CLINICAL RESEARCH IN INFECTIOUS DISEASES

STATISTICAL ANALYSIS PLAN

for

DMID Protocol

17-0076: A Phase II Study in Healthy Adults 18-64 Years Old to Assess the Safety, Reactogenicity and Immunogenicity of a Seqirus A/H7N9 Inactivated Influenza Vaccine Administered Intramuscularly With or Without MF59® Adjuvant

17-0076: NCT03682120

Version 1.0

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STUDY TITLE

Protocol Number Code:	DMID Protocol: 17-0076
Development Phase:	Phase II
Products:	Seqirus A/H7N9 Inactivated Influenza Vaccine Seqirus MF59® Adjuvant
Form/Route:	IM
Indication Studied:	Influenza A/H7N9
Sponsor:	Division of Microbiology and Infectious Diseases National Institute of Allergy and Infectious Diseases National Institutes of Health
Clinical Trial Initiation Date:	November 2, 2018
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This study was performed in compliance with Good Clinical Practice.

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LIST OF ABBREVIATIONS

AE	Adverse Event
ALT	Alanine Aminotransferase
BP	Blood Pressure
C	Celsius
CI	Confidence Interval
Cr	Creatinine
CRF	Case Report Form
CSR	Clinical Study Report
DHHS	U.S. Department of Health and Human Services
DMID	Division of Microbiology and Infectious Diseases
DSMB	Data and Safety Monitoring Board
eCRF	Electronic Case Report Form
F	Fahrenheit
FDA	U.S. Food and Drug Administration
GMT	Geometric Mean Titer
HAI	Hemagglutination inhibition antibody
Hgb	Hemoglobin
ICH	International Conference on Harmonisation
IIV	Inactivated Influenza Vaccine
IM	Intramuscularly
IRB	Institutional Review Board
MAAE	Medically Attended Adverse Event
mcg	Microgram
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligram
mITT	Modified Intention to Treat
N, n	Number
NA	Neuraminidase
Neut	Neutralizing Antibody
NIH	National Institutes of Health
NOCMC	New Onset Chronic Medical Condition

LIST OF ABBREVIATIONS *(continued)*

PIMMC	Potentially Immune Mediated Medical Condition
PP	Per-Protocol
PLT	Platelets
PT	Preferred Term
RCD	Reverse Cumulative Distribution
SAE	Serious Adverse Event
SD	Standard Deviation
SDCC	Statistical and Data Coordinating Center
SMC	Safety Monitoring Committee
SOC	System Organ Class
T. Bili	Total Bilirubin
WBC	White Blood Cell
WHO	World Health Organization

1. PREFACE

This Statistical Analysis Plan (SAP) for DMID Protocol 17-0076, "A Phase II Study in Healthy Adults 18-64 Years Old to Assess the Safety, Reactogenicity and Immunogenicity of a Seqirus A/H7N9 Inactivated Influenza Vaccine Administered Intramuscularly With or Without MF59 Adjuvant," describes and expands upon the statistical information presented in the protocol.

This document describes all planned analyses and provides reasons and justifications for these analyses. It also includes sample tables, figures, listings (TFLs) planned for final analyses included in the Clinical Study Report (CSR). Regarding the final analyses and CSR, this SAP follows the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Guidelines, as indicated in Topic E3 (Structure and Content of Clinical Study Reports), and more generally is consistent with Topic E8 (General Considerations for Clinical Trials) and Topic E9 (Statistical Principles for Clinical Trials). The structure and content of the SAP provides sufficient detail to meet the requirements identified by the FDA and ICH, while all work planned and reported for this SAP will follow internationally accepted guidelines published by the American Statistical Association and the Royal Statistical Society for statistical practice.

This document contains four sections: (1) a review of the study design, (2) general statistical considerations, (3) comprehensive statistical analysis methods for immunogenicity and safety outcomes, and (4) a list of proposed TFLs. Following any protocol amendment, this SAP will be reviewed and revised (if needed) to address any changes in the protocol impacting analysis. Any deviation from the final SAP will be described and justified in the CSR. The reader of this SAP is encouraged to also review the study protocol for details on conduct of the study and the operational aspects of clinical assessments.

2. INTRODUCTION

Since March of 2013 [1], avian influenza A/H7N9 viruses have continued to circulate in China causing discrete outbreaks (or waves) in humans with high mortality over the past 5 years. By late 2016, a fifth wave of outbreaks was identified in China and as of May 18, 2017, a total of 1,463 laboratory-confirmed human infections with avian influenza A/H7N9 virus have been reported by the World Health Organization [2, 3]. Since the onset of the fifth wave of H7N9 outbreaks in October 2016, more human cases of H7N9 infection have been reported in China than any prior H7N9 epidemic wave [3]. The U.S. Department of Health and Human Services (DHHS) recently assessed H7N9 influenza virus as having a significant potential to cause a pandemic, and the greatest risk of causing severe disease. As a result, DHHS has supported the production of fifth wave A/H7N9 inactivated influenza 9 vaccines (IIVs) for the U.S. stockpile and for an assessment of their safety and immunogenicity in clinical trials.

The goal of this clinical trial is to assess in healthy adults, ages 18-64, the safety, reactogenicity, and immunogenicity of two doses of a monovalent inactivated influenza A/H7N9 virus vaccine administered IM at different dosages given with or without MF59 adjuvant and to evaluate the potential of the dosage levels and adjuvant to enhance the immune response to A/H7N9 vaccine. The two doses of the A/H7N9 vaccine given with or without adjuvant will be administered approximately 21 days apart.

2.1. Purpose of the Analyses

These analyses will assess the safety and immunogenicity of two doses of A/H7N9 IIV administered IM with or without MF59 adjuvant approximately 21 days apart and will be included in the clinical study report.

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives

3.1.1. Primary

Safety:

- To assess the safety and reactogenicity following receipt of two doses of 2017 H7N9 IIV administered IM at different dosages approximately 21 days apart given with or without MF59 adjuvant.

Immunogenicity:

- To assess the serum hemagglutination inhibition (HAI) and neutralizing (Neut) antibody responses approximately 21 days following receipt of two doses of 2017 H7N9 IIV administered IM at different dosages approximately 21 days apart with or without MF59 adjuvant.

3.1.2. Secondary

Safety:

- To assess all unsolicited non-serious adverse events (AEs) following receipt of two doses of a 2017 H7N9 IIV administered IM at different dosages approximately 21 days apart with or without MF59 adjuvant
- To assess medically-attended adverse events (MAAEs) including new-onset chronic medical conditions (NOCMCs), potentially immune-mediated medical conditions (PIMMCs), and all serious adverse events (SAEs) following receipt of two doses of a 2017 H7N9 IIV administered IM at different dosages approximately 21 days apart with or without MF59 adjuvant

Immunogenicity:

- To assess the serum HAI and Neut antibody responses approximately 7 and 21 days following receipt of a single dose, and approximately 7 days following receipt of two doses of 2017 H7N9 IIV administered IM at different dosages approximately 21 days apart with or without MF59 adjuvant.

3.1.3. Exploratory

Immunogenicity:

- To assess the effects of age, sex, body mass index, and prior receipt of seasonal influenza vaccine(s) on serum HAI and Neut antibody responses following receipt of two doses of a 2017 H7N9 IIV administered IM at different dosages approximately 21 days apart with or without MF59 adjuvant.

- To assess, in at least a subset of samples, the cross-reactivity of serum HAI and Neut antibody responses to antigenically drifted variants of influenza A/H7 viruses following receipt of two doses of a 2017 H7N9 IIV administered IM at different dosages approximately 21 days apart with or without MF59 adjuvant.
- To assess the durability of serum HAI and Neut antibody responses at approximately 180 days following receipt of two doses of 2017 H7N9 IIV administered IM at different dosages approximately 21 days apart with or without MF59 adjuvant.
- To assess the neuraminidase (NA) content of the 2017 H7N9 IIV and determine the serum antibody responses to NA following receipt of 2017 H7N9 IIV. *Note: analysis plans for this objective will be described in an addendum to this SAP once the NA assay has been selected.*

3.2. Endpoints

3.2.1. Primary

Safety:

- Occurrence of study vaccine-related serious adverse events (SAEs) from the time of the first study vaccination through approximately 12 months after the last study vaccination.
- Occurrence of solicited injection site and systemic reactogenicity events from the time of each study vaccination through 7 days after each study vaccination.
- Occurrence of clinical safety laboratory adverse events from the time of each study vaccination through approximately 7 days after each study vaccination.

Immunogenicity:

- For HAI and Neut antibodies, percentage of subjects achieving seroconversion against the influenza 2017 H7N9 study vaccine strain (defined as either a pre-vaccination titer <1:10 and a post-vaccination titer ≥1:40 or a pre-vaccination titer ≥1:10 and a minimum four-fold rise in post-vaccination titer) at approximately 21 days after the second study vaccination (Study Day 43).
- For HAI and Neut antibodies, percentage of subjects achieving titer ≥1:40 against the influenza 2017 H7N9 study vaccine strain at approximately 21 days after the second study vaccination (Study Day 43).
- Geometric Mean Titers (GMTs) of serum HAI and Neut antibodies against the influenza 2017 H7N9 vaccine strain at approximately 21 days after the second study vaccination (Study Day 43).

3.2.2. Secondary

Safety:

- Occurrence of study vaccine-related unsolicited non-serious AEs from the time of each study vaccination through approximately 21 days after each study vaccination.
- Occurrence of all unsolicited adverse events, regardless of the assessment of seriousness or relatedness, from the time of each study vaccination through approximately 21 days after each study vaccination.
- Occurrence of MAAEs, including NOCMCs, and PIMMCs from the time of the first study vaccination through approximately 12 months after the last study vaccination.
- Occurrence of all SAEs, regardless of the assessment of relatedness, from the time of the first vaccination through approximately 12 months after the last study vaccination.

Immunogenicity:

- For HAI and Neut antibodies, percentage of subjects achieving seroconversion against the influenza 2017 H7N9 vaccine strain at approximately 7, 21, and 28 days after the first study vaccination (Study Days 8, 22, 29).
- For HAI and Neut antibodies, percentage of subjects achieving titers of 1:40 or greater against the influenza 2017 H7N9 vaccine strain at baseline and approximately 7, 21, and 28 days after the first study vaccination (Study Days 8, 22, 29).
- GMTs of serum HAI and Neut antibodies against the influenza 2017 H7N9 vaccine virus at baseline and approximately 7, 21, and 28 days after the first study vaccination (Study Days 8, 22, 29).

3.2.3. Exploratory

Immunogenicity:

- For HAI and Neut antibodies, percentage of subjects achieving seroconversion and the GMTs of serum HAI antibody against the 2017 H7N9 study vaccine strain approximately 21 and 180 days after the second study vaccination (Study Days 43 and 202), stratified by sex, body mass index, and prior receipt of seasonal influenza vaccine(s).
- For HAI and Neut antibodies, for at least a subset of subjects, percentage achieving seroconversion, percentage with titer ≥1:40, and GMTs against

antigenically drifted variants of influenza A/H7 viruses at baseline and approximately 21 and 180 days after the second study vaccination (Study Day 43 and 202).

- For HAI and Neut antibodies, percentage of subjects achieving seroconversion, percentage with titer ≥1:40, and GMTs against the 2017 H7N9 study vaccine strain at approximately 180 days after the second study vaccination (Study Day 202).
- Percentage of subjects with detectable levels of serum N9 NA specific antibody elicited by 2017 H7N9 vaccination, and the correlation of the NA content of 2017 H7N9 IIV with the elicited NA specific antibody responses at baseline and approximately 8 and 21 days after the first study vaccination (Study Day 1, 8 and 22) and 8, 21 and 180 days after the second study vaccination (Study Day, 29, 43 and 202). *Note: analysis plans for this endpoint will be described in an addendum to this SAP once the NA assay has been selected.*

3.3. Study Definitions and Derived Variables

For individual subjects, fold rise will be calculated as the ratio of: $\frac{post-vaccination\ titer}{pre-vaccination\ titer}$, where pre-vaccination value is always the result obtained at Day 1, prior to the priming vaccination.

Seroconversion for HAI and Neut assays is defined as either a pre-vaccination titer < 1:10 and a post-vaccination titer ≥ 1:40, or a pre-vaccination titer ≥ 1:10 and a minimum four-fold rise in post-vaccination titer [5].

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

The protocol follows a Phase II randomized, double blind study design enrolling 371 males and non-pregnant females, 18-64 years of age who are in good health as determined by medical history and physical examination, and meet all eligibility criteria, including erythrocyte sedimentation rate (ESR), hematology, and biochemistry parameters within acceptable range, and negative urine or serum pregnancy test (for females). This clinical trial is designed to assess the safety, reactogenicity, and immunogenicity of a monovalent inactivated influenza A/H7N9 virus vaccine at different dosages (3.75 mcg, 7.5 mcg, 15 mcg of HA per dose) with MF59 adjuvant, or at a dosage of 15 mcg per dose without adjuvant.

In this trial, subjects will be randomly assigned to 1 of 4 study groups with allocation 2:2:2:1 (see Table 1) stratified by site and prior receipt of at least one of the 2017-2018 and/or 2018-2019 seasonal influenza vaccine. The same dosage of vaccine with or without the same adjuvant will be given to subjects at both of their first and second study vaccinations. All study vaccinations will be administered IM approximately 21 days apart. Subjects assigned to study arm 1 will receive 3.75mcg A/H7N9 IIV and MF59, subjects assigned to study arm 2 will receive 7.5mcg A/H7N9 IIV and MF59, subjects assigned to study arm 3 will receive 15mcg A/H7N9 IIV and MF59, and subjects assigned to study arm 4 will receive 15mcg A/H7N9 unadjuvanted.

Reactogenicity will be measured by the occurrence of solicited injection site and systemic reactions from the time of each study vaccination through 7 days after each study vaccination. Unsolicited non-serious AEs will be collected from the time of each study vaccination through approximately 21 days after each study vaccination. SAEs, MAAEs, including NOCMCs, and PIMMCs, will be collected from the time of the first study vaccination through approximately 12 months after the last study vaccination. Clinical laboratory evaluations for safety will be performed on venous blood collected prior to each study vaccination and approximately 7 days after each study vaccination.

Immunogenicity testing will include performing HAI and Neut antibody assays against the 2017 A/H7N9 vaccine virus and drifted variants of the A/H7N9 virus on serum samples obtained immediately prior to each study vaccination (Days 1 and approximately Day 22), approximately 7 days after each study vaccination (Days 8 and 29), and approximately 21 and 180 days after the second study vaccination (Days 43 and 202).

Novel methods for identifying and assessing alternative correlates of protection against influenza infection are needed. To assess the NA specific antibody response to vaccination, it is first necessary to determine the NA content of inactivated influenza vaccine; this assay is under development. If successful, the NA content in a dosage specific manner can be correlated to the N9 NA-specific antibody responses elicited by the 2017 H7N9 IIV.

4.2. Discussion of Study Design, Including the Choice of Control Groups

This study uses a dose comparison concurrent control design. All subjects receive the same study product (A/H7N9 IIV) with differing dosages with or without MF59 adjuvant.

4.3. Selection of Study Population

The study population for this clinical trial is 371 males and non-pregnant females, 18-64 years of age, who are in good health and meet all eligibility criteria. The subjects will be recruited from the general population at the participating Vaccine Trial and Evaluation Unit (VTEU) sites that have substantial experience conducting large influenza vaccine studies.

4.4. Treatments

4.4.1. Treatments Administered

A/H7N9 Vaccine and MF59 Adjuvant will be administered.

4.4.2. Identity of Investigational Product

See the study protocol for details of study product formulation.

4.4.3. Method of Assigning Subjects to Treatment Groups (Randomization)

Enrollment/randomization will be performed through the enrollment module in the electronic data capture system maintained by the Statistical and Data Coordinating Center (SDCC).

Eligible subjects will be stratified by clinical site and prior receipt of at least one of the 2017-2018 and/or 2018-2019 seasonal influenza vaccines then randomly assigned with allocation (2:2:2:1) to one of 4 study arms indicated in Table 1. The treatment sequence was generated using permuted block randomization to provide an approximately balanced allocation to the study arms during the study.

4.4.4. Selection of Doses in the Study

Participants in this study are to receive two A/H7N9 vaccinations at HA doses of 3.75, 7.5, or 15 mcg with MF59 adjuvant, or at a HA dose of 15 mcg without adjuvant. The 3.75, 7.5, or 15 mcg with MF59 doses are selected to evaluate safety and immunogenicity of antigen sparing dose strategies. Per FDA Guidance [5], the 15mcg non-adjuvanted dose was selected to compare immune response with the 15 mcg adjuvanted vaccine.

4.4.5. Selection and Timing of Dose for Each Subject

Each subject is to be randomly assigned to a study group which will define the A/H7N9 vaccine dose and receipt of adjuvant for both planned study vaccinations. The first vaccination takes place on the day of randomization, and the second vaccination takes place approximately 21 days after the first vaccination (protocol defined window of 21-28 days post first vaccination).

4.4.6. Blinding

This trial is double-blinded; subjects, investigators, study personnel performing any study-related assessments following study vaccine administration, and laboratory personnel performing antibody assays are blinded to dosage within study vaccination schedule.

The randomization scheme was generated by the SDCC and provided to unblinded study personnel (i.e., pharmacists performing study vaccination preparations and unblinded study vaccine administrators) at the participating VTEU sites who will not be not involved in study-related assessments or have subject contact for data collection following study vaccine administration.

The Data and Safety Monitoring Board (DSMB) may receive data in aggregate and presented by group. The DSMB may also be provided with expected and observed rates of the expected AEs in an unblinded fashion, and may request treatment assignment be unblinded for an individual subject if required for safety assessment. The DSMB will review grouped and unblinded data in the closed session only.

4.4.7. Prior and Concomitant Therapy

Administration of any medications, therapies, or vaccines (including prescription and over-the-counter drugs as well as herbals, vitamins, and supplements) from 60 days prior to study vaccination through 180 days post final vaccination will be solicited from the participant during screening, enrollment, and follow-up. Any reported prior therapies from up to 30 days prior to vaccination through 180 days post final vaccination will be recorded in the appropriate data collection form.

Prior receipt of a licensed seasonal influenza vaccine over the current (2018-2019) and previous two seasons (2016-2017 and 2017-2018) is not exclusionary as long as it has been administered within the allowable window (protocol Section 5.1.2).

