[redacted]

FINAL REPORT

Testing Facility Study No. 2308-123

A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

SPONSOR:
Moderna TX, Inc.
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[redacted]

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REPORT APPROVAL

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Signing Reason: I approve this document
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PPD BS
Study Director

1. RESPONSIBLE PERSONNEL

Role/Phase	Name	Contact Information
Site Head / General Manager	PPD PhD, DSP	Address as cited for Testing Facility
Senior Director, Safety Evaluation	PPD , BS	Address as cited for Testing Facility
Senior Director, Laboratory Sciences	PPD BA	Address as cited for Testing Facility
Director, Operations	PPD BS, LAT	Address as cited for Testing Facility
Study Director	PPD , BS	Address as cited for Testing Facility
Supervisor, Toxicology Services	PPD BS, LATG	Address as cited for Testing Facility
Executive Director, Attending Veterinarian	PPD DVM, MS, DACLAM	Address as cited for Testing Facility
Report Coordinator	PPD MSc	Address as cited for Testing Facility
Individual Scientist (IS) at Testing Facility		
Staff Veterinarians	PPD DVM PPD , BVM&S, DVSc, DACLAM	Address as cited for Testing Facility
Clinical Pathology	PPD , DVM, DACVP	Address as cited for Testing Facility
Principal Investigator (PI)		
ELISA Assay	PPD PhD	National Institutes of Health (NIH) Building 40 Room 2608 40 Convent Drive Bethesda, MD 20892

2. SUMMARY

The objectives of this study were to determine the potential toxicity effects of mRNA-1273 when administered on Days 1 and 22 via intramuscular bolus injection in Crl:CD(SD) Sprague Dawley rats. The study design was as follows:

Text Table 1
Experimental Design

Group No.	Test Material	Dose Level (µg/dose)	Dose Volume (mL/kg)	Dose Concentration (µg/mL)	Main Study	
					No. of Males	No. of Females
1	Control Article	0	0.2	0	5	5
2	mRNA-1273	30	0.2	150	5	5
3	mRNA-1273	60	0.2	300	5	5
4	mRNA-1273	100	0.2	500	5	5

Crl:CD(SD) Sprague Dawley rats were administered the test or control article formulations by an intramuscular bolus injection on Days 1 and 22. A total of 2 doses were administered to each Crl:CD(SD) Sprague Dawley rat.

The following parameters and endpoints were evaluated in this study: viability, clinical signs, body weights, body weight gains, clinical pathology parameters (hematology and clinical chemistry) and immunogenicity.

There were no mRNA-1273-related mortalities, changes in body weight, or body weight gain.

mRNA-1273 elicited a significant, dose dependent antibody response on Day 35 following dose administrations on Days 1 and 22 at all dose levels.

mRNA-1273-related clinical observations were noted at 24 hours post each dose (i.e. Day 2 and 23) and generally consisted of transient, dose dependent edema with or without hindlimb impairment in all animals at ≥ 30 µg/dose. All edema and/or hindlimb impairment resolved 5 days following dose administration.

mRNA-1273-related hematology changes at Day 23 were consistent with inflammation and were seen at ≥ 30 µg/dose in both sexes. These findings included increases in neutrophil (range: 5.86x to 10.81x of control mean) and eosinophil (range: 2.60x to 4.67x of control mean) counts, decreases in mean albumin (range: 0.90x to 0.85x of control mean) and albumin/globulin ratio (range: 0.86x to 0.75x of control mean) at all dose levels, with increased mean globulin (range: 1.12x to 1.15x of control mean) in males at ≥60 µg/dose.

Other mRNA-1273-related changes observed at 30, 60, and/or 100 µg/dose consisted of decreases in mean reticulocyte (range: 0.80x to 0.65x of control mean), lymphocyte (range: 0.74x to 0.47x of control mean), and/or monocyte (range: 0.58x to 0.52x of control mean) counts. The decreases in reticulocyte counts were associated with mild decreases in red cell mass (erythrocytes, hemoglobin, and/or hematocrit) in the males at ≥30 µg/dose (hemoglobin range: 0.93x to 0.91x of control mean), and increases in RDW (red cell distribution width; range: 1.05x to 1.10x of control mean) at all doses.

Additional minor mRNA-1273-related changes most likely related to alterations in metabolic state and/or hydration status were also seen at 30, 60, and/or 100 µg/dose and included increases in mean creatinine (range: 1.26x to 1.43x of control mean), triglyceride (range: 1.66x to 2.30x of control mean), and/or cholesterol (range: 1.57x to 1.62x of control mean) concentrations. Mean glucose was also mildly increased (1.26x of control mean) in males at 100 µg/dose.

Administration of mRNA-1273 by intramuscular bolus injection on Days 1 and 22 to Crl:CD(SD) Sprague-Dawley rats was well tolerated up to 100 µg/dose.

3. INTRODUCTION

The objective of this study was to characterize the immunogenic response and potential toxicity of mRNA-1273 when administered via intramuscular injection on Days 1 and 22 to Sprague Dawley rats.

The design of this study was based on the following guidelines.

- ICH Harmonised Tripartite Guideline M3 (R2). *Guidance on Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals.*
- ICH Harmonised Tripartite Guideline S6 (R1). *Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals.*
- Note for Guidance on Preclinical Pharmacological and Toxicological Testing of Vaccines. The European Agency for the Evaluation of Medicinal Products, CPMP/SWP/465/95: Dec. 17, 1997.
- WHO guidelines on nonclinical evaluation of vaccines. World Health Organization, WHO Technical Report Series, No. 927, 2005.
- Final Rules of the Animal Welfare Act regulations (Code of Federal Regulations, Title 9)
- *Public Health Service Policy on Humane Care and Use of Laboratory Animals* (Office of Laboratory Animal Welfare, Current edition)
- *Guide for the Care and Use of Laboratory Animals* (National Research Council, Current edition)

The study protocol, last protocol amendment, and a deviation are presented in Appendix 1.

Study Initiation Date:	07 Feb 2020
Initiation of Dosing:	13 Feb 2020
Completion of In-life:	18 Mar 2020
Experimental Start Date:	10 Feb 2020
Experimental Completion Date:	23 Apr 2020

> 30 days !

4. MATERIALS AND METHODS

4.1. Test Materials

4.1.1. Test and Control Article Characterization

The Sponsor provided to the Testing Facility documentation of the identity, strength, purity, composition, and stability for the test article. A Certificate of Analysis was provided to the Testing Facility and is presented in Appendix 2.

Documentation of the strength, composition, stability, and other pertinent information for the control article was provided.

4.1.2. Test Material Identification

Text Table 2
Test Article Identification

Identification	mRNA-1273
Lot No.	8520100101
Expiration/Retest Date	07 Aug 2020
Purity	80%
Storage Conditions	Frozen at -60°C to -90°C, protected from light
Provided by	Moderna Therapeutics Inc.

Text Table 3
Control Article Identification

Identification	nCoV Formulation Buffer
Alternate Identification	Tris/Sucrose Buffer
Lot No.	DH-02271
Expiration/Retest Date	31 Jan 2021
Storage Conditions	Refrigerated at 2°C to 8°C, protected from light
Provided by	Moderna Therapeutics Inc.

4.2. Reserve Samples

Due to the study duration, a reserve sample was not collected.

4.3. Test Article Inventory and Disposition

The test materials (e.g., test and control articles) were received by the Testing Facility for distribution as needed. Records of the receipt, distribution, storage, and disposition of test materials (including empty containers of Sponsor-provided materials) were maintained. The remaining test article was discarded appropriately after completion of the study.

4.4. Dose Formulation and Analysis

4.4.1. Preparation of Formulations

Text Table 4
Formulation Frequency of Preparation

Dose Formulation	Administration Dose Form	Frequency of Preparation	Storage Conditions
Control	Solution	On each day of dosing	Controlled room temperature[a]
Test Article	Solution	On each day of dosing[b]	Controlled room temperature[a]

[a] Formulations were prepared fresh on each day of dosing and dispensed at room temperature to be used within 4 hours of release.
[b] Test article formulation preparation was based on the actual test article stock concentration presented in Appendix 2.

Any residual volumes from each dosing occasion were retained and stored frozen at -60°C to -90°C, and were discarded appropriately prior to report finalization.

4.4.2. Preparation Details

Dosing formulations were prepared prior to each dose administration according to the procedures described in the Protocol at appropriate concentrations to meet dose level requirements.

4.4.3. Sample Collection and Analysis

The test and control articles were used as received from the Sponsor; therefore, samples for dose formulation analysis were not collected by the Testing Facility.

4.5. Test System

4.5.1. Receipt

Charles River Laboratories ?

On 10 Feb 2020, Sprague Dawley rats (22/sex) were received from [redacted]. The animals were approximately 7 weeks old and weighed between 171 and 228 g at initiation of dosing.

4.5.2. Justification for Test System and Number of Animals

The current state of scientific knowledge and the applicable guidelines cited did not provide acceptable alternatives, in vitro or otherwise, to the use of live animals to accomplish the purpose of this study. "The development of knowledge necessary for the improvement of the health and well-being of humans as well as other animals requires in vivo experimentation with a wide variety of animal species" (Federal Register, 1985). "Whole animals are essential in research and testing because they best reflect the dynamic interactions between the various cells, tissues, and organs comprising the human body" (NIH Guide, 1993).

The rat is the usual rodent model used for evaluating the immunogenicity and toxicity of various classes of chemicals and for which there is a large historical database (US FDA CDER, 2006).

The total number of animals used in this study was considered to be the minimum required to properly characterize the effects of the test article and was designed such that it did not require an unnecessary number of animals to accomplish its objectives.

4.5.3. Animal Identification

Each animal was identified using a subcutaneously implanted electronic identification chip.

4.5.4. Environmental Acclimation

During the 3-day acclimation period, the animals were observed daily with respect to general health and any signs of disease. These examinations are not reported but are maintained in the study file.

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

Animals were randomly assigned to groups upon receipt. Before the initiation of dosing, any assigned animals considered unsuitable for use in the study were replaced by alternate animals obtained from the same shipment and maintained under the same environmental conditions.

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

4.5.6. Husbandry

4.5.6.1. Housing

The animals were pair- or group-housed in solid bottom cages with nonaromatic bedding. The housing was equipped with an automatic watering valve as specified in the *USDA Animal Welfare Act* (9 Code of Federal Regulations [CFR], Parts 1, 2 and 3) and as described in the *Guide for the Care and Use of Laboratory Animals* (National Research Council, Current edition). Each cage was clearly labeled with study, group, animal number, and sex.

CRL USA = Raleigh, North Carolina
Rat breeding Kingston, New York
Hollister, California

4.5.6.2. Animal Enrichment

Psychological/environmental enrichment was provided according to SOP.

4.5.6.3. Environmental Conditions

Target temperatures of 68°F to 79°F with a target relative humidity of 30% to 70% were maintained. A 12-hour light/12-hour dark cycle was maintained.

4.5.6.4. Food

Block Lab Diet® (Certified Rodent Diet #5002, PMI Nutrition International, Inc.) was provided ad libitum except during designated procedures. Results of analysis for nutritional components and environmental contaminants are provided by the supplier and are on file at the Testing Facility.

There are no known contaminants in the food that would interfere with this study.

4.5.6.5. Water

Tap water was available ad libitum to each animal via an automatic watering system.

There are no known contaminants in the water that would interfere with this study. The drinking water used was monitored for specified contaminants at periodic intervals according to Testing Facility SOP.

4.5.6.6. Veterinary Care

Veterinary care was available throughout the course of the study, and animals were examined by the veterinary staff as warranted by clinical signs or other changes. All veterinary examinations and recommended therapeutic treatments, if any, were documented in the study records and reviewed by the Study Director. The veterinary treatments and observations recorded after initiation of dosing are presented in Appendix 6.

4.6. Experimental Design

Text Table 5
Experimental Design

Group No.	Test Material	Dose Level (µg/dose)	Dose Concentration (µg /mL)	Dose Volume (mL/dose)	Animal Numbers	
					Male	Female
1	Control Article	0	0	0.2	1001, 1102, 1003-1005	1501-1505
2	mRNA-1273	30	150	0.2	2001-2005	2501-2505
3	mRNA-1273	60	300	0.2	3001-3005	3501-3505
4	mRNA-1273	100	500	0.2	4001-4005	4501-4504, 4605

4.6.1. Administration of Test Materials

The control and test article were administered once on Days 1 and 22 via intramuscular injection. The dose levels were 30, 60, and 100 µg/dose and administered at a dose volume of 0.2 mL/dose. The injection site areas and surrounding skin were shaved free of hair at least 48 hours prior to dose administration and as needed for evaluation of the injection site(s). Doses were administered via bolus intramuscular injection into one of the quadriceps (hind leg, thigh). A unique site was used for each injection (left quadricep on Day 1, right quadricep on Day 22). Care was taken to ensure that injection(s) were in the appropriate part of the muscle. The needle was inserted perpendicular to the skin surface. The location of the injection site was documented

for each dose. In addition, each injection site was marked with a large circle for the purposes of erythema and swelling evaluation. Each injection site was remarked at least once weekly. The control group received the control article in the same manner as the treated groups.

Under no circumstances were dose formulations subjected to vortexing or vigorous shaking to avoid disruption of the test article. Before withdrawing a dose formulation into syringes, the dose formulation container was gently swirled to achieve homogeneity. The dosing was conducted in a group number sequence order from Group 1 through Group 4, to minimize any potential risk of test article cross-contamination. Personal protective equipment (PPE) used during dose administration was changed between groups. Dose formulations were dispensed at room temperature shortly before dosing.

4.6.2. Justification of Route and Dose Levels

The intramuscular route is the intended route of administration of this test article in humans.

Doses were selected based on the aggregate toxicity data from various rat toxicity studies conducted using this lipid nanoparticle formulation. The high dose of 100 µg/dose was selected because it was the maximum feasible dose based on the concentration of the test article and the maximum intramuscular dose volume permitted in a rat. This dose was expected to elicit minor clinical observations including transient erythema and edema at the injection site. The mid- (60 µg/dose) and low- (30 µg/dose) doses were expected to produce minimal effects.

4.7. In-life Procedures, Observations, and Measurements

Text Table 6
General In-life Assessments

Parameter	Population(s)	Frequency (minimum required)	Comments
Mortality/Cageside Observations	All Animals	At least twice daily[a,b] (morning and afternoon) beginning upon arrival through termination/release.	Animals were observed within their cage unless necessary for identification or confirmation of possible findings
Detailed Clinical Observations	All Animals	Once daily from the day of receipt (Week -1) and throughout the study.[c]	Animals were removed from the cage. Observations included, but were not limited to, evaluation of the skin, fur, eyes, ears, nose, oral cavity, thorax, abdomen, external genitalia, limbs and feet, respiratory and circulatory effects, autonomic effects such as salivation, nervous system effects including tremors, convulsions, reactivity to handling, and unusual behavior.
Injection Site Observations	All Animals	Immediately post each dose, 6 hours post each dose, and 24 hours post each dose	The injection site was evaluated for the presence/absence of erythema and/or edema.
Individual Body Weights	All Animals	At receipt, Day -1, and once weekly during the study.	The body weights recorded at receipt are not reported but are maintained in the study file.

			Body weight changes were calculated for animals between each weighing interval.

[a] Included alternate animals until released from study.
[b] Except on days of receipt and necropsy where frequency was at least once daily.
[c] For observations that could not be attributed to an individual animal due to social housing (e.g., watery feces), the observation was noted to each animal in the socialized group.

4.8. Laboratory Evaluations

4.8.1. Clinical Pathology

Clinical pathology evaluations (hematology and clinical chemistry) were conducted on all animals on Day 23 (24 hours post the last dose). The materials and methods are described in Appendix 9.

4.8.2. Serum ELISA Assay

Blood samples (approximately 0.5 mL) were collected from all animals via the sublingual vein for ELISA assay of the test article predose on Day 1 and once on Day 35. The animals were not fasted prior to blood collection. After the final blood collection, the animals were euthanized by carbon dioxide inhalation followed by an SOP approved method to ensure death. The carcasses were discarded without further evaluation.

Blood samples were collected in non-additive, barrier-free serum separator tubes and allowed to clot at controlled room temperature until centrifuged at controlled room temperature. The resulting serum was divided into 2 approximately equal aliquots in pre-labeled cryovials. All aliquots were flash frozen on dry ice and stored frozen at -60°C to -90°C within 60 minutes of collection. Samples were shipped on dry ice to the Vaccine Research Center, National Institutes of Health, Bethesda, Maryland, for serum ELISA assay or to the Sponsor for possible future exploratory analysis (for a deviation see Appendix 1). Any possible future exploratory analysis conducted by the Sponsor and/or Vaccine Research Center, National Institutes of Health, will be outside the scope of this study and therefore not included in the report.

5. STATISTICS

All results presented in the tables of the report were calculated using non-rounded values as per the raw data rounding procedure and may not be exactly reproduced from the individual data presented. Text Table 7 defines the set of comparisons used in the statistical analyses described in this section.

Text Table 7
Statistical Comparisons

Control Group	Treatment Group
1	2, 3, 4

The raw data were tabulated within each time interval, and the mean and standard deviation were calculated for each endpoint by sex and group. For each endpoint, treatment groups were compared to the control group using the analysis outlined in Text Table 8.

Text Table 8
Statistical Analysis

Endpoints	Type of Analysis
Body Weights Body Weight Change Hematology Clinical Chemistry	Group Pair-wise Comparisons (General ANOVA)

5.1. Group Pair-wise Comparisons (General ANOVA)

Included below are the details of the statistical routines that were applied to the data, dependent on the data specific assumptions outlined as part of the routine. The actual analysis performed for each endpoint and collection interval is included in the summary tables. The experimental unit for statistical analysis was the individual animal.

If the control group had a sample size less than 3, no inferential statistics were calculated. If a particular endpoint and/or parameter within a given collection interval had the same value across all experimental units, no inferential statistics were calculated.

For endpoints and/or parameters where all groups with sample sizes of 3 or greater were included, the normality of the residuals and homogeneity of variances were tested to determine if the data were approximately normal or if a log transformation or rank transformation was required. Levene's test was used to assess homogeneity of group variances and Shapiro-Wilk's test was used to test the normality of the residuals (Milliken and Johnson, 1992; Royston, 1992).

For the raw data, if Levene's test was not significant ($p \geq 0.01$) and Shapiro-Wilk's test was not significant ($p \geq 0.01$), then a normal distribution was used. If either the Levene's test was significant ($p < 0.01$) or Shapiro-Wilk's test was significant ($p < 0.01$), normality and homogeneity of variances were tested with a log transformation used on the data.

For the log transformed data, if Levene's test was not significant ($p \geq 0.01$) and Shapiro-Wilk's test was not significant ($p \geq 0.01$), then a log normal distribution was used. If either the Levene's test was significant ($p < 0.01$) or Shapiro-Wilk's test was significant ($p < 0.01$), then a rank transformation was used on the data.

For raw or log transformed data, a one-way analysis of variance was used to test each endpoint for the effects of treatment (Zar, 1999). If the treatment effect was significant ($p < 0.05$), linear contrasts were constructed for a Dunnett's pair-wise comparison of treatment groups as described above.

For rank transformed data, a Kruskal-Wallis test was used to test each endpoint for the effects of treatment. If the treatment effect was significant ($p < 0.05$), a non-parametric Dunn's pair-wise comparison test of each treatment group with the control group was performed.

Results of all pair-wise comparisons are reported at the 0.05 and 0.01 significance levels. All endpoints were analyzed using two-tailed tests.

6. COMPUTER SYSTEMS

Critical computerized systems used in the study are listed below in Text Table 9 or presented in the appropriate Phase Report. All computerized systems used in the conduct of this study have been validated; when a particular system has not satisfied all requirements, appropriate

administrative and procedural controls were implemented to assure the quality and integrity of data.

Text Table 9
Critical Computerized Systems

System Name	Version No.	Description of Data Collected and/or Analyzed
DocuSign®	19	Collection of 21 CFR Part 11 compliant signature
Deviation Information Library	2.1	Deviations
Logbook	5.3	Electronic notebook and data collection system for veterinary communications, observations, and treatments.
ExyLIMS	3.0	A comprehensive laboratory information management system used to manage data, including but not limited to: instrumentation, test articles, standards, and samples.
NextDocs®	6.1	Electronic documentation management of Deviation Events and Corrective and Preventative Actions (CAPA).
Provantis™	9.4	Client-server, Oracle-based system used for electronic documentation and data management from compound receipt through reporting.
SAS®	9.2	The SAS® System is an integrated system of software products that enables a user to perform data entry, retrieval, data management, reporting, graphics, statistical analysis, and applications development.
Siemens Environmental Monitoring	3.11	Environmental monitoring, alarming, and reporting applications.
Niagara Framework® Software System	2.3	

7. RETENTION AND DISPOSITION OF RECORDS AND SAMPLES

All study-specific raw data, documentation, protocol, samples, and final reports from this study were archived at a [redacted] archival facility unless otherwise specified in the protocol. At least one year after issue of the draft report, the Sponsor will be contacted.

All records, retained samples and reports generated from phases or segments performed by the Sponsor or subcontractors for the Sponsor were maintained by that laboratory. Details regarding the retention of the materials were provided to the Study Director.

8. RESULTS

8.1. Mortality

(Appendix 3)

All animals survived to study termination.

8.2. Detailed Clinical, Veterinary, and Injection Site Observations

(Table 1, Appendix 4, Appendix 5 and Appendix 6)

There were mRNA-1273-related clinical and veterinary observations noted starting at around 24 hours post the Day 1 dose. These findings included edema with or without hindlimb impairment noted in all treated animals. There appeared to be a dose dependent trend to the hindlimb impairment caused by the edema noted within the quadriceps muscle. All hindlimb impairment and edema resolved by the end of the first study week (Day 3 and 6, respectively). The mRNA-1273-related clinical and veterinary observations noted following the Day 22 dose were similar to the Day 1 dose. Edema with or without hindlimb impairment was observed starting ~24 hours postdose; seemed dose dependent; was observed in animals at all treatment levels; and had completely resolved by Day 27.

Other clinical/veterinary observations were transient, not dose-responsive, occurred sporadically, noted for an animal in the control group, and/or are commonly seen within this strain, age and species.

8.3. Body Weight and Body Weight Gains

(Body weight - Figure 1, Table 2, and Appendix 7)

(Body weight gains - Figure 2, Table 3, and Appendix 8)

There were no mRNA-1273-related effects on body weights.

All fluctuations among individual and mean body weight values, regardless of statistical significance, were considered not test article-related due to the lack of dose response and/or negligible magnitude.

8.4. Hematology

(Appendix 9)

Administration of mRNA-1273 to rats was associated with hematology changes at 30, 60, and 100 µg/dose. These changes, presented in Text Table 4, occurred in red cell mass (red blood cell count, hemoglobin, and hematocrit), reticulocyte, neutrophil, lymphocyte, monocyte, eosinophil counts, and/or RDW.

Text Table 4
mRNA-1273-Related Hematology Changes

Group	1*		2		3		4	
Dose Level (µg/dose)	0		30		60		100	
Sex	M	F	M	F	M	F	M	F
Hemoglobin (g/dL) Day 23 (24 hr post)	17.42	16.44	**0.92x**	–	**0.91x**	–	**0.93x**	–
Erythrocytes (10^6x cells/µL) Day 23 (24 hr post)	8.600	8.618	**0.94x**	–	**0.94x**	–	**0.96x**	–
Hematocrit (%) Day 23 (24 hr post)	53.46	49.48	**0.93x**	–	**0.91x**	–	**0.93x**	–
Reticulocytes (10^3x cells/µL) Day 23 (24 hr post)	223.48	179.28	**0.78x**	**0.79x**	**0.77x**	**0.80x**	**0.77x**	**0.65x**
Neutrophils (10^3x cells/µL) Day 23 (24 hr post)	0.946	1.178	**9.79x**	**7.67x**	**10.81x**	**6.58x**	**8.26x**	**5.86x**
Lymphocytes (10^3x cells/µL) Day 23 (24 hr post)	7.978	6.004	**0.65x**	–	**0.58x**	0.74x	**0.47x**	0.61x
Monocytes (10^3x cells/µL) Day 23 (24 hr post)	0.220	0.124	–	–	**0.58x**	–	**0.52x**	–
Eosinophils (10^3x cells/µL) Day 23 (24 hr post)	0.040	0.054	**3.30x**	**4.67x**	**4.00x**	**3.26x**	**2.60x**	**3.48x**
RDW (%) Day 23 (24 hr post)	12.52	11.28	1.06x	1.05x	**1.08x**	**1.07x**	**1.10x**	**1.07x**

M = Males; F = Females
hr = hour; post = postdose
RDW = red cell distribution width
A dash (—) indicates absence of a mRNA-1273-related change. Numerical values indicate fold change of the treated group mean value relative to the control group mean value. **Bolded** values indicate the mean value was statistically different from controls ($p < 0.05$ or $p < 0.01$).
* Control group values are reported for comparison.

mRNA-1273-related changes consistent with inflammation were seen at ≥ 30 µg/dose in both sexes and included moderate increases in neutrophil (range: 5.86x to 10.81x of control mean) and eosinophil (range: 2.60x to 4.67x of control mean) counts. These effects correlated to other signals of inflammation described below (see Section 3.2).

mRNA-1273-related changes at 30, 60, and/or 100 µg/dose in both sexes consisted of mild to moderate decreases in mean reticulocyte (range: 0.80x to 0.65x of control mean), lymphocyte (range: 0.74x to 0.47x of control mean), and/or monocyte (range: 0.58x to 0.52x of control mean) counts. The decreases in reticulocyte counts were associated with mild decreases in red cell mass (red blood cell count, hemoglobin, and hematocrit) in the males at 30, 60, and 100 µg/dose (range: 0.91x to 0.96x of control mean), and mild increases in RDW (range: 1.05x to 1.10x) in both sexes at all doses.

All other fluctuations among individual and mean hematology values, regardless of statistical significance, were considered sporadic, consistent with biologic variation and/or negligible in magnitude, and not related to mRNA-1273 administration.

8.5. Clinical Chemistry

(Appendix 9)

Administration of mRNA-1273 to rats was associated with clinical chemistry changes at 30, 60, and 100 µg/dose. These changes, presented in Text Table 5, occurred in mean creatinine, albumin, globulin, albumin/globulin ratio, triglyceride, cholesterol, and/or glucose concentrations.

Text Table 5
mRNA-1273-Related Clinical Chemistry Changes

Group	1*		2		3		4	
Dose Level (µg/dose)	0		30		60		100	
Sex	M	F	M	F	M	F	M	F
Creatinine (mg/dL)								
Day 23 (24 hr post)	0.28	0.40	**1.36x**	**1.32x**	–	**1.26x**	**1.43x**	**1.37x**
Albumin (g/dL)								
Day 23 (24 hr post)	3.53	3.86	**0.90x**	**0.90x**	**0.87x**	**0.88x**	**0.88x**	**0.85x**
Globulin (g/dL)								
Day 23 (24 hr post)	3.12	3.47	–	–	1.12x	–	**1.15x**	–
Albumin/Globulin Ratio								
Day 23 (24 hr post)	1.13	1.12	**0.83x**	0.87x	**0.78x**	0.87x	**0.75x**	0.86x
Triglycerides (mg/dL)								
Day 23 (24 hr post)	40.0	35.5	**1.88x**	–	**2.30x**	2.02x	1.66x	–
Cholesterol (mg/dL)								
Day 23 (24 hr post)	55.6	76.9	**1.62x**	–	**1.57x**	–	**1.58x**	–
Glucose (mg/dL)								
Day 23 (24 hr post)	69.0	84.5	–	–	–	–	**1.26x**	–

M = Males F = Females
hr = hour; post = postdose
A dash (—) indicates absence of a mRNA-1273-related change. Numerical values indicate fold change of the treated group mean value relative to the control group mean value. **Bolded** values indicate the mean value was statistically different from controls ($p < 0.05$ or $p < 0.01$).
* Control group values are reported for comparison.

mRNA-1273-related changes consistent with inflammation were seen at 30, 60, and/or 100 µg/dose in both sexes, and included mild to moderate decreases in mean albumin (range: 0.90x to 0.85x of control mean) and albumin/globulin ratio (range: 0.86x to 0.75x of control mean), with increased mean globulin (range: 1.12x to 1.15x of control mean) in males at 60 and 100 µg/dose. These effects correlated to other signals of inflammation described above (see Section 8.4).

Other mRNA-1273-related changes noted at 30, 60, and/or 100 µg/dose in both sexes consisted of mild increases in mean creatinine (range: 1.26x to 1.43x of control mean), triglyceride (range: 1.66x to 2.30x of control mean), and/or cholesterol (range: 1.57x to 1.62x of control mean) concentrations. Mean glucose was also mildly increased (1.26x of control mean) in males at 100 µg/dose. This collection of changes was most likely related to mild alterations in metabolic state and hydration status.

All other fluctuations among individual and mean clinical chemistry values, regardless of statistical significance, were considered sporadic, consistent with biologic variation and/or negligible in magnitude, and not related to mRNA-1273 administration.

8.6. Serum ELISA Assay

(Appendix 10)

30, 60, and 100 µg doses of mRNA-1273 elicited significant antibody concentrations in rats by 34 days post initial and 13 days post 2nd immunization in a dose-independent manner. A summary of the group mean antibody titer levels on Day 35 are present below in Text Tables 6 and 7. Pretest antibody titer levels were not detectable and therefore are not presented with the tables below.

Text Table 6
mRNA-1273 Antibody Titer Levels in Males

Group	1	2	3	4
Dose Level (µg/dose)	0	30	60	100
Sex	M	M	M	M
Day 35	LOQ	2,486,970.54	3,571,545.26	2,361,125.79

LOQ is ≤ 100.00

Text Table 7
mRNA-1273 Antibody Titer Levels in Females

Group	1	2	3	4
Dose Level (µg/dose)	0	30	60	100
Sex	F	F	F	F
Day 35	LOQ	4,492,100.43	3,221,503.68	4,949,493.90

LOQ is ≤ 100.00

9. CONCLUSION

Administration of mRNA-1273 by intramuscular bolus injection on Days 1 and 22 to Crl:CD(SD) Sprague-Dawley rats was well tolerated up to 100 µg/dose.

