	1.216	0.400	0.580	0.072	0.024	0.034
		014	Recovery-Recovery Euthanasia 1	283.80	2.052	0.723	1.000	1.341	0.473	0.654	0.053	0.019	0.026
		015	Recovery-Recovery Euthanasia 1	379.20	2.133	0.563	1.000	1.268	0.334	0.594	0.083	0.022	0.039

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**Appendix 10**

**Organ Weights (g) and Ratios**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Male													
Group Number	Dose	Animal Number	Phase-Planned Sacrifice Group	BW (g)	Brain			Epididymis			Gland, Adrenal		
					ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN
2	30 µg/day	016	Dosing-Terminal Euthanasia	257.4	1.765	0.686	1.000	1.055	0.410	0.598	0.072	0.028	0.041
		017	Dosing-Terminal Euthanasia	284.4	1.949	0.685	1.000	0.885	0.311	0.454	0.066	0.023	0.034
		018	Dosing-Terminal Euthanasia	267.3	1.839	0.688	1.000	0.878	0.328	0.477	0.061	0.023	0.033
		019	Dosing-Terminal Euthanasia	289.1	1.772	0.613	1.000	1.129	0.391	0.637	0.099	0.034	0.056
		020	Dosing-Terminal Euthanasia	250.2	2.006	0.802	1.000	1.105	0.442	0.551	0.062	0.025	0.031
		021	Dosing-Terminal Euthanasia	269.6	2.062	0.765	1.000	1.058	0.392	0.513	0.068	0.025	0.033
		022	Dosing-Terminal Euthanasia	268.5	1.746	0.650	1.000	1.162	0.433	0.666	0.064	0.024	0.037
		023	Dosing-Terminal Euthanasia	274.5	1.830	0.667	1.000	1.119	0.408	0.611	0.095	0.035	0.052
		024	Dosing-Terminal Euthanasia	248.5	2.033	0.818	1.000	0.949	0.382	0.467	0.056	0.023	0.028
		025	Dosing-Terminal Euthanasia	302.2	2.157	0.714	1.000	1.286	0.426	0.596	0.084	0.028	0.039
		026	Recovery-Recovery Euthanasia 1	351.50	1.815	0.516	1.000	1.131	0.322	0.623	0.068	0.019	0.037
		027	Recovery-Recovery Euthanasia 1	340.00	1.818	0.535	1.000	1.023	0.301	0.563	0.078	0.023	0.043
		028	Recovery-Recovery Euthanasia 1	335.40	2.080	0.620	1.000	1.310	0.391	0.630	0.115	0.034	0.055
		029	Recovery-Recovery Euthanasia 1	350.40	2.062	0.588	1.000	1.259	0.359	0.611	0.101	0.029	0.049
		030	Recovery-Recovery Euthanasia 1	380.20	2.020	0.531	1.000	1.550	0.408	0.767	0.090	0.024	0.045

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**Appendix 10**

**Organ Weights (g) and Ratios**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Male													
Group Number	Dose	Animal Number	Phase-Planned Sacrifice Group	BW (g)	Brain			Epididymis			Gland, Adrenal		
					ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN
3	30 µg /day	031	Dosing-Terminal Euthanasia	244.7	1.808	0.739	1.000	1.116	0.456	0.617	0.075	0.031	0.041
		032	Dosing-Terminal Euthanasia	254.6	1.897	0.745	1.000	1.083	0.425	0.571	0.052	0.020	0.027
		033	Dosing-Terminal Euthanasia	301.1	1.945	0.646	1.000	0.970	0.322	0.499	0.077	0.026	0.040
		034	Dosing-Terminal Euthanasia	250.4	1.842	0.736	1.000	1.087	0.434	0.590	0.074	0.030	0.040
		035	Dosing-Terminal Euthanasia	235.8	1.922	0.815	1.000	1.018	0.432	0.530	0.081	0.034	0.042
		036	Dosing-Terminal Euthanasia	278.8	1.898	0.681	1.000	1.025	0.368	0.540	0.085	0.030	0.045
		037	Dosing-Terminal Euthanasia	273.2	1.861	0.681	1.000	0.953	0.349	0.512	0.077	0.028	0.041
		038	Dosing-Terminal Euthanasia	258.7	1.951	0.754	1.000	1.006	0.389	0.516	0.062	0.024	0.032
		039	Dosing-Terminal Euthanasia	262.2	1.947	0.743	1.000	1.159	0.442	0.595	0.064	0.024	0.033
		040	Dosing-Terminal Euthanasia	266.4	2.011	0.755	1.000	1.091	0.410	0.543	0.059	0.022	0.029
		041	Recovery-Recovery Euthanasia 1	339.00	1.922	0.567	1.000	1.394	0.411	0.725	0.069	0.020	0.036
		042	Recovery-Recovery Euthanasia 1	325.50	1.962	0.603	1.000	1.433	0.440	0.730	0.063	0.019	0.032
		043	Recovery-Recovery Euthanasia 1	344.20	1.939	0.563	1.000	1.401	0.407	0.723	0.070	0.020	0.036
		044	Recovery-Recovery Euthanasia 1	347.50	1.938	0.558	1.000	1.472	0.424	0.760	0.083	0.024	0.043
		045	Recovery-Recovery Euthanasia 1	315.60	1.943	0.616	1.000	1.302	0.413	0.670	0.099	0.031	0.051

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**Appendix 10**

**Organ Weights (g) and Ratios**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Male

Group Number	Dose	Animal Number	Phase-Planned Sacrifice Group	BW (g)	Gland, Prostate			Heart			Kidney		
					ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN
1	0 µg/day	001	Dosing-Terminal Euthanasia	269.7	0.704	0.261	0.384	0.946	0.351	0.516	1.935	0.717	1.055
		002	Dosing-Terminal Euthanasia	321.3	0.834	0.260	0.432	0.900	0.280	0.466	2.224	0.692	1.152
		003	Dosing-Terminal Euthanasia	300.0	0.799	0.266	0.410	0.925	0.308	0.474	2.439	0.813	1.250
		004	Dosing-Terminal Euthanasia	315.7	0.867	0.275	0.413	0.962	0.305	0.459	2.388	0.756	1.138
		005	Dosing-Terminal Euthanasia	294.1	0.766	0.260	0.397	0.879	0.299	0.456	2.197	0.747	1.140
		006	Dosing-Terminal Euthanasia	304.8	0.589	0.193	0.318	0.915	0.300	0.494	2.216	0.727	1.197
		007	Dosing-Terminal Euthanasia	304.1	0.585	0.192	0.309	1.053	0.346	0.556	2.288	0.752	1.208
		008	Dosing-Terminal Euthanasia	286.7	0.756	0.264	0.430	0.890	0.310	0.506	1.900	0.663	1.080
		009	Dosing-Terminal Euthanasia	276.4	0.724	0.262	0.372	0.906	0.328	0.466	2.042	0.739	1.049
		010	Dosing-Terminal Euthanasia	287.8	0.591	0.205	0.316	0.776	0.270	0.415	2.030	0.705	1.087
		011	Recovery-Recovery Euthanasia 1	329.10	0.884	0.269	0.407	1.011	0.307	0.465	2.406	0.731	1.107
		012	Recovery-Recovery Euthanasia 1	362.80	1.159	0.319	0.557	1.124	0.310	0.540	2.724	0.751	1.310
		013	Recovery-Recovery Euthanasia 1	304.00	1.450	0.477	0.691	0.790	0.260	0.377	2.060	0.678	0.982
		014	Recovery-Recovery Euthanasia 1	283.80	0.874	0.308	0.426	0.898	0.316	0.438	2.025	0.714	0.987
		015	Recovery-Recovery Euthanasia 1	379.20	1.299	0.343	0.609	1.311	0.346	0.615	2.814	0.742	1.319

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**Appendix 10**

**Organ Weights (g) and Ratios**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Male

Group Number	Dose	Animal Number	Phase-Planned Sacrifice Group	BW (g)	Gland, Prostate			Heart			Kidney		
					ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN
2	30 µg/day	016	Dosing-Terminal Euthanasia	257.4	0.697	0.271	0.395	0.964	0.375	0.546	1.965	0.763	1.113
		017	Dosing-Terminal Euthanasia	284.4	0.479	0.168	0.246	0.934	0.328	0.479	2.181	0.767	1.119
		018	Dosing-Terminal Euthanasia	267.3	0.520	0.195	0.283	0.801	0.300	0.436	2.195	0.821	1.194
		019	Dosing-Terminal Euthanasia	289.1	0.772	0.267	0.436	1.180	0.408	0.666	2.352	0.814	1.327
		020	Dosing-Terminal Euthanasia	250.2	0.658	0.263	0.328	0.880	0.352	0.439	2.020	0.807	1.007
		021	Dosing-Terminal Euthanasia	269.6	0.636	0.236	0.308	0.968	0.359	0.469	2.323	0.862	1.127
		022	Dosing-Terminal Euthanasia	268.5	0.683	0.254	0.391	0.838	0.312	0.480	2.064	0.769	1.182
		023	Dosing-Terminal Euthanasia	274.5	0.716	0.261	0.391	0.894	0.326	0.489	2.163	0.788	1.182
		024	Dosing-Terminal Euthanasia	248.5	0.950	0.382	0.467	0.785	0.316	0.386	2.182	0.878	1.073
		025	Dosing-Terminal Euthanasia	302.2	1.213	0.401	0.562	0.998	0.330	0.463	2.752	0.911	1.276
		026	Recovery-Recovery Euthanasia 1	351.50	0.869	0.247	0.479	1.038	0.295	0.572	2.282	0.649	1.257
		027	Recovery-Recovery Euthanasia 1	340.00	1.029	0.303	0.566	1.043	0.307	0.574	2.270	0.668	1.249
		028	Recovery-Recovery Euthanasia 1	335.40	1.306	0.389	0.628	1.152	0.343	0.554	2.440	0.727	1.173
		029	Recovery-Recovery Euthanasia 1	350.40	0.884	0.252	0.429	1.171	0.334	0.568	2.364	0.675	1.146
		030	Recovery-Recovery Euthanasia 1	380.20	1.008	0.265	0.499	1.091	0.287	0.540	2.347	0.617	1.162

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**Appendix 10**

**Organ Weights (g) and Ratios**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Male

Group Number	Dose	Animal Number	Phase-Planned Sacrifice Group	BW (g)	Gland, Prostate			Heart			Kidney		
					ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN
3	30 µg /day	031	Dosing-Terminal Euthanasia	244.7	0.709	0.290	0.392	0.807	0.330	0.446	1.808	0.739	1.000
		032	Dosing-Terminal Euthanasia	254.6	0.580	0.228	0.306	0.805	0.316	0.424	1.998	0.785	1.053
		033	Dosing-Terminal Euthanasia	301.1	0.781	0.259	0.402	0.984	0.327	0.506	2.209	0.734	1.136
		034	Dosing-Terminal Euthanasia	250.4	0.500	0.200	0.271	0.837	0.334	0.454	1.720	0.687	0.934
		035	Dosing-Terminal Euthanasia	235.8	0.724	0.307	0.377	0.767	0.325	0.399	1.828	0.775	0.951
		036	Dosing-Terminal Euthanasia	278.8	0.767	0.275	0.404	0.898	0.322	0.473	2.325	0.834	1.225
		037	Dosing-Terminal Euthanasia	273.2	0.651	0.238	0.350	1.127	0.413	0.606	2.067	0.757	1.111
		038	Dosing-Terminal Euthanasia	258.7	0.545	0.211	0.279	0.853	0.330	0.437	2.221	0.859	1.138
		039	Dosing-Terminal Euthanasia	262.2	0.836	0.319	0.429	0.853	0.325	0.438	1.981	0.756	1.017
		040	Dosing-Terminal Euthanasia	266.4	0.662	0.248	0.329	0.864	0.324	0.430	2.095	0.786	1.042
		041	Recovery-Recovery Euthanasia 1	339.00	0.909	0.268	0.473	1.091	0.322	0.568	2.470	0.729	1.285
		042	Recovery-Recovery Euthanasia 1	325.50	0.823	0.253	0.419	0.958	0.294	0.488	1.963	0.603	1.001
		043	Recovery-Recovery Euthanasia 1	344.20	1.169	0.340	0.603	1.085	0.315	0.560	2.293	0.666	1.183
		044	Recovery-Recovery Euthanasia 1	347.50	1.088	0.313	0.561	1.088	0.313	0.561	2.331	0.671	1.203
		045	Recovery-Recovery Euthanasia 1	315.60	1.234	0.391	0.635	1.104	0.350	0.568	2.359	0.747	1.214

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**Appendix 10**

**Organ Weights (g) and Ratios**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Male													
Group Number	Dose	Animal Number	Phase-Planned Sacrifice Group	BW (g)	Liver			Spleen			Testis		
					ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN
1	0 µg/day	001	Dosing-Terminal Euthanasia	269.7	8.285	3.072	4.517	0.503	0.187	0.274	3.436	1.274	1.874
		002	Dosing-Terminal Euthanasia	321.3	9.334	2.905	4.834	0.669	0.208	0.346	3.283	1.022	1.700
		003	Dosing-Terminal Euthanasia	300.0	8.844	2.948	4.533	0.598	0.199	0.307	3.689	1.230	1.891
		004	Dosing-Terminal Euthanasia	315.7	8.552	2.709	4.076	0.689	0.218	0.328	3.599	1.140	1.715
		005	Dosing-Terminal Euthanasia	294.1	8.495	2.888	4.406	0.604	0.205	0.313	3.500	1.190	1.815
		006	Dosing-Terminal Euthanasia	304.8	8.099	2.657	4.375	0.537	0.176	0.290	2.828	0.928	1.528
		007	Dosing-Terminal Euthanasia	304.1	8.327	2.738	4.397	0.635	0.209	0.335	2.729	0.897	1.441
		008	Dosing-Terminal Euthanasia	286.7	7.583	2.645	4.309	0.607	0.212	0.345	3.189	1.112	1.812
		009	Dosing-Terminal Euthanasia	276.4	7.937	2.872	4.079	0.590	0.213	0.303	3.296	1.192	1.694
		010	Dosing-Terminal Euthanasia	287.8	7.762	2.697	4.155	0.519	0.180	0.278	3.178	1.104	1.701
		011	Recovery-Recovery Euthanasia 1	329.10	8.169	2.482	3.759	0.602	0.183	0.277	3.522	1.070	1.621
		012	Recovery-Recovery Euthanasia 1	362.80	9.132	2.517	4.390	0.647	0.178	0.311	3.802	1.048	1.828
		013	Recovery-Recovery Euthanasia 1	304.00	7.466	2.456	3.559	0.542	0.178	0.258	3.191	1.050	1.521
		014	Recovery-Recovery Euthanasia 1	283.80	7.437	2.621	3.624	0.655	0.231	0.319	3.421	1.205	1.667
		015	Recovery-Recovery Euthanasia 1	379.20	10.744	2.833	5.037	0.597	0.157	0.280	3.800	1.002	1.782

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**Appendix 10**

**Organ Weights (g) and Ratios**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Male													
Group Number	Dose	Animal Number	Phase-Planned Sacrifice Group	BW (g)	Liver			Spleen			Testis		
					ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN
2	30 µg/day	016	Dosing-Terminal Euthanasia	257.4	7.531	2.926	4.267	0.790	0.307	0.448	3.506	1.362	1.986
		017	Dosing-Terminal Euthanasia	284.4	7.900	2.778	4.053	0.782	0.275	0.401	3.547	1.247	1.820
		018	Dosing-Terminal Euthanasia	267.3	8.757	3.276	4.762	0.775	0.290	0.421	3.004	1.124	1.633
		019	Dosing-Terminal Euthanasia	289.1	8.317	2.877	4.694	0.626	0.217	0.353	3.508	1.213	1.980
		020	Dosing-Terminal Euthanasia	250.2	7.481	2.990	3.729	0.747	0.299	0.372	3.406	1.361	1.698
		021	Dosing-Terminal Euthanasia	269.6	7.714	2.861	3.741	0.933	0.346	0.452	3.582	1.329	1.737
		022	Dosing-Terminal Euthanasia	268.5	7.203	2.683	4.125	0.697	0.260	0.399	3.037	1.131	1.739
		023	Dosing-Terminal Euthanasia	274.5	7.457	2.717	4.075	0.767	0.279	0.419	3.480	1.268	1.902
		024	Dosing-Terminal Euthanasia	248.5	7.389	2.973	3.635	0.646	0.260	0.318	3.480	1.400	1.712
		025	Dosing-Terminal Euthanasia	302.2	8.131	2.691	3.770	0.937	0.310	0.434	4.133	1.368	1.916
		026	Recovery-Recovery Euthanasia 1	351.50	9.462	2.692	5.213	0.674	0.192	0.371	3.169	0.902	1.746
		027	Recovery-Recovery Euthanasia 1	340.00	8.740	2.571	4.807	0.710	0.209	0.391	2.955	0.869	1.625
		028	Recovery-Recovery Euthanasia 1	335.40	8.136	2.426	3.912	0.703	0.210	0.338	3.595	1.072	1.728
		029	Recovery-Recovery Euthanasia 1	350.40	9.145	2.610	4.435	0.727	0.207	0.353	3.828	1.092	1.856
		030	Recovery-Recovery Euthanasia 1	380.20	9.353	2.460	4.630	0.801	0.211	0.397	3.744	0.985	1.853

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**Appendix 10**

**Organ Weights (g) and Ratios**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Male													
Group Number	Dose	Animal Number	Phase-Planned Sacrifice Group	BW (g)	Liver			Spleen			Testis		
					ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN
3	30 µg /day	031	Dosing-Terminal Euthanasia	244.7	7.476	3.055	4.135	0.850	0.347	0.470	3.361	1.374	1.859
		032	Dosing-Terminal Euthanasia	254.6	7.377	2.897	3.889	0.775	0.304	0.409	3.475	1.365	1.832
		033	Dosing-Terminal Euthanasia	301.1	8.757	2.908	4.502	0.838	0.278	0.431	2.980	0.990	1.532
		034	Dosing-Terminal Euthanasia	250.4	6.773	2.705	3.677	0.680	0.272	0.369	2.942	1.175	1.597
		035	Dosing-Terminal Euthanasia	235.8	7.037	2.984	3.661	0.799	0.339	0.416	3.422	1.451	1.780
		036	Dosing-Terminal Euthanasia	278.8	7.802	2.798	4.111	0.736	0.264	0.388	3.126	1.121	1.647
		037	Dosing-Terminal Euthanasia	273.2	8.310	3.042	4.465	0.976	0.357	0.524	3.090	1.131	1.660
		038	Dosing-Terminal Euthanasia	258.7	7.656	2.959	3.924	0.883	0.341	0.453	3.263	1.261	1.672
		039	Dosing-Terminal Euthanasia	262.2	7.155	2.729	3.675	0.730	0.278	0.375	3.445	1.314	1.769
		040	Dosing-Terminal Euthanasia	266.4	7.529	2.826	3.744	0.717	0.269	0.357	3.612	1.356	1.796
		041	Recovery-Recovery Euthanasia 1	339.00	8.953	2.641	4.658	0.478	0.141	0.249	3.415	1.007	1.777
		042	Recovery-Recovery Euthanasia 1	325.50	8.199	2.519	4.179	0.671	0.206	0.342	4.027	1.237	2.052
		043	Recovery-Recovery Euthanasia 1	344.20	8.854	2.572	4.566	0.624	0.181	0.322	3.508	1.019	1.809
		044	Recovery-Recovery Euthanasia 1	347.50	9.468	2.725	4.885	0.782	0.225	0.404	3.825	1.101	1.974
		045	Recovery-Recovery Euthanasia 1	315.60	8.320	2.636	4.282	0.747	0.237	0.384	3.694	1.170	1.901

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**Appendix 10**

**Organ Weights (g) and Ratios**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Male

Thymus

Group Number	Dose	Animal Number	Phase-Planned Sacrifice Group	BW (g)	ABS	OW:BW	OW:BRN
1	0 µg/day	001	Dosing-Terminal Euthanasia	269.7	0.581	0.215	0.317
		002	Dosing-Terminal Euthanasia	321.3	0.611	0.190	0.316
		003	Dosing-Terminal Euthanasia	300.0	0.643	0.214	0.330
		004	Dosing-Terminal Euthanasia	315.7	0.681	0.216	0.325
		005	Dosing-Terminal Euthanasia	294.1	0.522	0.177	0.271
		006	Dosing-Terminal Euthanasia	304.8	0.556	0.182	0.300
		007	Dosing-Terminal Euthanasia	304.1	0.657	0.216	0.347
		008	Dosing-Terminal Euthanasia	286.7	0.484	0.169	0.275
		009	Dosing-Terminal Euthanasia	276.4	0.653	0.236	0.336
		010	Dosing-Terminal Euthanasia	287.8	0.526	0.183	0.282
		011	Recovery-Recovery Euthanasia 1	329.10	0.397	0.121	0.183
		012	Recovery-Recovery Euthanasia 1	362.80	0.407	0.112	0.196
		013	Recovery-Recovery Euthanasia 1	304.00	0.519	0.171	0.247
		014	Recovery-Recovery Euthanasia 1	283.80	0.583	0.205	0.284
		015	Recovery-Recovery Euthanasia 1	379.20	0.563	0.148	0.264

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**Appendix 10**

**Organ Weights (g) and Ratios**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Male

Thymus

Group Number	Dose	Animal Number	Phase-Planned Sacrifice Group	BW (g)	ABS	OW:BW	OW:BRN
2	30 µg/day	016	Dosing-Terminal Euthanasia	257.4	0.351	0.136	0.199
		017	Dosing-Terminal Euthanasia	284.4	0.650	0.229	0.334
		018	Dosing-Terminal Euthanasia	267.3	0.466	0.174	0.253
		019	Dosing-Terminal Euthanasia	289.1	0.412	0.143	0.233
		020	Dosing-Terminal Euthanasia	250.2	0.409	0.163	0.204
		021	Dosing-Terminal Euthanasia	269.6	0.479	0.178	0.232
		022	Dosing-Terminal Euthanasia	268.5	0.562	0.209	0.322
		023	Dosing-Terminal Euthanasia	274.5	0.469	0.171	0.256
		024	Dosing-Terminal Euthanasia	248.5	0.353	0.142	0.174
		025	Dosing-Terminal Euthanasia	302.2	0.522	0.173	0.242
		026	Recovery-Recovery Euthanasia 1	351.50	0.572	0.163	0.315
		027	Recovery-Recovery Euthanasia 1	340.00	0.492	0.145	0.271
		028	Recovery-Recovery Euthanasia 1	335.40	0.530	0.158	0.255
		029	Recovery-Recovery Euthanasia 1	350.40	0.525	0.150	0.255
030	Recovery-Recovery Euthanasia 1	380.20	0.649	0.171	0.321		

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**Appendix 10**

**Organ Weights (g) and Ratios**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Male

Thymus

Group Number	Dose	Animal Number	Phase-Planned Sacrifice Group	BW (g)	ABS	OW:BW	OW:BRN
3	30 µg /day	031	Dosing-Terminal Euthanasia	244.7	0.306	0.125	0.169
		032	Dosing-Terminal Euthanasia	254.6	0.550	0.216	0.290
		033	Dosing-Terminal Euthanasia	301.1	0.573	0.190	0.295
		034	Dosing-Terminal Euthanasia	250.4	0.332	0.133	0.180
		035	Dosing-Terminal Euthanasia	235.8	0.343	0.145	0.178
		036	Dosing-Terminal Euthanasia	278.8	0.460	0.165	0.242
		037	Dosing-Terminal Euthanasia	273.2	0.454	0.166	0.244
		038	Dosing-Terminal Euthanasia	258.7	0.359	0.139	0.184
		039	Dosing-Terminal Euthanasia	262.2	0.396	0.151	0.203
		040	Dosing-Terminal Euthanasia	266.4	0.427	0.160	0.212
		041	Recovery-Recovery Euthanasia 1	339.00	0.348	0.103	0.181
		042	Recovery-Recovery Euthanasia 1	325.50	0.525	0.161	0.268
		043	Recovery-Recovery Euthanasia 1	344.20	0.366	0.106	0.189
		044	Recovery-Recovery Euthanasia 1	347.50	0.416	0.120	0.215
		045	Recovery-Recovery Euthanasia 1	315.60	0.480	0.152	0.247

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**Appendix 10**

**Organ Weights (g) and Ratios**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Female													
Group Number	Dose	Animal Number	Phase-Planned Sacrifice Group	BW (g)	Brain			Gland, Adrenal			Heart		
					ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN
1	0 µg/day	046	Dosing-Terminal Euthanasia	185.6	1.734	0.934	1.000	0.067	0.036	0.039	0.670	0.361	0.386
		047	Dosing-Terminal Euthanasia	213.7	1.948	0.912	1.000	0.086	0.040	0.044	0.807	0.378	0.414
		048	Dosing-Terminal Euthanasia	183.1	1.928	1.053	1.000	0.075	0.041	0.039	0.757	0.413	0.393
		049	Dosing-Terminal Euthanasia	192.4	1.836	0.954	1.000	0.067	0.035	0.036	0.659	0.343	0.359
		050	Dosing-Terminal Euthanasia	206.6	1.913	0.926	1.000	0.107	0.052	0.056	0.640	0.310	0.335
		051	Dosing-Terminal Euthanasia	207.2	1.837	0.887	1.000	0.100	0.048	0.054	0.865	0.417	0.471
		052	Dosing-Terminal Euthanasia	201.7	1.905	0.944	1.000	0.094	0.047	0.049	0.738	0.366	0.387
		053	Dosing-Terminal Euthanasia	202.0	1.907	0.944	1.000	0.080	0.040	0.042	0.833	0.412	0.437
		054	Dosing-Terminal Euthanasia	207.8	1.797	0.865	1.000	0.114	0.055	0.063	0.803	0.386	0.447
		055	Dosing-Terminal Euthanasia	187.2	1.805	0.964	1.000	0.092	0.049	0.051	0.678	0.362	0.376
		056	Recovery-Recovery Euthanasia 1	230.00	1.854	0.806	1.000	0.093	0.040	0.050	0.759	0.330	0.409
		057	Recovery-Recovery Euthanasia 1	202.70	1.804	0.890	1.000	0.077	0.038	0.043	0.689	0.340	0.382
		058	Recovery-Recovery Euthanasia 1	203.30	1.668	0.820	1.000	0.084	0.041	0.050	0.702	0.345	0.421
		059	Recovery-Recovery Euthanasia 1	200.80	1.938	0.965	1.000	0.100	0.050	0.052	0.691	0.344	0.357
		060	Recovery-Recovery Euthanasia 1	231.40	1.904	0.823	1.000	0.079	0.034	0.041	0.815	0.352	0.428

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**Appendix 10**

**Organ Weights (g) and Ratios**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Female													
Group Number	Dose	Animal Number	Phase-Planned Sacrifice Group	BW (g)	Brain			Gland, Adrenal			Heart		
					ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN
2	30 µg/day	061	Dosing-Terminal Euthanasia	201.9	1.753	0.868	1.000	0.091	0.045	0.052	0.842	0.417	0.480
		062	Dosing-Terminal Euthanasia	188.0	1.846	0.982	1.000	0.076	0.040	0.041	0.733	0.390	0.397
		063	Dosing-Terminal Euthanasia	180.5	1.678	0.930	1.000	0.082	0.045	0.049	0.875	0.485	0.521
		064	Dosing-Terminal Euthanasia	197.0	1.834	0.931	1.000	0.096	0.049	0.052	0.699	0.355	0.381
		065	Dosing-Terminal Euthanasia	196.8	1.808	0.919	1.000	0.073	0.037	0.040	0.733	0.372	0.405
		066	Dosing-Terminal Euthanasia	194.9	1.844	0.946	1.000	0.076	0.039	0.041	0.669	0.343	0.363
		067	Dosing-Terminal Euthanasia	198.0	1.845	0.932	1.000	0.113	0.057	0.061	0.775	0.391	0.420
		068	Dosing-Terminal Euthanasia	175.3	1.713	0.977	1.000	0.069	0.039	0.040	0.607	0.346	0.354
		069	Dosing-Terminal Euthanasia	211.6	1.762	0.833	1.000	0.108	0.051	0.061	0.861	0.407	0.489
		070	Dosing-Terminal Euthanasia	201.6	1.785	0.885	1.000	0.102	0.051	0.057	0.779	0.386	0.436
		071	Recovery-Recovery Euthanasia 1	216.00	2.093	0.969	1.000	0.088	0.041	0.042	0.778	0.360	0.372
		072	Recovery-Recovery Euthanasia 1	216.00	1.759	0.814	1.000	0.070	0.032	0.040	0.939	0.435	0.534
		073	Recovery-Recovery Euthanasia 1	205.20	1.900	0.926	1.000	0.087	0.042	0.046	0.690	0.336	0.363
		074	Recovery-Recovery Euthanasia 1	209.20	1.850	0.884	1.000	0.104	0.050	0.056	0.890	0.425	0.481
		075	Recovery-Recovery Euthanasia 1	220.40	1.764	0.800	1.000	0.103	0.047	0.058	1.032	0.468	0.585

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**Appendix 10**  
**Organ Weights (g) and Ratios**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Female													
Group Number	Dose	Animal Number	Phase-Planned Sacrifice Group	BW (g)	Brain			Gland, Adrenal			Heart		
					ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN
3	30 µg /day	076	Dosing-Terminal Euthanasia	192.2	1.758	0.915	1.000	0.024e	0.012e	0.014e	0.686	0.357	0.390
		077	Dosing-Terminal Euthanasia	190.0	1.757	0.925	1.000	0.074	0.039	0.042	0.748	0.394	0.426
		078	Dosing-Terminal Euthanasia	201.5	1.899	0.942	1.000	0.094	0.047	0.049	0.843	0.418	0.444
		079	Dosing-Terminal Euthanasia	200.8	1.806	0.899	1.000	0.095	0.047	0.053	0.720	0.359	0.399
		080	Dosing-Terminal Euthanasia	199.4	1.896	0.951	1.000	0.113	0.057	0.060	0.707	0.355	0.373
		081	Dosing-Terminal Euthanasia	185.4	1.868	1.008	1.000	0.069	0.037	0.037	0.615	0.332	0.329
		082	Dosing-Terminal Euthanasia	184.3	1.842	0.999	1.000	0.072	0.039	0.039	0.640	0.347	0.347
		083	Dosing-Terminal Euthanasia	192.1	1.822	0.948	1.000	0.124	0.065	0.068	0.881	0.459	0.484
		084	Dosing-Terminal Euthanasia	191.9	2.001	1.043	1.000	0.097	0.051	0.048	0.678	0.353	0.339
		085	Dosing-Terminal Euthanasia	180.6	1.758	0.973	1.000	0.078	0.043	0.044	0.655	0.363	0.373
		086	Recovery-Recovery Euthanasia 1	210.30	1.785	0.849	1.000	0.099	0.047	0.055	0.719	0.342	0.403
		087	Recovery-Recovery Euthanasia 1	237.80	1.819	0.765	1.000	0.092	0.039	0.051	0.930	0.391	0.511
		088	Recovery-Recovery Euthanasia 1	182.40	1.918	1.052	1.000	0.089	0.049	0.046	0.760	0.417	0.396
		089	Recovery-Recovery Euthanasia 1	212.50	1.862	0.876	1.000	0.079	0.037	0.042	0.776	0.365	0.417
090	Recovery-Recovery Euthanasia 1	208.80	1.841	0.882	1.000	0.091	0.044	0.049	0.920	0.441	0.500		

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**Appendix 10**

**Organ Weights (g) and Ratios**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Female													
Group Number	Dose	Animal Number	Phase-Planned Sacrifice Group	BW (g)	Kidney			Liver			Ovary		
					ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN
1	0 µg/day	046	Dosing-Terminal Euthanasia	185.6	1.528	0.823	0.881	5.132	2.765	2.960	0.105	0.057	0.061
		047	Dosing-Terminal Euthanasia	213.7	1.491	0.698	0.765	6.077	2.844	3.120	0.126	0.059	0.065
		048	Dosing-Terminal Euthanasia	183.1	1.521	0.831	0.789	4.935	2.695	2.560	0.124	0.068	0.064
		049	Dosing-Terminal Euthanasia	192.4	1.416	0.736	0.771	5.284	2.746	2.878	0.103	0.054	0.056
		050	Dosing-Terminal Euthanasia	206.6	1.638	0.793	0.856	5.809	2.812	3.037	0.129	0.062	0.067
		051	Dosing-Terminal Euthanasia	207.2	1.545	0.746	0.841	5.489	2.649	2.988	0.085	0.041	0.046
		052	Dosing-Terminal Euthanasia	201.7	1.563	0.775	0.820	5.626	2.789	2.953	0.118	0.059	0.062
		053	Dosing-Terminal Euthanasia	202.0	1.514	0.750	0.794	5.556	2.750	2.913	0.130	0.064	0.068
		054	Dosing-Terminal Euthanasia	207.8	1.653	0.795	0.920	5.314	2.557	2.957	0.137	0.066	0.076
		055	Dosing-Terminal Euthanasia	187.2	1.404	0.750	0.778	5.349	2.857	2.963	0.110	0.059	0.061
		056	Recovery-Recovery Euthanasia 1	230.00	1.694	0.737	0.914	6.030	2.622	3.252	0.149	0.065	0.080
		057	Recovery-Recovery Euthanasia 1	202.70	1.340	0.661	0.743	5.280	2.605	2.927	0.090	0.044	0.050
		058	Recovery-Recovery Euthanasia 1	203.30	1.392	0.685	0.835	5.299	2.606	3.177	0.097	0.048	0.058
		059	Recovery-Recovery Euthanasia 1	200.80	1.560	0.777	0.805	5.176	2.578	2.671	0.114	0.057	0.059
		060	Recovery-Recovery Euthanasia 1	231.40	1.660	0.717	0.872	6.028	2.605	3.166	0.171	0.074	0.090