Use of concomitant medications is allowed prior to and during the trial with the exception of medications and therapies that might interfere with the evaluation of the investigational product. Medications in this category include the prohibited medication per the Subject Exclusion Criteria (protocol Section 5.1.2). In addition, the site principal investigator or appropriate sub-investigator may identify other medications that should not be used due to a risk to subject safety or assessment of reactogenicity and immunogenicity.

4.4.8. Treatment Compliance

All subjects are to receive two doses of study product administered in the clinic.

4.5. Immunogenicity and Safety Variables

See Table 2 and Table 3 for schedule of study procedures.

4.5.1. Safety Variables

Safety will be assessed by the frequency and severity of:

1. SAEs occurring from the time of the first study vaccination through approximately 12 months after the last study vaccination.
2. Solicited AEs – reactogenicity events occurring from the time of each study vaccination through 7 days after each study vaccination:
   a) Injection site reactions including pruritus, ecchymosis, erythema, induration/swelling, pain, and tenderness.
   b) Systemic reactions including fever, feverishness, fatigue, malaise, myalgia, arthralgia, headache, and nausea.
3. Clinical safety laboratory AEs occurring from the time of each study vaccination through approximately 7 days after each study vaccination. Parameters to be evaluated include white blood cells (WBC), hemoglobin (Hgb), platelets (PLT), alanine aminotransferase (ALT), total bilirubin (T. Bili), and creatinine (Cr).
4. Unsolicited AEs – non-serious AEs occurring from the time of each study vaccination through approximately 21 days after each study vaccination.
5. MAAEs, including NOCMCs, and PIMMCs occurring from the time of the first study vaccination through approximately 12 months after the last study vaccination.

Grading scales for injection site and systemic solicited reactions, vital signs, and clinical laboratory parameters are provided in Table 9, Table 10, Table 11, and Table 12.

4.5.2. Immunogenicity Variables

Individual HAI and Neut results will be reported by the central immunology laboratory for the homologous vaccine strain, A/Hong Kong/125/2017 (H7N9), and heterologous strains, A/Shanghai/2/2013 (H7N9) and A/Guangdong/17SF003/2016xPR8/17SF003/2016xPR8 (H7N9). Assay results are reported as a reciprocal titer with values of $10*2^k$, where k=0, 1, 2, etc. The lower limit of detection for the HAI and Neut assays is 1:10; values below the limit of detection are imputed for analysis as one-half the limit of detection (10/2 = 5). For analysis, the geometric mean (calculated on natural log scale) of repeated results for each sample will be computed and used as the response for all subsequent calculations. The variation arising from multiple measurements for an individual at a single time point is not used in subsequent calculations. See Section 3.3 for definitions of derived variables for the analysis of HAI and Neut data.

To assess the Neuraminidase Antigen (NA) specific antibody response to vaccination, it is first necessary to determine the NA content of inactivated influenza vaccine; this assay is under development. If successful, the NA content in a dosage specific manner can be correlated to the N9 NA-specific antibody responses elicited by the 2017 H7N9 IIV. An addendum to the SAP will be generated to outline the planned analyses when assay development is complete.

All immunogenicity data will be uploaded into the SDCC's electronic data capture system.

5. SAMPLE SIZE CONSIDERATIONS

This study is planned to enroll 106 subjects in each adjuvanted study arm and 53 subjects in the unadjuvanted study arm. Randomization at each site will be stratified by prior receipt of season influenza vaccines, however there is no enrollment target for these strata. The sample size for this study was selected to obtain preliminary estimates in a time critical manner. While this study is not designed to test any specific null hypothesis, the following tables illustrate the precision and power that is available for select estimates and comparisons of interest.

Table 4 indicates the probability of observing one or more safety events, such as solicited injection site or systemic reactogenicity events or an unsolicited non-serious AE of a particular type for a single study arm (N = 53, 106) and for all subjects receiving adjuvanted vaccine (N = 318).

Binomial confidence intervals (CI) are widest (have the least precision) when the response rate is 50%. Table 5 is presented to indicate the worst-case scenario for precision of observed exact (Clopper-Pearson) binomial confidence intervals.

Table 6 illustrates the minimum detectable differences in the proportion of subjects responding (e.g., attaining seroconversion or a titer ≥1:40) between two adjuvanted study arms within each stratum using a two-sided Likelihood Ratio Test and alpha = 0.05.

Power calculations assume n=100 per adjuvanted group and n=50 for the unadjuvanted group. Based on previous DMID A/H7N9 trials it is expected 5% of enrolled subjects in this stratum may be excluded from analysis of the primary endpoint. In the event that only 100 subjects are actually enrolled in a study arm, the small dropout rates anticipated would have a minimal impact on the calculations presented in Table 7.

Per FDA guidance [5,6], for differences in HAI antibody response rates, the lower confidence limit on the appropriate point estimate excluding equality (i.e., 0 for the difference parameter) may be sufficient to demonstrate the added value of the adjuvant. Table 7 shows the lower bound of the 95% confidence interval for the difference in the proportion of responders between the adjuvanted and unadjuvanted arms (e.g. 15 mcg + MF59 minus 15 mcg unadjuvanted) assuming the proportion of responders in the unadjuvanted arm is 0.10 and considering a range for the proportion of responders in the adjuvanted arm ranges from 0.50 to 0.90.

6. GENERAL STATISTICAL CONSIDERATIONS

6.1. General Principles

All continuous variables will be summarized using the following descriptive statistics: n (non-missing sample size), mean, standard deviation, median, maximum and minimum. The frequency and percentages (based on the non-missing sample size) of observed levels will be reported for all categorical measures. In general, all data will be listed, sorted by site, study arm and subject, and when appropriate by visit number within subject. All summary tables will be structured with a column for each study arm in the following order:

- Arm 1: 3.75 mcg A/H7N9 + MF59
- Arm 2: 7.5 mcg A/H7N9 + MF59
- Arm 3: 15 mcg A/H7N9 + MF59
- Arm 4: 15 mcg A/H7N9

All tables will be annotated with the total population size relevant to that table/arm, including any missing observations.

6.2. Timing of Analyses

6.2.1. CSR

Once the last subject completes the visit that occurs approximately at Day 387, the clinical database will be cleaned, monitored, and locked. The CSR will be completed when all safety data through Day 387 and all humoral immunogenicity data through Day 202 are completed and uploaded.

Upon receipt of humoral immunogenicity against homologous influenza A/Hong Kong/125/2017 (H7N9) virus through Day 202 and non-clinical data lock, a subset of predefined “topline tables” will be generated by the SDCC concurrently with CSR generation. These tables will include summaries of safety and immunogenicity data and will represent the final analyses of primary endpoints; as such no p-value adjustment is required. These analyses may be made available to the sponsor for planning subsequent trials and to the lead PI for publication. Tables to be included in the topline set are indicated with the symbol * in the title.

Analysis of exploratory immunogenicity endpoints may be performed and released as the data are available from the research laboratory. Any such analyses would be considered the final analysis for the endpoint and included in the CSR. Additional exploratory immunogenicity endpoint data not available at the time of CSR preparation may be included in an addendum to the CSR.

6.3. Analysis Populations

6.3.1. Safety Population

The Safety Analysis population includes all subjects who received at least one study vaccination.

6.3.2. Modified Intention-to-Treat (mITT) Population

The modified intent-to-treat (mITT) population includes all subjects who received at least one study vaccination and contributed both pre- and at least one post-study vaccination venous blood samples for immunogenicity testing (HAI or Neut antibody assays) for which valid results were reported. For analyses using the mITT population, subjects will be grouped based on randomized study arm.

6.3.3. Per-Protocol Population

The Per-Protocol (PP) population includes all subjects in the mITT subset with the following exclusions:

- Data from all available visits for subjects found to be ineligible at baseline.
- Data from all visits subsequent to major protocol deviations, such as:
  - Second study vaccination not received,
  - Second study vaccination received out of window,
  - Receipt of non-study licensed live vaccine within 30 days before or after each study vaccination,
  - Receipt of non-study licensed inactivated vaccine within 14 days before or after each study vaccination,
  - Receipt of immunosuppressive therapy (e.g., corticosteroids) within 30 days before or after each study vaccination.
- Data **from** any visit that occurs out of window:
  - Visit 3 data collected before 6 days or after 10 days post first study vaccination
  - Visit 4 data collected before 20 days or after 29 days post first study vaccination.
  - Visit 6 data collected before 6 days or after 10 days post second study vaccination.
    - For subjects who did not receive the second study vaccination, visit 6 data collected before 27 days or after 31 days post first study vaccination.
  - Visit 7 data collected before 20 days or after 29 days post second study vaccination.
    - For subjects who did not receive the second study vaccination, visit 7 data collected before 41 days or after 50 days post first study vaccination.

- Visit 10 data collected before 165 days or after 195 days post second study vaccination.
    - For subjects who did not receive the second study vaccination, visit 10 data collected before 200 days or after 216 days post first study vaccination.

For analyses using the PP population, subjects will be grouped based on study vaccinations received.

6.4. Covariates and Subgroups

As a protocol defined exploratory analysis, HAI antibody response following the second vaccination will be summarized stratified by the following covariates: age (categorical: 18-34, 35-49, 50-64), sex (male, female), body mass index (<30, ≥30), and prior receipt of seasonal influenza vaccine(s) (receipt of 2017-2018 or 2018-2019, or receipt of neither), and these covariates will be considered in statistical modeling as described in Section 8.3. As these analyses are exploratory the study was not powered for any subgroup analyses.

6.5. Missing Data

All attempts will be made to collect all data Per-Protocol. As missing data are expected to be minimal, no imputation will be performed for missing values. Any data point that appears to be erroneous or inexplicable based on clinical judgment will be investigated as a possible outlier. If data points are identified as outliers, sensitivity analyses will be performed to examine the impact of including or excluding the outliers. Any substantive differences in these analyses will be reported.

6.6. Interim Analyses and Data Monitoring

Interim analyses will only be used to terminate this trial in the event that unanticipated safety events deemed to be of sufficient concern require such action by the sponsor. These assessments will not be made on the basis of testing a formal statistical hypothesis; therefore, p-value adjustment will not be made to any analyses. A DSMB will be convened by DMID to review study progress and participant, clinical, safety, and reactogenicity and immunogenicity data.

Clinical, safety, and reactogenicity data through approximately 180 days after the second study vaccination will represent the primary clinical database for this trial. Once the last subject completes the visit that occurs approximately 180 days after second study vaccination and all HAI and Neut results are received, a “topline” subset of the immunogenicity and safety tables will be provided to DMID on an expedited timeline. These analyses may be made available to the sponsor for planning subsequent trials and to the lead PI for publication and will be considered the final analysis of these data.

Emergent public health needs may dictate additional interim safety, reactogenicity, and/or immunogenicity analyses be performed on available information at any time during the trial. If this occurs, immunogenicity data will be analyzed as results are available from the central immunogenicity laboratory.

6.6.1. Interim Safety Review

An interim safety review may include enrollment and demographic information, medical history, concomitant medications, physical assessments, clinical laboratory values, dosing compliance, and solicited and unsolicited AE/SAEs. Additional data may be requested by the DSMB, and interim statistical reports may be generated as deemed necessary and appropriate by DMID. The DSMB may receive data in aggregate and presented by study arm. The DSMB may also be provided with expected and observed rates of the expected AEs in an unblinded fashion and may request the treatment assignment be unblinded for an individual subject if required for safety assessment. The DSMB will review grouped and unblinded data in the closed session only. The DSMB will meet and review this data at scheduled time points or ad hoc as needed during this trial as defined in the DSMB charter. As an outcome of each review/meeting, the DSMB will make a recommendation as to the advisability of proceeding with study vaccinations (as applicable), and to continue, modify, or terminate this trial. Summaries prepared for the DSMB are defined separately in a report shell reviewed and approved by the DSMB.

Additionally, this trial will be monitored to determine if any of the halting rules described in Protocol Section 9.5 are met.

6.6.2. Interim Immunogenicity Review

Clinical, safety, and reactogenicity data through approximately 180 days after the second study vaccination will represent the primary clinical database for this trial. Once the last subject completes the visit that occurs approximately 180 days after second study vaccination and all HAI and Neut results are received, a “topline” subset of the immunogenicity and safety tables will be provided to DMID on an expedited timeline. These analyses may be made available to the sponsor for planning subsequent trials and to the lead PI for publication and will be considered the final analysis of these data.

Should emergent public health needs dictate interim immunogenicity review, immune responses will be summarized in terms of strain-specific 2017 A/H7N9 HAI and Neut antibody titers**.** Any immunogenicity reports would be provided by the SDCC to the DMID Scientific Lead and CPM, and the DSMB. Reports would include data summarized by treatment arm.

6.7. Multicenter Studies

Although randomization was stratified by site, data will be pooled across all clinical sites for all analyses. Center effects are not anticipated because the sites are using standardized procedures for vaccination and assessment of solicited and unsolicited AEs, and the study relies on a central laboratory for immunogenicity assessments.

6.8. Multiple Comparisons/Multiplicity

This study was designed to obtain preliminary estimates of safety and immune response to the A/H7N9 vaccination in healthy adults. The study was not designed to test any specific null hypothesis, and as such no adjustment for multiple comparisons will be performed.

7. STUDY SUBJECTS

7.1. Subject Disposition

Table 13 will present a summary of the reasons that subjects were screened but not enrolled.

The number and percentage of enrolled subjects excluded from each analysis population by study arm are presented in Table 14. A listing of subjects excluded from each analysis population will be presented in Listing 5.

The disposition of subjects in the study will be tabulated by study arm in Table 15. The table will show the total number of subjects screened, randomized, receiving the first study vaccination, receiving the second study vaccination, completing the blood draw for the primary immunogenicity endpoints, and completing the last visit.

A flowchart showing the disposition of study subjects, adapted from the CONSORT Statement [4] will be included and will present the number of subjects screened, randomized, lost to follow up, and analyzed, by study arm (see Figure 1).

A listing of subjects who were discontinued from treatment or terminated from study follow-up and the reason will be included in Listing 2.

7.2. Protocol Deviations

A summary of subject-specific protocol deviations will be presented by the deviation category and deviation type, study arm, and age stratum for all enrolled subjects in Table 8. Major deviations that will be reviewed for possible exclusion of immunogenicity results from the PP population include deviations related to eligibility/enrollment, treatment administration schedule, follow-up visit schedule, and receipt of exclusionary vaccines or medications. All subject-specific protocol deviations and non subject-specific protocol deviations will be included in Listing 3 and Listing 4.

8. IMMUNOGENICITY EVALUATION

Analysis of all immune responses will be conducted using the PP population. In addition, primary endpoint analyses will be conducted with the mITT population. Immune responses in terms of strain-specific A/H7N9 HAI and Neut antibody titers will be summarized by study arm at each time point. Descriptive summary statistics will be provided for all assays and time points including number of subjects with non-missing results, percentage of subjects with titers ≥1:40, percentage of subjects achieving seroconversion, and GMTs along with corresponding 95% CI. Exact confidence intervals will be presented for proportional endpoints. Summaries of primary and secondary immunogenicity endpoints are presented in Table 23, Table 24, Table 25, and Table 26.

Reverse cumulative distribution (RCD) curves will be presented for post-vaccination HAI and Neut antibody titers. Plots for each assay will be generated with 4 panels (8 days post vaccination 1, 21 days post vaccination 1, 8 days post vaccination 2, 21 days post vaccination 2, and 180 days post vaccination 2), and separate curves within each panel for each study arm, as shown in Figure 2, Figure 3, Figure 4, and Figure 5.

Figures depicting the HAI and Neut GMT over time will also be presented as shown in Figure 6, Figure 7, Figure 8, and Figure 9.

The spearman correlation between HAI and Neut antibody titers will be calculated at each time point over all groups. The correlation will be depicted in scatter plots as Figure 10 and Figure 11.

Individual HAI and Neut assay results will be provided in Listing 8 and Listing 9.

8.1. Primary Immunogenicity Analysis

The primary immunogenicity endpoints HAI and Neut seroconversion, percentage of subjects with titer ≥1:40, and GMTs against the homologous A/H7N9 vaccine strain 21 days after the second vaccination will be summarized as described above. Regression modelling of seroconversion and log titers is planned as described in Section 8.3.2.

8.2. Secondary Immunogenicity Analyses

The secondary immunogenicity endpoints HAI and Neut seroconversion, percentage of subjects with titer ≥40, and GMTs against the homologous A/H7N9 vaccine strain 8 and 21 days after the first vaccination and 8 days after the second vaccination will be summarized as described above. No formal hypothesis testing is planned.

8.3. Exploratory Immunogenicity Analyses

Immunogenicity data summaries and analysis for exploratory endpoints will be presented for the PP populations.

8.3.1. Covariate Analysis

As an exploratory analysis, seroconversion and GMT of serum antibody for both HAI and Neut at 21 and 180 days after second vaccination will be summarized by study arm stratified

by age (categorized as those subjects ages 18-34, 35-49, 50-64) in Table 27, Table 28, Table 29, and Table 30, by sex in Table 31, Table 32, Table 33, and Table 34 by BMI in Table 35, Table 36, Table 37, and Table 38, and by prior receipt of seasonal influenza vaccines in Table 39, Table 40, Table 41, and Table 42. These stratified summaries will be presented for the PP population. It is anticipated that subjects will have little to no pre-existing antibody at baseline, so seroconversion and titer ≥40 endpoints will be similar.

8.3.2. Regression Modeling

Logistic and multivariate linear regression will be utilized to test for the effects of the HA antigen dose and the MF59 adjuvant on seroconversion and GMT, respectively, for the PP population. Similar models will be fit for HAI and Neut Antibodies. Separate models will be fit for data from Day 21 post dose 2 and Day 180 post dose 2.

Logistic regression will be fit to examine the relationship of HAI seroconversion at 21 days after the 2nd study vaccination with study arm. If the available titer data meets the required assumptions of normality after log transformation, multiple linear regression will be fit to examine the relationship of log transformed titers at 21 days after the 2nd study vaccination with study arm. Both models will be fit with and without adjustment for the following covariates (Z): age category (19-34 years, 35-49 years, 50-64 years), sex (female, male), BMI (<30, ≥30), and prior receipt of seasonal influenza vaccine (none in past 2 seasons, at least once in past 2 seasons). Modeling assumptions will be checked using standard diagnostic methods (e.g., using the INFLUENCE option in PROC LOGISTIC or PROC GLM). Parameter estimates and odds ratio estimates for the logistic models will be presented in Table 43, Table 44, Table 45, Table 46, Table 47, Table 48, Table 49, and Table 50. Parameter estimates for the multiple linear regression models will be presented in Table 51, Table 52, Table 53, Table 54, Table 55, Table 56, Table 57, and Table 58.