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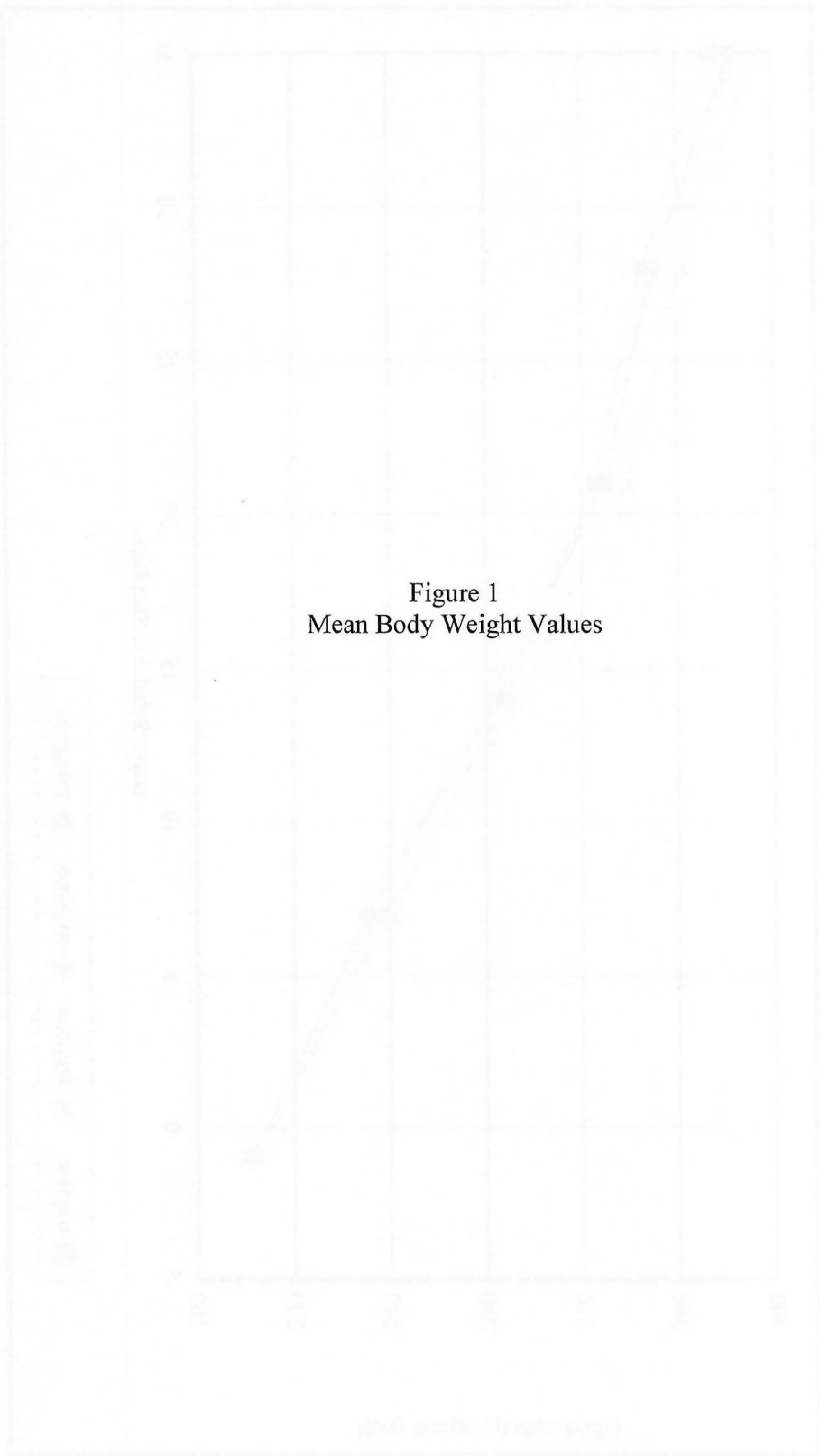
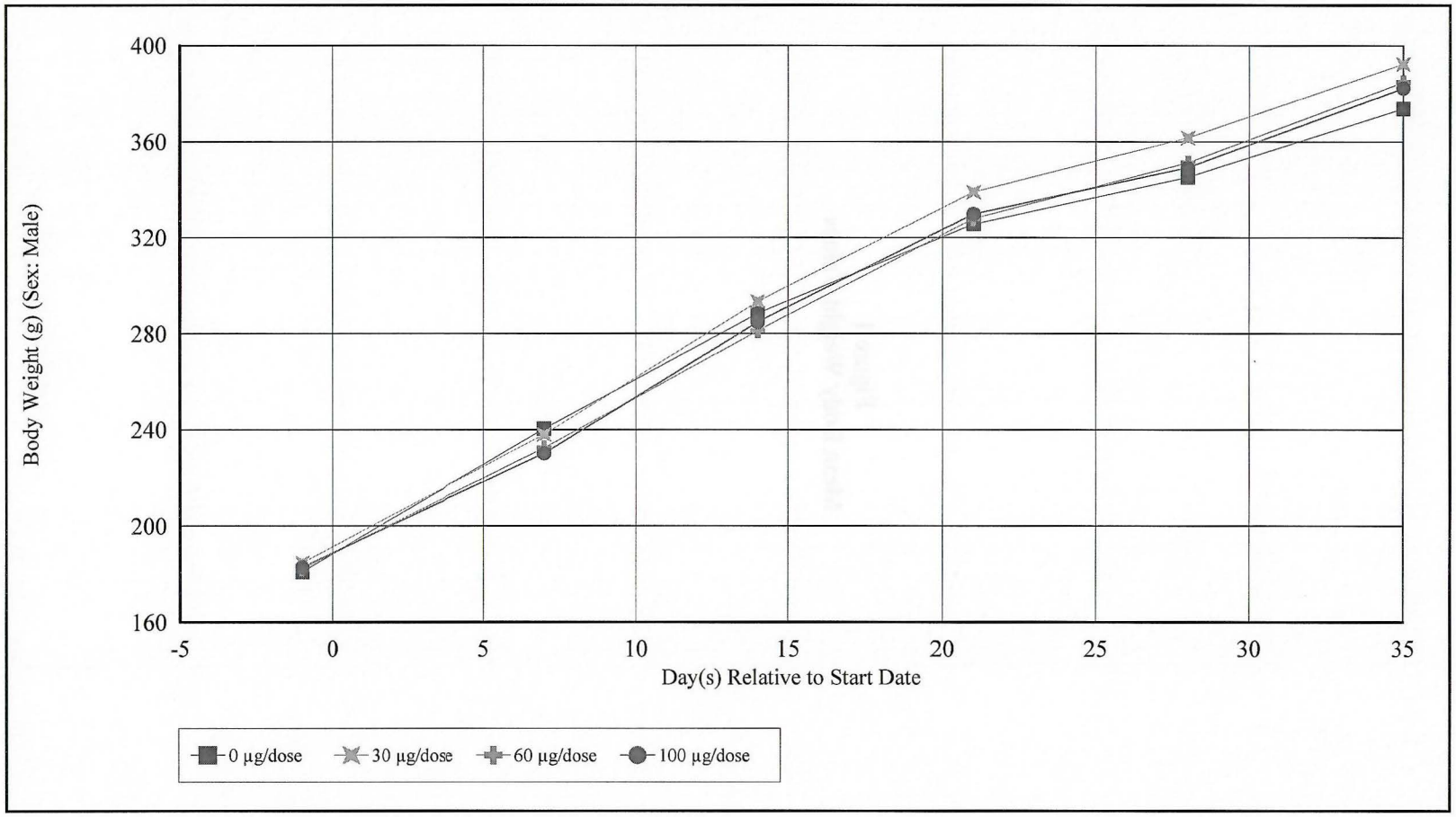


Figure 1
Mean Body Weight Values

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Mean Body Weight Values



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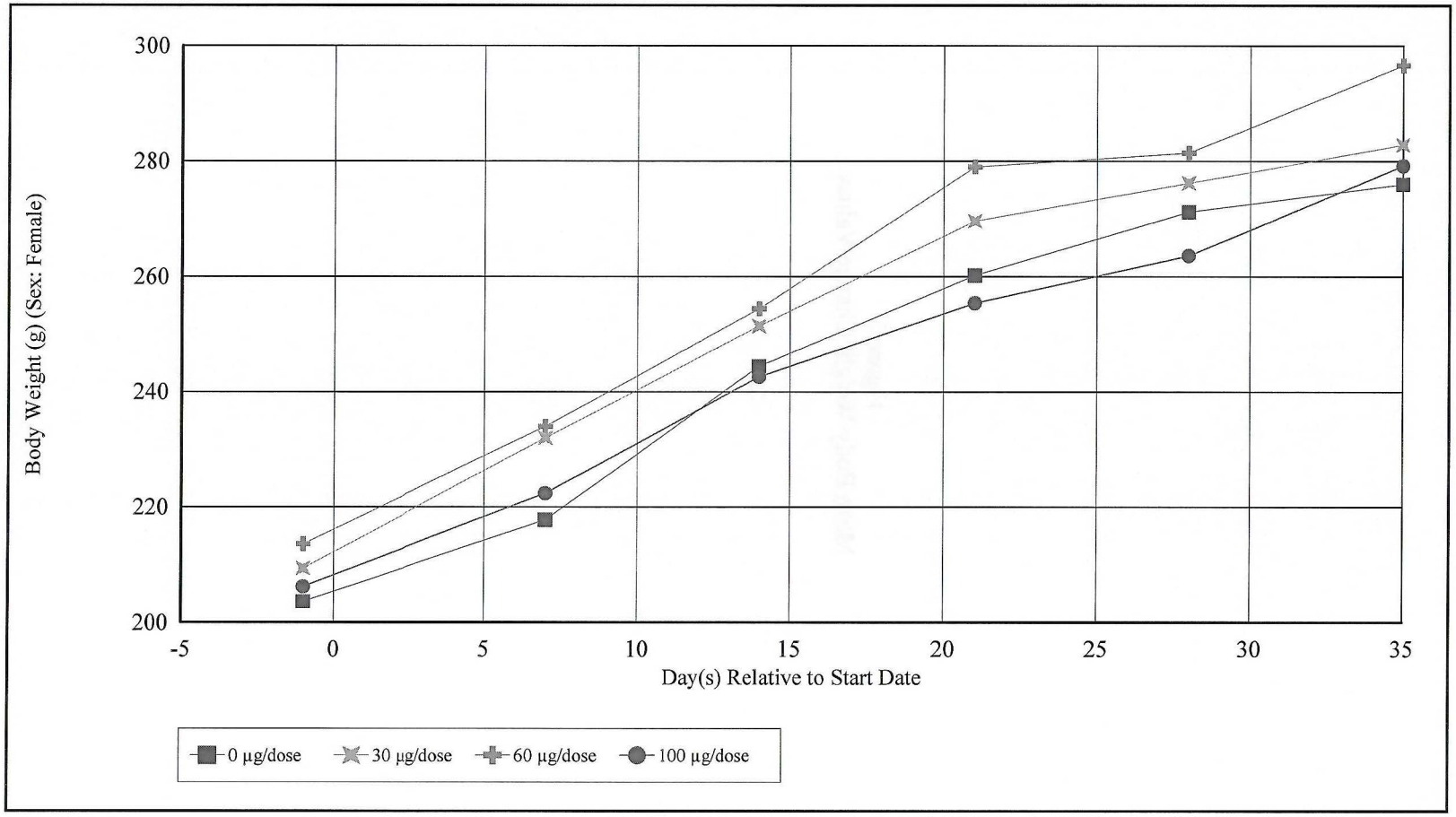
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Mean Body Weight Values



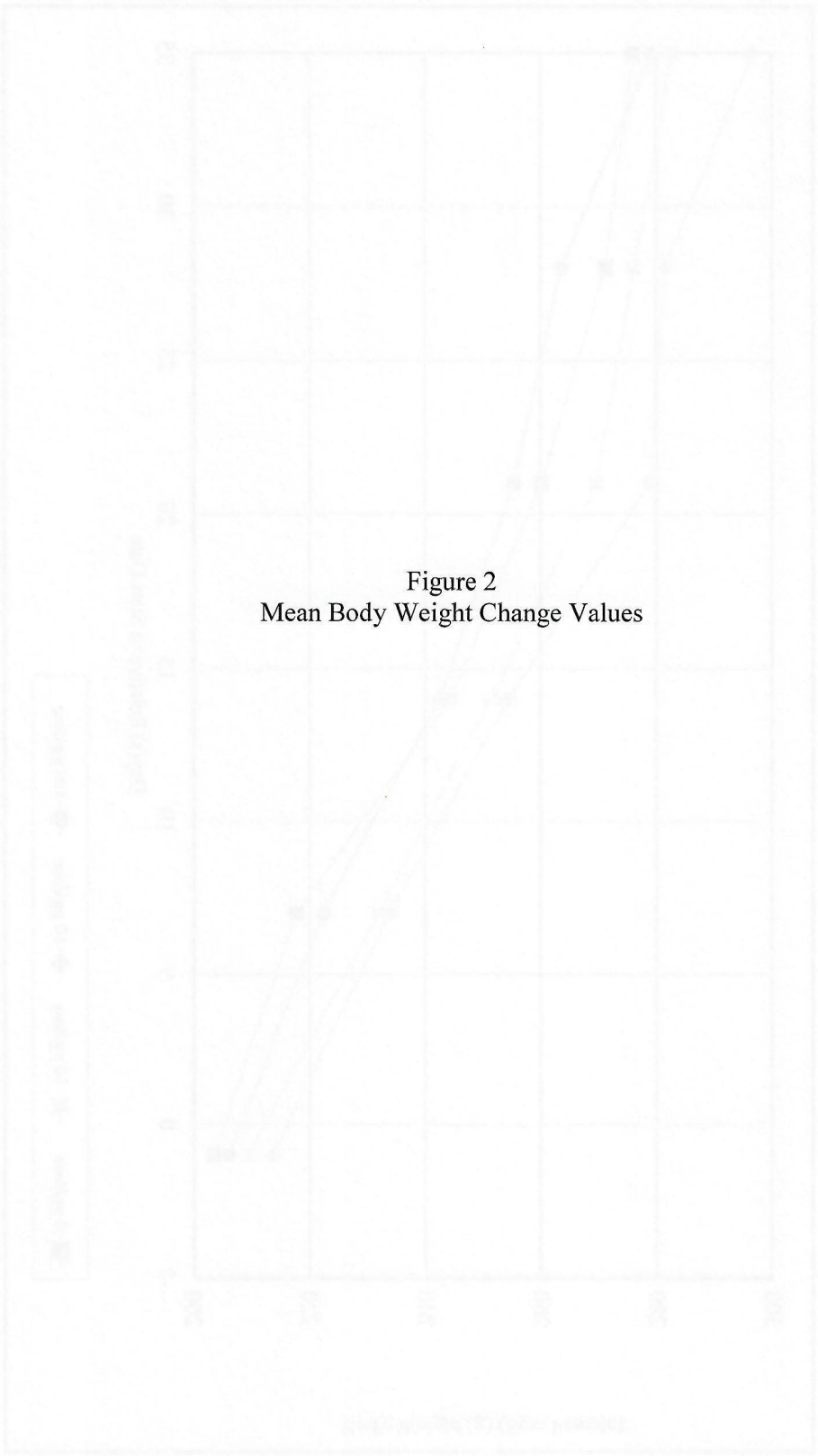
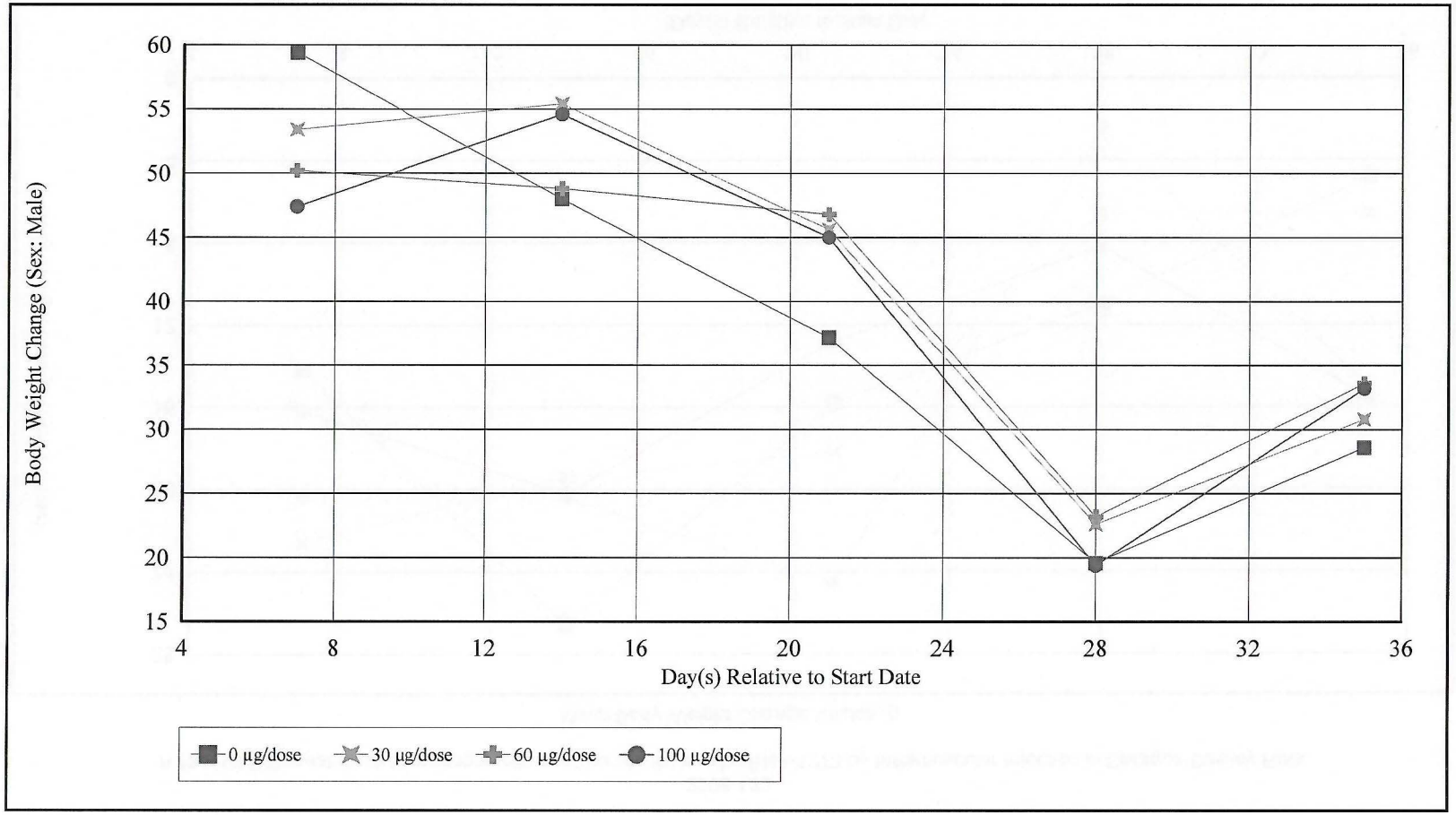


Figure 2
Mean Body Weight Change Values

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Mean Body Weight Change Values, g



2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Mean Body Weight Change Values, g

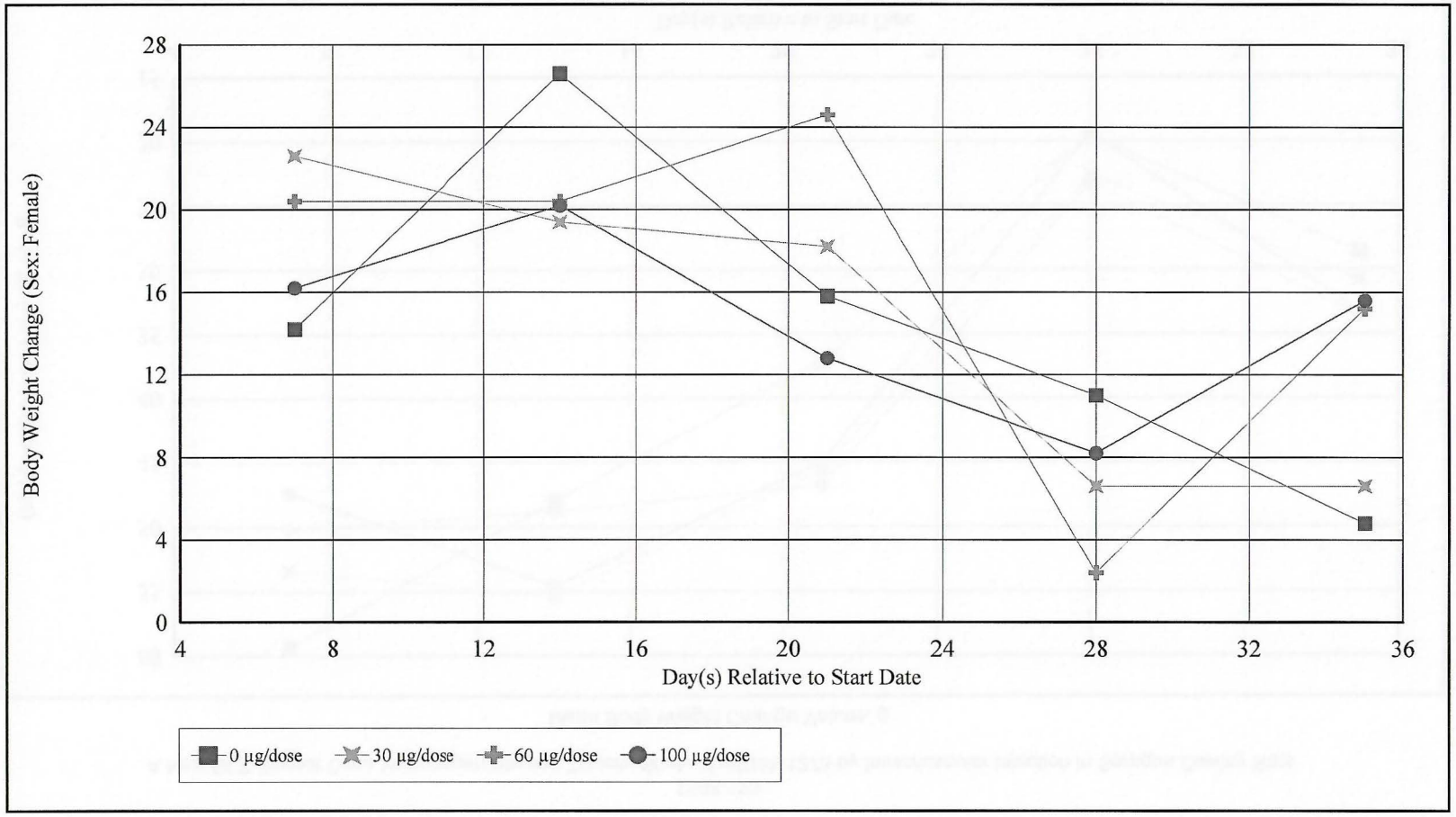


Table 1
Summary of Detailed Clinical Observations

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Summary of Detailed Clinical Observations

Observation Type: All Types	Male			
From Day 1 (Start Date) to 35 (Start Date)	0 µg/dose	30 µg/dose	60 µg/dose	100 µg/dose
Total Number of Animals:	5	5	5	5
-EXTERNAL APPEARANCE				
Limb function impaired				
Number of Times Recorded	0	1	5	5
Number of Animals Affected	-	1	5	5
Material around eyes, Black				
Number of Times Recorded	0	0	1	0
Number of Animals Affected	-	-	1	-
Material around nose, Red				
Number of Times Recorded	0	0	1	2
Number of Animals Affected	-	-	1	2
Thin				
Number of Times Recorded	0	0	6	0
Number of Animals Affected	-	-	2	-
-PELAGE/SKIN				
Abrasion(s)				
Number of Times Recorded	0	0	2	0
Number of Animals Affected	-	-	2	-
Edema				
Number of Times Recorded	0	10	30	29
Number of Animals Affected	-	5	5	5
Hair sparse				
Number of Times Recorded	0	5	39	0
Number of Animals Affected	-	1	3	-
Scabbed area				
Number of Times Recorded	0	0	20	6
Number of Animals Affected	-	-	3	1
Skin discolored, Brown				
Number of Times Recorded	0	0	2	0
Number of Animals Affected	-	-	1	-
Skin discolored, Red				
Number of Times Recorded	0	0	0	6
Number of Animals Affected	-	-	-	1
Unkempt appearance				
Number of Times Recorded	0	0	0	9
Number of Animals Affected	-	-	-	3

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Summary of Detailed Clinical Observations

Observation Type: All Types From Day 1 (Start Date) to 35 (Start Date)	Female 0 µg/dose	30 µg/dose	60 µg/dose	100 µg/dose
Total Number of Animals:	5	5	5	5
-EXTERNAL APPEARANCE				
Limb function impaired				
Number of Times Recorded	0	0	4	5
Number of Animals Affected	-	-	4	5
Material around eyes, Black				
Number of Times Recorded	0	0	0	0
Material around nose, Red				
Number of Times Recorded	0	0	0	0
Thin				
Number of Times Recorded	0	0	0	0
-PELAGE/SKIN				
Abrasion(s)				
Number of Times Recorded	0	0	0	0
Edema				
Number of Times Recorded	0	13	31	30
Number of Animals Affected	-	5	5	5
Hair sparse				
Number of Times Recorded	6	24	72	116
Number of Animals Affected	1	2	3	2
Scabbed area				
Number of Times Recorded	0	0	0	0
Skin discolored, Brown				
Number of Times Recorded	0	0	0	0
Skin discolored, Red				
Number of Times Recorded	0	0	0	0
Unkempt appearance				
Number of Times Recorded	0	0	0	0

Table 2
Summary of Body Weight Values

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Summary of Body Weight Values

Body Weight (g)

Sex: Male Day(s) Relative to Start Date		0 µg/dose	30 µg/dose	60 µg/dose	100 µg/dose
-1	Mean	181.0	184.6	182.2	182.8
	SD	10.27	6.54	8.17	10.80
	N	5	5	5	5
7	Mean	240.4	238.0	232.4	230.2
	SD	9.50	11.02	10.53	14.87
	N	5	5	5	5
14	Mean	288.4	293.4	281.2	284.8
	SD	10.95	17.62	7.05	20.75
	N	5	5	5	5
21	Mean	325.6	339.0	328.0	329.8
	SD	13.97	22.75	11.18	22.35
	N	5	5	5	5
28	Mean	345.2	361.6	351.2	349.2
	SD	12.77	24.47	12.70	22.54
	N	5	5	5	5

Anova & Dunnett

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Summary of Body Weight Values

Body Weight (g)

Sex: Male Day(s) Relative to Start Date		0 µg/dose	30 µg/dose	60 µg/dose	100 µg/dose
35	Mean	373.8	392.4	384.8	382.4
	SD	15.25	26.54	18.05	21.90
	N	5	5	5	5

Anova & Dunnett

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Summary of Body Weight Values

Body Weight (g)

Sex: Female Day(s) Relative to Start Date		0 µg/dose	30 µg/dose	60 µg/dose	100 µg/dose
-1	Mean	203.6	209.4	213.6	206.2
	SD	8.73	4.93	8.08	3.49
	N	5	5	5	5
7	Mean	217.8	232.0	234.0	222.4
	SD	12.11	6.16	15.35	6.66
	N	5	5	5	5
14	Mean	244.4	251.4	254.4	242.6
	SD	17.46	8.62	15.71	8.29
	N	5	5	5	5
21	Mean	260.2	269.6	279.0	255.4
	SD	20.72	15.19	22.30	10.14
	N	5	5	5	5
28	Mean	271.2	276.2	281.4	263.6
	SD	26.34	8.93	18.77	14.38
	N	5	5	5	5

Anova & Dunnett

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Summary of Body Weight Values

Body Weight (g)

Sex: Female Day(s) Relative to Start Date		0 µg/dose	30 µg/dose	60 µg/dose	100 µg/dose
35	Mean	276.0	282.8	296.6	279.2
	SD	20.06	15.93	30.39	21.18
	N	5	5	5	5

Anova & Dunnett

Table 3
Summary of Body Weight Change Values

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Summary of Body Weight Change Values, g

Body Weight Change

Sex: Male Day(s) Relative to Start Date		0 µg/dose	30 µg/dose	60 µg/dose	100 µg/dose
-1 → 7	Mean	59.4	53.4	50.2 a	47.4 b
	SD	2.19	5.59	2.59	5.86
	N	5	5	5	5
7 → 14	Mean	48.0	55.4	48.8	54.6
	SD	5.48	10.14	8.29	6.07
	N	5	5	5	5
14 → 21	Mean	37.2	45.6	46.8	45.0
	SD	8.01	5.98	12.58	5.24
	N	5	5	5	5
21 → 28	Mean	19.6	22.6	23.2	19.4
	SD	4.83	5.59	3.70	5.81
	N	5	5	5	5
28 → 35	Mean	28.6	30.8	33.6	33.2
	SD	5.50	5.76	8.65	5.26
	N	5	5	5	5

Anova & Dunnett: a = $p < 0.05$; b = $p < 0.01$

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Summary of Body Weight Change Values, g

Body Weight Change

Sex: Female Day(s) Relative to Start Date		0 µg/dose	30 µg/dose	60 µg/dose	100 µg/dose
-1 → 7	Mean	14.2	22.6	20.4	16.2
	SD	4.97	6.02	7.57	5.97
	N	5	5	5	5
7 → 14	Mean	26.6	19.4	20.4	20.2
	SD	9.32	3.44	7.20	5.50
	N	5	5	5	5
14 → 21	Mean	15.8	18.2	24.6	12.8
	SD	3.63	7.79	7.54	9.01
	N	5	5	5	5
21 → 28	Mean	11.0	6.6	2.4	8.2
	SD	9.14	7.80	9.56	6.61
	N	5	5	5	5
28 → 35	Mean	4.8	6.6	15.2	15.6
	SD	11.45	8.79	13.33	7.44
	N	5	5	5	5

Anova & Dunnett

Appendix 1
Deviation, Amended Protocol, and Protocol

DEVIATION

The deviation that occurred during the study was authorized/acknowledged by the Study Director, assessed for impact, and documented in the study records. The following unplanned protocol deviation was not considered to have impacted the overall integrity of the study or the interpretation of the study results and conclusions.

Laboratory Evaluations

- The serum aliquot 2 samples were shipped to PPD at the Vaccine Research Center, Bethesda, Maryland. The protocol had specified shipment directly to the Principal Investigator PPD There was no impact on study.

[redacted]

PROTOCOL AMENDMENT No. 03

Testing Facility Study No. 2308-123

A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Status: non-GLP

SPONSOR:
Moderna TX, Inc.
200 Technology Square
Cambridge, MA 02139
USA

TESTING FACILITY:
[redacted]

SUMMARY OF CHANGES AND JUSTIFICATIONS

Note: When applicable, additions are indicated in **bold underlined** text and deletions are indicated in ~~**bold strikethrough**~~ text in the affected sections of the document.

Item or Section(s)	Justification
Amendment 1	**Effective Date of Change: 12 Feb 2020**
9.1. Administration of Test Article(s)	Removal of the requirement for isoflurane sedation prior to dose based upon a small pilot dose conducted at the Testing Facility increasing the IACUC accepted dose volume for non-sedated intramuscular injections in rats. Removal of marking a dot at the site of needle insertion to allow for better assessment of any changes at the injection site.
Attachment B	Correction to shipment schedule as sample analysis is not required following each collection.
Amendment 2	**Effective Date of Change: 11 Mar 2020**
4.Responsible Personnel 12.3. Serum Analysis for ELISA Assay	Identification of the Principal Investigator at the Sponsor-designated laboratory for ELISA Assay Analysis. Removal of the Principal Investigator at Moderna as any analysis done at their laboratories will be exploratory. Clarification that there will be a full report provided by the Sponsor-designated laboratory.
5.2. Test Article Identification. 5.3. Control Article Identification	Addition of Test and Control Article information based upon receipt of Certificate of Analysis.
12. Serum Collection for ELISA Assay	Clarification of collection interval.
Attachment B	Addition of the shipment address for the Sponsor-designated laboratory for ELISA Assay Analysis; clarification of which samples will be shipped to each laboratory.
Amendment 3	**Effective Date of Change: 21 Apr 2020**
4. Responsible Personnel 12.3. Serum Analysis for ELISA Assay	Clarification that only the ELISA Assay Analysis raw data and interpretation statements will be included in the final report instead of a full sub-report.

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1. OBJECTIVE(S)

The objective of this study is to characterize the immunogenic response and potential toxicity of mRNA-1273 when administered via intramuscular injection on Days 1 and 22 to Sprague Dawley rats.

2. PROPOSED STUDY SCHEDULE

Actual dates will be included in the Final Report.

Experimental Starting/Animal Arrival Date:	10 Feb 2020 (First date of study-specific data collection)
Initiation of Dosing:	13 Feb 2020
Completion of In-life:	18 Mar 2020 (Last date of necropsy)
Experimental Completion Date:	To be included in the Final Report (Last date on which data are collected)
Draft Report:	6 weeks (Following last day of necropsy or last sample analyzed)
Final Report:	The date on which the Study Director signs the final report.

3. SPONSOR

Role	Name/Contact Information
Sponsor Representative	PPD ALM Address: The same as cited for Sponsor Tel PPD E-mail: PPD
Alternate Sponsor Representative	PPD MS Address: The same as cited for Sponsor Tel PPD E-mail: PPD

4. RESPONSIBLE PERSONNEL

Role/Phase	Name/Contact Information
Study Director	PPD BS Tel PPD E-m PPD
Alternate Contact	PPD Tel PPD E-mail PPD
Testing Facility Management	PPD Tel PPD

Role/Phase	Name/Contact Information
	E-mail PPD
Individual Scientist (IS)	
Clinical Pathologist	Will be included in the Final Report
Principal Investigator (PI)	
ELISA Assay	PPD PhD Tel PPD E-mail: PPD

Each IS and PI are required to report all deviations or other circumstances that could affect the quality or integrity of the study to the Study Director in a timely manner for authorization/acknowledgement. Each IS ~~and PI~~ will provide a report addressing their assigned phase of the study, which will be included as an appendix to the Final Report.

The IS Phase Report will include the following:

- A listing of critical computerized systems used in the conduct and/or interpretation of the assigned study phase

The PI Phase Report will include the following**, if applicable**:

- The archive site for all records, samples, specimens and reports generated from the phase or segment (alternatively, details regarding the retention of the materials may be provided to the Study Director for inclusion in the Final Report), if applicable
- A listing of critical computerized systems used in the conduct and/or interpretation of the assigned study phase

5. TEST MATERIALS

5.1. Test Article Characterization

A Certificate of Analysis or equivalent documentation will be provided for inclusion in the Final Report (if available).