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**Appendix 10**

**Organ Weights (g) and Ratios**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Female													
Group Number	Dose	Animal Number	Phase-Planned Sacrifice Group	BW (g)	Kidney			Liver			Ovary		
					ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN
2	30 µg/day	061	Dosing-Terminal Euthanasia	201.9	1.579	0.782	0.901	6.265	3.103	3.574	0.121	0.060	0.069
		062	Dosing-Terminal Euthanasia	188.0	1.595	0.848	0.864	5.849	3.111	3.168	0.071	0.038	0.038
		063	Dosing-Terminal Euthanasia	180.5	1.550	0.859	0.924	4.987	2.763	2.972	0.087	0.048	0.052
		064	Dosing-Terminal Euthanasia	197.0	1.528	0.776	0.833	5.364	2.723	2.925	0.106	0.054	0.058
		065	Dosing-Terminal Euthanasia	196.8	1.621	0.824	0.897	6.048	3.073	3.345	0.120	0.061	0.066
		066	Dosing-Terminal Euthanasia	194.9	1.662	0.853	0.901	5.055	2.594	2.741	0.115	0.059	0.062
		067	Dosing-Terminal Euthanasia	198.0	1.720	0.869	0.932	5.548	2.802	3.007	0.124	0.063	0.067
		068	Dosing-Terminal Euthanasia	175.3	1.614	0.921	0.942	4.941	2.819	2.884	0.121	0.069	0.071
		069	Dosing-Terminal Euthanasia	211.6	1.766	0.835	1.002	6.512	3.078	3.696	0.095	0.045	0.054
		070	Dosing-Terminal Euthanasia	201.6	1.708	0.847	0.957	5.921	2.937	3.317	0.093	0.046	0.052
		071	Recovery-Recovery Euthanasia 1	216.00	1.620	0.750	0.774	5.605	2.595	2.678	0.125	0.058	0.060
		072	Recovery-Recovery Euthanasia 1	216.00	1.591	0.737	0.904	6.056	2.804	3.443	0.078	0.036	0.044
		073	Recovery-Recovery Euthanasia 1	205.20	1.482	0.722	0.780	5.460	2.661	2.874	0.170	0.083	0.089
		074	Recovery-Recovery Euthanasia 1	209.20	1.723	0.824	0.931	5.655	2.703	3.057	0.166	0.079	0.090
		075	Recovery-Recovery Euthanasia 1	220.40	1.828	0.829	1.036	6.258	2.839	3.548	0.113	0.051	0.064

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**Appendix 10**

**Organ Weights (g) and Ratios**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Female													
Group Number	Dose	Animal Number	Phase-Planned Sacrifice Group	BW (g)	Kidney			Liver			Ovary		
					ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN
3	30 µg /day	076	Dosing-Terminal Euthanasia	192.2	1.596	0.830	0.908	5.669	2.950	3.225	0.015e	0.008e	0.009e
		077	Dosing-Terminal Euthanasia	190.0	1.529	0.805	0.870	5.637	2.967	3.208	0.092	0.048	0.052
		078	Dosing-Terminal Euthanasia	201.5	1.750	0.868	0.922	6.241	3.097	3.286	0.116	0.058	0.061
		079	Dosing-Terminal Euthanasia	200.8	1.794	0.893	0.993	6.541	3.257	3.622	0.127	0.063	0.070
		080	Dosing-Terminal Euthanasia	199.4	1.684	0.845	0.888	6.451	3.235	3.402	0.139	0.070	0.073
		081	Dosing-Terminal Euthanasia	185.4	1.669	0.900	0.893	5.539	2.988	2.965	0.116	0.063	0.062
		082	Dosing-Terminal Euthanasia	184.3	1.402	0.761	0.761	5.071	2.751	2.753	0.096	0.052	0.052
		083	Dosing-Terminal Euthanasia	192.1	1.756	0.914	0.964	5.806	3.022	3.187	0.119	0.062	0.065
		084	Dosing-Terminal Euthanasia	191.9	1.590	0.829	0.795	5.941	3.096	2.969	0.110	0.057	0.055
		085	Dosing-Terminal Euthanasia	180.6	1.394	0.772	0.793	5.208	2.884	2.962	0.087	0.048	0.049
		086	Recovery-Recovery Euthanasia 1	210.30	1.615	0.768	0.905	5.322	2.531	2.982	0.147	0.070	0.082
		087	Recovery-Recovery Euthanasia 1	237.80	1.823	0.767	1.002	6.706	2.820	3.687	0.169	0.071	0.093
		088	Recovery-Recovery Euthanasia 1	182.40	1.725	0.946	0.899	5.371	2.945	2.800	0.119	0.065	0.062
		089	Recovery-Recovery Euthanasia 1	212.50	1.737	0.817	0.933	5.787	2.723	3.108	0.112	0.053	0.060
090	Recovery-Recovery Euthanasia 1	208.80	1.670	0.800	0.907	5.952	2.851	3.233	0.112	0.054	0.061		

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**Appendix 10**

**Organ Weights (g) and Ratios**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Group Number	Dose	Animal Number	Phase-Planned Sacrifice Group	BW (g)	Female					
					Spleen			Thymus		
					ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN
1	0 µg/day	046	Dosing-Terminal Euthanasia	185.6	0.356	0.192	0.205	0.457	0.246	0.264
		047	Dosing-Terminal Euthanasia	213.7	0.501	0.234	0.257	0.426	0.199	0.219
		048	Dosing-Terminal Euthanasia	183.1	0.348	0.190	0.180	0.373	0.204	0.193
		049	Dosing-Terminal Euthanasia	192.4	0.516	0.268	0.281	0.538	0.280	0.293
		050	Dosing-Terminal Euthanasia	206.6	0.490	0.237	0.256	0.573	0.277	0.300
		051	Dosing-Terminal Euthanasia	207.2	0.416	0.201	0.226	0.413	0.199	0.225
		052	Dosing-Terminal Euthanasia	201.7	0.532	0.264	0.279	0.527	0.261	0.277
		053	Dosing-Terminal Euthanasia	202.0	0.389	0.193	0.204	0.396	0.196	0.208
		054	Dosing-Terminal Euthanasia	207.8	0.425	0.205	0.237	0.493	0.237	0.274
		055	Dosing-Terminal Euthanasia	187.2	0.409	0.218	0.227	0.392	0.209	0.217
		056	Recovery-Recovery Euthanasia 1	230.00	0.565	0.246	0.305	0.410	0.178	0.221
		057	Recovery-Recovery Euthanasia 1	202.70	0.413	0.204	0.229	0.392	0.193	0.217
		058	Recovery-Recovery Euthanasia 1	203.30	0.332	0.163	0.199	0.496	0.244	0.297
		059	Recovery-Recovery Euthanasia 1	200.80	0.380	0.189	0.196	0.336	0.167	0.173
		060	Recovery-Recovery Euthanasia 1	231.40	0.516	0.223	0.271	0.505	0.218	0.265

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**Appendix 10**

**Organ Weights (g) and Ratios**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Group Number	Dose	Animal Number	Phase-Planned Sacrifice Group	BW (g)	Female					
					Spleen			Thymus		
					ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN
2	30 µg/day	061	Dosing-Terminal Euthanasia	201.9	0.712	0.353	0.406	0.447	0.221	0.255
		062	Dosing-Terminal Euthanasia	188.0	0.694	0.369	0.376	0.380	0.202	0.206
		063	Dosing-Terminal Euthanasia	180.5	0.640	0.355	0.381	0.530	0.294	0.316
		064	Dosing-Terminal Euthanasia	197.0	0.884	0.449	0.482	0.372	0.189	0.203
		065	Dosing-Terminal Euthanasia	196.8	0.785	0.399	0.434	0.400	0.203	0.221
		066	Dosing-Terminal Euthanasia	194.9	0.552	0.283	0.299	0.495	0.254	0.268
		067	Dosing-Terminal Euthanasia	198.0	0.598	0.302	0.324	0.387	0.195	0.210
		068	Dosing-Terminal Euthanasia	175.3	0.552	0.315	0.322	0.121	0.069	0.071
		069	Dosing-Terminal Euthanasia	211.6	0.674	0.319	0.383	0.478	0.226	0.271
		070	Dosing-Terminal Euthanasia	201.6	0.705	0.350	0.395	0.357	0.177	0.200
		071	Recovery-Recovery Euthanasia 1	216.00	0.476	0.220	0.227	0.429	0.199	0.205
		072	Recovery-Recovery Euthanasia 1	216.00	0.411	0.190	0.234	0.463	0.214	0.263
		073	Recovery-Recovery Euthanasia 1	205.20	0.482	0.235	0.254	0.406	0.198	0.214
		074	Recovery-Recovery Euthanasia 1	209.20	0.504	0.241	0.272	0.460	0.220	0.249
		075	Recovery-Recovery Euthanasia 1	220.40	0.500	0.227	0.283	0.431	0.196	0.244

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**Appendix 10**

**Organ Weights (g) and Ratios**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Group Number	Dose	Animal Number	Phase-Planned Sacrifice Group	BW (g)	Female					
					Spleen			Thymus		
					ABS	OW:BW	OW:BRN	ABS	OW:BW	OW:BRN
3	30 µg /day	076	Dosing-Terminal Euthanasia	192.2	0.601	0.313	0.342	0.339	0.176	0.193
		077	Dosing-Terminal Euthanasia	190.0	0.583	0.307	0.332	0.399	0.210	0.227
		078	Dosing-Terminal Euthanasia	201.5	0.610	0.303	0.321	0.374	0.186	0.197
		079	Dosing-Terminal Euthanasia	200.8	0.712	0.355	0.394	0.410	0.204	0.227
		080	Dosing-Terminal Euthanasia	199.4	0.635	0.318	0.335	0.518	0.260	0.273
		081	Dosing-Terminal Euthanasia	185.4	0.543	0.293	0.291	0.419	0.226	0.224
		082	Dosing-Terminal Euthanasia	184.3	0.677	0.367	0.368	0.363	0.197	0.197
		083	Dosing-Terminal Euthanasia	192.1	0.684	0.356	0.375	0.402	0.209	0.221
		084	Dosing-Terminal Euthanasia	191.9	0.587	0.306	0.293	0.295	0.154	0.147
		085	Dosing-Terminal Euthanasia	180.6	0.567	0.314	0.323	0.387	0.214	0.220
		086	Recovery-Recovery Euthanasia 1	210.30	0.378	0.180	0.212	0.413	0.196	0.231
		087	Recovery-Recovery Euthanasia 1	237.80	0.532	0.224	0.292	0.425	0.179	0.234
		088	Recovery-Recovery Euthanasia 1	182.40	0.347	0.190	0.181	0.317	0.174	0.165
		089	Recovery-Recovery Euthanasia 1	212.50	0.461	0.217	0.248	0.418	0.197	0.224
090	Recovery-Recovery Euthanasia 1	208.80	0.518	0.248	0.281	0.388	0.186	0.211		

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**Appendix 11**  
**Individual Macroscopic and Microscopic Observations w/Correlations**  
**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

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**Footnotes**

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NOS = Not otherwise specified.

Note: All tissues are considered as macroscopically unremarkable unless noted in the individual animal listings.

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**Appendix 11**

**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
001	M	1	0 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Gland, Parathyroid	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone Marrow, Sternum	Bone, Sternum	Brain	Epididymis
Esophagus	Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary
Gland, Seminal Vesicle	Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart	Joint
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Liver	Lung
Lymph Node, Draining	Lymph Node, Inguinal	Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic
Nerve, Peripheral	Pancreas	Site, Injection	Skin	Small Intestine, Duodenum
Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord	Spleen	Stomach
Testis	Thymus	Tongue	Trachea	Ureter
Urinary Bladder				

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**Appendix 11**

**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
002	M	1	0 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Gland, Parathyroid	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	
Gland, Thyroid	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	
Lymph Node, Inguinal	No macroscopic observations on tissue				Missing	

The following required protocol tissues were not examined microscopically:

Lymph Node, Inguinal

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone Marrow, Sternum	Bone, Sternum	Brain	Epididymis
Esophagus	Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary
Gland, Seminal Vesicle	Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart	Joint
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Liver	Lung
Lymph Node, Draining	Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral
Pancreas	Site, Injection	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord	Spleen	Stomach	Testis
Thymus	Tongue	Trachea	Ureter	Urinary Bladder

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**Appendix 11**

**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
003	M	1	0 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Kidney	No macroscopic observations on tissue				Dilatation, Pelvis, Unilateral, Minimal	
Lung	Abnormal color, Dark, Focal, 0.3-0.5 cm, Left lobe			Not Correlated	Tissue is unremarkable	
Lymph Node, Inguinal	Abnormal size, Enlarged, Right			Not Correlated	Tissue is unremarkable	
Nerve, Optic	No macroscopic observations on tissue				Tissue Comment: examined along with the eye sections	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

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**Appendix 11**

**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
003	M	1	0 µg/day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone Marrow, Sternum	Bone, Sternum	Brain	Epididymis
Esophagus	Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary
Gland, Seminal Vesicle	Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart	Joint
Large Intestine, Cecum	Large Intestine, Colon	Liver	Lymph Node, Draining	Lymph Node, Mesenteric
Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral	Pancreas	Skin
Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord	Spleen
Stomach	Testis	Thymus	Tongue	Trachea
Ureter	Urinary Bladder			

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**Appendix 11**

**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
004	M	1	0 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone Marrow, Sternum	Bone, Sternum	Brain	Epididymis
Esophagus	Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary
Gland, Seminal Vesicle	Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart	Joint
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Liver	Lung
Lymph Node, Draining	Lymph Node, Inguinal	Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic
Nerve, Peripheral	Pancreas	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord	Spleen	Stomach	Testis
Thymus	Tongue	Trachea	Ureter	Urinary Bladder

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**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
005	M	1	0 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Gland, Parathyroid	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone Marrow, Sternum	Bone, Sternum	Brain	Epididymis
Esophagus	Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary
Gland, Seminal Vesicle	Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart	Joint
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Liver	Lung
Lymph Node, Draining Nerve, Peripheral	Lymph Node, Inguinal Pancreas	Lymph Node, Mesenteric Skin	Muscle, Skeletal Small Intestine, Duodenum	Nerve, Optic Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord	Spleen	Stomach	Testis
Thymus	Tongue	Trachea	Ureter	Urinary Bladder

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
006	M	1	0 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone Marrow, Sternum	Bone, Sternum	Brain	Epididymis
Esophagus	Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary
Gland, Seminal Vesicle	Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart	Joint
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Liver	Lung
Lymph Node, Mesenteric Site, Injection	Muscle, Skeletal Skin	Nerve, Optic Small Intestine, Duodenum	Nerve, Peripheral Small Intestine, Ileum	Pancreas Small Intestine, Jejunum
Spinal Cord	Spleen	Stomach	Testis	Thymus
Tongue	Trachea	Ureter	Urinary Bladder	

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**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
007	M	1	0 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone Marrow, Sternum	Bone, Sternum	Brain	Epididymis
Esophagus	Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary
Gland, Seminal Vesicle	Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart	Joint
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Liver	Lung
Lymph Node, Inguinal	Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral
Pancreas	Site, Injection	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord	Spleen	Stomach	Testis
Thymus	Tongue	Trachea	Ureter	Urinary Bladder

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
008	M	1	0 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Gland, Parathyroid	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone Marrow, Sternum	Bone, Sternum	Brain	Epididymis
Esophagus	Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary
Gland, Seminal Vesicle	Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart	Joint
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Liver	Lung
Lymph Node, Draining Nerve, Peripheral	Lymph Node, Inguinal Pancreas	Lymph Node, Mesenteric Skin	Muscle, Skeletal Small Intestine, Duodenum	Nerve, Optic Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord	Spleen	Stomach	Testis
Thymus	Tongue	Trachea	Ureter	Urinary Bladder

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
009	M	1	0 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Gland, Parathyroid	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone Marrow, Sternum	Bone, Sternum	Brain	Epididymis
Esophagus	Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary
Gland, Seminal Vesicle	Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart	Joint
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Liver	Lung
Lymph Node, Draining Nerve, Peripheral	Lymph Node, Inguinal Pancreas	Lymph Node, Mesenteric Site, Injection	Muscle, Skeletal Skin	Nerve, Optic Small Intestine, Duodenum
Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord	Spleen	Stomach
Testis	Thymus	Tongue	Trachea	Ureter
Urinary Bladder				

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
010	M	1	0 µg/day	17	Dosing	Terminal Euthanasia

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone Marrow, Sternum	Bone, Sternum	Brain
Epididymis	Esophagus	Eye	Gland, Adrenal
Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary	Gland, Parathyroid
Gland, Pituitary	Gland, Prostate	Gland, Salivary	Gland, Seminal Vesicle
Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart	Joint
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Liver
Lung	Lymph Node, Draining	Lymph Node, Inguinal	Lymph Node, Mesenteric
Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral	Pancreas
Site, Injection	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord	Spleen	Stomach
Testis	Thymus	Tongue	Trachea
Ureter	Urinary Bladder		

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
011	M	1	0 µg/day	22	Recovery	Recovery Euthanasia 1
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Lymph Node, Draining	No macroscopic observations on tissue				Missing	
Adipose Tissue	Abnormal color, Dark, Focal /Comments: Abdominal			Correlated	Inflammation, Mild	
	Abnormal consistency, Firm, Focal			Correlated	Fibrosis, Minimal	
	Abnormal consistency, Firm, Focal			Correlated	Inflammation, Mild	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum	Joint	Liver	Lymph Node, Inguinal	Site, Injection
Spleen				

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
012	M	1	0 µg/day	22	Recovery	Recovery Euthanasia 1
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum      Joint      Liver      Lymph Node, Draining      Site, Injection  
 Spleen

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
013	M	1	0 µg/day	22	Recovery	Recovery Euthanasia 1
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum      Joint      Liver      Lymph Node, Draining      Site, Injection  
Spleen

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
014	M	1	0 µg/day	22	Recovery	Recovery Euthanasia 1

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum	Joint	Liver	Lymph Node, Draining
Lymph Node, Inguinal	Site, Injection	Spleen	

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
015	M	1	0 µg/day	22	Recovery	Recovery Euthanasia 1

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum	Joint	Liver	Lymph Node, Draining
Lymph Node, Inguinal	Site, Injection	Spleen	

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
016	M	2	30 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Joint	No macroscopic observations on tissue				Inflammation, Extra-capsular, Minimal	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	
Site, Injection	No macroscopic observations on tissue				Edema, Mild Inflammation, Moderate	
Spleen	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
016	M	2	30 µg/day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Epididymis	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary	Gland, Seminal Vesicle
Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Lung	Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic
Nerve, Peripheral	Pancreas	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord	Stomach	Testis	Thymus
Tongue	Trachea	Ureter	Urinary Bladder	

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
017	M	2	30 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Joint	No macroscopic observations on tissue				Inflammation, Extra-capsular, Minimal	
Liver	Abnormal surface, Raised, Focal, < 0.3 cm			Not Correlated	Vacuolation, Hepatocyte; Periportal, Minimal	
Lung	Abnormal color, Pale, Focal, Right caudal lobe			Not Correlated	Tissue is unremarkable	
Lymph Node, Draining	Abnormal size, Enlarged, Left			Correlated	Increased cellularity, Germinal center, Mild	
	Abnormal size, Enlarged, Left			Correlated	Increased cellularity, Plasma cell, Mild	
Site, Injection	Abnormal color, Dark, Focal, 0.3-0.5 cm			Correlated	Edema, Mild	
	Abnormal color, Dark, Focal, 0.3-0.5 cm			Correlated	Inflammation, Moderate	
	Abnormal consistency, Firm, Focal			Correlated	Edema, Mild	
	Abnormal consistency, Firm, Focal			Correlated	Inflammation, Moderate	
Spleen	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	
					Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
017	M	2	30 µg/day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Epididymis	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary	Gland, Seminal Vesicle
Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Lymph Node, Inguinal	Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic
Nerve, Peripheral	Pancreas	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord	Stomach	Testis	Thymus
Tongue	Trachea	Ureter	Urinary Bladder	

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<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
018	M	2	30 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Gland, Pituitary	No macroscopic observations on tissue				Cyst, Pars anterior (distalis), Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Plasma cell, Moderate	
Site, Injection	No macroscopic observations on tissue				Edema, Mild Inflammation, Mild	
Spleen	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

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<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
018	M	2	30 µg/day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Epididymis	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Prostate	Gland, Salivary	Gland, Seminal Vesicle	Gland, Thyroid
Gut-Associated Lymphoid Tissue	Heart	Joint	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Liver	Lung	Lymph Node, Inguinal	Lymph Node, Mesenteric
Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral	Pancreas	Skin
Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord	Stomach
Testis	Thymus	Tongue	Trachea	Ureter
Urinary Bladder				

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<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
019	M	2	30 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Kidney	No macroscopic observations on tissue				Tubular basophilia, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild Increased cellularity, Plasma cell, Mild	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild	
Site, Injection	No macroscopic observations on tissue				Edema, Mild Inflammation, Mild	
Spleen	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:  
No Tissues to list

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**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
019	M	2	30 µg/day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Epididymis	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary	Gland, Seminal Vesicle
Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart	Joint	Large Intestine, Cecum
Large Intestine, Colon	Liver	Lung	Lymph Node, Mesenteric	Muscle, Skeletal
Nerve, Optic	Nerve, Peripheral	Pancreas	Skin	Small Intestine, Duodenum
Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord	Stomach	Testis
Thymus	Tongue	Trachea	Ureter	Urinary Bladder

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
020	M	2	30 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Gland, Parathyroid	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild Increased cellularity, Plasma cell, Mild	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild	
Site, Injection	Abnormal consistency, Firm, Focal, Site, Injection, 9			Correlated	Edema, Mild	
	Abnormal consistency, Firm, Focal, Site, Injection, 9			Correlated	Inflammation, Moderate	
Spleen	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:  
No Tissues to list

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
020	M	2	30 µg/day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Epididymis	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary	Gland, Seminal Vesicle
Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart	Joint	Kidney
Large Intestine, Cecum	Large Intestine, Colon	Lung	Lymph Node, Mesenteric	Muscle, Skeletal
Nerve, Optic	Nerve, Peripheral	Pancreas	Skin	Small Intestine, Duodenum
Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord	Stomach	Testis
Thymus	Tongue	Trachea	Ureter	Urinary Bladder

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
021	M	2	30 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Gland, Mammary	No macroscopic observations on tissue				Missing	
Gland, Parathyroid	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Missing	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild Increased cellularity, Plasma cell, Minimal	
Site, Injection	No macroscopic observations on tissue				Edema, Moderate Inflammation, Mild	
Spleen	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Ureter	No macroscopic observations on tissue				Both Missing	

The following required protocol tissues were not examined microscopically:

Gland, Mammary                      Lymph Node, Draining                      Ureter

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
021	M	2	30 µg/day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Epididymis	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Parathyroid
Gland, Pituitary	Gland, Prostate	Gland, Salivary	Gland, Seminal Vesicle	Gland, Thyroid
Gut-Associated Lymphoid Tissue	Heart	Joint	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Lung	Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic
Nerve, Peripheral	Pancreas	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord	Stomach	Testis	Thymus
Tongue	Trachea	Urinary Bladder		

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
022	M	2	30 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Gland, Parathyroid	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild Increased cellularity, Plasma cell, Minimal	
Site, Injection	Abnormal color, Pale, Diffuse			Correlated	Edema, Mild	
	Abnormal color, Pale, Diffuse			Correlated	Inflammation, Mild	
Spleen	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:  
No Tissues to list

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<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
022	M	2	30 µg/day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Epididymis	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary	Gland, Seminal Vesicle
Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart	Joint	Kidney
Large Intestine, Cecum	Large Intestine, Colon	Liver	Lung	Lymph Node, Inguinal
Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral	Pancreas
Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord
Stomach	Testis	Thymus	Tongue	Trachea
Ureter	Urinary Bladder			

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
023	M	2	30 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Gland, Parathyroid	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild	
Site, Injection	No macroscopic observations on tissue				Inflammation, Mild	
Spleen	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
023	M	2	30 µg/day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Epididymis	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary	Gland, Seminal Vesicle
Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart	Joint	Kidney
Large Intestine, Cecum	Large Intestine, Colon	Liver	Lung	Lymph Node, Draining
Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral	Pancreas
Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord
Stomach	Testis	Thymus	Tongue	Trachea
Ureter	Urinary Bladder			

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<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
024	M	2	30 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Plasma cell, Mild	
Site, Injection	No macroscopic observations on tissue				Edema, Mild Inflammation, Mild	
Spleen	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:  
 No Tissues to list

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
024	M	2	30 µg/day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Epididymis	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary	Gland, Seminal Vesicle
Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart	Joint	Kidney
Large Intestine, Cecum	Large Intestine, Colon	Liver	Lung	Lymph Node, Inguinal
Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral	Pancreas
Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord
Stomach	Testis	Thymus	Tongue	Trachea
Ureter	Urinary Bladder			

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
025	M	2	30 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Joint	No macroscopic observations on tissue				Inflammation, Extra-capsular, Minimal	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Plasma cell, Moderate	
Site, Injection	No macroscopic observations on tissue				Edema, Mild Inflammation, Mild	
Spleen	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Hematopoietic cell, Minimal	
Ureter	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	

The following required protocol tissues were not examined microscopically:

No Tissues to list

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
025	M	2	30 µg/day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Epididymis	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary	Gland, Seminal Vesicle
Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Lung	Lymph Node, Inguinal	Lymph Node, Mesenteric	Muscle, Skeletal
Nerve, Optic	Nerve, Peripheral	Pancreas	Skin	Small Intestine, Duodenum
Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord	Stomach	Testis
Thymus	Tongue	Trachea	Ureter	Urinary Bladder

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
026	M	2	30 µg/day	22	Recovery	Recovery Euthanasia 1
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Lymph Node,	Abnormal size, Enlarged			Correlated	Increased cellularity, Germinal center, Minimal	
Draining	Abnormal size, Enlarged			Correlated	Increased cellularity, Plasma cell, Minimal	
	Abnormal size, Enlarged			Correlated	Infiltration, Macrophage, Minimal	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum      Joint      Liver      Lymph Node, Inguinal      Spleen

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<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
027	M	2	30 µg/day	22	Recovery	Recovery Euthanasia 1
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum      Joint      Liver      Spleen

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<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
028	M	2	30 µg/day	22	Recovery	Recovery Euthanasia 1
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Plasma cell, Minimal	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum      Joint      Liver      Lymph Node, Inguinal      Spleen

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<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
029	M	2	30 µg/day	22	Recovery	Recovery Euthanasia 1
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Plasma cell, Minimal Infiltration, Macrophage, Mild	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum      Joint      Liver      Spleen

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<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
030	M	2	30 µg/day	22	Recovery	Recovery Euthanasia 1
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild Increased cellularity, Plasma cell, Minimal Infiltration, Macrophage, Minimal	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	
Spleen	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum      Joint      Liver

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**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
031	M	3	30 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Gland, Pituitary	No macroscopic observations on tissue				Cyst, Pars anterior (distalis), Minimal	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	
Site, Injection	No macroscopic observations on tissue				Edema, Moderate Inflammation, Moderate	
Spleen	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Ureter	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	

The following required protocol tissues were not examined microscopically:

No Tissues to list

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**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
031	M	3	30 µg /day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Epididymis	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Prostate	Gland, Salivary	Gland, Seminal Vesicle	Gland, Thyroid
Gut-Associated Lymphoid Tissue	Heart	Joint	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Lung	Lymph Node, Inguinal	Lymph Node, Mesenteric	Muscle, Skeletal
Nerve, Optic	Nerve, Peripheral	Pancreas	Skin	Small Intestine, Duodenum
Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord	Stomach	Testis
Thymus	Tongue	Trachea	Ureter	Urinary Bladder

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**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
032	M	3	30 µg /day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Plasma cell, Minimal	
Site, Injection	No macroscopic observations on tissue				Edema, Mild Inflammation, Moderate	
Spleen	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

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**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
032	M	3	30 µg /day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Epididymis	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary	Gland, Seminal Vesicle
Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart	Joint	Kidney
Large Intestine, Cecum	Large Intestine, Colon	Liver	Lung	Lymph Node, Inguinal
Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral	Pancreas
Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord
Stomach	Testis	Thymus	Tongue	Trachea
Ureter	Urinary Bladder			

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**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
033	M	3	30 µg /day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild Increased cellularity, Plasma cell, Moderate	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild	
Site, Injection	No macroscopic observations on tissue				Edema, Mild Inflammation, Mild	
Spleen	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:  
No Tissues to list

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
033	M	3	30 µg /day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Epididymis	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary	Gland, Seminal Vesicle
Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart	Joint	Kidney
Large Intestine, Cecum	Large Intestine, Colon	Lung	Lymph Node, Mesenteric	Muscle, Skeletal
Nerve, Optic	Nerve, Peripheral	Pancreas	Skin	Small Intestine, Duodenum
Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord	Stomach	Testis
Thymus	Tongue	Trachea	Ureter	Urinary Bladder

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
034	M	3	30 µg /day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Gland, Parathyroid	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild Increased cellularity, Plasma cell, Minimal	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild	
Site, Injection	No macroscopic observations on tissue				Edema, Mild Inflammation, Moderate	
Spleen	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:  
No Tissues to list

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<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
034	M	3	30 µg /day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Epididymis	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary	Gland, Seminal Vesicle
Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart	Joint	Kidney
Large Intestine, Cecum	Large Intestine, Colon	Lung	Lymph Node, Mesenteric	Muscle, Skeletal
Nerve, Optic	Nerve, Peripheral	Pancreas	Skin	Small Intestine, Duodenum
Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord	Stomach	Testis
Thymus	Tongue	Trachea	Ureter	Urinary Bladder

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
035	M	3	30 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Gland, Parathyroid	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	
Gland, Pituitary	No macroscopic observations on tissue				Cyst, Pars anterior (distalis), Minimal	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild Increased cellularity, Plasma cell, Mild	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild Increased cellularity, Plasma cell, Minimal	
Site, Injection	Abnormal consistency, Firm, Focal			Correlated	Edema, Mild	
	Abnormal consistency, Firm, Focal			Correlated	Inflammation, Moderate	
Spleen	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Hematopoietic cell, Minimal	
Stomach	No macroscopic observations on tissue				Erosion, Nonglandular mucosa, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
035	M	3	30 µg /day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Epididymis	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Prostate	Gland, Salivary	Gland, Seminal Vesicle	Gland, Thyroid
Gut-Associated Lymphoid Tissue	Heart	Joint	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Lung	Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic
Nerve, Peripheral	Pancreas	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord	Testis	Thymus	Tongue
Trachea	Ureter	Urinary Bladder		

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
036	M	3	30 µg /day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Gland, Prostate	No macroscopic observations on tissue				Infiltration mononuclear cell, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild Increased cellularity, Plasma cell, Minimal	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	
Site, Injection	No macroscopic observations on tissue				Inflammation, Mild	
Spleen	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
036	M	3	30 µg /day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Epididymis	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Salivary	Gland, Seminal Vesicle	Gland, Thyroid
Gut-Associated Lymphoid Tissue	Heart	Joint	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Liver	Lung	Lymph Node, Mesenteric	Muscle, Skeletal
Nerve, Optic	Nerve, Peripheral	Pancreas	Skin	Small Intestine, Duodenum
Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord	Stomach	Testis
Thymus	Tongue	Trachea	Ureter	Urinary Bladder

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
037	M	3	30 µg /day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Kidney	No macroscopic observations on tissue				Infiltration mononuclear cell, Unilateral, Minimal	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Site, Injection	No macroscopic observations on tissue				Edema, Mild Inflammation, Moderate	
Spleen	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
037	M	3	30 µg /day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Epididymis	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary	Gland, Seminal Vesicle
Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart	Joint	Large Intestine, Cecum
Large Intestine, Colon	Lung	Lymph Node, Draining	Lymph Node, Inguinal	Lymph Node, Mesenteric
Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral	Pancreas	Skin
Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord	Stomach
Testis	Thymus	Tongue	Trachea	Ureter
Urinary Bladder				

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
038	M	3	30 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild Increased cellularity, Plasma cell, Mild	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild	
Site, Injection	No macroscopic observations on tissue				Edema, Mild Inflammation, Mild	
Spleen	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

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<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
038	M	3	30 µg /day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Epididymis	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary	Gland, Seminal Vesicle
Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart	Joint	Kidney
Large Intestine, Cecum	Large Intestine, Colon	Lung	Lymph Node, Mesenteric	Muscle, Skeletal
Nerve, Optic	Nerve, Peripheral	Pancreas	Skin	Small Intestine, Duodenum
Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord	Stomach	Testis
Thymus	Tongue	Trachea	Ureter	Urinary Bladder

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
039	M	3	30 µg /day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Plasma cell, Minimal	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild	
Site, Injection	Abnormal consistency, Firm, Focal, Site, Injection, 9			Correlated	Edema, Mild	
	Abnormal consistency, Firm, Focal, Site, Injection, 9			Correlated	Inflammation, Mild	
Spleen	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:  
 No Tissues to list

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<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
039	M	3	30 µg /day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Epididymis	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary	Gland, Seminal Vesicle
Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart	Joint	Kidney
Large Intestine, Cecum	Large Intestine, Colon	Lung	Lymph Node, Mesenteric	Muscle, Skeletal
Nerve, Optic	Nerve, Peripheral	Pancreas	Skin	Small Intestine, Duodenum
Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord	Stomach	Testis
Thymus	Tongue	Trachea	Ureter	Urinary Bladder

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<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
040	M	3	30 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild Increased cellularity, Plasma cell, Mild	
Site, Injection	Abnormal color, Pale, Diffuse			Correlated	Edema, Mild	
	Abnormal color, Pale, Diffuse			Correlated	Inflammation, Mild	
Spleen	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Ureter	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	

The following required protocol tissues were not examined microscopically:

No Tissues to list

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**Appendix 11**

**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
040	M	3	30 µg /day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Epididymis	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Prostate	Gland, Salivary	Gland, Seminal Vesicle
Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart	Joint	Kidney
Large Intestine, Cecum	Large Intestine, Colon	Liver	Lung	Lymph Node, Inguinal
Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral	Pancreas
Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord
Stomach	Testis	Thymus	Tongue	Trachea
Ureter	Urinary Bladder			

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**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
041	M	3	30 µg /day	22	Recovery	Recovery Euthanasia 1
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild Increased cellularity, Plasma cell, Minimal Infiltration, Macrophage, Minimal	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum      Joint      Liver      Lymph Node, Inguinal      Spleen

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
042	M	3	30 µg /day	22	Recovery	Recovery Euthanasia 1
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Plasma cell, Minimal Infiltration, Macrophage, Minimal	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum      Joint      Liver      Spleen

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
043	M	3	30 µg /day	22	Recovery	Recovery Euthanasia 1
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild Increased cellularity, Plasma cell, Minimal Infiltration, Macrophage, Mild	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum      Joint      Liver      Lymph Node, Inguinal      Spleen