Model 1A: Logistic Regression (without covariate adjustment):

$$logit[P(seroconversion)] = \beta_0 + \beta_1 \times Study\ Arm + \varepsilon$$

Model 1B: Logistic Regression (with covariate adjustment):

$$logit[P(seroconversion)] = \beta_0 + \beta_1 \times Study\ Arm + \beta_2 \times Z + \varepsilon$$

Model 2A: Multiple Linear Regression (without covariate adjustment):

$$log(titer) = \beta_0 + \beta_1 \times Study\ Arm + \varepsilon$$

Model 2B: Multiple Linear Regression (with covariate adjustment):

$$log(titer) = \beta_0 + \beta_1 \times Study\ Arm + \beta_2 \times Z + \varepsilon$$

Subjects missing data for one or more covariates will be excluded from Models 1B and 2B.

8.3.3. Analysis of Heterologous Strain

HAI and Neut antibody responses against antigenically drifted variants of influenza A/H7 viruses including A/Shanghai/2/2013 and A/Guangdong/17SF003/2016xPR8 will be summarized for the Per-Protocol population as described in Section 8 and presented in

Table 59, Table 60, Table 61, Table 62, Figure 12, Figure 13, Figure 14, Figure 15, Figure 16, Figure 17, Figure 18, and Figure 19. A scatter plot of the correlation between HAI and Neut antibody responses for each of the drifted strains will be presented in Figure 20 , Figure 21, Figure 22, and Figure 23. A scatter plot of the correlation between response to the vaccine strain and each heterologous strain will be presented in Figure 24 and Figure 25. No formal hypothesis testing or modeling for the exploratory analysis of heterologous strains is planned.

8.3.4. NA Serum Antibody Responses

Descriptions of the NA assays and planned analyses will be described in an addendum to this SAP.

9. SAFETY EVALUATION

All summaries and analysis of safety data will be presented for the Safety Analysis Population. Safety summaries will be presented overall and grouped by study arm overall and by age stratum.

Continuous variables will be summarized using the following descriptive statistics: n (non-missing sample size), mean, standard deviation, median, maximum and minimum. All categorical measures will be summarized by the frequency and percentages of observed levels. The denominator for the percentages may be based on the number of non-missing observations for an assessment or based on the number of subjects in a population. This will be described for each table.

9.1. Demographic and Other Baseline Characteristics

Summaries of age, sex, ethnicity, race, BMI, and prior receipt of seasonal influenza vaccine will be presented by site in Table 18 and Table 19 and by study arm overall in Table 20 and Table 21. Age will be summarized as a continuous variable as well as by strata categories. Ethnicity is categorized as Hispanic or Latino, or not Hispanic and not Latino. In accordance with NIH reporting policy, subjects may self-designate as belonging to more than one race or may refuse to identify a race, the latter reflected in the electronic case report form (eCRF) as "No" to each racial option. BMI will be summarized as a continuous as well as categorical variable, categorized as (<30, ≥30). Self-reported history of prior receipt of seasonal influenza vaccine will be categorized as follows: 2017-2018, 2018-2019, receipt of none, or unknown. Demographic information for individual subjects will be provided in Listing 6.

9.1.1. Prior and Concurrent Illnesses and Medical Conditions

All current illnesses and past or pre-existing medical conditions will be coded using Medical Dictionary for Regulatory Activities (MedDRA®) version 20.0 or higher.

Summaries of subjects' prior and concurrent medical conditions will be presented by study arm in Table 22.

Individual subject listings will be presented for all reported medical history including prior and concurrent medical conditions in Listing 7.

9.1.2. Prior and Concurrent Medications

Concomitant medications will be coded to the Anatomical Therapeutic Classification using the WHO Drug Dictionary. The use of concomitant medications during the study will be summarized by ATC1 and ATC2 code and study arm for the Safety population in Table 108. A listing of concomitant medications will be presented in Listing 17.

9.2. Measurements of Treatment Compliance

All subjects are to receive 2 study vaccinations administered in the clinic. The number of study vaccinations administered to subjects will be presented by study arm and by site, overall in Table 16 and Table 17 and as part of the subject disposition in Table 15.

Listing 1 presents subjects who received investigational product with randomized study arm and study product received for each vaccination.

9.3. Adverse Events

A summary of all adverse events is provided in Table 63. A summary of those events that occurred in ≥5% of subjects in any treatment group is provided in Table 64.

9.3.1. Solicited Events and Symptoms

Systemic solicited adverse events were collected pre-vaccination, and systemic and injection site solicited adverse events were collected at-least 20 minutes post-vaccination and then daily for 7 days after each vaccination and graded on a scale of 0 (absent), 1 (mild), 2 (moderate) and 3 (severe). Systemic events include fever, feverishness, fatigue, malaise, myalgia, arthralgia, headache, and nausea. The grading scale for systemic events, including quantitative grading for fever, is included in Table 10. Injection site events include pruritus, ecchymosis, erythema, induration/swelling, pain, and tenderness. Ecchymosis, erythema, and induration are measured by both functional and measurement grading scales as defined in Table 9.

When calculating the incidence of solicited events, each subject will be counted once at the highest severity following the applicable vaccination, and any repetitions will be ignored. For summaries presented separately for each vaccination, the denominator for percentages will be the number of subjects who received the respective vaccination with non-missing data for the event summarized. For summaries over all vaccinations the denominator will be the number of subjects who received at least one vaccination with non-missing data for the event summarized.

The number and percentage of subjects reporting at least one solicited adverse event of any severity will be summarized for each solicited symptom, any systemic symptom, any injection site symptom, and any symptoms. For each event the denominator is the number of subjects who received the applicable vaccination with non-missing data for the specific event. The 95% CI calculated using Clopper-Pearson methodology from a binomial distribution (SAS Proc Freq with a binomial option) will be presented in Table 65, Table 66, and Table 67. Logistic regression models will be fit to estimate the effect of study arm on the probability of reporting any injection site event or reporting any systemic event in Table 68 and Table 69. If statistically significant effects are observed in the model for local events or systemic events, then additional models will be fit for each individual event of that type.

$$logit[P(Event)] = \beta_0 + \beta_1 \times Study\ Arm + \varepsilon,$$

For each systemic and injection site event, any systemic event, any injection site event, and any solicited event, the maximum severity over 7 days after each vaccination will be summarized for the Safety population. The number and percentage of subjects reporting each event will be summarized by the maximum severity and treatment group overall and by age stratum, separately for each vaccination and over all vaccinations. For each event the denominator is the number of subjects who received the applicable vaccination with non-missing data for the specific event. The 95% CI calculated using Clopper-Pearson

methodology from a binomial distribution (SAS Proc Freq with a binomial option) will be presented in Table 70, Table 71, and Table 72.

The number of subjects reporting a solicited adverse event will be summarized for each day post vaccination for each vaccination and for all vaccinations combined both as summary in Table 73, Table 74, and Table 75 and graphically in a bar chart in Figure 26 and Figure 27. A comparison of the event rate for each treatment group between vaccination 1 and vaccination 2 will be presented, including p-values from McNemar's test performed over all subjects for injection site and systemic symptoms in Table 76 and Table 77.

Systemic and injection site solicited events reported by subject will be presented in Listing 10 and Listing 11, sorted by subject ID, vaccination number, parameter, and study day.

9.3.2. Unsolicited Adverse Events

When calculating the incidence of unsolicited AEs (i.e., on a per subject basis), each subject will only be counted once at the highest severity and/or relationship, and any repetitions of AEs within a subject will be ignored; the denominator will be the total number of subjects in the safety population. All AEs reported will be included in the summaries and analyses.

The number and percentage of subjects reporting at least one unsolicited AE will be summarized by MedDRA system organ class and preferred term. A 95% CI will be presented for the percentage of subjects reporting any unsolicited AE (serious or non-serious) for each MedDRA system organ class and preferred term over all study vaccinations in Table 78.

The following summaries for unsolicited AEs will be presented by MedDRA system organ class, preferred term, and study arm:

- Incidence of AEs by severity and relationship to study product in Table 79;
- Incidence of non-serious, related AEs by severity in Table 80;
- Incidence of AEs over time (Days 1-8, Days 9-22 post each study vaccination) in Table 81;
- Incidence of non-serious, related AEs over time (Days 1-8, Days 9-22 post each study vaccination) in Table 82 – note this table presents results for secondary safety endpoint, "Occurrence of study vaccine-related unsolicited non-serious AEs from the time of each study vaccination through approximately 21 days after each study vaccination";
- Total frequency of AEs over time (Days 1-8, Days 9-22 post each study vaccination) in Table 83;
- Subject listing of non-serious AEs of moderate or greater severity in Table 87;
- Bar chart displaying total frequency of AEs by severity and MedDRA system organ class, Study arm, and Age Stratum in Figure 28;

- Bar chart displaying incidence of AEs by severity and MedDRA system organ class, Study arm, and Age Stratum in Figure 29;
- Bar chart displaying total frequency and incidence of AEs by relationship to study product and MedDRA system organ class and study arm in Figure 30 and Figure 31.

9.4. Deaths, Serious Adverse Events and other Significant Adverse Events

The following listings will be presented including Subject ID, Age (years) AE Description, AE Onset Date/End Date, Last Vaccination Received/Days Post Vaccination, Reason Reported as an SAE, Relationship to Treatment, Alternate Etiology if not Related, Outcome, and Duration of Event (days):

- Deaths and Serious Adverse Events in Table 84;
- Potentially Immune-Mediated Medical Conditions in Table 85;
- New Onset Chronic Medical Conditions in Table 86;

A listing of all reported AEs by subject will be presented in Listing 11, sorted by Study arm, Subject ID, and AE Number.

9.5. Pregnancies

For any subjects in the Safety population who became pregnant during the study, every attempt will be made to follow these subjects to completion of pregnancy to document the outcome, including information regarding any complications with pregnancy and/or delivery. Listing 18, Listing 19, Listing 20, Listing 21, and Listing 22 will present any study pregnancies and their outcomes.

9.6. Clinical Laboratory Evaluations

Clinical safety laboratory parameters (WBC, Hgb, PLT, ALT, T. Bili, Cr) will be collected from each subject prior to each study vaccination and approximately 7 days after each study vaccination. These evaluations will be performed by the central clinical laboratory. The grading scale for clinical laboratory evaluations is presented in Table 12. Clinical laboratory evaluations assessed on Day 1 prior to the first study vaccination will be considered as baseline.

The distribution of laboratory results by severity, study day, and study arm will be presented in Table 88, Table 89, Table 90, Table 91, Table 92, Table 93, and Table 94. Descriptive statistics including mean, standard deviation, median, minimum and maximum values by study day will be summarized for each parameter and for the change from baseline for each parameter in Table 95, Table 96, Table 97, Table 98, Table 99, and Table 100. Box plots illustrating the change from baseline for each laboratory parameter will be presented in Figure 25, Figure 26, Figure 27, Figure 28, Figure 29, and Figure 30. Subject visits with

abnormal laboratory results, Grade 1 severity or higher, will be presented in Table 101 and Table 102 for Chemistry and Hematology parameters, respectively.

A complete listing of individual clinical laboratory results will be presented in Listing 13 and Listing 14 for chemistry and hematology, respectively, sorted by subject ID, parameter, and visit number.

9.7. Vital Signs and Physical Evaluations

Oral temperature, systolic blood pressure, diastolic blood pressure, and pulse will be assessed prior to study vaccination on Day 1 and Day 22. The grading scale for vital sign evaluations is presented in Table 11. Summaries of vital signs by maximum severity will be tabulated by visit and study arm in Table 103, Table 104, Table 105, Table 106, and Table 107. A listing of vital signs will be presented in Listing 15.

Targeted physical examinations will be performed, if indicated, based on a subject's medical history. A listing of physical exam findings will be presented (Listing 16).

9.8. Concomitant Medications

Concomitant medications will be collected for the 30 days prior to the first study vaccination through 21 days after the second study vaccination. Concomitant medications will be coded to the Anatomical Therapeutic Classification using the WHO Drug Dictionary. The use of prior and concomitant medications taken during the study will be recorded on the CRFs. A by-subject listing of concomitant medication use will be presented (Listing 17). The use of concomitant medications during the study will be summarized by ATC1, ATC2 code, study arm for the Safety population (Table 108).

10. REPORTING CONVENTIONS

P-values ≥0.001 and ≤0.999 will be reported to 3 decimal places; p-values less than 0.001 will be reported as "<0.001"; p-values greater than 0.999 will be reported as "> 0.999". The mean, standard deviation, and any other statistics other than quantiles, will be reported to one decimal place greater than the original data. Quantiles, such as median, or minimum and maximum will use the same number of decimal places as the original data. Proportions will be presented as two decimal places; values <0.01 will be presented as "<0.01". Percentages will be reported to the nearest whole number; non-zero values < 1% will be presented as "<1"; values greater than 99% but less than 100% will be presented as >99. Estimated parameters, not on the same scale as raw observations (e.g. regression coefficients) will be reported to 3 significant figures.

11. TECHNICAL DETAILS

SAS version 9.4 or above will be used to generate all tables, figures and listings.

12. SUMMARY OF CHANGES IN THE CONDUCT OF THE STUDY OR PLANNED ANALYSES

This SAP does not include any changes from the analyses described in the protocol.

13. REFERENCES

1. Gao, R., et al., *Human infection with a novel avian-origin influenza A (H7N9) virus.* N Engl J Med, 2013. **368**(20): p. 1888-97.
2. *Analysis of recent scientific information on avian influenza A(H7N9) virus.* WHO Influenza Update, 2017.
3. Human infection with avian influenza A(H7N9) virus – China: 18 May 2017. WHO Emergencies preparedness, response, 2017.
4. Drummond R. CONSORT Revised: Improving the Reporting of Randomized Clinical Trials. JAMA. 2001; 285(15):2006-2007.
5. FDA Guidance for Industry: Clinical Data Needed to Support the Licensure of Seasonal Inactivated Influenza Vaccines (US DHHS, FDA, CBER, May 2007).
6. FDA Guidance for Industry: Clinical Data Needed to Support the Licensure of Pandemic Influenza Vaccines (US DHHS, FDA, CBER, May 2007).

14. APPENDICES

Table, figure, and listing shells are presented in Appendices 1, 2, and 3. Tables and figures included in the topline set are indicated by *.

APPENDIX 1. TABLE MOCK-UPS

LIST OF TABLES

LIST OF TABLES

9.1 Overall Study Design and Plan Description

Table 1: Study Design

Study Arms	Day 1	Day 22
Study Arm 1, n=106	Seqirus H7N9 vaccine 3.75 mcg plus MF59 adjuvant	Seqirus H7N9 vaccine 3.75 mcg plus MF59 adjuvant
Study Arm 2, n=106	Seqirus H7N9 vaccine 7.5 mcg plus MF59 adjuvant	Seqirus H7N9 vaccine 7.5 mcg plus MF59 adjuvant
Study Arm 3, n=106	Seqirus H7N9 vaccine 15 mcg plus MF59 adjuvant	Seqirus H7N9 vaccine 15 mcg plus MF59 adjuvant
Study Arm 4, n=53	Seqirus H7N9 vaccine 15 mcg unadjuvanted	Seqirus H7N9 vaccine 15 mcg unadjuvanted

9.5.1 Efficacy/Immunogenicity and Safety Measurements Assessed and Flow Chart

Table 2: Schedule of Study Procedures – Vaccination Period

Study Visit Number	**V00**	**V01**	**V02****	**V03**	**V04**	**V05****	**V06**	**V07**
Study Day post 1st vaccination	**Screening (Optional) D -28 to -1**	**Enrollment Vac 1 D1**	**D4±1d**	**D8+2d**	**D22+7d**	***D25***	***D29***	***D43***
Study Day post 2nd vaccination					**Vac 2 D1**	**D4±1d**	**D8+2d**	**D22+7d**
Study Procedure/Evaluation								
Obtain Informed Consent∞	X	X¬						
Collect Demographic Information	X	X†*						
Review Eligibility Criteria	X	X†¬[1]			X†[1]			
Medical History@	X	X†¬	X	X	X†	X	X	X
Concomitant Medications	Xς	X†¬ς	Xς	Xς	X†ς	Xς	Xς	Xς
Vital Signs$ (Oral Temperature%, Pulse, and BP)	X	X†			X†[2]			
Height and Weight	X	X†*						
Physical Examination[3]	X	X†*		{X}	{X}†		{X}	{X}
Urine or Serum Pregnancy Test	X^	X†^			X†^			
Venous Blood Collection for ESR	X≠	X≠*						
Venous Blood Collection for Clinical Safety Laboratory Evaluations~		X†		X	X†		X	
Venous Blood Collection for Immunogenicity Assays		X†		X	X†Ψ		X	X
Serum Sample Collected for Future Research[4]		X†		X	X†		X	X
Enrollment in AdvantageEDC℠ and Randomization		X†						
Pre-Administration Reactogenicity Assessments		X†			X†			
Study Vaccination		X			X			

Table 2: Schedule of Study Procedures – Vaccination Period *(continued)*

Study Visit Number	**V00**	**V01**	**V02****	**V03**	**V04**	**V05****	**V06**	**V07**
Study Day post 1st vaccination	**Screening (Optional) D -28 to -1**	**Enrollment Vac 1 D1**	**D4±1d**	**D8+2d**	**D22+7d**	***D25***	***D29***	***D43***
Study Day post 2nd vaccination					**Vac 2 D1**	**D4±1d**	**D8+2d**	**D22+7d**
Study Procedure/Evaluation								
20-minute Evaluation After Study Vaccination		X			X			
Examine Study Vaccination Site		X		X	X		X	
Post-Administration Reactogenicity Assessments		X			X			
Distribute Memory Aid and Study-Related Materials		X			X			
Review Memory Aid			X	X		X	X	
AE/SAE Assessment		X[&]	X[&]	X[&]	X[&]	X[&]	X[&]	X

** Phone call assessment
∞ Prior to study procedures.
† Prior to study vaccination.
[1] Review results of clinical screening (ESR) or safety laboratory evaluations.
¬ Review/confirm information or activity in subjects previously consented and screened
@ Complete medical history will be obtained by interview of subjects at the first visit (either screening [optional] or on Day 1 prior to the first study vaccination) and interim medical history will be obtained by interview of subjects at subsequent visits.
ς Receipt of non-study influenza vaccines will be solicited through approximately 180 days after the last study vaccination, and reported in the eCRF.
* Not required if done at the optional screening visit
$ Vital signs assessed on Day 1 prior to the first study vaccination will be considered as baseline.
% Subjects must not eat or drink anything hot or cold, or smoke within 10 minutes prior to taking oral temperature.
[2] Vital signs are not required for subjects who are discontinued from receipt of the second study vaccination and are being followed for safety.
[3] At the screening (or baseline if not done at screening) visit, a physical examination will be performed on all subjects to include the following organs and organ systems: skin, head and neck, lungs, heart, liver, spleen, extremities, lymph nodes, and nervous system.
{} Targeted physical examination if indicated based on review of interim medical history.
^ Will be performed on all women of childbearing potential at screening (optional) and within 24 hours prior to each study vaccination and results must be negative and known prior to each study vaccination.
≠ To be performed locally by the site. The ESR value must be confirmed as <30 mm/hr prior to randomization and first study vaccination.
~ Includes WBC, Hgb, PLT, ALT, T. Bili, Cr
Ψ Subjects who do not receive the second study vaccination will continue with follow-up safety assessments (may be conducted by phone call) rather than in person continuing through approximately 12 months after their first study vaccination. These subjects will also be encouraged to provide a venous blood sample for anti-viral antibody assays at approximately 21 and 180 days after their first study vaccination
[4] For subjects who have consented to collection of serum for future use
& Inclusive of reactogenicity assessments performed on the day of each study vaccination through 7 days after each study vaccination.