5.2. Test Article Identification

Identification:	mRNA-1273
Alternate Identification:	No alternate ID
Moderna Lot No.:	8520100101
Expiration/Retest Date[a]:	07Aug2020
Physical Description:	White to off-white dispersion. Essentially free of particulates.
Purity:	80%
Correction Factor:	None
Concentration[b]:	0.5 mg/mL

Storage Conditions:	Frozen (-60 to -90°C)
Provided by:	Sponsor
Test Article Contact	PPD Tel: PPD E-mail: PPD

[a] The Study Director should be informed in the event that the Sponsor has updated information (e.g., retest or stability data) that could affect the validity of the study, during or after its completion, then the Study Director should be informed.

[b] Test Article formulation preparation will be based on the actual Test Article stock concentration listed in the Summary of Analysis.

5.3. Control Article Identification

	Control Article
Identification:	Tris/Sucrose Buffer
Alternate Identification:	No alternate ID
Batch/Lot No.:	Details will be documented in the raw data and specified in the Study Report
Expiration/Retest Date:	Details will be documented in the raw data and specified in the Study Report
Physical Description:	Details will be documented in the raw data and specified in the Study Report
Storage Conditions:	Refrigerated (2 to 8°C)
Provided by:	Sponsor
Characterization:	The Sponsor will provide documentation on the strength, purity, composition, stability, and other pertinent information on each batch of control article, unless otherwise noted.

5.4. Reserve Samples

No reserve sample will be collected.

5.5. Test Article Inventory and Disposition

Records of the receipt, distribution, storage, and disposition of test materials (including empty containers of Sponsor-provided materials) will be maintained until study finalization.

All unused Sponsor-supplied bulk test materials, with the exception of reserve samples, will be returned to the Sponsor following issuance of the Draft Report unless otherwise requested (documentation will be retained in the study record). An earlier shipment of these materials may also be requested and authorized by the Study Director and Sponsor. See Attachment A for shipping details.

5.6. Safety

A Safety Data Sheet (SDS), or equivalent documentation, will be provided by the Sponsor (if available). It is the responsibility of the Sponsor to notify the Testing Facility of any special handling requirements of the test article. Otherwise routine safety precautions will be followed. Appropriate gloves, safety glasses and arm covers will be worn by individuals working with neat test material(s) or formulations.

6. DOSE FORMULATION AND ANALYSIS

6.1. Preparation of Formulations

Dose formulations will be divided into aliquots where required to allow to be dispensed on each dosing occasion.

Preparation Details

Dose Formulation	Frequency of Preparation	Storage Conditions
Control Article	On each day of dosing	Refrigerated (2 to 8°C)
Test Article	On each day of dosing[a]	Room Temperature (≤ 4 hours) Or Refrigerated (2-8°C, ≤ 8 hours)

[a] Test Article formulation preparation will be based on the actual Test Article stock concentration listed in the Summary of Analysis.

Any residual volumes from each dosing occasion will be retained under Frozen (-60 to -90°C) conditions unless otherwise requested by the Study Director.

6.2. Preparation Details

Dosing formulations will be prepared freshly on the day of dosing according to the procedure described in Section 6.2.2. at appropriate concentrations to meet dose level requirements.

6.2.1. Preparation of Control Article

Dose formulation preparations will be performed under a Biological safety cabinet using aseptic procedures.

The Control Article, consisting of 10.7 mM Sodium Acetate, 20 mM Tris and 8.7% (w/v) sucrose, will be dispensed on the day of each dose (Days 1 and 22) for administration to Group 1 control animals and will be used as required to dilute the bulk Test Article for administration to Groups 2 to 4 animals. The aliquots will be stored under refrigerated conditions set to maintain 2-8°C until use. Refrigerated aliquots will be equilibrated to room temperature for at least 30 minutes prior to the start of dosing and used with 4 hours of being brought to room temperature. Any residual volumes will be retained, but not reused.

6.2.2. Preparation of Test Article Dose Formulation

Dose formulation preparations will be performed under a biological safety cabinet using sterile aseptic procedures.

The bulk Test Article stock will be removed from the freezer and allowed to thaw at room temperature for approximately 1 hour before dose formulation preparation on the day of each dose (Days 1 and 22). When possible, bulk test article in each stock vial will be used only once.

The dosing formulations will be prepared by diluting the appropriate bulk Test Article with the Control Article as necessary to the target concentration for administration and should not be filtered. The storage of prepared dose formulations should not exceed 4 hours at room

temperature or 8 hours at refrigerated conditions from the time of preparation to the dose administration. If the dosing formulations are stored refrigerated (2-8°C), they will be used for dose administration within 4 hours of being brought to room temperature. Refrigerated dose formulations will be equilibrated to room temperature for at least 30 minutes prior to the start of dosing. The formulations will NOT be vortexed or sonicated but may be gently swirled to reach visual homogeneity during formulation. Stock solution vials will be used only on the day of dose formulation preparation once thawed and will not be used on subsequent days.

Any residual volumes of formulated Test Article will be stored in a freezer set to maintain -60 to -90°C and discarded prior to report finalization as directed by the Sponsor Representative or Study Director.

6.3. Sample Collection and Analysis

Dose formulation samples will not be collected.

7. TEST SYSTEM

Species:	Rat
Strain:	CD® [Crl:CD®(SD)]
Condition:	Purpose-bred, naïve
Source:	[redacted]
	The source used will be documented in the raw data.
Number Ordered:	
Male:	22
Female:	22
Number on Study:	
Male:	20
Female:	20
Expected Age at Arrival:	Ordered to be 6 weeks of age at arrival
Expected Weight at Arrival:	Commensurate with age; males will generally weigh 97 to 335g and females will generally weigh 89 to 245g as measured within 3 days of arrival. The actual range will be documented in the data.

The actual age and weight of animals received will be listed in the Final Report.

7.1. Animal Identification

Method: Each animal will be assigned an animal number to be used in Provantis™ and will be implanted with a microchip bearing a unique identification number. The individual animal number, implant number, and the Testing Facility study number will comprise a unique identification for each animal. The animal cage will be identified by the study number, animal number, group number, and sex.

7.2. Environmental Acclimation

Duration: At least 3 days

Details: During this acclimation period, all animals will be observed daily for any clinical signs of disease, and all animals will be given a detailed clinical examination within 3 days of the first dose administration.

7.3. Selection, Assignment, Replacement and Disposition of Animals

Assignment and Randomization: Animals will be randomly assigned to groups upon receipt. Males and females will be randomized separately.

All animals with any evidence of disease or physical abnormalities will not be selected for study.

Replacement: Before the initiation of dosing, any assigned animals considered unsuitable for use in the study will be replaced by alternate animals maintained under the same environmental conditions.

After initiation of dosing, study animals may be replaced during the replacement period with alternate animals in the event of accidental injury, non-test article-related health issues, or similar circumstances. Any data generated will not be included in the report unless deemed appropriate by the Study Director.

Alternate animals may be used as replacements per Testing Facility SOP.

Disposition: Extra animals obtained for this study, but not placed on study will be either transferred to a Testing Facility stock or training colony or euthanized and discarded.

The disposition of all animals will be documented in the study records.

8. HUSBANDRY

8.1. Housing

Housing:	Pair-housed, when possible (animals may be housed 2 to 3/cage during acclimation and in-life depending on study design). Housing set-up is as specified in the USDA Animal Welfare Act (9 CFR, Parts 1, 2 and 3) and as described in the *Guide for the Care and Use of Laboratory Animals*. Animals will be separated during designated procedures/activities or will be separated as required for monitoring and/or health purposes, as deemed appropriate by Study Director and/or Clinical Veterinarian.
Caging:	Solid bottom cages with nonaromatic bedding. The bedding will be from an approved supplier and documented in the study data.

8.2. Animal Enrichment

Supplemental Enrichment:	Animal enrichment will be provided according to Testing Facility SOP.

8.3. Environmental Conditions

Temperature and Humidity:	Temperature and humidity will be maintained according to Testing Facility SOP.
Lighting:	Fluorescent lighting will be provided via an automatic timer for approximately 12 hours per day. On occasion, the dark cycle may be interrupted intermittently due to study-related activities.

8.4. Food

Diet:	The basal diet will be block Lab Diet® Certified Rodent Diet #5002, PMI Nutrition International, Inc.
Frequency:	Ad libitum, except during designated procedures
Analysis:	Results of analysis for nutritional components and environmental contaminants are provided by the supplier and are on file at the Testing Facility. There are no known contaminants in the food that would interfere with this study.

8.5. Water

Type:	Tap water

Frequency: Supplied ad libitum to all animals via an automatic water system unless otherwise indicated.

Analysis: Periodic analysis of the water is performed per Testing Facility SOP and results of these analyses are on file at the Testing Facility. It is considered that there are no known contaminants in the water that would interfere with the outcome of the study.

8.6. Veterinary Care

Veterinary care will be available throughout the course of the study and animals will be examined by the veterinary staff as warranted by clinical signs or other changes. In the event that animals show signs of illness or distress, the responsible veterinarian may make initial recommendations about treatment of the animal(s) and/or alteration of study procedures, which must be approved by the Study Director (or scientific designee). Treatment of the animal(s) for minor injuries or ailments may be approved without prior consultation with the Sponsor representative when such treatment does not impact fulfillment of the study objectives. If the condition of the animal(s) warrants significant therapeutic intervention or alterations in study procedures, the Sponsor representative will be contacted, when possible, to discuss appropriate action. If the condition of the animal(s) is such that emergency measures must be taken, the Study Director (or scientific designee) and/or veterinarian will attempt to consult with the Sponsor representative prior to responding to the medical crisis, but the Study Director (or scientific designee) and/or veterinarian has authority to act immediately at his/her discretion to alleviate suffering. The Sponsor representative will be fully informed of any such events.

9. EXPERIMENTAL DESIGN

Group No.	Test Material	Dose Level (µg/dose)	Dose Volume (mL/dose)	Dose Concentration (µg/mL)	Main Study	
					No. of Males	No. of Females
1	Control Article	0	0.2	0	5	5
2	mRNA-1273	30		150	5	5
3		60		300	5	5
4		100		500	5	5

No. = Number

9.1. Administration of Test Article(s)

Dose Route: Intramuscular injection

Frequency/Duration: The test article and control article will be administered once on Days 1 and 22.

Special Requirement: Under no circumstances will the dose formulations be subjected to vortexing and vigorously shaking to avoid disruption of the Test Article. Before withdrawing a dose formulation into syringes, the dose formulation container will be gently swirled to achieve homogeneity and

this step will be documented. The dosing will be conducted in a group number sequence order from Group 1 through Group 4, to minimize any potential risk of Test Article cross-contamination. Personal protective equipment (PPE) used in dosing will be changed between groups. Refrigerated dose formulations will be equilibrated to room temperature for at least 30 minutes prior to the start of dosing.

Details: The injection site areas and surrounding skin will be shaved free of hair at least 48 hours prior to dose administration. Doses will be administered via bolus intramuscular injection into one of the quadriceps (hind leg, thigh). Isoflurane inhalation may be used, if necessary (i.e. difficult animal to dose), in accordance with Testing Facility SOP. A unique site will be used for each injection (left quadricep on Day 1, right quadricep on Day 22).

Care will be taken to ensure that injection(s) are in the appropriate part of the muscle. The needle will be inserted perpendicular to the skin surface. The location of the injection site will be documented for each dose. In addition, each injection site will be marked with a larger circle for the purposes of erythema and swelling evaluation. Each injection site will be remarked at least once weekly and prior to necropsy.

10. IN-LIFE PROCEDURES, OBSERVATIONS, AND MEASUREMENTS

Standard In-life Assessments

Parameter	Population(s)	Frequency (minimum required)	Comments
Mortality/Cageside Observations	All surviving animals	At least twice daily (morning and afternoon) beginning upon arrival through termination/release.[a,b]	Animals will be observed within their cage unless necessary for identification or confirmation of possible findings. Animals will be observed for morbidity, mortality, injury, and availability of food and water. Any animals in poor health will be identified for further monitoring and possible euthanasia.

Parameter	Population(s)	Frequency (minimum required)	Comments
Detailed Clinical Observations	All animals	Daily; from at least Week -1 and throughout the study.[c]	Animals are removed from the cage. Observations will include, but will not be limited to, evaluation of the skin, fur, eyes, ears, nose, oral cavity, thorax, abdomen, external genitalia, limbs and feet, respiratory and circulatory effects, autonomic effects such as salivation, nervous system effects including tremors, convulsions, reactivity to handling, and unusual behavior.
Individual Body Weight	All animals	Within 3 days of arrival, Day -1, and once weekly throughout the study.	Not collected from animals found dead.
Injection Site Observations	All animals	Immediately post dose, 6 hours and 24 hours post dose	

[a] Procedures on alternate animals will be conducted per Testing Facility SOP.
[b] Except on days of receipt and necropsy where frequency will be at least once daily.
[c] For observations that cannot be attributed to an individual animal due to social housing (e.g., watery feces), the observation will be noted to each animal in the socialized group.

11. CLINICAL PATHOLOGY

11.1. Sample Collection

Clinical Pathology Sample Collection

Group Nos.	Time Point(s)	Hematology	Clinical Chemistry
All animals	Day 23 (24 hours post the last dose)	X	X
Unscheduled Euthanasia (when possible)	See the Unscheduled Euthanasia section of this protocol.		

Volume (mL)[a]:	NA	0.5 mL	0.8 mL
Fasting Required:	Free access to drinking water but will be fasted overnight (at least 8 hours) prior to blood collection.		
Anticoagulant:	NA	K_2EDTA	Serum Gel Separator
Special Requirements:	NA	NA	NA
Processing:	NA	None	Serum

X = Sample to be collected; NA = Not applicable
[a] Additional blood samples may be obtained (e.g. due to sample quality) if permissible sampling frequency and blood volume are not exceeded.

Blood Sample Collection Method: Sublingual, or another suitable vein

Blood Sample Special Instructions: The blood will be collected in dose group order, to minimize any potential risk of cross-contamination.

The following clinical pathology tests will be conducted on available samples and the data will be interpreted by a Clinical Pathologist.

11.2. Hematology

Hematology Parameters

Leukocyte count (total and absolute differential)	Mean corpuscular hemoglobin (calculated)
Erythrocyte count	Mean corpuscular volume
Hemoglobin	Mean corpuscular hemoglobin concentration (calculated)
Hematocrit	RDW
Absolute reticulocytes	Platelet count
	Blood smear (preserve and stain)[a]

[a] Blood smear review may be performed on select animals per Testing Facility SOP.

11.3. Clinical Chemistry

Clinical Chemistry Parameters

Alkaline phosphatase	Globulin and A/G (albumin/globulin) ratio (calculated)
Total bilirubin (with direct bilirubin if total bilirubin exceeds 1 mg/dL)	Glucose
	Total cholesterol
Aspartate aminotransferase	Triglycerides
Alanine aminotransferase	Electrolytes (sodium, potassium, chloride)
Urea nitrogen	Calcium
Creatinine	Phosphorus
Total protein	
Albumin	

12. SERUM COLLECTION FOR ELISA ASSAY

12.1. Sample Collection

Serum Collection for ELISA Assay

	Collection Intervals	
Group Nos.	**Predose on Day 1**	**Day 35**
1-4	X	X

X = Sample to be collected

Method/Comments: Sublingual or other suitable vein

Volume (mL): 0.5 mL

Anticoagulant: Serum Separator, non-additive; barrier free

Whole Blood Storage: Ambient and allowed to clot until centrifuged.

Processing:	Serum, Two aliquots of approximately equal volume
Final Storage Temperature:	Frozen (-60 to -90°C) Serum samples will be placed in frozen (-60 to -90°C) storage within 60 minutes of collection. The samples in aliquot tubes will be frozen immediately over dry ice.

12.2. Serum Shipment

Additional Container Label Requirements:	Study number, animal number, matrix of sample, interval and timepoint, analysis type, and aliquot number.
Bioanalytical Sample Shipping Contact:	All samples to be analyzed will be shipped to the designated Test Site, see Attachment B for shipping details.

12.3. Serum Analysis for ELISA Assay

Analysis Performed By:	ELISA assay of the serum samples will be performed by the Sponsor-designated laboratory, NIH. The samples shipped to the Sponsor's laboratory will be for possible future exploratory analysis.
Reporting:	~~**A Report will be prepared by the Sponsor-designated laboratory and**~~ **An interpretation of the data and the raw data itself will be** submitted to the Testing Facility for inclusion as an appendix in the main study Final Report. If future exploratory analysis does occur for the samples at the Sponsor's laboratory; this analysis will be outside the scope of this study and therefore not included in the Final Report.

13. TERMINAL PROCEDURES

Terminal procedures are summarized in the following tables:

Terminal Procedures

Group No.	Necropsy Procedures			Histology Processing	Microscopic Evaluation
	Necropsy	Tissue Collection	Organ Weights		
Found dead or unscheduled euthanasia	X	X	NA	NA	NA

Terminal Procedure Tables Footnotes:

X = Procedure to be conducted; NA = Not applicable.
"Histology Processing" = embedded in paraffin, sectioned, mounted on glass slides, and stained with hematoxylin and eosin.

13.1. Method of Euthanasia

Euthanasia will be by carbon dioxide inhalation followed by a Testing Facility SOP approved method to ensure death, e.g. exsanguination.

13.2. Unscheduled Euthanasia

Moribund animals will be subject to Testing Facility SOP criteria and procedures. If possible, the samples below will be collected from animals euthanized early, following veterinary consultation. A veterinary consultation is not required if the samples are collected following anesthesia or euthanasia. Blood collection methods utilized for animals euthanized early may include suitable methods other than those presented in the respective blood collection section(s) of this protocol.

Sample Type	Groups	Volume	Anticoagulant
Hematology	1-4	0.5 mL	K_2EDTA
Clinical Chemistry		0.8 mL	Serum Gel Separator
Serum (ELISA Assay)		0.5 mL	Serum Separator non-additive; barrier free

Necropsy examinations will be performed 7 days a week. Animals that are found dead or euthanized early after regular working hours will be refrigerated and necropsies performed at the start of the next day.

13.3. Scheduled Euthanasia

Animals surviving until study termination will be euthanized by the methods described above and discarded without any further evaluation.

13.4. Necropsy

Animals euthanized early or found dead as detailed in the Terminal Procedures table will be subjected to a complete necropsy examination, which will include evaluation of the carcass and musculoskeletal system; all external surfaces and orifices; cranial cavity and external surfaces of the brain; and thoracic, abdominal, and pelvic cavities with their associated organs and tissues.

All animals will be examined carefully for external abnormalities including palpable masses.

Images may be generated for illustration of or consultation on gross observations. These images will not be used for data generation or interpretation and will not be archived or included in the Final Report.

14. STATISTICAL ANALYSIS

The following presents a proposed statistical analysis plan. Statistical plans are data dependent, and this analysis plan may require modification if standard data assumptions are not met. Other conceptually equivalent statistical testing routines may also be employed at the discretion of the statistician. The actual analysis plan will be documented in the Final Report.

The raw data will be tabulated within each time interval, and the appropriate summary statistics will be calculated for each endpoint, sex, and group. For each endpoint, treatment groups will be compared to the control group using the analysis outlined below. Data for some endpoints, as indicated, will be transformed by either a log or rank transformation prior to conducting the specified analysis. Statistical Comparisons

Control Group	Comparison Group(s)
1	2, 3, 4

14.1. Group Pair-wise Comparison (General ANOVA)

Endpoints:
- Body Weight and Body Weight Change
- Hematology
- Clinical Chemistry

Description: If the control group has a sample size less than 3, no inferential statistics will be calculated. If a particular endpoint and/or parameter within a given collection interval have the same value across all experimental units, no inferential statistics will be calculated.

Otherwise, for endpoints and/or parameters where all groups with sample sizes of 3 or greater are included, the system will test the normality of the residuals and homogeneity of variances to see whether the data is approximately normal or whether a log transformation or rank transformation should be used. Levene's test will be used to assess homogeneity of group variances and Shapiro-Wilk's test will be used to test the normality of the residuals.[1,2]

On the raw data, if Levene's test is not significant ($p \geq 0.01$) and Shapiro-Wilk's test is not significant ($p \geq 0.01$), then a normal distribution will be used. If either the Levene's test is significant ($p < 0.01$) or Shapiro-Wilk's test is significant ($p < 0.01$), normality and homogeneity of variances will be tested with a log transformation used on the data.

On the log transformed data, if Levene's test is not significant ($p \geq 0.01$) and Shapiro-Wilk's test is not significant ($p \geq 0.01$), then a log normal distribution will be used. If either the Levene's test is significant ($p < 0.01$) or Shapiro-Wilk's test is significant ($p < 0.01$), then a rank transformation will be used on the data.

Raw or Log Transformed Data:

A one-way analysis of variance will be used to test each endpoint for the effects of treatment.[3]

If the treatment effect is significant ($p < 0.05$), linear contrasts will be constructed for a Dunnett's pair-wise comparison of treatment groups as described above.

Rank Transformed Data:

A Kruskal-Wallis test will be used to test each endpoint for the effects of treatment.

If the treatment effect is significant ($p<0.05$), a non-parametric Dunn's pair-wise comparison test of each treatment group with the control group.

Results of all pair-wise comparisons will be reported at the 0.05 and 0.01 significance levels. All endpoints will be analyzed using two-tailed tests unless indicated otherwise.

15. COMPUTERIZED SYSTEMS

The actual systems and versions used will be documented in the Final Report.

Computer System Name	Description
CCI	Collection of Part 11 compliant signature(s).
	A comprehensive laboratory information management system used to manage data, including but not limited to: instrumentation, test articles, standards, and samples.
	Electronic notebook and data collection system for veterinary communications, observations, and treatments.
	Electronic documentation management of deviation events and Corrective and Preventative Actions (CAPA).
	Client-server, Oracle-based system used for electronic documentation and data management from compound receipt through reporting.
	An integrated system of software products that enables a user to perform data entry, retrieval, data management, reporting, graphics, statistical analysis, and applications development.
	Environmental monitoring, alarming, and reporting applications.

16. REGULATORY COMPLIANCE

This study is not within the scope of regulations governing the conduct of nonclinical laboratory studies and is not intended to comply with such regulations.

17. AMENDMENTS AND DEVIATIONS

Changes to the approved protocol shall be made in the form of an amendment, which will be signed and dated by the Study Director. Every reasonable effort will be made to discuss any necessary protocol changes in advance with the Sponsor. The Study Director will notify the Sponsor of deviations that may result in a significant impact on the study as soon as possible.

18. RETENTION AND DISPOSITION OF RECORDS, SAMPLES, AND SPECIMENS

All study-specific raw data, electronic data, documentation, protocol, retained samples and specimens, and Interim (if applicable) and Final Reports will be archived per Testing Facility SOP. All retained materials will be archived at [redacted] Laboratories-MWN, unless specified by the Sponsor. At least 1 year after issue of the Draft Report, the Sponsor will be contacted.

Samples for clinical pathology evaluations are discarded per Testing Facility SOP unless otherwise indicated in the table below.

Disposition of residual/retained analytical samples will be as described in the table below. See Attachment A for shipping details.

Disposition of Residual/Retained Samples

Sample Type	Disposition	Schedule
Dose Formulations	Archive	Samples will be maintained for a minimum of 6 months following issuance of the Draft Report or at an alternate time point prior to finalization as requested and authorized by the Study Director in consultation with the Sponsor Representative.

Records to be maintained will include, but will not be limited to, documentation and data for the following:

- Deviations, Protocol amendments, and Protocol
- Study schedule
- Study-related correspondence
- Test system receipt, health, and husbandry
- Test and control article receipt, identification, preparation, and analysis
- In-life measurements and observations
- Clinical pathology sample collection and evaluation
- Statistical analysis results

19. STUDY CLASSIFICATION

Study Category:	Pharmacology
Study Type:	Repeat Dose Toxicity
Study Design:	Parallel
Primary Treatment CAS Registry Number:	Insert from Sponsor Not Available
Primary Treatment Unique Ingredient ID:	Insert from Sponsor Not Available
Class of Compound:	mRNA in Lipid Nanoparticle
Administration Dose Form:	LNP dispersion

20. REPORTING

A comprehensive Draft Report will be prepared following completion of the study and will be finalized following consultation with the Sponsor. The report will include all information necessary to provide a complete and accurate description of the experimental methods and results and any circumstances that may have affected the quality or integrity of the study.

The Sponsor will receive an electronic version of the Final Report provided in Adobe Acrobat PDF format (hyperlinked and searchable at final). The PDF document will be created from native electronic files to the extent possible, including text and tables generated by the Testing Facility. Report components not available in native electronic files and/or original signature pages will be scanned and converted to PDF image files for incorporation.

Reports should be finalized within 6 months of issue of the Draft Report. If the Sponsor has not provided comments to the report within 6 months of draft issue, the report will be finalized by the Testing Facility unless other arrangements are made by the Sponsor.

20.1. SEND Datasets

At the request of the Sponsor, SEND datasets will be generated and provided outside the context of the Final Report. These datasets will not be subject to QA Audit nor will they be used as the basis for the Study Director interpretation of the study results. SEND datasets will be provided following the Final Report(s).

When work in support of this study is conducted at a Test Site (i.e., Bioanalysis, TK modeling, etc.), an electronic version of all data should be provided to Testing Facility.

21. JUSTIFICATIONS AND GUIDELINES

21.1. Justification of Test System and Number of Animals

The current state of scientific knowledge and the applicable guidelines cited in this Protocol do not provide acceptable alternatives, in vitro or otherwise, to the use of live animals to accomplish the purpose of this study. "The development of knowledge necessary for the improvement of the health and well-being of humans as well as other animals requires in vivo experimentation with a wide variety of animal species."[4] "Whole animals are essential in research and testing because they best reflect the dynamic interactions between the various cells, tissues, and organs comprising the human body."[5]

The rat is the usual rodent model used for evaluating the immunogenicity and toxicity of various classes of chemicals and for which there is a large historical database.[6]

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

21.2. Justification of Route and Dose Levels

The intramuscular route is the intended route of administration of this test article in humans.

Doses were selected based on the aggregate toxicity data from various rat toxicity studies conducted using this lipid nanoparticle formulation. The high dose of 100 ug/dose was selected because it is the maximum feasible dose based on the concentration of the test article and the maximum intramuscular dose volume permitted in a rat. This dose is expected to elicit minor clinical observations including transient erythema and edema at the injection site. The mid- (60 ug/dose) and low- (30 ug/dose) doses are expected to produce minimal effects

21.3. Guidelines for Study

The design of this study was based on the study objective(s), the overall product development strategy for the Test Article, and the following study design guidelines:

- ICH Harmonised Tripartite Guideline M3 (R2). *Guidance on Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals.*
- ICH Harmonised Tripartite Guideline S6 (R1). *Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals.*
- Note for Guidance on Preclinical Pharmacological and Toxicological Testing of Vaccines. The European Agency for the Evaluation of Medicinal Products, CPMP/SWP/465/95: Dec. 17, 1997.
- WHO guidelines on nonclinical evaluation of vaccines. World Health Organization, WHO Technical Report Series, No. 927, 2005.

22. ANIMAL WELFARE

This study will comply with all applicable sections of the Final Rules of the Animal Welfare Act regulations (Code of Federal Regulations, Title 9), the *Public Health Service Policy on Humane Care and Use of Laboratory Animals* from the Office of Laboratory Animal Welfare, and the *Guide for the Care and Use of Laboratory Animals* from the National Research Council.[7,8] The protocol and any amendments or procedures involving the care or use of animals in this study will be reviewed and approved by the Testing Facility Institutional Animal Care and Use Committee before the initiation of such procedures.

If an animal is determined to be in overt pain/distress or appears moribund and is beyond the point where recovery appears reasonable, the animal will be euthanized for humane reasons in accordance with the *American Veterinary Medical Association (AVMA) Guidelines on Euthanasia* and with the procedures outlined in the protocol.[9]

By approving this protocol, the Sponsor affirms that there are no acceptable non-animal alternatives for this study, that this study is required by a relevant government regulatory agency(ies) and that it does not unnecessarily duplicate any previous experiments.

22.1. Institutional Animal Care and Use Committee Approval

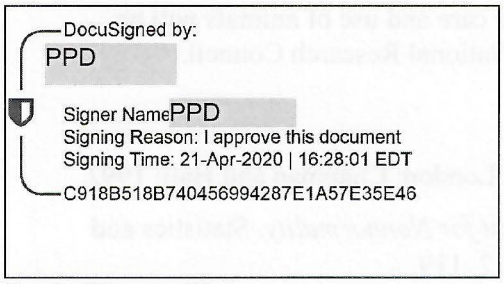
The protocol and any amendment(s) or procedures involving the care and use of animals in this study will be reviewed and approved by CR-MWN Institutional Animal Care and Use Committee (IACUC) before conduct. During the study, the care and use of animals will be conducted with guidance from the guidelines of the USA National Research Council.

23. REFERENCES

1. Milliken GA, Johnson DE. *Analysis of messy data*. London: Chapman and Hall; 1992.
2. Royston JP. *Approximating the Shapiro-Wilk W Test for Nonnormality*. Statistics and Computing 2. London: Chapman and Hall; 1992:117–119.
3. Zar JH. *Biostatistical Analysis*. 4th ed. New Jersey: Prentice Hall; 1999.
4. *Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training*, Federal Register, 1985 May 20; 50(97).
5. *Position Statement on the Use of Animals in Research*, 1993 Feb 26; NIH Guide 22(8).
6. *Guidance for Industry, Investigators, and Reviewers: Exploratory IND Studies.* US FDA Center for Drug Evaluation and Research (CDER), 2006 Jan.
7. Office of Laboratory Animal Welfare. *Public Health Services Policy on Humane Care and Use of Laboratory Animals*. Bethesda, MD: National Institutes of Health. Current edition.
8. National Research Council. *Guide for the Care and Use of Laboratory Animals*. Washington, DC: National Academy Press. Current edition.
9. American Veterinary Medical Association. *AVMA Guidelines on Euthanasia*. Current edition.

TESTING FACILITY APPROVAL

The signature below indicates that the Study Director approves the study protocol amendment.



Study Director/Date

SPONSOR APPROVAL

The protocol amendment was approved by the Sponsor by e-mail on the date designated below. The correspondence giving approval will be archived, as appropriate with other Sponsor communications.

21 Apr 2020
Date of Sponsor Approval

ATTACHMENT A

Tissue Weighing, Collection, Processing and Evaluation Table

Organ	Macroscopic Evaluation and Collection
Animal ID	X
Artery, aorta	X
Body cavity, nasal	X
Bone marrow, sternum	X
Bone marrow smear	X[a]
Bone, femur	X (1)
Bone, sternum	X
Brain	X
Epididymis	X (2)[b]
Esophagus	X
Eye	X (2)[b]
Ganglion, dorsal root, lumbar	X
Gland, adrenal	X (2)
Gland, clitoral	X (2)
Gland, lacrimal	X (2) (extra-orbital)
Gland, Harderian	X (2)
Gland, mammary	X
Gland, parathyroid	X (2)
Gland, pituitary	X
Gland, preputial	X (2)
Gland, prostate	X
Gland, salivary, submandibular	X (2)
Gland, salivary, sublingual	X (2)
Gland salivary, parotid	X (2)
Gland, seminal vesicle	X (2)
Gland, thyroid	X (2)
Gland, Zymbal's	X (2)
Gut-associated lymphoid tissue[c]	X
Heart	X
Joint, femorotibial	X (1)
Kidney	X (2)
Large intestine, cecum	X
Large intestine, colon	X
Large intestine, rectum	X
Larynx	X
Liver	X
Lung	X
Lymph node(s) draining administration site(s): Inguinal	X
Lymph node, mandibular	X (2)
Lymph node, mesenteric	X
Muscle, skeletal	X (2)

Organ	Macroscopic Evaluation and Collection
Nerve, optic	X (2)[b]
Nerve, sciatic	X (2)
Nerve, tibial	X (2)
Ovary	X (2)
Oviduct	X (2)
Pancreas	X
Site(s), administration	X
Skin	X
Small intestine, duodenum	X
Small intestine, ileum	X
Small intestine, jejunum	X
Spinal cord	X
Spleen	X
Stomach	X
Testis	X (2)[b]
Thymus	X
Tongue	X
Trachea	X
Ureter	X (2)
Urinary bladder	X
Uterus/Cervix	X
Vagina	X

X = Procedure to be conducted. - = Not applicable. (1) = one side. (2) = both sides.
Macroscopic abnormalities in the organs listed and in other organs will be sampled at necropsy, processed for histology and examined microscopically.