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
044	M	3	30 µg /day	22	Recovery	Recovery Euthanasia 1
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Plasma cell, Minimal Infiltration, Macrophage, Mild	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Infiltration, Macrophage, Minimal	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	
Spleen	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum      Joint      Liver

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
045	M	3	30 µg /day	22	Recovery	Recovery Euthanasia 1
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Plasma cell, Minimal	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum      Joint      Liver      Lymph Node, Inguinal      Spleen

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**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Animal #	Sex	Group #	Dose	Day of Death	Phase	Status
046	F	1	0 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Gland, Adrenal	No macroscopic observations on tissue				Tissue Comment: medulla missing unilaterally	
Site, Injection	Abnormal color, Dark, Focal, < 0.3 cm, Site, Injection, 9			Correlated	Inflammation, Minimal	
Urinary Bladder	No macroscopic observations on tissue				Missing	

The following required protocol tissues were not examined microscopically:

Urinary Bladder

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone Marrow, Sternum	Bone, Sternum	Brain	Cervix
Esophagus	Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary	Gland, Thyroid
Gut-Associated Lymphoid Tissue	Heart	Joint	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Liver	Lung	Lymph Node, Draining	Lymph Node, Inguinal
Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral	Ovary
Oviduct	Pancreas	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord	Spleen	Stomach	Thymus
Tongue	Trachea	Ureter	Uterus	Vagina

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
047	F	1	0 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Gland, Parathyroid	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone Marrow, Sternum	Bone, Sternum	Brain	Cervix
Esophagus	Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary	Gland, Thyroid
Gut-Associated Lymphoid Tissue	Heart	Joint	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Liver	Lung	Lymph Node, Draining	Lymph Node, Inguinal
Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral	Ovary
Oviduct	Pancreas	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord	Spleen	Stomach	Thymus
Tongue	Trachea	Ureter	Urinary Bladder	Uterus
Vagina				

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
048	F	1	0 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Eye	No macroscopic observations on tissue				Rosettes retina, Minimal	
Gland, Harderian	No macroscopic observations on tissue				Degeneration/Necrosis, Minimal Infiltration mononuclear cell, Minimal	
Kidney	No macroscopic observations on tissue				Infiltration mononuclear cell, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone Marrow, Sternum	Bone, Sternum	Brain	Cervix
Esophagus	Gland, Adrenal	Gland, Lacrimal, Extraorbital	Gland, Mammary	Gland, Parathyroid
Gland, Pituitary	Gland, Salivary	Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart
Joint	Large Intestine, Cecum	Large Intestine, Colon	Liver	Lung
Lymph Node, Inguinal	Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral
Ovary	Oviduct	Pancreas	Site, Injection	Skin
Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord	Spleen
Stomach	Thymus	Tongue	Trachea	Ureter
Urinary Bladder	Uterus	Vagina		

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
049	F	1	0 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Gland, Harderian	No macroscopic observations on tissue				Infiltration mononuclear cell, Minimal	
Gland, Pituitary	No macroscopic observations on tissue				Cyst, Minimal	
Gland, Salivary	No macroscopic observations on tissue				Hypertrophy, Minimal	
Gut-Associated Lymphoid Tissue	No macroscopic observations on tissue				Missing	

The following required protocol tissues were not examined microscopically:

- Gut-Associated
- Lymphoid Tissue

The following tissues are unremarkable microscopically:

- |                              |                        |                          |                                  |                      |
|------------------------------|------------------------|--------------------------|----------------------------------|----------------------|
| Artery, Aorta                | Bone Marrow, Sternum   | Bone, Sternum            | Brain                            | Cervix               |
| Esophagus                    | Eye                    | Gland, Adrenal           | Gland, Lacrimal,<br>Extraorbital | Gland, Mammary       |
| Gland, Parathyroid           | Gland, Thyroid         | Heart                    | Joint                            | Kidney               |
| Large Intestine, Cecum       | Large Intestine, Colon | Liver                    | Lung                             | Lymph Node, Draining |
| Lymph Node, Inguinal         | Lymph Node, Mesenteric | Muscle, Skeletal         | Nerve, Optic                     | Nerve, Peripheral    |
| Ovary                        | Oviduct                | Pancreas                 | Site, Injection                  | Skin                 |
| Small Intestine,<br>Duodenum | Small Intestine, Ileum | Small Intestine, Jejunum | Spinal Cord                      | Spleen               |
| Stomach                      | Thymus                 | Tongue                   | Trachea                          | Ureter               |
| Urinary Bladder              | Uterus                 | Vagina                   |                                  |                      |

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**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
050	F	1	0 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Gland, Adrenal	No macroscopic observations on tissue				Tissue Comment: Adrenal medulla missing unilaterally	
Gland, Parathyroid	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	
Gland, Pituitary	No macroscopic observations on tissue				Tissue Comment: Pars distalis only	
Gut-Associated Lymphoid Tissue	No macroscopic observations on tissue				Missing	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	
Ureter	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	

The following required protocol tissues were not examined microscopically:

- Gut-Associated
- Lymphoid Tissue

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
050	F	1	0 µg/day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone Marrow, Sternum	Bone, Sternum	Brain	Cervix
Esophagus	Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary	Gland, Thyroid
Heart	Joint	Kidney	Large Intestine, Cecum	Large Intestine, Colon
Liver	Lung	Lymph Node, Draining	Lymph Node, Inguinal	Lymph Node, Mesenteric
Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral	Ovary	Oviduct
Pancreas	Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum
Spinal Cord	Spleen	Stomach	Thymus	Tongue
Trachea	Ureter	Urinary Bladder	Uterus	Vagina

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<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
051	F	1	0 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Gland, Adrenal	No macroscopic observations on tissue				Tissue Comment: Adrenal medulla missing unilaterally	
Gland, Harderian	No macroscopic observations on tissue				Degeneration/Necrosis, Minimal	
Kidney	No macroscopic observations on tissue				Infiltration mononuclear cell, Minimal	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	
Ureter	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	

The following required protocol tissues were not examined microscopically:  
 No Tissues to list

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
051	F	1	0 µg/day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone Marrow, Sternum	Bone, Sternum	Brain	Cervix
Esophagus	Eye	Gland, Adrenal	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Salivary	Gland, Thyroid	Gut-Associated Lymphoid Tissue
Heart	Joint	Large Intestine, Cecum	Large Intestine, Colon	Liver
Lung	Lymph Node, Draining	Lymph Node, Inguinal	Lymph Node, Mesenteric	Muscle, Skeletal
Nerve, Optic	Nerve, Peripheral	Ovary	Oviduct	Pancreas
Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord
Spleen	Stomach	Thymus	Tongue	Trachea
Ureter	Urinary Bladder	Uterus	Vagina	

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

Animal #	Sex	Group #	Dose	Day of Death	Phase	Status
052	F	1	0 µg/day	17	Dosing	Terminal Euthanasia
Tissue	Macroscopic Observations / comments			Status	Microscopic Observations / comments	
Gland, Parathyroid	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone Marrow, Sternum	Bone, Sternum	Brain	Cervix
Esophagus	Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary	Gland, Thyroid
Gut-Associated Lymphoid Tissue	Heart	Joint	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Liver	Lung	Lymph Node, Draining	Lymph Node, Inguinal
Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral	Ovary
Oviduct	Pancreas	Site, Injection	Skin	Small Intestine, Duodenum
Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord	Spleen	Stomach
Thymus	Tongue	Trachea	Ureter	Urinary Bladder
Uterus	Vagina			

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
053	F	1	0 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Joint	No macroscopic observations on tissue				Physcal dysplasia, Focal, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone Marrow, Sternum	Bone, Sternum	Brain	Cervix
Esophagus	Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary	Gland, Thyroid
Gut-Associated Lymphoid Tissue	Heart	Kidney	Large Intestine, Cecum	Large Intestine, Colon
Liver	Lung	Lymph Node, Draining	Lymph Node, Inguinal	Lymph Node, Mesenteric
Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral	Ovary	Oviduct
Pancreas	Site, Injection	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord	Spleen	Stomach	Thymus
Tongue	Trachea	Ureter	Urinary Bladder	Uterus
Vagina				

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<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
054	F	1	0 µg/day	17	Dosing	Terminal Euthanasia

<b>Tissue</b>	<b>Macroscopic Observations / comments</b>	<b>Status</b>	<b>Microscopic Observations / comments</b>
Gland, Pituitary	No macroscopic observations on tissue		Tissue Comment: Pars distalis only

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone Marrow, Sternum	Bone, Sternum	Brain	Cervix
Esophagus	Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital
Gland, Mammary	Gland, Parathyroid	Gland, Pituitary	Gland, Salivary	Gland, Thyroid
Gut-Associated Lymphoid Tissue	Heart	Joint	Kidney	Large Intestine, Cecum
Large Intestine, Colon	Liver	Lung	Lymph Node, Draining	Lymph Node, Inguinal
Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral	Ovary
Oviduct	Pancreas	Site, Injection	Skin	Small Intestine, Duodenum
Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord	Spleen	Stomach
Thymus	Tongue	Trachea	Ureter	Urinary Bladder
Uterus	Vagina			

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**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
055	F	1	0 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Gland, Harderian	No macroscopic observations on tissue				Infiltration mononuclear cell, Minimal	
Gland, Parathyroid	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	
Lung	No macroscopic observations on tissue				Infiltration mixed cell, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

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**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
055	F	1	0 µg/day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone Marrow, Sternum	Bone, Sternum	Brain	Cervix
Esophagus	Eye	Gland, Adrenal	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Salivary	Gland, Thyroid	Gut-Associated Lymphoid Tissue
Heart	Joint	Kidney	Large Intestine, Cecum	Large Intestine, Colon
Liver	Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral
Ovary	Oviduct	Pancreas	Skin	Small Intestine, Duodenum
Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord	Spleen	Stomach
Thymus	Tongue	Trachea	Ureter	Urinary Bladder
Uterus	Vagina			

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**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

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<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
056	F	1	0 µg/day	22	Recovery	Recovery Euthanasia 1

---

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum	Joint	Liver	Lymph Node, Draining
Lymph Node, Inguinal	Site, Injection	Spleen	

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**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
057	F	1	0 µg/day	22	Recovery	Recovery Euthanasia 1
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum      Joint      Liver      Lymph Node, Draining      Site, Injection  
 Spleen

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

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<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
058	F	1	0 µg/day	22	Recovery	Recovery Euthanasia 1

---

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum	Joint	Liver	Lymph Node, Draining
Lymph Node, Inguinal	Site, Injection	Spleen	

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**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

---

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
059	F	1	0 µg/day	22	Recovery	Recovery Euthanasia 1

---

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum	Joint	Liver	Lymph Node, Draining
Lymph Node, Inguinal	Site, Injection	Spleen	

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
060	F	1	0 µg/day	22	Recovery	Recovery Euthanasia 1
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum      Joint      Liver      Site, Injection      Spleen

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
061	F	2	30 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Plasma cell, Moderate	
Site, Injection	No macroscopic observations on tissue				Edema, Mild Inflammation, Mild	
Spleen	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Hematopoietic cell, Minimal	
Stomach	No macroscopic observations on tissue				Infiltration mononuclear cell, Serosa, Focal, Minimal	
Ureter	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	

The following required protocol tissues were not examined microscopically:

No Tissues to list

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
061	F	2	30 µg/day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Cervix	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Salivary	Gland, Thyroid	Gut-Associated Lymphoid Tissue
Heart	Joint	Kidney	Large Intestine, Cecum	Large Intestine, Colon
Lung	Lymph Node, Inguinal	Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic
Nerve, Peripheral	Ovary	Oviduct	Pancreas	Skin
Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord	Thymus
Tongue	Trachea	Ureter	Urinary Bladder	Uterus
Vagina				

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
062	F	2	30 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Gland, Parathyroid	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	
Gland, Pituitary	No macroscopic observations on tissue				Tissue Comment: Missing, pars nervosa	
Kidney	No macroscopic observations on tissue				Tubular basophilia, Minimal	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Plasma cell, Moderate	
Oviduct	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	
Pancreas	No macroscopic observations on tissue				Atrophy, Acinar cell, Minimal Infiltration mononuclear cell, Interstitium, Focal, Minimal	
Site, Injection	Abnormal consistency, Firm, Focal, Site, Injection, 9			Correlated	Edema, Mild	
	Abnormal consistency, Firm, Focal, Site, Injection, 9			Correlated	Inflammation, Mild	
Spleen	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
062	F	2	30 µg/day	17	Dosing	Terminal Euthanasia

<b>Tissue</b>	<b>Macroscopic Observations / comments</b>	<b>Status</b>	<b>Microscopic Observations / comments</b>
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The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Cervix	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Salivary	Gland, Thyroid	Gut-Associated Lymphoid Tissue
Heart	Joint	Large Intestine, Cecum	Large Intestine, Colon	Lung
Lymph Node, Inguinal	Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral
Ovary	Oviduct	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord	Stomach	Thymus	Tongue
Trachea	Ureter	Urinary Bladder	Uterus	Vagina

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
063	F	2	30 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Gland, Mammary	No macroscopic observations on tissue				Missing	
Gland, Parathyroid	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Plasma cell, Moderate	
Site, Injection	No macroscopic observations on tissue				Edema, Mild Inflammation, Mild	
Skin	No macroscopic observations on tissue				Missing	
Spleen	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Hematopoietic cell, Minimal	
Ureter	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	
The following required protocol tissues were not examined microscopically:						
Gland, Mammary	Skin					

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
063	F	2	30 µg/day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Cervix	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Parathyroid
Gland, Pituitary	Gland, Salivary	Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart
Joint	Kidney	Large Intestine, Cecum	Large Intestine, Colon	Lung
Lymph Node, Inguinal	Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral
Ovary	Oviduct	Pancreas	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord	Stomach	Thymus	Tongue
Trachea	Ureter	Urinary Bladder	Uterus	Vagina

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
064	F	2	30 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Plasma cell, Moderate	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	
Pancreas	No macroscopic observations on tissue				Atrophy, Acinar cell, Minimal	
Site, Injection	Abnormal consistency, Firm, Focal			Correlated	Edema, Mild	
	Abnormal consistency, Firm, Focal			Correlated	Inflammation, Mild	
Spleen	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
064	F	2	30 µg/day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Cervix	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Salivary	Gland, Thyroid	Gut-Associated Lymphoid Tissue
Heart	Joint	Kidney	Large Intestine, Cecum	Large Intestine, Colon
Lung	Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral
Ovary	Oviduct	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord	Stomach	Thymus	Tongue
Trachea	Ureter	Urinary Bladder	Uterus	Vagina

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
065	F	2	30 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Gland, Parathyroid	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	
Kidney	No macroscopic observations on tissue				Infiltration mononuclear cell, Minimal	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Plasma cell, Minimal	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild	
Pancreas	No macroscopic observations on tissue				Atrophy, Acinar cell, Minimal	
Site, Injection	No macroscopic observations on tissue				Edema, Mild Inflammation, Moderate	
Spleen	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	
Ureter	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	

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<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
065	F	2	30 µg/day	17	Dosing	Terminal Euthanasia

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Cervix	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Salivary	Gland, Thyroid	Gut-Associated Lymphoid Tissue
Heart	Joint	Large Intestine, Cecum	Large Intestine, Colon	Lung
Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral	Ovary
Oviduct	Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum
Spinal Cord	Stomach	Thymus	Tongue	Trachea
Ureter	Urinary Bladder	Uterus	Vagina	

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<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
066	F	2	30 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Kidney	No macroscopic observations on tissue				Infiltration mononuclear cell, Minimal	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	
Site, Injection	Abnormal color, Pale, Diffuse			Correlated	Edema, Mild	
	Abnormal color, Pale, Diffuse			Correlated	Inflammation, Moderate	
Spleen	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
066	F	2	30 µg/day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Cervix	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Salivary	Gland, Thyroid	Gut-Associated Lymphoid Tissue
Heart	Joint	Large Intestine, Cecum	Large Intestine, Colon	Lung
Lymph Node, Draining	Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral
Ovary	Oviduct	Pancreas	Skin	Small Intestine, Duodenum
Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord	Stomach	Thymus
Tongue	Trachea	Ureter	Urinary Bladder	Uterus
Vagina				

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<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
067	F	2	30 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Gland, Parathyroid	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	
Joint	No macroscopic observations on tissue				Inflammation, Extra-capsular, Minimal	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Lung	No macroscopic observations on tissue				Infiltration mixed cell, Focal, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Plasma cell, Moderate	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Plasma cell, Minimal	
Site, Injection	Abnormal consistency, Firm, Focal			Correlated	Edema, Mild	
	Abnormal consistency, Firm, Focal			Correlated	Inflammation, Mild	
Spleen	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

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**Appendix 11**

**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
067	F	2	30 µg/day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Cervix	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Salivary	Gland, Thyroid	Gut-Associated Lymphoid Tissue
Heart	Kidney	Large Intestine, Cecum	Large Intestine, Colon	Lymph Node, Mesenteric
Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral	Ovary	Oviduct
Pancreas	Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum
Spinal Cord	Stomach	Thymus	Tongue	Trachea
Ureter	Urinary Bladder	Uterus	Vagina	

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
068	F	2	30 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild Increased cellularity, Plasma cell, Moderate	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild	
Site, Injection	No macroscopic observations on tissue				Edema, Mild Inflammation, Mild	
Spleen	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
068	F	2	30 µg/day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Cervix	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Salivary	Gland, Thyroid	Gut-Associated Lymphoid Tissue
Heart	Joint	Kidney	Large Intestine, Cecum	Large Intestine, Colon
Lung	Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral
Ovary	Oviduct	Pancreas	Skin	Small Intestine, Duodenum
Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord	Stomach	Thymus
Tongue	Trachea	Ureter	Urinary Bladder	Uterus
Vagina				

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
069	F	2	30 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Eye	No macroscopic observations on tissue				Mineralization, Cornea, Focal, Minimal	
Gland, Parathyroid	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	
Gut-Associated Lymphoid Tissue	No macroscopic observations on tissue				Mineralization, Germinal center, Focal, Minimal /Comments: associated with fibrosis and mixed inflammation	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Plasma cell, Mild	
Site, Injection	Abnormal color, Dark, Focal, 1-2 cm, Site, Injection, 9			Correlated	Edema, Mild	
	Abnormal color, Dark, Focal, 1-2 cm, Site, Injection, 9			Correlated	Inflammation, Mild	
	Abnormal consistency, Firm, Focal, Site, Injection, 9			Correlated	Edema, Mild	
	Abnormal consistency, Firm, Focal, Site, Injection, 9			Correlated	Inflammation, Mild	
Spleen	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:  
No Tissues to list

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**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
069	F	2	30 µg/day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Cervix	Esophagus
Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary	Gland, Parathyroid
Gland, Pituitary	Gland, Salivary	Gland, Thyroid	Heart	Joint
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Lung	Lymph Node, Inguinal
Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral	Ovary
Oviduct	Pancreas	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord	Stomach	Thymus	Tongue
Trachea	Ureter	Urinary Bladder	Uterus	Vagina

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
070	F	2	30 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Gland, Harderian	No macroscopic observations on tissue				Infiltration mononuclear cell, Minimal	
Joint	No macroscopic observations on tissue				Inflammation, Extra-capsular, Minimal	
Kidney	No macroscopic observations on tissue				Infiltration mononuclear cell, Minimal	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Lymph Node, Draining	Abnormal size, Enlarged, Left			Correlated	Increased cellularity, Germinal center, Mild	
	Abnormal size, Enlarged, Left			Correlated	Increased cellularity, Plasma cell, Moderate	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild Increased cellularity, Plasma cell, Minimal	
Pancreas	No macroscopic observations on tissue				Atrophy, Acinar cell, Minimal	
Site, Injection	Abnormal color, Pale, Diffuse			Correlated	Edema, Moderate	
	Abnormal color, Pale, Diffuse			Correlated	Inflammation, Moderate	
Spleen	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Hematopoietic cell, Minimal	
Ureter	No macroscopic observations on tissue				One-of-pair Missing	

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
070	F	2	30 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Ureter	No macroscopic observations on tissue				Tissue is unremarkable	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Cervix	Esophagus
Eye	Gland, Adrenal	Gland, Lacrimal, Extraorbital	Gland, Mammary	Gland, Parathyroid
Gland, Pituitary	Gland, Salivary	Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart
Large Intestine, Cecum	Large Intestine, Colon	Lung	Lymph Node, Mesenteric	Muscle, Skeletal
Nerve, Optic	Nerve, Peripheral	Ovary	Oviduct	Skin
Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord	Stomach
Thymus	Tongue	Trachea	Ureter	Urinary Bladder
Uterus	Vagina			

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
071	F	2	30 µg/day	22	Recovery	Recovery Euthanasia 1
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Plasma cell, Minimal	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	
Spleen	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	
Adipose Tissue	Abnormal color, Dark, Multifocal /Comments: Neck, Ventral, Yellow			Correlated	Infiltration mononuclear cell, Mild /Comments: hemosiderophages	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum      Joint      Liver      Lymph Node, Inguinal

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
072	F	2	30 µg/day	22	Recovery	Recovery Euthanasia 1
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Plasma cell, Minimal Infiltration, Macrophage, Minimal	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum      Joint      Liver      Lymph Node, Inguinal      Spleen

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
073	F	2	30 µg/day	22	Recovery	Recovery Euthanasia 1
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Plasma cell, Minimal	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum      Joint      Liver      Spleen

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
074	F	2	30 µg/day	22	Recovery	Recovery Euthanasia 1
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Joint	No macroscopic observations on tissue				Physcal dysplasia, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild Increased cellularity, Plasma cell, Minimal Infiltration, Macrophage, Mild	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	
Spleen	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum      Liver      Lymph Node, Inguinal

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
075	F	2	30 µg/day	22	Recovery	Recovery Euthanasia 1
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Infiltration, Macrophage, Mild	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum      Joint      Liver      Lymph Node, Inguinal      Spleen

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
076	F	3	30 µg /day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Eye	No macroscopic observations on tissue				Rosettes retina, Minimal	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Plasma cell, Mild	
Site, Injection	No macroscopic observations on tissue				Edema, Mild Inflammation, Mild	
Spleen	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
076	F	3	30 µg /day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Cervix	Esophagus
Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary	Gland, Parathyroid
Gland, Pituitary	Gland, Salivary	Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart
Joint	Kidney	Large Intestine, Cecum	Large Intestine, Colon	Lung
Lymph Node, Inguinal	Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral
Ovary	Oviduct	Pancreas	Skin	Small Intestine, Duodenum
Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord	Stomach	Thymus
Tongue	Trachea	Ureter	Urinary Bladder	Uterus
Vagina				

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<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
077	F	3	30 µg /day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Gland, Harderian	No macroscopic observations on tissue				Degeneration/Necrosis, Minimal	
Gland, Pituitary	No macroscopic observations on tissue				Cyst, Minimal	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Plasma cell, Minimal	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	
Site, Injection	Abnormal consistency, Firm, Focal			Correlated	Edema, Mild	
	Abnormal consistency, Firm, Focal			Correlated	Inflammation, Mild	
Spleen	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

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<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
077	F	3	30 µg /day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Cervix	Esophagus
Eye	Gland, Adrenal	Gland, Lacrimal, Extraorbital	Gland, Mammary	Gland, Parathyroid
Gland, Salivary	Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart	Joint
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Lung	Lymph Node, Mesenteric
Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral	Ovary	Oviduct
Pancreas	Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum
Spinal Cord	Stomach	Thymus	Tongue	Trachea
Ureter	Urinary Bladder	Uterus	Vagina	

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
078	F	3	30 µg /day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Gland, Parathyroid	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Plasma cell, Minimal	
Site, Injection	No macroscopic observations on tissue				Edema, Mild Inflammation, Mild	
Spleen	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:  
No Tissues to list

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<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
078	F	3	30 µg /day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Cervix	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Salivary	Gland, Thyroid	Gut-Associated Lymphoid Tissue
Heart	Joint	Kidney	Large Intestine, Cecum	Large Intestine, Colon
Lung	Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral
Ovary	Oviduct	Pancreas	Skin	Small Intestine, Duodenum
Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord	Stomach	Thymus
Tongue	Trachea	Ureter	Urinary Bladder	Uterus
Vagina				

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**Appendix 11**

**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
079	F	3	30 µg /day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Gland, Parathyroid	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	
Lymph Node, Draining	Abnormal size, Enlarged			Correlated	Increased cellularity, Germinal center, Minimal	
	Abnormal size, Enlarged			Correlated	Increased cellularity, Plasma cell, Mild	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	
Site, Injection	Abnormal consistency, Firm, Focal			Correlated	Edema, Mild	
	Abnormal consistency, Firm, Focal			Correlated	Inflammation, Mild	
Spleen	Abnormal size, Enlarged			Correlated	Increased cellularity, Germinal center, Minimal	
	Abnormal size, Enlarged			Correlated	Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

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**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
079	F	3	30 µg /day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Cervix	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Salivary	Gland, Thyroid	Gut-Associated Lymphoid Tissue
Heart	Joint	Kidney	Large Intestine, Cecum	Large Intestine, Colon
Liver	Lung	Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic
Nerve, Peripheral	Ovary	Oviduct	Pancreas	Skin
Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord	Stomach
Thymus	Tongue	Trachea	Ureter	Urinary Bladder
Uterus	Vagina			

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
080	F	3	30 µg/day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Gland, Adrenal	No macroscopic observations on tissue				Hypertrophy, Cortex, Present	
Gland, Parathyroid	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	
Gland, Pituitary	No macroscopic observations on tissue				Cyst, Minimal	
Joint	No macroscopic observations on tissue				Inflammation, Extra-capsular, Minimal	
Lymph Node, Draining	Abnormal size, Enlarged			Correlated	Increased cellularity, Germinal center, Minimal	
	Abnormal size, Enlarged			Correlated	Increased cellularity, Plasma cell, Mild	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	
Site, Injection	Abnormal consistency, Firm, Focal			Correlated	Edema, Moderate	
	Abnormal consistency, Firm, Focal			Correlated	Inflammation, Moderate	
Spleen	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:  
No Tissues to list

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**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
080	F	3	30 µg /day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Cervix	Esophagus
Eye	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary	Gland, Parathyroid
Gland, Salivary	Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart	Kidney
Large Intestine, Cecum	Large Intestine, Colon	Liver	Lung	Lymph Node, Mesenteric
Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral	Ovary	Oviduct
Pancreas	Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum
Spinal Cord	Stomach	Thymus	Tongue	Trachea
Ureter	Urinary Bladder	Uterus	Vagina	

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
081	F	3	30 µg /day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Gland, Harderian	No macroscopic observations on tissue				Degeneration/Necrosis, Minimal	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Plasma cell, Moderate	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild Increased cellularity, Plasma cell, Minimal	
Site, Injection	Abnormal consistency, Firm, Focal, Site, Injection, 9			Correlated	Edema, Mild	
	Abnormal consistency, Firm, Focal, Site, Injection, 9			Correlated	Inflammation, Mild	
Spleen	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

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**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
081	F	3	30 µg /day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Cervix	Esophagus
Eye	Gland, Adrenal	Gland, Lacrimal, Extraorbital	Gland, Mammary	Gland, Parathyroid
Gland, Pituitary	Gland, Salivary	Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart
Joint	Kidney	Large Intestine, Cecum	Large Intestine, Colon	Lung
Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral	Ovary
Oviduct	Pancreas	Skin	Small Intestine, Duodenum	Small Intestine, Ileum
Small Intestine, Jejunum	Spinal Cord	Stomach	Thymus	Tongue
Trachea	Ureter	Urinary Bladder	Uterus	Vagina

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
082	F	3	30 µg /day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Gland, Adrenal	No macroscopic observations on tissue				Tissue Comment: Medulla not in section unilaterally	
Gland, Harderian	No macroscopic observations on tissue				Infiltration mononuclear cell, Minimal	
Gland, Parathyroid	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	
Joint	No macroscopic observations on tissue				Inflammation, Extra-capsular, Minimal	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Lymph Node, Draining	Abnormal size, Enlarged			Correlated	Increased cellularity, Plasma cell, Mild	
Lymph Node, Inguinal	Abnormal size, Enlarged, Left			Correlated	Increased cellularity, Germinal center, Minimal	
Site, Injection	Abnormal consistency, Firm, Focal			Correlated	Edema, Mild	
	Abnormal consistency, Firm, Focal			Correlated	Inflammation, Mild	
Spleen	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
082	F	3	30 µg /day	17	Dosing	Terminal Euthanasia

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Cervix	Esophagus
Eye	Gland, Adrenal	Gland, Lacrimal, Extraorbital	Gland, Mammary	Gland, Parathyroid
Gland, Pituitary	Gland, Salivary	Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Lung	Lymph Node, Mesenteric
Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral	Ovary	Oviduct
Pancreas	Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum
Spinal Cord	Stomach	Thymus	Tongue	Trachea
Ureter	Urinary Bladder	Uterus	Vagina	

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
083	F	3	30 µg /day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Eye	No macroscopic observations on tissue				Rosettes retina, Minimal	
Joint	No macroscopic observations on tissue				Inflammation, Extra-capsular, Minimal	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild Increased cellularity, Plasma cell, Minimal	
Site, Injection	No macroscopic observations on tissue				Edema, Mild Inflammation, Mild	
Spleen	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:  
No Tissues to list

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
083	F	3	30 µg /day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Cervix	Esophagus
Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary	Gland, Parathyroid
Gland, Pituitary	Gland, Salivary	Gland, Thyroid	Gut-Associated Lymphoid Tissue	Heart
Kidney	Large Intestine, Cecum	Large Intestine, Colon	Lung	Lymph Node, Mesenteric
Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral	Ovary	Oviduct
Pancreas	Skin	Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum
Spinal Cord	Stomach	Thymus	Tongue	Trachea
Ureter	Urinary Bladder	Uterus	Vagina	

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
084	F	3	30 µg /day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Large Intestine, Colon	No macroscopic observations on tissue				Infiltration mixed cell, Mucosa, Minimal	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	
Site, Injection	Abnormal consistency, Firm, Focal			Correlated	Edema, Mild	
	Abnormal consistency, Firm, Focal			Correlated	Inflammation, Mild	
Spleen	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Hematopoietic cell, Minimal	
Ureter	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	

The following required protocol tissues were not examined microscopically:

No Tissues to list

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
084	F	3	30 µg /day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Cervix	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Salivary	Gland, Thyroid	Gut-Associated Lymphoid Tissue
Heart	Joint	Kidney	Large Intestine, Cecum	Liver
Lung	Lymph Node, Draining	Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic
Nerve, Peripheral	Ovary	Oviduct	Pancreas	Skin
Small Intestine, Duodenum	Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord	Stomach
Thymus	Tongue	Trachea	Ureter	Urinary Bladder
Uterus	Vagina			

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
085	F	3	30 µg /day	17	Dosing	Terminal Euthanasia
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Bone Marrow, Sternum	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	
Gland, Parathyroid	No macroscopic observations on tissue				One-of-pair Missing Tissue is unremarkable	
Liver	No macroscopic observations on tissue				Vacuolation, Hepatocyte; Periportal, Minimal	
Lymph Node, Draining	Abnormal size, Enlarged			Correlated	Increased cellularity, Germinal center, Mild	
	Abnormal size, Enlarged			Correlated	Increased cellularity, Plasma cell, Mild	
Lymph Node, Inguinal	Abnormal size, Enlarged, Left			Correlated	Increased cellularity, Germinal center, Mild	
	Abnormal size, Enlarged, Left			Correlated	Increased cellularity, Plasma cell, Minimal	
Site, Injection	Abnormal consistency, Firm, Focal			Correlated	Edema, Mild	
	Abnormal consistency, Firm, Focal			Correlated	Inflammation, Mild	
Spleen	No macroscopic observations on tissue				Increased cellularity, Hematopoietic cell, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
085	F	3	30 µg /day	17	Dosing	Terminal Euthanasia

The following tissues are unremarkable microscopically:

Artery, Aorta	Bone, Sternum	Brain	Cervix	Esophagus
Eye	Gland, Adrenal	Gland, Harderian	Gland, Lacrimal, Extraorbital	Gland, Mammary
Gland, Parathyroid	Gland, Pituitary	Gland, Salivary	Gland, Thyroid	Gut-Associated Lymphoid Tissue
Heart	Joint	Kidney	Large Intestine, Cecum	Large Intestine, Colon
Lung	Lymph Node, Mesenteric	Muscle, Skeletal	Nerve, Optic	Nerve, Peripheral
Ovary	Oviduct	Pancreas	Skin	Small Intestine, Duodenum
Small Intestine, Ileum	Small Intestine, Jejunum	Spinal Cord	Stomach	Thymus
Tongue	Trachea	Ureter	Urinary Bladder	Uterus
Vagina				

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
086	F	3	30 µg /day	22	Recovery	Recovery Euthanasia 1
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Joint	No macroscopic observations on tissue				Physcal dysplasia, Minimal	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum      Liver      Lymph Node, Inguinal      Spleen

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
087	F	3	30 µg /day	22	Recovery	Recovery Euthanasia 1
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Infiltration, Macrophage, Mild	
Lymph Node,	Abnormal size, Enlarged			Correlated	Increased cellularity, Germinal center, Minimal	
Inguinal	Abnormal size, Enlarged			Correlated	Increased cellularity, Plasma cell, Minimal	
	Abnormal size, Enlarged			Correlated	Infiltration, Macrophage, Minimal	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum      Joint      Liver      Spleen

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
088	F	3	30 µg /day	22	Recovery	Recovery Euthanasia 1
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal Increased cellularity, Plasma cell, Minimal Infiltration, Macrophage, Mild	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum      Joint      Liver      Spleen

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**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
089	F	3	30 µg /day	22	Recovery	Recovery Euthanasia 1
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Lymph Node, Draining	Abnormal size, Enlarged			Correlated	Increased cellularity, Germinal center, Minimal	
	Abnormal size, Enlarged			Correlated	Increased cellularity, Plasma cell, Minimal	
	Abnormal size, Enlarged			Correlated	Infiltration, Macrophage, Minimal	
Lymph Node, Inguinal	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	
Spleen	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum      Joint      Liver

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**Appendix 11**

**Individual Macroscopic and Microscopic Observations w/Correlations**

**20GR142 : 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

<b>Animal #</b>	<b>Sex</b>	<b>Group #</b>	<b>Dose</b>	<b>Day of Death</b>	<b>Phase</b>	<b>Status</b>
090	F	3	30 µg /day	22	Recovery	Recovery Euthanasia 1
<b>Tissue</b>	<b>Macroscopic Observations / comments</b>			<b>Status</b>	<b>Microscopic Observations / comments</b>	
Lymph Node, Draining	No macroscopic observations on tissue				Increased cellularity, Germinal center, Mild Increased cellularity, Plasma cell, Minimal Infiltration, Macrophage, Mild	
Site, Injection	No macroscopic observations on tissue				Inflammation, Minimal	
Spleen	No macroscopic observations on tissue				Increased cellularity, Germinal center, Minimal	

The following required protocol tissues were not examined microscopically:

No Tissues to list

The following tissues are unremarkable microscopically:

Bone Marrow, Sternum      Joint      Liver      Lymph Node, Inguinal

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**Test Article:** BNT162b2(V9), BNT162b3c

Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Erythema Grade-Left(ERL)**

Males						
Group #	Animal #	Dosing Day: 1 Session: S1-Predose	Dosing Day: 2 Session: S2-4 HPD	Dosing Day: 3 Session: S3-24 HPD	Dosing Day: 4 Session: S4-48 HPD	Dosing Day: 4 Session: S5-72 HPD
1	001	ER-0:...	ER-0:...	ER-0:...	-	-
	002	ER-0:...	ER-0:...	ER-0:...	-	-
	003	ER-0:...	ER-0:...	ER-0:...	-	-
	004	ER-0:...	ER-0:...	ER-0:...	-	-
	005	ER-0:...	ER-0:...	ER-0:...	-	-
	006	ER-0:...	ER-0:...	ER-0:...	-	-
	007	ER-0:...	ER-0:...	ER-0:...	-	-
	008	ER-0:...	ER-0:...	ER-0:...	-	-
	009	ER-0:...	ER-0:...	ER-0:...	-	-
	010	ER-0:...	ER-0:...	ER-0:...	-	-
	011	ER-0:...	ER-0:...	ER-0:...	-	-
	012	ER-0:...	ER-0:...	ER-0:...	-	-
	013	ER-0:...	ER-0:...	ER-0:...	-	-
	014	ER-0:...	ER-0:...	ER-0:...	-	-
	015	ER-0:...	ER-0:...	ER-0:...	-	-
2	016	ER-0:...	ER-0:...	ER-0:...	-	-
	017	ER-0:...	ER-0:...	ER-0:...	-	-
	018	ER-0:...	ER-0:...	ER-0:...	-	-
	019	ER-0:...	ER-0:...	ER-0:...	-	-
	020	ER-0:...	ER-0:...	ER-0:...	-	-
	021	ER-0:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...