Table 3: Schedule of Study Procedures - Follow-Up Period (Including early termination and unscheduled visits)

Study Visit Number	V08**	V09**	V10	V11**	Early Termination (if needed)	Unscheduled (if needed)
Study Day post first study vaccination	*D82*	*D142*	*D202*	*D387*		
Study Day post second study vaccination	**D61±7d**	**D121±14d**	**D181±14d**	**D366±14d**		
Study Procedure/Evaluation						
Medical History[@]			X		X	X (if indicated)
Concomitant Medications	X[ς]	X[ς]	X[ς]		X (if within 21 days after last study vaccination and receipt of any non-study influenza vaccine will be recorded if within 180 days after the 2nd study vaccination)	X (if prior to 21 days after last study vaccination and receipt of any non-study influenza vaccine will be recorded if within 180 days after the 2nd study)
Vital Signs (Oral Temperature[%], Pulse, and BP)					X (may be obtained if indicated)	X (may be obtained if indicated)
Physical Examination[3]			{X}		{X}	{X}
Venous Blood Collection for Clinical Safety Laboratory Evaluations~					X (if within 7 days after the last study vaccination)	X (if indicated)
Venous Blood Collection for Immunogenicity Assays			X		X (if within 21 days after last study vaccination)	X (if prior to 21 days after last study vaccination)
Serum Sample Collected for Future Research[4]			X		X(if within 21 days after last study vaccination	X(if prior to 21 days after last study vaccination

Table 3: Schedule of Study Procedures - Follow-Up Period (Including early termination and unscheduled visits) *(continued)*

Study Visit Number	V08**	V09**	V10	V11**	Early Termination (if needed)	Unscheduled (if needed)
Study Day post first study vaccination	*D82*	*D142*	*D202*	*D387*		
Study Day post second study vaccination	**D61±7d**	**D121±14d**	**D181±14d**	**D366±14d**		
Study Procedure/Evaluation						
Examine Study Vaccination Site					X (if within 7 days after last study vaccination)	X (if within 7 days after last study vaccination)
Post-Administration Reactogenicity Assessments					X (if within 7 days after last study vaccination)	X (if within 7 days after last study vaccination)
Review Memory Aid					X (if within 7 days after last study vaccination)	X (if within 7 days after last study vaccination)
AE/SAE Assessment	X[#]	X[#!]	X[#]	X[#]	X[#]	X[#]

** Phone call assessment

[@] Complete medical history will be obtained by interview of subjects at screening (optional) or on Day 1 prior to the first study vaccination and interim medical history will be obtained by interview of subjects at follow-up visits after the first study vaccination.

[ç] Receipt of non-study influenza vaccines will be solicited through approximately 180 days after the last study vaccination, and reported in the eCRF.

[%] Subjects must not eat or drink anything hot or cold, or smoke within 10 minutes prior to taking oral temperature.

{} Targeted physical examination if indicated based on review of interim medical history.

~ Includes WBC, Hgb, PLT, ALT, T. Bili, Cr

[Ψ] Subjects who do not receive the second study vaccination will continue with follow-up safety assessments (may be conducted by phone call) rather than in person continuing through approximately 12 months after their first study vaccination. These subjects will also be encouraged to provide a venous blood sample for anti-viral antibody assays at approximately 21 and 180 days after their first study vaccination

[4] For subjects who have consented to collection of serum for future use

[#] AEs will be limited to SAEs and MAAEs, including NOCMCs and PIMMCs if after 21 days after last study vaccination

9.7.1 Sample Size

Table 4: Power (%) to Detect Safety Events

Event Frequency	N = 53	N = 106	N = 318
≥10% Very Common	>99	>99	>99
≥1% Common	41	65	95
≥0.1% Uncommon	5	10	27
≥0.01% Rare	<1	1	3

Table 5: Precisions of Binomial Confidence Intervals

N	95% CI
53	36-64
106	40-60
318	44-56

Table 6: Minimum Detectable Difference in Proportion Responders with 80% Power

Assumed Proportion of subjects with titer ≥40 in comparator arm	Minimum Detectable Difference (N = 100)
0.40	0.20
0.50	0.29
0.60	0.19
0.70	0.17
0.80	0.14
0.90	0.09

Table 7: Lower Confidence Bound for Difference in Proportion of Responders Between Adjuvanted (N = 100) and Unadjuvanted (N = 50) Arms, 18-64 Years Stratum

Adjuvanted Study Arm	Unadjuvanted Study Arm	Difference	Lower Confidence Bound[a]
0.50	0.10	0.40	0.26
0.60	0.10	0.50	0.36
0.70	0.10	0.60	0.46
0.80	0.10	0.70	0.56
0.90	0.10	0.80	0.67

[a] Farrington-Manning confidence limits.

10.2 Protocol Deviations

Table 8: Distribution of Protocol Deviations by Category, Type, and Study arm - All Enrolled Subjects

Category	Deviation Type	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)		Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)		Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)		Study Arm 4 15 mcg A/H7N9 (N=X)		All Subjects (N=X)	
		# of Subj.	# of Dev.	# of Subj.	# of Dev.	# of Subj.	# of Dev.	# of Subj.	# of Dev.	# of Subj.	# of Dev.
Eligibility/enrollment	Any type										
	Did not meet inclusion criterion	x	x	x	x	x	x	x	x	x	x
	Met exclusion criterion										
	ICF not signed prior to study procedures										
	Other										
Treatment administration schedule	Any type										
	Out of window visit										
	Missed visit/visit not conducted										
	Missed treatment administration										
	Delayed treatment administration										
	Other										
Follow-up visit schedule	Any type										
	Out of window visit										
	Missed visit/visit not conducted										
	Other										
Protocol procedure/assessment	Any type										
	Incorrect version of ICF signed										
	Blood not collected										
	Too few aliquots obtained										
	Specimen result not obtained										

Table 8: Distribution of Protocol Deviations by Category, Type, and Study arm - All Enrolled Subjects *(continued)*

Category	Deviation Type	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)		Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)		Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)		Study Arm 4 15 mcg A/H7N9 (N=X)		All Subjects (N=X)	
		# of Subj.	# of Dev.	# of Subj.	# of Dev.	# of Subj.	# of Dev.	# of Subj.	# of Dev.	# of Subj.	# of Dev.
	Required procedure not conducted										
	Required procedure done incorrectly										
	Study product temperature excursion										
	Specimen temperature excursion										
	Other										
Treatment administration	Any type										
	Required procedure done incorrectly										
	Study product temperature excursion										
	Other										
Blinding policy/procedure	Any type										
	Treatment unblinded										
	Other										
Note: N = Number of subjects enrolled											

12.2.2 Displays of Adverse Events

Table 9: Solicited Adverse Event Grading Scale – Local

Local (Injection Site) Reactogenicity Grading			
Local (Injection Site) Reaction	**Mild (Grade 1)**	**Moderate (Grade 2)**	**Severe (Grade 3)**
Pain – experienced without touching the injection site (spontaneous discomfort)	Subject is aware of pain, but it does not interfere with daily activity, **and** no pain medication is taken	Subject is aware of pain; there is interference with daily activity **or** it requires repeated use of a non-narcotic pain reliever for >24 hours	Subject is aware of pain, **and** it prevents daily activity or requires any use of a narcotic pain reliever
Tenderness – hurts only when injection site is touched or the arm is moved	The area immediately surrounding the injection site hurts only when touched or with arm motion, **and** it does **not** interfere with daily activity	The area immediately surrounding the injection site hurts when touched or with arm motion, **and** it interferes with daily activity	The area immediately surrounding the injection site hurts when touched or with arm motion, **and** it prevents daily activity
Pruritus (Itching)	Does not interfere with daily activity	Interferes with daily activity	Prevents daily activity
Ecchymosis (Bruising)*	Does not interfere with daily activity	Interferes with daily activity	Prevents daily activity
Erythema (Redness)*	Does not interfere with daily activity	Interferes with daily activity	Prevents daily activity
Induration (Hardness)/Swelling*	Does not interfere with daily activity	Interferes with daily activity	Prevents daily activity
Local (Injection Site) Reactogenicity Measurements			
Local (Injection Site) Reaction	**Small (Grade 1)**	**Medium (Grade 2)**	**Large (Grade 3)**
Ecchymosis (Bruising)*	<20 mm	20 mm – 50 mm	>50 mm
Erythema (Redness)*	<20 mm	20 mm – 50 mm	>50 mm
Induration (Hardness)/Swelling*	<20 mm	20 mm – 50 mm	>50 mm

Table 10: Solicited Adverse Event Grading Scale - Systemic

Subjective Systemic Reactogenicity Grading			
Systemic (Subjective)	**Mild (Grade 1)**	**Moderate (Grade 2)**	**Severe (Grade 3)**
Feverishness (Chills/Shivering/Sweating)	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Fatigue (Tiredness)	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Malaise (General Unwell Feeling)	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Myalgia (Body Aches/Muscular Pain)*	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Arthralgia (Joint Pain)*	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Headache	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Nausea	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Quantitative Systemic Reactogenicity Grading			
Systemic (Quantitative)	**Mild (Grade 1)**	**Moderate (Grade 2)**	**Severe (Grade 3)**
Fever[#] - oral	38.0°C – 38.4°C 100.4°F – 101.1°F	38.5°C – 38.9°C 101.2°F – 102.0°F	>38.9°C >102.0°F

* Not at injection site.

[#] Oral temperature assessed on Day 1 prior to the first study vaccination will be considered as baseline. A fever can be considered not related to the study product if an alternative etiology can be documented.

Table 11: Vital Signs Adverse Event Grading Scale

For all individuals, pulse and blood pressure[#] will be graded as follows:			
Physiologic Parameter	**Mild (Grade 1)**	**Moderate (Grade 2)**	**Severe (Grade 3)**
Bradycardia - beats per minute	45 – 46	40 – 44	<40
Tachycardia - beats per minute	101 – 130	131 – 155	>155
Hypotension (systolic) mmHg	80 – 84	75 – 79	<75
Hypotension (diastolic) mmHg	50 – 54	45 – 49	<45
Hypertension (systolic) mmHg	151 – 155	156 – 160	>160
Hypertension (diastolic) mmHg	96 – 100	101 – 105	>105
[#] Pulse and blood pressure assessed on Day 1 prior to the first study vaccination will be considered as baseline.			

12.4.1 Individual Laboratory Measurements and Abnormal Laboratory Values

Table 12: Laboratory Adverse Event Grading Scale

Hematology	**Mild (Grade 1)**	**Moderate (Grade 2)**	**Severe (Grade 3)**
WBC $10^3/\mu L$ (Decrease)	2.5 – 3.9	1.5 – 2.4	<1.5
WBC $10^3/\mu L$ (Increase)	10.6 – 15.0	15.1 – 20.0	>20.0
Hgb g/dL (Decrease) (Female)	10.1 – 11.4	8.5 – 10	<8.5
Hgb g/dL (Decrease) (Male)	11.0 – 12.4	9.5 – 10.9	<9.5
Platelets $10^3/\mu L$ (Decrease)	125 – 139	100 – 124	<100
Platelets $10^3/\mu L$ (Increase)	416 – 550	551– 750	>750
Chemistry	**Mild (Grade 1)**	**Moderate (Grade 2)**	**Severe (Grade 3)**
ALT IU/L (Increase) (Female)	44 – 100	101 – 200	>200
ALT IU/L (Increase) (Male)	61 – 138	139 – 275	>275
Total Bilirubin mg/dL (Increase) – when accompanied by any increase in ALT	1.30 – 1.59	1.60 – 1.80	>1.80
Total Bilirubin mg/dL (Increase) – when ALT is normal	1.30 – 1.89	1.90 – 2.40	>2.40
Creatinine mg/dL (Increase) (Female)	1.1 – 1.7	1.8 – 2.0	>2.0
Creatinine mg/dL (Increase) (Male)	1.4 – 1.7	1.8 – 2.0	>2.0

14.1 Description of Study Subjects

14.1.1 Disposition of Subjects

Table 13: Ineligibility Summary of Screen Failures

Inclusion/Exclusion Category	Inclusion/Exclusion Criterion	n[a]	%[b]
Inclusion and Exclusion	Number of subjects failing any eligibility criterion	x	x
Inclusion	Any inclusion criterion	x	x
	[inclusion criterion 1]	x	x
	[inclusion criterion 2]	x	x
	[inclusion criterion 3]	x	x
Exclusion	Any exclusion criterion	x	x
	[exclusion criterion 1]	x	x
	[exclusion criterion 2]	x	x
	[exclusion criterion 3]	x	x

[a] More than one criterion may be marked per subject.

[b] Denominator for percentages is the total number of screen failures.

Table 14: Analysis Populations by Study Arm, All Enrolled Subjects

Analysis Populations	Reason Subjects Excluded	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)		Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)		Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)		Study Arm 4 15 mcg A/H7N9 (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%	n	%	n	%
Safety Population	Any Reason	x	xx	x	xx	x	xx	x	xx	x	xx
	Study Vaccination 1 Not Received										
Modified Intent to Treat	Any Reason										
	Study Vaccination 1 Not Received										
	No Baseline Results Available										
	No Post-Vaccination Results Available										
Per-Protocol, All Visits	Found to be Ineligible After Baseline										
Per-Protocol, Day 8	Any Reason										
	Study Vaccination 1 Not Received										
	No Baseline Results Available										
	Ineligible at Baseline										
	Receipt of Non-Study Vaccination										
	Receipt of Immunosuppressive Medication										
	No Day 9 Result Reported by Lab										
	Lost to Follow-up Before Day 9										
	Day 9 Visit Out of Window										
Per-Protocol, Day 22	Any Reason										
	Study Vaccination 1 Not Received										
	No Baseline Results Available										
	Ineligible at Baseline										

Table 14: Analysis Populations by Study arm* *(continued)*

Analysis Populations	Reason Subjects Excluded	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)		Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)		Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)		Study Arm 4 15 mcg A/H7N9 (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%	n	%	n	%
	Receipt of Non-Study Vaccination										
	Receipt of Immunosuppressive Medication										
	No Day 22 Result Reported by Lab										
	Lost to Follow-up Before Day 22										
	Day 22 Visit Out of Window										
Per-Protocol, Day 29	Any Reason										
	Study Vaccination 1 Not Received										
	No Baseline Results Available										
	Ineligible at Baseline										
	Study Vaccination 2 Not Received										
	Study Vaccination 2 Out of Window										
	Receipt of Non-Study Vaccination										
	Receipt of Immunosuppressive Medication										
	No Day 29 Result Reported by Lab										
	Lost to Follow-up Before Day 29										
	Day 29 Visit Out of Window										
Per-Protocol, Day 43	Any Reason										
	Study Vaccination 1 Not Received										
	No Baseline Results Available										
	Ineligible at Baseline										
	Study Vaccination 2 Not Received										
	Study Vaccination 2 Out of Window										

Table 14: Analysis Populations by Study arm* *(continued)*

Analysis Populations	Reason Subjects Excluded	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)		Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)		Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)		Study Arm 4 15 mcg A/H7N9 (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%	n	%	n	%
	Receipt of Non-Study Vaccination										
	Receipt of Immunosuppressive Medication										
	No Day 43 Result Reported by Lab										
	Lost to Follow-up Before Day 43										
	Day 43 Visit Out of Window										
Per-Protocol, Day 202	Any Reason										
	Study Vaccination 1 Not Received										
	No Baseline Results Available										
	Ineligible at Baseline										
	Study Vaccination 2 Not Received										
	Study Vaccination 2 Out of Window										
	Receipt of Non-Study Vaccination										
	Receipt of Immunosuppressive Medication										
	No Day 202 Result Reported by Lab										
	Lost to Follow-up Before Day 202										
	Day 202 Visit Out of Window										
Note: N = Number of subjects randomized.											

Table 15: Subject Disposition by Study Arm - All Randomized Subjects

Subject Disposition	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)		Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)		Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)		Study Arm 4 15 mcg A/H7N9 (N=X)		All Subjects (N=X)	
	n	%	n	%	n	%	n	%	n	%
Screened	x	--	x	--	x	--	x	--	x	--
Enrolled/Randomized	x	100	x	100	x	100	x	100	x	100
Received Vaccination 1	x	xx	x	xx	x	xx	x	xx	x	xx
Received Vaccination 2	x	xx	x	xx	x	xx	x	xx	x	xx
Received All Scheduled Vaccinations [a]	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Blood Draw for Primary Immunogenicity Analysis (Day 43)	x	xx	x	xx	x	xx	x	xx	x	xx
Included in Per-Protocol Primary Immunogenicity Analysis (Day 43)[b]	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Primary Follow-up (Day 43)[a]	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Final Study Visit (Day 387)	x	xx	x	xx	x	xx	x	xx	x	xx

Note: N = Number of subjects randomized

[a] Refer to Early Terminations or Discontinued Subjects Listing for reasons subjects discontinued from study vaccinations or terminated early.