[a] Two bone marrow smears will be collected from the femur at scheduled and unscheduled necropsies (for possible examination). Smears will not be collected from animals that are found dead or from animals that were euthanized moribund and then stored in the refrigerator prior to necropsy. Bone marrow smears are allowed to air dry and are not fixed in formalin.

[b] Eyes and optic nerves are preserved in Davidson's fixative. Testes and epididymides are preserved in modified Davidson's fixative.

[c] From small intestine: Peyer's patch or solitary lymphoid follicle.

[d] Weigh with gland, thyroid.

ATTACHMENT B

Shipment of Samples and Study Records

Samples will be shipped on Monday through Wednesday for next day delivery for domestic shipments and expedited delivery for International shipments using the Conditions for Shipment(s) listed below.

Sample Matrix	Sample Type	Aliquot of Sample	Proposed Shipment	Conditions for Shipment	Recipient/Address
Serum	Serum for Possible Future Analysis	Aliquot 1	After the last collection interval	on dry ice Temperature monitor to be included in shipment	PPD Moderna TX, Inc. 200 Technology Square Cambridge, MA 02139 USA Tel PPD E-mail: PPD
Serum	Serum for ELISA Assay	Aliquot 2	After the last collection interval	on dry ice Temperature monitor to be included in shipment	PPD , PhD 2608 40 Convent Drive Bethesda MD 20892 Tel:PPD E-mail: PPD

[redacted]

[redacted]

FINAL PROTOCOL

Testing Facility Study No. 2308-123

A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Status: non-GLP

SPONSOR:
Moderna TX, Inc.
200 Technology Square
Cambridge, MA 02139
USA

TESTING FACILITY:

[redacted]

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1. OBJECTIVE(S)

The objective of this study is to characterize the immunogenic response and potential toxicity of mRNA-1273 when administered via intramuscular injection on Days 1 and 22 to Sprague Dawley rats.

2. PROPOSED STUDY SCHEDULE

Actual dates will be included in the Final Report.

Experimental Starting/Animal Arrival Date:	10 Feb 2020 (First date of study-specific data collection)
Initiation of Dosing:	13 Feb 2020
Completion of In-life:	18 Mar 2020 (Last date of necropsy)
Experimental Completion Date:	To be included in the Final Report (Last date on which data are collected)
Draft Report:	6 weeks (Following last day of necropsy or last sample analyzed)
Final Report:	The date on which the Study Director signs the final report.

3. SPONSOR

Role	Name/Contact Information
Sponsor Representative	PPD ALM Address: The same as cited for Sponsor Tel: PPD E-mail: PPD
Alternate Sponsor Representative	PPD MS Address: The same as cited for Sponsor Tel: PPD E-mail: PPD

4. RESPONSIBLE PERSONNEL

Role/Phase	Name/Contact Information
Study Director	PPD BS Tel: PPD E-m PPD
Alternate Contact	PPD , PhD PPD E-mail PPD
Testing Facility Management	PPD BS PPD

Role/Phase	Name/Contact Information
	E-mail: PPD
Individual Scientist (IS)	
Clinical Pathologist	Will be included in the Final Report
Principal Investigator (PI)	
ELISA Assay	PPD Tel: PPD E-mail PPD

Each IS and PI are required to report all deviations or other circumstances that could affect the quality or integrity of the study to the Study Director in a timely manner for authorization/acknowledgement. Each IS and PI will provide a report addressing their assigned phase of the study, which will be included as an appendix to the Final Report.

The IS Phase Report will include the following:

- A listing of critical computerized systems used in the conduct and/or interpretation of the assigned study phase

The PI Phase Report will include the following:

- The archive site for all records, samples, specimens and reports generated from the phase or segment (alternatively, details regarding the retention of the materials may be provided to the Study Director for inclusion in the Final Report), if applicable
- A listing of critical computerized systems used in the conduct and/or interpretation of the assigned study phase

5. TEST MATERIALS

5.1. Test Article Characterization

A Certificate of Analysis or equivalent documentation will be provided for inclusion in the Final Report (if available).

5.2. Test Article Identification

Identification:	mRNA-1273
Alternate Identification:	No alternate ID
Moderna Lot No.:	8520100101
Expiration/Retest Date[a]:	To be added by amendment
Physical Description:	White to off-white dispersion. Essentially free of particulates.
Purity:	To be added by amendment
Correction Factor:	None
Concentration[b]:	0.5 mg/mL

Storage Conditions:	Frozen (-60 to -90°C)
Provided by:	Sponsor
Test Article Contact:	PPD Tel PPD E-mail: PPD

[a] The Study Director should be informed in the event that the Sponsor has updated information (e.g., retest or stability data) that could affect the validity of the study, during or after its completion, then the Study Director should be informed.

[b] Test Article formulation preparation will be based on the actual Test Article stock concentration listed in the Summary of Analysis.

5.3. Control Article Identification

	Control Article
Identification:	Tris/Sucrose Buffer
Alternate Identification:	No alternate ID
Batch/Lot No.:	Details will be documented in the raw data and specified in the Study Report
Expiration/Retest Date:	Details will be documented in the raw data and specified in the Study Report
Physical Description:	Details will be documented in the raw data and specified in the Study Report
Storage Conditions:	Refrigerated (2 to 8°C)
Provided by:	Sponsor
Characterization:	The Sponsor will provide documentation on the strength, purity, composition, stability, and other pertinent information on each batch of control article, unless otherwise noted.

5.4. Reserve Samples

No reserve sample will be collected.

5.5. Test Article Inventory and Disposition

Records of the receipt, distribution, storage, and disposition of test materials (including empty containers of Sponsor-provided materials) will be maintained until study finalization.

All unused Sponsor-supplied bulk test materials, with the exception of reserve samples, will be returned to the Sponsor following issuance of the Draft Report unless otherwise requested (documentation will be retained in the study record). An earlier shipment of these materials may also be requested and authorized by the Study Director and Sponsor. See Attachment A for shipping details.

5.6. Safety

A Safety Data Sheet (SDS), or equivalent documentation, will be provided by the Sponsor (if available). It is the responsibility of the Sponsor to notify the Testing Facility of any special handling requirements of the test article. Otherwise routine safety precautions will be followed. Appropriate gloves, safety glasses and arm covers will be worn by individuals working with neat test material(s) or formulations.

6. DOSE FORMULATION AND ANALYSIS

6.1. Preparation of Formulations

Dose formulations will be divided into aliquots where required to allow to be dispensed on each dosing occasion.

Preparation Details

Dose Formulation	Frequency of Preparation	Storage Conditions
Control Article	On each day of dosing	Refrigerated (2 to 8°C)
Test Article	On each day of dosing[a]	Room Temperature (≤ 4 hours) Or Refrigerated (2-8°C, ≤ 8 hours)

[a] Test Article formulation preparation will be based on the actual Test Article stock concentration listed in the Summary of Analysis.

Any residual volumes from each dosing occasion will be retained under Frozen (-60 to -90°C) conditions unless otherwise requested by the Study Director.

6.2. Preparation Details

Dosing formulations will be prepared freshly on the day of dosing according to the procedure described in Section 6.2.2. at appropriate concentrations to meet dose level requirements.

6.2.1. Preparation of Control Article

Dose formulation preparations will be performed under a Biological safety cabinet using aseptic procedures.

The Control Article, consisting of 10.7 mM Sodium Acetate, 20 mM Tris and 8.7% (w/v) sucrose, will be dispensed on the day of each dose (Days 1 and 22) for administration to Group 1 control animals and will be used as required to dilute the bulk Test Article for administration to Groups 2 to 4 animals. The aliquots will be stored under refrigerated conditions set to maintain 2-8°C until use. Refrigerated aliquots will be equilibrated to room temperature for at least 30 minutes prior to the start of dosing and used with 4 hours of being brought to room temperature. Any residual volumes will be retained, but not reused.

6.2.2. Preparation of Test Article Dose Formulation

Dose formulation preparations will be performed under a biological safety cabinet using sterile aseptic procedures.

The bulk Test Article stock will be removed from the freezer and allowed to thaw at room temperature for approximately 1 hour before dose formulation preparation on the day of each dose (Days 1 and 22). When possible, bulk test article in each stock vial will be used only once.

The dosing formulations will be prepared by diluting the appropriate bulk Test Article with the Control Article as necessary to the target concentration for administration and should not be filtered. The storage of prepared dose formulations should not exceed 4 hours at room

temperature or 8 hours at refrigerated conditions from the time of preparation to the dose administration. If the dosing formulations are stored refrigerated (2-8°C), they will be used for dose administration within 4 hours of being brought to room temperature. Refrigerated dose formulations will be equilibrated to room temperature for at least 30 minutes prior to the start of dosing. The formulations will NOT be vortexed or sonicated but may be gently swirled to reach visual homogeneity during formulation. Stock solution vials will be used only on the day of dose formulation preparation once thawed and will not be used on subsequent days.

Any residual volumes of formulated Test Article will be stored in a freezer set to maintain -60 to -90°C and discarded prior to report finalization as directed by the Sponsor Representative or Study Director.

6.3. Sample Collection and Analysis

Dose formulation samples will not be collected.

7. TEST SYSTEM

Species:	Rat
Strain:	CD® [Crl:CD®(SD)]
Condition:	Purpose-bred, naïve
Source:	[redacted]
	The source used will be documented in the raw data.
Number Ordered:	
Male:	22
Female:	22
Number on Study:	
Male:	20
Female:	20
Expected Age at Arrival:	Ordered to be 6 weeks of age at arrival
Expected Weight at Arrival:	Commensurate with age; males will generally weigh 97 to 335g and females will generally weigh 89 to 245g as measured within 3 days of arrival. The actual range will be documented in the data.

The actual age and weight of animals received will be listed in the Final Report.

7.1. Animal Identification

Method: Each animal will be assigned an animal number to be used in Provantis™ and will be implanted with a microchip bearing a unique identification number. The individual animal number, implant number, and the Testing Facility study number will comprise a unique identification for each animal. The animal cage will be identified by the study number, animal number, group number, and sex.

7.2. Environmental Acclimation

Duration: At least 3 days

Details: During this acclimation period, all animals will be observed daily for any clinical signs of disease, and all animals will be given a detailed clinical examination within 3 days of the first dose administration.

7.3. Selection, Assignment, Replacement and Disposition of Animals

Assignment and Randomization: Animals will be randomly assigned to groups upon receipt. Males and females will be randomized separately.

All animals with any evidence of disease or physical abnormalities will not be selected for study.

Replacement: Before the initiation of dosing, any assigned animals considered unsuitable for use in the study will be replaced by alternate animals maintained under the same environmental conditions.

After initiation of dosing, study animals may be replaced during the replacement period with alternate animals in the event of accidental injury, non-test article-related health issues, or similar circumstances. Any data generated will not be included in the report unless deemed appropriate by the Study Director.

Alternate animals may be used as replacements per Testing Facility SOP.

Disposition: Extra animals obtained for this study, but not placed on study will be either transferred to a Testing Facility stock or training colony or euthanized and discarded.

The disposition of all animals will be documented in the study records.

8. HUSBANDRY

8.1. Housing

Housing:	Pair-housed, when possible (animals may be housed 2 to 3/cage during acclimation and in-life depending on study design). Housing set-up is as specified in the USDA Animal Welfare Act (9 CFR, Parts 1, 2 and 3) and as described in the *Guide for the Care and Use of Laboratory Animals*. Animals will be separated during designated procedures/activities or will be separated as required for monitoring and/or health purposes, as deemed appropriate by Study Director and/or Clinical Veterinarian.
Caging:	Solid bottom cages with nonaromatic bedding. The bedding will be from an approved supplier and documented in the study data.

8.2. Animal Enrichment

Supplemental Enrichment:	Animal enrichment will be provided according to Testing Facility SOP.

8.3. Environmental Conditions

Temperature and Humidity:	Temperature and humidity will be maintained according to Testing Facility SOP.
Lighting:	Fluorescent lighting will be provided via an automatic timer for approximately 12 hours per day. On occasion, the dark cycle may be interrupted intermittently due to study-related activities.

8.4. Food

Diet:	The basal diet will be block Lab Diet® Certified Rodent Diet #5002, PMI Nutrition International, Inc.
Frequency:	Ad libitum, except during designated procedures
Analysis:	Results of analysis for nutritional components and environmental contaminants are provided by the supplier and are on file at the Testing Facility. There are no known contaminants in the food that would interfere with this study.

8.5. Water

Type:	Tap water

Frequency: Supplied ad libitum to all animals via an automatic water system unless otherwise indicated.

Analysis: Periodic analysis of the water is performed per Testing Facility SOP and results of these analyses are on file at the Testing Facility. It is considered that there are no known contaminants in the water that would interfere with the outcome of the study.

8.6. Veterinary Care

Veterinary care will be available throughout the course of the study and animals will be examined by the veterinary staff as warranted by clinical signs or other changes. In the event that animals show signs of illness or distress, the responsible veterinarian may make initial recommendations about treatment of the animal(s) and/or alteration of study procedures, which must be approved by the Study Director (or scientific designee). Treatment of the animal(s) for minor injuries or ailments may be approved without prior consultation with the Sponsor representative when such treatment does not impact fulfillment of the study objectives. If the condition of the animal(s) warrants significant therapeutic intervention or alterations in study procedures, the Sponsor representative will be contacted, when possible, to discuss appropriate action. If the condition of the animal(s) is such that emergency measures must be taken, the Study Director (or scientific designee) and/or veterinarian will attempt to consult with the Sponsor representative prior to responding to the medical crisis, but the Study Director (or scientific designee) and/or veterinarian has authority to act immediately at his/her discretion to alleviate suffering. The Sponsor representative will be fully informed of any such events.

9. EXPERIMENTAL DESIGN

Group No.	Test Material	Dose Level (µg/dose)	Dose Volume (mL/dose)	Dose Concentration (µg/mL)	Main Study	
					No. of Males	No. of Females
1	Control Article	0	0.2	0	5	5
2	mRNA-1273	30		150	5	5
3		60		300	5	5
4		100		500	5	5

No. = Number

9.1. Administration of Test Article(s)

Dose Route: Intramuscular injection

Frequency/Duration: The test article and control article will be administered once on Days 1 and 22.

Special Requirement: Under no circumstances will the dose formulations be subjected to vortexing and vigorously shaking to avoid disruption of the Test Article. Before withdrawing a dose formulation into syringes, the dose formulation container will be gently swirled to achieve homogeneity and

this step will be documented. The dosing will be conducted in a group number sequence order from Group 1 through Group 4, to minimize any potential risk of Test Article cross-contamination. Personal protective equipment (PPE) used in dosing will be changed between groups. Refrigerated dose formulations will be equilibrated to room temperature for at least 30 minutes prior to the start of dosing.

Details: The injection site areas and surrounding skin will be shaved free of hair at least 48 hours prior to dose administration. Doses will be administered via bolus intramuscular injection into one of the quadriceps (hind leg, thigh) after isoflurane inhalation in accordance with Testing Facility SOP. A unique site will be used for each injection (left quadricep on Day 1, right quadricep on Day 22).

Care will be taken to ensure that injection(s) are in the appropriate part of the muscle. The needle will be inserted perpendicular to the skin surface. The location of the injection site will be documented for each dose. In addition, each injection site will be marked with a single large dot at the exact site of needle insertion and a larger circle centered on that dot, for the purposes of erythema and swelling evaluation. Each injection site will be remarked at least once weekly and prior to necropsy.

10. IN-LIFE PROCEDURES, OBSERVATIONS, AND MEASUREMENTS

Standard In-life Assessments

Parameter	Population(s)	Frequency (minimum required)	Comments
Mortality/Cageside Observations	All surviving animals	At least twice daily (morning and afternoon) beginning upon arrival through termination/release.[a,b]	Animals will be observed within their cage unless necessary for identification or confirmation of possible findings. Animals will be observed for morbidity, mortality, injury, and availability of food and water. Any animals in poor health will be identified for further monitoring and possible euthanasia.

Parameter	Population(s)	Frequency (minimum required)	Comments
Detailed Clinical Observations	All animals	Daily; from at least Week -1 and throughout the study.[c]	Animals are removed from the cage. Observations will include, but will not be limited to, evaluation of the skin, fur, eyes, ears, nose, oral cavity, thorax, abdomen, external genitalia, limbs and feet, respiratory and circulatory effects, autonomic effects such as salivation, nervous system effects including tremors, convulsions, reactivity to handling, and unusual behavior.
Individual Body Weight	All animals	Within 3 days of arrival, Day -1, and once weekly throughout the study.	Not collected from animals found dead.
Injection Site Observations	All animals	Immediately post dose, 6 hours and 24 hours post dose	

[a] Procedures on alternate animals will be conducted per Testing Facility SOP.
[b] Except on days of receipt and necropsy where frequency will be at least once daily.
[c] For observations that cannot be attributed to an individual animal due to social housing (e.g., watery feces), the observation will be noted to each animal in the socialized group.

11. CLINICAL PATHOLOGY

11.1. Sample Collection

Clinical Pathology Sample Collection

Group Nos.	Time Point(s)	Hematology	Clinical Chemistry
All animals	Day 23 (24 hours post the last dose)	X	X
Unscheduled Euthanasia (when possible)	See the Unscheduled Euthanasia section of this protocol.		

Volume (mL)[a]:	NA	0.5 mL	0.8 mL
Fasting Required:	Free access to drinking water but will be fasted overnight (at least 8 hours) prior to blood collection.		
Anticoagulant:	NA	K_2EDTA	Serum Gel Separator
Special Requirements:	NA	NA	NA
Processing:	NA	None	Serum

X = Sample to be collected; NA = Not applicable
[a] Additional blood samples may be obtained (e.g. due to sample quality) if permissible sampling frequency and blood volume are not exceeded.

Blood Sample Collection Method: Sublingual, or another suitable vein

Blood Sample Special Instructions: The blood will be collected in dose group order, to minimize any potential risk of cross-contamination.

The following clinical pathology tests will be conducted on available samples and the data will be interpreted by a Clinical Pathologist.

11.2. Hematology

Hematology Parameters

Leukocyte count (total and absolute differential)	Mean corpuscular hemoglobin (calculated)
Erythrocyte count	Mean corpuscular volume
Hemoglobin	Mean corpuscular hemoglobin concentration (calculated)
Hematocrit	RDW
Absolute reticulocytes	Platelet count
	Blood smear (preserve and stain)[a]

[a] Blood smear review may be performed on select animals per Testing Facility SOP.

11.3. Clinical Chemistry

Clinical Chemistry Parameters

Alkaline phosphatase	Globulin and A/G (albumin/globulin) ratio (calculated)
Total bilirubin (with direct bilirubin if total bilirubin exceeds 1 mg/dL)	Glucose
	Total cholesterol
Aspartate aminotransferase	Triglycerides
Alanine aminotransferase	Electrolytes (sodium, potassium, chloride)
Urea nitrogen	Calcium
Creatinine	Phosphorus
Total protein	
Albumin	

12. SERUM COLLECTION FOR ELISA ASSAY

12.1. Sample Collection

Serum Collection for ELISA Assay

	Collection Intervals	
Group Nos.	**Predose**	**Day 35**
1-4	X	X

X = Sample to be collected

Method/Comments: Sublingual or other suitable vein

Volume (mL): 0.5 mL

Anticoagulant: Serum Separator, non-additive; barrier free

Whole Blood Storage: Ambient and allowed to clot until centrifuged.

Processing:	Serum, Two aliquots of approximately equal volume
Final Storage Temperature:	Frozen (-60 to -90°C) Serum samples will be placed in frozen (-60 to -90°C) storage within 60 minutes of collection. The samples in aliquot tubes will be frozen immediately over dry ice.

12.2. Serum Shipment

Additional Container Label Requirements:	Study number, animal number, matrix of sample, interval and timepoint, analysis type, and aliquot number.
Bioanalytical Sample Shipping Contact:	All samples to be analyzed will be shipped to the designated Test Site, see Attachment B for shipping details.

12.3. Serum Analysis for ELISA Assay

Analysis Performed By:	ELISA assay of the serum samples will be performed by the Sponsor.
Reporting:	A memo Report will be prepared and submitted to the Testing Facility for inclusion as an appendix in the main study Final Report.

13. TERMINAL PROCEDURES

Terminal procedures are summarized in the following tables:

Terminal Procedures

Group No.	Necropsy Procedures			Histology Processing	Microscopic Evaluation
	Necropsy	Tissue Collection	Organ Weights		
Found dead or unscheduled euthanasia	X	X	NA	NA	NA

Terminal Procedure Tables Footnotes:

X = Procedure to be conducted; NA = Not applicable.
"Histology Processing" = embedded in paraffin, sectioned, mounted on glass slides, and stained with hematoxylin and eosin.

13.1. Method of Euthanasia

Euthanasia will be by carbon dioxide inhalation followed by a Testing Facility SOP approved method to ensure death, e.g. exsanguination.

13.2. Unscheduled Euthanasia

Moribund animals will be subject to Testing Facility SOP criteria and procedures. If possible, the samples below will be collected from animals euthanized early, following veterinary consultation. A veterinary consultation is not required if the samples are collected following anesthesia or euthanasia. Blood collection methods utilized for animals euthanized early may include suitable methods other than those presented in the respective blood collection section(s) of this protocol.

Sample Type	Groups	Volume	Anticoagulant
Hematology	1-4	0.5 mL	K_2EDTA
Clinical Chemistry		0.8 mL	Serum Gel Separator
Serum (ELISA Assay)		0.5 mL	Serum Separator non-additive; barrier free

Necropsy examinations will be performed 7 days a week. Animals that are found dead or euthanized early after regular working hours will be refrigerated and necropsies performed at the start of the next day.

13.3. Scheduled Euthanasia

Animals surviving until study termination will be euthanized by the methods described above and discarded without any further evaluation.

13.4. Necropsy

Animals euthanized early or found dead as detailed in the Terminal Procedures table will be subjected to a complete necropsy examination, which will include evaluation of the carcass and musculoskeletal system; all external surfaces and orifices; cranial cavity and external surfaces of the brain; and thoracic, abdominal, and pelvic cavities with their associated organs and tissues.

All animals will be examined carefully for external abnormalities including palpable masses.

Images may be generated for illustration of or consultation on gross observations. These images will not be used for data generation or interpretation and will not be archived or included in the Final Report.

14. STATISTICAL ANALYSIS

The following presents a proposed statistical analysis plan. Statistical plans are data dependent, and this analysis plan may require modification if standard data assumptions are not met. Other conceptually equivalent statistical testing routines may also be employed at the discretion of the statistician. The actual analysis plan will be documented in the Final Report.

The raw data will be tabulated within each time interval, and the appropriate summary statistics will be calculated for each endpoint, sex, and group. For each endpoint, treatment groups will be compared to the control group using the analysis outlined below. Data for some endpoints, as

indicated, will be transformed by either a log or rank transformation prior to conducting the specified analysis. Statistical Comparisons

Control Group	Comparison Group(s)
1	2, 3, 4

14.1. Group Pair-wise Comparison (General ANOVA)

Endpoints:

- Body Weight and Body Weight Change
- Hematology
- Clinical Chemistry

Description: If the control group has a sample size less than 3, no inferential statistics will be calculated. If a particular endpoint and/or parameter within a given collection interval have the same value across all experimental units, no inferential statistics will be calculated.

Otherwise, for endpoints and/or parameters where all groups with sample sizes of 3 or greater are included, the system will test the normality of the residuals and homogeneity of variances to see whether the data is approximately normal or whether a log transformation or rank transformation should be used. Levene's test will be used to assess homogeneity of group variances and Shapiro-Wilk's test will be used to test the normality of the residuals.[1,2]

On the raw data, if Levene's test is not significant ($p \geq 0.01$) and Shapiro-Wilk's test is not significant ($p \geq 0.01$), then a normal distribution will be used. If either the Levene's test is significant ($p < 0.01$) or Shapiro-Wilk's test is significant ($p < 0.01$), normality and homogeneity of variances will be tested with a log transformation used on the data.

On the log transformed data, if Levene's test is not significant ($p \geq 0.01$) and Shapiro-Wilk's test is not significant ($p \geq 0.01$), then a log normal distribution will be used. If either the Levene's test is significant ($p < 0.01$) or Shapiro-Wilk's test is significant ($p < 0.01$), then a rank transformation will be used on the data.

Raw or Log Transformed Data:

A one-way analysis of variance will be used to test each endpoint for the effects of treatment.[3]

If the treatment effect is significant ($p < 0.05$), linear contrasts will be constructed for a Dunnett's pair-wise comparison of treatment groups as described above.

Rank Transformed Data:

A Kruskal-Wallis test will be used to test each endpoint for the effects of treatment.

If the treatment effect is significant ($p<0.05$), a non-parametric Dunn's pair-wise comparison test of each treatment group with the control group.

Results of all pair-wise comparisons will be reported at the 0.05 and 0.01 significance levels. All endpoints will be analyzed using two-tailed tests unless indicated otherwise.

15. COMPUTERIZED SYSTEMS

The actual systems and versions used will be documented in the Final Report.

Computer System Name	Description
CCI	ollection of Part 11 compliant signature(s).
	A comprehensive laboratory information management system used o manage data, including but not limited to: instrumentation, test rticles, standards, and samples.
	lectronic notebook and data collection system for veterinary ommunications, observations, and treatments.
	lectronic documentation management of deviation events and orrective and Preventative Actions (CAPA).
	lient-server, Oracle-based system used for electronic ocumentation and data management from compound receipt hrough reporting.
	n integrated system of software products that enables a user to erform data entry, retrieval, data management, reporting, raphics, statistical analysis, and applications development.
	nvironmental monitoring, alarming, and reporting applications.

16. REGULATORY COMPLIANCE

This study is not within the scope of regulations governing the conduct of nonclinical laboratory studies and is not intended to comply with such regulations.

17. AMENDMENTS AND DEVIATIONS

Changes to the approved protocol shall be made in the form of an amendment, which will be signed and dated by the Study Director. Every reasonable effort will be made to discuss any necessary protocol changes in advance with the Sponsor. The Study Director will notify the Sponsor of deviations that may result in a significant impact on the study as soon as possible.

18. RETENTION AND DISPOSITION OF RECORDS, SAMPLES, AND SPECIMENS

All study-specific raw data, electronic data, documentation, protocol, retained samples and specimens, and Interim (if applicable) and Final Reports will be archived per Testing Facility SOP. All retained materials will be archived at [redacted], unless specified by the Sponsor. At least 1 year after issue of the Draft Report, the Sponsor will be contacted.

Samples for clinical pathology evaluations are discarded per Testing Facility SOP unless otherwise indicated in the table below.

Disposition of residual/retained analytical samples will be as described in the table below. See Attachment A for shipping details.

Disposition of Residual/Retained Samples

Sample Type	Disposition	Schedule
Dose Formulations	Archive	Samples will be maintained for a minimum of 6 months following issuance of the Draft Report or at an alternate time point prior to finalization as requested and authorized by the Study Director in consultation with the Sponsor Representative.

Records to be maintained will include, but will not be limited to, documentation and data for the following:

- Deviations, Protocol amendments, and Protocol
- Study schedule
- Study-related correspondence
- Test system receipt, health, and husbandry
- Test and control article receipt, identification, preparation, and analysis
- In-life measurements and observations
- Clinical pathology sample collection and evaluation
- Statistical analysis results

19. STUDY CLASSIFICATION

Study Category:	Pharmacology
Study Type:	Repeat Dose Toxicity
Study Design:	Parallel
Primary Treatment CAS Registry Number:	Insert from Sponsor Not Available
Primary Treatment Unique Ingredient ID:	Insert from Sponsor Not Available
Class of Compound:	mRNA in Lipid Nanoparticle
Administration Dose Form:	LNP dispersion

20. REPORTING

A comprehensive Draft Report will be prepared following completion of the study and will be finalized following consultation with the Sponsor. The report will include all information necessary to provide a complete and accurate description of the experimental methods and results and any circumstances that may have affected the quality or integrity of the study.

The Sponsor will receive an electronic version of the Final Report provided in Adobe Acrobat PDF format (hyperlinked and searchable at final). The PDF document will be created from native electronic files to the extent possible, including text and tables generated by the Testing Facility. Report components not available in native electronic files and/or original signature pages will be scanned and converted to PDF image files for incorporation.

Reports should be finalized within 6 months of issue of the Draft Report. If the Sponsor has not provided comments to the report within 6 months of draft issue, the report will be finalized by the Testing Facility unless other arrangements are made by the Sponsor.

20.1. SEND Datasets

At the request of the Sponsor, SEND datasets will be generated and provided outside the context of the Final Report. These datasets will not be subject to QA Audit nor will they be used as the basis for the Study Director interpretation of the study results. SEND datasets will be provided following the Final Report(s).

When work in support of this study is conducted at a Test Site (i.e., Bioanalysis, TK modeling, etc.), an electronic version of all data should be provided to Testing Facility.

21. JUSTIFICATIONS AND GUIDELINES

21.1. Justification of Test System and Number of Animals

The current state of scientific knowledge and the applicable guidelines cited in this Protocol do not provide acceptable alternatives, in vitro or otherwise, to the use of live animals to accomplish the purpose of this study. "The development of knowledge necessary for the improvement of the health and well-being of humans as well as other animals requires in vivo experimentation with a wide variety of animal species."[4] "Whole animals are essential in research and testing because they best reflect the dynamic interactions between the various cells, tissues, and organs comprising the human body."[5]

The rat is the usual rodent model used for evaluating the immunogenicity and toxicity of various classes of chemicals and for which there is a large historical database.[6]

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

21.2. Justification of Route and Dose Levels

The intramuscular route is the intended route of administration of this test article in humans.

Doses were selected based on the aggregate toxicity data from various rat toxicity studies conducted using this lipid nanoparticle formulation. The high dose of 100 ug/dose was selected because it is the maximum feasible dose based on the concentration of the test article and the maximum intramuscular dose volume permitted in a rat. This dose is expected to elicit minor clinical observations including transient erythema and edema at the injection site. The mid- (60 ug/dose) and low- (30 ug/dose) doses are expected to produce minimal effects

21.3. Guidelines for Study

The design of this study was based on the study objective(s), the overall product development strategy for the Test Article, and the following study design guidelines:

- ICH Harmonised Tripartite Guideline M3 (R2). *Guidance on Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals.*
- ICH Harmonised Tripartite Guideline S6 (R1). *Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals.*
- Note for Guidance on Preclinical Pharmacological and Toxicological Testing of Vaccines. The European Agency for the Evaluation of Medicinal Products, CPMP/SWP/465/95: Dec. 17, 1997.
- WHO guidelines on nonclinical evaluation of vaccines. World Health Organization, WHO Technical Report Series, No. 927, 2005.

22. ANIMAL WELFARE

This study will comply with all applicable sections of the Final Rules of the Animal Welfare Act regulations (Code of Federal Regulations, Title 9), the *Public Health Service Policy on Humane Care and Use of Laboratory Animals* from the Office of Laboratory Animal Welfare, and the *Guide for the Care and Use of Laboratory Animals* from the National Research Council.[7,8] The protocol and any amendments or procedures involving the care or use of animals in this study will be reviewed and approved by the Testing Facility Institutional Animal Care and Use Committee before the initiation of such procedures.

If an animal is determined to be in overt pain/distress or appears moribund and is beyond the point where recovery appears reasonable, the animal will be euthanized for humane reasons in accordance with the *American Veterinary Medical Association (AVMA) Guidelines on Euthanasia* and with the procedures outlined in the protocol.[9]

By approving this protocol, the Sponsor affirms that there are no acceptable non-animal alternatives for this study, that this study is required by a relevant government regulatory agency(ies) and that it does not unnecessarily duplicate any previous experiments.

22.1. Institutional Animal Care and Use Committee Approval

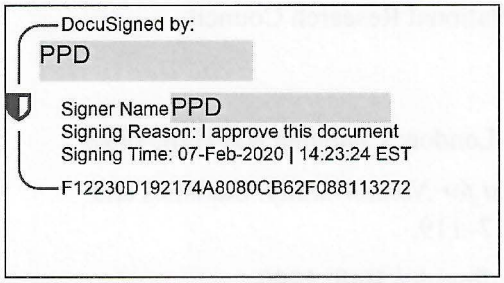
The protocol and any amendment(s) or procedures involving the care and use of animals in this study will be reviewed and approved by CR-MWN Institutional Animal Care and Use Committee (IACUC) before conduct. During the study, the care and use of animals will be conducted with guidance from the guidelines of the USA National Research Council.