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2	022	ER-0:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...
	023	ER-0:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...
	024	ER-0:...	ER-0:...	ER-0:...	-	-
	025	ER-0:...	ER-0:...	ER-1:...	-	-
	026	ER-0:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...
	027	ER-0:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...
	028	ER-0:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...
	029	ER-0:...	ER-0:...	ER-0:...	-	-
	030	ER-0:...	ER-0:...	ER-0:...	-	-
	3	031	ER-0:...	ER-0:...	ER-0:...	ER-0:...
032		ER-0:...	ER-0:...	ER-0:...	-	-
033		ER-0:...	ER-0:...	ER-0:...	-	-
034		ER-0:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...
035		ER-0:...	ER-0:...	ER-0:...	-	-
036		ER-0:...	ER-0:...	ER-0:...	-	-
037		ER-0:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...
038		ER-0:...	ER-0:...	ER-0:...	-	-
039		ER-0:...	ER-0:...	ER-0:...	-	-
040		ER-0:...	ER-0:...	ER-0:...	-	-
041		ER-0:...	ER-0:...	ER-1:...	-	-
042		ER-0:...	ER-0:...	ER-0:...	-	-

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3	043	ER-0:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...
	044	ER-0:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...
	045	ER-0:...	ER-0:...	ER-0:...	ER-1:...	ER-0:...

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Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Erythema Grade-Left(ERL)**

Males						
Group #	Animal #	Dosing Day: 6 Session: S6-120 HPD	Day: 7 Session: S7-144 HPD	Day: 8 Session: S1-Predose	Session: S2-4 HPD	Day: 9 Session: S3-24 HPD
1	001	-	-	ER-0:...	ER-0:...	ER-0:...
	002	-	-	ER-0:...	ER-0:...	ER-0:...
	003	-	-	ER-0:...	ER-0:...	ER-0:...
	004	-	-	ER-0:...	ER-0:...	ER-0:...
	005	-	-	ER-0:...	ER-0:...	ER-0:...
	006	-	-	ER-0:...	ER-0:...	ER-0:...
	007	-	-	ER-0:...	ER-0:...	ER-0:...
	008	-	-	ER-0:...	ER-0:...	ER-0:...
	009	-	-	ER-0:...	ER-0:...	ER-0:...
	010	-	-	ER-0:...	ER-0:...	ER-0:...
	011	-	-	ER-0:...	ER-0:...	ER-0:...
	012	-	-	ER-0:...	ER-0:...	ER-0:...
	013	-	-	ER-0:...	ER-0:...	ER-0:...
	014	-	-	ER-0:...	ER-0:...	ER-0:...
	015	-	-	ER-0:...	ER-0:...	ER-0:...
2	016	-	-	ER-0:...	ER-0:...	ER-0:...
	017	-	-	ER-0:...	ER-0:...	ER-0:...
	018	-	-	ER-0:...	ER-0:...	ER-0:...
	019	-	-	ER-0:...	ER-0:...	ER-0:...
	020	-	-	ER-0:...	ER-0:...	ER-0:...
	021	-	-	ER-0:...	ER-0:...	ER-0:...

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2	022	-	-	ER-0:...	ER-0:...	ER-1:...
	023	-	-	ER-0:...	ER-0:...	ER-0:...
	024	-	-	ER-0:...	ER-0:...	ER-1:...
	025	-	-	ER-0:...	ER-0:...	ER-1:...
	026	-	-	ER-0:...	ER-0:...	ER-1:...
	027	-	-	ER-0:...	ER-0:...	ER-1:...
	028	-	-	ER-0:...	ER-0:...	ER-1:...
	029	-	-	ER-0:...	ER-0:...	ER-1:...
	030	-	-	ER-0:...	ER-0:...	ER-0:...
	3	031	-	-	ER-0:...	ER-0:...
032		-	-	ER-0:...	ER-0:...	ER-1:...
033		-	-	ER-0:...	ER-0:...	ER-1:...
034		-	-	ER-0:...	ER-0:...	ER-1:...
035		-	-	ER-0:...	ER-0:...	ER-1:...
036		-	-	ER-0:...	ER-0:...	ER-1:...
037		ER-0:...	ER-0:...	ER-0:...	ER-0:...	ER-1:...
038		-	-	ER-0:...	ER-0:...	ER-1:...
039		-	-	ER-0:...	ER-0:...	ER-0:...
040		-	-	ER-0:...	ER-0:...	ER-1:...
041		-	-	ER-0:...	ER-0:...	ER-1:...
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3	043	ER-0:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...
	044	ER-0:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...
	045	ER-0:...	ER-0:...	ER-0:...	ER-0:...	ER-1:...

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Males						
Group #	Animal #	Dosing Day: 10 Session: S4-48 HPD	Day: 11 Session: S5-72 HPD	Day: 13 Session: S6-120 HPD	Day: 14 Session: S7-144 HPD	Day: 15 Session: S1-Predose
1	001	-	-	-	-	ER-0:...
	002	-	-	-	-	ER-0:...
	003	-	-	-	-	ER-0:...
	004	-	-	-	-	ER-0:...
	005	-	-	-	-	ER-0:...
	006	-	-	-	-	ER-0:...
	007	-	-	-	-	ER-0:...
	008	-	-	-	-	ER-0:...
	009	-	-	-	-	ER-0:...
	010	-	-	-	-	ER-0:...
	011	-	-	-	-	ER-0:...
	012	-	-	-	-	ER-0:...
	013	-	-	-	-	ER-0:...
	014	-	-	-	-	ER-0:...
	015	-	-	-	-	ER-0:...
2	016	-	-	-	-	ER-0:...
	017	-	-	-	-	ER-0:...
	018	ER-0:...	ER-0:...	-	-	ER-0:...
	019	ER-0:...	ER-0:...	-	-	ER-0:...
	020	ER-0:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...
	021	ER-0:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...

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2	022	ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...
	023	ER-1:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...
	024	ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...
	025	ER-1:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...
	026	ER-1:...	ER-1:...	ER-1:...	ER-0:...	ER-0:...
	027	ER-0:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...
	028	ER-1:...	ER-1:...	ER-1:...	ER-0:...	ER-0:...
	029	ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...
	030	ER-0:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...
	3	031	ER-1:...	ER-1:...	ER-0:...	ER-0:...
032		ER-1:...	ER-0:...	-	-	ER-0:...
033		ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...
034		ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...
035		ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...
036		ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...
037		ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...
038		ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...
039		ER-0:...	ER-0:...	-	-	ER-0:...
040		ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...
041		ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...
042		ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...

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3	043	ER-1:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...
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1	001	ER-0:...	ER-0:...	-	-	-
	002	ER-0:...	ER-0:...	-	-	-
	003	ER-0:...	ER-0:...	-	-	-
	004	ER-0:...	ER-0:...	-	-	-
	005	ER-0:...	ER-0:...	-	-	-
	006	ER-0:...	ER-0:...	-	-	-
	007	ER-0:...	ER-0:...	-	-	-
	008	ER-0:...	ER-0:...	-	-	-
	009	ER-0:...	ER-0:...	-	-	-
	010	ER-0:...	ER-0:...	-	-	-
	011	ER-0:...	ER-0:...	-	-	-
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	013	ER-0:...	ER-0:...	-	-	-
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2	016	ER-0:...	ER-0:...	ER-0:...	-	-
	017	ER-0:...	ER-0:...	-	-	-
	018	ER-0:...	ER-0:...	ER-0:...	-	-
	019	ER-0:...	ER-0:...	ER-0:...	-	-
	020	ER-0:...	ER-0:...	ER-0:...	-	-
	021	ER-0:...	ER-0:...	ER-0:...	-	-

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2	022	ER-0:...	ER-0:...	ER-0:...	-	-
	023	ER-0:...	ER-0:...	ER-0:...	-	-
	024	ER-0:...	ER-0:...	ER-0:...	-	-
	025	ER-0:...	ER-0:...	ER-0:...	-	-
	026	ER-0:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...
	027	ER-0:...	ER-0:...	ER-0:...	ER-0:...	-
	028	ER-0:...	ER-0:...	ER-0:...	ER-0:...	-
	029	ER-0:...	ER-0:...	-	-	-
	030	ER-0:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...
	3	031	ER-0:...	ER-0:...	ER-1:...	-
032		ER-0:...	ER-0:...	-	-	-
033		ER-0:...	ER-0:...	ER-1:...	-	-
034		ER-0:...	ER-0:...	ER-0:...	-	-
035		ER-0:...	ER-0:...	ER-0:...	-	-
036		ER-0:...	ER-0:...	ER-0:...	-	-
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040		ER-0:...	ER-0:...	ER-0:...	-	-
041		ER-1:...	ER-0:...	ER-1:...	ER-0:...	ER-0:...
042		ER-0:...	ER-0:...	ER-0:...	ER-0:...	-

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StudyTitle: 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY  
Test Article: BNT162b2(V9), BNT162b3c

Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

Erythema Grade-Left(ERL)

Males						
Group #	Animal #	Dosing Day: 15 Session: S2-4 HPD	Day: 16 Session: S3-24 HPD	Day: 17 Session: S4-48 HPD	Recovery Day: 1 Session: S5-72 HPD	Day: 3 Session: S6-120 HPD
3	043	ER-0:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...
	044	ER-0:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...
	045	ER-0:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...

S = Scheduled Animal Room, U = UnScheduled Animal Room, N = Scheduled Necropsy, n = UnScheduled Necropsy

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Repeat Dose Toxicity/Toxicity with Recovery

Erythema Grade-Left(ERL)

Males

Group #	Animal #	Recovery Day: 4 Session: S7-144 HPD
1	001	-
	002	-
	003	-
	004	-
	005	-
	006	-
	007	-
	008	-
	009	-
	010	-
	011	-
	012	-
	013	-
	014	-
	015	-
2	016	-
	017	-
	018	-
	019	-
	020	-
	021	-

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Repeat Dose Toxicity/Toxicity with Recovery

**Erythema Grade-Left(ERL)**

Males		
Group #	Animal #	Recovery Day: 4 Session: S7-144 HPD
2	022	-
	023	-
	024	-
	025	-
	026	ER-0:...
	027	-
	028	-
	029	-
	030	ER-0:...
	3	031
032		-
033		-
034		-
035		-
036		-
037		-
038		-
039		-
040		-
041		ER-0:...
042		-

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Repeat Dose Toxicity/Toxicity with Recovery

**Erythema Grade-Left(ERL)**

**Males**

Group #	Animal #	Recovery Day: 4 Session: S7-144 HPD
3	043	ER-0:...
	044	ER-0:...
	045	ER-0:...

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Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Erythema Grade-Left(ERL)**

Females						
Group #	Animal #	Dosing Day: 1 Session: S1-Predose	Day: 2 Session: S2-4 HPD	Day: 3 Session: S3-24 HPD	Day: 4 Session: S4-48 HPD	Day: 4 Session: S5-72 HPD
1	046	ER-0:...	ER-0:...	ER-0:...	-	-
	047	ER-0:...	ER-0:...	ER-0:...	-	-
	048	ER-0:...	ER-0:...	ER-0:...	-	-
	049	ER-0:...	ER-0:...	ER-0:...	-	-
	050	ER-0:...	ER-0:...	ER-0:...	-	-
	051	ER-0:...	ER-0:...	ER-0:...	-	-
	052	ER-0:...	ER-0:...	ER-0:...	-	-
	053	ER-0:...	ER-0:...	ER-0:...	-	-
	054	ER-0:...	ER-0:...	ER-0:...	-	-
	055	ER-0:...	ER-0:...	ER-0:...	-	-
	056	ER-0:...	ER-0:...	ER-0:...	-	-
	057	ER-0:...	ER-0:...	ER-0:...	-	-
	058	ER-0:...	ER-0:...	ER-0:...	-	-
	059	ER-0:...	ER-0:...	ER-0:...	-	-
060	ER-0:...	ER-0:...	ER-0:...	-	-	
2	061	ER-0:...	ER-0:...	ER-0:...	-	-
	062	ER-0:...	ER-0:...	ER-1:...	ER-1:...	ER-1:...
	063	ER-0:...	ER-0:...	ER-1:...	ER-1:...	ER-0:...
	064	ER-0:...	ER-0:...	ER-1:...	ER-1:...	ER-1:...
	065	ER-0:...	ER-0:...	ER-0:...	-	-
	066	ER-0:...	ER-0:...	ER-1:...	ER-1:...	ER-1:...

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Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Erythema Grade-Left(ERL)**

Females						
Group #	Animal #	Dosing Day: 1		Day: 2	Day: 3	Day: 4
		Session: S1-Predose	Session: S2-4 HPD	Session: S3-24 HPD	Session: S4-48 HPD	Session: S5-72 HPD
2	067	ER-0:...	ER-0:...	ER-1:...	ER-1:...	ER-1:...
	068	ER-0:...	ER-0:...	ER-0:...	-	-
	069	ER-0:...	ER-0:...	ER-1:...	ER-1:...	ER-1:...
	070	ER-0:...	ER-0:...	ER-0:...	-	-
	071	ER-0:...	ER-0:...	ER-1:...	-	-
	072	ER-0:...	ER-0:...	ER-1:...	ER-1:...	ER-1:...
	073	ER-0:...	ER-0:...	ER-1:...	ER-1:...	ER-1:...
	074	ER-0:...	ER-0:...	ER-1:...	ER-1:...	ER-1:...
	075	ER-0:...	ER-0:...	ER-1:...	ER-1:...	ER-1:...
	3	076	ER-0:...	ER-0:...	ER-1:...	-
077		ER-0:...	ER-0:...	ER-1:...	-	-
078		ER-0:...	ER-0:...	ER-1:...	-	-
079		ER-0:...	ER-0:...	ER-1:...	ER-1:...	ER-1:...
080		ER-0:...	ER-0:...	ER-1:...	ER-1:...	ER-1:...
081		ER-0:...	ER-0:...	ER-1:...	-	-
082		ER-0:...	ER-0:...	ER-1:...	-	-
083		ER-0:...	ER-0:...	ER-1:...	ER-1:...	ER-1:...
084		ER-0:...	ER-0:...	ER-1:...	ER-1:...	ER-1:...
085		ER-0:...	ER-0:...	ER-1:...	ER-1:...	ER-1:...
086	ER-0:...	ER-0:...	ER-1:...	-	-	
087	ER-0:...	ER-0:...	ER-1:...	ER-1:...	ER-1:...	

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Repeat Dose Toxicity/Toxicity with Recovery

Erythema Grade-Left(ERL)

Females

Group #	Animal #	Dosing Day: 1 Session: S1-Predose	Session: S2-4 HPD	Day: 2 Session: S3-24 HPD	Day: 3 Session: S4-48 HPD	Day: 4 Session: S5-72 HPD
3	088	ER-0:...	ER-0:...	ER-1:...	ER-1:...	ER-1:...
	089	ER-0:...	ER-0:...	ER-1:...	-	-
	090	ER-0:...	ER-0:...	ER-1:...	-	-

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Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Erythema Grade-Left(ERL)**

Females						
Group #	Animal #	Dosing Day: 6 Session: S6-120 HPD	Day: 7 Session: S7-144 HPD	Day: 8 Session: S1-Predose	Session: S2-4 HPD	Day: 9 Session: S3-24 HPD
1	046	-	-	ER-0:...	ER-0:...	ER-0:...
	047	-	-	ER-0:...	ER-0:...	ER-0:...
	048	-	-	ER-0:...	ER-0:...	ER-0:...
	049	-	-	ER-0:...	ER-0:...	ER-0:...
	050	-	-	ER-0:...	ER-0:...	ER-0:...
	051	-	-	ER-0:...	ER-0:...	ER-0:...
	052	-	-	ER-0:...	ER-0:...	ER-0:...
	053	-	-	ER-0:...	ER-0:...	ER-0:...
	054	-	-	ER-0:...	ER-0:...	ER-0:...
	055	-	-	ER-0:...	ER-0:...	ER-0:...
	056	-	-	ER-0:...	ER-0:...	ER-0:...
	057	-	-	ER-0:...	ER-0:...	ER-0:...
	058	-	-	ER-0:...	ER-0:...	ER-0:...
	059	-	-	ER-0:...	ER-0:...	ER-0:...
060	-	-	ER-0:...	ER-0:...	ER-0:...	
2	061	-	-	ER-0:...	ER-0:...	ER-1:...
	062	ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-1:...
	063	ER-0:...	ER-0:...	ER-0:...	ER-0:...	ER-1:...
	064	ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-1:...
	065	-	-	ER-0:...	ER-0:...	ER-1:...
	066	ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-1:...

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Repeat Dose Toxicity/Toxicity with Recovery

**Erythema Grade-Left(ERL)**

Females						
Group #	Animal #	Dosing Day: 6 Session: S6-120 HPD	Day: 7 Session: S7-144 HPD	Day: 8 Session: S1-Predose	Session: S2-4 HPD	Day: 9 Session: S3-24 HPD
2	067	ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-1:...
	068	-	-	ER-0:...	ER-0:...	ER-1:...
	069	ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-1:...
	070	-	-	ER-0:...	ER-0:...	ER-1:...
	071	-	-	ER-0:...	ER-0:...	ER-1:...
	072	ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-1:...
	073	ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-1:...
	074	ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-1:...
	075	ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-1:...
	3	076	-	-	ER-0:...	ER-0:...
077		-	-	ER-0:...	ER-0:...	ER-1:...
078		-	-	ER-0:...	ER-0:...	ER-1:...
079		ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-1:...
080		ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-1:...
081		-	-	ER-0:...	ER-0:...	ER-1:...
082		-	-	ER-0:...	ER-0:...	ER-1:...
083		ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-1:...
084		ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-1:...
085		ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-1:...
086	-	-	ER-0:...	ER-0:...	ER-1:...	
087	ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-1:...	

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Repeat Dose Toxicity/Toxicity with Recovery

Erythema Grade-Left(ERL)

Females

Group #	Animal #	Dosing Day: 6 Session: S6-120 HPD	Day: 7 Session: S7-144 HPD	Day: 8 Session: S1-Predose	Session: S2-4 HPD	Day: 9 Session: S3-24 HPD
3	088	ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-1:...
	089	-	-	ER-0:...	ER-0:...	ER-1:...
	090	-	-	ER-0:...	ER-0:...	ER-1:...

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Repeat Dose Toxicity/Toxicity with Recovery

**Erythema Grade-Left(ERL)**

Females						
Group #	Animal #	Dosing Day: 10 Session: S4-48 HPD	Day: 11 Session: S5-72 HPD	Day: 13 Session: S6-120 HPD	Day: 14 Session: S7-144 HPD	Day: 15 Session: S1-Predose
1	046	-	-	-	-	ER-0:...
	047	-	-	-	-	ER-0:...
	048	-	-	-	-	ER-0:...
	049	-	-	-	-	ER-0:...
	050	-	-	-	-	ER-0:...
	051	-	-	-	-	ER-0:...
	052	-	-	-	-	ER-0:...
	053	-	-	-	-	ER-0:...
	054	-	-	-	-	ER-0:...
	055	-	-	-	-	ER-0:...
	056	-	-	-	-	ER-0:...
	057	-	-	-	-	ER-0:...
	058	-	-	-	-	ER-0:...
	059	-	-	-	-	ER-0:...
060	-	-	-	-	ER-0:...	
2	061	ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...
	062	ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...
	063	ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...
	064	ER-1:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...
	065	ER-1:...	ER-1:...	ER-1:...	ER-0:...	ER-0:...
	066	ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...

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Females						
Group #	Animal #	Dosing Day: 10 Session: S4-48 HPD	Day: 11 Session: S5-72 HPD	Day: 13 Session: S6-120 HPD	Day: 14 Session: S7-144 HPD	Day: 15 Session: S1-Predose
2	067	ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...
	068	ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...
	069	ER-1:...	ER-0:...	-	-	ER-0:...
	070	ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...
	071	ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...
	072	ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...
	073	ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...
	074	ER-1:...	ER-1:...	ER-1:...	ER-0:...	ER-0:...
	075	ER-1:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...
	3	076	ER-1:...	ER-1:...	ER-1:...	ER-0:...
077		ER-1:...	ER-1:...	ER-1:...	ER-0:...	ER-0:...
078		ER-1:...	ER-1:...	ER-1:...	ER-0:...	ER-0:...
079		ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...
080		ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...
081		ER-1:...	ER-1:...	ER-1:...	ER-0:...	ER-0:...
082		ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...
083		ER-1:...	ER-1:...	ER-1:...	ER-0:...	ER-0:...
084		ER-1:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...
085		ER-1:...	ER-1:...	ER-1:...	ER-0:...	ER-0:...
086	ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...	
087	ER-1:...	ER-1:...	ER-1:...	ER-0:...	ER-0:...	

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Erythema Grade-Left(ERL)

Females

Group #	Animal #	Dosing Day: 10 Session: S4-48 HPD	Day: 11 Session: S5-72 HPD	Day: 13 Session: S6-120 HPD	Day: 14 Session: S7-144 HPD	Day: 15 Session: S1-Predose
3	088	ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...
	089	ER-1:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...
	090	ER-1:...	ER-1:...	ER-1:...	ER-0:...	ER-0:...

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Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Erythema Grade-Left(ERL)**

Females						
Group #	Animal #	Dosing Day: 15 Session: S2-4 HPD	Day: 16 Session: S3-24 HPD	Day: 17 Session: S4-48 HPD	Recovery Day: 1 Session: S5-72 HPD	Day: 3 Session: S6-120 HPD
1	046	ER-0:...	ER-0:...	-	-	-
	047	ER-0:...	ER-0:...	-	-	-
	048	ER-0:...	ER-0:...	-	-	-
	049	ER-0:...	ER-0:...	-	-	-
	050	ER-0:...	ER-0:...	-	-	-
	051	ER-0:...	ER-0:...	-	-	-
	052	ER-0:...	ER-0:...	-	-	-
	053	ER-0:...	ER-0:...	-	-	-
	054	ER-0:...	ER-0:...	-	-	-
	055	ER-0:...	ER-0:...	-	-	-
	056	ER-0:...	ER-0:...	-	-	-
	057	ER-0:...	ER-0:...	-	-	-
	058	ER-0:...	ER-0:...	-	-	-
	059	ER-0:...	ER-0:...	-	-	-
060	ER-0:...	ER-0:...	-	-	-	
2	061	ER-0:...	ER-0:...	ER-0:...	-	-
	062	ER-0:...	ER-1:...	ER-1:...	-	-
	063	ER-0:...	ER-1:...	ER-1:...	-	-
	064	ER-0:...	ER-1:...	ER-0:...	-	-
	065	ER-0:...	ER-1:...	ER-0:...	-	-
	066	ER-0:...	ER-1:...	ER-0:...	-	-

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**Dermal Assessment Left/Right Report with Individual Values**

Pfizer

**Study:** 20GR142  
**StudyTitle:** 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY  
**Test Article:** BNT162b2(V9), BNT162b3c

Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Erythema Grade-Left(ERL)**

Females						
Group #	Animal #	Dosing Day: 15 Session: S2-4 HPD	Day: 16 Session: S3-24 HPD	Day: 17 Session: S4-48 HPD	Recovery Day: 1 Session: S5-72 HPD	Day: 3 Session: S6-120 HPD
2	067	ER-0:...	ER-1:...	ER-0:...	-	-
	068	ER-0:...	ER-1:...	ER-0:...	-	-
	069	ER-0:...	ER-1:...	ER-0:...	-	-
	070	ER-0:...	ER-0:...	ER-0:...	-	-
	071	ER-0:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...
	072	ER-0:...	ER-1:...	ER-0:...	ER-1:...	ER-0:...
	073	ER-0:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...
	074	ER-0:...	ER-0:...	ER-0:...	ER-0:...	ER-0:...
	075	ER-0:...	ER-1:...	ER-1:...	ER-1:...	ER-0:...
	3	076	ER-0:...	ER-1:...	ER-1:...	-
077		ER-0:...	ER-1:...	ER-1:...	-	-
078		ER-0:...	ER-1:...	ER-1:...	-	-
079		ER-0:...	ER-1:...	ER-0:...	-	-
080		ER-0:...	ER-1:...	ER-1:...	-	-
081		ER-0:...	ER-1:...	ER-1:...	-	-
082		ER-0:...	ER-1:...	ER-1:...	-	-
083		ER-0:...	ER-1:...	ER-0:...	-	-
084		ER-0:...	ER-1:...	ER-1:...	-	-
085		ER-0:...	ER-1:...	ER-1:...	-	-
086	ER-0:...	ER-1:...	ER-0:...	ER-0:...	ER-0:...	
087	ER-0:...	ER-1:...	ER-1:...	ER-1:...	ER-0:...	

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Erythema Grade-Left(ERL)

Females						
Group #	Animal #	Dosing Day: 15 Session: S2-4 HPD	Day: 16 Session: S3-24 HPD	Day: 17 Session: S4-48 HPD	Recovery Day: 1 Session: S5-72 HPD	Day: 3 Session: S6-120 HPD
3	088	ER-0:...	ER-1:...	ER-1:...	ER-1:...	ER-1:...
	089	ER-0:...	ER-1:...	ER-1:...	ER-1:...	ER-0:...
	090	ER-0:...	ER-1:...	ER-1:...	ER-1:...	ER-0:...

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Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

Erythema Grade-Left(ERL)

Females

Group #	Animal #	Recovery Day: 4 Session: S7-144 HPD
1	046	-
	047	-
	048	-
	049	-
	050	-
	051	-
	052	-
	053	-
	054	-
	055	-
	056	-
	057	-
	058	-
2	059	-
	060	-
	061	-
	062	-
	063	-
	064	-
	065	-
066	-	

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Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Erythema Grade-Left(ERL)**

**Females**

Group #	Animal #	Recovery Day: 4 Session: S7-144 HPD
2	067	-
	068	-
	069	-
	070	-
	071	ER-0:...
	072	ER-0:...
	073	ER-0:...
	074	ER-0:...
	075	ER-0:...
3	076	-
	077	-
	078	-
	079	-
	080	-
	081	-
	082	-
	083	-
	084	-
	085	-
	086	ER-0:...
	087	ER-0:...

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Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Erythema Grade-Left(ERL)**

**Females**

Group #	Animal #	Recovery Day: 4 Session: S7-144 HPD
3	088	ER-0:...
	089	ER-0:...
	090	ER-0:...

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Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

Erythema Grade-Right(ERR)

Males

Group #	Animal #	Dosing Day: 1	Session: S1-Predose	Session: S2-4 HPD
1	001	ER-0:...		ER-0:...
	002	ER-0:...		ER-0:...
	003	ER-0:...		ER-0:...
	004	ER-0:...		ER-0:...
	005	ER-0:...		ER-0:...
	006	ER-0:...		ER-0:...
	007	ER-0:...		ER-0:...
	008	ER-0:...		-
	009	ER-0:...		ER-0:...
	010	ER-0:...		-
	011	ER-0:...		-
	012	ER-0:...		-
	013	ER-0:...		-
	014	ER-0:...		-
	015	ER-0:...		-
2	016	ER-0:...		-
	017	ER-0:...		-
	018	ER-0:...		-
	019	ER-0:...		-
	020	ER-0:...		-
	021	ER-0:...		-

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Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Erythema Grade-Right(ERR)**

Males				
Group #	Animal #	Dosing Day: 1	Session: S1-Predose      Session: S2-4 HPD	
2	022	ER-0:...	-	
	023	ER-0:...	-	
	024	ER-0:...	-	
	025	ER-0:...	-	
	026	ER-0:...	-	
	027	ER-0:...	-	
	028	ER-0:...	-	
	029	ER-0:...	-	
	030	ER-0:...	-	
	3	031	ER-0:...	-
032		ER-0:...	-	
033		ER-0:...	-	
034		ER-0:...	-	
035		ER-0:...	-	
036		ER-0:...	-	
037		ER-0:...	-	
038		ER-0:...	-	
039		ER-0:...	-	
040		ER-0:...	-	
041		ER-0:...	-	
042		ER-0:...	-	

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Repeat Dose Toxicity/Toxicity with Recovery

**Erythema Grade-Right(ERR)**

**Males**

Group #	Animal #	Dosing Day: 1	Session: S1-Predose	Session: S2-4 HPD
3	043	ER-0:...	-	-
	044	ER-0:...	-	-
	045	ER-0:...	-	-

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Repeat Dose Toxicity/Toxicity with Recovery

**Erythema Grade-Right(ERR)**

**Females**

Group #	Animal #	Dosing Day: 1	Session: S1-Predose	Session: S2-4 HPD
1	046	ER-0:...	ER-0:...	ER-0:...
	047	ER-0:...	ER-0:...	ER-0:...
	048	ER-0:...	ER-0:...	ER-0:...
	049	ER-0:...	ER-0:...	ER-0:...
	050	ER-0:...	ER-0:...	ER-0:...
	051	ER-0:...	ER-0:...	ER-0:...
	052	ER-0:...	ER-0:...	ER-0:...
	053	ER-0:...	ER-0:...	ER-0:...
	054	ER-0:...	ER-0:...	ER-0:...
	055	ER-0:...	ER-0:...	ER-0:...
	056	ER-0:...	ER-0:...	ER-0:...
	057	ER-0:...	ER-0:...	ER-0:...
	058	ER-0:...	ER-0:...	ER-0:...
	059	ER-0:...	-	-
	060	ER-0:...	-	-
2	061	ER-0:...	-	-
	062	ER-0:...	-	-
	063	ER-0:...	-	-
	064	ER-0:...	-	-
	065	ER-0:...	-	-
	066	ER-0:...	-	-

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Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Erythema Grade-Right(ERR)**

**Females**

Group #	Animal #	Dosing Day: 1	Session: S1-Predose	Session: S2-4 HPD
2	067	ER-0:...		-
	068	ER-0:...		-
	069	ER-0:...		-
	070	ER-0:...		-
	071	ER-0:...		-
	072	ER-0:...		-
	073	ER-0:...		-
	074	ER-0:...		-
	075	ER-0:...		-
3	076	ER-0:...		-
	077	ER-0:...		-
	078	ER-0:...		-
	079	ER-0:...		-
	080	ER-0:...		-
	081	ER-0:...		-
	082	ER-0:...		-
	083	ER-0:...		-
	084	ER-0:...		-
	085	ER-0:...		-
086	ER-0:...		-	
087	ER-0:...		-	

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Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Erythema Grade-Right(ERR)**

**Females**

Group #	Animal #	Dosing Day: 1	Session: S1-Predose	Session: S2-4 HPD
3	088	ER-0:...	-	-
	089	ER-0:...	-	-
	090	ER-0:...	-	-

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Repeat Dose Toxicity/Toxicity with Recovery

**Edema Grade-Left(EDL)**

Males						
Group #	Animal #	Dosing Day: 1 Session: S1-Predose	Day: 2 Session: S2-4 HPD	Day: 3 Session: S3-24 HPD	Day: 4 Session: S4-48 HPD	Day: 4 Session: S5-72 HPD
1	001	ED-0:...	ED-0:...	ED-0:...	-	-
	002	ED-0:...	ED-0:...	ED-0:...	-	-
	003	ED-0:...	ED-0:...	ED-0:...	-	-
	004	ED-0:...	ED-0:...	ED-0:...	-	-
	005	ED-0:...	ED-0:...	ED-0:...	-	-
	006	ED-0:...	ED-0:...	ED-0:...	-	-
	007	ED-0:...	ED-0:...	ED-0:...	-	-
	008	ED-0:...	ED-0:...	ED-0:...	-	-
	009	ED-0:...	ED-0:...	ED-0:...	-	-
	010	ED-0:...	ED-0:...	ED-0:...	-	-
	011	ED-0:...	ED-0:...	ED-0:...	-	-
	012	ED-0:...	ED-0:...	ED-0:...	-	-
	013	ED-0:...	ED-0:...	ED-0:...	-	-
	014	ED-0:...	ED-0:...	ED-0:...	-	-
	015	ED-0:...	ED-0:...	ED-0:...	-	-
2	016	ED-0:...	ED-0:...	ED-0:...	-	-
	017	ED-0:...	ED-0:...	ED-0:...	-	-
	018	ED-0:...	ED-0:...	ED-0:...	-	-
	019	ED-0:...	ED-0:...	ED-1:...	-	-
	020	ED-0:...	ED-0:...	ED-1:...	-	-
	021	ED-0:...	ED-0:...	ED-2:...	ED-1:...	ED-0:...