[b] Refer to Subjects Excluded from Analysis Populations Listing for reasons subjects are excluded from the Per-Protocol population.

Table 16: Dates of First Study Vaccination by Site and Study Arm - Safety Population

Dates of Dosing	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)	Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)	Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)	Study Arm 4 15 mcg A/H7N9 (N=X)	All Subjects (N=X)
[Site 1]					
Total (Entire period of enrollment)	x	x	x	x	x
DDMMMYYYY-DDMMMYYYY					
….					
[Site 2]					
Total (Entire period of enrollment)	x	x	x	x	x
DDMMMYYYY-DDMMMYYYY					
….					
[Repeat for all sites]					
Note: N = Number of subjects in the Safety population.enrolled.					

Table with similar format:

Table 17: Dates of Second Study Vaccination by Site, Study Arm, and Age Stratum - Safety Population

14.1.2 Demographic Data

Table 18: Summary of Categorical Demographic and Baseline Characteristics by Site - All Enrolled Subjects

Variable	Characteristic	[Site 1] (N=X)		[Site 2] (N=X)		[Site 3] (N=X)		[Site 4] (N=X)		[Site 5] (N=X)		[Site 6] (N=X)		[Site 7] (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Sex	Male	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Female																
BMI	< 30																
	≥ 30																
Ethnicity	Not Hispanic or Latino	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	xx	xx
	Hispanic or Latino																
	Not Reported																
	Unknown																
Race	American Indian or Alaska Native	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	xx	xx
	Asian																
	Native Hawaiian or Other Pacific Islander																
	Black or African American																
	White																
	Multi-Racial																
	Unknown																
Prior Seasonal Influenza Vaccination	2016-2017 only																
	2017-2018 only																
	2018-2019 only																
	None																
	Unknown																

Note: N = Number of subjects enrolled

Table 19: Summary of Continuous Demographic and Baseline Characteristics by Site - All Enrolled Subjects

Variable	Statistic	[Site 1] (N=X)	[Site 2] (N=X)	[Site 3] (N=X)	[Site 4] (N=X)	[Site 5] (N=X)	[Site 6] (N=X)	[Site 7] (N=X)	All Subjects (N=X)
Age	Mean	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Median	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum	x	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x	x
BMI	Mean	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Median	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum	x	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x	x
Note: N = Number of subjects enrolled									

Table 20: Summary of Categorical Demographic and Baseline Characteristics by Study Arm - All Enrolled Subjects

Variable	Characteristic	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)		Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)		Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)		Study Arm 4 15 mcg A/H7N9 (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%	n	%	n	%
Sex	Male										
	Female										
BMI	< 30										
	≥ 30										
Ethnicity	Not Hispanic or Latino										
	Hispanic or Latino										
	Not Reported										
	Unknown										
Race	American Indian or Alaska Native										
	Asian										
	Native Hawaiian or Other Pacific Islander										
	Black or African American										
	White										
	Multi-Racial										
	Unknown										
Prior Seasonal Influenza Vaccination	2016-2017 only										
	2017-2018 only										
	2018-2019 only										
	Neither										
	Unknown										
Note: N = Number of subjects enrolled											

Table 21: Summary of Continuous Baseline Characteristics by Study Arm - All Enrolled Subjects

Variable	Statistic	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)	Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)	Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)	Study Arm 4 15 mcg A/H7N9 (N=X)	All Subjects (N=X)
Age	Mean	x.x	x.x	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x	x.x	x.x
	Median	x	x	x	x	x
	Minimum	x	x	x	x	x
	Maximum	x	x	x	x	x
BMI	Mean	x.x	x.x	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x	x.x	x.x
	Median	x	x	x	x	x
	Minimum	x	x	x	x	x
	Maximum	x	x	x	x	x
Note: N = Number of subjects enrolled.						

14.1.3 Summary of Prior or Concurrent Medical Conditions

Table 22: Summary of Subjects with Prior or Concurrent Medical Conditions by MedDRA System Organ Class and Study Arm - Safety Population

MedDRA System Organ Class	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)		Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)		Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)		Study Arm 4 15 mcg A/H7N9 (N=X)		All Subjects (N=X)	
	n	%	n	%	n	%	n	%	n	%
Any SOC	x	xx	x	xx	x	xx	x	xx	x	xx
[SOC 1]	x	xx	x	xx	x	xx	x	xx	x	xx
[SOC 2]	x	xx	x	xx	x	xx	x	xx	x	xx
…										
Note: N=Number of subjects in the Safety population; n = Number of subjects reporting medical history within the specified SOC. A subject is only counted once per SOC.										

14.2 Immunogenicity Tables

14.2.1 Immune Response Against 2017 A/H7N9

Table 23: Summaries of Hemagglutination Inhibition Antibody Against A/Hong Kong/125/2017 (H7N9) by Study Day and Study Arm - Modified Intent-to-Treat Population*

Time Point	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)	Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)	Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)	Study Arm 4 15 mcg A/H7N9 (N=X)
Day 1 (Pre-Vaccination 1)				
n	x	x	x	x
GMT (95% CI)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)
Titer ≥ 1:40 - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
7 Days Post Vaccination 1				
n	x	x	x	x
GMT (95% CI)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)
Seroconversion - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Titer ≥ 1:40 - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
21 Days Post Vaccination 1				
n	x	x	x	x
GMT (95% CI)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)
Seroconversion - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Titer ≥ 1:40 - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
7 Days Post Vaccination 2				
n	x	x	x	x
GMT (95% CI)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)
Seroconversion - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Titer ≥ 1:40 - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)

Table 23: Summaries of Hemagglutination Inhibition Antibody Against 2017 A/H7N9 by Study Day and Study arm, Modified Intent-to-Treat Population *(continued)*

Time Point	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)	Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)	Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)	Study Arm 4 15 mcg A/H7N9 (N=X)
21 Days Post Vaccination 2				
n	x	x	x	x
GMT (95% CI)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)
Seroconversion - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Titer ≥ 1:40 - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
180 Days Post Vaccination 2				
n	x	x	x	x
GMT (95% CI)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)
Seroconversion - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Titer ≥ 1:40 - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)

Note: N=number of subjects in the Modified Intent-to-Treat population.; n = Number of subjects with available results.
GMT = Geometric Mean Titer; CI = Confidence Interval.
[a]95% CIs calculated using Clopper-Pearson exact methods.

Tables with similar format:

Table 24: Summaries of Hemagglutination Inhibition Antibody Against A/Hong Kong/125/2017 (H7N9) by Study Day and Study Arm - Per-Protocol Population*

Table 25: Summaries of Neutralizing Antibody Against A/Hong Kong/125/2017 (H7N9) by Study Day and Study Arm - Modified Intent-to-Treat Population*

Table 26: Summaries of Neutralizing Antibody Against A/Hong Kong/125/2017 (H7N9) by Study Day and Study Arm - Per-Protocol Population*

Table 27: Summary of Hemagglutination Inhibition Antibody Against A/Hong Kong/125/2017 (H7N9) by Study Arm and Age Categories at 21 Days Post Second Vaccination - Per-Protocol Population

	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)	**Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)**	**Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)**	**Study Arm 4 15 mcg A/H7N9 (N=X)**
Age 19-34 years				
n	x	x	x	x
GMT (95% CI)	xxx.x(xxx.x,xxx.x)	xxx.x(xxx.x,xxx.x)	xxx.x(xxx.x,xxx.x)	xxx.x(xxx.x,xxx.x)
Seroconversion - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Titer ≥ 1:40 - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Age 35-49 years				
n	x	x	x	x
GMT (95% CI)	xxx.x(xxx.x,xxx.x)	xxx.x(xxx.x,xxx.x)	xxx.x(xxx.x,xxx.x)	xxx.x(xxx.x,xxx.x)
Seroconversion - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Titer ≥ 1:40 - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Age 50-64 years				
n	x	x	x	x
GMT (95% CI)	xxx.x(xxx.x,xxx.x)	xxx.x(xxx.x,xxx.x)	xxx.x(xxx.x,xxx.x)	xxx.x(xxx.x,xxx.x)
Seroconversion - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Titer ≥ 1:40 - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)

Note: N=number of subjects in the Modified Intent-to-Treat population.; n = Number of subjects with available results.
GMT = Geometric Mean Titer; CI = Confidence Interval.
[a]95% CIs calculated using Clopper-Pearson exact methods.

Tables with similar format:

Table 28: Summary of Hemagglutination Inhibition Antibody Against A/Hong Kong/125/2017 (H7N9) by Study Arm and Age Categories at 180 Days Post Second Vaccination - Per-Protocol Population

Table 29: Summary of Neutralizing Antibody Against A/Hong Kong/125/2017 (H7N9) by Study Arm and Age Categories at 21 Days Post Second Vaccination - Per-Protocol Population

Table 30: Summary of Neutralizing Antibody Against A/Hong Kong/125/2017 (H7N9) by Study Arm and Age Categories at 180 Days Post Second Vaccination - Per-Protocol Population

Table 31: Summary of Hemagglutination Inhibition Antibody Against 2017 A/H7N9 by Study Arm and Sex at 21 Days Post Second Vaccination - Per-Protocol Population

	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)	Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)	Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)	Study Arm 4 15 mcg A/H7N9 (N=X)
Female				
n	x	x	x	x
GMT (95% CI)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)
Seroconversion - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Titer ≥ 1:40 - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Male				
n	x	x	x	x
GMT (95% CI)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)
Seroconversion - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Titer ≥ 1:40 - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)

Note: N = Number of subjects in the Per-Protocol population; n = Number of subjects with available results.
GMT = Geometric Mean Titer; CI = Confidence Interval.
[a] 95% CIs calculated using Clopper-Pearson exact methods.

Tables with similar format:

Table 32: Summary of Hemagglutination Inhibition Antibody Against 2017 A/H7N9 by Study Arm and Sex at 180 Days Post Second Vaccination - Per-Protocol Population

Table 33: Summary of Neutralizing Antibody Against 2017 A/H7N9 by Study Arm and Sex at 21 Days Post Second Vaccination - Per-Protocol Population

Table 34: Summary of Neutralizing Antibody Against 2017 A/H7N9 by Study Arm and Sex at 180 Days Post Second Vaccination - Per-Protocol Population

Table 35: Summary of Hemagglutination Inhibition Antibody Against 2017 A/H7N9 by Study Arm and BMI at 21 Days Post Second Vaccination - Per-Protocol Population

	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)	Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)	Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)	Study Arm 4 15 mcg A/H7N9 (N=X)
BMI < 30				
n	x	x	x	x
GMT (95% CI)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)
Seroconversion - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Titer ≥ 1:40 - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
BMI ≥ 30				
n	x	x	x	x
GMT (95% CI)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)
Seroconversion - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Titer ≥ 1:40 - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)

Note: N = Number of subjects in the Per-Protocol population; n = Number of subjects with available results.
GMT = Geometric Mean Titer; CI = Confidence Interval.
[a] 95% CIs calculated using Clopper-Pearson exact methods.

Tables with similar format:

Table 36: Summary of Hemagglutination Inhibition Antibody Against 2017 A/H7N9 by Study Arm and BMI at 180 Days Post Second Vaccination - Per-Protocol Population

Table 37: Summary of Neutralizing Antibody Against 2017 A/H7N9 by Study Arm and BMI at 21 Days Post Second Vaccination - Per-Protocol Population

Table 38: Summary of Neutralizing Antibody Against 2017 A/H7N9 by Study Arm and BMI at 180 Days Post Second Vaccination - Per-Protocol Population

Table 39: Summary of Hemagglutination Inhibition Antibody Against A/Hong Kong/125/2017 (H7N9) by Study Arm and Prior Seasonal Influenza Vaccination at 21 Days Post Second Vaccination - Per-Protocol Population

	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)	Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)	Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)	Study Arm 4 15 mcg A/H7N9 (N=X)
Did Not Receive 2017-2018 or 2018-2019 Seasonal Influenza Vaccination				
n	x	x	x	x
GMT (95% CI)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)
Seroconversion - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Titer ≥ 1:40 - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Received 2017-2018 or 2018-2019 Seasonal Influenza Vaccination				
n	x	x	x	x
GMT (95% CI)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)
Seroconversion - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Titer ≥ 1:40 - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)

Note: N = Number of subjects in the Per-Protocol population; n = Number of subjects with available results.

GMT = Geometric Mean Titer; CI = Confidence Interval.

[a] 95% CIs calculated using Clopper-Pearson exact methods.

Tables with similar format:

Table 40: Summary of Hemagglutination Inhibition Antibody Against A/Hong Kong/125/2017 (H7N9) by Study Arm, Age Stratum and Prior Seasonal Influenza Vaccination at 180 Days Post Second Vaccination - Per-Protocol Population

Table 41: Summary of Neutralizing Antibody Against A/Hong Kong/125/2017 (H7N9) by Study Arm, Age Stratum and Prior Seasonal Influenza Vaccination at 21 Days Post Second Vaccination - Per-Protocol Population

Table 42: Summary of Neutralizing Antibody Against A/Hong Kong/125/2017 (H7N9) by Study Arm, Age Stratum and Prior Seasonal Influenza Vaccination at 180 Days Post Second Vaccination - Per-Protocol Population

Table 43: Logistic Regression Model to Evaluate the Relationship of HA Antigen Dose and MF59 Adjuvant with HAI Seroconversion Against A/Hong Kong/125/2017 (H7N9) at 21 Days Post Second Study Vaccination - Per-Protocol Population

Model Parameter	Parameter Estimate	SE	p-value	Odds Ratio	95%CI
Intercept	xxx.x	xxx.x	x.xxx	-	-
Study Arm					
15 mcg without MF59 adjuvant (reference)	-	-	-	-	-
3.75 mcg with MF59 adjuvant	xxx.x	xxx.x	x.xxx	xx.x	xx.x-xx.x
7.5 mcg with MF59 adjuvant	xxx.x	xxx.x	x.xxx	xx.x	xx.x-xx.x
15 mcg MF59 adjuvant	xxx.x	xxx.x	x.xxx	xx.x	xx.x-xx.x
Note: N = Number of subjects with results available at 21 days post second vaccination in the Per-Protocol population. XX subjects missing covariate data were excluded from this analysis.					

Tables with similar format:

Table 44: Logistic Regression Model to Evaluate the Relationship of HA Antigen Dose and MF59 Adjuvant with Neut Seroconversion Against A/Hong Kong/125/2017 (H7N9) at 21 Days Post Second Study Vaccination - Per-Protocol Population

Table 45: Logistic Regression Model to Evaluate the Relationship of HA Antigen Dose and MF59 Adjuvant with HAI Seroconversion Against A/Hong Kong/125/2017 (H7N9) at 180 Days Post Second Study Vaccination - Per-Protocol Population

Table 46: Logistic Regression Model to Evaluate the Relationship of HA Antigen Dose and MF59 Adjuvant with Neut Seroconversion Against A/Hong Kong/125/2017 (H7N9) at 180 Days Post Second Study Vaccination - Per-Protocol Population

Table 47: Logistic Regression Model to Evaluate the Relationship of HA Antigen Dose and MF59 Adjuvant with HAI Seroconversion Against A/Hong Kong/125/2017 (H7N9) at 21 Days Post Second Study Vaccination, Adjusted for Baseline Covariates - Per-Protocol Population

Model Parameter	Parameter Estimate	SE	p-value	Odds Ratio	95%CI
Intercept	xxx.x	xxx.x	x.xxx	-	-
Study Arm					
15 mcg without MF59 Adjuvant (reference)	-	-	-	-	-
3.75 mcg with MF59 Adjuvant	xxx.x	xxx.x	x.xxx	xx.x	xx.x-xx.x
7.5 mcg with MF59 Adjuvant	xxx.x	xxx.x	x.xxx	xx.x	xx.x-xx.x
15 mcg with MF59 Adjuvant	xxx.x	xxx.x	x.xxx	xx.x	xx.x-xx.x
Age					
19-34 (reference)	-	-	-	-	-
35-49	xxx.x	xxx.x	x.xxx	xx.x	xx.x-xx.x
50-64	xxx.x	xxx.x	x.xxx	xx.x	xx.x-xx.x
Sex					
Female (reference)	-	-	-	-	-
Male	xxx.x	xxx.x	x.xxx	xx.x	xx.x-xx.x
BMI					
<30 (reference)	-	-	-	-	-
≥30	xxx.x	xxx.x	x.xxx	xx.x	xx.x-xx.x
Prior Receipt of Influenza Vaccine					
Did Not Receive 2017-2018 or 2018-2019 Seasonal Influenza Vaccine (reference)	-	-	-	-	-
Received 2017-2018 or 2018-2019 Seasonal Influenza Vaccine	xxx.x	xxx.x	x.xxx	xx.x	xx.x-xx.x
Note: N = Number of subjects with results available at 21 days post second vaccination in the Per-Protocol population. XX subjects missing covariate data were excluded from this analysis.					