23. REFERENCES

1. Milliken GA, Johnson DE. *Analysis of messy data*. London: Chapman and Hall; 1992.
2. Royston JP. *Approximating the Shapiro-Wilk W Test for Nonnormality*. Statistics and Computing 2. London: Chapman and Hall; 1992:117–119.
3. Zar JH. *Biostatistical Analysis*. 4th ed. New Jersey: Prentice Hall; 1999.
4. *Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training*, Federal Register, 1985 May 20; 50(97).
5. *Position Statement on the Use of Animals in Research*, 1993 Feb 26; NIH Guide 22(8).
6. *Guidance for Industry, Investigators, and Reviewers: Exploratory IND Studies*. US FDA Center for Drug Evaluation and Research (CDER), 2006 Jan.
7. Office of Laboratory Animal Welfare. *Public Health Services Policy on Humane Care and Use of Laboratory Animals*. Bethesda, MD: National Institutes of Health. Current edition.
8. National Research Council. *Guide for the Care and Use of Laboratory Animals*. Washington, DC: National Academy Press. Current edition.
9. American Veterinary Medical Association. *AVMA Guidelines on Euthanasia*. Current edition.

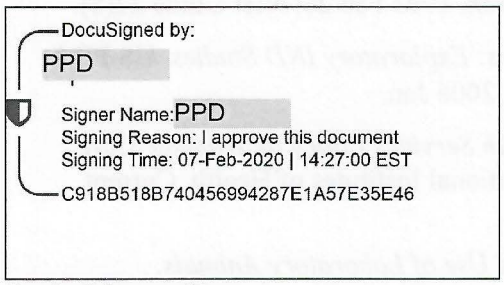
TESTING FACILITY APPROVAL

The signature below indicates that Testing Facility Management approves the Study Director identified in this protocol and acknowledges the study.



Testing Facility Management/Date

The signature below indicates that the Study Director approves the study protocol.



Study Director/Date

SPONSOR APPROVAL

The protocol was approved by the Sponsor by e-mail on the date designated below. The correspondence giving approval will be archived, as appropriate with other Sponsor communications.

07 Feb 2020
Date of Sponsor Approval

ATTACHMENT A

Tissue Weighing, Collection, Processing and Evaluation Table

Organ	Macroscopic Evaluation and Collection
Animal ID	X
Artery, aorta	X
Body cavity, nasal	X
Bone marrow, sternum	X
Bone marrow smear	X[a]
Bone, femur	X (1)
Bone, sternum	X
Brain	X
Epididymis	X (2)[b]
Esophagus	X
Eye	X (2)[b]
Ganglion, dorsal root, lumbar	X
Gland, adrenal	X (2)
Gland, clitoral	X (2)
Gland, lacrimal	X (2) (extra-orbital)
Gland, Harderian	X (2)
Gland, mammary	X
Gland, parathyroid	X (2)
Gland, pituitary	X
Gland, preputial	X (2)
Gland, prostate	X
Gland, salivary, submandibular	X (2)
Gland, salivary, sublingual	X (2)
Gland salivary, parotid	X (2)
Gland, seminal vesicle	X (2)
Gland, thyroid	X (2)
Gland, Zymbal's	X (2)
Gut-associated lymphoid tissue[c]	X
Heart	X
Joint, femorotibial	X (1)
Kidney	X (2)
Large intestine, cecum	X
Large intestine, colon	X
Large intestine, rectum	X
Larynx	X
Liver	X
Lung	X
Lymph node(s) draining administration site(s): Inguinal	X
Lymph node, mandibular	X (2)
Lymph node, mesenteric	X
Muscle, skeletal	X (2)

Organ	Macroscopic Evaluation and Collection
Nerve, optic	X (2)[b]
Nerve, sciatic	X (2)
Nerve, tibial	X (2)
Ovary	X (2)
Oviduct	X (2)
Pancreas	X
Site(s), administration	X
Skin	X
Small intestine, duodenum	X
Small intestine, ileum	X
Small intestine, jejunum	X
Spinal cord	X
Spleen	X
Stomach	X
Testis	X (2)[b]
Thymus	X
Tongue	X
Trachea	X
Ureter	X (2)
Urinary bladder	X
Uterus/Cervix	X
Vagina	X

X = Procedure to be conducted. - = Not applicable. (1) = one side. (2) = both sides.
Macroscopic abnormalities in the organs listed and in other organs will be sampled at necropsy, processed for histology and examined microscopically.

[a] Two bone marrow smears will be collected from the femur at scheduled and unscheduled necropsies (for possible examination). Smears will not be collected from animals that are found dead or from animals that were euthanized moribund and then stored in the refrigerator prior to necropsy. Bone marrow smears are allowed to air dry and are not fixed in formalin.

[b] Eyes and optic nerves are preserved in Davidson's fixative. Testes and epididymides are preserved in modified Davidson's fixative.

[c] From small intestine: Peyer's patch or solitary lymphoid follicle.

[d] Weigh with gland, thyroid.

ATTACHMENT B

Shipment of Samples and Study Records

Samples will be shipped on Monday through Wednesday for next day delivery for domestic shipments and expedited delivery for International shipments using the Conditions for Shipment(s) listed below.

Sample Matrix	Sample Type	Aliquot of Sample	Proposed Shipment	Conditions for Shipment	ent/Address
Serum	Serum for ELISA Assay	All	After each collection interval	on dry ice Temperature monitor to be included in shipment	PPD Moderna TX, Inc. 200 Technology Square Cambridge, MA 02139 USA Tel PPD E-mail: PPD

Appendix 2
Test Article Characterization

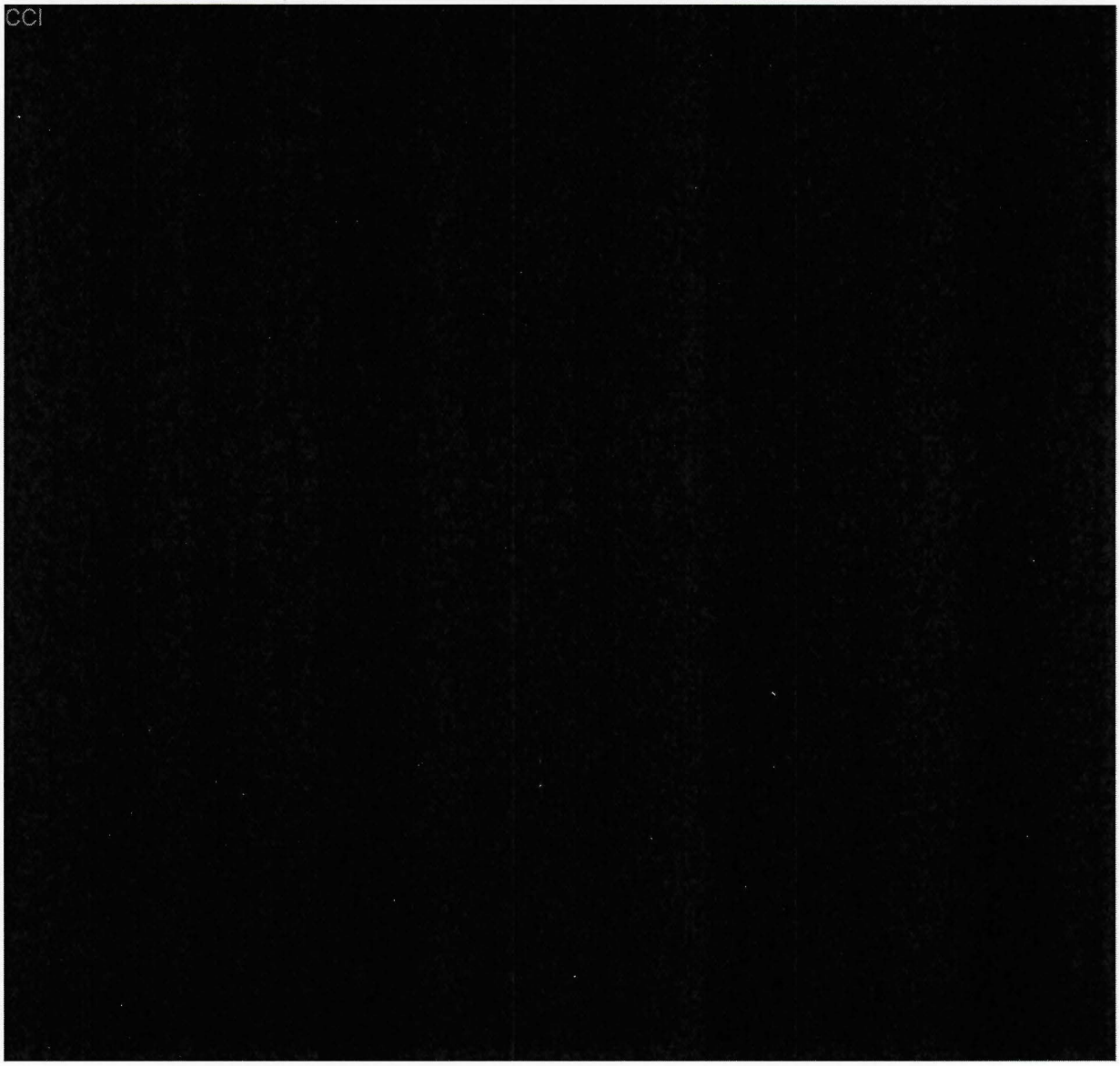
Document Number: COA-0363 Version: 2.0 Final Date:
mRNA-1273 Drug Product Interim Certificate of Analysis Lot 8520100101

moderna

1 Moderna Way • Norwood, MA 02062
phone 617-714-6500 • fax 617-583-1998

CERTIFICATE OF ANALYSIS

CCI



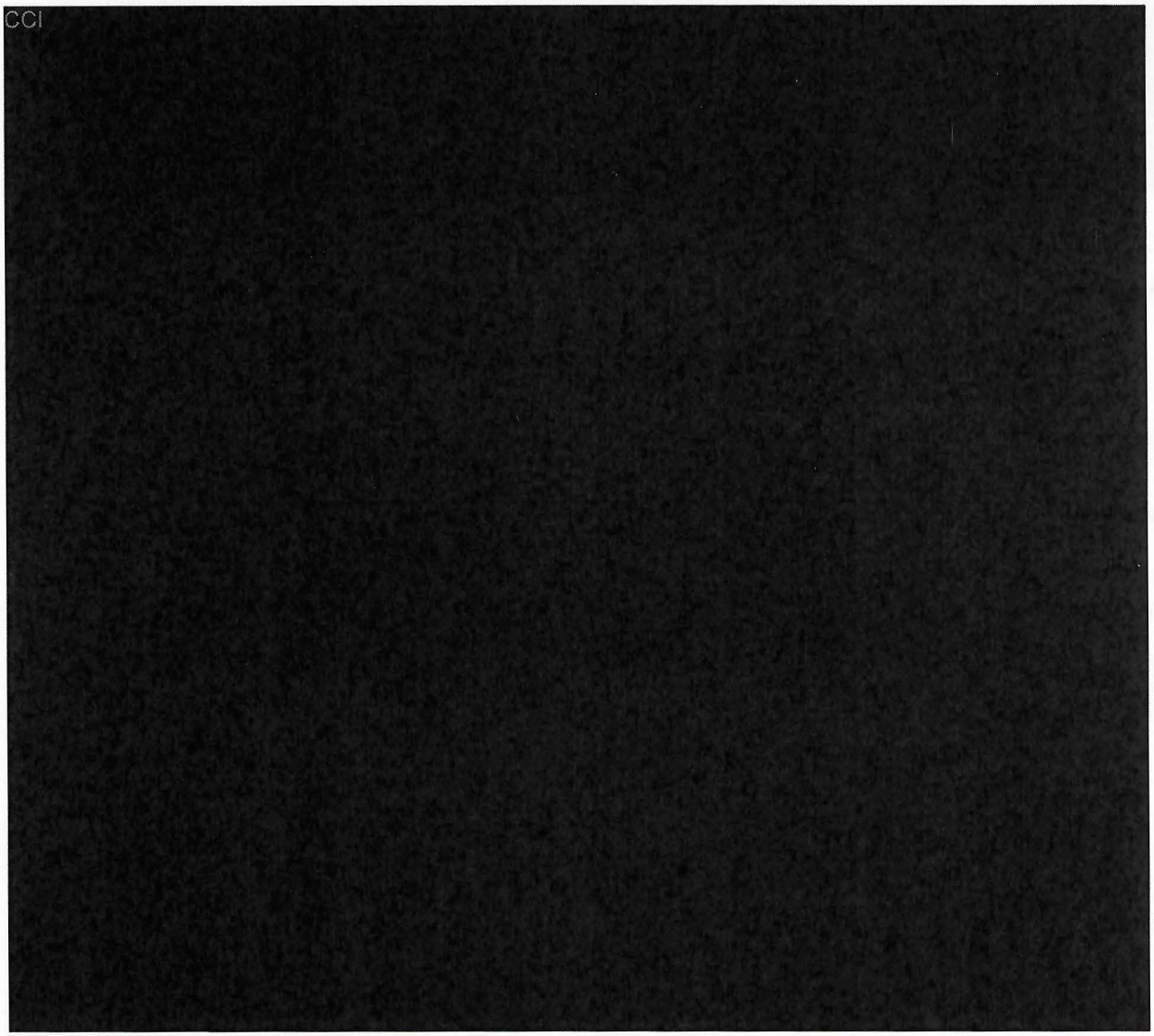
VERSION NUMBER 2.0

Document Number: COA-0363 Version: 2.0 Final Date:
mRNA-1273 Drug Product Interim Certificate of Analysis Lot 8520100101

moderna

1 Moderna Way • Norwood, MA 02062
phone 617-714-6500 • fax 617-583-1998

CERTIFICATE OF ANALYSIS



Document Number: COA-0363 Version: 2.0 Final Date:
mRNA-1273 Drug Product Interim Certificate of Analysis Lot 8520100101

moderna

1 Moderna Way • Norwood, MA 02062
phone 617-714-6500 • fax 617-583-1998

CERTIFICATE OF ANALYSIS

CCI [redacted]

Product Attribute	Method	Parameter	Specification	Result

Revision History:

1.0 – Original
2.0 – Removed "Interim" from title; added USP <71> sterility test result (SOP-0378)

Department	Signature	Date
QC Review:	PPD [redacted]	
QA Review:		

Appendix 3
Record of Animal Fate and Disposition

Abbreviations
EuDis – Euthanized and discarded

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Record of Animal Fate and Disposition

Sex: Male Day(s): 1 to 35 Relative to Start Date

0 µg/dose	Fate	Removal Day
1001	EuDis	35
1003	EuDis	35
1004	EuDis	35
1005	EuDis	35
1102	EuDis	35

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Record of Animal Fate and Disposition

Sex: Male Day(s): 1 to 35 Relative to Start Date

30 µg/dose	Fate	Removal Day
2001	EuDis	35
2002	EuDis	35
2003	EuDis	35
2004	EuDis	35
2005	EuDis	35

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Record of Animal Fate and Disposition

Sex: Male Day(s): 1 to 35 Relative to Start Date

60 µg/dose	Fate	Removal Day
3001	EuDis	35
3002	EuDis	35
3003	EuDis	35
3004	EuDis	35
3005	EuDis	35

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Record of Animal Fate and Disposition

Sex: Male Day(s): 1 to 35 Relative to Start Date

100 µg/dose	Fate	Removal Day
4001	EuDis	35
4002	EuDis	35
4003	EuDis	35
4004	EuDis	35
4005	EuDis	35

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Record of Animal Fate and Disposition

Sex: Female Day(s): 1 to 35 Relative to Start Date

0 µg/dose	Fate	Removal Day
1501	EuDis	35
1502	EuDis	35
1503	EuDis	35
1504	EuDis	35
1505	EuDis	35

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Record of Animal Fate and Disposition

Sex: Female Day(s): 1 to 35 Relative to Start Date

30 µg/dose	Fate	Removal Day
2501	EuDis	35
2502	EuDis	35
2503	EuDis	35
2504	EuDis	35
2505	EuDis	35

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Record of Animal Fate and Disposition

Sex: Female Day(s): 1 to 35 Relative to Start Date

60 µg/dose	Fate	Removal Day
3501	EuDis	35
3502	EuDis	35
3503	EuDis	35
3504	EuDis	35
3505	EuDis	35

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Record of Animal Fate and Disposition

Sex: Female Day(s): 1 to 35 Relative to Start Date

100 µg/dose	Fate	Removal Day
4501	EuDis	35
4502	EuDis	35
4503	EuDis	35
4504	EuDis	35
4605	EuDis	35

Appendix 4
Individual Detailed Clinical Observations

On occasion, clinical findings may have been observed more than once during the interval and were documented accordingly in the raw data. The individual clinical observations table of this appendix reports the findings observed, not the number of times observed within an interval.

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Detailed Clinical Observations

Sex: Male	Animal	Observation Type: Routine	From Day -3 (Start Date) to 35 (Start Date)
0 µg/dose	1001	Normal	-3, -2, -1, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
	1003	Normal	-3, -2, -1, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
	1004	Normal	-3, -2, -1, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
	1005	Normal	-3, -2, -1, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
	1102	Normal	-3, -2, -1, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
30 µg/dose	2001	Normal	-3, -2, -1, 1, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
		Edema, Hind limb/left	2, 3
	2002	Normal	-3, -2, -1, 1, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
		Edema, Hind limb/left	2, 3
		Hair sparse, Face	18, 19, 20, 21, 22
	2003	Normal	-3, -2, -1, 1, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
		Limb function impaired, Hind limb/left	2
		Edema, Hind limb/left	2, 3
	2004	Normal	-3, -2, -1, 1, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
		Edema, Hind limb/left	2, 3

Values=Interval seen

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Detailed Clinical Observations

Sex: Male	Animal	Observation Type: Routine	From Day -3 (Start Date) to 35 (Start Date)
30 µg/dose	2005	Normal	-3, -2, -1, 1, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
		Edema, Hind limb/left	2, 3
60 µg/dose	3001	Normal	-3, -2, -1, 1, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
		Limb function impaired, Hind limb/left	2
		Edema, Hind limb/left	2, 3, 4, 5
		Edema, Hind limb/right	24, 25
	3002	Normal	-3, -2, -1, 1, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20
		Limb function impaired, Hind limb/left	2
		Edema, Hind limb/left	2, 3, 4, 5
		Edema, Hind limb/right	24, 25
		Hair sparse, Face	21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
		Scabbed area, Face	26, 27, 28, 29, 30, 31, 32, 33, 34, 35
	3003	Normal	-3, -2, -1, 1, 7, 8, 9, 10, 11, 12, 26, 27, 28, 29, 30, 35
		Limb function impaired, Hind limb/left	2
		Thin	4, 5, 6
		Abrasion(s), Face	31
		Edema, Hind limb/left	2, 3, 4, 5
		Edema, Hind limb/right	24, 25
		Hair sparse, Face	13, 14, 15, 16, 17, 18, 19, 20, 21, 22
		Scabbed area, Face	32, 33, 34
		Scabbed area, Hind limb/left	21
		Skin discolored, Hind limb/left, Brown	22, 23
	3004	Normal	-3, -2, -1, 1, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18, 19, 20, 21, 22, 23, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
		Limb function impaired, Hind limb/left	2
		Material around nose, Red	17

Values=Interval seen

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Detailed Clinical Observations

Sex: Male	Animal	Observation Type: Routine	From Day -3 (Start Date) to 35 (Start Date)
60 µg/dose	3004	Thin	4, 5, 6
		Edema, Hind limb/left	2, 3, 4, 5
		Edema, Hind limb/right	24
	3005	Normal	-3, -2, -1, 1, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 27, 28
		Limb function impaired, Hind limb/left	2
		Material around eyes, Eye/right, Black	2
		Abrasion(s), Inguinal region/left	29
		Edema, Hind limb/left	2, 3, 4, 5
		Edema, Hind limb/right	24, 25, 26
		Hair sparse, Anogenital region	29, 30, 31, 32, 33, 34, 35
		Hair sparse, Inguinal region/left	29, 30, 31, 32, 33, 34, 35
		Scabbed area, Inguinal region/left	30, 31, 32, 33, 34, 35
100 µg/dose	4001	Normal	-3, -2, -1, 1, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
		Limb function impaired, Hind limb/left	2
		Edema, Hind limb/left	2, 3, 4, 5, 6
		Edema, Hind limb/right	24
		Unkempt appearance	3, 4, 5
	4002	Normal	-3, -2, -1, 1, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 27, 28, 29, 30, 31, 32, 33, 34, 35
		Limb function impaired, Hind limb/left	2
		Edema, Hind limb/left	2, 3, 4, 5
		Edema, Hind limb/right	24, 25, 26
		Unkempt appearance	3, 4, 5
	4003	Normal	-3, -2, -1, 1, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 19, 20, 27, 28, 29, 30, 31, 32, 33, 34, 35
		Limb function impaired, Hind limb/left	2
		Material around nose, Red	18
		Edema, Hind limb/left	2, 3, 4, 5

Values=Interval seen

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Detailed Clinical Observations

Sex: Male	Animal	Observation Type: Routine	From Day -3 (Start Date) to 35 (Start Date)
100 µg/dose	4003	Edema, Hind limb/right	24, 25
		Scabbed area, Hind limb/left	21, 22, 23, 24, 25, 26
	4004	Normal	-3, -2, -1, 1, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18, 19, 20, 21, 22, 23, 25, 26, 27, 28, 29
		Limb function impaired, Hind limb/left	2
		Material around nose, Red	17
		Edema, Hind limb/left	2, 3, 4, 5
		Edema, Hind limb/right	24
		Skin discolored, Tail, Red	30, 31, 32, 33, 34, 35
		Unkempt appearance	3, 4, 5
	4005	Normal	-3, -2, -1, 1, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
		Limb function impaired, Hind limb/left	2
		Edema, Hind limb/left	2, 3, 4, 5
		Edema, Hind limb/right	24

Values=Interval seen

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Detailed Clinical Observations

Sex: Female	Animal	Observation Type: Routine	From Day -3 (Start Date) to 35 (Start Date)
0 µg/dose	1501	Normal	-3, -2, -1, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
	1502	Normal	-3, -2, -1, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
		Hair sparse, Face	17, 18, 19, 20, 21, 22
	1503	Normal	-3, -2, -1, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
	1504	Normal	-3, -2, -1, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
	1505	Normal	-3, -2, -1, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
30 µg/dose	2501	Normal	-3, -2, -1, 1, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28
		Edema, Hind limb/left	2, 3
		Hair sparse, Cervical region	29, 30, 31, 32, 33, 34, 35
		Hair sparse, Face	29, 30, 31, 32, 33, 34, 35
		Hair sparse, Shoulder/left	29, 30, 31, 32, 33, 34, 35
	2502	Normal	-3, -2, -1, 1, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
		Edema, Hind limb/left	2, 3
	2503	Normal	-3, -2, -1, 1, 5, 6, 7, 8, 9, 10, 11, 12, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
		Edema, Hind limb/left	2, 3, 4
		Hair sparse, Cervical region	13, 14, 15
	2504	Normal	-3, -2, -1, 1, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35

Values=Interval seen

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Detailed Clinical Observations

Sex: Female	Animal	Observation Type: Routine	From Day -3 (Start Date) to 35 (Start Date)
30 µg/dose	2504	Edema, Hind limb/left	2, 3, 4
	2505	Normal	-3, -2, -1, 1, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
		Edema, Hind limb/left	2, 3, 4
60 µg/dose	3501	Normal	-3, -2, -1, 1, 6, 7, 8, 9, 10, 11, 12
		Limb function impaired, Hind limb/left	2
		Edema, Hind limb/left	2, 3, 4, 5
		Edema, Hind limb/right	24, 25, 26
		Hair sparse, Forefoot/left	13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33
		Hair sparse, Forefoot/right	13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33
		Hair sparse, Forelimb/left	34, 35
		Hair sparse, Forelimb/right	34, 35
	3502	Normal	-3, -2, -1, 1, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 25
		Limb function impaired, Hind limb/left	2
		Edema, Hind limb/left	2, 3, 4, 5
		Edema, Hind limb/right	24
		Hair sparse, Cervical region	26, 27, 28, 29, 30, 31, 32, 33, 34, 35
		Hair sparse, Thoracic region	26, 27, 28, 29, 30, 31, 32, 33, 34, 35
	3503	Normal	-3, -2, -1, 1, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 28, 35
		Limb function impaired, Hind limb/left	2
		Edema, Hind limb/left	2, 3, 4, 5
		Edema, Hind limb/right	24, 25, 26, 27
		Hair sparse, Cervical region	29, 30, 31, 32, 33, 34
	3504	Normal	-3, -2, -1, 1, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
		Limb function impaired, Hind limb/left	2

Values=Interval seen

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Detailed Clinical Observations

Sex: Female	Animal	Observation Type: Routine	From Day -3 (Start Date) to 35 (Start Date)
60 µg/dose	3504	Edema, Hind limb/left	2, 3, 4, 5, 6
		Edema, Hind limb/right	24
	3505	Normal	-3, -2, -1, 1, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
		Edema, Hind limb/left	2, 3, 4, 5
		Edema, Hind limb/right	24
100 µg/dose	4501	Normal	-3, -2, -1, 1, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
		Limb function impaired, Hind limb/left	2
		Edema, Hind limb/left	2, 3, 4, 5, 6
		Edema, Hind limb/right	24
	4502	Normal	-3, -2, -1, 1, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
		Limb function impaired, Hind limb/left	2
		Edema, Hind limb/left	2, 3, 4, 5
		Edema, Hind limb/right	24
	4503	Normal	-3, -2, -1, 1, 7, 8, 9, 10, 11, 12, 13, 14
		Limb function impaired, Hind limb/left	2
		Edema, Hind limb/left	2, 3, 4, 5, 6
		Edema, Hind limb/right	24, 25, 26
		Hair sparse, Cervical region	15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
		Hair sparse, Shoulder/right	17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31
	4504	Normal	-3, -2, -1, 1, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
		Limb function impaired, Hind limb/left	2
		Edema, Hind limb/left	2, 3, 4
		Edema, Hind limb/right	24

Values=Interval seen

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Detailed Clinical Observations

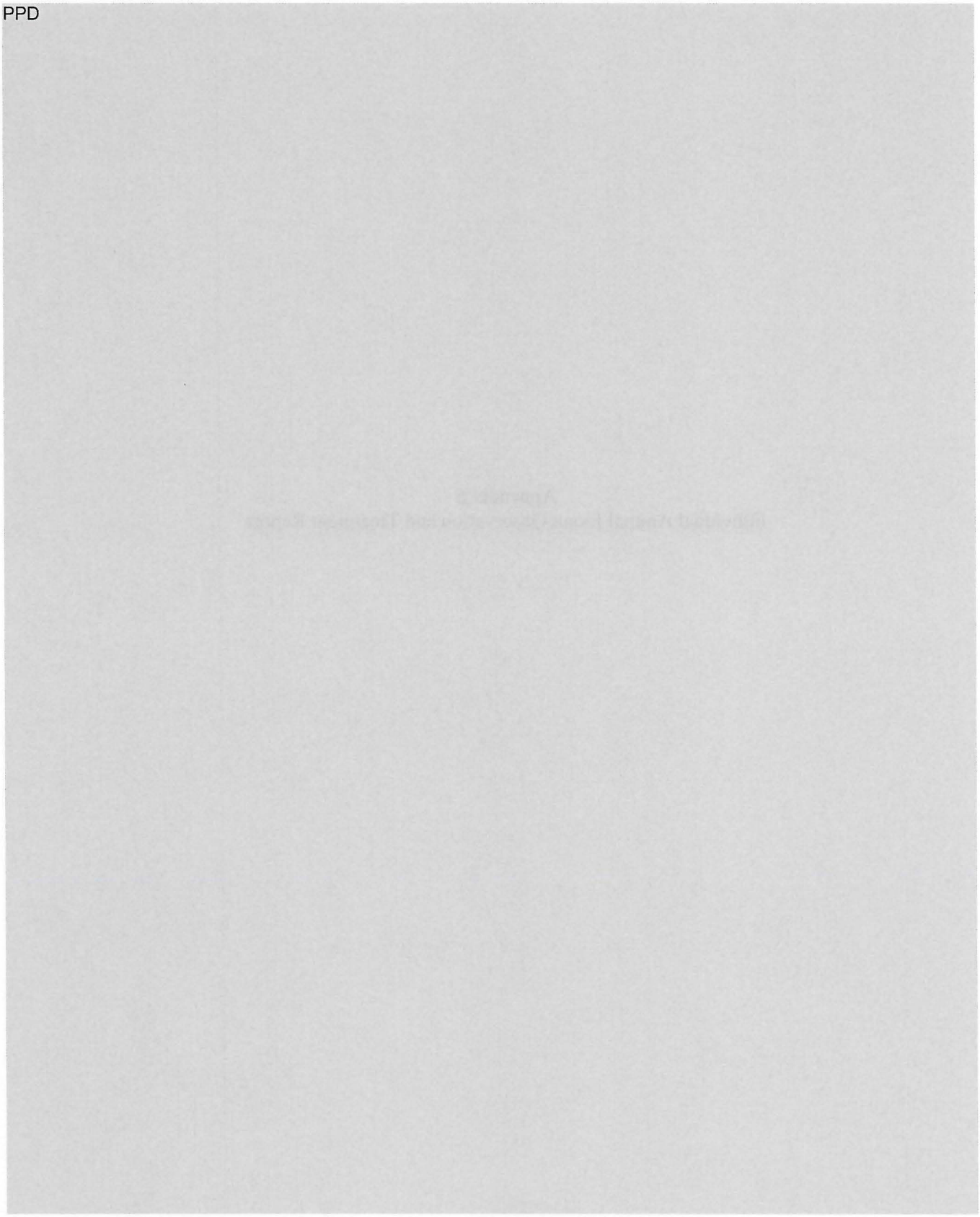
Sex: Female	Animal	Observation Type: Routine	From Day -3 (Start Date) to 35 (Start Date)
100 µg/dose	4605	Normal	-3, -2, -1, 1, 7, 8, 9, 10, 11, 12, 13, 14
		Limb function impaired, Hind limb/left	2
		Edema, Hind limb/left	2, 3, 4, 5, 6
		Edema, Hind limb/right	24, 25
		Hair sparse, Cervical region	15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
		Hair sparse, Face	15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
		Hair sparse, Shoulder/left	17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35
		Hair sparse, Shoulder/right	17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35

Values=Interval seen

Appendix 5
Individual Injection Site Observations

PPD

PPD



Appendix 6
Individual Animal Exam Observation and Treatment Report

The following abbreviations may be used throughout the table to document general medical information, as well as wound/integument descriptions and food enrichment.