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Repeat Dose Toxicity/Toxicity with Recovery

**Edema Grade-Left(EDL)**

Males						
Group #	Animal #	Dosing Day: 1		Day: 2	Day: 3	Day: 4
		Session: S1-Predose	Session: S2-4 HPD	Session: S3-24 HPD	Session: S4-48 HPD	Session: S5-72 HPD
2	022	ED-0:...	ED-0:...	ED-2:...	ED-2:...	ED-1:...
	023	ED-0:...	ED-0:...	ED-2:...	ED-2:...	ED-1:...
	024	ED-0:...	ED-0:...	ED-0:...	-	-
	025	ED-0:...	ED-0:...	ED-1:...	-	-
	026	ED-0:...	ED-0:...	ED-2:...	ED-2:...	ED-1:...
	027	ED-0:...	ED-0:...	ED-2:...	ED-2:...	ED-1:...
	028	ED-0:...	ED-0:...	ED-2:...	ED-2:...	ED-1:...
	029	ED-0:...	ED-0:...	ED-1:...	-	-
	030	ED-0:...	ED-0:...	ED-1:...	-	-
	3	031	ED-0:...	ED-0:...	ED-2:...	ED-2:...
032		ED-0:...	ED-0:...	ED-0:...	-	-
033		ED-0:...	ED-0:...	ED-1:...	-	-
034		ED-0:...	ED-0:...	ED-2:...	ED-2:...	ED-1:...
035		ED-0:...	ED-0:...	ED-0:...	-	-
036		ED-0:...	ED-0:...	ED-1:...	-	-
037		ED-0:...	ED-0:...	ED-2:...	ED-2:...	ED-2:...
038		ED-0:...	ED-0:...	ED-1:...	-	-
039		ED-0:...	ED-0:...	ED-1:...	-	-
040		ED-0:...	ED-0:...	ED-1:...	-	-
041		ED-0:...	ED-0:...	ED-1:...	-	-
042		ED-0:...	ED-0:...	ED-1:...	-	-

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**Edema Grade-Left(EDL)**

Males						
Group #	Animal #	Dosing Day: 1 Session: S1-Predose	Day: 2 Session: S2-4 HPD	Day: 3 Session: S3-24 HPD	Day: 4 Session: S4-48 HPD	Day: 4 Session: S5-72 HPD
3	043	ED-0:...	ED-0:...	ED-2:...	ED-2:...	ED-2:...
	044	ED-0:...	ED-0:...	ED-2:...	ED-2:...	ED-2:...
	045	ED-0:...	ED-0:...	ED-2:...	ED-2:...	ED-2:...

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Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Edema Grade-Left(EDL)**

Males						
Group #	Animal #	Dosing Day: 6 Session: S6-120 HPD	Day: 7 Session: S7-144 HPD	Day: 8 Session: S1-Predose	Session: S2-4 HPD	Day: 9 Session: S3-24 HPD
1	001	-	-	ED-0:...	ED-0:...	ED-0:...
	002	-	-	ED-0:...	ED-0:...	ED-0:...
	003	-	-	ED-0:...	ED-0:...	ED-0:...
	004	-	-	ED-0:...	ED-0:...	ED-0:...
	005	-	-	ED-0:...	ED-0:...	ED-0:...
	006	-	-	ED-0:...	ED-0:...	ED-0:...
	007	-	-	ED-0:...	ED-0:...	ED-0:...
	008	-	-	ED-0:...	ED-0:...	ED-0:...
	009	-	-	ED-0:...	ED-0:...	ED-0:...
	010	-	-	ED-0:...	ED-0:...	ED-0:...
	011	-	-	ED-0:...	ED-0:...	ED-0:...
	012	-	-	ED-0:...	ED-0:...	ED-0:...
	013	-	-	ED-0:...	ED-0:...	ED-0:...
	014	-	-	ED-0:...	ED-0:...	ED-0:...
	015	-	-	ED-0:...	ED-0:...	ED-0:...
2	016	-	-	ED-0:...	ED-0:...	ED-0:...
	017	-	-	ED-0:...	ED-0:...	ED-0:...
	018	-	-	ED-0:...	ED-0:...	ED-2:...
	019	-	-	ED-0:...	ED-0:...	ED-2:...
	020	-	-	ED-0:...	ED-0:...	ED-2:...
	021	-	-	ED-0:...	ED-0:...	ED-2:...

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**Edema Grade-Left(EDL)**

Males						
Group #	Animal #	Dosing Day: 6 Session: S6-120 HPD	Day: 7 Session: S7-144 HPD	Day: 8 Session: S1-Predose	Session: S2-4 HPD	Day: 9 Session: S3-24 HPD
2	022	-	-	ED-0:...	ED-0:...	ED-3:...
	023	-	-	ED-0:...	ED-0:...	ED-3:...
	024	-	-	ED-0:...	ED-0:...	ED-3:...
	025	-	-	ED-0:...	ED-0:...	ED-3:...
	026	-	-	ED-0:...	ED-0:...	ED-3:...
	027	-	-	ED-0:...	ED-0:...	ED-2:...
	028	-	-	ED-0:...	ED-0:...	ED-3:...
	029	-	-	ED-0:...	ED-0:...	ED-3:...
	030	-	-	ED-0:...	ED-0:...	ED-2:...
	3	031	-	-	ED-0:...	ED-0:...
032		-	-	ED-0:...	ED-0:...	ED-2:...
033		-	-	ED-0:...	ED-0:...	ED-3:...
034		-	-	ED-0:...	ED-0:...	ED-2:...
035		-	-	ED-0:...	ED-0:...	ED-3:...
036		-	-	ED-0:...	ED-0:...	ED-2:...
037		ED-2:...	ED-1:...	ED-0:...	ED-0:...	ED-3:...
038		-	-	ED-0:...	ED-0:...	ED-3:...
039		-	-	ED-0:...	ED-0:...	ED-2:...
040		-	-	ED-0:...	ED-0:...	ED-3:...
041		-	-	ED-0:...	ED-0:...	ED-3:...
042		-	-	ED-0:...	ED-0:...	ED-3:...

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Dermal Assessment Left/Right Report with Individual Values

Pfizer

Study: 20GR142  
StudyTitle: 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY  
Test Article: BNT162b2(V9), BNT162b3c

Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

Edema Grade-Left(EDL)

Males

Group #	Animal #	Dosing Day: 6 Session: S6-120 HPD	Day: 7 Session: S7-144 HPD	Day: 8 Session: S1-Predose	Session: S2-4 HPD	Day: 9 Session: S3-24 HPD
3	043	ED-2:...	ED-1:...	ED-0:...	ED-0:...	ED-3:...
	044	ED-2:...	ED-1:...	ED-0:...	ED-0:...	ED-3:...
	045	ED-2:...	ED-1:...	ED-0:...	ED-0:...	ED-3:...

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Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Edema Grade-Left(EDL)**

Males						
Group #	Animal #	Dosing Day: 10 Session: S4-48 HPD	Day: 11 Session: S5-72 HPD	Day: 13 Session: S6-120 HPD	Day: 14 Session: S7-144 HPD	Day: 15 Session: S1-Predose
1	001	-	-	-	-	ED-0:...
	002	-	-	-	-	ED-0:...
	003	-	-	-	-	ED-0:...
	004	-	-	-	-	ED-0:...
	005	-	-	-	-	ED-0:...
	006	-	-	-	-	ED-0:...
	007	-	-	-	-	ED-0:...
	008	-	-	-	-	ED-0:...
	009	-	-	-	-	ED-0:...
	010	-	-	-	-	ED-0:...
	011	-	-	-	-	ED-0:...
	012	-	-	-	-	ED-0:...
	013	-	-	-	-	ED-0:...
	014	-	-	-	-	ED-0:...
	015	-	-	-	-	ED-0:...
2	016	-	-	-	-	ED-0:...
	017	-	-	-	-	ED-0:...
	018	ED-2:...	ED-1:...	-	-	ED-0:...
	019	ED-2:...	ED-1:...	-	-	ED-0:...
	020	ED-2:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
	021	ED-2:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...

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**Edema Grade-Left(EDL)**

Males						
Group #	Animal #	Dosing Day: 10 Session: S4-48 HPD	Day: 11 Session: S5-72 HPD	Day: 13 Session: S6-120 HPD	Day: 14 Session: S7-144 HPD	Day: 15 Session: S1-Predose
2	022	ED-3:...	ED-2:...	ED-1:...	ED-1:...	ED-0:...
	023	ED-3:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
	024	ED-3:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
	025	ED-3:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
	026	ED-3:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
	027	ED-2:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
	028	ED-3:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
	029	ED-3:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
	030	ED-2:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
	3	031	ED-3:...	ED-2:...	ED-1:...	ED-0:...
032		ED-2:...	ED-1:...	-	-	ED-0:...
033		ED-3:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
034		ED-3:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
035		ED-3:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
036		ED-2:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
037		ED-3:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
038		ED-3:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
039		ED-2:...	ED-1:...	-	-	ED-0:...
040		ED-3:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
041		ED-3:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
042		ED-3:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...

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Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

Edema Grade-Left(EDL)

Males						
Group #	Animal #	Dosing Day: 10 Session: S4-48 HPD	Day: 11 Session: S5-72 HPD	Day: 13 Session: S6-120 HPD	Day: 14 Session: S7-144 HPD	Day: 15 Session: S1-Predose
3	043	ED-3:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
	044	ED-3:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
	045	ED-3:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...

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Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Edema Grade-Left(EDL)**

Males						
Group #	Animal #	Dosing Day: 15 Session: S2-4 HPD	Day: 16 Session: S3-24 HPD	Day: 17 Session: S4-48 HPD	Recovery Day: 1 Session: S5-72 HPD	Day: 3 Session: S6-120 HPD
1	001	ED-0:...	ED-0:...	-	-	-
	002	ED-0:...	ED-0:...	-	-	-
	003	ED-0:...	ED-0:...	-	-	-
	004	ED-0:...	ED-0:...	-	-	-
	005	ED-0:...	ED-0:...	-	-	-
	006	ED-0:...	ED-0:...	-	-	-
	007	ED-0:...	ED-0:...	-	-	-
	008	ED-0:...	ED-0:...	-	-	-
	009	ED-0:...	ED-0:...	-	-	-
	010	ED-0:...	ED-0:...	-	-	-
	011	ED-0:...	ED-0:...	-	-	-
	012	ED-0:...	ED-0:...	-	-	-
	013	ED-0:...	ED-0:...	-	-	-
	014	ED-0:...	ED-0:...	-	-	-
	015	ED-0:...	ED-0:...	-	-	-
2	016	ED-0:...	ED-2:...	ED-2:...	-	-
	017	ED-0:...	ED-0:...	-	-	-
	018	ED-0:...	ED-2:...	ED-2:...	-	-
	019	ED-0:...	ED-2:...	ED-2:...	-	-
	020	ED-0:...	ED-2:...	ED-2:...	-	-
	021	ED-0:...	ED-2:...	ED-2:...	-	-

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**Edema Grade-Left(EDL)**

Males						
Group #	Animal #	Dosing Day: 15 Session: S2-4 HPD	Day: 16 Session: S3-24 HPD	Day: 17 Session: S4-48 HPD	Recovery Day: 1 Session: S5-72 HPD	Day: 3 Session: S6-120 HPD
2	022	ED-0:...	ED-2:...	ED-2:...	-	-
	023	ED-0:...	ED-2:...	ED-2:...	-	-
	024	ED-0:...	ED-2:...	ED-2:...	-	-
	025	ED-0:...	ED-2:...	ED-2:...	-	-
	026	ED-1:...	ED-2:...	ED-2:...	ED-2:...	ED-0:...
	027	ED-0:...	ED-3:...	ED-3:...	ED-1:...	-
	028	ED-0:...	ED-3:...	ED-3:...	ED-1:...	-
	029	ED-1:...	ED-1:...	-	-	-
	030	ED-0:...	ED-2:...	ED-2:...	ED-2:...	ED-1:...
	3	031	ED-0:...	ED-2:...	ED-3:...	-
032		ED-0:...	ED-1:...	-	-	-
033		ED-0:...	ED-2:...	ED-2:...	-	-
034		ED-0:...	ED-2:...	ED-2:...	-	-
035		ED-0:...	ED-2:...	ED-2:...	-	-
036		ED-1:...	ED-2:...	ED-2:...	-	-
037		ED-1:...	ED-2:...	ED-2:...	-	-
038		ED-1:...	ED-2:...	ED-2:...	-	-
039		ED-0:...	ED-2:...	ED-2:...	-	-
040		ED-0:...	ED-2:...	ED-2:...	-	-
041		ED-1:...	ED-3:...	ED-3:...	ED-2:...	ED-0:...
042		ED-0:...	ED-2:...	ED-2:...	ED-1:...	-

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Males						
Group #	Animal #	Dosing Day: 15 Session: S2-4 HPD	Day: 16 Session: S3-24 HPD	Day: 17 Session: S4-48 HPD	Recovery Day: 1 Session: S5-72 HPD	Day: 3 Session: S6-120 HPD
3	043	ED-0:...	ED-3:...	ED-3:...	ED-2:...	ED-0:...
	044	ED-1:...	ED-3:...	ED-3:...	ED-2:...	ED-0:...
	045	ED-0:...	ED-2:...	ED-2:...	ED-2:...	ED-0:...

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Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

Edema Grade-Left(EDL)

Males

Group #	Animal #	Recovery Day: 4 Session: S7-144 HPD
1	001	-
	002	-
	003	-
	004	-
	005	-
	006	-
	007	-
	008	-
	009	-
	010	-
	011	-
	012	-
	013	-
	014	-
	015	-
2	016	-
	017	-
	018	-
	019	-
	020	-
	021	-

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Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Edema Grade-Left(EDL)**

Males		
Group #	Animal #	Recovery Day: 4 Session: S7-144 HPD
2	022	-
	023	-
	024	-
	025	-
	026	ED-1:...
	027	-
	028	-
	029	-
	030	ED-1:...
	3	031
032		-
033		-
034		-
035		-
036		-
037		-
038		-
039		-
040		-
041		ED-1:...
042		-

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Repeat Dose Toxicity/Toxicity with Recovery

Edema Grade-Left(EDL)

Males

Group #	Animal #	Recovery Day: 4 Session: S7-144 HPD
3	043	ED-0:...
	044	ED-0:...
	045	ED-0:...

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Repeat Dose Toxicity/Toxicity with Recovery

**Edema Grade-Left(EDL)**

Females						
Group #	Animal #	Dosing Day: 1 Session: S1-Predose	Day: 2 Session: S2-4 HPD	Day: 3 Session: S3-24 HPD	Day: 4 Session: S4-48 HPD	Day: 4 Session: S5-72 HPD
1	046	ED-0:...	ED-0:...	ED-0:...	-	-
	047	ED-0:...	ED-0:...	ED-0:...	-	-
	048	ED-0:...	ED-0:...	ED-0:...	-	-
	049	ED-0:...	ED-0:...	ED-0:...	-	-
	050	ED-0:...	ED-0:...	ED-0:...	-	-
	051	ED-0:...	ED-0:...	ED-0:...	-	-
	052	ED-0:...	ED-0:...	ED-0:...	-	-
	053	ED-0:...	ED-0:...	ED-0:...	-	-
	054	ED-0:...	ED-0:...	ED-0:...	-	-
	055	ED-0:...	ED-0:...	ED-0:...	-	-
	056	ED-0:...	ED-0:...	ED-0:...	-	-
	057	ED-0:...	ED-0:...	ED-0:...	-	-
	058	ED-0:...	ED-0:...	ED-0:...	-	-
	059	ED-0:...	ED-0:...	ED-0:...	-	-
	060	ED-0:...	ED-0:...	ED-0:...	-	-
2	061	ED-0:...	ED-0:...	ED-1:...	-	-
	062	ED-0:...	ED-0:...	ED-2:...	ED-2:...	ED-2:...
	063	ED-0:...	ED-0:...	ED-2:...	ED-2:...	ED-2:...
	064	ED-0:...	ED-0:...	ED-2:...	ED-2:...	ED-2:...
	065	ED-0:...	ED-0:...	ED-1:...	-	-
	066	ED-0:...	ED-0:...	ED-2:...	ED-2:...	ED-2:...

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Females						
Group #	Animal #	Dosing Day: 1 Session: S1-Predose	Day: 2 Session: S2-4 HPD	Day: 3 Session: S3-24 HPD	Day: 4 Session: S4-48 HPD	Day: 4 Session: S5-72 HPD
2	067	ED-0:...	ED-0:...	ED-2:...	ED-2:...	ED-2:...
	068	ED-0:...	ED-0:...	ED-1:...	-	-
	069	ED-0:...	ED-0:...	ED-2:...	ED-2:...	ED-2:...
	070	ED-0:...	ED-0:...	ED-1:...	-	-
	071	ED-0:...	ED-0:...	ED-1:...	-	-
	072	ED-0:...	ED-0:...	ED-2:...	ED-2:...	ED-2:...
	073	ED-0:...	ED-0:...	ED-2:...	ED-2:...	ED-2:...
	074	ED-0:...	ED-0:...	ED-2:...	ED-2:...	ED-2:...
	075	ED-0:...	ED-0:...	ED-2:...	ED-2:...	ED-2:...
	3	076	ED-0:...	ED-0:...	ED-1:...	-
077		ED-0:...	ED-0:...	ED-1:...	-	-
078		ED-0:...	ED-0:...	ED-1:...	-	-
079		ED-0:...	ED-0:...	ED-2:...	ED-2:...	ED-2:...
080		ED-0:...	ED-0:...	ED-2:...	ED-2:...	ED-2:...
081		ED-0:...	ED-0:...	ED-1:...	-	-
082		ED-0:...	ED-0:...	ED-1:...	-	-
083		ED-0:...	ED-0:...	ED-2:...	ED-2:...	ED-2:...
084		ED-0:...	ED-0:...	ED-2:...	ED-2:...	ED-2:...
085		ED-0:...	ED-0:...	ED-2:...	ED-2:...	ED-2:...
086	ED-0:...	ED-0:...	ED-1:...	-	-	
087	ED-0:...	ED-0:...	ED-2:...	ED-2:...	ED-2:...	

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**Edema Grade-Left(EDL)**

Females						
Group #	Animal #	Dosing Day: 1 Session: S1-Predose	Dosing Day: 2 Session: S2-4 HPD	Dosing Day: 3 Session: S3-24 HPD	Dosing Day: 4 Session: S4-48 HPD	Dosing Day: 5 Session: S5-72 HPD
3	088	ED-0:...	ED-0:...	ED-2:...	ED-2:...	ED-2:...
	089	ED-0:...	ED-0:...	ED-1:...	-	-
	090	ED-0:...	ED-1:...	ED-1:...	-	-

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Females						
Group #	Animal #	Dosing Day: 6 Session: S6-120 HPD	Day: 7 Session: S7-144 HPD	Day: 8 Session: S1-Predose	Session: S2-4 HPD	Day: 9 Session: S3-24 HPD
1	046	-	-	ED-0:...	ED-0:...	ED-0:...
	047	-	-	ED-0:...	ED-0:...	ED-0:...
	048	-	-	ED-0:...	ED-0:...	ED-0:...
	049	-	-	ED-0:...	ED-0:...	ED-0:...
	050	-	-	ED-0:...	ED-0:...	ED-0:...
	051	-	-	ED-0:...	ED-0:...	ED-0:...
	052	-	-	ED-0:...	ED-0:...	ED-0:...
	053	-	-	ED-0:...	ED-0:...	ED-0:...
	054	-	-	ED-0:...	ED-0:...	ED-0:...
	055	-	-	ED-0:...	ED-0:...	ED-0:...
	056	-	-	ED-0:...	ED-0:...	ED-0:...
	057	-	-	ED-0:...	ED-0:...	ED-0:...
	058	-	-	ED-0:...	ED-0:...	ED-0:...
	059	-	-	ED-0:...	ED-0:...	ED-0:...
060	-	-	ED-0:...	ED-0:...	ED-0:...	
2	061	-	-	ED-0:...	ED-0:...	ED-2:...
	062	ED-2:...	ED-2:...	ED-0:...	ED-0:...	ED-3:...
	063	ED-2:...	ED-2:...	ED-0:...	ED-0:...	ED-2:...
	064	ED-2:...	ED-2:...	ED-0:...	ED-0:...	ED-2:...
	065	-	-	ED-0:...	ED-0:...	ED-3:...
	066	ED-2:...	ED-2:...	ED-0:...	ED-0:...	ED-3:...

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**Dermal Assessment Left/Right Report with Individual Values**

Pfizer

**Study:** 20GR142  
**StudyTitle:** 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY  
**Test Article:** BNT162b2(V9), BNT162b3c

Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Edema Grade-Left(EDL)**

Females						
Group #	Animal #	Dosing Day: 6 Session: S6-120 HPD	Day: 7 Session: S7-144 HPD	Day: 8 Session: S1-Predose	Session: S2-4 HPD	Day: 9 Session: S3-24 HPD
2	067	ED-2:...	ED-2:...	ED-0:...	ED-0:...	ED-3:...
	068	-	-	ED-0:...	ED-0:...	ED-3:...
	069	ED-2:...	ED-2:...	ED-0:...	ED-0:...	ED-2:...
	070	-	-	ED-0:...	ED-0:...	ED-3:...
	071	-	-	ED-0:...	ED-0:...	ED-3:...
	072	ED-2:...	ED-2:...	ED-0:...	ED-0:...	ED-3:...
	073	ED-2:...	ED-2:...	ED-0:...	ED-0:...	ED-2:...
	074	ED-2:...	ED-2:...	ED-0:...	ED-0:...	ED-3:...
	075	ED-2:...	ED-2:...	ED-0:...	ED-0:...	ED-2:...
	3	076	-	-	ED-0:...	ED-0:...
077		-	-	ED-0:...	ED-0:...	ED-3:...
078		-	-	ED-0:...	ED-0:...	ED-3:...
079		ED-2:...	ED-2:...	ED-0:...	ED-0:...	ED-3:...
080		ED-2:...	ED-2:...	ED-0:...	ED-0:...	ED-3:...
081		-	-	ED-0:...	ED-0:...	ED-2:...
082		-	-	ED-0:...	ED-0:...	ED-3:...
083		ED-2:...	ED-2:...	ED-0:...	ED-0:...	ED-3:...
084		ED-2:...	ED-2:...	ED-0:...	ED-0:...	ED-2:...
085		ED-2:...	ED-2:...	ED-0:...	ED-0:...	ED-3:...
086	-	-	ED-0:...	ED-0:...	ED-2:...	
087	ED-2:...	ED-2:...	ED-0:...	ED-0:...	ED-3:...	

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Repeat Dose Toxicity/Toxicity with Recovery

Edema Grade-Left(EDL)

Females

Group #	Animal #	Dosing Day: 6 Session: S6-120 HPD ED-2:...	Day: 7 Session: S7-144 HPD ED-2:...	Day: 8 Session: S1-Predose ED-0:...	Session: S2-4 HPD ED-0:...	Day: 9 Session: S3-24 HPD ED-2:...
3	088					
	089	-	-			
	090	-	-			

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Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Edema Grade-Left(EDL)**

Females						
Group #	Animal #	Dosing Day: 10 Session: S4-48 HPD	Day: 11 Session: S5-72 HPD	Day: 13 Session: S6-120 HPD	Day: 14 Session: S7-144 HPD	Day: 15 Session: S1-Predose
1	046	-	-	-	-	ED-0:...
	047	-	-	-	-	ED-0:...
	048	-	-	-	-	ED-0:...
	049	-	-	-	-	ED-0:...
	050	-	-	-	-	ED-0:...
	051	-	-	-	-	ED-0:...
	052	-	-	-	-	ED-0:...
	053	-	-	-	-	ED-0:...
	054	-	-	-	-	ED-0:...
	055	-	-	-	-	ED-0:...
	056	-	-	-	-	ED-0:...
	057	-	-	-	-	ED-0:...
	058	-	-	-	-	ED-0:...
	059	-	-	-	-	ED-0:...
060	-	-	-	-	ED-0:...	
2	061	ED-2:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
	062	ED-3:...	ED-3:...	ED-1:...	ED-0:...	ED-0:...
	063	ED-2:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
	064	ED-2:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
	065	ED-3:...	ED-3:...	ED-1:...	ED-0:...	ED-0:...
	066	ED-3:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...

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**Edema Grade-Left(EDL)**

Females						
Group #	Animal #	Dosing Day: 10 Session: S4-48 HPD	Day: 11 Session: S5-72 HPD	Day: 13 Session: S6-120 HPD	Day: 14 Session: S7-144 HPD	Day: 15 Session: S1-Predose
2	067	ED-3:...	ED-3:...	ED-1:...	ED-0:...	ED-0:...
	068	ED-3:...	ED-3:...	ED-1:...	ED-0:...	ED-0:...
	069	ED-2:...	ED-1:...	-	-	ED-0:...
	070	ED-3:...	ED-3:...	ED-1:...	ED-0:...	ED-0:...
	071	ED-3:...	ED-3:...	ED-1:...	ED-0:...	ED-0:...
	072	ED-3:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
	073	ED-2:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
	074	ED-3:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
	075	ED-2:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
	3	076	ED-3:...	ED-3:...	ED-1:...	ED-0:...
077		ED-3:...	ED-3:...	ED-2:...	ED-0:...	ED-0:...
078		ED-3:...	ED-3:...	ED-2:...	ED-1:...	ED-0:...
079		ED-3:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
080		ED-3:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
081		ED-3:...	ED-2:...	ED-0:...	ED-0:...	ED-0:...
082		ED-3:...	ED-2:...	ED-0:...	ED-0:...	ED-0:...
083		ED-3:...	ED-3:...	ED-0:...	ED-0:...	ED-0:...
084		ED-2:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...
085		ED-3:...	ED-3:...	ED-1:...	ED-0:...	ED-0:...
086	ED-2:...	ED-2:...	ED-1:...	ED-0:...	ED-0:...	
087	ED-3:...	ED-3:...	ED-1:...	ED-0:...	ED-0:...	

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Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Edema Grade-Left(EDL)**

Females						
Group #	Animal #	Dosing Day: 10 Session: S4-48 HPD	Day: 11 Session: S5-72 HPD	Day: 13 Session: S6-120 HPD	Day: 14 Session: S7-144 HPD	Day: 15 Session: S1-Predose
3	088	ED-3:...	ED-3:...	ED-1:...	ED-0:...	ED-0:...
	089	ED-2:...	ED-2:...	ED-0:...	ED-0:...	ED-0:...
	090	ED-2:...	ED-2:...	ED-2:...	ED-0:...	ED-0:...

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Repeat Dose Toxicity/Toxicity with Recovery

**Edema Grade-Left(EDL)**

Females						
Group #	Animal #	Dosing Day: 15 Session: S2-4 HPD	Day: 16 Session: S3-24 HPD	Day: 17 Session: S4-48 HPD	Recovery Day: 1 Session: S5-72 HPD	Day: 3 Session: S6-120 HPD
1	046	ED-0:...	ED-0:...	-	-	-
	047	ED-0:...	ED-0:...	-	-	-
	048	ED-0:...	ED-0:...	-	-	-
	049	ED-0:...	ED-0:...	-	-	-
	050	ED-0:...	ED-0:...	-	-	-
	051	ED-0:...	ED-0:...	-	-	-
	052	ED-0:...	ED-0:...	-	-	-
	053	ED-0:...	ED-0:...	-	-	-
	054	ED-0:...	ED-0:...	-	-	-
	055	ED-0:...	ED-0:...	-	-	-
	056	ED-0:...	ED-0:...	-	-	-
	057	ED-0:...	ED-0:...	-	-	-
	058	ED-0:...	ED-0:...	-	-	-
	059	ED-0:...	ED-0:...	-	-	-
	060	ED-0:...	ED-0:...	-	-	-
2	061	ED-0:...	ED-2:...	ED-2:...	-	-
	062	ED-0:...	ED-3:...	ED-3:...	-	-
	063	ED-0:...	ED-3:...	ED-3:...	-	-
	064	ED-0:...	ED-3:...	ED-2:...	-	-
	065	ED-0:...	ED-2:...	ED-2:...	-	-
	066	ED-0:...	ED-3:...	ED-3:...	-	-

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Repeat Dose Toxicity/Toxicity with Recovery

**Edema Grade-Left(EDL)**

Females						
Group #	Animal #	Dosing Day: 15 Session: S2-4 HPD	Day: 16 Session: S3-24 HPD	Day: 17 Session: S4-48 HPD	Recovery Day: 1 Session: S5-72 HPD	Day: 3 Session: S6-120 HPD
2	067	ED-0:...	ED-3:...	ED-2:...	-	-
	068	ED-0:...	ED-2:...	ED-2:...	-	-
	069	ED-0:...	ED-3:...	ED-2:...	-	-
	070	ED-0:...	ED-2:...	ED-2:...	-	-
	071	ED-0:...	ED-3:...	ED-3:...	ED-2:...	ED-1:...
	072	ED-0:...	ED-3:...	ED-3:...	ED-3:...	ED-1:...
	073	ED-0:...	ED-2:...	ED-2:...	ED-2:...	ED-1:...
	074	ED-0:...	ED-2:...	ED-1:...	ED-2:...	ED-1:...
	075	ED-0:...	ED-3:...	ED-3:...	ED-3:...	ED-0:...
	3	076	ED-0:...	ED-3:...	ED-3:...	-
077		ED-0:...	ED-3:...	ED-3:...	-	-
078		ED-0:...	ED-3:...	ED-3:...	-	-
079		ED-0:...	ED-3:...	ED-2:...	-	-
080		ED-0:...	ED-3:...	ED-3:...	-	-
081		ED-0:...	ED-3:...	ED-3:...	-	-
082		ED-0:...	ED-3:...	ED-2:...	-	-
083		ED-0:...	ED-3:...	ED-3:...	-	-
084		ED-0:...	ED-3:...	ED-2:...	-	-
085		ED-0:...	ED-2:...	ED-3:...	-	-
086	ED-0:...	ED-2:...	ED-2:...	ED-2:...	ED-1:...	
087	ED-0:...	ED-3:...	ED-3:...	ED-3:...	ED-1:...	

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**Edema Grade-Left(EDL)**

Females						
Group #	Animal #	Dosing Day: 15 Session: S2-4 HPD	Day: 16 Session: S3-24 HPD	Day: 17 Session: S4-48 HPD	Recovery Day: 1 Session: S5-72 HPD	Day: 3 Session: S6-120 HPD
3	088	ED-0:...	ED-3:...	ED-3:...	ED-3:...	ED-1:...
	089	ED-0:...	ED-2:...	ED-2:...	ED-3:...	ED-0:...
	090	ED-0:...	ED-2:...	ED-2:...	ED-2:...	ED-1:...

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Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

Edema Grade-Left(EDL)

Females

Group #	Animal #	Recovery Day: 4 Session: S7-144 HPD
1	046	-
	047	-
	048	-
	049	-
	050	-
	051	-
	052	-
	053	-
	054	-
	055	-
	056	-
	057	-
	058	-
2	059	-
	060	-
	061	-
	062	-
	063	-
	064	-
	065	-
	066	-

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Repeat Dose Toxicity/Toxicity with Recovery

Edema Grade-Left(EDL)

Females

Group #	Animal #	Recovery Day: 4 Session: S7-144 HPD
2	067	-
	068	-
	069	-
	070	-
	071	ED-0:...
	072	ED-0:...
	073	ED-0:...
	074	ED-0:...
	075	ED-0:...
3	076	-
	077	-
	078	-
	079	-
	080	-
	081	-
	082	-
	083	-
	084	-
	085	-
	086	ED-0:...
	087	ED-0:...

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Repeat Dose Toxicity/Toxicity with Recovery

**Edema Grade-Left(EDL)**

**Females**

Group #	Animal #	Recovery Day: 4 Session: S7-144 HPD
3	088	ED-0:...
	089	ED-0:...
	090	ED-0:...