Tables with similar format:

Table 48: Logistic Regression Model to Evaluate the Relationship of HA Antigen Dose and MF59 Adjuvant with Neut Seroconversion Against A/Hong Kong/125/2017 (H7N9) at 21 Days Post Second Study Vaccination, Adjusted for Baseline Covariates - Per-Protocol Population

Table 49: Logistic Regression Model to Evaluate the Relationship of HA Antigen Dose and MF59 Adjuvant with HAI Seroconversion Against A/Hong Kong/125/2017 (H7N9) at 180 Days Post Second Study Vaccination, Adjusted for Baseline Covariates - Per-Protocol Population

Table 50: Logistic Regression Model to Evaluate the Relationship of HA Antigen Dose and MF59 Adjuvant with Neut Seroconversion Against A/Hong Kong/125/2017 (H7N9) at 180 Days Post Second Study Vaccination, Adjusted for Baseline Covariates - Per-Protocol Population

Table 51: Multiple Linear Regression Model to Evaluate the Relationship of HA Antigen Dose and MF59 Adjuvant with Log-Adjusted HAI Titer at 21 Days Post Second Study Vaccination - Per-Protocol Population

Model Parameter	Parameter Estimate	SE	95%CI	p-value
Intercept	xxx.x	xxx.x	-	x.xxx
Study Arm				
15 mcg without MF59 adjuvant (reference)	-	-	-	-
3.75 mcg with MF59 adjuvant	xxx.x	xxx.x	xx.x-xx.x	x.xxx
7.5 mcg with MF59 adjuvant	xxx.x	xxx.x	xx.x-xx.x	x.xxx
15 mcg with MF59 adjuvant	xxx.x	xxx.x	xx.x-xx.x	x.xxx
Note: N = Number of subjects with results available at 21 days post second vaccination in the Per-Protocol population. XX subjects missing covariate data were excluded from this analysis				

Tables with similar format:

Table 52: Multiple Linear Regression Model to Evaluate the Relationship of HA Antigen Dose and MF59 Adjuvant with Log-Adjusted Neut Titer at 21 Days Post Second Study Vaccination - Per-Protocol Population

Table 53: Multiple Linear Regression Model to Evaluate the Relationship of HA Antigen Dose and MF59 Adjuvant with Log-Adjusted HAI Titer at 180 Days Post Second Study Vaccination - Per-Protocol Population

Table 54: Multiple Linear Regression Model to Evaluate the Relationship of HA Antigen Dose and MF59 Adjuvant with Log-Adjusted Neut Titer at 180 Days Post Second Study Vaccination - Per-Protocol Population

Table 55: Multiple Linear Regression Model to Evaluate the Relationship of HA Antigen Dose and MF59 Adjuvant with Log-Adjusted HAI Titer at 21 Days Post Second Study Vaccination, Adjusted for Baseline Covariates - Per-Protocol Population

Model Parameter	Parameter Estimate	SE	95%CI	p-value
Intercept	xxx.x	xxx.x	-	x.xxx
Study Arm				
15 mcg without MF59 adjuvant (reference)	-	-	-	-
3.75 mcg with MF59 adjuvant	xxx.x	xxx.x	xx.x-xx.x	x.xxx
7.5 mcg with MF59 adjuvant	xxx.x	xxx.x	xx.x-xx.x	x.xxx
15 mcg with MF59 adjuvant	xxx.x	xxx.x	xx.x-xx.x	x.xxx
Age				
19-34 (reference)	-	-	-	-
35-49	xxx.x	xxx.x	xx.x-xx.x	x.xxx
50-64	xxx.x	xxx.x	xx.x-xx.x	x.xxx
Sex				
Female (reference)	-	-	-	-
Male	xxx.x	xxx.x	xx.x-xx.x	x.xxx
BMI				
<30 (reference)	-	-	-	-
≥30	xxx.x	xxx.x	xx.x-xx.x	x.xxx
Prior Receipt of Influenza Vaccine				
Did Not Receive 2017-2018 or 2018-2019 Seasonal Influenza Vaccine (reference)	-	-	-	-
Received 2017-2018 or 2018-2019 Seasonal Influenza Vaccine	xxx.x	xxx.x	xx.x-xx.x	x.xxx
Note: N = Number of subjects with results available at 21 days post second vaccination in the Per-Protocol population. XX subjects missing covariate data were excluded from this analysis				

Tables with similar format:

Table 56: Multiple Linear Regression Model to Evaluate the Relationship of HA Antigen Dose and MF59 Adjuvant with Log-Adjusted Neut Titer at 21 Days Post Second Study Vaccination, Adjusted for Baseline Covariates, Per-Protocol Population

Table 57: Multiple Linear Regression Model to Evaluate the Relationship of HA Antigen Dose and MF59 Adjuvant with Log-Adjusted HAI Titer at 180 Days Post Second Study Vaccination, Adjusted for Baseline Covariates, Per-Protocol Population

Table 58: Multiple Linear Regression Model to Evaluate the Relationship of HA Antigen Dose and MF59 Adjuvant with Log-Adjusted Neut Titer at 180 Days Post Second Study Vaccination, Adjusted for Baseline Covariates, Per-Protocol Population

Table 59: Summaries of Hemagglutination Inhibition Antibody Against A/Shanghai/2/2013 (H7N9) by Study Day and Study Arm, Per-Protocol Population*

Time Point	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)	Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)	Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)	Study Arm 4 15 mcg A/H7N9 (N=X)
Day 1 (Pre Vaccination 1)				
n	x	x	x	x
GMT (95% CI)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)
Titer ≥ 1:40 - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Day 21 Post Vaccination 2				
n	x	x	x	x
GMT (95% CI)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x)
Seroconversion - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Titer ≥ 1:40 - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Day 180 Post Vaccination 2				
n	x	x	x	x
GMT (95% CI)	xxx.x (xxx.x,xxx.x) xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x) xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x) xxx.x (xxx.x,xxx.x)	xxx.x (xxx.x,xxx.x) xxx.x (xxx.x,xxx.x)
Seroconversion - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Titer ≥ 1:40 - % (95% CI[a])	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)

N = Number of subjects in the Per-Protocol Population; n = number of subjects with available results;
GMT = Geometric Mean Titer; CI = Confidence Interval
[a]95% CIs calculated using Clopper-Pearson exact methods.

Tables with similar format:

Table 60: Summaries of Hemagglutination Inhibition Antibody Against A/Guangdong/17SF003/2016 (H7N9) by Study Day and Study Arm, Per-Protocol Population*

Table 61: Summaries of Neutralizing Antibody Against A/Shanghai/2/2013 (H7N9) by Study Day and Study Arm, Per-Protocol Population*

Table 62: Summaries of Neutralizing Antibody Against A/Guangdong/17SF003/2016 (H7N9) by Study Day and Study Arm, Per-Protocol Population*

14.3 Safety Data

14.3.1 Displays of Adverse Events

Table 63: Overall Summary of Adverse Events – Safety Population*

	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)		Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)		Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)		Study Arm 4 15 mcg A/H7N9 (N=X)		All Subjects (N=X)	
Subjects[a] with	n	%	n	%	n	%	n	%	n	%
At least one injection site solicited adverse event	x	x	x	x	x	x	x	x	x	x
At least one systemic solicited adverse event	x	x	x	x	x	x	x	x	x	x
At least one unsolicited adverse event	x	x	x	x	x	x	x	x	x	x
At least one related unsolicited adverse event	x	x	x	x	x	x	x	x	x	x
Mild (Grade 1)	x	x	x	x	x	x	x	x	x	x
Moderate (Grade 2)	x	x	x	x	x	x	x	x	x	x
Severe (Grade 3)	x	x	x	x	x	x	x	x	x	x
At least one severe (Grade 3) unsolicited adverse event	x	x	x	x	x	x	x	x	x	x
Related	x	x	x	x	x	x	x	x	X	x
Unrelated	x	x	x	x	x	x	x	x	X	x
At least one serious adverse event[b]	x	x	x	x	x	x	x	x	x	x
At least one related, serious adverse event	x	x	x	x	x	x	x	x	x	x
At least one adverse event leading to early termination[c]	x	x	x	x	x	x	x	x	x	x
At least one medically attended adverse event	x	x	x	x	x	x	x	x	x	x

Table 63: Overall Summary of Adverse Events *(continued)*

	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)		**Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)**		**Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)**		**Study Arm 4 15 mcg A/H7N9 (N=X)**		**All Subjects (N=X)**	
Subjects[a] with	n	%	n	%	n	%	n	%	n	%
At least one new onset chronic medical condition	x	x	x	x	x	x	x	x	x	x
At least one potentially immune mediated medical condition	x	x	x	x	x	x	x	x	x	x

Note: N = Number of subjects in the Safety population.
[a] Subjects are counted once for each category regardless of the number of events.
[b] A listing of Serious Adverse Events is included in Section 14.3.2.
[c] As reported on the Adverse Event eCRF.

Table 64: Number of Adverse Events Occurring in 5% of Subjects in Any Study Arm by MedDRA® System Organ Class and Preferred Term, and Treatment Group - Safety Population

[Implementation note: This table includes solicited events, unsolicited events, and clinical laboratory events. Sort by SOC then PT]

Preferred Term	MedDRA System Organ Class	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)			Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)			Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)			Study Arm 4 15 mcg A/H7N9 (N=X)			All Subjects (N=X)		
		n	%	Events	n	%	Events	n	%	Events	n	%	Events	n	%	Events
Serious Adverse Events																
All	All	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
PT1	SOC1	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Etc.	Etc.															
Other (Non-serious) Adverse Events																
All	All	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
PT1	SOC1	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Etc	Etc															

Note: N = number of subjects in the Safety population (number of subjects at risk); n= number of subjects reporting event; Events = total frequency of events reported.
MedDRA Version X.X.

14.3.1.1 Solicited Adverse Events

Table 65: Number and Percentage of Subjects Experiencing Solicited Events with 95% Confidence Intervals by Symptom and Study Arm – Post Any Study Vaccination - Safety Population

Symptom	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)		Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)		Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)		Study Arm 4 15 mcg A/H7N9 (N=X)	
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
Any Symptom	x	xx (xx-xx)	x	xx (xx-xx)	x	xx (xx-xx)	x	xx (xx-xx)
Any Systemic Symptom								
Fever								
Feverishness								
Fatigue								
Malaise								
Myalgia								
Arthralgia								
Headache								
Nausea								
Any Injection Site Symptom								
Pain								
Tenderness								
Pruritus								
Ecchymosis								
Ecchymosis (measurement)								
Erythema								
Erythema (measurement)								
Induration/Swelling								

Table 65: Number and Percentage of Subjects Experiencing Solicited Events with 95% Confidence Intervals by Symptom and Study Arm – Post Any Study Vaccination - Safety Population *(continued)*

Symptom	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)		Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)		Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)		Study Arm 4 15 mcg A/H7N9 (N=X)	
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
Induration/Swelling (measurement)								
Note: N = Number of subjects in the Safety population. 95% CI estimated using Clopper-Pearson exact method								

Tables with similar format:

Table 66: Number and Percentage of Subjects Experiencing Solicited Events with 95% Confidence Intervals by Symptom and Study arm – Post Study Vaccination 1 – Safety Population

[Footnote update] N = Number of subjects in the Safety population who received the first vaccination.

Table 67: Number and Percentage of Subjects Experiencing Solicited Events with 95% Confidence Intervals by Symptom and Study arm– Post Study Vaccination 2 – Safety Population

[Footnote update] N = Number of subjects in the Safety population who received the second vaccination.

Table 68: Logistic Regression Model to Evaluate the Relationship of HA Antigen Dose and MF59 Adjuvant with Reporting Any Injection Site Event - Post Any Study Vaccination – Safety Population

Model Parameter	Parameter Estimate		SE	p-value	Odds Ratio	95%CI
Intercept	xxx.x		xxx.x	x.xxx	-	-
Study Arm						
15 mcg with MF59 adjuvant (reference)	-		-	-	-	-
3.75 mcg with MF59 adjuvant	xxx.x		xxx.x	x.xxx	xx.x	xx.x-xx.x
7.5 mcg with MF59 adjuvant	xxx.x		xxx.x	x.xxx	xx.x	xx.x-xx.x
15 mcg without MF59 adjuvant	xxx.x		xxx.x	x.xxx	xx.x	xx.x-xx.x
N = Number of subjects in the Safety population.						

Table with similar format:

Table 69: Logistic Regression Model to Evaluate the Relationship of HA Antigen Dose and MF59 Adjuvant with Reporting Any Systemic Event - Post Any Study Vaccination – Safety Population

Table 70: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity and Study Arm– Post Any Study Vaccination – Safety Population

Symptom	Severity	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)		Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)		Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)		Study Arm 4 15 mcg A/H7N9 (N=X)	
		n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
Any Symptom	None	x	xx (xx-xx)	x	xx (xx-xx)	x	xx (xx-xx)	x	xx (xx-xx)
	Mild								
	Moderate								
	Severe								
Any Systemic Symptom	None	x	xx (xx-xx)	x	xx (xx-xx)	x	xx (xx-xx)	x	xx (xx-xx)
	Mild								
	Moderate								
	Severe								
Fever	None								
	Mild								
	Moderate								
	Severe								
Feverishness	None								
	Mild								
	Moderate								
	Severe								
Fatigue	None								
	Mild								
	Moderate								
	Severe								
Malaise	None								

Table 70: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity and Study arm – Post Any Study Vaccination – Safety Population *(continued)*

Symptom	Severity	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)		Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)		Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)		Study Arm 4 15 mcg A/H7N9 (N=X)	
		n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
	Mild								
	Moderate								
	Severe								
Myalgia	None								
	Mild								
	Moderate								
	Severe								
Arthralgia	None								
	Mild								
	Moderate								
	Severe								
Headache	None								
	Mild								
	Moderate								
	Severe								
Nausea	None								
	Mild								
	Moderate								
	Severe								
Any Injection Site Symptom	None								

Table 70: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity and Study arm – Post Any Study Vaccination – Safety Population *(continued)*

Symptom	Severity	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)		Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)		Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)		Study Arm 4 15 mcg A/H7N9 (N=X)	
		n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
	Mild								
	Moderate								
	Severe								
Pain	None								
	Mild								
	Moderate								
	Severe								
Tenderness	None								
	Mild								
	Moderate								
	Severe								
Pruritus	None								
	Mild								
	Moderate								
	Severe								
Ecchymosis	None								
	Mild								
	Moderate								
	Severe								
Ecchymosis (measurement)	None								

Table 70: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity and Study arm – Post Any Study Vaccination – Safety Population *(continued)*

Symptom	Severity	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)		Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)		Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)		Study Arm 4 15 mcg A/H7N9 (N=X)	
		n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
	Mild								
	Moderate								
	Severe								
Erythema	None								
	Mild								
	Moderate								
	Severe								
Erythema (measurement)	None								
	Mild								
	Moderate								
	Severe								
Induration/Swelling	None								
	Mild								
	Moderate								
	Severe								
Induration/Swelling (measurement)	None								
	Mild								
	Moderate								
	Severe								

Table 70: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity and Study arm – Post Any Study Vaccination – Safety Population *(continued)*

Symptom	Severity	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)		Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)		Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)		Study Arm 4 15 mcg A/H7N9 (N=X)	
		n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
Note: N = Number of subjects in the Safety population. 95% CI estimated using Clopper-Pearson exact method. Severity is the maximum severity reported over all solicited symptoms post dosing for each subject.									

Tables with similar format:

Table 71: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity and Study arm– Post Study Vaccination 1 – Safety Population

[Footnote Update] N = Number of subjects in the Safety population who received the first study vaccination.

Table 72: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity and Study arm – Post Study Vaccination 2 – Safety Population

[Footnote Update] N = Number of subjects in the Safety population who received the second study vaccination.

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Table 73: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, Day Post Study Vaccination, and Study arm – Post Any Study Vaccination – Safety Population

Symptom	Severity	Pre-Vac.		Post-Vac.		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Study Arm 1: 3.75 mcg A/H7N9 + MF59 (N=X)																					
All Subjects																					
Any Symptom	None																				
	Mild																				
	Moderate																				
	Severe																				
Any Systemic Symptom	None																				
	Mild																				
	Moderate																				
	Severe																				
Fever	None																				
	Mild																				
	Moderate																				
	Severe																				
Feverishness	None																				
	Mild																				
	Moderate																				
	Severe																				
Fatigue	None																				
	Mild																				
	Moderate																				
	Severe																				

Table 73: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, Day Post Study Vaccination, and Study arm – Post Any Study Vaccination *(continued)*

Symptom	Severity	Pre-Vac.		Post-Vac.		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Malaise	None																				
	Mild																				
	Moderate																				
	Severe																				
Myalgia	None																				
	Mild																				
	Moderate																				
	Severe																				
Arthralgia	None																				
	Mild																				
	Moderate																				
	Severe																				
Headache	None																				
	Mild																				
	Moderate																				
	Severe																				
Nausea	None																				
	Mild																				
	Moderate																				
	Severe																				
Any Injection Site Symptom	None																				
	Mild																				
	Moderate																				

Table 73: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, Day Post Study Vaccination, and Study arm – Post Any Study Vaccination *(continued)*

Symptom	Severity	Pre-Vac.		Post-Vac.		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Severe																				
Pain	None																				
	Mild																				
	Moderate																				
	Severe																				
Tenderness	None																				
	Mild																				
	Moderate																				
	Severe																				
Pruritus	None																				
	Mild																				
	Moderate																				
	Severe																				
Ecchymosis	None																				
	Mild																				
	Moderate																				
	Severe																				
Ecchymosis (measurement)	None																				
	Mild																				
	Moderate																				
	Severe																				
Erythema	None																				
	Mild																				

Table 73: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, Day Post Study Vaccination, and Study arm – Post Any Study Vaccination *(continued)*

Symptom	Severity	Pre-Vac.		Post-Vac.		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Moderate																				
	Severe																				
Erythema (measurement)	None																				
	Mild																				
	Moderate																				
	Severe																				
Induration/Swelling	None																				
	Mild																				
	Moderate																				
	Severe																				
Induration/Swelling (measurement)	None																				
	Mild																				
	Moderate																				
	Severe																				
[repeat for all study arms]																					

Note: N = Number of subjects in the Safety population. Severity is the maximum severity reported post dosing for each subject for each day.

Tables with similar format:

Table 74: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, Day Post Study Vaccination, and Study arm – Post Study Vaccination 1 – Safety Population

Table 75: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, Day Post Study Vaccination, and Study arm – Post Study Vaccination 2 – Safety Population

Table 76: Number and Percentage of Subjects Experiencing Solicited Systemic Events for Dose 1 Compared with Dose 2 by Study Arm – Safety Population

		Study Vaccination 2		
Study Arm	**Study Vaccination 1**	**Subjects with No Symptoms**	**Subjects with Mild or Greater Symptoms**	**Total Number of Subjects n (Percent) [p-value*]**
Study Arm 1 3.75 mcg A/H7N9 + MF59	Subjects with No Symptoms	x (%)	x (%)	x (%)
	Subjects with Mild or Greater Symptoms	x (%)	x (%)	x (%)
	Total Number of Subjects	x (%)	x (%)	x (100%) [0.xxx]
Study Arm 2 7.5 mcg A/H7N9 + MF59	Subjects with No Symptoms	x (%)	x (%)	x (%)
	Subjects with Mild or Greater Symptoms	x (%)	x (%)	x (%)
	Total Number of Subjects	x (%)	x (%)	x (100%) [0.xxx]
Study Arm 3 15 mcg A/H7N9 + MF59	Subjects with No Symptoms	x (%)	x (%)	x (%)
	Subjects with Mild or Greater Symptoms	x (%)	x (%)	x (%)
	Total Number of Subjects	x (%)	x (%)	x (100%) [0.xxx]
Study Arm 4 15 mcg A/H7N9	Subjects with No Symptoms	x (%)	x (%)	x (%)
	Subjects with Mild or Greater Symptoms	x (%)	x (%)	x (%)
	Total Number of Subjects	x (%)	x (%)	x (100%) [0.xxx]

Note: Denominators for percentages are the number of subjects in the Safety population who received both the first and second study vaccination. [x] subjects did not get the second dose and are not included in this table.
* P-value is calculated from McNemar's test for each study arm.