Abbreviations Used Throughout Medical Record Comments				
Abbreviation	**Meaning**		**Abbreviation**	**Meaning**
ABD	Abdominal		HCC	Hematology, coagulation, clinical chemistry
~, approx.	Approximately		HFR	Hindfoot right
AD, EAR	Right ear		HFL	Hindfoot left
AF	Animal fasted		HLL	Hindlimb left
AFN	Appetite and feces normal		HLR	Hindlimb right
ANG	Anogenital		HR	Heart rate in beats per minute
AS, EAL	Left ear		HS	Hair sparse
AU	Both ears		IDC	Interdigital cyst
AXL	Axillary left		IGL	Inguinal left
AXR	Axillary right		IGR	Inguinal right
BAR	Bright, alert, and responsive		IM	Intramuscular
BG	Blood glucose		IP	Intraperitoneal
BID	Twice a day		IV	Intravenous
BHV	Behavior		L	Left
BLD	Basal Laboratory Diet		LRS	Lactated Ringer's Solution
BPM, bpm	Beats per minute		LUM	Lumbar
BF	Baby food		M	Mild
BT	Body temperature		MM	Mucous membranes
BW	Body weight		MOD	moderate
CHX	Chlorhexidine		MOU	Mouth
Clin Med	Clinical Medicine		M-W-F	Monday, Wednesday, Friday
CMP	Clinical Medicine Pharmacy		NA	Not applicable
CRA	Cranial		NAD	Nothing abnormal detected
CRT	Capillary refill time		NBS	Neurobehavioral Sciences
CRV	Cervical		NC	No change in condition
d/c, D/C	Discontinue(d)		Neo/poly/bac	Neomycin, Polymyxin, Bacitracin
DOR	Dorsal		NR	Not required/Not administered
d/x, D/X	Diagnosis		NSAID	Nonsteroidal anti-inflammatory drug
EE	Environmental enrichment		NSF	No significant findings
EENT	Ears, eyes, nose, and throat		Obs	Observations
ENB	Entire body		OD, EYR	Right eye
ENV	Enviro-dri		OS, EYL	Left eye
EXP	Expiration		OU	Both eyes
FBX	Foraging box		PE	Planned event
FE	Food enrichment		PO	Oral
FFL	Forefoot left		PU/PD	Polyuria/Polydipsia
FFR	Forefoot right		PRN, prn	As needed
FLL	Forelimb left		QD	Once daily
FLR	Forelimb right			

Abbreviations Used Throughout Medical Record Comments, Continued				
Abbreviation	Meaning		Abbreviation	Meaning
QID	Four times a day		SRG	Surgery
QAR	Quiet, alert, and responsive		SSD	Silver sulfadiazine
R	Right		TAO	Triple antibiotic ointment
RE	Respiratory effort		TA, TM	Test article, Test material
RF	Recently fed		TID	Three times a day
RR, rpm	Respiratory rate in breaths per minute		THR	Thoracic region
RRC	Room recently cleaned		TPR	Temperature, pulse, and respirations
S/R	Suture removal		TX	Treatment
SC/SQ	Subcutaneous		TXØ	Treatment completed/ discontinued
SD	Study Director		TXΔ	Treatment changed
SEV	Severe		UN	Product unavailable at this time
SH	Socially housed/ pair housed		VD	Ventrodorsal
SHL	Shoulder left		VEN	Ventral
SHO	Shoulder right		Vet	Veterinarian
SID	Once a day		VMS	Veterinary Management System
SN	Serial number		W/	With
SOP	Standard operating procedure		WNL	Within normal limits
			X	Times (i.e., 2X weekly)
Wound/Integument Descriptions				
B	Black		PLU	Plantar ulcer
CL	Closed		PU	Purulent
D	Dry		RM	Red material
DP	Deep		S	Scabbed
E	Erythemic		SU	Superficial
MO	Moist		SW	Swelling
OP	Open		U	Ulcerated
P	Purple			
Enrichment Food Abbreviations				
A	Apples		FM	Mardi Gras foraging mix
B	Bananas		FN	Fruit and Nut Foraging Mix
C	Carrots		FV	Fruit and veggie medley
CC	Criticare		G	Grapes
CR	Imitation Crab Meat		GB	Green Beans
DG	Diet Gel		GR	Granola
DM	Purina Dietetic Management		MF	Marshmallow Fluff
DT	Diamond Twists		MJ	Monkey Jumble
FB	Fruity Bites		O	Oranges
EN	Purina EN Gastroenteric Canned Diet		PB	Peanut Butter
ENV	Enviro-dri		TH	Timothy Hay
FC	Fruit Crunchies		VB	Veggie Bites
FDC	Frozen Dixie Cup		VC	Veggie Crunchies
FG	Fruity Gems		Y	Yam/ Sweet Potato

2308-123

A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

0 µg/dose	Individual Animal Exam Observation and Treatment Report: Male			
	Study Day	Animal Number	Activity	Entry Summary
	2	1001	Treatment	Category: Assessment; Treatment: Gen Ob; Frequency: Daily; Treatment Date: 14-FEB-20; Date and Time Performed: 14-FEB-20, 01:42:00 PM
	3	1001	Treatment	Category: Assessment; Treatment: Gen ob - reevaluation; Frequency: Daily; Treatment Date: 15-FEB-20; Date and Time Performed: 15-FEB-20, 07:53:00 AM
	3	1001	Treatment	Category: Assessment; Treatment: Gen Ob-Reeval; Frequency: Daily; Treatment Date: 15-FEB-20; Date and Time Performed: 15-FEB-20, 07:54:00 AM
	4	1001	Treatment	Category: Assessment; Treatment: Gen Ob; Frequency: Daily; Treatment Date: 16-FEB-20; Date and Time Performed: 16-FEB-20, 07:04:00 AM
	5	1001	Treatment	Category: Assessment; Treatment: Gen Ob; Frequency: Daily; Treatment Date: 17-FEB-20; Date and Time Performed: 17-FEB-20, 01:53:00 PM
	6	1001	Treatment	Category: Assessment; Treatment: Gen Ob; Frequency: Daily; Treatment Date: 18-FEB-20; Date and Time Performed: 18-FEB-20, 09:07:00 AM

2308-123

A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

30 µg/dose	Individual Animal Exam Observation and Treatment Report: Male			
	Study Day	Animal Number	Activity	Entry Summary
	24	2001	Treatment	Category: Assessment; Treatment: Gen Ob - G2/3/4; Frequency: Daily; Treatment Date: 07-MAR-20; Date and Time Performed: 07-MAR-20, 08:51:00 AM
	25	2001	Treatment	Category: Assessment; Treatment: Gen Ob - G2/3/4; Frequency: Daily; Treatment Date: 08-MAR-20; Date and Time Performed: 08-MAR-20, 09:11:00 AM
	26	2001	Treatment	Category: Assessment; Treatment: Gen Ob - G2/3/4; Frequency: Daily; Treatment Date: 09-MAR-20; Date and Time Performed: 09-MAR-20, 11:09:00 AM

2308-123

A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

60 µg/dose	Individual Animal Exam Observation and Treatment Report: Male			
	Study Day	Animal Number	Activity	Entry Summary
	29	3002	Assessment	Animal has small scabs on each side of the face however the animal appears non-painful and healthy otherwise at this time. Trim nails and offer EE. Monitor and re-evaluate in two weeks.
	29	3002	Examination	Obs: Activity/Gait/Locomotion; Obs: Activity/Gait/Locomotion, Normal
	29	3002	Examination	Obs: Attitude; Obs: Bright, Alert, Responsive
	29	3002	Examination	Obs: General Body Condition; Obs: Body Condition, Normal
	29	3002	Examination	Obs: Integumentary System; Obs: Skin, Scab; Obs: Head; Obs: Bilateral; Obs: Small
	29	3002	Examination	Obs: Pain Assessment; Obs: Non-painful
	29	3002	Treatment	Category: Enrichment; Treatment: Environmental Enrichment; Route: Offer PRN; Frequency: Once Weekly; Treatment Date: 12-MAR-20; Date and Time Performed: 12-MAR-20, 10:40:00 AM; Comments: 1 shepherd shack, 1 cocoon, 1 nestlet
	29	3002	Treatment	Category: Other; Treatment: Trim Nails; Frequency: Weekly PRN; Treatment Date: 12-MAR-20; Date and Time Performed: 12-MAR-20, 10:40:00 AM; Comments: Completed
	36	3002	Reassessment	Animal was euthanized and discarded on 18-MAR-2020. Confirmed in Provantis.
	29	3005	Assessment	Animal has a small dry scabbed area in the left inguinal region however the animal appears unaffected and healthy otherwise at this time. Monitor twice weekly and re-evaluate in one week to ensure scabbed area remains dry.
	29	3005	Examination	Obs: Activity/Gait/Locomotion; Obs: Activity/Gait/Locomotion, Normal
	29	3005	Examination	Obs: Attitude; Obs: Bright, Alert, Responsive
	29	3005	Examination	Obs: General Body Condition; Obs: Body Condition, Normal
	29	3005	Examination	Obs: Integumentary System; Obs: Skin, Scab; Obs: Inguinal; Obs: Left; Obs: Small; Obs: Dry
	29	3005	Examination	Obs: Pain Assessment; Obs: Non-painful
	29	3005	Treatment	Category: Assessment; Treatment: Monitor; Frequency: 2X Weekly - Thurs; Treatment Date: 12-MAR-20; Date and Time Performed: 12-MAR-20, 10:48:00 AM
	33	3005	Examination	Obs: Other; Obs: No Change
	33	3005	Treatment	Category: Assessment; Treatment: Monitor; Frequency: 2X Weekly - Thurs; Treatment Date: 16-MAR-20; Date and Time Performed: 16-MAR-20, 01:41:00 PM
	36	3005	Reassessment	Animal was euthanized and discarded on 18-MAR-2020. Confirmed in Provantis.

2308-123

A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

General Observation		
Observation Date	Activity	Entry Summary
2/13/2020	General Observation	Dosing of all animals was observed on day 1 by veterinarian. Animals showed no evidence of pain or distress during the dosing procedure or immediately following it. All animals appeared clinically normal cage-side afterwards. Monitor daily via gen ob and re-evaluate in two days to ensure that animals remain normal following injection of volume above IACUC recommended limits.
2/14/2020	General Observation	All dosed animals were examined. Group 1 animals appear clinically normal. Some group 2 animals have mild swelling in the left hind limb injection site with mildly abnormal ambulation observed. All animals in groups 3 and 4 have mild-moderate swelling in the left hind limb injection site with abnormal ambulation and mild-moderate impairment of the left hind limb observed. No animals reacted painfully to palpation of the left hind limb. All animals appear currently stable. Continue to monitor daily by general observation. Any animals with more severe clinical signs will be placed on individual consult. If swelling or limb impairment significantly increases in severity, or animals respond painfully to palpation, consider administration of single dose of NSAIDs. Vet review: JK 14FEB2020
2/15/2020	General Observation	All target study animals were observed. All appear healthy overall Group 2 animals: mild or no swelling, HLL injection site Groups 3/4 animals: mild to moderate swelling, HLL injection site No impairment observed in any group, no one appeared painful. Continue to perform daily observations, re-evaluate in 1 week or sooner as necessary. Vet Review SLA 16FEB2020
2/16/2020	General Observation	All target study animals were observed. All appear healthy overall. Group 1 animals appear normal Group 2 animals: mild or no swelling, HLL injection site Groups 3/4 animals: mild or no swelling, HLL injection site No impairment observed in any group, no one appeared painful. Vet Review SLA 16FEB2020
2/17/2020	General Observation	All target study animals were observed. All appear healthy overall. Group 1 animals appear normal Group 2 animals: appear normal Groups 3/4 animals: mild or no swelling, HLL injection site No impairment observed in any group, all appear non-painful. Vet review: JK 17FEB2020

2308-123

A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

2/18/2020	General Observation	All target study animals appear normal at this time. No swelling was observed and all animals are ambulating normally. No further monitoring via general observation necessary at this time. Vet review: JK 18FEB2020
3/6/2020	General Observation	All animals on study were examined due to the observations made after the first dose was administered. All animals in group 1 appear normal at this time. Animals in group 2 have mild to moderate swelling of the right hind limb with mild limb impairment of the right hind limb. Animals in groups 3 and 4 have moderate to severe swelling of the right hind limb with moderate limb impairment of the right hind limb. All animals appear non-painful upon palpation and appear stable overall at this time. Monitor all animals in groups 2, 3, and 4 daily via general observation for changes. Any animals found with additional or more severe symptoms will be placed on individual consult.
3/7/2020	General Observation	All animals in groups 2, 3, and 4 were observed. Group 2: a few animals have mild swelling HLR; they appear normal otherwise. Group 3: animals have moderate swelling HLR; they appear normal otherwise. Group 4: a few animals have mild swelling HLR with no impairment; most of the animals in group 4 have moderate swelling HLR with no impairment; a couple of group 4 animals have severe swelling HLR with mild impairment of that limb. All in group 4 appear healthy otherwise. No animals appear to be in pain at this time.
3/8/2020	General Observation	All animals in groups 2, 3, and 4 were observed. Group 2: animals have either mild or no swelling HLR and appear healthy, no impairment. Group 3: one animal has no swelling HLR; the others have mild swelling HLR; all appear healthy, no impairment. Group 4: animals have mild or moderate swelling HLR; all appear healthy, no impairment.
3/9/2020	General Observation	All animals in groups 2, 3, and 4 were examined. All animals are ambulating normally and no swelling was noted. All animals appear healthy overall at this time. No further monitoring or treatments via general observation necessary at this time.

Appendix 7
Individual Body Weight Values

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Body Weight Values

Sex: Male Body Weight (g)

0 µg/dose	Day(s) Relative to Start Date					
	-1	7	14	21	28	35
1001	196	253	295	321	338	357
1003	175	236	287	322	342	375
1004	187	248	303	348	362	392
1005	176	233	282	327	354	385
1102	171	232	275	310	330	360

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Body Weight Values

Sex: Male Body Weight (g)

30 µg/dose	Day(s) Relative to Start Date					
	-1	7	14	21	28	35
2001	175	222	274	317	331	363
2002	187	249	301	345	373	396
2003	189	241	311	366	389	424
2004	181	232	275	314	341	368
2005	191	246	306	353	374	411

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Body Weight Values

Sex: Male Body Weight (g)

60 µg/dose	Day(s) Relative to Start Date					
	-1	7	14	21	28	35
3001	189	240	284	341	366	403
3002	187	239	277	339	361	406
3003	176	223	274	317	335	370
3004	171	219	279	320	343	372
3005	188	241	292	323	351	373

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Body Weight Values

Sex: Male Body Weight (g)

100 µg/dose	Day(s) Relative to Start Date					
	-1	7	14	21	28	35
4001	183	234	292	337	357	393
4002	172	210	256	305	319	359
4003	192	238	293	340	354	385
4004	172	221	273	309	337	363
4005	195	248	310	358	379	412

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Body Weight Values

Sex: Female Body Weight (g)

0 µg/dose	Day(s) Relative to Start Date					
	-1	7	14	21	28	35
1501	201	216	255	275	283	280
1502	209	221	251	269	282	284
1503	196	203	225	237	253	252
1504	196	213	227	239	236	261
1505	216	236	264	281	302	303

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Body Weight Values

Sex: Female Body Weight (g)

30 µg/dose	Day(s) Relative to Start Date					
	-1	7	14	21	28	35
2501	214	233	255	273	273	282
2502	213	242	264	289	289	299
2503	211	227	241	247	266	257
2504	207	227	248	273	281	292
2505	202	231	249	266	272	284

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Body Weight Values

Sex: Female Body Weight (g)

60 µg/dose	Day(s) Relative to Start Date					
	-1	7	14	21	28	35
3501	228	261	279	311	309	348
3502	210	230	241	263	262	272
3503	210	230	261	294	287	295
3504	209	224	245	265	283	292
3505	211	225	246	262	266	276

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Body Weight Values

Sex: Female Body Weight (g)

100 µg/dose	Day(s) Relative to Start Date					
	-1	7	14	21	28	35
4501	206	223	236	248	263	280
4502	206	232	252	262	268	280
4503	203	214	232	250	255	265
4504	204	219	247	247	247	258
4605	212	224	246	270	285	313

Appendix 8
Individual Body Weight Change Values

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Body Weight Change Values, g

Sex: Male Body Weight Change

0 µg/dose	Day(s) Relative to Start Date				
	-1 → 7	7 → 14	14 → 21	21 → 28	28 → 35
1001	57	42	26	17	19
1003	61	51	35	20	33
1004	61	55	45	14	30
1005	57	49	45	27	31
1102	61	43	35	20	30

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Body Weight Change Values, g

Sex: Male Body Weight Change

30 µg/dose	Day(s) Relative to Start Date				
	-1 → 7	7 → 14	14 → 21	21 → 28	28 → 35
2001	47	52	43	14	32
2002	62	52	44	28	23
2003	52	70	55	23	35
2004	51	43	39	27	27
2005	55	60	47	21	37

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Body Weight Change Values, g

Sex: Male Body Weight Change

60 µg/dose	Day(s) Relative to Start Date				
	-1 → 7	7 → 14	14 → 21	21 → 28	28 → 35
3001	51	44	57	25	37
3002	52	38	62	22	45
3003	47	51	43	18	35
3004	48	60	41	23	29
3005	53	51	31	28	22

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Body Weight Change Values, g

Sex: Male Body Weight Change

100 µg/dose	Day(s) Relative to Start Date				
	-1 → 7	7 → 14	14 → 21	21 → 28	28 → 35
4001	51	58	45	20	36
4002	38	46	49	14	40
4003	46	55	47	14	31
4004	49	52	36	28	26
4005	53	62	48	21	33

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Body Weight Change Values, g

Sex: Female Body Weight Change

0 µg/dose	Day(s) Relative to Start Date				
	-1 → 7	7 → 14	14 → 21	21 → 28	28 → 35
1501	15	39	20	8	-3
1502	12	30	18	13	2
1503	7	22	12	16	-1
1504	17	14	12	-3	25
1505	20	28	17	21	1

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Body Weight Change Values, g

Sex: Female Body Weight Change

30 µg/dose	Day(s) Relative to Start Date				
	-1 → 7	7 → 14	14 → 21	21 → 28	28 → 35
2501	19	22	18	0	9
2502	29	22	25	0	10
2503	16	14	6	19	-9
2504	20	21	25	8	11
2505	29	18	17	6	12

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Body Weight Change Values, g

Sex: Female Body Weight Change

60 µg/dose	Day(s) Relative to Start Date				
	-1 → 7	7 → 14	14 → 21	21 → 28	28 → 35
3501	33	18	32	-2	39
3502	20	11	22	-1	10
3503	20	31	33	-7	8
3504	15	21	20	18	9
3505	14	21	16	4	10

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Body Weight Change Values, g

Sex: Female Body Weight Change

100 µg/dose	Day(s) Relative to Start Date				
	-1 → 7	7 → 14	14 → 21	21 → 28	28 → 35
4501	17	13	12	15	17
4502	26	20	10	6	12
4503	11	18	18	5	10
4504	15	28	0	0	11
4605	12	22	24	15	28

Appendix 9
Clinical Pathology Report

[redacted]

[redacted]

FINAL REPORT

Study Phase: Clinical Pathology

Testing Facility Study No. 2308-123

TESTING FACILITY:
[redacted]

[redacted]

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REPORT APPROVAL

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Clinical Pathologist

1. SUMMARY

This study was conducted for Moderna TX, Inc., to characterize the immunogenic response and potential toxicity of the test article, mRNA-1273, when administered via intramuscular (IM) injection once per day on Days 1 and 22 to Sprague Dawley CD® [Crl:CD®(SD)] rats.

mRNA-1273 was administered to Sprague Dawley CD® [Crl:CD®(SD)] rats as an IM injection on Days 1 and 22 at dose levels of 30, 60, and 100 µg/dose. Clinical pathology evaluations were conducted on main study animals as detailed below (see Text Table 2).

mRNA-1273-related changes consistent with inflammation were seen at ≥ 30 µg/dose in both sexes. These findings included moderate increases in neutrophil (range: 5.86x to 10.81x of control mean) and eosinophil (range: 2.60x to 4.67x of control mean) counts, along with mild to moderate decreases in mean albumin (range: 0.90x to 0.85x of control mean) and albumin/globulin ratio (range: 0.86x to 0.75x of control mean) in both sexes at all dose levels, with increased mean globulin (range: 1.12x to 1.15x of control mean) in males at 60 and 100 µg/dose.

Other mRNA-1273-related changes observed at 30, 60, and/or 100 µg/dose consisted of mild to moderate decreases in mean reticulocyte (range: 0.80x to 0.65x of control mean), lymphocyte (range: 0.74x to 0.47x of control mean), and/or monocyte (range: 0.58x to 0.52x of control mean) counts. The decreases in reticulocyte counts were associated with mild decreases in red cell mass (erythrocytes, hemoglobin, and/or hematocrit) in the males at 30, 60, and 100 µg/dose (hemoglobin range: 0.96x to 0.91x of control mean), and mild increases in RDW (red cell distribution width; range: 1.05x to 1.10x of control mean) in both sexes at all doses.

Additional minor mRNA-1273-related changes most likely related to alterations in metabolic state and/or hydration status were also seen at 30, 60, and/or 100 µg/dose in both sexes and included mild increases in mean creatinine (range: 1.26x to 1.43x of control mean), triglyceride (range: 1.66x to 2.30x of control mean), and/or cholesterol (range: 1.57x to 1.62x of control mean) concentrations. Mean glucose was also mildly increased (1.26x of control mean) in males at 100 µg/dose.

2. MATERIALS AND METHODS

2.1. Group Assignments

Animals were assigned to the study as indicated in Text Table 1.

Text Table 1
Group Assignments

Group No.	Dose Level (µg/dose)	No. of Animals	
		Male	Female
1	0	5	5
2	30	5	5
3	60	5	5
4	100	5	5

2.2. Hematology and Clinical Chemistry

Samples were collected according to Text Table 2 and analyzed for protocol designated endpoints.

Text Table 2
Clinical Pathology Sample Collection

Group No.	Time Point(s)	Hematology	Clinical Chemistry
All animals	Day 23 (24 hr post the last dose)	X	X
Target Volume (mL):	NA	0.5 mL	0.8 mL
Method:	The order of bleeding was by dose group order, to minimize any potential risk of cross-contamination		
Collection Site:	Sublingual vein		
Fasting Required:	The animals had access to drinking water but were fasted overnight (at least 8 hours) prior to scheduled blood collection.		
Anticoagulant:	NA	K_2EDTA	Serum Gel Separator
Processing:	NA	None	Serum

X = Sample was collected; NA = Not applicable; hr = hour; post = postdose.

2.3. Data Collection and Analysis Software

Data Collection and Analysis Software is listed in Text Table 3.

Text Table 3
Data Collection and Analysis Software

Hematology	Advia 2120i v6.9
Clinical Chemistry	AU5800 v05.03

3. RESULTS AND DISCUSSION

For the purpose of this report, treated animals' values were compared to control animals' values. Fold change (x) in clinical pathology parameters was determined by comparing the mRNA-1273 group mean to the respective control group mean.

3.1. Hematology

(Table 1 and Appendix 1)

Administration of mRNA-1273 to rats was associated with hematology changes at 30, 60, and 100 µg/dose. These changes, presented in Text Table 4, occurred in red cell mass (red blood cell count, hemoglobin, and hematocrit), reticulocyte, neutrophil, lymphocyte, monocyte, eosinophil counts, and/or RDW.

Text Table 4
mRNA-1273-Related Hematology Changes

Group	1*		2		3		4	
Dose Level (µg/dose)	0		30		60		100	
Sex	M	F	M	F	M	F	M	F
Hemoglobin (g/dL)								
Day 23 (24 hr post)	17.42	16.44	**0.92x**	–	**0.91x**	–	**0.93x**	–
Erythrocytes (10^6x cells/µL)								
Day 23 (24 hr post)	8.600	8.618	**0.94x**	–	**0.94x**	–	**0.96x**	–
Hematocrit (%)								
Day 23 (24 hr post)	53.46	49.48	**0.93x**	–	**0.91x**	–	**0.93x**	–
Reticulocytes (10^3x cells/µL)								
Day 23 (24 hr post)	223.48	179.28	**0.78x**	**0.79x**	**0.77x**	**0.80x**	**0.77x**	**0.65x**
Neutrophils (10^3x cells/µL)								
Day 23 (24 hr post)	0.946	1.178	**9.79x**	**7.67x**	**10.81x**	**6.58x**	**8.26x**	**5.86x**
Lymphocytes (10^3x cells/µL)								
Day 23 (24 hr post)	7.978	6.004	**0.65x**	–	**0.58x**	0.74x	**0.47x**	0.61x
Monocytes (10^3x cells/µL)								
Day 23 (24 hr post)	0.220	0.124	–	–	**0.58x**	–	**0.52x**	–
Eosinophils (10^3x cells/µL)								
Day 23 (24 hr post)	0.040	0.054	**3.30x**	**4.67x**	**4.00x**	**3.26x**	**2.60x**	**3.48x**
RDW (%)								
Day 23 (24 hr post)	12.52	11.28	1.06x	1.05x	**1.08x**	**1.07x**	**1.10x**	**1.07x**

M = Males F = Females
hr = hour; post = postdose
RDW = red cell distribution width
A dash (—) indicates absence of a mRNA-1273-related change. Numerical values indicate fold change of the treated group mean value relative to the control group mean value. **Bolded** values indicate the mean value was statistically different from controls ($p < 0.05$ or $p < 0.01$).
* Control group values are reported for comparison

mRNA-1273-related changes consistent with inflammation were seen at ≥ 30 µg/dose in both sexes and included moderate increases in neutrophil (range: 5.86x to 10.81x of control mean) and eosinophil (range: 2.60x to 4.67x of control mean) counts. These effects correlated to other signals of inflammation described below (see Section 3.2).

mRNA-1273-related changes at 30, 60, and/or 100 µg/dose in both sexes consisted of mild to moderate decreases in mean reticulocyte (range: 0.80x to 0.65x of control mean), lymphocyte (range: 0.74x to 0.47x of control mean), and/or monocyte (range: 0.58x to 0.52x of control mean) counts. The decreases in reticulocyte counts were associated with mild decreases in red cell mass (red blood cell count, hemoglobin, and hematocrit) in the males at 30, 60, and 100 µg/dose (range: 0.91x to 0.96x of control mean), and mild increases in RDW (range: 1.05x to 1.10x) in both sexes at all doses.

All other fluctuations among individual and mean hematology values, regardless of statistical significance, were considered sporadic, consistent with biologic variation and/or negligible in magnitude, and not related to mRNA-1273 administration.

3.2. Clinical Chemistry

(Table 2 and Appendix 2)

Administration of mRNA-1273 to rats was associated with clinical chemistry changes at 30, 60, and 100 µg/dose. These changes, presented in Text Table 5, occurred in mean creatinine, albumin, globulin, albumin/globulin ratio, triglyceride, cholesterol, and/or glucose concentrations.

Text Table 5
mRNA-1273-Related Clinical Chemistry Changes

Group	1*		2		3		4	
Dose Level (µg/dose)	0		30		60		100	
Sex	M	F	M	F	M	F	M	F
Creatinine (mg/dL)								
Day 23 (24 hr post)	0.28	0.40	**1.36x**	**1.32x**	–	**1.26x**	**1.43x**	**1.37x**
Albumin (g/dL)								
Day 23 (24 hr post)	3.53	3.86	**0.90x**	**0.90x**	**0.87x**	**0.88x**	**0.88x**	**0.85x**
Globulin (g/dL)								
Day 23 (24 hr post)	3.12	3.47	–	–	1.12x	–	**1.15x**	–
Albumin/Globulin Ratio								
Day 23 (24 hr post)	1.13	1.12	**0.83x**	0.87x	**0.78x**	0.87x	**0.75x**	0.86x
Triglycerides (mg/dL)								
Day 23 (24 hr post)	40.0	35.5	**1.88x**	–	**2.30x**	2.02x	1.66x	–
Cholesterol (mg/dL)								
Day 23 (24 hr post)	55.6	76.9	**1.62x**	–	**1.57x**	–	**1.58x**	–

Group	1*		2		3		4	
Dose Level (µg/dose)	0		30		60		100	
Sex	M	F	M	F	M	F	M	F
Glucose (mg/dL)								
Day 23 (24 hr post)	69.0	84.5	–	–	–	–	**1.26x**	–

M = Males F = Females
hr = hour; post = postdose
A dash (—) indicates absence of a mRNA-1273-related change. Numerical values indicate fold change of the treated group mean value relative to the control group mean value. **Bolded** values indicate the mean value was statistically different from controls ($p < 0.05$ or $p < 0.01$).
* Control group values are reported for comparison.

mRNA-1273-related changes consistent with inflammation were seen at 30, 60, and/or 100 µg/dose in both sexes, and included mild to moderate decreases in mean albumin (range: 0.90x to 0.85x of control mean) and albumin/globulin ratio (range: 0.86x to 0.75x of control mean), with increased mean globulin (range: 1.12x to 1.15x of control mean) in males at 60 and 100 µg/dose. These effects correlated to other signals of inflammation described above (see Section 3.1).

Other mRNA-1273-related changes noted at 30, 60, and/or 100 µg/dose in both sexes consisted of mild increases in mean creatinine (range: 1.26x to 1.43x of control mean), triglyceride (range: 1.66x to 2.30x of control mean), and/or cholesterol (range: 1.57x to 1.62x of control mean) concentrations. Mean glucose was also mildly increased (1.26x of control mean) in males at 100 µg/dose. This collection of changes was most likely related to mild alterations in metabolic state and hydration status.

All other fluctuations among individual and mean clinical chemistry values, regardless of statistical significance, were considered sporadic, consistent with biologic variation and/or negligible in magnitude, and not related to mRNA-1273 administration.

4. CONCLUSIONS

Administration of mRNA-1273 to Sprague Dawley rats as an IM injection on Days 1 and 22 at dose levels of 30, 60, and 100 µg/dose elicited hematology and clinical chemistry changes at all dose levels.

mRNA-1273-related changes consistent with inflammation were seen at ≥ 30 µg/dose in both sexes. These findings included moderate increases in neutrophil and/or eosinophil counts, along with mild to moderate decreases in albumin and albumin/globulin ratio at ≥ 30 µg/dose, with increased globulin in males at ≥ 30 µg/dose.

Other mRNA-1273-related changes observed at ≥ 30 µg/dose consisted of mild to moderate decreases in reticulocyte, lymphocyte, and/or monocyte counts. The decreases in reticulocyte counts were associated with mild decreases in red cell mass (red blood cell count, hemoglobin, and hematocrit) in males at all dose levels, and mild increases in RDW in both sexes at all doses.

Additional minor mRNA-1273-related changes additional minor changes most likely related to alterations in metabolic state and/or hydration status were also seen at ≥ 30 µg/dose in both sexes and included mild increases in creatinine, triglyceride, and/or cholesterol concentrations. Glucose was also mildly increased in males at 100 µg/dose.