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Repeat Dose Toxicity/Toxicity with Recovery

**Edema Grade-Right(EDR)**

Males			
Group #	Animal #	Dosing Day: 1	
		Session: S1-Predose	Session: S2-4 HPD
1	001	ED-0:...	ED-0:...
	002	ED-0:...	ED-0:...
	003	ED-0:...	ED-0:...
	004	ED-0:...	ED-0:...
	005	ED-0:...	ED-0:...
	006	ED-0:...	ED-0:...
	007	ED-0:...	ED-0:...
	008	ED-0:...	-
	009	ED-0:...	ED-0:...
	010	ED-0:...	-
	011	ED-0:...	-
	012	ED-0:...	-
	013	ED-0:...	-
	014	ED-0:...	-
	015	ED-0:...	-
2	016	ED-0:...	-
	017	ED-0:...	-
	018	ED-0:...	-
	019	ED-0:...	-
	020	ED-0:...	-
	021	ED-0:...	-

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Repeat Dose Toxicity/Toxicity with Recovery

**Edema Grade-Right(EDR)**

Males				
Group #	Animal #	Dosing Day: 1	Session: S1-Predose	Session: S2-4 HPD
2	022	ED-0:...		-
	023	ED-0:...		-
	024	ED-0:...		-
	025	ED-0:...		-
	026	ED-0:...		-
	027	ED-0:...		-
	028	ED-0:...		-
	029	ED-0:...		-
	030	ED-0:...		-
	3	031	ED-0:...	
032		ED-0:...		-
033		ED-0:...		-
034		ED-0:...		-
035		ED-0:...		-
036		ED-0:...		-
037		ED-0:...		-
038		ED-0:...		-
039		ED-0:...		-
040		ED-0:...		-
041		ED-0:...		-
042		ED-0:...		-

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**Edema Grade-Right(EDR)**

**Males**

Group #	Animal #	Dosing Day: 1	Session: S1-Predose	Session: S2-4 HPD
3	043	ED-0:...		-
	044	ED-0:...		-
	045	ED-0:...		-

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**Test Article:** BNT162b2(V9), BNT162b3c

Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Edema Grade-Right(EDR)**

**Females**

Group #	Animal #	Dosing Day: 1	Session: S1-Predose	Session: S2-4 HPD
1	046	ED-0:...	ED-0:...	ED-0:...
	047	ED-0:...	ED-0:...	ED-0:...
	048	ED-0:...	ED-0:...	ED-0:...
	049	ED-0:...	ED-0:...	ED-0:...
	050	ED-0:...	ED-0:...	ED-0:...
	051	ED-0:...	ED-0:...	ED-0:...
	052	ED-0:...	ED-0:...	ED-0:...
	053	ED-0:...	ED-0:...	ED-0:...
	054	ED-0:...	ED-0:...	ED-0:...
	055	ED-0:...	ED-0:...	ED-0:...
	056	ED-0:...	ED-0:...	ED-0:...
	057	ED-0:...	ED-0:...	ED-0:...
	058	ED-0:...	ED-0:...	ED-0:...
	059	ED-0:...	ED-0:...	-
060	ED-0:...	ED-0:...	-	
2	061	ED-0:...	ED-0:...	-
	062	ED-0:...	ED-0:...	-
	063	ED-0:...	ED-0:...	-
	064	ED-0:...	ED-0:...	-
	065	ED-0:...	ED-0:...	-
	066	ED-0:...	ED-0:...	-

S = Scheduled Animal Room, U = UnScheduled Animal Room, N = Scheduled Necropsy, n = UnScheduled Necropsy

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Dermal Assessment Left/Right Report with Individual Values

Pfizer

Study: 20GR142  
StudyTitle: 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY  
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Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

Edema Grade-Right(EDR)

Females

Group #	Animal #	Dosing Day: 1	Session: S1-Predose	Session: S2-4 HPD
2	067	ED-0:...		-
	068	ED-0:...		-
	069	ED-0:...		-
	070	ED-0:...		-
	071	ED-0:...		-
	072	ED-0:...		-
	073	ED-0:...		-
	074	ED-0:...		-
	075	ED-0:...		-
3	076	ED-0:...		-
	077	ED-0:...		-
	078	ED-0:...		-
	079	ED-0:...		-
	080	ED-0:...		-
	081	ED-0:...		-
	082	ED-0:...		-
	083	ED-0:...		-
	084	ED-0:...		-
	085	ED-0:...		-
	086	ED-0:...		-
087	ED-0:...		-	

S = Scheduled Animal Room, U = UnScheduled Animal Room, N = Scheduled Necropsy, n = UnScheduled Necropsy

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**Dermal Assessment Left/Right Report with Individual Values**

Pfizer

**Study:** 20GR142  
**StudyTitle:** 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY  
**Test Article:** BNT162b2(V9), BNT162b3c

Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Edema Grade-Right(EDR)**

**Females**

Group #	Animal #	Dosing Day: 1	Session: S1-Predose	Session: S2-4 HPD
3	088	ED-0:...		-
	089	ED-0:...		-
	090	ED-0:...		-

S = Scheduled Animal Room, U = UnScheduled Animal Room, N = Scheduled Necropsy, n = UnScheduled Necropsy

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**Body Temperature Report with Individual Values**

Pfizer

**Study:** 20GR142

**StudyTitle:** 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY

**Test Article:** BNT162b2(V9), BNT162b3c

Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Body Temp(BT)-(°C)**

Males						
Group #	Animal #	PID Day: 6 Session: S1-Predose	Dosing Day: 1 Session: S1-Predose	Day: 2 Session: S2-4 HPD	Day: 8 Session: S3-24 HPD	Day: 8 Session: S1-Predose
1	001	36.8	36.1	35.8	37.4	37.7
	002	36.2	35.9	36.0	38.8	37.7
	003	36.9	36.5	36.1	38.2	36.7
	004	36.0	37.8	36.4	38.7	36.9
	005	37.1	36.8	35.6	38.3	37.7
	006	36.5	37.1	36.8	38.1	36.7
	007	36.0	37.2	36.4	38.5	37.4
	008	36.9	37.8	35.6	38.1	37.6
	009	36.2	37.0	36.5	38.8	37.6
	010	37.5	37.2	35.6	38.2	36.9
	011	36.7	37.1	36.2	38.3	37.5
	012	36.5	36.9	35.2	38.3	36.6
	013	35.6	36.8	36.2	38.2	37.9
	014	37.8	37.1	35.2	38.5	37.7
	015	37.7	37.1	36.0	38.2	37.3
2	016	36.4	37.0	36.1	38.3	36.7
	017	36.8	36.9	36.1	39.2	37.1
	018	37.5	37.0	36.3	39.2	37.9
	019	36.0	36.8	37.0	38.7	36.9
	020	36.1	37.1	35.9	38.5	36.7
	021	36.0	36.9	35.9	39.3	36.9

S = Scheduled Animal Room, U = UnScheduled Animal Room, N = Scheduled Necropsy, n = UnScheduled Necropsy

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**Body Temperature Report with Individual Values**

Pfizer

**Study:** 20GR142

**StudyTitle:** 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY

**Test Article:** BNT162b2(V9), BNT162b3c

Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Body Temp(BT)-(°C)**

Males						
Group #	Animal #	PID Day: 6 Session: S1-Predose	Dosing Day: 1 Session: S1-Predose	Day: 2 Session: S2-4 HPD	Day: 8 Session: S3-24 HPD	Day: 8 Session: S1-Predose
2	022	36.9	37.1	35.5	39.1	37.7
	023	36.6	37.1	35.8	38.4	36.9
	024	37.4	36.9	35.0	38.5	37.3
	025	37.5	38.5	35.1	39.1	38.4
	026	36.1	36.9	36.9	39.1	36.6
	027	37.7	36.8	36.7	38.8	36.9
	028	37.7	37.0	35.5	38.9	37.4
	029	36.3	37.1	36.6	38.4	36.8
	030	35.2	36.8	35.5	39.3	38.5
	3	031	38.2	36.8	36.3	38.8
032		36.3	37.0	36.1	39.4	36.6
033		37.0	36.9	36.4	38.9	37.0
034		37.9	36.9	35.6	38.6	36.4
035		38.2	37.1	35.3	38.4	37.9
036		36.8	37.2	36.2	38.7	37.1
037		37.0	36.7	36.0	39.0	37.0
038		36.2	37.0	35.7	39.2	37.6
039		36.8	36.8	36.0	39.1	36.8
040		36.0	37.4	36.2	39.0	37.6
041		35.9	36.9	36.4	38.6	37.6
042		36.0	36.7	36.4	38.8	37.4

S = Scheduled Animal Room, U = UnScheduled Animal Room, N = Scheduled Necropsy, n = UnScheduled Necropsy

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**Body Temperature Report with Individual Values**

Pfizer

**Study:** 20GR142

**StudyTitle:** 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY

**Test Article:** BNT162b2(V9), BNT162b3c

Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Body Temp(BT)-(°C)**

Males						
Group #	Animal #	PID Day: 6 Session: S1-Predose	Dosing Day: 1 Session: S1-Predose	Day: 2 Session: S2-4 HPD	Day: 2 Session: S3-24 HPD	Day: 8 Session: S1-Predose
3	043	36.4	37.2	36.6	39.5	37.3
	044	36.3	37.0	35.9	39.8	38.0
	045	37.0	37.1	36.1	39.5	37.4

S = Scheduled Animal Room, U = UnScheduled Animal Room, N = Scheduled Necropsy, n = UnScheduled Necropsy

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**Test Article:** BNT162b2(V9), BNT162b3c

Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Body Temp(BT)-(°C)**

Males							
Group #	Animal #	Dosing Day: 8 Session: S2-4 HPD	Day: 9 Session: S3-24 HPD	Day: 15 Session: S1-Predose	Session: S2-4 HPD	Day: 16 Session: S3-24 HPD	
1	001	34.6	37.0	37.6	36.8	37.3	
	002	34.5	36.9	37.4	36.5	36.7	
	003	34.7	37.1	37.8	37.2	37.2	
	004	34.9	36.9	38.8	36.8	37.1	
	005	36.3	37.0	38.0	37.7	36.9	
	006	36.4	37.1	37.3	37.0	37.0	
	007	35.5	36.9	37.4	36.8	37.1	
	008	35.5	36.6	37.9	37.3	37.1	
	009	36.2	36.3	37.9	36.9	37.3	
	010	37.2	36.5	37.4	37.4	36.7	
	011	36.4	36.8	38.6	37.0	37.0	
	012	36.6	37.4	38.2	37.8	37.4	
	013	36.8	37.6	37.6	37.5	37.0	
	014	36.9	37.6	38.2	37.7	36.3	
	015	37.2	37.6	37.9	38.0	36.7	
2	016	36.0	39.0	37.4	37.5	38.6	
	017	36.1	38.4	37.8	38.1	38.5	
	018	36.0	37.5	38.5	38.8	38.4	
	019	36.7	37.9	37.8	38.5	37.6	
	020	37.2	38.1	37.2	37.9	37.5	
	021	36.4	38.3	37.6	38.1	38.9	

S = Scheduled Animal Room, U = UnScheduled Animal Room, N = Scheduled Necropsy, n = UnScheduled Necropsy

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Pfizer

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**Test Article:** BNT162b2(V9), BNT162b3c

Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Body Temp(BT)-(°C)**

Males							
Group #	Animal #	Dosing Day: 8 Session: S2-4 HPD	Day: 9 Session: S3-24 HPD	Day: 15 Session: S1-Predose	Session: S2-4 HPD	Day: 16 Session: S3-24 HPD	
2	022	35.1	37.8	37.9	38.4	38.5	
	023	35.9	37.1	37.2	37.9	37.5	
	024	36.1	39.0	38.2	38.0	38.8	
	025	36.4	39.2	38.7	38.8	38.4	
	026	37.3	37.4	36.6	37.7	37.7	
	027	37.4	37.7	38.3	37.6	37.4	
	028	37.2	37.6	37.0	37.9	38.3	
	029	37.4	37.9	37.5	37.5	38.5	
	030	37.8	37.9	38.4	37.9	38.3	
	3	031	36.7	38.6	37.3	38.5	38.5
032		35.8	38.4	37.1	37.8	38.0	
033		36.7	38.4	37.1	38.2	38.0	
034		36.2	38.6	36.8	38.0	38.2	
035		37.0	38.5	38.1	38.8	39.1	
036		36.3	38.6	36.8	37.6	38.5	
037		37.4	38.8	37.1	37.6	38.5	
038		36.2	38.4	37.8	37.8	38.6	
039		36.2	38.6	37.0	37.8	38.0	
040		38.1	38.4	38.8	38.5	39.0	
041		36.1	37.9	37.7	38.2	37.8	
042		36.9	37.0	38.7	38.1	38.4	

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Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

Body Temp(BT)-(°C)

Males

Group #	Animal #	Dosing Day: 8 Session: S2-4 HPD	Day: 9 Session: S3-24 HPD	Day: 15 Session: S1-Predose	Session: S2-4 HPD	Day: 16 Session: S3-24 HPD
3	043	36.9	38.4	37.4	38.5	38.7
	044	36.6	38.3	37.6	37.5	38.7
	045	36.2	38.0	37.7	37.2	37.9

S = Scheduled Animal Room, U = UnScheduled Animal Room, N = Scheduled Necropsy, n = UnScheduled Necropsy

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**Body Temperature Report with Individual Values**

Pfizer

**Study:** 20GR142

**StudyTitle:** 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY

**Test Article:** BNT162b2(V9), BNT162b3c

Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Body Temp(BT)-(°C)**

Females						
Group #	Animal #	PID Day: 6 Session: S1-Predose	Dosing Day: 1 Session: S1-Predose	Day: 2 Session: S2-4 HPD	Day: 2 Session: S3-24 HPD	Day: 8 Session: S1-Predose
1	046	38.3	37.4	37.0	37.7	38.2
	047	37.1	37.8	38.6	37.3	37.7
	048	38.7	38.0	38.2	37.7	37.9
	049	38.0	36.8	37.8	38.0	37.7
	050	38.0	38.0	38.2	37.5	38.0
	051	37.5	38.6	38.7	38.2	38.3
	052	38.5	37.6	38.2	37.8	37.8
	053	37.8	37.5	38.8	38.0	37.9
	054	37.7	38.4	37.6	37.6	38.8
	055	36.8	37.2	38.5	37.9	37.9
	056	38.5	37.0	37.7	37.0	38.0
	057	37.8	37.8	38.0	37.0	37.6
	058	37.8	35.9	36.9	37.3	38.0
	059	36.5	37.9	37.7	36.7	37.5
060	37.2	37.7	38.0	37.5	37.8	
2	061	36.2	36.9	37.8	37.6	37.9
	062	37.4	38.3	38.5	38.1	37.6
	063	37.4	37.4	38.2	37.5	38.0
	064	36.9	36.4	39.4	36.6	37.9
	065	38.5	38.3	38.1	38.9	37.7
	066	36.6	38.2	37.9	37.1	38.1

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**Body Temperature Report with Individual Values**

Pfizer

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**Test Article:** BNT162b2(V9), BNT162b3c

Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Body Temp(BT)-(°C)**

**Females**

Group #	Animal #	PID Day: 6 Session: S1-Predose	Dosing Day: 1 Session: S1-Predose	Session: S2-4 HPD	Day: 2 Session: S3-24 HPD	Day: 8 Session: S1-Predose
2	067	36.8	38.4	38.7	37.8	38.3
	068	38.1	37.7	38.7	37.3	38.0
	069	37.8	36.7	39.0	39.0	37.7
	070	36.6	37.9	38.7	37.1	37.8
	071	37.3	37.1	37.1	37.8	37.6
	072	36.3	36.6	37.8	37.9	37.8
	073	38.1	37.4	39.3	38.2	38.2
	074	37.3	36.4	38.1	37.5	37.9
	075	36.6	38.3	38.6	38.0	37.5
	3	076	38.5	37.9	38.7	38.2
077		37.7	36.9	38.8	38.0	38.0
078		37.6	38.3	38.6	38.1	37.9
079		37.6	38.0	37.6	38.1	37.9
080		38.1	38.8	38.5	37.7	38.0
081		38.0	36.6	38.5	37.8	37.8
082		38.8	37.6	39.0	38.7	37.7
083		37.4	37.9	38.1	37.5	38.1
084		36.5	38.2	39.1	38.4	37.7
085		38.2	37.6	38.9	37.9	37.6
	086	38.6	37.6	37.9	37.9	38.0
	087	36.8	38.0	39.0	38.9	39.0

S = Scheduled Animal Room, U = UnScheduled Animal Room, N = Scheduled Necropsy, n = UnScheduled Necropsy

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Body Temperature Report with Individual Values

Pfizer

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Test Article: BNT162b2(V9), BNT162b3c

Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

Body Temp(BT)-(°C)

Females

Group #	Animal #	PID Day: 6 Session: S1-Predose	Dosing Day: 1 Session: S1-Predose	Day: 2 Session: S2-4 HPD	Day: 8 Session: S3-24 HPD	Day: 8 Session: S1-Predose
3	088	38.6	38.8	38.7	37.8	37.9
	089	38.0	38.6	38.5	37.9	37.9
	090	36.1	37.9	38.3	37.9	38.1

S = Scheduled Animal Room, U = UnScheduled Animal Room, N = Scheduled Necropsy, n = UnScheduled Necropsy

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**Body Temperature Report with Individual Values**

Pfizer

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Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Body Temp(BT)-(°C)**

**Females**

Group #	Animal #	Dosing Day: 8 Session: S2-4 HPD	Day: 9 Session: S3-24 HPD	Day: 15 Session: S1-Predose	Session: S2-4 HPD	Day: 16 Session: S3-24 HPD
1	046	37.4	37.1	36.8	36.8	37.0
	047	38.0	37.0	37.3	37.0	37.7
	048	37.3	36.6	37.5	37.7	37.0
	049	37.0	37.8	37.0	37.8	37.7
	050	37.3	37.3	37.3	37.1	36.8
	051	37.9	38.3	37.1	39.0	37.3
	052	37.5	37.5	37.8	37.8	36.9
	053	38.0	37.7	37.1	38.3	37.1
	054	37.7	37.9	36.9	39.0	37.3
	055	37.7	37.4	37.2	36.5	36.7
	056	37.9	37.1	37.0	38.3	37.4
	057	38.7	37.1	37.3	39.1	37.5
	058	37.7	36.8	37.7	38.4	37.0
	059	36.9	38.0	37.2	38.5	37.5
	060	37.1	37.7	36.9	37.9	37.1
2	061	37.2	38.2	38.0	37.5	37.7
	062	38.0	38.6	38.1	38.9	37.7
	063	37.8	37.4	37.5	38.5	38.1
	064	37.8	37.9	38.1	39.2	37.6
	065	37.6	37.9	38.3	37.8	37.7
	066	37.5	38.5	37.1	37.6	37.0

S = Scheduled Animal Room, U = UnScheduled Animal Room, N = Scheduled Necropsy, n = UnScheduled Necropsy

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**Body Temperature Report with Individual Values**

Pfizer

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**Test Article:** BNT162b2(V9), BNT162b3c

Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

**Body Temp(BT)-(°C)**

**Females**

Group #	Animal #	Dosing Day: 8 Session: S2-4 HPD	Day: 9 Session: S3-24 HPD	Day: 15 Session: S1-Predose	Session: S2-4 HPD	Day: 16 Session: S3-24 HPD
2	067	37.6	38.9	38.3	38.8	37.9
	068	37.5	38.6	37.7	37.2	37.8
	069	39.2	38.1	37.5	38.2	37.8
	070	38.5	38.9	38.3	38.0	38.5
	071	37.8	38.5	37.8	37.3	37.3
	072	37.9	38.9	37.9	37.7	37.6
	073	37.9	37.8	38.1	38.1	37.4
	074	37.4	38.7	38.5	37.8	37.6
	075	37.9	38.5	38.7	38.3	37.7
	3	076	38.1	38.9	38.2	38.3
077		39.0	38.0	38.1	37.5	38.0
078		38.3	38.9	37.7	38.5	37.9
079		38.7	38.5	38.4	37.2	38.1
080		37.7	38.9	37.8	37.0	38.3
081		38.3	38.0	37.8	37.9	37.9
082		38.1	39.3	38.3	38.6	38.2
083		38.2	38.9	38.0	37.0	37.9
084		37.8	38.5	37.9	38.4	37.8
085		38.1	38.8	38.0	38.6	37.3
086	38.4	38.9	37.7	38.6	37.8	
087	39.4	38.9	38.0	38.7	37.9	

S = Scheduled Animal Room, U = UnScheduled Animal Room, N = Scheduled Necropsy, n = UnScheduled Necropsy

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Body Temperature Report with Individual Values

Pfizer

Study: 20GR142

StudyTitle: 17-DAY INTRAMUSCULAR TOXICITY STUDY IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY

Test Article: BNT162b2(V9), BNT162b3c

Rat/Wistar Han

Repeat Dose Toxicity/Toxicity with Recovery

Body Temp(BT)-(°C)

Females

Group #	Animal #	Dosing Day: 8 Session: S2-4 HPD	Day: 9 Session: S3-24 HPD	Day: 15 Session: S1-Predose	Session: S2-4 HPD	Day: 16 Session: S3-24 HPD
3	088	38.0	38.0	38.2	38.8	37.7
	089	38.2	38.1	37.9	38.3	38.6
	090	37.9	38.3	38.1	38.0	37.2

S = Scheduled Animal Room, U = UnScheduled Animal Room, N = Scheduled Necropsy, n = UnScheduled Necropsy

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**C O N F I D E N T I A L**



**OPHTHALMOLOGY REPORT:**

**17-DAY INTRAMUSCULAR TOXICITY STUDY OF BNT162B2 (V9) AND  
BNT162B3C IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY**

**Testing Facility Study Number: 20GR142**

**Alternative Test Article Identifier(s):**

PF-07302048: Generic number for COVID-19 vaccine program

BNT162b2 (V9): BNT162b2 (Version 9); RBP020.2; PF-07305885

BNT162b3c: BNT162b3; RBP020.8; PF-07315256

**TESTING FACILITY:**

Pfizer

Drug Safety Research & Development

Eastern Point Road

Groton, CT 06340 USA

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Page 537

Report for Study 20GR142

Ophthalmology Report for Study 20GR142

**SIGNATURES**

I confirm that this report accurately reflects my interpretation of the ophthalmology data.

(b) (6)

Clinical Veterinarian  
Ophthalmology

For signatures see the [Document Approval Record](#).

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FDA-CBER-2021-5683-0709979

**GLP COMPLIANCE STATEMENT**

This portion of the study was conducted in compliance with Good Laboratory Practice for Nonclinical Laboratory Studies regulations as set forth in the Code of Federal Regulations (21 CFR Part 58).

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## 1. INTRODUCTION AND OBJECTIVE

BNT162b2 (Version 9 [V9]) and BNT162b3c are candidate COVID-19 vaccines, which are based on an RNA platform and express the SARS-CoV-2 spike protein or its derivatives. The objective of this study was to determine the toxicity and development of a specific immune response to the antigens in each of the vaccine candidates following administration of intramuscular (IM) doses once weekly for a total of 3 doses to Wistar Han (CrI:WI[Han]) rats. The reversibility of effects was evaluated following a 3-week recovery phase.

Group designations and doses are indicated in the table below.

Group Number	Test Article or Vehicle Dose ( $\mu\text{g RNA}$ )/Dose Day	Dose Volume ( $\mu\text{L/injection site}$ ) <sup>a</sup>	Animal Numbers	
			Males	Females
1	0 <sup>b</sup>	60	1-15	46-60
2	30 <sup>c</sup>	60	16-30	61-75
3	30 <sup>d</sup>	60	31-45	76-90

- Each animal received a single intramuscular injection on each dose day.
- Sterile saline.
- BNT162b2 (V9).
- BNT162b3c.

Doses were administered by a single intramuscular injection (60  $\mu\text{L}$ ) on each dosing day (Days 1, 8, and 15) into the left hindlimb quadriceps muscle.

The first 10 animals/sex/group, by ascending animal order, were designated for necropsy at the end of the dosing phase. The remaining animals were retained for the recovery phase.

## 2. MATERIALS AND METHODS

Ophthalmic examinations were performed on animals (Groups 1-3) prior to the initiation of dosing (PID) on PID Day 7 for males and PID Day 8 for females, except for Animal 88 examined on PID Day 9, and on Day 15 for males and Day 16 for females. Tropicamide 1% was administered topically to each eye to facilitate the examination. Indirect ophthalmoscopy was used for examinations. Handheld slit lamp biomicroscopy was also used at the discretion of the examiner.

## 3. DATA ACQUISITION

Pristima Preclinical Data Management Suite (Version 7.4.3) was used to record ophthalmology data.

#### 4. DATA MANAGEMENT AND ARCHIVES

All raw data and the original report pertaining to this phase of the study are retained at Pfizer, DSRD, Groton, CT (USA). A copy of this report is appended to the study report.

Materials including raw data and documents electronically archived are retained in the Pfizer OpenLab archive system or locked and retained in the source computerized system, as defined per SOP.

#### 5. RESULTS

An incidence summary of ophthalmic findings is presented in [Table 2](#). Individual animal ophthalmic findings are included in [Appendix 3](#).

Ophthalmic examinations of rats performed prior to initiation of dosing were within normal limits, except for incidental findings noted in the following animals: mild unilateral vitreous hemorrhage in Animal 8, minimal unilateral tortuous retinal vessels in Animal 10, minimal unilateral vitreous hyaloid remnant in Animal 11, and mild unilateral keratic precipitates in Animal 14 and Animal 41.

No test article-related ophthalmic findings were observed in rats at the end of the dosing phase.

The mild unilateral keratic precipitates observed on Day 16 in Animal 49 is a recognized spontaneous finding in Wistar Han rats and was not considered test article related (Williams, 2013). The Day 15 ophthalmic findings in Animals 8, 10, 11, 14, and 41 were consistent with those observed on PID Day 7.

Ophthalmic examinations were not conducted during the recovery phase due to the lack of test article-related changes at the end of the dosing phase.

#### 6. INTEGRATED SUMMARY AND DISCUSSION OF RESULTS

Clinical ophthalmic parameters of rats examined in this study were not affected following 3 intramuscular doses of BNT162b2 (V9) or BNT162b3c administered 1 week apart.

#### 7. REFERENCES

Williams, DL. Laboratory animal ophthalmology. In: Gelatt KN, Gilger BC, Kern TJ, eds. *Veterinary Ophthalmology*. 5th ed. Vol 2. Ames, IA: Wiley-Blackwell; 2013:1698.

## Document Approval Record

<b>Document Name:</b>	DSRD Ophthalmology Report
<b>Document Title:</b>	20GR142: DSRD Ophthalmology Report

<b>Signed By:</b>	<b>Date(GMT)</b>	<b>Signing Capacity</b>
(b) (6)	04-Nov-2020 18:45:48	Author Approval



## PHASE REPORT

### 17-DAY INTRAMUSCULAR TOXICITY STUDY OF BNT162B2 (V9) AND BNT162B3C IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY 20GR142 (WORK ORDER 4)

**SERVICE PERFORMED BY:**

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Version summary:

VERSION	ISSUE DATE	CHANGE
0.1	24 Sept 2020	Draft report
0.2	05 Oct 2020	Sponsor review and data table added in Appendix
0.3	07 Oct 2020	Typo edits, margins and data table adaptation
1.0	29 Oct 2020	Final report



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## 1. PURPOSE

This Phase Report describes the activities completed by VisMederi applying the Microneutralization (MN) assay for serological detection of SARS-CoV-2 specific neutralizing antibodies in animal sera relative to the "Work order 4" agreed between VisMederi Srl and Pfizer.

## 2. STUDY MANAGEMENT

The BNT162b2 (V9) and BNT162b3c candidate COVID-19 vaccines, based on an RNA platform and target the SARS-CoV-2 spike protein, were evaluated through the 20GR142 study for toxicity and immune response development.

BNT162b2 (V9) and BNT162b3c were administered by intramuscular (IM) doses once weekly for a total of 3 doses to male and female Wistar Han (CrI:WI[Han]) rats. Animals received the vehicle or test article at doses of 30 µg RNA/Dose Day followed by a 3-week recovery phase. Group designations and doses are indicated in the table below.

Experimental Design				
Group Number	Test Article or Vehicle Dose/Dose Day (µg/Dose Day)	Dose Volume (µL/injection site) <sup>a</sup>	Animal Numbers	
			Males	Females
1	0 <sup>b</sup>	60	1-15	46-60
2	30 <sup>c</sup>	60	16-30	61-75
3	30 <sup>d</sup>	60	31-45	76-90

a. Each animal received a single injection on each dose day.

b. Sterile saline

c. BNT162b2(V9)

d. BNT162b3c



Doses were administered by a single intramuscular injection on each dosing day (60 µL) administered into the left hindlimb quadriceps muscle on Days 1, 8, and 15.

The first 10 animals/sex/group, by ascending animal order, were designated for necropsy at the end of the dosing phase. The remaining animals were retained for the recovery phase.

Samples for antibody response to the vaccine components were collected prior to dose initiation (PID) on PID Day 8 (Day -5), during the dosing phase on Day 17, and during the recovery phase (RP) on RP Day 21 (Day 38).

VisMederi performed immunogenicity tests on rats samples, testing for detection of neutralizing antibody titers to wild type live Sars-CoV-2 virus.

The assay was performed according to VisMederi internal working instruction "Microneutralization CPE-based assay for SARS-COV-2" (WI-MNSARS-CoV-2), in accordance with the Good Clinical Laboratory Practice 2009/2013 (GCLP).

VisMederi received, on August 24<sup>th</sup> 2020, 210 rat's serum samples, from Pfizer DSRD – Eastern Point Road, Groton, CT 06340, USA, for study 20GR142 with BNT162b2 (V9) and BNT162b3c. In particular, the shipment contained prior to initiation of dosing (PID) Day 8 (Day -5) and dosing phase Day 17 time-points samples of 90 animals and recovery phase (RP) Day 21 (Day 38) time-points from 30 rats.

Upon arrival, all samples passed a visual check of the physical characteristics and correspondence with material shipping inventory, according to the SOP-HBM of VisMederi, and they were stored in a freezer at -20°C (VM-F-009).





Each serum sample of study 20GR142 has been tested in duplicate for serological detection of SARS-CoV-2 specific neutralizing antibodies.

The SARS-CoV-2 2019 live wild type virus 2019-nCoV strain 2019-nCov/Italy-INMI1 was obtained by VisMederi Srl from the European Virus Archive Global (EVAg).

The strain information are available at the following link:

<https://www.european-virus-archive.com/virus/human-2019-ncov-strain-2019-ncovitaly-inmi1>

The virus growth was carried out by VisMederi Research Srl, according to VisMederi Research procedure "Virus Growth in cell culture" (SOP-VGC) in epithelial cell line, VERO E6 cells (from kidney of a normal monkey Cercopithecus aethiops) provided by the American Type Culture Collection (ATCC - CRL 1586).

The internal virus batch applied for MN analyses was VMR\_SARSCOV2VEROE6\_280420\_C1.

The Microneutralization assay for SARS-CoV-2 on rat sera samples were performed on 8<sup>th</sup> – 11<sup>th</sup> September 2020 in the VisMederi BSL3 laboratories in accordance to the SOP-HSAL of VisMederi.

#### QA Statement and Regulatory Statement

The work was conducted in accordance with the procedures in force and following the GCLP guidelines and under ISO 9001:2015.

All the laboratory staff involved was trained in recording the raw data of the study in a timely and accurate manner, and aware of the responsibility of the quality of the data produced.

Independent laboratory audits are conducted periodically to ensure the quality of work and data integrity.

Equipment used are periodically maintained, calibrated and qualified as appropriate.



All the documentation related to the study is archived in a secure place in compliance with the ISO 27001 (both in electronic and paper format).

No significant laboratory events or deviations have occurred during the study that could have impacted the generated results.

### 3. TEST PROCEDURE

The MN-CPE (Microneutralization based on Cytopathic effect) method is a specific technique used for the identification of virus-specific neutralizing antibodies against live viruses which are able to prevent the virus infection. This assay is a fundamental test in virology, immunology, vaccine assessment and epidemiology studies.

The assay was performed following the VisMederi procedure "WI-MNSARS-CoV-2", and the main phases are described as follows:

- Virus Titration
- Back titration
- Microneutralization

#### Virus titration

The virus, ten-fold serially diluted in suitable MN medium, was transferred to a plate containing confluent VERO E6 cell monolayers.

After incubation of 3 days the plate was observed under an inverted microscope and the wells were scored as positive/negative for Cytopathic effect (CPE).

The titer was calculated using the Reed-Muench method, obtaining  $10^{7.59}$  TCID<sub>50</sub>/mL as result. The stock virus was then applied in the MN assay at a proper dilution in order to contain 2000TCID<sub>50</sub>/mL in the working virus solution.



MN assay

Serum samples were heat inactivated for 30 minutes at 56°C, then two-fold serially diluted starting from 1:10 up to 1:5120 and were mixed with an equal volume of viral solution.

Duplicate runs for each sample were performed in two different plates.

The serum-virus mixture was incubated for 1 hour at 37°C, in a humidified atmosphere with 5% CO<sub>2</sub>. After the incubation time, 100 µl of the mixture for each dilution was added in duplicate to a cell plate containing a healthy and sub confluent-to confluent VERO E6 cell lawn and incubated for 3 days in the CO<sub>2</sub> incubator at 37°C and 5% CO<sub>2</sub>. The readout was achieved through inverted optical microscopy in order to discriminate wells as positive/negative for Cytopathic effect (CPE).

The Microneutralization titer (MNT) of each titrated sample corresponded to the reciprocal of the highest sample dilution able to protect from CPE at least 50% of the cell monolayer. If no neutralization was observed (MNT <10) an arbitrary value of 5 was reported.

Back titration and reference samples

To verify the virus workload in the solution applied in the assay, the virus working solution was titrated in each MN session. The back titrations performed in both sessions for this study confirmed virus titers within the defined acceptance range of (b) (4)

In addition, each test session included runs of specific reference sera: a positive and a negative serum.

The positive control (PCS) used in every test run, is a human plasma sample collected from a COVID-19 convalescent patient. The sample code TLS-8 was previously tested



by MN and by ELISA for SARS-CoV-2 antibody titer, providing high positive response confirmed by multiple repetitions.

The negative control sample (NCS) used was a human serum depleted of IgA, IgM and IgG, provided by Sigma Aldrich, cod. S5393 batch 108M4791V.

#### 4. ACCEPTANCE CRITERIA

In agreement with WI-MNSARS-CoV-2, the following internal quality controls have been satisfied in each session of analysis for the Study 20GR142 samples, therefore results were considered reliable and acceptable.

Virus titer evaluation:

- The back titration of the working viral solution lies within the defined target range of (b) (4)

MN results acceptability of each MN plate:

- The cell control (CC) showed a healthy cell monolayer and no evidence of CPE
- The virus control (VC) wells showed cytopathic effect.

MN results acceptability of each sample:

- The duplicate neutralization titers of each serum sample were within a range of  $\pm$ (b) (4)

MN results acceptability of each analysis session:

- the positive control sample (PCS) showed a positive titer, in agreement with previous data,
- the negative control sample (NCS) with absent antibody titer showed a negative response.

Since all the acceptability criteria were met, no retest was necessary.



**5. DATA RELEASE**

Test results were recorded through dedicated forms, attachments of the VisMederi WI "WI-MNSARS-CoV-2", and transferred in an excel data entry sheet: PFZ\_20GR142-WO4\_MN-SarsCov2\_V2\_20200924\_GL.xlsx

This report shows the full set of data in Appendix 1 and 2 tables.

Data entry description

The data tables present three sections:

- Sample identification
- Raw Data
- Derived values as geometric mean of duplicate tests

Each subject is identified in a row of table by Sample ID, gender and administered dose of vaccine. Any Study day is showed in following columns as duplicate results "T1A" and "T1B", each one is used for a replicate titer of the same sample. Last columns shows the geometric mean calculated from the two replicate titers for each study visit.

The following table shows geometric mean titers for grouped subjects by sex and for vaccine administered.