Table with similar format:

Table 77: Number and Percentage of Subjects Experiencing Solicited Injection Site Events for Dose 1 Compared with Dose 2 by Study arm and Age Stratum – Safety Population

14.3.1.2 Unsolicited Adverse Events

Table 78: Number and Percentage of Subjects Experiencing Unsolicited Adverse Events with 95% Confidence Intervals by MedDRA® System Organ Class and Preferred Term, and Study Arm – Safety Population

		Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)		Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)		Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)		Study Arm 4 15 mcg A/H7N9 (N=X)	
MedDRA® System Organ Class	**MedDRA® Preferred Term**	**n**	**% (95% CI)**	**n**	**% (95% CI)**	**n**	**% (95% CI)**	**n**	**% (95% CI)**
Any SOC	Any PT	x	xx (xx-xx)	x	xx (xx-xx)	x	xx (xx-xx)	x	xx (xx-xx)
[SOC 1]	Any PT								
	[PT 1]								
	[PT 2]								
[SOC 2]	Any PT								
	[PT 1]								
	[PT 2]								
Note: N = Number of subjects in the Safety population. This table presents number and percentage of subjects. A subject is only counted once per PT.									

Table 79: Number and Percentage of Subjects Experiencing Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, Relationship, and Study Arm – Safety Population

MedDRA System Organ Class	MedDRA Preferred Term	Any Incidence		Severity [1]						Relationship to Treatment [2]			
				Mild		Moderate		Severe		Not Related		Related	
		n	%	n	%	n	%	n	%	n	%	n	%
Study Arm 1: 3.75 mcg A/H7N9 + MF59 (N = X)													
All Subjects													
Any SOC	Any PT	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
[SOC 1]	Any PT												
	[PT 1]												
	[PT 2]												
[SOC 2]	Any PT												
	[PT 1]												
	[PT 2]												
[Repeat for all study arms]													

Note: N = Number of subjects in the Safety population.
[1] For severity, a subject is counted once per preferred term and is summarized according to their highest severity.
[2] For relationship, a subject is only counted once per preferred term and is summarized according to their closest relationship.

Table 80: Number and Percentage of Subjects Experiencing Non-Serious Related Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, and Study Arm – Safety Population

MedDRA System Organ Class	MedDRA Preferred Term	Any Incidence		Severity [1]					
				Mild		Moderate		Severe	
		n	%	n	%	n	%	n	%
Study Arm 1: 3.75 mcg A/H7N9 + MF59 (N=X)									
All Subjects									
Any SOC	Any PT	x	xx	x	xx	x	xx	x	xx
[SOC 1]	Any PT	x	xx	x	xx	x	xx	x	xx
	[PT 1]								
	[PT 2]								
[SOC 2]	Any PT								
	[PT 1]								
	[PT 2]								
[Repeat for all study arms]									

Note: N = Number of subjects in the Safety population. This table presents number and percentage of subjects.
[1] For severity, a subject is counted once per preferred term and is summarized according to their highest severity.

Table 81: Number and Percentage of Subjects Experiencing Unsolicited Adverse Events Within 21 Days Post Study Vaccination by MedDRA System Organ Class and Preferred Term, Day Post Vaccination, and Study Arm – Safety Population

		Day 1-8 Post Vac 1		Day 9-22 Post Vac 1		Day 1-22 Post Vac 1		Day 1-8 Post Vac 2		Day 9-22 Post Vac 2		Day 1-22 Post Vac 2		Day 1-22 Post Any Vaccination	
MedDRA System Organ Class	**MedDRA Preferred Term**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Study Arm 1: 3.75 mcg A/H7N9 + MF59, (N=X)															
All Subjects															
Any SOC	Any PT	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
[SOC 1]	Any PT														
	[PT 1]														
	[PT 2]														
[SOC 2]	Any PT														
	[PT 1]														
	[PT 2]														
[Repeat for all study arms]															
Note: N = Number of subjects in the Safety Population. This table presents number and percentage of subjects. For each time period, a subject is only counted once per PT.															

Table 82: Number and Percentage of Subjects Experiencing Non-Serious, Related Unsolicited Adverse Events Within 21 Days Post Vaccination by MedDRA System Organ Class and Preferred Term, Study Vaccination, and Study Arm – Safety Population

		Day 1-8 Post Vac 1		Day 9-22 Post Vac 1		Day 1-22 Post Vac 1		Day 1-8 Post Vac 2		Day 9-22 Post Vac 2		Day 1-22 Post Vac 2		Day 1-22 Post Any Vaccination	
MedDRA System Organ Class	**MedDRA Preferred Term**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Study Arm 1: 3.75 mcg A/H7N9 + MF59 (N=X)															
All Subjects															
Any SOC	Any PT	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
[SOC 1]	Any PT														
	[PT 1]														
	[PT 2]														
[SOC 2]	Any PT														
	[PT 1]														
	[PT 2]														
[Repeat for all study arms]															

Note: N = Number of subjects in the Safety population. This table presents number and percentage of subjects. For each time period, a subject is only counted once per PT.

Table 83: Number of Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Day Post Vaccination, and Study Arm – Safety Population

		Day 1-8 Post Vac 1	Day 9-22 Post Vac 1	Day 1-22 Post Vac 1	Day 1-8 Post Vac 2	Day 9-22 Post Vac 2	Day 1-22 Post Vac 2	Day 1-22 Post Any Vaccination
MedDRA System Organ Class	**MedDRA Preferred Term**	**# of Events**	**# of Events**	**# of Events**	**# of Events**	**# of Events**	**# of Events**	**# of Events**
Study Arm 1: 3.75 mcg A/H7N9 + MF59 (N=X)								
All Subjects								
Any SOC	Any PT	x	x	x	x	x	x	x
[SOC 1]	Any PT							
	[PT 1]							
	[PT 2]							
[SOC 2]	Any PT							
	[PT 1]							
	[PT 2]							
[Repeat for all study arms]								

Note: N = Number of subjects in the Safety population. This table presents number of events; A subject may be counted multiple times.

14.3.2 Listings of Serious and Significant Adverse Events

Table 84: Listing of Serious Adverse Events – Safety Population

[Implementation Note: This listing is included in the table shells document, as it is included in the body of the CSR. If the event is ongoing (no stop date), indicate "ongoing" in the "Duration" column. If more than one reason is selected for the reason reported as an SAE, list all reasons in the column, separated by a comma. In the "If Not Related, Alternate Etiology" column, merge the 2 data fields for collecting alternate etiology, separate by a colon. In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification.]

Adverse Event	Associated with Vac #	# of Days Post Associated Vac (Duration)	# of Days Post Vac the Event Became Serious	Reason Reported as an SAE	Severity	Relationship to Study Treatment	In Not Related, Alternative Etiology	Action Taken with Study Treatment	Subject Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Subject ID: , Study arm: , AE Number:												
Comments:												
Subject ID: , Study arm: , AE Number:												
Comments:												

Table 85: Listing of Potentially Immune-Mediated Medical Conditions – Safety Population

[Implementation Note: This listing is included in the tables section, as it is included in the body of the CSR. If the event is ongoing (no stop date), indicate "ongoing" in the "Duration" column. In the "If Not Related, Alternate Etiology" column, merge the 2 data fields for collecting alternate etiology, separate by a colon.]

Adverse Event	Associated with Vac #	# of Days Post Associated Vac (Duration)	SAE? Severity	Relationship to Study Treatment	In Not Related, Alternative Etiology	Action Taken with Study Treatment	Subject Discontinued Due to AE	Outcome	MAAE? NOCMC?	MedDRA System Organ Class	MedDRA Preferred Term
	Subject ID: , Study arm: , AE Number:										
			SAE: No Mild								
	Comments:										
	Subject ID: , Study arm: , AE Number:										
	Comments:										

Tables with similar format:

Table 86: Listing of New Onset Chronic Medical Conditions – Safety Population

Table 87: Listing of Non-Serious, Unsolicited, Moderate or Severe Adverse Events – Safety Population

14.3.3 Narratives of Deaths, Other Serious and Significant Adverse Events

(not included in SAP, but this is a placeholder for the CSR)

14.3.4 Displays of Laboratory Results

Table 88: Laboratory Results by Parameter, Maximum Severity, Study Day, and Study Arm – All Laboratory Parameters – Safety Population

Treatment Group	Study Day	N	None		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%
Study Arm 1 3.75 mcg A/H7N9 + MF59	Baseline	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Day 8											
	Day 22											
	Day 29											
	Max Severity Post Baseline											
[Repeat for all Study Arms]												

Note: N = Number of subjects in the Safety population.
The "Max Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments.

Tables with similar format:

Table 89: Laboratory Results by Parameter, Maximum Severity, Study Day, and Study arm – Hemoglobin – Safety Population

Table 90: Laboratory Results by Parameter, Maximum Severity, Study Day, and Study arm – Alanine aminotransferase (ALT) – Safety Population

Table 91: Laboratory Results by Parameter, Maximum Severity, Study Day, and Study arm – Total Bilirubin – Safety Population

Table 92: Laboratory Results by Parameter, Maximum Severity, Study Day, and Study arm – Creatinine – Safety Population

Table 93: Laboratory Results by Parameter, Maximum Severity, Study Day, and Study Arm – White Blood Cells – Safety Population

Treatment Group	Study Day	N	None		Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Study Arm 1 3.75 mcg A/H7N9 + MF59	Baseline	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Day 8																	
	Day 22																	
	Day 29																	
	Max Severity Post Baseline																	
[Repeat for all Study Arms]																		

Note: N = Number of subjects in the Safety population.
The "Max Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments.

Table with similar format:

Table 94: Laboratory Results by Parameter, Maximum Severity, Study Day, and Study Arm – Platelets – Safety Population

Table 95: Laboratory Summary Statistics of Value and Change from Baseline by Parameter, Study Day, and Study Arm – White Blood Cells - Safety Population

Treatment Group	Study Day	Value					Change from Baseline				
		N	Mean	Standard Deviation	Median	Min, Max	N	Mean	Standard Deviation	Median	Min, Max
Study Arm 1 3.75 mcg A/H7N9 + MF59	Baseline	x	xx.x	xx.x	xx	xx, xx	NA	NA	NA	NA	NA
	Day 8	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
	Day 22	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
	Day 29	x	xx.x	xx.x	xx	xx, xx	x	xx.x	xx.x	xx	xx, xx
[Repeat for all Study Arms]											
N = Number of subjects in the Safety population											

Tables with similar format:

Table 96: Laboratory Summary Statistics of Value and Change from Baseline by Parameter, Study Day, and Study Arm – Hemoglobin - Safety Population

Table 97: Laboratory Summary Statistics of Value and Change from Baseline by Parameter, Study Day, and Study Arm – Platelets - Safety Population

Table 98: Laboratory Summary Statistics of Value and Change from Baseline by Parameter, Study Day, and Study Arm – Alanine aminotransferase (ALT) - Safety Population

Table 99: Laboratory Summary Statistics of Value and Change from Baseline by Parameter, Study Day, and Study Arm – Total Bilirubin - Safety Population

Table 100: Laboratory Summary Statistics of Value and Change from Baseline by Parameter, Study Day, and Study Arm – Creatinine - Safety Population

14.3.4.5 Clinical Laboratory Reference Ranges

(Placeholder for the CSR)

14.3.5 Abnormal Laboratory Value Listings (by Subject)

Table 101: Listing of Abnormal Laboratory Results - Chemistry

Subject ID	Study Arm	Sex	Age (years)	Planned Time Point	Actual Study Day	Laboratory Parameter (Units)	Result (Severity)	Relationship to Treatment	If Not Related, Alternate Etiology	Action Taken with Study Treatment	Subject Discontinued Due to Result?

Table 102: Listing of Abnormal Laboratory Results - Hematology

Subject ID	Study Arm	Sex	Age (years)	Planned Time Point	Actual Study Day	Laboratory Parameter (Units)	Result (Severity)	Relationship to Treatment	If Not Related, Alternate Etiology	Action Taken with Study Treatment	Subject Discontinued Due to Result?

14.3.6 Displays of Vital Signs

Table 103: Vital Signs by Assessment, Maximum Severity, Study Day, and Study Arm – Any Assessment - Safety Population

Treatment Group	Study Day	N	None		Mild		Moderate		Severe		Missing	
			n	%	n	%	n	%	n	%	n	%
Study Arm 1 3.75 mcg A/H7N9 + MF59	Baseline	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Day 22											
	Max Severity Post Baseline											
[Repeat for all Study Arms]												
Note: N = Number of subjects in the Safety population. The "Max Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments.												

Table with similar format:

Table 104: Vital Signs by Assessment, Maximum Severity, Study Day, and Study Arm – Oral Temperature - Safety Population

Table 105: Vital Signs by Assessment, Maximum Severity, Study Day, and Study Arm – Systolic Blood Pressure - Safety Population

Treatment Group	Study Day	N	None		Mild (Low)		Mild (High)		Moderate (Low)		Moderate (High)		Severe (Low)		Severe (High)		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Study Arm 1 3.75 mcg A/H7N9 + MF59	Baseline	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Day 22																	
	Max Severity Post Baseline																	
[Repeat for all Study Arms]																		

Note: N = Number of subjects in the Safety population.

The "Max Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments.

Tables with similar format:

Table 106: Vital Signs by Assessment, Maximum Severity, Study Day, and Study Arm – Diastolic Blood Pressure - Analysis Population

Table 107: Vital Signs by Assessment, Maximum Severity, Study Day, and Study Arm – Pulse - Safety Population

14.4 Summary of Concomitant Medications

Table 108: Number and Percentage of Subjects with Prior and Concurrent Medications by WHO Drug Classification and Study Arm- Safety Population

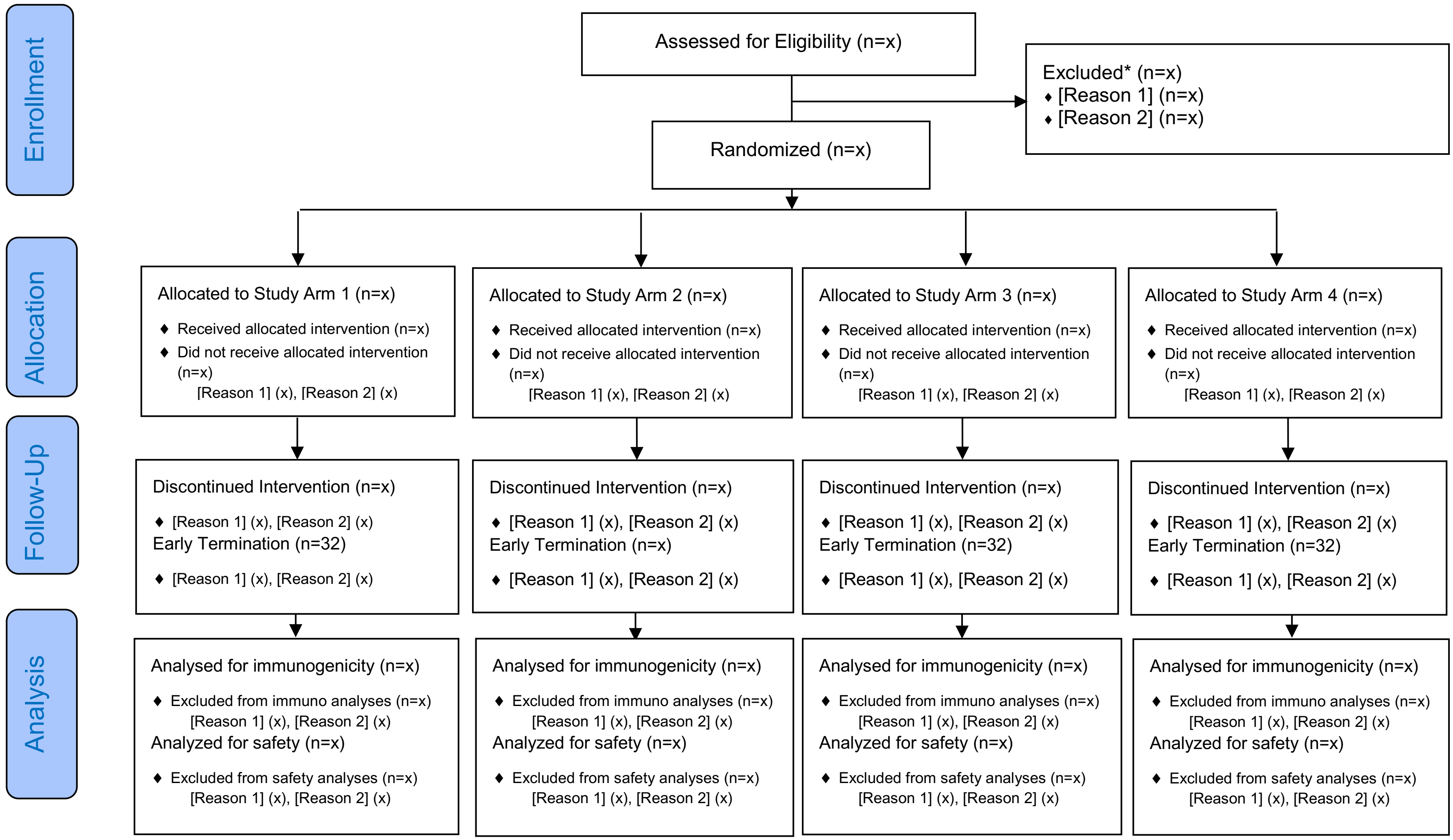
WHO Drug Code Level 1, Anatomic Group	WHO Drug Code Level 2, Therapeutic Subgroup	Study Arm 1 3.75 mcg A/H7N9 + MF59 (N=X)		Study Arm 2 7.5 mcg A/H7N9 + MF59 (N=X)		Study Arm 3 15 mcg A/H7N9 + MF59 (N=X)		Study Arm 4 15 mcg A/H7N9 (N=X)	
		n	%	n	%	n	%	n	%
Any Level 1 Codes	Any Level 2 Codes	x	xx	x	xx	x	xx	x	xx
[ATC Level 1 - 1]	Any [ATC 1 – 1]								
	[ATC 2 - 1]								
	[ATC 2 - 2]								
	[ATC 2 - 3]								
[ATC Level 1 – 2]	[ATC 2 - 1]								
	[ATC 2 - 2]								
	[ATC 2 - 3]								
N= Number of subjects in the Safety population; n=Number of subjects reporting taking at least one medication in the specific WHO Drug Class.									