Table 2
Summary of Clinical Chemistry Values

Abbreviations for Clinical Chemistry Parameters

24PD - 24 hour postdose
AST - Aspartate Aminotransferase
ALT - Alanine Aminotransferase
ALP - Alkaline Phosphatase

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Summary of Clinical Chemistry Values

Sex: Male Day(s) Relative to Start Date			0 µg/dose	30 µg/dose	60 µg/dose	100 µg/dose
Sodium (mEq/L)	23 (24PD) [g]	Mean	141.8	140.0	139.7	139.7
		SD	1.45	1.85	1.21	1.00
		N	5	5	5	5
Potassium (mEq/L)	23 (24PD) [g1]	Mean	5.26	5.40	6.01	5.86
		SD	0.410	0.359	1.035	0.833
		N	5	5	5	5
Chloride (mEq/L)	23 (24PD) [g]	Mean	99.1	97.7	97.3	98.0
		SD	0.63	1.21	1.53	1.46
		N	5	5	5	5
Calcium (mg/dL)	23 (24PD) [g]	Mean	9.96	9.85	9.72	9.77
		SD	0.297	0.315	0.276	0.283
		N	5	5	5	5
Phosphorus (mg/dL)	23 (24PD) [g]	Mean	8.25	8.64	8.84	8.89
		SD	0.490	0.384	0.351	0.212
		N	5	5	5	5
ALP (U/L)	23 (24PD) [g]	Mean	223.7	204.5	186.2	204.6
		SD	66.54	55.76	27.38	43.53
		N	5	5	5	5
Total Bilirubin (mg/dL)	23 (24PD) [g]	Mean	0.14	0.14	0.15	0.13
		SD	0.020	0.016	0.016	0.012
		N	5	5	5	5

[g] - Anova & Dunnett
[g1] - Anova & Dunnett(Log)

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Summary of Clinical Chemistry Values

Sex: Male Day(s) Relative to Start Date			0 µg/dose	30 µg/dose	60 µg/dose	100 µg/dose
AST (U/L)	23 (24PD) [g]	Mean	120.3	138.5	131.6	119.8
		SD	17.41	38.93	23.98	19.71
		N	5	5	5	5
ALT (U/L)	23 (24PD) [g]	Mean	32.4	33.9	34.6	34.5
		SD	2.72	3.40	6.89	3.86
		N	5	5	5	5
Urea Nitrogen (mg/dL)	23 (24PD) [g]	Mean	13.6	14.0	12.4	11.9
		SD	0.88	1.57	1.46	0.67
		N	5	5	5	5
Creatinine (mg/dL)	23 (24PD) [g]	Mean	0.28	0.36 b	0.34 b	0.37 b
		SD	0.037	0.031	0.007	0.019
		N	5	5	5	5
Total Protein (g/dL)	23 (24PD) [g]	Mean	6.65	6.53	6.54	6.66
		SD	0.117	0.330	0.507	0.363
		N	5	5	5	5
Albumin (g/dL)	23 (24PD) [g]	Mean	3.53	3.16 b	3.06 b	3.06 b
		SD	0.083	0.183	0.170	0.128
		N	5	5	5	5
Globulin (g/dL)	23 (24PD) [g]	Mean	3.12	3.37	3.48	3.60 a
		SD	0.068	0.156	0.345	0.256
		N	5	5	5	5

[g] - Anova & Dunnett: a = $p < 0.05$; b = $p < 0.01$

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Summary of Clinical Chemistry Values

Sex: Male Day(s) Relative to Start Date			0 µg/dose	30 µg/dose	60 µg/dose	100 µg/dose
Albumin/ Globulin	23 (24PD) [g]	Mean	1.13	0.94 b	0.88 b	0.85 b
		SD	0.033	0.026	0.045	0.039
		N	5	5	5	5
Triglyceride (mg/dL)	23 (24PD) [g]	Mean	40.0	75.1 a	92.1 b	66.4
		SD	7.38	29.16	25.71	10.25
		N	5	5	5	5
Cholesterol (mg/dL)	23 (24PD) [g]	Mean	55.6	89.6 b	87.1 b	87.7 b
		SD	5.68	13.50	8.59	15.39
		N	5	5	5	5
Glucose (mg/dL)	23 (24PD) [g1]	Mean	69.0	70.7	79.7	86.5 b
		SD	5.18	10.27	3.12	1.16
		N	5	5	5	5

[g] - Anova & Dunnett: a = p < 0.05; b = p < 0.01
[g1] - Kruskal-Wallis & Dunn: b = p < 0.01

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Summary of Clinical Chemistry Values

Sex: Female Day(s) Relative to Start Date			0 µg/dose	30 µg/dose	60 µg/dose	100 µg/dose
Sodium (mEq/L)	23 (24PD) [g]	Mean	140.6	139.3	139.1	139.7
		SD	0.99	2.85	1.80	2.71
		N	5	5	5	5
Potassium (mEq/L)	23 (24PD) [g]	Mean	4.92	5.61	5.83 a	5.92 b
		SD	0.364	0.488	0.616	0.316
		N	5	5	5	5
Chloride (mEq/L)	23 (24PD) [g]	Mean	100.2	97.6	98.3	99.9
		SD	0.72	2.24	1.99	1.58
		N	5	5	5	5
Calcium (mg/dL)	23 (24PD) [g]	Mean	10.07	10.10	9.76	9.69
		SD	0.466	0.249	0.436	0.300
		N	5	5	5	5
Phosphorus (mg/dL)	23 (24PD) [g1]	Mean	5.91	7.66 b	7.20	7.29 a
		SD	0.211	1.014	0.520	0.509
		N	5	5	5	5
ALP (U/L)	23 (24PD) [g]	Mean	104.7	107.7	106.8	100.5
		SD	18.04	16.18	15.59	18.82
		N	5	5	5	5
Total Bilirubin (mg/dL)	23 (24PD) [g]	Mean	0.14	0.20	0.16	0.16
		SD	0.017	0.054	0.032	0.016
		N	5	5	5	5

[g] - Anova & Dunnett: a = $p < 0.05$; b = $p < 0.01$
[g1] - Kruskal-Wallis & Dunn: a = $p < 0.05$; b = $p < 0.01$

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Summary of Clinical Chemistry Values

Sex: Female Day(s) Relative to Start Date			0 µg/dose	30 µg/dose	60 µg/dose	100 µg/dose
AST (U/L)	23 (24PD) [g]	Mean	105.4	126.7	123.9	114.4
		SD	12.06	14.82	7.81	29.61
		N	5	5	5	5
ALT (U/L)	23 (24PD) [g]	Mean	32.5	34.4	30.2	34.8
		SD	8.56	5.33	4.51	9.98
		N	5	5	5	5
Urea Nitrogen (mg/dL)	23 (24PD) [g]	Mean	14.6	14.0	16.1	14.1
		SD	0.96	1.96	2.08	1.38
		N	5	5	5	5
Creatinine (mg/dL)	23 (24PD) [g]	Mean	0.40	0.48 a	0.45	0.48 a
		SD	0.039	0.061	0.011	0.039
		N	5	5	5	5
Total Protein (g/dL)	23 (24PD) [g]	Mean	7.34	7.00	6.85	6.68 a
		SD	0.584	0.213	0.246	0.148
		N	5	5	5	5
Albumin (g/dL)	23 (24PD) [g]	Mean	3.86	3.44 a	3.38 a	3.26 b
		SD	0.418	0.212	0.190	0.078
		N	5	5	5	5
Globulin (g/dL)	23 (24PD) [g]	Mean	3.47	3.56	3.47	3.41
		SD	0.336	0.260	0.131	0.160
		N	5	5	5	5

[g] - Anova & Dunnett: a = $p < 0.05$; b = $p < 0.01$

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Summary of Clinical Chemistry Values

Sex: Female Day(s) Relative to Start Date			0 µg/dose	30 µg/dose	60 µg/dose	100 µg/dose
Albumin/ Globulin	23 (24PD) [g]	Mean	1.12	0.97	0.97	0.96
		SD	0.134	0.113	0.061	0.056
		N	5	5	5	5
Triglyceride (mg/dL)	23 (24PD) [g1]	Mean	35.5	58.1	71.6	58.3
		SD	5.87	30.85	36.63	15.65
		N	5	5	5	5
Cholesterol (mg/dL)	23 (24PD) [g]	Mean	76.9	70.5	69.2	77.2
		SD	20.42	20.58	20.19	23.38
		N	5	5	5	5
Glucose (mg/dL)	23 (24PD) [g]	Mean	84.5	80.5	83.5	94.1
		SD	10.80	5.52	5.20	5.65
		N	5	5	5	5

[g] - Anova & Dunnett
[g1] - Anova & Dunnett(Log)

Table 1
Summary of Hematology Values

Abbreviations for Hematology Parameters

MCV - Mean Corpuscular Volume
MCH - Mean Corpuscular Hemoglobin
MCHC - Mean Corpuscular Hemoglobin Concentration
RDW - Red Blood Cell Distribution Width
24PD - 24 hour postdose

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Summary of Hematology Values

Sex: Male Day(s) Relative to Start Date			0 µg/dose	30 µg/dose	60 µg/dose	100 µg/dose
Leukocytes (10^3 cells/ µL)	23 (24PD) [g]	Mean	9.30	14.96 a	15.36 a	11.90
		SD	0.868	2.523	3.446	4.306
		N	5	5	5	5
Erythrocytes (10^6 cells/ µL)	23 (24PD) [g]	Mean	8.600	8.070	8.116	8.294
		SD	0.5361	0.2528	0.2856	0.2586
		N	5	5	5	5
Hemoglobin (g/dL)	23 (24PD) [g]	Mean	17.42	16.06 b	15.88 b	16.28 b
		SD	0.726	0.261	0.327	0.311
		N	5	5	5	5
Hematocrit (%)	23 (24PD) [g]	Mean	53.46	49.28 b	48.40 b	49.86 b
		SD	1.876	0.950	1.125	1.514
		N	5	5	5	5
MCV (fL)	23 (24PD) [g]	Mean	62.30	61.10	59.66	60.10
		SD	2.887	2.312	1.370	1.251
		N	5	5	5	5
MCH (pg)	23 (24PD) [g]	Mean	20.30	19.92	19.56	19.62
		SD	0.840	0.760	0.488	0.249
		N	5	5	5	5
MCHC (g/dL)	23 (24PD) [g]	Mean	32.54	32.58	32.82	32.68
		SD	0.251	0.249	0.217	0.540
		N	5	5	5	5

[g] - Anova & Dunnett: a = $p < 0.05$; b = $p < 0.01$

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Summary of Hematology Values

Sex: Male Day(s) Relative to Start Date			0 µg/dose	30 µg/dose	60 µg/dose	100 µg/dose
Platelets (10^3 cells/ µL)	23 (24PD) [g]	Mean	823.2	1007.6	960.0	990.6
		SD	345.70	97.55	127.35	61.37
		N	5	5	5	5
Absolute Reticulocyte (10^3 cells/µL)	23 (24PD) [g1]	Mean	223.48	174.84 a	171.70 a	172.88 a
		SD	46.622	19.888	23.256	12.307
		N	5	5	5	5
Neutrophils (10^3 cells/ µL)	23 (24PD) [g1]	Mean	0.946	9.258 b	10.230 b	7.814 b
		SD	0.1880	2.1675	3.0448	3.4915
		N	5	5	5	5
Lymphocytes (10^3 cells/ µL)	23 (24PD) [g1]	Mean	7.978	5.200 b	4.614 b	3.754 b
		SD	0.9159	0.6885	0.8708	1.0540
		N	5	5	5	5
Monocytes (10^3 cells/ µL)	23 (24PD) [g1]	Mean	0.220	0.156	0.128 a	0.114 a
		SD	0.0863	0.0261	0.0370	0.0498
		N	5	5	5	5
Eosinophils (10^3 cells/ µL)	23 (24PD) [g2]	Mean	0.040	0.132 b	0.200 b	0.104 b
		SD	0.0187	0.0363	0.0711	0.0114
		N	5	5	5	5
Basophils (10^3 cells/ µL)	23 (24PD) [g1]	Mean	0.048	0.072	0.072	0.044
		SD	0.0259	0.0390	0.0130	0.0261
		N	5	5	5	5

[g] - Kruskal-Wallis & Dunn
[g1] - Anova & Dunnett: a = $p < 0.05$; b = $p < 0.01$
[g2] - Anova & Dunnett(Log): b = $p < 0.01$

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Summary of Hematology Values

Sex: Male Day(s) Relative to Start Date			0 µg/dose	30 µg/dose	60 µg/dose	100 µg/dose
Other Cells (10^3 cells/ µL)	23 (24PD) [g]	Mean	0.080	0.144 a	0.112	0.074
		SD	0.0235	0.0329	0.0421	0.0297
		N	5	5	5	5
RDW (%)	23 (24PD) [g]	Mean	12.52	13.28	13.58 b	13.76 b
		SD	0.319	0.507	0.581	0.434
		N	5	5	5	5

[g] - Anova & Dunnett: a = p < 0.05; b = p < 0.01

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Summary of Hematology Values

Sex: Female Day(s) Relative to Start Date			0 µg/dose	30 µg/dose	60 µg/dose	100 µg/dose
Leukocytes (10^3 cells/ µL)	23 (24PD) [g]	Mean	7.46	14.70 b	12.62	11.00
		SD	1.787	1.290	3.267	4.926
		N	5	5	5	5
Erythrocytes (10^6 cells/ µL)	23 (24PD) [g1]	Mean	8.618	8.482	8.922	8.904
		SD	0.2997	0.2472	0.2408	0.7889
		N	5	5	5	5
Hemoglobin (g/dL)	23 (24PD) [g]	Mean	16.44	16.00	16.78	17.12
		SD	0.270	0.339	0.460	0.918
		N	5	5	5	5
Hematocrit (%)	23 (24PD) [g2]	Mean	49.48	47.84	50.62	51.74
		SD	1.201	1.009	1.420	3.428
		N	5	5	5	5
MCV (fL)	23 (24PD) [g]	Mean	57.44	56.44	56.70	58.22
		SD	1.474	2.051	1.294	1.411
		N	5	5	5	5
MCH (pg)	23 (24PD) [g]	Mean	19.08	18.90	18.82	19.28
		SD	0.606	0.696	0.487	0.719
		N	5	5	5	5
MCHC (g/dL)	23 (24PD) [g]	Mean	33.22	33.48	33.16	33.12
		SD	0.377	0.217	0.241	0.563
		N	5	5	5	5

[g] - Anova & Dunnett: b = p < 0.01
[g1] - Kruskal-Wallis & Dunn
[g2] - Anova & Dunnett(Log)

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Summary of Hematology Values

Sex: Female Day(s) Relative to Start Date			0 µg/dose	30 µg/dose	60 µg/dose	100 µg/dose
Platelets (10^3 cells/ µL)	23 (24PD) [g]	Mean	1194.2	1025.2	1009.0	1000.0
		SD	181.67	94.24	139.91	77.09
		N	5	5	5	5
Absolute Reticulocyte (10^3 cells/µL)	23 (24PD) [g]	Mean	179.28	140.96	143.24	116.72 b
		SD	20.125	39.100	20.084	14.832
		N	5	5	5	5
Neutrophils (10^3 cells/ µL)	23 (24PD) [g]	Mean	1.178	9.036 b	7.754 b	6.900 b
		SD	0.3355	1.6046	2.0583	3.2773
		N	5	5	5	5
Lymphocytes (10^3 cells/ µL)	23 (24PD) [g]	Mean	6.004	4.992	4.426	3.670
		SD	1.4705	0.7987	1.2039	1.6383
		N	5	5	5	5
Monocytes (10^3 cells/ µL)	23 (24PD) [g]	Mean	0.124	0.170	0.108	0.102
		SD	0.0279	0.0752	0.0438	0.0342
		N	5	5	5	5
Eosinophils (10^3 cells/ µL)	23 (24PD) [g1]	Mean	0.054	0.252 b	0.176 b	0.188 b
		SD	0.0089	0.0676	0.0873	0.0589
		N	5	5	5	5
Basophils (10^3 cells/ µL)	23 (24PD) [g]	Mean	0.034	0.114 a	0.072	0.066
		SD	0.0182	0.0559	0.0370	0.0321
		N	5	5	5	5

[g] - Anova & Dunnett: a = p < 0.05; b = p < 0.01
[g1] - Anova & Dunnett(Log): b = p < 0.01

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A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Summary of Hematology Values

Sex: Female Day(s) Relative to Start Date			0 µg/dose	30 µg/dose	60 µg/dose	100 µg/dose
Other Cells (10^3 cells/ µL)	23 (24PD) [g]	Mean	0.066	0.136	0.084	0.076
		SD	0.0207	0.0647	0.0207	0.0467
		N	5	5	5	5
RDW (%)	23 (24PD) [g1]	Mean	11.28	11.88	12.06 a	12.06 a
		SD	0.507	0.482	0.344	0.321
		N	5	5	5	5

[g] - Anova & Dunnett(Log)
[g1] - Anova & Dunnett: a = p < 0.05

Table 2
Summary of Clinical Chemistry Values

Abbreviations for Clinical Chemistry Parameters

24PD - 24 hour postdose
AST - Aspartate Aminotransferase
ALT - Alanine Aminotransferase
ALP - Alkaline Phosphatase

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A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Summary of Clinical Chemistry Values

Sex: Male Day(s) Relative to Start Date			0 µg/dose	30 µg/dose	60 µg/dose	100 µg/dose
Sodium (mEq/L)	23 (24PD) [g]	Mean	141.8	140.0	139.7	139.7
		SD	1.45	1.85	1.21	1.00
		N	5	5	5	5
Potassium (mEq/L)	23 (24PD) [g1]	Mean	5.26	5.40	6.01	5.86
		SD	0.410	0.359	1.035	0.833
		N	5	5	5	5
Chloride (mEq/L)	23 (24PD) [g]	Mean	99.1	97.7	97.3	98.0
		SD	0.63	1.21	1.53	1.46
		N	5	5	5	5
Calcium (mg/dL)	23 (24PD) [g]	Mean	9.96	9.85	9.72	9.77
		SD	0.297	0.315	0.276	0.283
		N	5	5	5	5
Phosphorus (mg/dL)	23 (24PD) [g]	Mean	8.25	8.64	8.84	8.89
		SD	0.490	0.384	0.351	0.212
		N	5	5	5	5
ALP (U/L)	23 (24PD) [g]	Mean	223.7	204.5	186.2	204.6
		SD	66.54	55.76	27.38	43.53
		N	5	5	5	5
Total Bilirubin (mg/dL)	23 (24PD) [g]	Mean	0.14	0.14	0.15	0.13
		SD	0.020	0.016	0.016	0.012
		N	5	5	5	5

[g] - Anova & Dunnett
[g1] - Anova & Dunnett(Log)

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A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Summary of Clinical Chemistry Values

Sex: Male Day(s) Relative to Start Date			0 µg/dose	30 µg/dose	60 µg/dose	100 µg/dose
AST (U/L)	23 (24PD) [g]	Mean	120.3	138.5	131.6	119.8
		SD	17.41	38.93	23.98	19.71
		N	5	5	5	5
ALT (U/L)	23 (24PD) [g]	Mean	32.4	33.9	34.6	34.5
		SD	2.72	3.40	6.89	3.86
		N	5	5	5	5
Urea Nitrogen (mg/dL)	23 (24PD) [g]	Mean	13.6	14.0	12.4	11.9
		SD	0.88	1.57	1.46	0.67
		N	5	5	5	5
Creatinine (mg/dL)	23 (24PD) [g]	Mean	0.28	0.36 b	0.34 b	0.37 b
		SD	0.037	0.031	0.007	0.019
		N	5	5	5	5
Total Protein (g/dL)	23 (24PD) [g]	Mean	6.65	6.53	6.54	6.66
		SD	0.117	0.330	0.507	0.363
		N	5	5	5	5
Albumin (g/dL)	23 (24PD) [g]	Mean	3.53	3.16 b	3.06 b	3.06 b
		SD	0.083	0.183	0.170	0.128
		N	5	5	5	5
Globulin (g/dL)	23 (24PD) [g]	Mean	3.12	3.37	3.48	3.60 a
		SD	0.068	0.156	0.345	0.256
		N	5	5	5	5

[g] - Anova & Dunnett: a = $p < 0.05$; b = $p < 0.01$

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A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Summary of Clinical Chemistry Values

Sex: Male Day(s) Relative to Start Date			0 µg/dose	30 µg/dose	60 µg/dose	100 µg/dose
Albumin/ Globulin	23 (24PD) [g]	Mean	1.13	0.94 b	0.88 b	0.85 b
		SD	0.033	0.026	0.045	0.039
		N	5	5	5	5
Triglyceride (mg/dL)	23 (24PD) [g]	Mean	40.0	75.1 a	92.1 b	66.4
		SD	7.38	29.16	25.71	10.25
		N	5	5	5	5
Cholesterol (mg/dL)	23 (24PD) [g]	Mean	55.6	89.6 b	87.1 b	87.7 b
		SD	5.68	13.50	8.59	15.39
		N	5	5	5	5
Glucose (mg/dL)	23 (24PD) [g1]	Mean	69.0	70.7	79.7	86.5 b
		SD	5.18	10.27	3.12	1.16
		N	5	5	5	5

[g] - Anova & Dunnett: a = $p < 0.05$; b = $p < 0.01$
[g1] - Kruskal-Wallis & Dunn: b = $p < 0.01$

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A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Summary of Clinical Chemistry Values

Sex: Female Day(s) Relative to Start Date			0 µg/dose	30 µg/dose	60 µg/dose	100 µg/dose
Sodium (mEq/L)	23 (24PD) [g]	Mean	140.6	139.3	139.1	139.7
		SD	0.99	2.85	1.80	2.71
		N	5	5	5	5
Potassium (mEq/L)	23 (24PD) [g]	Mean	4.92	5.61	5.83 a	5.92 b
		SD	0.364	0.488	0.616	0.316
		N	5	5	5	5
Chloride (mEq/L)	23 (24PD) [g]	Mean	100.2	97.6	98.3	99.9
		SD	0.72	2.24	1.99	1.58
		N	5	5	5	5
Calcium (mg/dL)	23 (24PD) [g]	Mean	10.07	10.10	9.76	9.69
		SD	0.466	0.249	0.436	0.300
		N	5	5	5	5
Phosphorus (mg/dL)	23 (24PD) [g1]	Mean	5.91	7.66 b	7.20	7.29 a
		SD	0.211	1.014	0.520	0.509
		N	5	5	5	5
ALP (U/L)	23 (24PD) [g]	Mean	104.7	107.7	106.8	100.5
		SD	18.04	16.18	15.59	18.82
		N	5	5	5	5
Total Bilirubin (mg/dL)	23 (24PD) [g]	Mean	0.14	0.20	0.16	0.16
		SD	0.017	0.054	0.032	0.016
		N	5	5	5	5

[g] - Anova & Dunnett: a = $p < 0.05$; b = $p < 0.01$
[g1] - Kruskal-Wallis & Dunn: a = $p < 0.05$; b = $p < 0.01$

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A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Summary of Clinical Chemistry Values

Sex: Female Day(s) Relative to Start Date			0 µg/dose	30 µg/dose	60 µg/dose	100 µg/dose
AST (U/L)	23 (24PD) [g]	Mean	105.4	126.7	123.9	114.4
		SD	12.06	14.82	7.81	29.61
		N	5	5	5	5
ALT (U/L)	23 (24PD) [g]	Mean	32.5	34.4	30.2	34.8
		SD	8.56	5.33	4.51	9.98
		N	5	5	5	5
Urea Nitrogen (mg/dL)	23 (24PD) [g]	Mean	14.6	14.0	16.1	14.1
		SD	0.96	1.96	2.08	1.38
		N	5	5	5	5
Creatinine (mg/dL)	23 (24PD) [g]	Mean	0.40	0.48 a	0.45	0.48 a
		SD	0.039	0.061	0.011	0.039
		N	5	5	5	5
Total Protein (g/dL)	23 (24PD) [g]	Mean	7.34	7.00	6.85	6.68 a
		SD	0.584	0.213	0.246	0.148
		N	5	5	5	5
Albumin (g/dL)	23 (24PD) [g]	Mean	3.86	3.44 a	3.38 a	3.26 b
		SD	0.418	0.212	0.190	0.078
		N	5	5	5	5
Globulin (g/dL)	23 (24PD) [g]	Mean	3.47	3.56	3.47	3.41
		SD	0.336	0.260	0.131	0.160
		N	5	5	5	5

[g] - Anova & Dunnett: a = $p < 0.05$; b = $p < 0.01$

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A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Summary of Clinical Chemistry Values

Sex: Female Day(s) Relative to Start Date			0 µg/dose	30 µg/dose	60 µg/dose	100 µg/dose
Albumin/ Globulin	23 (24PD) [g]	Mean	1.12	0.97	0.97	0.96
		SD	0.134	0.113	0.061	0.056
		N	5	5	5	5
Triglyceride (mg/dL)	23 (24PD) [g1]	Mean	35.5	58.1	71.6	58.3
		SD	5.87	30.85	36.63	15.65
		N	5	5	5	5
Cholesterol (mg/dL)	23 (24PD) [g]	Mean	76.9	70.5	69.2	77.2
		SD	20.42	20.58	20.19	23.38
		N	5	5	5	5
Glucose (mg/dL)	23 (24PD) [g]	Mean	84.5	80.5	83.5	94.1
		SD	10.80	5.52	5.20	5.65
		N	5	5	5	5

[g] - Anova & Dunnett
[g1] - Anova & Dunnett(Log)

Appendix 1
Individual Hematology Values

Manual Evaluation – Blood Cell Morphology:

All Parameters:

Multi-species Ranges:	0	-	Does not meet reporting criteria

Echinocyte (Burr Cells):

Multi-species Ranges:	3+	-	≥100 cells

Acanthocyte, Spherocyte, Schistocyte, Keratocyte or Blister Cell, and Howell-Jolly Bodies:

Multi-species Ranges:	1+	-	2-5 cells
	2+	-	6-10 cells
	3+	-	≥11 cells

Polychromasia:

Multi-species Ranges:	1+	-	4-12 cells
	2+	-	13-25 cells
	3+	-	≥26 cells

Basophilic Stippling, Pappenheimer Bodies, Heinz Bodies, Eccentrocytes, and Ghost Cells:

Multi-species Ranges:	1+	-	1-3 cells
	2+	-	4-10 cells
	3+	-	≥11 cells

Unclassified Poikilocytosis:

Multi-species Ranges:	1+	-	3-10 cells
	2+	-	11-20 cells
	3+	-	≥21 cells

Codes for Individual Hematology Values

MCV - Mean Corpuscular Volume
MCH - Mean Corpuscular Hemoglobin
MCHC - Mean Corpuscular Hemoglobin Concentration
RDW - Red Blood Cell Distribution Width
24PD - 24 hour postdose

Blood Cell Morphology Parameters

RBC - Red blood cell = Erythrocyte
Poik - Poikilocytes
NCC - Neutrophil Cytoplasmic Change
CAC - Consistent with automated count

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Individual Hematology Values

Sex: Male

0 µg/dose	Day(s) Relative to Start Date	Leukocytes (10^3 cells/ µL)	Erythrocytes (10^6 cells/ µL)	Hemoglobin (g/dL)	Hematocrit (%)	MCV (fL)	MCH (pg)
1001	23 (24PD)	10.2	9.26	18.4	55.8	60.3	19.9
1003	23 (24PD)	8.3	8.66	16.7	51.3	59.2	19.3
1004	23 (24PD)	9.1	7.81	16.7	51.8	66.3	21.4
1005	23 (24PD)	10.2	8.43	17.6	54.0	64.1	20.9
1102	23 (24PD)	8.7	8.84	17.7	54.4	61.6	20.0

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Individual Hematology Values

Sex: Male

0 µg/dose	Day(s) Relative to Start Date	MCHC (g/dL)	Platelets (10^3 cells/ µL)	Absolute Reticulocyte (10^3 cells/ µL)	Neutrophils (10^3 cells/ µL)	Lymphocytes (10^3 cells/ µL)	Monocytes (10^3 cells/ µL)
1001	23 (24PD)	32.9	915	212.8	1.00	8.77	0.26
1003	23 (24PD)	32.6	1079	168.5	1.07	6.91	0.18
1004	23 (24PD)	32.2	1018	236.6	1.15	7.53	0.33
1005	23 (24PD)	32.5	221	294.5	0.69	9.09	0.23
1102	23 (24PD)	32.5	883	205.0	0.82	7.59	0.10

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A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Hematology Values

Sex: Male

0 µg/dose	Day(s) Relative to Start Date	Eosinophils (10^3 cells/ µL)	Basophils (10^3 cells/ µL)	Other Cells (10^3 cells/ µL)	RDW (%)
1001	23 (24PD)	0.06	0.05	0.09	12.6
1003	23 (24PD)	0.03	0.02	0.10	12.3
1004	23 (24PD)	0.06	0.04	0.05	12.7
1005	23 (24PD)	0.03	0.04	0.10	12.9
1102	23 (24PD)	0.02	0.09	0.06	12.1

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A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Hematology Values

Sex: Male

30 µg/dose	Day(s) Relative to Start Date	Leukocytes (10^3 cells/ µL)	Erythrocytes (10^6 cells/ µL)	Hemoglobin (g/dL)	Hematocrit (%)	MCV (fL)	MCH (pg)
2001	23 (24PD)	12.5	8.44	15.8	48.8	57.9	18.8
2002	23 (24PD)	14.7	8.19	16.1	49.5	60.4	19.6
2003	23 (24PD)	14.0	7.80	16.2	49.9	63.9	20.7
2004	23 (24PD)	19.2	8.02	16.4	50.3	62.7	20.5
2005	23 (24PD)	14.5	7.90	15.8	47.9	60.6	20.0

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A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Hematology Values

Sex: Male

30 µg/dose	Day(s) Relative to Start Date	MCHC (g/dL)	Platelets (10^3 cells/ µL)	Absolute Reticulocyte (10^3 cells/ µL)	Neutrophils (10^3 cells/ µL)	Lymphocytes (10^3 cells/ µL)	Monocytes (10^3 cells/ µL)
2001	23 (24PD)	32.4	895	154.5	7.41	4.63	0.17
2002	23 (24PD)	32.5	1118	174.7	8.48	5.75	0.12
2003	23 (24PD)	32.4	1047	205.8	9.26	4.29	0.15
2004	23 (24PD)	32.6	1063	178.4	12.95	5.60	0.19
2005	23 (24PD)	33.0	915	160.8	8.19	5.73	0.15

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A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Hematology Values

Sex: Male

30 µg/dose	Day(s) Relative to Start Date	Eosinophils (10^3 cells/ µL)	Basophils (10^3 cells/ µL)	Other Cells (10^3 cells/ µL)	RDW (%)
2001	23 (24PD)	0.11	0.06	0.10	13.1
2002	23 (24PD)	0.15	0.06	0.15	14.1
2003	23 (24PD)	0.08	0.04	0.13	13.4
2004	23 (24PD)	0.17	0.14	0.15	12.8
2005	23 (24PD)	0.15	0.06	0.19	13.0

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A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Hematology Values

Sex: Male

60 µg/dose	Day(s) Relative to Start Date	Leukocytes (10^3 cells/ µL)	Erythrocytes (10^6 cells/ µL)	Hemoglobin (g/dL)	Hematocrit (%)	MCV (fL)	MCH (pg)
3001	23 (24PD)	20.6	8.39	15.9	48.8	58.2	18.9
3002	23 (24PD)	14.1	8.01	15.8	48.0	59.9	19.7
3003	23 (24PD)	11.2	7.83	15.4	46.7	59.6	19.7
3004	23 (24PD)	14.6	7.90	16.0	48.8	61.8	20.2
3005	23 (24PD)	16.3	8.45	16.3	49.7	58.8	19.3

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Hematology Values

Sex: Male

60 µg/dose	Day(s) Relative to Start Date	MCHC (g/dL)	Platelets (10^3 cells/ µL)	Absolute Reticulocyte (10^3 cells/ µL)	Neutrophils (10^3 cells/ µL)	Lymphocytes (10^3 cells/ µL)	Monocytes (10^3 cells/ µL)
3001	23 (24PD)	32.5	1141	207.4	14.15	5.85	0.12
3002	23 (24PD)	32.9	1021	170.9	8.64	4.90	0.12
3003	23 (24PD)	33.1	811	176.9	6.36	4.54	0.09
3004	23 (24PD)	32.8	883	157.0	9.77	4.32	0.12
3005	23 (24PD)	32.8	944	146.3	12.23	3.46	0.19

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Hematology Values

Sex: Male

60 µg/dose	Day(s) Relative to Start Date	Eosinophils (10^3 cells/ µL)	Basophils (10^3 cells/ µL)	Other Cells (10^3 cells/ µL)	RDW (%)
3001	23 (24PD)	0.22	0.07	0.16	12.9
3002	23 (24PD)	0.26	0.06	0.11	14.2
3003	23 (24PD)	0.12	0.06	0.05	13.6
3004	23 (24PD)	0.13	0.09	0.14	14.1
3005	23 (24PD)	0.27	0.08	0.10	13.1

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Hematology Values

Sex: Male

100 µg/dose	Day(s) Relative to Start Date	Leukocytes (10^3 cells/ µL)	Erythrocytes (10^6 cells/ µL)	Hemoglobin (g/dL)	Hematocrit (%)	MCV (fL)	MCH (pg)
4001	23 (24PD)	8.1	8.30	16.4	51.6	62.1	19.8
4002	23 (24PD)	6.6	8.58	16.6	50.9	59.3	19.3
4003	23 (24PD)	16.5	8.05	16.0	48.1	59.8	19.8
4004	23 (24PD)	14.1	8.52	16.5	50.2	58.9	19.4
4005	23 (24PD)	14.3	8.02	15.9	48.5	60.4	19.8

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Hematology Values

Sex: Male

100 µg/dose	Day(s) Relative to Start Date	MCHC (g/dL)	Platelets (10^3 cells/ µL)	Absolute Reticulocyte (10^3 cells/ µL)	Neutrophils (10^3 cells/ µL)	Lymphocytes (10^3 cells/ µL)	Monocytes (10^3 cells/ µL)
4001	23 (24PD)	31.8	986	185.6	5.34	2.44	0.08
4002	23 (24PD)	32.6	931	185.2	3.28	3.14	0.06
4003	23 (24PD)	33.2	967	163.6	11.83	4.19	0.18
4004	23 (24PD)	33.0	975	158.6	8.45	5.22	0.15
4005	23 (24PD)	32.8	1094	171.4	10.17	3.78	0.10

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Hematology Values

Sex: Male

100 µg/dose	Day(s) Relative to Start Date	Eosinophils (10^3 cells/ µL)	Basophils (10^3 cells/ µL)	Other Cells (10^3 cells/ µL)	RDW (%)
4001	23 (24PD)	0.10	0.02	0.06	13.7
4002	23 (24PD)	0.09	0.02	0.03	13.1
4003	23 (24PD)	0.10	0.04	0.10	14.3
4004	23 (24PD)	0.12	0.08	0.08	13.9
4005	23 (24PD)	0.11	0.06	0.10	13.8

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Blood Cell Morphology

Sex: Male

0 µg/dose	Day(s) Relative to Start Date	Blood Cell Morphology	Nucleated RBC	Polychrom-asia	Heinz Bodies	Basophilic Stippling	Pappenheimer Bodies
1005	23 (24PD)	Findings	0	1+	0	0	0