Table 1: Overview of GMTs for each dose group, by sampling day and sex

Study Day	Sex	Saline	30µg BNT162b2(V9)	30µg BNT162b3c
PID Day 8 (Day -5)	Male	5	5	5
	Female	5	5	5
Day 17	Male	5	1114	993
	Female	5	2501	1810
RP Day 21 (Day 38)	Male	5	5120	3880
	Female	5	5120	3880

PID = prior to dose initiation; RP = Recovery Phase



Administration of 3 once weekly doses of BNT162b2 (V9) or BNT162b3c elicited SARS-CoV-2 neutralizing antibody responses in males and females at the end of the dosing (Day 17) and recovery phases (Day 21) of the study. SARS-CoV-2 neutralizing antibody responses were not observed in animals prior to vaccine administration or in saline-administered control animals.

## 6. REFERENCES

- Manenti A, Maggetti M, Casa E, et al (2020). Evaluation of SARS-CoV-2 neutralizing antibodies using of a CPE-based Colorimetric live virus microneutralization assay in human serum samples. Journal of Medical Virology. doi: 10.1002/jmv.25986.
- Reed, L.J.; Muench, H. (1938). "A simple method of estimating fifty percent endpoints". The American Journal of Hygiene. 27: 493–497.
- Algaissi A, Hashem AM. (2020). Evaluation of MERS-CoV Neutralizing Antibodies in Sera Using Live Virus Microneutralization Assay. Methods in molecular biology (Clifton, N.J.) vol. 2099: 107-116.
- Good Clinical Laboratory Practice GCLP – 2009/2013
- OECD Principles on Good Laboratory Practice (ENV/MC/CHEM(98)17)
- UNI EN ISO 9001:2015
- UNI EN ISO 27001:2017
- "WI-MNSARS-CoV-2" Working Instruction "Microneutralization CPE-based assay for Sars-Cov-2"
- "HSAL" Handling and safety for activities in BSL2 and BSL3 Laboratories – VisMederi procedure
- "HBM" Handling Of Biological Material – Vismederi procedure
- "HCC" Handling Cell Cultures – VisMederi Research procedure
- "MRR" Management and Release of Results – VisMederi procedure
- "VGC" Virus Growth in Cell culture – VisMederi Research procedure



**7. APPENDICES**

Appendix 1: data table for Male

Sample ID	Gender	Dose	Dose Units	T1A-DAY8	T1A-DAY17	T1A-DAY21	T1B-DAY8	T1B-DAY17	T1B-DAY21	Geometric Mean Day8	Geometric Mean Day17	Geometric Mean Day21
001M	Male	0	µg/kg	5	5		5	5		5.0	5.0	
002M	Male	0	µg/kg	5	5		5	5		5.0	5.0	
003M	Male	0	µg/kg	5	5		5	5		5.0	5.0	
004M	Male	0	µg/kg	5	5		5	5		5.0	5.0	
005M	Male	0	µg/kg	5	5		5	5		5.0	5.0	
006M	Male	0	µg/kg	5	5		5	5		5.0	5.0	
007M	Male	0	µg/kg	5	5		5	5		5.0	5.0	
008M	Male	0	µg/kg	5	5		5	5		5.0	5.0	
009M	Male	0	µg/kg	5	5		5	5		5.0	5.0	
010M	Male	0	µg/kg	5	5		5	5		5.0	5.0	
011M	Male	0	µg/kg	5	5	5	5	5	5	5.0	5.0	5.0
012M	Male	0	µg/kg	5	5	5	5	5	5	5.0	5.0	5.0
013M	Male	0	µg/kg	5	5	5	5	5	5	5.0	5.0	5.0
014M	Male	0	µg/kg	5	5	5	5	5	5	5.0	5.0	5.0
015M	Male	0	µg/kg	5	5	5	5	5	5	5.0	5.0	5.0
016M	Male	30	µg/kg	5	2560		5	2560		5.0	2560.0	
017M	Male	30	µg/kg	5	640		5	640		5.0	640.0	
018M	Male	30	µg/kg	5	2560		5	1280		5.0	1810.2	
019M	Male	30	µg/kg	5	2560		5	2560		5.0	2560.0	
020M	Male	30	µg/kg	5	320		5	640		5.0	452.5	
021M	Male	30	µg/kg	5	2560		5	2560		5.0	2560.0	
022M	Male	30	µg/kg	5	640		5	1280		5.0	905.1	
023M	Male	30	µg/kg	5	1280		5	1280		5.0	1280.0	
024M	Male	30	µg/kg	5	1280		5	1280		5.0	1280.0	
025M	Male	30	µg/kg	5	1280		5	1280		5.0	1280.0	
026M	Male	30	µg/kg	5	320	5120	5	320	5120	5.0	320.0	5120.0
027M	Male	30	µg/kg	5	640	5120	5	320	5120	5.0	452.5	5120.0
028M	Male	30	µg/kg	5	1280	5120	5	1280	5120	5.0	1280.0	5120.0
029M	Male	30	µg/kg	5	320	5120	5	640	5120	5.0	452.5	5120.0
030M	Male	30	µg/kg	5	2560	5120	5	5120	5120	5.0	3620.4	5120.0
031M	Male	30	µg/kg	5	2560		5	2560		5.0	2560.0	
032M	Male	30	µg/kg	5	320		5	320		5.0	320.0	
033M	Male	30	µg/kg	5	2560		5	2560		5.0	2560.0	
034M	Male	30	µg/kg	5	1280		5	2560		5.0	1810.2	
035M	Male	30	µg/kg	5	160		5	160		5.0	160.0	
036M	Male	30	µg/kg	5	640		5	640		5.0	640.0	
037M	Male	30	µg/kg	5	160		5	320		5.0	226.3	
038M	Male	30	µg/kg	5	1280		5	1280		5.0	1280.0	
039M	Male	30	µg/kg	5	320		5	320		5.0	320.0	
040M	Male	30	µg/kg	5	2560		5	2560		5.0	2560.0	
041M	Male	30	µg/kg	5	2560	5120	5	5120	5120	5.0	3620.4	5120.0
042M	Male	30	µg/kg	5	1280	5120	5	1280	5120	5.0	1280.0	5120.0
043M	Male	30	µg/kg	5	2560	5120	5	2560	5120	5.0	2560.0	5120.0
044M	Male	30	µg/kg	5	640	2560	5	640	2560	5.0	640.0	2560.0
045M	Male	30	µg/kg	5	1280	2560	5	1280	2560	5.0	1280.0	2560.0



Appendix 2: data table for Female

Sample ID	Gender	Dose	Dose Units	T1A-DAY8	T1A-DAY17	T1A-DAY21	T1B-DAY8	T1B-DAY17	T1B-DAY21	Geometric Mean Day8	Geometric Mean Day17	Geometric Mean Day21
046F	Female	0	µg/kg	5	5		5	5		5.0	5.0	
047F	Female	0	µg/kg	5	5		5	5		5.0	5.0	
048F	Female	0	µg/kg	5	5		5	5		5.0	5.0	
049F	Female	0	µg/kg	5	5		5	5		5.0	5.0	
050F	Female	0	µg/kg	5	5		5	5		5.0	5.0	
051F	Female	0	µg/kg	5	5		5	5		5.0	5.0	
052F	Female	0	µg/kg	5	5		5	5		5.0	5.0	
053F	Female	0	µg/kg	5	5		5	5		5.0	5.0	
054F	Female	0	µg/kg	5	5		5	5		5.0	5.0	
055F	Female	0	µg/kg	5	5		5	5		5.0	5.0	
056F	Female	0	µg/kg	5	5	5	5	5	5	5.0	5.0	5.0
057F	Female	0	µg/kg	5	5	5	5	5	5	5.0	5.0	5.0
058F	Female	0	µg/kg	5	5	5	5	5	5	5.0	5.0	5.0
059F	Female	0	µg/kg	5	5	5	5	5	5	5.0	5.0	5.0
060F	Female	0	µg/kg	5	5	5	5	5	5	5.0	5.0	5.0
061F	Female	30	µg/kg	5	5120		5	5120		5.0	5120.0	
062F	Female	30	µg/kg	5	1280		5	1280		5.0	1280.0	
063F	Female	30	µg/kg	5	640		5	640		5.0	640.0	
064F	Female	30	µg/kg	5	2560		5	2560		5.0	2560.0	
065F	Female	30	µg/kg	5	5120		5	5120		5.0	5120.0	
066F	Female	30	µg/kg	5	2560		5	2560		5.0	2560.0	
067F	Female	30	µg/kg	5	5120		5	5120		5.0	5120.0	
068F	Female	30	µg/kg	5	2560		5	2560		5.0	2560.0	
069F	Female	30	µg/kg	5	5120		5	5120		5.0	5120.0	
070F	Female	30	µg/kg	5	1280		5	1280		5.0	1280.0	
071F	Female	30	µg/kg	5	2560	5120	5	2560	5120	5.0	2560.0	5120.0
072F	Female	30	µg/kg	5	2560	5120	5	5120	5120	5.0	3620.4	5120.0
073F	Female	30	µg/kg	5	5120	5120	5	5120	5120	5.0	5120.0	5120.0
074F	Female	30	µg/kg	5	1280	5120	5	1280	5120	5.0	1280.0	5120.0
075F	Female	30	µg/kg	5	1280	5120	5	1280	5120	5.0	1280.0	5120.0
076F	Female	30	µg/kg	5	1280		5	1280		5.0	1280.0	
077F	Female	30	µg/kg	5	1280		5	1280		5.0	1280.0	
078F	Female	30	µg/kg	5	1280		5	1280		5.0	1280.0	
079F	Female	30	µg/kg	5	5120		5	5120		5.0	5120.0	
080F	Female	30	µg/kg	5	640		5	640		5.0	640.0	
081F	Female	30	µg/kg	5	5120		5	5120		5.0	5120.0	
082F	Female	30	µg/kg	5	1280		5	1280		5.0	1280.0	
083F	Female	30	µg/kg	5	1280		5	1280		5.0	1280.0	
084F	Female	30	µg/kg	5	5120		5	5120		5.0	5120.0	
085F	Female	30	µg/kg	5	2560		5	2560		5.0	2560.0	
086F	Female	30	µg/kg	5	320	1280	5	320	1280	5.0	320.0	1280.0
087F	Female	30	µg/kg	5	5120	5120	5	5120	5120	5.0	5120.0	5120.0
088F	Female	30	µg/kg	5	1280	5120	5	2560	5120	5.0	1810.2	5120.0
089F	Female	30	µg/kg	5	640	5120	5	640	5120	5.0	640.0	5120.0
090F	Female	30	µg/kg	5	5120	5120	5	5120	5120	5.0	5120.0	5120.0



**C O N F I D E N T I A L**



**CLINICAL PATHOLOGY REPORT: 17-DAY INTRAMUSCULAR TOXICITY  
STUDY OF BNT162B2 (V9) AND BNT162B3C IN WISTAR HAN RATS WITH A  
3-WEEK RECOVERY**

**Testing Facility Study Number: 20GR142**

**Alternative Test Article Identifier(s):**

PF-07302048: Generic number for COVID-19 vaccine program

BNT162b2 (V9): BNT162b2 (Version 9); RBP020.2; PF-07305885

BNT162b3c: BNT162b3; RBP020.8; PF-07315256

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## SIGNATURES

I was responsible for the principal investigator activities conducted in support of this study and confirm that this report accurately reflects my interpretation of the clinical pathology data and that my portions of the study were conducted in compliance with GLP regulations with the exceptions noted; (see [GLP Compliance Statement](#)).

(b) (6)

Clinical Pathologist  
Principal Investigator

## Quality Assurance Statement Signature

The signature for the following individual applies only to the Pearl River, NY [Quality Assurance Statement](#) contained in this study report.

(b) (6)

Pfizer Inc, Pearl River, NY.

For signatures see the [Document Approval Record](#) located on the last page of this report.

### **GLP COMPLIANCE STATEMENT**

This portion of the study was conducted in compliance with Good Laboratory Practice for Nonclinical Laboratory Studies regulations as set forth in the Code of Federal Regulations (21 CFR Part 58) with the exception of the analyses of alpha-1 acid glycoprotein (A1AGP) and alpha-2-macroglobulin (A2M) which were conducted under non-GLP conditions, but according to fit-for-purpose methods. This exception did not have an impact on the integrity or data interpretation of the study.

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## 1. INTRODUCTION

BNT162b2 (Version 9 [V9]) and BNT162b3c are candidate COVID-19 vaccines, which consist of an LNP-encapsulated RNA encoding the SARS-CoV-2 spike protein or its derivatives, were administered by intramuscular (IM) doses once weekly for a total of 3 doses to male and female Wistar Han (CrI:WI[Han]) rats. Animals received the vehicle or test article at doses of 0 or 30 µg RNA/Dose Day followed by a 3-week recovery phase. Group designations and doses are indicated in the table below.

Experimental Design				
Group Number	Test Article or Vehicle Dose (µg RNA/Dose Day)	Dose Volume (µL/injection site) <sup>a</sup>	Animal Numbers	
			Males	Females
1	0 <sup>b</sup>	60	1-15	46-60
2	30 <sup>c</sup>	60	16-30	61-75
3	30 <sup>d</sup>	60	31-45	76-90

- a. Each animal received a single injection on each dose day.
- b. Sterile saline.
- c. BNT162b2 (V9).
- d. BNT162b3c.

Doses were administered by a single intramuscular injection on each dosing day (60 µL) administered into the left hindlimb quadriceps muscle on Days 1, 8, and 15.

The first 10 animals/sex/group, by ascending animal order, were designated for necropsy at the end of the dosing phase. The remaining animals were retained for the recovery phase.

## 2. MATERIALS AND METHODS

Clinical laboratory measurements were completed at the Testing Facility (Pfizer DSRD, Groton, CT) and clinical laboratory measurements interpretation was completed at the Test Site (Pfizer DSRD, Pearl River, NY).

### 2.1. Clinical Laboratory Measurements

Clinical laboratory parameters were evaluated in samples collected from all animals as listed in each section below.

Bone marrow smears were prepared for all animals. Bone marrow smear slides were stained with May-Grunwald Giemsa and were not examined.

Clinical Pathology Report for Study 20GR142

Schedule for Collection of Samples for Clinical Laboratory Measurements			
Parameter	Day of Study		
	Dosing Phase		Recovery Phase
	Day 4	Day 17 <sup>c</sup>	Day 22
Hematology	X <sup>a,c</sup>	X <sup>c</sup>	X <sup>c</sup>
Coagulation	NA	X <sup>c</sup>	X <sup>c</sup>
Clinical Chemistry (Core Chemistry)	X <sup>b,c</sup>	X <sup>c</sup>	X <sup>c</sup>
Clinical Chemistry (Other Biomarkers – Acute Phase Proteins)/Serum <sup>d</sup>	X <sup>b,c</sup>	X <sup>c</sup>	X <sup>c</sup>
Urinalysis	NA	X	X

NA = Not applicable; X = Scheduled Collection.

- a. First 7 animals/sex/group.
- b. Last 8 animals/sex/group.
- c. Blood samples were collected from animals in a fasted state, with the exception of same day redraws.
- d. Assay performed using shared clinical chemistry sample.
- e. Evaluated on animals scheduled for necropsy.

Blood Collection			
Parameter	Collection Condition	Approximate Blood Volume	Anticoagulant
Clinical Chemistry	Nonterminal <sup>a, b</sup>	0.7 mL	None-Serum Separator Tube
Clinical Chemistry	Terminal	2.5 mL	None-Serum Separator Tube
Hematology	Nonterminal <sup>a,b</sup>	0.5 mL	K <sub>2</sub> EDTA
Hematology	Terminal	2.0 mL	K <sub>2</sub> EDTA
Coagulation	Terminal	2.0 mL	3.2% sodium citrate
Biomarkers (Clinical Chemistry)	Nonterminal <sup>a,b</sup>	using shared sample	None-Serum Separator Tube
Biomarkers (Clinical Chemistry)	Terminal	Using shared sample	None-Serum Separator Tube

- a. Blood samples were collected under anesthesia.
- b. This volume was based on collecting blood for one parameter per group of animals and the other parameter on another group of animals.

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### 2.1.1. Hematology and Coagulation

Blood samples were analyzed for:

Red Blood Cells (RBC)	Red Cell Distribution Width (RDW)
Hemoglobin (HGB)	Reticulocytes (RETIC)
Hematocrit (HCT)	Platelets (PLT)
Mean Cell Volume (MCV)	Mean Platelet Volume (MPV)
Mean Cell Hemoglobin (MCH)	White Blood Cells (WBC)
Mean Cell Hemoglobin Concentration (MCHC)	White Cell Differential

Blood smears were prepared for the first 7 animals on Day 4 and all animals on Dosing Phase Day 17 and Recovery Phase Day 21 (Groups 1-3).

Blood cell morphology was evaluated microscopically on 5 animals of each sex from all groups at both scheduled necropsies (ie, at dosing and recovery phases).

Blood samples were analyzed for:

Activated Partial Thromboplastin Time (APTT)	Prothrombin Time (PT_Rat)
Fibrinogen (FIB)	

### 2.1.2. Clinical Chemistry

#### Core Chemistry

Serum samples were analyzed for:

Alanine Aminotransferase (ALT)	Globulin (GLOB)
Aspartate Aminotransferase (AST)	Albumin/Globulin Ratio (AG)
Alkaline Phosphatase (ALP)	Blood Urea Nitrogen (BUN)
Gamma Glutamyltransferase (GGT)	Creatinine (CREA)
Bilirubin, Total (TBIL)	Phosphorus (PHOS)
Cholesterol (CHOL)	Calcium (CA)
Triglyceride (TRIG)	Sodium (NA)
Glucose (GLUC)	Potassium (K)
Total Protein (TP)	Chloride (CL)
Albumin (ALB)	

Serum indices for hemolysis, icterus, and lipemia were performed.

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**Other Biomarkers**

**Serum Biomarker Sample Collection**

Serum samples were analyzed for:

alpha-1-acid glycoprotein (A1AGP)	alpha-2-macroglobulin (A2M)
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**2.1.3. Urinalysis**

Urine samples were collected overnight at scheduled necropsy. Urine samples were analyzed for:

Color	Protein (PRO)
Clarity	Blood
pH	Bilirubin (BIL)
Glucose Urine (GLU)	Specific Gravity (SG)
Ketones (KET)	Volume

Microscopic examination of sediment for formed elements was performed on 5 animals of each sex from all dose groups at both scheduled necropsies (ie, dosing and recovery phases).

**2.2. Statistical Analysis**

Statistical analyses of hematology, coagulation, clinical chemistry, and urinalysis data was conducted in Pristima. All analyses were performed separately for each sex.

Descriptive statistics were generated for each parameter and group at each scheduled sampling time or each time interval. Statistical tests were conducted at the 5% and 1% significance levels.

Analyses of hematology, coagulation, clinical chemistry, and urinalysis parameters were done on measurements collected for each animal at the scheduled sampling times or time intervals.

A nonparametric (rank-transform) one way analysis of variance (ANOVA) on all groups was conducted, with two-sided pairwise comparisons of Groups 2 and 3 to Group 1 using Dunnett's test. Average ranks were assigned to ties.

**3. DATA ACQUISITION**

Cerner HNA Millennium Laboratory Information System (Version 2018.01) was used to record clinical laboratory measurement data.

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#### 4. DATA MANAGEMENT AND ARCHIVES

Raw data, documentation, protocol and amendments, final report, and any specimens generated at the Test Facility as the result of the study are retained at Pfizer, Groton, CT.

Materials including raw data and documents electronically archived are retained in the Pfizer OpenLab archive system or locked and retained in the source computerized system, as defined per SOP.

Materials are retained in accordance with the Enterprise Records Retention Schedule.

#### 5. RESULTS

##### 5.1. Clinical Laboratory Measurements

###### 5.1.1. Hematology and Coagulation

Group mean hematology and coagulation data are presented in [Table 6](#). Individual animal hematology and coagulation data are included in [Appendix 7](#). Results indicated below are test article group mean values compared with control group mean values.

###### Dosing Phase

Test article-related hematology and coagulation findings were similar in rats administered either BNT162b2 (V9) or BNT162b3c and included higher mean white blood cell (WBC) counts and fibrinogen concentrations, lower (Day 4) and higher (Day 17) reticulocyte counts, and lower red blood cell mass (red blood cell [RBC] count, hemoglobin [HGB] and hematocrit [HCT], as represented by HCT in [Text Table 1](#)) compared with controls.

Higher WBC primarily involved neutrophils, monocytes and large unstained cells (LUC) but also affected eosinophils and basophils. They were present on Days 4 and 17, with higher counts on Day 17 than Day 4. On Day 17, there were also test article-related higher fibrinogen concentrations in both sexes. Hypersegmented neutrophils were present on peripheral blood smears of test article-treated animals.

In addition, there were test article-related transiently lower reticulocyte counts on Day 4, and higher reticulocytes on Day 17 (females only) with attendant expected changes in RBC indices (higher mean cell hemoglobin concentration [MCHC; males] on Day 4; lower mean cell hemoglobin [MCH] and higher red cell distribution width [RDW] on Day 17; both sexes). These were associated with lower RBC mass on Days 4 & 17 (comparable on both days or slightly lower on Day 17).

**Text Table 1. Test Article-Related Hematology and Coagulation Parameter Effects  
(Mean Control Values and Ratio Relative to Control Mean)**

Parameter	Dose (µg RNA/Dose Day)					
	Test Article	Males			Females	
	Vehicle	BNT162b2(V9)	BNT162b3c	Vehicle	BNT162b2(V9)	BNT162b3c
	0	30	30	0	30	30
HCT (%)						
4D	48.04	0.90x	0.91x	44.91	0.93x	0.93x
17D	42.61	0.90x	0.92x	41.67	0.91x	0.89x
MCH (pg)						
4D	18.51	-	-	18.37	-	-
17D	18.27	0.96x	-	18.62	0.97x	0.96x
MCHC (g/dL)						
4D	31.24	1.04x	1.03x	32.34	-	-
17D	32.46	-	-	33.18	-	-
RDW (%)						
4D	12.27	-	-	11.11	-	-
17D	11.63	1.21x	1.18x	11.33	1.18x	1.18x
RETIC (10e3/uL)						
4D	392.1	0.27x	0.27x	301.7	0.43x	0.44x
17D	178.8	-	-	168.9	1.31x	1.20x
WBC (10e3/uL)						
4D	7.60	1.41x	1.28x	6.01	1.30x	1.43x
17D	3.84	2.30x	2.24x	2.16	2.64x	2.95x
NEUT (10e3/uL)						
4D	1.083	2.28x	2.00x	0.920	2.51x	3.13x
17D	0.674	6.60x	6.46x	0.409	6.04x	7.04x
MONO (10e3/uL)						
4D	0.109	1.83x	1.96x	0.093	1.89x	2.52x
17D	0.071	3.30x	3.58x	0.056	2.75x	3.14x
EO (10e3/uL)						
4D	0.081	-	-	0.057	-	2.16x
17D	0.056	2.52x	2.18x	0.029	3.17x	3.34x
BASO (10e3/uL)						
4D	0.016	1.88x	2.31x	0.009	1.89x	2.67x
17D	0.003	5.67x	6.33x	0.001	8.00x	10.00x
LUC (10e3/uL)						
4D	0.046	4.07x	3.98x	0.030	4.20x	4.43x
17D	0.026	8.04x	12.42x	0.010	13.20x	19.00x

**Text Table 1. Test Article-Related Hematology and Coagulation Parameter Effects (Mean Control Values and Ratio Relative to Control Mean) - Continued**

Parameter	Dose (µg RNA/Dose Day)					
	Males			Females		
Test Article	Vehicle	BNT162b2(V9)	BNT162b3c	Vehicle	BNT162b2(V9)	BNT162b3c
	0	30	30	0	30	30
FIB (mg/dL)						
17D	253.1	2.36x	2.39x	217.2	2.49x	2.59x

Control mean values and the ratio of the test article-related findings relative to control means are listed.

- = Not test article related; BASO = Basophil, absolute; D = Day; EO = Eosinophil, absolute; FIB = Fibrinogen; HCT = Hematocrit; LUC = Large unstained cells, absolute; MCH = Mean cell hemoglobin; MCHC = Mean cell hemoglobin concentration; MONO = Monocyte, absolute; NEUT = Neutrophil, absolute; RDW = Red cell distribution width; RETIC = Reticulocyte, absolute; WBC = White blood cells.

**Recovery Phase**

All test article related changes were fully reversed after a 3-week recovery period, with the exception of higher RDW (Text Table 2).

**Text Table 2. Test Article-Related Hematology and Coagulation Parameter Effects (Mean Control Values and Ratio Relative to Control Mean)**

Parameter	Dose (µg RNA/Dose Day)					
	Males			Females		
Test Article	Vehicle	BNT162b2(V9)	BNT162b3c	Vehicle	BNT162b2(V9)	BNT162b3c
	0	30	30	0	30	30
RDW (%)						
R22	11.93	1.13x	1.12x	10.80	1.21x	1.23x

Control mean values and the ratio of the test article-related findings relative to control means are listed.

R = Recovery Day; RDW = Red cell distribution width.

Other statistically significant or apparent differences between test article and control group hematology and coagulation parameters were not test article related due to one or more of the following: small magnitude of the difference, inconsistent direction of the difference, and general overlap in magnitude of individual values with controls.

**5.1.2. Clinical Chemistry**

Group mean clinical chemistry data are presented in [Table 7](#). Individual animal clinical chemistry data are included in [Appendix 8](#). Results indicated below are test article group mean values compared with control group mean values.

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## Dosing Phase

Test article-related clinical chemistry findings were similar in rats administered 30 µg RNA/dosing day of either BNT162b2 (V9) or BNT162b3c and included higher mean alpha-1 acid glycoprotein (A1AGP) and alpha-2-macroglobulin (A2M) and lower albumin:globulin (AG) ratios (primarily due to lower albumin with slight contribution from higher globulins) on Days 4 and 17 in both sexes compared with controls (Text Table 3).

**Text Table 3. Test Article-Related Clinical Chemistry Parameter Effects (Mean Control Values and Ratio Relative to Control Mean)**

Parameter	Dose (µg RNA/Dose Day)					
	Males			Females		
Test Article	Vehicle	BNT162b2(V9)	BNT162b3c	Vehicle	BNT162b2(V9)	BNT162b3c
	0	30	30	0	30	30
ALB (g/dL)						
4D	3.98	0.93x	0.92x	4.16	0.86x	0.90x
17D	3.50	-	-	3.60	0.85x	0.86x
GLOB (g/dL)						
4D	2.13	-	-	2.10	-	1.05x
17D	1.89	1.10x	1.07x	1.84	1.04x	-
AG						
4D	1.88	0.90x	0.90x	1.98	0.86x	0.85x
17D	1.85	0.89x	0.89x	1.96	0.82x	0.85x
A1AGP						
4D	174.358	9.42x	13.49x	239.774	7.95x	6.99x
17D	47.672	38.51x	42.40x	95.959	15.55x	17.21x
A2M						
4D	113.4	20.44x	34.99x	212.1	3.32x	4.18x
17D	14.0	70.76x	128.16x	33.1	15.74x	17.89x

Control mean values and the ratio of the test article-related findings relative to control means are listed.

- = Not test article related; A1AGP = alpha-1 acid glycoprotein; A2M = alpha-2-macroglobulin; AG = Albumin/globulin ratio; ALB = Albumin; D = Day; GLOB = Globulin; TP = Protein, total.

## Recovery Phase

All test article related changes were fully reversed after a 22-day recovery period, with the exception of higher globulins in males administered BNT162b2 (V9) and females administered BNT162b2 (V9) and BNT162b3c, and lower AG ratio in females administered BNT162b2 (V9) (see [Text Table 4](#)).

**Text Table 4. Test Article-Related Clinical Chemistry Parameter Effects (Mean Control Values and Ratio Relative to Control Mean)**

Parameter	Dose (µg RNA/Dose Day)					
	Males			Females		
	Vehicle	BNT162b2(V9)	BNT162b3c	Vehicle	BNT162b2(V9)	BNT162b3c
	0	30	30	0	30	30
GLOB (g/dL)						
R22	2.10	1.08x	-	2.26	1.06x	1.07x
AG						
R22	1.76	-	-	1.90	0.91x	-

Control mean values and the ratio of the test article-related findings relative to control means are listed.  
 - = Not test article related; AG = Albumin/globulin ratio; GLOB = Globulin; R = Recovery Day.

Other statistically significant or apparent differences between test article and control group clinical chemistry parameters were not test article related due small magnitude of the difference and general overlap in magnitude of individual values with controls.

**5.1.3. Urinalysis**

Group mean urinalysis data are presented in [Table 8](#). Individual animal urinalysis data are included in [Appendix 9](#).

**Dosing and Recovery Phases**

There were no test article-related findings on urinalysis.

All statistically significant or apparent differences in urinalysis parameters between test article and control group were not test article related due small magnitude of the difference and general overlap in magnitude of individual values with controls.

**6. INTEGRATED SUMMARY AND DISCUSSION OF RESULTS**

Male and female Wistar-Han rats were administered either BNT162b2 (V9) or BNT162b3c at 30 µg RNA/Dose Day by intramuscular (IM) injection once weekly for 3 weeks, resulting in nonadverse findings in hematology and clinical chemistry parameters compared with control animals.

All clinical pathology findings (type and magnitude) were generally comparable between rats administered BNT162b2 (V9) or BNT162b3c, and consistent with expected immune responses to vaccines or secondary to inflammation. The main findings were present in males and females on Days 4 and/or 17 and included higher acute phase proteins (alpha-1

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acid glycoprotein [A1AGP; 7.0x – 42x controls], alpha-2-macroglobulin [A2M; 3.3x – 128x] and fibrinogen [2.4x-2.6x]), lower albumin:globulin (AG; 0.90x - 0.82x; primarily due to lower albumin [0.93x – 0.85x] with slight contribution from globulins [1.04x – 1.10x]), and higher WBC (1.28x - 2.95x; primarily involving neutrophils, monocytes and LUC, which typically represent large mononuclear cells). Hypersegmented neutrophils present on peripheral blood smears were considered to be secondary to the robust increases in neutrophil counts and likely related to mobilization of bone marrow storage neutrophils and prolonged neutrophil lifespan in circulation (Ulich et al, 1988). Collectively, these findings were consistent with expected immune responses to vaccines. Microscopic correlates included minimally increased cellularity of hematopoietic cells (primarily myeloid) in the bone marrow and the spleen, minimal to moderate mixed cell inflammation at the injection site and increased cellularity in germinal centers of lymphoid organs.

In addition, there were transiently lower reticulocyte counts on Day 4 (0.44x - 0.27x), and higher reticulocytes on Day 17 (1.20x - 1.31x; females only), with minor lower red cell mass on Days 4 and 17 (HCT; 0.93x - 0.89x). Lower reticulocytes were interpreted to be a transient effect of innate immune responses (Abreu et al, 2018; Brooks et al, 2017; Kim et al, 2014; Wrighting & Andrews, 2006).

All test article related changes were fully reversed after a 3-week recovery period, with the exception of higher RDW in males and females administered BNT162b2 (V9) (1.13x and 1.21x, respectively) and BNT162b3c (1.12x and 1.23x, respectively), higher globulins in males administered BNT162b2 (V9) (1.08x) and females administered BNT162b2 (V9) (1.06x) and BNT162b3c (1.07x), and lower AG ratio in females administered BNT162b2 (V9) (0.91x).

In conclusion, clinical pathology findings in rats administered BNT162b2 (V9) or BNT162b3c were consistent with expected immune responses to vaccines or secondary to inflammation and included higher acute phase proteins (A1AGP, A2M and fibrinogen), higher WBC (primarily neutrophils, monocytes and LUC), lower red blood cell mass and transiently lower reticulocytes.

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**Medical Quality Assurance**

***Quality Assurance Statement***

**Title:** 17-DAY INTRAMUSCULAR TOXICITY STUDY OF BNT162B2 (V9) AND BNT162B3C IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY

**Study:** 20GR142

In accordance with Pfizer policies and Medical Quality Assurance procedures for Good Laboratory Practice (GLP), the conduct of this portion of this study has been inspected and/or audited as follows.

<b>Phase Inspected</b>	<b>Audit/Inspection Date GMT</b>	<b>Reporting Date GMT</b>
Test Site Protocol Review	24-Jun-2020 to 25-Jun-2020	25-Jun-2020
Protocol Amendment #1	02-Jul-2020 to 02-Jul-2020	02-Jul-2020
Protocol Amendment #4	04-Sep-2020 to 04-Sep-2020	04-Sep-2020
Report: Clinical Pathology	20-Oct-2020 to 30-Oct-2020	03-Nov-2020
Report: Pathology	20-Oct-2020 to 30-Oct-2020	03-Nov-2020

In addition Routine Facility and Process audits are conducted in accordance with MQA SOPs and Site Monitoring Plans.

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## Document Approval Record

<b>Document Name:</b>	Clinical Pathology Report
<b>Document Title:</b>	20GR142 Clinical Pathology Report

<b>Signed By:</b>	<b>Date(GMT)</b>	<b>Signing Capacity</b>
(b) (6)	09-Nov-2020 21:24:21	Quality Assurance Approval
	10-Nov-2020 20:16:43	Author Approval

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**C O N F I D E N T I A L**



**ANATOMIC PATHOLOGY REPORT: 17-DAY INTRAMUSCULAR TOXICITY  
STUDY OF BNT162B2 (V9) AND BNT162B3C IN WISTAR HAN RATS WITH A  
3-WEEK RECOVERY**

**Testing Facility Study Number: 20GR142**

**Alternative Test Article Identifier(s):**

PF-07302048: Generic number for COVID-19 vaccine program

BNT162b2 (V9): BNT162b2 (Version 9); RBP020.2; PF-07305885

BNT162b3c: BNT162b3; RBP020.8; PF-07315256

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## SIGNATURES

I was responsible for the principal investigator activities conducted in support of this study and confirm that this report accurately reflects my interpretation of the organ weight, macroscopic, and microscopic data and that my portions of the study were conducted in compliance with GLP regulations (see [GLP Compliance Statement](#)).

(b) (6)



### Quality Assurance Statement Signature

The signature for the following individual applies only to the Pearl River, NY [Quality Assurance Statement](#) contained in this study report.

(b) (6)



Pfizer Inc, Pearl River, NY.

For signatures see the [Document Approval Record](#) located on the last page of this report.

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### **GLP COMPLIANCE STATEMENT**

This portion of the study was conducted in compliance with Good Laboratory Practice for Nonclinical Laboratory Studies regulations as set forth in the Code of Federal Regulations (21 CFR Part 58).

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**OTHER STUDY PERSONNEL**

The following study personnel were involved in the conduct of this study:

Peer Review Pathologist:

(b) (6)

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## 1. INTRODUCTION

BNT162b2 (Version 9 [V9]) and BNT162b3c are candidate COVID-19 vaccines, which consist of an LNP-encapsulated RNA encoding the SARS-CoV-2 spike protein or its derivatives, were administered intramuscularly (IM) once weekly for a total of 3 doses to male and female Wistar Han (CrI:WI[Han]) rats. Animals received the vehicle or test article at doses of 30 µg RNA/dosing day followed by a 3-week recovery phase. Group designations and doses are indicated in the table below.

Experimental Design				
Group Number	Test Article or Vehicle Dose (µg RNA/Dose Day)	Dose Volume (µL/injection site) <sup>a</sup>	Animal Numbers	
			Males	Females
1	0 <sup>b</sup>	60	1-15	46-60
2	30 <sup>c</sup>	60	16-30	61-75
3	30 <sup>d</sup>	60	31-45	76-90

a. Each animal received a single injection on each dose day.

b. Sterile saline.

c. BNT162b2(V9).

d. BNT162b3c.

Doses were administered by a single intramuscular injection (60 µL) on each dosing day (Days 1, 8, and 15) into the left hindlimb quadriceps muscle.

The first 10 animals/sex/group, by ascending animal order, were designated for necropsy at the end of the dosing phase (Day 17). The remaining animals were retained for the recovery phase.

## 2. MATERIALS AND METHODS

Necropsy, organ weights, macroscopic examination, tissue collection, tissue processing, and slide preparation were completed at the Testing Facility (Pfizer DSRD, Groton, CT) and microscopic examination and peer review were completed at the Test Site (Pfizer DSRD, Pearl River, NY).

### 2.1. Postmortem Observations

#### 2.1.1. Euthanasia

Animals were euthanized by gas anesthesia (isoflurane) followed by exsanguination.



**2.1.2. Necropsy**

**2.1.2.1. Scheduled Necropsy**

Animals from the dosing phase were fasted overnight and euthanized on Dosing Phase Day 17, 2 days after the last dose (first 10 animals/sex/group). Animals from the recovery phase were fasted overnight and euthanized on Recovery Phase Day 22 (remaining 5 animals/sex/group). Complete necropsies, tissue collection, organ weights, and macroscopic tissue evaluation were performed on all animals. Necropsy included macroscopic examination of the external surface of the body, the thoracic and abdominal cavities and their contents, and the collection of all protocol-defined tissues.

**2.1.2.2. Tissue Collection, Organ Weights and Tissues Processed for Slide Preparation – Dosing Phase**

Tissues Collected	Organs Weighed (All Dose Groups)	Tissues Processed for Slide Preparation (X)		
		Dose Group		
		Group 1	Group 2	Group 3
Artery, Aorta		X	X	X
Bone Marrow, Sternum		X	X	X
Bone, Sternum		X	X	X
Brain	X	X	X	X
Cervix		X	X	X
Epididymis	X	X	X	X
Esophagus		X	X	X
Eye		X	X	X
Gland, Adrenal	X	X	X	X
Gland, Harderian		X	X	X
Gland, Lacrimal (Extraorbital)		X	X	X
Gland, Mammary		X	X	X
Gland, Parathyroid		X	X	X
Gland, Pituitary		X	X	X
Gland, Prostate	X	X	X	X
Gland, Salivary		X	X	X
Gland, Seminal Vesicle		X	X	X
Gland, Thyroid		X	X	X
Gut-Associated Lymphoid Tissue		X	X	X
Heart	X	X	X	X
Joint		X	X	X
Kidney	X	X	X	X
Large Intestine, Cecum		X	X	X
Large Intestine, Colon		X	X	X
Larynx				

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Tissues Collected	Organs Weighed (All Dose Groups)	Tissues Processed for Slide Preparation (X)		
		Dose Group		
		Group 1	Group 2	Group 3
Liver	X	X	X	X
Lung		X	X	X
Lymph Node, Draining		X	X	X
Lymph Node, Inguinal		X	X	X
Lymph Node, Mesenteric		X	X	X
Macroscopic Findings		X	X	X
Muscle, Skeletal		X	X	X
Nerve, Optic		X	X	X
Nerve, Peripheral		X	X	X
Ovary	X	X	X	X
Oviduct		X	X	X
Pancreas		X	X	X
Site, Injection		X	X	X
Skin		X	X	X
Small Intestine, Duodenum		X	X	X
Small Intestine, Ileum		X	X	X
Small Intestine, Jejunum		X	X	X
Spinal Cord		X	X	X
Spleen	X	X	X	X
Stomach		X	X	X
Testis	X	X	X	X
Thymus	X	X	X	X
Tongue		X	X	X
Trachea		X	X	X
Ureter		X	X	X
Urinary Bladder		X	X	X
Uterus		X	X	X
Vagina		X	X	X

**2.1.2.3. Tissue Collection, Organ Weights and Tissues Processed for Slide Preparation – Recovery Phase**

Tissues Collected	Organs Weighed (All Dose Groups)	Tissues Processed for Slide Preparation (X)		
		Dose Group		
		Group 1	Group 2	Group 3
Artery, Aorta				
Bone Marrow, Sternum		X	X	X
Bone, Sternum				
Brain	X			

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Tissues Collected	Organs Weighed (All Dose Groups)	Tissues Processed for Slide Preparation (X)		
		Dose Group		
		Group 1	Group 2	Group 3
Cervix				
Epididymis	X			
Esophagus				
Eye				
Gland, Adrenal	X			
Gland, Harderian				
Gland, Lacrimal (Extraorbital)				
Gland, Mammary				
Gland, Parathyroid				
Gland, Pituitary				
Gland, Prostate	X			
Gland, Salivary				
Gland, Seminal Vesicle				
Gland, Thyroid				
Gut-Associated Lymphoid Tissue				
Heart	X			
Joint		X	X	X
Kidney	X			
Large Intestine, Cecum				
Large Intestine, Colon				
Larynx				
Liver	X	X	X	X
Lung				
Lymph Node, Draining		X	X	X
Lymph Node, Inguinal		X	X	X
Lymph Node, Mesenteric				
Macroscopic Findings		X	X	X
Muscle, Skeletal		X	X	X
Nerve, Optic				
Nerve, Peripheral				
Ovary	X			
Oviduct				
Pancreas				
Site, Injection		X	X	X
Skin				
Small Intestine, Duodenum				
Small Intestine, Ileum				
Small Intestine, Jejunum				
Spinal Cord				
Spleen	X	X	X	X

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Tissues Collected	Organs Weighed (All Dose Groups)	Tissues Processed for Slide Preparation (X)		
		Dose Group		
		Group 1	Group 2	Group 3
Stomach				
Testis	X			
Thymus	X			
Tongue				
Trachea				
Ureter				
Urinary Bladder				
Uterus				
Vagina				

**2.1.3. Organ Weights**

Designated organs from animals in Groups 1-3 were weighed at scheduled necropsy. Organ-to-body weight and organ-to-brain weight ratios were calculated.

**2.1.4. Tissue Processing**

Representative samples of collected tissues were fixed in 10% neutral buffered formalin except for eye with optic nerve attached (Davidson’s), and testis and epididymis (modified Davidson’s). All tissues processed for slide preparation were stained with hematoxylin and eosin.

**2.1.5. Microscopic Examination**

For the dosing phase, all tissues (excluding larynx) collected from all dosing phase animals were examined microscopically. For the recovery phase, tissues (bone marrow sternum, joint, liver, draining lymph node, inguinal lymph node, injection site, and spleen) from recovery animals in the control group and test article dose groups were examined microscopically. Microscopic findings were graded on a scale of 1 to 5 as minimal, mild, moderate, marked, or severe; findings not graded were listed as present.

**2.1.6. Peer Review**

Following completion of the tissue evaluation by the Anatomic Pathologists, a peer review evaluation was performed by another Pfizer Pathologist.

**2.2. Statistical Analysis**

Statistical analyses of organ weight data were conducted in Pristima with the methods outlined below. All analyses were performed separately for each sex.

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Descriptive statistics were generated for each parameter and group at each scheduled sampling time or each time interval. Statistical tests were conducted at the 5% and 1% significance levels.

Analyses of organ weight parameters were done on measurements collected for each animal at the scheduled sampling times or time intervals. In addition, organ weight to body weight and organ weight to brain weight ratios were analyzed.

A nonparametric (rank-transform) one way analysis of variance (ANOVA) on all groups was conducted, with two-sided pairwise comparisons of Groups 2 and 3 to Group 1 using Dunnett's test. Average ranks were assigned to ties.

### **3. DATA ACQUISITION**

Pristima Preclinical Data Management Suite (Version 7.4.3) was used to record pathology data.

### **4. DATA MANAGEMENT AND ARCHIVES**

Raw data, documentation, protocol and amendments, final report, and any specimens generated at the Test Facility as the result of the study are retained at Pfizer, Groton, CT.

Materials including raw data and documents electronically archived are retained in the Pfizer OpenLab archive system or locked and retained in the source computerized system, as defined per SOP.

Materials are retained in accordance with the Enterprise Records Retention Schedule.

### **5. RESULTS**

#### **5.1. Unscheduled Euthanasia and Deaths**

All animals survived until scheduled necropsy.

#### **5.2. Postmortem Observations**

##### **5.2.1. Organ Weights**

Group mean organ weight data are presented in [Table 9](#). Individual animal organ weight data are included in [Appendix 10](#). Results indicated below are test article group mean values compared with control group mean values.

**Dosing Phase**

Test article-related organ weight changes included higher absolute and relative (to body and brain weight) spleen weights in males and females administered BNT162b2 (V9) or BNT162b3c.

Higher group mean absolute and relative spleen weights were noted at 30 µg RNA/dosing day in BNT162b2 (V9) administered males (1.29x – 1.42x) and females (1.55x – 1.62x) and BNT162b3c administered males (1.34x – 1.52x) and females (1.41x – 1.47x) relative to control group means.

**Text Table 1. Ratios of Test Article-Related Mean Absolute and Relative (To Body Weight and Brain Weight) Organ Weights Compared with Mean Controls**

Dose (µg RNA/dosing day)		Males			Females		
		0	30 <sup>d</sup>	30 <sup>e</sup>	0	30 <sup>d</sup>	30 <sup>e</sup>
		Mean	Ratio		Mean	Ratio	
Spleen	Absolute (g)	0.5951	<b>1.29x</b>	<b>1.34x</b>	0.4382	<b>1.55x</b>	<b>1.41x</b>
	OW:BW <sup>a</sup>	0.2008	<b>1.42x</b>	<b>1.52x</b>	0.2202	<b>1.59x</b>	<b>1.47x</b>
	OW:BN <sup>b</sup>	0.3120	<b>1.29x</b>	<b>1.34x</b>	0.2353	<b>1.62x</b>	<b>1.43x</b>
Brain <sup>c</sup>	Absolute (g)	1.9061	1.01x	1.00x	1.8610	0.96x	0.99x
	OW:BW <sup>a</sup>	0.6449	1.10x	1.13x	0.9383	0.98x	1.02x
Terminal BW <sup>c</sup>	Absolute (g)	296.06	0.92x	0.89x	198.73	0.98x	0.97x

BN = Brain weight; BW = Body weight; g = grams OW = Organ weight.

a. Organ weight relative to terminal body weight.

b. Organ weight relative to brain weight.

c. Included for evaluating organ to brain weight and body weight ratios.

d. BNT162b2(V9)

e. BNT162b3c

**Bold** = test article related.

**Recovery Phase**

No test article-related organ weight changes were noted for either test article.

The spleen weights (absolute and relative to brain weight) were statistically increased in males administered BNT162b2 (V9). A similar change was not observed in females administered BNT162b2 (V9). A microscopic correlate was not identified in males (ie, no evidence of increased cellularity of hematopoietic cells), although one male had minimally

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increased cellularity of germinal centers in the spleen. A similar increase in spleen weight was not identified in either males or females administered BNT162b3c. Therefore, the higher spleen weights in recovery males administered BNT162b2 (V9) was considered incidental and unrelated to vaccine administration, consistent with full recovery of the higher spleen weights observed at the end of dosing phase.

Other statistically significant or apparent alterations in mean absolute or relative organ weights were not test article-related because they did not occur in a dose-related pattern, were of low magnitude, lacked a macroscopic or microscopic correlate, occurred only in relative data, or occurred only in absolute data, but lost significance when evaluated relative to brain or body weight.

### 5.2.2. Macroscopic Findings

An incidence summary of macroscopic observations is presented in [Table 10](#). Individual animal macroscopic observations are included in [Appendix 11](#).

#### Dosing Phase

Test article-related macroscopic findings included large draining lymph nodes (abnormal size, enlarged) and dark/pale and/or firm injection sites (abnormal color, dark/pale and/or abnormal consistency, firm) in animals administered BNT162b2 (V9) or BNT162b3c, and large spleen and inguinal lymph nodes (abnormal size, enlarged) in animals administered BNT162b3c.

The macroscopic observation of large draining lymph nodes was present in BNT162b2 (V9) administered males and females and BNT162b3c administered females; large inguinal lymph nodes were observed in BNT162b3c administered females; pale/dark injection sites were observed in BNT162b2 (V9) administered males and females and BNT162b3c administered males; and firm injection sites were observed in BNT162b2 (V9) or BNT162b3c administered males and females. The macroscopic observation of enlarged spleen was limited to a single BNT162b3c administered female.

**Text Table 2. Group Incidences of Test Article-Related Macroscopic Findings**

Finding	Males			Females		
	Dose ( $\mu$ g RNA/dosing day)			Dose ( $\mu$ g RNA/dosing day)		
	0	30 <sup>b</sup>	30 <sup>c</sup>	0	30 <sup>b</sup>	30 <sup>c</sup>
Number Examined	10	10	10	10	10	10
Lymph Node, Draining						
Abnormal size, enlarged	-	1	-	-	1	4
Lymph Node, Inguinal						

**Text Table 2. Group Incidences of Test Article-Related Macroscopic Findings - Cont'd**

Finding	Males			Females		
	Dose ( $\mu\text{g}$ RNA/dosing day)			Dose ( $\mu\text{g}$ RNA/dosing day)		
	0	30 <sup>b</sup>	30 <sup>c</sup>	0	30 <sup>b</sup>	30 <sup>c</sup>
Number Examined	10	10	10	10	10	10
Abnormal size, enlarged	1 <sup>a</sup>	-	-	-	-	2
Site, Injection						
Abnormal color, dark/pale	-	2	1	1	3	-
Abnormal consistency, firm	-	2	2	-	4	7
Spleen						
Abnormal size, enlarged	-	-	-	-	-	1

- = No finding present.

a. = No microscopic correlates.

b. BNT162b2(V9).

c. BNT162b3c.

### Recovery Phase

Test article-related macroscopic findings observed at the end of recovery phase were limited to large draining lymph nodes (abnormal size, enlarged) in one male administered BNT162b2 (V9) and 1 female administered BNT162b3c and large inguinal lymph nodes (abnormal size, enlarged) in 1 female administered BNT162b3c, indicating a partial recovery of these findings. Pale/dark and/or firm injection sites and enlarged spleen were not observed at the end of recovery phase in BNT162b2 (V9) or BNT162b3c administered males and females, indicating a complete recovery of these findings.

**Text Table 3. Group Incidences of Test Article-Related Macroscopic Findings**

Finding	Males			Females		
	Dose ( $\mu\text{g}$ RNA/dosing day)			Dose ( $\mu\text{g}$ RNA/dosing day)		
	0	30 <sup>a</sup>	30 <sup>b</sup>	0	30 <sup>a</sup>	30 <sup>b</sup>
Number Examined	5	5	5	5	5	5
Lymph Node, Draining						
Abnormal size, enlarged	-	1	-	-	-	1
Lymph Node, Inguinal						
Abnormal size, enlarged	-	-	-	-	-	1

- = No finding present.

a. BNT162b2(V9).

b. BNT162b3c.

The remaining macroscopic findings were not test article-related effects because they were consistent with spontaneously occurring findings, the findings were distributed randomly



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among groups, or their appearance was similar to findings in controls from this and/or previous studies.

### 5.2.3. Microscopic Findings

An expanded incidence summary of microscopic observations is presented in [Table 11](#). Individual animal microscopic observations are included in [Appendix 11](#).

#### Dosing Phase

Organs with test article-related microscopic findings included the injection site (mixed cell inflammation and edema), draining and inguinal lymph nodes (increased cellularity, plasma cells and germinal centers), liver (hepatocellular vacuolation), spleen (increased cellularity, hematopoietic cells and germinal centers), and bone marrow (increased cellularity, hematopoietic cells) in both males and females administered BNT162b2 (V9) or BNT162b3c. Inflammation at the injection site and increased cellularity of germinal centers in the lymph nodes were also observed in control animals but the incidence and/or severity was/were low and within the limits of the expected normal response to intramuscular injection of saline in these animals.

**Text Table 4. Group Incidences (with Severities) of Test Article-Related Microscopic Findings**

Finding	Males			Females		
	Dose ( $\mu\text{g}$ RNA/dosing day)			Dose ( $\mu\text{g}$ RNA/dosing day)		
	0	30 <sup>b</sup>	30 <sup>c</sup>	0	30 <sup>b</sup>	30 <sup>c</sup>
Site, Injection <sup>a</sup>	10	10	10	10	10	10
Inflammation	4	10	10	5	10	10
Minimal (Grade 1)	4	-	-	5	-	-
Mild (Grade 2)	-	7	5	-	7	9
Moderate (Grade 3)	-	3	5	-	3	1
Edema	-	9	9	-	10	10
Mild (Grade 2)	-	8	8	-	9	9
Moderate (Grade 3)	-	1	1	-	1	1
Lymph Node, Draining <sup>a</sup>	10	9	10	10	10	10
Increased cellularity, Plasma cell	-	7	8	-	9	7
Minimal (Grade 1)	-	1	4	-	1	1
Mild (Grade 2)	-	4	3	-	1	5
Moderate (Grade 3)	-	2	1	-	7	1
Increased cellularity, Germinal center	2	6	8	2	5	6
Minimal (Grade 1)	1	2	2	1	3	4
Mild (Grade 2)	1	4	6	1	2	2
Lymph Node, Inguinal <sup>a</sup>	9	10	10	10	10	10
Increased cellularity, Plasma cell	-	1	1	-	2	4

**Text Table 4. Group Incidences (with Severities) of Test Article-Related Microscopic Findings - Continued**

Finding	Males			Females		
	Dose ( $\mu\text{g}$ RNA/dosing day)			Dose ( $\mu\text{g}$ RNA/dosing day)		
	0	30 <sup>b</sup>	30 <sup>c</sup>	0	30 <sup>b</sup>	30 <sup>c</sup>
Minimal (Grade 1)	-	1	1	-	2	4
Increased cellularity, Germinal center	1	5	6	1	6	9
Minimal (Grade 1)	-	1	1	1	3	6
Mild (Grade 2)	1	4	5	-	3	3
Liver <sup>a</sup>	10	10	10	10	10	10
Vacuolation, Hepatocyte; Periportal	-	5	7	-	10	7
Minimal (Grade 1)	-	5	7	-	10	7
Spleen <sup>a</sup>	10	10	10	10	10	10
Increased cellularity, hematopoietic cell	-	10	10	-	9	10
Minimal (Grade 1)	-	10	10	-	9	10
Increased cellularity, Germinal center	-	5	5	-	6	5
Minimal (Grade 1)	-	5	5	-	6	5
Bone marrow, Sternum <sup>a</sup>	10	10	10	10	10	10
Increased cellularity, hematopoietic cell	-	10	10	-	10	10
Minimal (Grade 1)	-	10	10	-	10	10

- = No finding present.

a. Number examined.

b. BNT162b2(V9).

c. BNT162b3c.

Mixed cell inflammation at the injection site was characterized by large numbers of neutrophils with fewer plasma cells, macrophages, and lymphocytes admixed with abundant pale eosinophilic fluid (edema) and small amounts of cellular debris, fibrin, and hemorrhage. Inflammatory cells frequently infiltrated and expanded the epimysium, perimysium, and endomysium and separated and surrounded the myofibers and/or blood vessels in the skeletal muscle. Occasionally, inflammatory cells extended into the subcutaneous tissue/dermis of the overlying skin and into the extra-capsular tissue of the joint.

Increased cellularity in germinal center was observed in the lymph nodes and spleen compared to controls.

Increased cellularity of plasma cells in the lymph nodes was characterized by infiltration of variable numbers of plasma cells in the cortical, medullary, and subcapsular sinuses. Plasma cells were immature in appearance and were interpreted to likely represent plasmablasts.

Increased cellularity of hematopoietic cells in the bone marrow and spleen was characterized by increased hematopoietic precursor cells (primarily myeloid precursors) within the bone marrow or splenic red pulp compared to controls.

Vacuolation of the periportal hepatocytes in the liver was characterized by small clear round membrane bound structures within cytoplasm of these cells.

**Recovery Phase**

Test article-related microscopic findings noted at the end of the dosing phase including edema at the injection site, hepatocellular vacuolation in the liver, and increased cellularity of hematopoietic cells in the spleen and bone marrow were not observed at the end of recovery phase in BNT162b2 (V9) or BNT162b3c administered males and females, indicating a complete recovery of these findings. Inflammation at the injection site was characterized by mostly lymphocytes and plasma cells with few neutrophils (indicating partial recovery) and no edema (full recovery). However, increased cellularity of plasma cells and germinal centers in the draining and inguinal lymph nodes, and increased cellularity of the germinal centers in the spleen partially recovered, as the incidence and/or severity of these findings were lower in recovery phase animals as compared to dosing phase animals in both males and females administered BNT162b2 (V9) or BNT162b3c. At the end of recovery phase, mature plasma cells had replaced the plasmablasts identified in the inguinal and draining lymph nodes in the dosing phase animals. In recovery phase animals, infiltration of macrophages was observed in the draining lymph nodes (minimal to mild) in both sexes administered BNT162b2 (V9) or BNT162b3c and in the inguinal lymph nodes (minimal) in both sexes administered BNT162b3c. This finding was considered indicative of a reparative process (consequence of phagocytosis), which can be seen following inflammatory reactions at the injection sites.

**Text Table 5. Group Incidences (with Severities) of Test Article-Related Microscopic Findings**

Finding	Males			Females		
	Dose (µg RNA/dosing day)			Dose (µg RNA/dosing day)		
	0	30 <sup>b</sup>	30 <sup>c</sup>	0	30 <sup>b</sup>	30 <sup>c</sup>
Site, Injection <sup>a</sup>	5	5	5	5	5	5
Inflammation	-	5	5	-	5	5
Minimal (Grade 1)	-	5	5	-	5	5
Lymph Node, Draining <sup>a</sup>	4	5	5	5	5	5
Increased cellularity, Plasma cell	-	4	5	-	4	3
Minimal (Grade 1)	-	4	5	-	4	3
Increased cellularity, Germinal center	-	4	4	1	3	5
Minimal (Grade 1)	-	3	2	1	2	4
Mild (Grade 2)	-	1	2	-	1	1
Infiltration, Macrophage	-	3	4	-	3	4
Minimal (Grade 1)	-	2	2	-	1	1
Mild (Grade 2)	-	1	2	-	2	3

**Text Table 5. Group Incidences (with Severities) of Test Article-Related Microscopic Findings - Continued**

Finding	Males			Females		
	Dose ( $\mu\text{g}$ RNA/dosing day)			Dose ( $\mu\text{g}$ RNA/dosing day)		
	0	30 <sup>b</sup>	30 <sup>c</sup>	0	30 <sup>b</sup>	30 <sup>c</sup>
Lymph Node, Inguinal <sup>a</sup>	5	5	5	5	5	5
Increased cellularity, Plasma cell	-	-	-	-	-	1
Minimal (Grade 1)	-	-	-	-	-	1
Increased cellularity, Germinal center	2	3	2	2	1	3
Minimal (Grade 1)	2	3	2	2	1	3
Infiltration, Macrophage	-	-	1	-	-	1
Minimal (Grade 1)	-	-	1	-	-	1
Spleen <sup>a</sup>	5	5	5	5	5	5
Increased cellularity, Germinal center	-	1	1	-	2	2
Minimal (Grade 1)	-	1	1	-	2	2

- = No finding present.

a. Number examined.

b. BNT162b2(V9).

c. BNT162b3c.

The remaining microscopic findings were not test article-related effects because they were consistent with spontaneously occurring findings, the findings were distributed randomly among groups, or their appearance was similar to findings in controls from this and/or previous studies.

## 6. INTEGRATED SUMMARY AND DISCUSSION OF RESULTS

BNT162b2 (Version 9 [V9]) and BNT162b3c, candidate COVID-19 vaccines, were administered by intramuscular (IM) doses once weekly for a total of 3 doses to male and female Wistar Han (CrI:WI[Han]) rats at 30  $\mu\text{g}$  RNA/dosing day followed by a 3-week recovery phase.

All test article-related pathology findings with both vaccine candidates were interpreted as nonadverse, as there was no evidence of systemic toxicity or clinical signs of illness or lameness.

At the end of the dosing phase, test article-related mixed cell inflammation (mild to moderate) and edema (mild to moderate) at the injection site were consistent with those typically associated with the IM administration of lipid nanoparticle (LNP)-encapsulated mRNA vaccines (Hassett et al, 2019). These findings correlated with macroscopic observations of abnormal color (dark/pale) and consistency (firm). At the end of the 3-week recovery phase, full recovery occurred for macroscopic findings of pale/dark and firm

injection sites and the microscopic finding of edema, whereas partial recovery occurred for inflammation at the injection sites.

At the end of the dosing phase, test article-related findings in the lymph nodes (increased cellularity of plasma cells [minimal to moderate] and germinal centers [minimal to mild]), spleen (increased cellularity of hematopoietic cells [minimal] and germinal centers [minimal]), and the bone marrow (minimal increased cellularity of hematopoietic cells) were secondary to immune activation and/or inflammation at the injection site. The presence of plasma cells (interpreted as plasmablasts) in the draining and inguinal lymph nodes was interpreted to reflect a robust immunological response to the vaccines. These observations correlated with macroscopic observations of abnormal size (enlarged) in the lymph nodes and spleen and increased splenic weights. At the end of the 3-week recovery phase, full recovery occurred for higher spleen weights, macroscopic finding of enlarged spleen, and microscopic findings of increased cellularity of hematopoietic cells in the spleen and bone marrow, whereas partial recovery occurred for macroscopic findings of enlarged draining and inguinal lymph nodes, microscopic findings of increased cellularity of plasma cells and germinal centers in the draining and inguinal lymph nodes, and increased cellularity of the germinal centers in the spleen.

At the end of the dosing phase, test article-related microscopic finding of minimal portal hepatocyte vacuolation was not associated with hepatic tissue damage or liver enzyme alterations. This change might be related to hepatic clearance of the pegylated lipid in the LNP (Ivens et al, 2015). At the end of 3-week recovery phase, this finding was completely recovered.

In conclusion, administration of BNT162b2 (Version 9 [V9]) or BNT162b3c, at 30 µg RNA/dosing day by intramuscular (IM) administration once weekly to Wistar Han rats for 3 weeks did not result in any adverse findings. All test article-related effects were nonadverse, and except for hepatocyte vacuolation, effects were consistent with expected immune responses to vaccines and/or secondary to inflammation. Full or partial recovery occurred in both males and females administered BNT162b2 (V9) or BNT162b3c for all findings by the end of the recovery phase.

## 7. REFERENCES

Hassett KJ, Benenato KE, Jacquinet E, et al. Optimization of lipid nanoparticles for intramuscular administration of mRNA vaccines. *Mol Ther Nucleic Acids* 2019;15:1-11.

Ivens IA, Achanzar W, Baumann A, et al. PEGylated biopharmaceuticals: current experience and considerations for nonclinical development. *Toxicol Pathol* 2015;43(7):959-83.



**Medical Quality Assurance**

***Quality Assurance Statement***

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**Title:** 17-DAY INTRAMUSCULAR TOXICITY STUDY OF BNT162B2 (V9) AND BNT162B3C IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY

**Study:** 20GR142

In accordance with Pfizer policies and Medical Quality Assurance procedures for Good Laboratory Practice (GLP), the conduct of this portion of this study has been inspected and/or audited as follows.

<b>Phase Inspected</b>	<b>Audit/Inspection Date GMT</b>	<b>Reporting Date GMT</b>
Test Site Protocol Review	24-Jun-2020 to 25-Jun-2020	25-Jun-2020
Protocol Amendment #1	02-Jul-2020 to 02-Jul-2020	02-Jul-2020
Protocol Amendment #4	04-Sep-2020 to 04-Sep-2020	04-Sep-2020
Report: Clinical Pathology	20-Oct-2020 to 30-Oct-2020	03-Nov-2020
Report: Pathology	20-Oct-2020 to 30-Oct-2020	03-Nov-2020

In addition Routine Facility and Process audits are conducted in accordance with MQA SOPs and Site Monitoring Plans.

(b) (6)

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## Document Approval Record

<b>Document Name:</b>	Anatomic Pathology
<b>Document Title:</b>	20GR142 Anatomic Pathology

<b>Signed By:</b>	<b>Date(GMT)</b>	<b>Signing Capacity</b>
(b) (6)	09-Nov-2020 17:49:26	Quality Assurance Approval
(b) (6)	09-Nov-2020 17:55:46	Scientific Review
(b) (6)	09-Nov-2020 19:54:09	Author Approval

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### Non-GMP CoA

Material not for human use  
 Version 3

**Product:** CoVVAC  
**Batch:** RBP020.2LNP  
**Lot:** CoVVAC/270320

Test	Method	Result
Appearance	Visual Inspection (224/SOP/011)	(b) (4)
RNA identity	CE (223/SOP/016)	
RNA integrity	CE (223/SOP/016)	
RNA content	Ribogreen Assay (221/SOP/018)	
RNA encapsulation	Ribogreen assay +/- LNP disruption (221/SOP/018)	
ALC-0315 content	HPLC-CAD (222/SOP/044)	
ALC-0159 content	HPLC-CAD (222/SOP/044)	
DSPC content	HPLC-CAD (222/SOP/044)	
Cholesterol content	HPLC-CAD (222/SOP/044)	
Particle size (Z <sub>avg</sub> )	Dynamic light scattering (224/SOP/002)	
Polydispersity index (PDI)	Dynamic light scattering (224/SOP/002)	
pH	pH (224/SOP/016)	
Osmolality	Freezing point depression (224/SOP/009)	
Endotoxins/Pyrogens	Turbidimetric, kinetic LAL assay (Ph.Eur. 2.6.14/ USP<85>)	
Bioburden	Membrane filtration method 225/SOP/001	

Store at: -70°C

Date: 09.04.20

Date: 09.04.20

(b) (6)

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**Non-GMP CoA**  
 Material not for human use  
 Version 2

**Product:** CorVac BNT162b3c  
**Batch:** RBP020.8 LNP  
**Lot:** BCV/040620

Test	Method	Result
Appearance	Visual Inspection (224/SOP/011)	(b) (4)
RNA identity	CE (223/SOP/015)	
RNA integrity	CE (223/SOP/015)	
RNA content	Ribogreen Assay (221/SOP/018)	
RNA encapsulation	Ribogreen assay +/- LNP disruption (221/SOP/018)	
ALC-0315 identification and content	HPLC-CAD (222/SOP/044)	
ALC-0159 identification and content	HPLC-CAD (222/SOP/044)	
DSPC identification and content	HPLC-CAD (222/SOP/044)	
Cholesterol identification and content	HPLC-CAD (222/SOP/044)	
Particle size (Z <sub>avg</sub> )	Dynamic light scattering (224/SOP/002)	
Polydispersity index (PDI)	Dynamic light scattering (224/SOP/002)	
pH	pH (224/SOP/016)	
Osmolality	Freezing point depression (224/SOP/009)	
Endotoxins/Pyrogens	Turbidimetric, kinetic LAL assay (Ph.Eur. 2.6.14/ USP<85>)	
Bioburden	Membrane filtration method 225/SOP/001	

**Store at: -70°C**

Date: 03.07.2020

Date: 03.07.2020

(b) (6)

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## Medical Quality Assurance

### *Quality Assurance Statement*

**Title:** 17-DAY INTRAMUSCULAR TOXICITY STUDY OF BNT162B2 (V9) AND BNT162B3C IN WISTAR HAN RATS WITH A 3-WEEK RECOVERY

**Study:** 20GR142

In accordance with Pfizer policies and Medical Research Quality Assurance procedures for Good Laboratory Practice (GLP), the conduct of this study has been inspected and/or audited as follows. The Individual Quality Assurance Statement for study phase(s) conducted at other site(s) are contained within this report.

<b>Phase Inspected</b>	<b>Audit/Inspection Date GMT</b>	<b>Reporting Date GMT</b>
Protocol Review	29-Jun-2020 to 29-Jun-2020	30-Jun-2020
Protocol Amendment #1	07-Jul-2020 to 07-Jul-2020	07-Jul-2020
In-life: Dosing	13-Jul-2020 to 14-Jul-2020	16-Jul-2020
In-life: Dosing	13-Jul-2020 to 14-Jul-2020	16-Jul-2020
Protocol Amendment #2	16-Jul-2020 to 16-Jul-2020	16-Jul-2020
In-life: Clin Path Blood Collection	22-Jul-2020 to 23-Jul-2020	24-Jul-2020
In-life: Necropsy	22-Jul-2020 to 22-Jul-2020	24-Jul-2020
Protocol Amendment #3	28-Jul-2020 to 28-Jul-2020	03-Aug-2020
Protocol Amendment #4	08-Sep-2020 to 08-Sep-2020	08-Sep-2020
Report: Nonclinical Study	14-Oct-2020 to 03-Nov-2020	03-Nov-2020

In addition Routine Facility and Process audits are conducted in accordance with MQA SOPs and Site Monitoring Plans.

(b) (6)

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## Document Approval Record

**Document Name:** Study 20GR142 - 17-Day Intramuscular Toxicity Study of BNT162B2 (V9) and BNT162B3C in Wistar Han Rats with a 3-Week Recovery

**Document Title:** Final Report - 17-Day Intramuscular Toxicity Study of BNT162B2 (V9) and BNT162B3C in Wistar Han Rats with a 3-Week Recovery

<b>Signed By:</b>	<b>Date(GMT)</b>	<b>Signing Capacity</b>
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