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Blood Cell Morphology

Sex: Male

0 µg/dose	Day(s) Relative to Start Date	Howell-Jolly Bodies	Echinocyte (Burr Cells)	Spherocyte	Schistocyte	Acanthocyte	Keratocyte, Blister Cell
1005	23 (24PD)	0	0	0	0	0	0

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Blood Cell Morphology

Sex: Male

0 µg/dose	Day(s) Relative to Start Date	Eccentrocyte	Unclassified Poik	Ghost Cells	Rouleaux	RBC Agg-lutination	NCC
1005	23 (24PD)	0	0	0	0	0	0

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Blood Cell Morphology

Sex: Male

0 µg/dose	Day(s) Relative to Start Date	Smudge Cells	Pyknotic Cells	Reactive Lymphocyte	Reactive Monocytes	Leukocyte Agglutination	Platelet Estimate Count
1005	23 (24PD)	0	0	0	0	0	CAC

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Blood Cell Morphology

Sex: Male

0 µg/dose	Day(s) Relative to Start Date	Platelet Clumps	Large Platelets
1005	23 (24PD)	0	0

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Hematology Values

Sex: Female

0 µg/dose	Day(s) Relative to Start Date	Leukocytes (10^3 cells/ µL)	Erythrocytes (10^6 cells/ µL)	Hemoglobin (g/dL)	Hematocrit (%)	MCV (fL)	MCH (pg)
1501	23 (24PD)	5.4	8.22	16.4	48.5	58.9	19.9
1502	23 (24PD)	6.1	8.40	16.1	48.3	57.5	19.2
1503	23 (24PD)	7.3	8.70	16.6	50.6	58.2	19.1
1504	23 (24PD)	8.8	8.93	16.3	49.1	55.0	18.2
1505	23 (24PD)	9.7	8.84	16.8	50.9	57.6	19.0

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Hematology Values

Sex: Female

0 µg/dose	Day(s) Relative to Start Date	MCHC (g/dL)	Platelets (10^3 cells/ µL)	Absolute Reticulocyte (10^3 cells/ µL)	Neutrophils (10^3 cells/ µL)	Lymphocytes (10^3 cells/ µL)	Monocytes (10^3 cells/ µL)
1501	23 (24PD)	33.8	1068	208.5	0.83	4.38	0.13
1502	23 (24PD)	33.3	1184	155.9	1.09	4.74	0.11
1503	23 (24PD)	32.8	999	172.0	1.00	5.95	0.17
1504	23 (24PD)	33.2	1253	189.1	1.26	7.27	0.11
1505	23 (24PD)	33.0	1467	170.9	1.71	7.68	0.10

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Hematology Values

Sex: Female

0 µg/dose	Day(s) Relative to Start Date	Eosinophils (10^3 cells/ µL)	Basophils (10^3 cells/ µL)	Other Cells (10^3 cells/ µL)	RDW (%)
1501	23 (24PD)	0.04	0.01	0.05	11.4
1502	23 (24PD)	0.06	0.02	0.06	10.8
1503	23 (24PD)	0.06	0.05	0.07	11.1
1504	23 (24PD)	0.05	0.04	0.05	11.0
1505	23 (24PD)	0.06	0.05	0.10	12.1

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Hematology Values

Sex: Female

30 µg/dose	Day(s) Relative to Start Date	Leukocytes (10^3 cells/ µL)	Erythrocytes (10^6 cells/ µL)	Hemoglobin (g/dL)	Hematocrit (%)	MCV (fL)	MCH (pg)
2501	23 (24PD)	13.8	8.65	15.7	47.2	54.5	18.1
2502	23 (24PD)	15.5	8.25	15.6	46.7	56.7	19.0
2503	23 (24PD)	16.6	8.81	16.2	48.3	54.9	18.4
2504	23 (24PD)	13.9	8.45	16.1	47.7	56.4	19.1
2505	23 (24PD)	13.8	8.25	16.4	49.3	59.7	19.9

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Hematology Values

Sex: Female

30 µg/dose	Day(s) Relative to Start Date	MCHC (g/dL)	Platelets (10^3 cells/ µL)	Absolute Reticulocyte (10^3 cells/ µL)	Neutrophils (10^3 cells/ µL)	Lymphocytes (10^3 cells/ µL)	Monocytes (10^3 cells/ µL)
2501	23 (24PD)	33.2	874	122.8	7.28	5.90	0.12
2502	23 (24PD)	33.5	1000	161.6	9.38	5.59	0.13
2503	23 (24PD)	33.5	1097	93.3	11.52	4.08	0.30
2504	23 (24PD)	33.8	1051	131.4	8.08	5.12	0.17
2505	23 (24PD)	33.4	1104	195.7	8.92	4.27	0.13

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Hematology Values

Sex: Female

30 µg/dose	Day(s) Relative to Start Date	Eosinophils (10^3 cells/ µL)	Basophils (10^3 cells/ µL)	Other Cells (10^3 cells/ µL)	RDW (%)
2501	23 (24PD)	0.24	0.15	0.07	11.7
2502	23 (24PD)	0.22	0.04	0.09	11.6
2503	23 (24PD)	0.35	0.17	0.21	11.5
2504	23 (24PD)	0.28	0.14	0.11	11.9
2505	23 (24PD)	0.17	0.07	0.20	12.7

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Hematology Values

Sex: Female

60 µg/dose	Day(s) Relative to Start Date	Leukocytes (10^3 cells/ µL)	Erythrocytes (10^6 cells/ µL)	Hemoglobin (g/dL)	Hematocrit (%)	MCV (fL)	MCH (pg)
3501	23 (24PD)	12.0	9.05	17.0	51.5	56.9	18.8
3502	23 (24PD)	12.9	8.50	16.5	49.3	58.0	19.4
3503	23 (24PD)	17.2	9.01	16.8	50.6	56.1	18.7
3504	23 (24PD)	8.0	9.09	17.4	52.5	57.7	19.1
3505	23 (24PD)	13.1	8.96	16.2	49.2	54.8	18.1

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Hematology Values

Sex: Female

60 µg/dose	Day(s) Relative to Start Date	MCHC (g/dL)	Platelets (10^3 cells/ µL)	Absolute Reticulocyte (10^3 cells/ µL)	Neutrophils (10^3 cells/ µL)	Lymphocytes (10^3 cells/ µL)	Monocytes (10^3 cells/ µL)
3501	23 (24PD)	32.9	1028	165.8	7.34	4.15	0.11
3502	23 (24PD)	33.5	1112	116.5	7.34	5.24	0.05
3503	23 (24PD)	33.3	941	151.4	10.57	5.89	0.15
3504	23 (24PD)	33.1	807	153.8	4.93	2.75	0.08
3505	23 (24PD)	33.0	1157	128.7	8.59	4.10	0.15

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Hematology Values

Sex: Female

60 µg/dose	Day(s) Relative to Start Date	Eosinophils (10^3 cells/ µL)	Basophils (10^3 cells/ µL)	Other Cells (10^3 cells/ µL)	RDW (%)
3501	23 (24PD)	0.25	0.04	0.08	12.4
3502	23 (24PD)	0.10	0.08	0.07	12.0
3503	23 (24PD)	0.29	0.13	0.12	12.2
3504	23 (24PD)	0.12	0.04	0.07	12.2
3505	23 (24PD)	0.12	0.07	0.08	11.5

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Hematology Values

Sex: Female

100 µg/dose	Day(s) Relative to Start Date	Leukocytes (10^3 cells/ µL)	Erythrocytes (10^6 cells/ µL)	Hemoglobin (g/dL)	Hematocrit (%)	MCV (fL)	MCH (pg)
4501	23 (24PD)	18.4	9.61	17.6	54.4	56.6	18.4
4502	23 (24PD)	12.9	9.84	18.3	56.0	57.0	18.6
4503	23 (24PD)	6.5	8.08	16.1	48.5	60.0	19.9
4504	23 (24PD)	6.7	8.27	16.3	48.4	58.5	19.7
4605	23 (24PD)	10.5	8.72	17.3	51.4	59.0	19.8

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Hematology Values

Sex: Female

100 µg/dose	Day(s) Relative to Start Date	MCHC (g/dL)	Platelets (10^3 cells/ µL)	Absolute Reticulocyte (10^3 cells/ µL)	Neutrophils (10^3 cells/ µL)	Lymphocytes (10^3 cells/ µL)	Monocytes (10^3 cells/ µL)
4501	23 (24PD)	32.4	998	97.4	12.14	5.61	0.15
4502	23 (24PD)	32.7	876	122.4	7.27	5.15	0.12
4503	23 (24PD)	33.2	1059	118.8	3.89	2.37	0.06
4504	23 (24PD)	33.7	1070	108.3	4.39	1.96	0.09
4605	23 (24PD)	33.6	997	136.7	6.81	3.26	0.09

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Hematology Values

Sex: Female

100 µg/dose	Day(s) Relative to Start Date	Eosinophils (10^3 cells/ µL)	Basophils (10^3 cells/ µL)	Other Cells (10^3 cells/ µL)	RDW (%)
4501	23 (24PD)	0.23	0.11	0.14	12.4
4502	23 (24PD)	0.22	0.07	0.11	11.9
4503	23 (24PD)	0.11	0.03	0.03	12.3
4504	23 (24PD)	0.14	0.04	0.05	12.1
4605	23 (24PD)	0.24	0.08	0.05	11.6

Appendix 2
Individual Clinical Chemistry Values

Codes for Individual Clinical Chemistry Values

AST - Aspartate Aminotransferase
ALT - Alanine Aminotransferase
ALP - Alkaline Phosphatase
24PD - 24 hour postdose

Hemolytic Index Result Reference Guide

0 - No Hemolysis
1 - Slight Hemolysis
2 - Hemolyzed

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Clinical Chemistry Values

Sex: Male

0 µg/dose	Day(s) Relative to Start Date	Sodium (mEq/L)	Potassium (mEq/L)	Chloride (mEq/L)	Calcium (mg/dL)	Phosphorus (mg/dL)	ALP (U/L)	Total Bilirubin (mg/dL)	AST (U/L)	ALT (U/L)	Urea Nitrogen (mg/dL)
1001	23 (24PD)	140	5.6	99	10.0	8.4	129	0.2	135	33	14
1003	23 (24PD)	144	5.2	100	9.7	7.5	247	0.1	113	34	13
1004	23 (24PD)	142	5.3	98	10.1	8.7	270	0.1	119	28	13
1005	23 (24PD)	142	4.6	100	10.4	8.2	289	0.2	96	32	13
1102	23 (24PD)	141	5.6	99	9.7	8.6	183	0.2	139	35	15

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Clinical Chemistry Values

Sex: Male

0 µg/dose	Day(s) Relative to Start Date	Creatinine (mg/dL)	Total Protein (g/dL)	Albumin (g/dL)	Globulin (g/dL)	Albumin/ Globulin	Triglyceride (mg/dL)	Cholesterol (mg/dL)	Glucose (mg/dL)	Hemolytic Index
1001	23 (24PD)	0.3	6.7	3.6	3.1	1.2	34	55	68	1
1003	23 (24PD)	0.3	6.6	3.5	3.1	1.1	52	63	64	0
1004	23 (24PD)	0.3	6.5	3.5	3.0	1.2	42	59	66	0
1005	23 (24PD)	0.3	6.8	3.6	3.2	1.1	33	49	78	0
1102	23 (24PD)	0.2	6.6	3.4	3.2	1.1	39	52	69	1

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Clinical Chemistry Values

Sex: Male

30 µg/dose	Day(s) Relative to Start Date	Sodium (mEq/L)	Potassium (mEq/L)	Chloride (mEq/L)	Calcium (mg/dL)	Phosphorus (mg/dL)	ALP (U/L)	Total Bilirubin (mg/dL)	AST (U/L)	ALT (U/L)	Urea Nitrogen (mg/dL)
2001	23 (24PD)	142	5.0	99	10.1	9.2	209	0.1	99	31	12
2002	23 (24PD)	141	5.6	98	9.6	8.2	166	0.1	162	39	15
2003	23 (24PD)	139	5.1	98	10.2	8.6	299	0.1	109	31	16
2004	23 (24PD)	141	5.5	98	9.5	8.8	169	0.1	193	36	14
2005	23 (24PD)	137	5.9	96	10.0	8.4	179	0.2	129	34	15

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Clinical Chemistry Values

Sex: Male

30 µg/dose	Day(s) Relative to Start Date	Creatinine (mg/dL)	Total Protein (g/dL)	Albumin (g/dL)	Globulin (g/dL)	Albumin/ Globulin	Triglyceride (mg/dL)	Cholesterol (mg/dL)	Glucose (mg/dL)	Hemolytic Index
2001	23 (24PD)	0.3	6.0	2.9	3.1	0.9	65	108	58	0
2002	23 (24PD)	0.4	6.6	3.2	3.4	1.0	79	98	68	0
2003	23 (24PD)	0.4	6.8	3.3	3.6	0.9	67	86	83	0
2004	23 (24PD)	0.4	6.7	3.3	3.4	1.0	43	74	66	0
2005	23 (24PD)	0.4	6.5	3.1	3.4	0.9	122	83	79	0

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Clinical Chemistry Values

Sex: Male

60 µg/dose	Day(s) Relative to Start Date	Sodium (mEq/L)	Potassium (mEq/L)	Chloride (mEq/L)	Calcium (mg/dL)	Phosphorus (mg/dL)	ALP (U/L)	Total Bilirubin (mg/dL)	AST (U/L)	ALT (U/L)	Urea Nitrogen (mg/dL)
3001	23 (24PD)	141	5.8	98	10.1	9.2	193	0.1	141	36	13
3002	23 (24PD)	140	7.8	97	9.8	9.2	150	0.2	122	46	13
3003	23 (24PD)	140	5.6	99	9.4	8.6	194	0.1	108	30	12
3004	23 (24PD)	138	5.5	95	9.8	8.7	223	0.2	169	33	10
3005	23 (24PD)	140	5.3	98	9.5	8.5	172	0.2	118	28	14

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Clinical Chemistry Values

Sex: Male

60 µg/dose	Day(s) Relative to Start Date	Creatinine (mg/dL)	Total Protein (g/dL)	Albumin (g/dL)	Globulin (g/dL)	Albumin/ Globulin	Triglyceride (mg/dL)	Cholesterol (mg/dL)	Glucose (mg/dL)	Hemolytic Index
3001	23 (24PD)	0.3	7.1	3.2	3.9	0.8	83	84	74	0
3002	23 (24PD)	0.3	6.1	2.9	3.2	0.9	126	90	81	0
3003	23 (24PD)	0.3	6.0	2.9	3.1	0.9	112	84	82	0
3004	23 (24PD)	0.3	7.0	3.3	3.7	0.9	63	100	80	0
3005	23 (24PD)	0.4	6.6	3.0	3.5	0.9	77	78	82	1

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Clinical Chemistry Values

Sex: Male

100 µg/dose	Day(s) Relative to Start Date	Sodium (mEq/L)	Potassium (mEq/L)	Chloride (mEq/L)	Calcium (mg/dL)	Phosphorus (mg/dL)	ALP (U/L)	Total Bilirubin (mg/dL)	AST (U/L)	ALT (U/L)	Urea Nitrogen (mg/dL)
4001	23 (24PD)	140	5.8	99	9.7	9.1	228	0.1	133	35	12
4002	23 (24PD)	140	7.3	100	9.7	8.8	171	0.1	132	32	12
4003	23 (24PD)	141	5.2	97	9.3	8.9	146	0.1	133	32	12
4004	23 (24PD)	138	5.5	97	10.0	8.6	244	0.1	112	41	13
4005	23 (24PD)	139	5.5	98	10.0	9.1	234	0.1	89	32	12

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Clinical Chemistry Values

Sex: Male

100 µg/dose	Day(s) Relative to Start Date	Creatinine (mg/dL)	Total Protein (g/dL)	Albumin (g/dL)	Globulin (g/dL)	Albumin/ Globulin	Triglyceride (mg/dL)	Cholesterol (mg/dL)	Glucose (mg/dL)	Hemolytic Index
4001	23 (24PD)	0.4	6.5	3.1	3.5	0.9	65	96	87	0
4002	23 (24PD)	0.4	6.6	3.1	3.6	0.9	83	80	85	0
4003	23 (24PD)	0.4	6.2	2.9	3.3	0.9	68	64	87	0
4004	23 (24PD)	0.4	7.1	3.3	3.8	0.8	59	101	88	0
4005	23 (24PD)	0.4	6.9	3.1	3.9	0.8	58	97	87	0

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Clinical Chemistry Values

Sex: Female

0 µg/dose	Day(s) Relative to Start Date	Sodium (mEq/L)	Potassium (mEq/L)	Chloride (mEq/L)	Calcium (mg/dL)	Phosphorus (mg/dL)	ALP (U/L)	Total Bilirubin (mg/dL)	AST (U/L)	ALT (U/L)	Urea Nitrogen (mg/dL)
1501	23 (24PD)	139	5.4	100	9.9	6.2	96	0.2	117	24	14
1502	23 (24PD)	141	5.0	101	10.9	5.8	106	0.1	105	29	14
1503	23 (24PD)	142	4.6	101	9.8	5.9	126	0.1	118	26	14
1504	23 (24PD)	141	5.1	100	9.8	5.9	80	0.2	98	38	16
1505	23 (24PD)	141	4.5	99	10.0	5.7	117	0.1	90	45	15

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Clinical Chemistry Values

Sex: Female

0 µg/dose	Day(s) Relative to Start Date	Creatinine (mg/dL)	Total Protein (g/dL)	Albumin (g/dL)	Globulin (g/dL)	Albumin/ Globulin	Triglyceride (mg/dL)	Cholesterol (mg/dL)	Glucose (mg/dL)	Hemolytic Index
1501	23 (24PD)	0.3	7.2	3.9	3.3	1.2	31	59	88	0
1502	23 (24PD)	0.4	8.3	4.5	3.8	1.2	42	90	100	0
1503	23 (24PD)	0.4	6.9	3.7	3.2	1.2	32	64	75	0
1504	23 (24PD)	0.4	6.9	3.7	3.2	1.2	42	65	73	0
1505	23 (24PD)	0.4	7.3	3.4	3.9	0.9	31	106	86	0

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Clinical Chemistry Values

Sex: Female

30 µg/dose	Day(s) Relative to Start Date	Sodium (mEq/L)	Potassium (mEq/L)	Chloride (mEq/L)	Calcium (mg/dL)	Phosphorus (mg/dL)	ALP (U/L)	Total Bilirubin (mg/dL)	AST (U/L)	ALT (U/L)	Urea Nitrogen (mg/dL)
2501	23 (24PD)	135	6.2	95	10.0	8.5	110	0.2	152	29	14
2502	23 (24PD)	139	5.0	98	10.2	6.7	99	0.2	115	42	15
2503	23 (24PD)	143	5.4	101	10.4	8.1	91	0.2	116	34	12
2504	23 (24PD)	141	5.9	97	10.3	8.6	134	0.3	123	30	17
2505	23 (24PD)	139	5.5	97	9.7	6.5	105	0.2	127	37	12

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Clinical Chemistry Values

Sex: Female

30 µg/dose	Day(s) Relative to Start Date	Creatinine (mg/dL)	Total Protein (g/dL)	Albumin (g/dL)	Globulin (g/dL)	Albumin/ Globulin	Triglyceride (mg/dL)	Cholesterol (mg/dL)	Glucose (mg/dL)	Hemolytic Index
2501	23 (24PD)	0.5	6.8	3.2	3.5	0.9	33	46	73	2
2502	23 (24PD)	0.5	7.3	3.6	3.7	1.0	57	94	84	0
2503	23 (24PD)	0.5	6.9	3.6	3.3	1.1	59	59	79	0
2504	23 (24PD)	0.6	6.9	3.6	3.4	1.1	33	65	79	1
2505	23 (24PD)	0.4	7.1	3.2	4.0	0.8	109	89	88	1

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Clinical Chemistry Values

Sex: Female

60 µg/dose	Day(s) Relative to Start Date	Sodium (mEq/L)	Potassium (mEq/L)	Chloride (mEq/L)	Calcium (mg/dL)	Phosphorus (mg/dL)	ALP (U/L)	Total Bilirubin (mg/dL)	AST (U/L)	ALT (U/L)	Urea Nitrogen (mg/dL)
3501	23 (24PD)	142	5.4	101	9.3	7.0	106	0.1	133	30	16
3502	23 (24PD)	139	5.5	97	9.8	7.8	81	0.2	118	32	15
3503	23 (24PD)	138	6.8	98	10.5	7.6	120	0.2	125	26	18
3504	23 (24PD)	138	5.5	97	9.5	7.2	119	0.2	129	37	18
3505	23 (24PD)	139	6.0	99	9.8	6.5	108	0.2	114	26	14

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Clinical Chemistry Values

Sex: Female

60 µg/dose	Day(s) Relative to Start Date	Creatinine (mg/dL)	Total Protein (g/dL)	Albumin (g/dL)	Globulin (g/dL)	Albumin/ Globulin	Triglyceride (mg/dL)	Cholesterol (mg/dL)	Glucose (mg/dL)	Hemolytic Index
3501	23 (24PD)	0.5	6.5	3.1	3.4	0.9	53	66	89	0
3502	23 (24PD)	0.5	6.7	3.3	3.4	1.0	63	73	78	1
3503	23 (24PD)	0.5	7.1	3.6	3.6	1.0	135	79	79	2
3504	23 (24PD)	0.5	7.0	3.6	3.4	1.1	43	37	88	1
3505	23 (24PD)	0.4	7.0	3.3	3.7	0.9	64	91	83	0

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Clinical Chemistry Values

Sex: Female

100 µg/dose	Day(s) Relative to Start Date	Sodium (mEq/L)	Potassium (mEq/L)	Chloride (mEq/L)	Calcium (mg/dL)	Phosphorus (mg/dL)	ALP (U/L)	Total Bilirubin (mg/dL)	AST (U/L)	ALT (U/L)	Urea Nitrogen (mg/dL)
4501	23 (24PD)	142	5.7	101	10.1	7.9	98	0.2	79	30	16
4502	23 (24PD)	136	6.4	97	9.8	7.6	80	0.2	161	27	15
4503	23 (24PD)	141	6.0	101	9.7	6.9	89	0.2	109	28	12
4504	23 (24PD)	137	5.5	99	9.3	6.7	106	0.2	115	39	14
4605	23 (24PD)	142	6.1	101	9.5	7.5	129	0.2	108	51	14

2308-123
A Non-GLP Repeat Dose Immunogenicity and Toxicity Study of mRNA-1273 by Intramuscular Injection in Sprague Dawley Rats

Individual Clinical Chemistry Values

Sex: Female

100 µg/dose	Day(s) Relative to Start Date	Creatinine (mg/dL)	Total Protein (g/dL)	Albumin (g/dL)	Globulin (g/dL)	Albumin/ Globulin	Triglyceride (mg/dL)	Cholesterol (mg/dL)	Glucose (mg/dL)	Hemolytic Index
4501	23 (24PD)	0.6	6.9	3.2	3.7	0.9	77	101	88	0
4502	23 (24PD)	0.5	6.7	3.4	3.3	1.0	49	54	88	1
4503	23 (24PD)	0.5	6.7	3.2	3.5	0.9	56	58	96	1
4504	23 (24PD)	0.5	6.7	3.3	3.4	1.0	71	70	99	1
4605	23 (24PD)	0.5	6.5	3.2	3.2	1.0	39	103	100	1

Appendix 10
Serum Analysis Results
(Sections 1 to 2)

Appendix 10
Section 1
Interpretation Statement

Immunogenicity of mRNA-1273 in Rats

PPD
Lead, Coronavirus Vaccines and Immunopathogenesis Team
NIH, NIAID, Vaccine Research Center, Viral Pathogenesis Laboratory
April 23, 2020

Principal Investigator PPD
Program Managers PPD and PPD
Sera collection and animal care: NIH NIAID VRC Translational Research Program
ELISA Assay: Catherine Liu
Data analysis PPD an PPD

Immunizations: completed by Moderna, Inc.

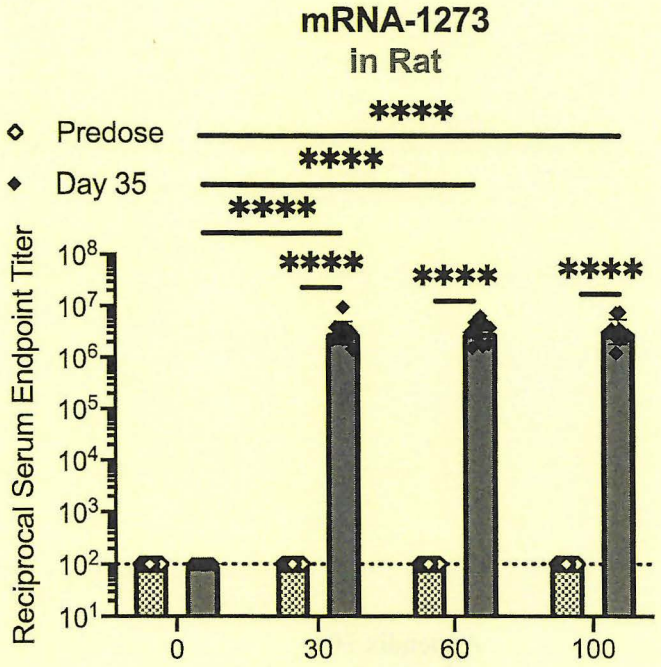

Figure 1. Immunogenicity of mRNA-1273 in rats. Rats were immunized with mRNA-1273 on study day 1 and 22. Sera from pre-immunized (open diamonds) and post-immunized (solid diamonds) animals (study days 1 and 35 respectively) were analyzed by ELISA to assess binding to SARS-CoV-2 stabilized prefusion spike protein (SARS-CoV-2 S-2P). Each symbol represents an individual animal, bars represent geometric mean titers (GMT), and error bars indicate geometric standard deviation (SD). Two-way ANOVA was used to compare pre-dose responses to post-immunization responses and mRNA dose levels (**** = p-value < 0.0001).

Results: 30, 60, and 100 µg doses of mRNA-1273 elicited significant spike-specific antibody in rats post-immunization in a dose-independent manner.

Appendix 10
Section 2
Individual Vaccine Titer Values

Individual Vaccine Titer Values

Group No.	Animal Number	Sex[a]	Barcode	Vaccine	Interval/ Study Day	Dose (µg/kg/dose)	Endpoint Titer
1	1001	M	C12060841	mRNA1273	Pretest	N/A	100.00
1	1003	M	C12060842	mRNA1273	Pretest	N/A	100.00
1	1004	M	C12060843	mRNA1273	Pretest	N/A	100.00
1	1005	M	C12060844	mRNA1273	Pretest	N/A	100.00
1	1102	M	C12060879	mRNA1273	Pretest	N/A	100.00
1	1501	F	C12060845	mRNA1273	Pretest	N/A	100.00
1	1502	F	C12060846	mRNA1273	Pretest	N/A	100.00
1	1503	F	C12060847	mRNA1273	Pretest	N/A	100.00
1	1504	F	C12060848	mRNA1273	Pretest	N/A	100.00
1	1505	F	C12060849	mRNA1273	Pretest	N/A	100.00
2	2001	M	C12060850	mRNA1273	Pretest	N/A	100.00
2	2002	M	C12060851	mRNA1273	Pretest	N/A	100.00
2	2003	M	C12060852	mRNA1273	Pretest	N/A	100.00
2	2004	M	C12060853	mRNA1273	Pretest	N/A	100.00
2	2005	M	C12060854	mRNA1273	Pretest	N/A	100.00
2	2501	F	C12060855	mRNA1273	Pretest	N/A	100.00
2	2502	F	C12060856	mRNA1273	Pretest	N/A	100.00
2	2503	F	C12060857	mRNA1273	Pretest	N/A	100.00
2	2504	F	C12060858	mRNA1273	Pretest	N/A	100.00
2	2505	F	C12060859	mRNA1273	Pretest	N/A	100.00
3	3001	M	C12060860	mRNA1273	Pretest	N/A	100.00
3	3002	M	C12060861	mRNA1273	Pretest	N/A	100.00
3	3003	M	C12060862	mRNA1273	Pretest	N/A	100.00
3	3004	M	C12060863	mRNA1273	Pretest	N/A	100.00
3	3005	M	C12060864	mRNA1273	Pretest	N/A	100.00
3	3501	F	C12060865	mRNA1273	Pretest	N/A	100.00
3	3502	F	C12060866	mRNA1273	Pretest	N/A	100.00
3	3503	F	C12060867	mRNA1273	Pretest	N/A	100.00
3	3504	F	C12060868	mRNA1273	Pretest	N/A	100.00
3	3505	F	C12060869	mRNA1273	Pretest	N/A	100.00
4	4001	M	C12060870	mRNA1273	Pretest	N/A	100.00
4	4002	M	C12060871	mRNA1273	Pretest	N/A	100.00
4	4003	M	C12060872	mRNA1273	Pretest	N/A	100.00
4	4004	M	C12060873	mRNA1273	Pretest	N/A	100.00
4	4005	M	C12060874	mRNA1273	Pretest	N/A	100.00
4	4501	F	C12060875	mRNA1273	Pretest	N/A	100.00
4	4502	F	C12060876	mRNA1273	Pretest	N/A	100.00
4	4503	F	C12060877	mRNA1273	Pretest	N/A	100.00
4	4504	F	C12060878	mRNA1273	Pretest	N/A	100.00
4	4605	F	C12060880	mRNA1273	Pretest	N/A	100.00

[a] M = Male; F = Female

Individual Vaccine Titer Values

Group No.	Animal Number	Sex	Barcode	Vaccine	Interval/ Study Day	Dose (µg/kg/dose)	Endpoint Titer
1	1001	M	C12148994	mRNA1273	35	0	100.00
1	1003	M	C12148995	mRNA1273	35	0	100.00
1	1004	M	C12148996	mRNA1273	35	0	100.00
1	1005	M	C12148997	mRNA1273	35	0	100.00
1	1102	M	C12148998	mRNA1273	35	0	100.00
1	1501	F	C12148999	mRNA1273	35	0	100.00
1	1502	F	C12149000	mRNA1273	35	0	100.00
1	1503	F	C12149001	mRNA1273	35	0	100.00
1	1504	F	C12149002	mRNA1273	35	0	100.00
1	1505	F	C12149003	mRNA1273	35	0	100.00
2	2001	M	C12149004	mRNA1273	35	30	1,467,954.63
2	2002	M	C12149005	mRNA1273	35	30	2,272,581.67
2	2003	M	C12149006	mRNA1273	35	30	2,320,373.64
2	2004	M	C12149007	mRNA1273	35	30	3,904,077.92
2	2005	M	C12149008	mRNA1273	35	30	2,469,864.85
2	2501	F	C12149009	mRNA1273	35	30	3,170,547.44
2	2502	F	C12149010	mRNA1273	35	30	3,592,253.40
2	2503	F	C12149011	mRNA1273	35	30	2,320,373.64
2	2504	F	C12149012	mRNA1273	35	30	3,823,666.93
2	2505	F	C12149013	mRNA1273	35	30	9,553,678.72
3	3001	M	C12149014	mRNA1273	35	60	1,698,171.66
3	3002	M	C12149015	mRNA1273	35	60	4,423,326.64
3	3003	M	C12149016	mRNA1273	35	60	3,105,244.73
3	3004	M	C12149017	mRNA1273	35	60	3,823,666.93
3	3005	M	C12149018	mRNA1273	35	60	4,807,316.32
3	3501	F	C12149019	mRNA1273	35	60	6,300,894.21
3	3502	F	C12149020	mRNA1273	35	60	1,562,528.33
3	3503	F	C12149021	mRNA1273	35	60	1,845,590.21
3	3504	F	C12149022	mRNA1273	35	60	2,574,838.73
3	3505	F	C12149023	mRNA1273	35	60	3,823,666.93
4	4001	M	C12149024	mRNA1273	35	100	3,105,244.73
4	4002	M	C12149025	mRNA1273	35	100	2,469,864.85
4	4003	M	C12149026	mRNA1273	35	100	2,740,723.98
4	4004	M	C12149027	mRNA1273	35	100	2,272,581.67
4	4005	M	C12149028	mRNA1273	35	100	1,217,213.71
4	4501	F	C12149029	mRNA1273	35	100	7,598,852.03
4	4502	F	C12149030	mRNA1273	35	100	3,592,235.40
4	4503	F	C12149031	mRNA1273	35	100	3,592,235.40
4	4504	F	C12149032	mRNA1273	35	100	2,521,805.64
4	4605	F	C12149033	mRNA1273	35	100	7,442,341.01

[a] M = Male; F = Female