APPENDIX 2. FIGURE MOCK-UPS

LIST OF FIGURES

10.1 Disposition of Subjects Figures

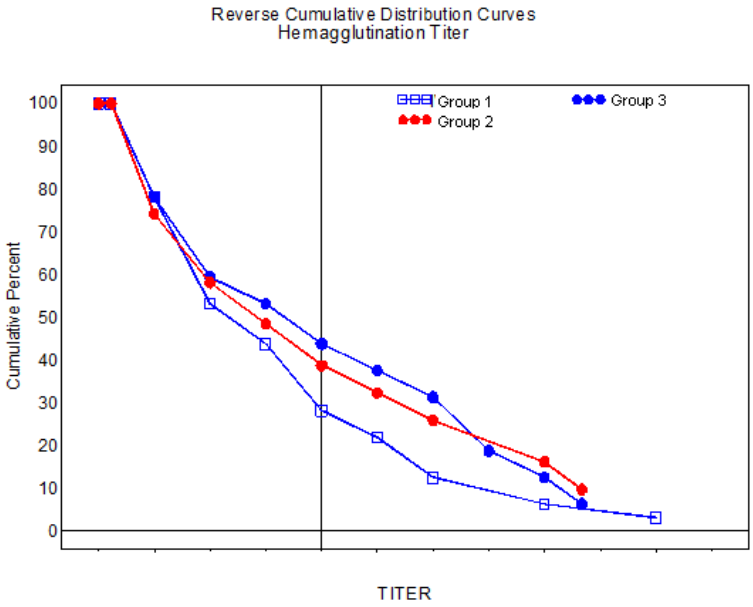
Figure 1: CONSORT Flow Diagram



14.2.2 Immunogenicity Figures

Figure 2: Reverse Cumulative Distribution of Hemagglutination Inhibition Antibody against A/Hong Kong/125/2017 (H7N9) by Study Day, and Study Arm - Modified Intent to Treat Population

[Implementation Note: A generic sample figure is shown below. The RCD curves should be presented in a single figure with separate panels for each study day (Baseline, Day 8, Day 22, Day 29, Day 43, Day 202). Figures generated for preliminary report will include data from all available visits at the time of report generation. Visit labels should be included in the panel headers. Within each panel individual curves should be used for each study arm (four curves).]



Figures with similar format:

Figure 3: Reverse Cumulative Distribution of Hemagglutination Inhibition Antibody against A/Hong Kong/125/2017 (H7N9) by Study Day, and Study Arm - Per-Protocol Population

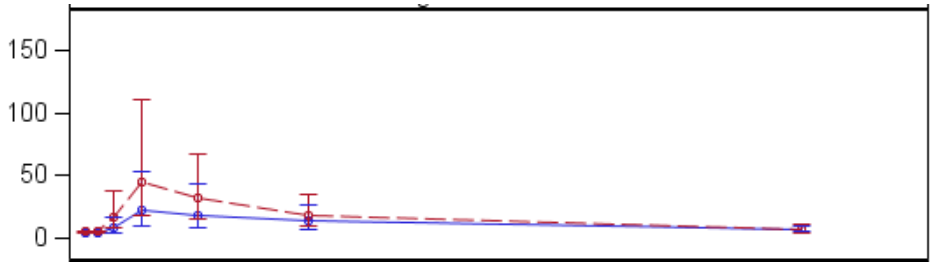
Figure 4: Reverse Cumulative Distribution of Neutralizing Antibody Against A/Hong Kong/125/2017 (H7N9) by Study Day, and Study Arm - Modified Intent-to-Treat Population

Figure 5: Reverse Cumulative Distribution of Neutralizing Antibody against A/Hong Kong/125/2017 (H7N9) by Study Day, and Study Arm - Per-Protocol Population

Figure 6: Geometric Mean Titers of Hemagglutination Inhibition Antibody Against A/Hong Kong/125/2017 (H7N9) by Study Day, and Study Arm - Modified Intent-to-Treat Population

[Implementation Note: A generic sample figure is shown below. Planned Study Day is plotted along the x-axis, with visit labels as tick labels. Titer is plotted on the y-axis on the log-10 scale. GMT should be plotted at each visit with upper and lower error bars for the 95% CI for each treatment group with different marker shapes/colors for each study arm. Each study arm should have a separate color and marker shape.]

Note: this figure will be generated for the preliminary report including data through Day 43, then re-generated for the final CSR to include all data through Day 202.



Figures with similar format:

Figure 7: Geometric Mean Titers of Hemagglutination Inhibition Antibody against A/Hong Kong/125/2017 (H7N9) by Study Day and Study Arm - Per-Protocol Population

Figure 8: Geometric Mean Titers of Neutralizing Antibody against A/Hong Kong/125/2017 (H7N9) Study Day and Study Arm - Modified Intent-to-Treat Population

Figure 9: Geometric Mean Titers of Neutralizing Antibody against A/Hong Kong/125/2017 (H7N9) by Study Day and Study Arm - Per-Protocol Population

Figure 10: Correlation of Hemagglutination Inhibition Antibody and Neutralizing Antibody Against A/Hong Kong/125/2017 (H7N9) by Study Day and Study Arm - Modified Intent-to-Treat Population

[Implementation Note: A generic sample figure is shown below. The scatter plots should be presented in a single figure with separate panels for each visit (Baseline, D8, D22, D29, D43, D202. Visit labels should be included in the panel header. Within each panel distinct marker types and colors should be used to indicate the study arms, with treatment group labels included in a legend.). Each study arm should have a unique color and marker shape. The spearman correlation should be calculated over all subjects and annotated within each panel as "Spearman Correlation (r=0.xx, p=0.xx)".]

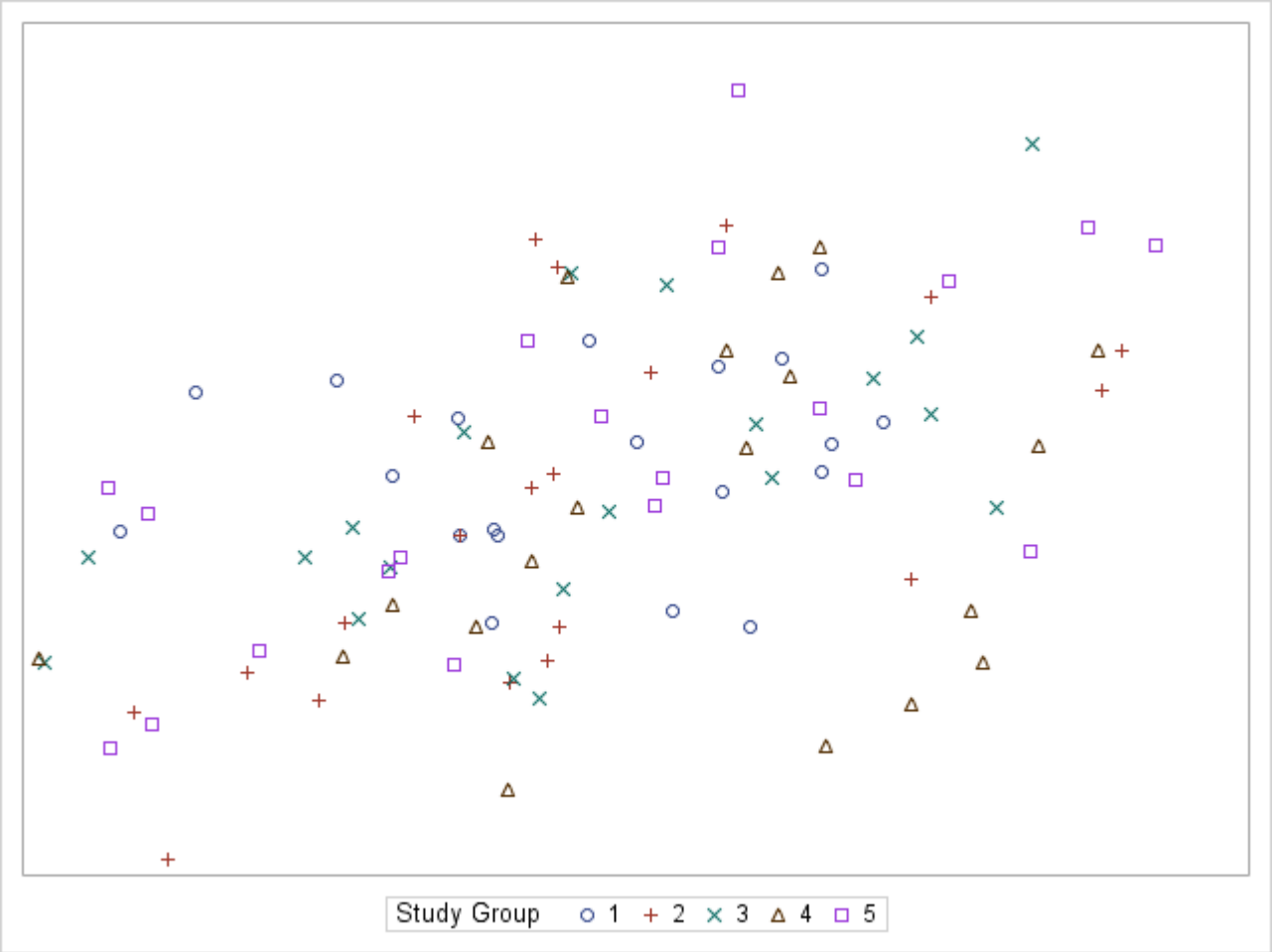


Figure with Similar format:

Figure 11: Correlation of Hemagglutination Inhibition Antibody and Neutralizing Antibody Against A/Hong Kong/125/2017 (H7N9) by Study Day and Study Arm - Per-Protocol Population

Figure 12: Reverse Cumulative Distribution of Hemagglutination Inhibition Antibody against A/Shanghai/2/2013 (H7N9) by Study Day and Study Arm - Per-Protocol Population

[Implementation Note: A generic sample figure is shown below. The RCD curves should be presented in a single figure with separate panels for each study day (Baseline[Day1], Day 8, Day 22, Day 29, Day 43, Day 202. Visit labels should be included in the panel headers. Within each panel individual curves should be used for each study arm (four curves). Each study arm should have a separate color.]

[Implementation Note: repeat for all heterologous strains]

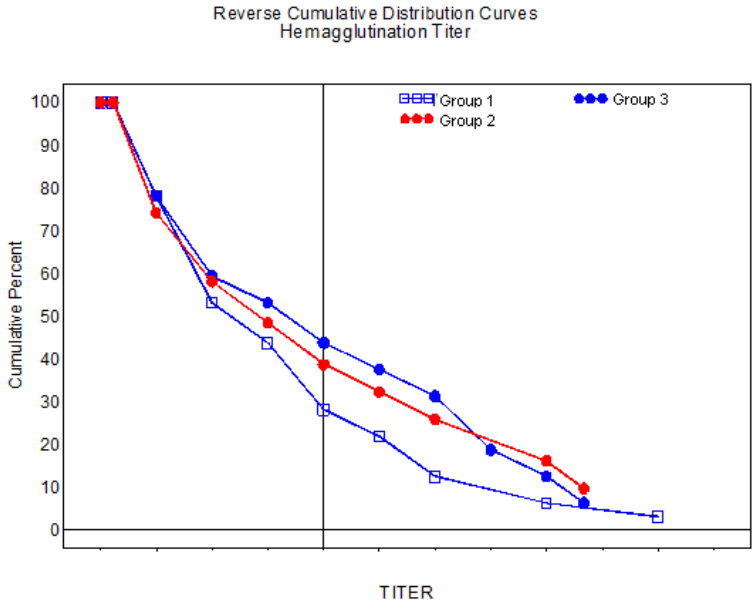


Figure with Similar Format:

Figure 13: Reverse Cumulative Distribution of Hemagglutination Inhibition Antibody against A/Guangdong/17SF003/2016 (H7N9) by Study Day and Study Arm - Per-Protocol Population

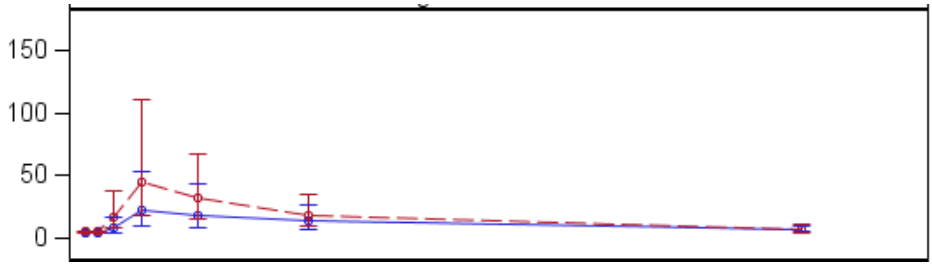
Figure 14: Reverse Cumulative Distribution of Neutralizing Antibody against A/Shanghai/2/2013 (H7N9) by Study Day and Study Arm - Per-Protocol Population

Figure 15: Reverse Cumulative Distribution of Neutralizing Antibody against A/Guangdong/17SF003/2016 (H7N9) by Study Day and Study Arm - Per-Protocol Population

Figure 16: Geometric Mean Titers of Hemagglutination Inhibition Antibody against A/Shanghai/2/2013 (H7N9) by Study Day and Study Arm - Per-Protocol Population

[Implementation Note: A generic sample figure is shown below. Planned Study Day is plotted along the x-axis, with visit labels as tick labels. Titer is plotted on the y-axis on the log-10 scale. GMT should be plotted at each visit with upper and lower error bars for the 95% CI for each treatment group with different marker shapes/colors for each study arm.]

[Implementation Note: repeat for all heterologous strains]



Figures with similar format:

Figure 17: Geometric Mean Titers of Neutralizing Antibody against A/Guangdong/17SF003/2016 (H7N9) by Study Day and Study Arm - Per-Protocol Population

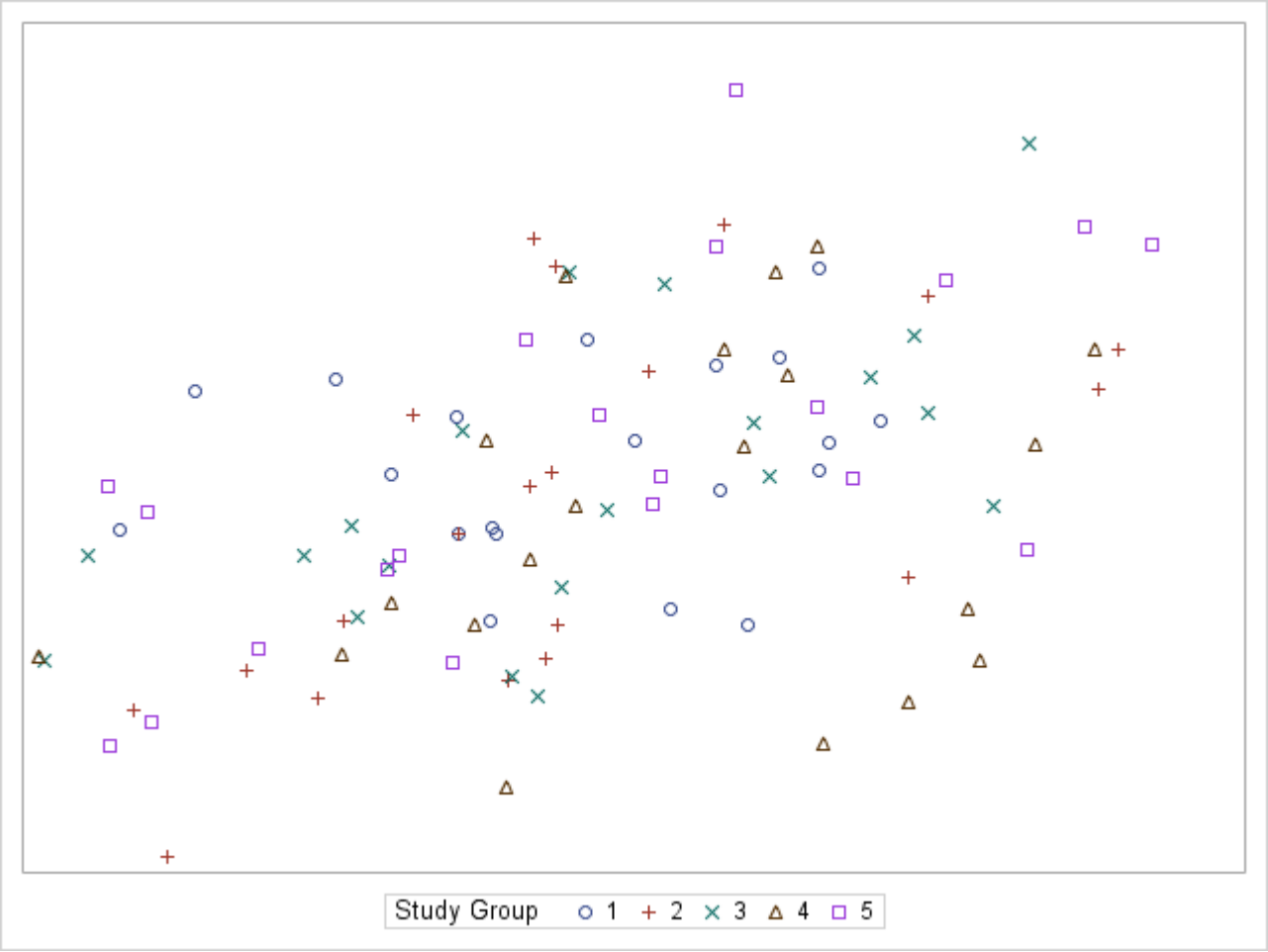
Figure 18: Geometric Mean Titers of Hemagglutination Inhibition Antibody against A/Shanghai/2/2013 (H7N9) by Study Day and Study Arm - Per-Protocol Population

Figure 19: Geometric Mean Titers of Neutralizing Antibody against A/Guangdong/17SF003/2016 (H7N9) by Study Day and Study Arm - Per-Protocol Population

Figure 20: Correlation of Hemagglutination Inhibition Antibody and Neutralizing Antibody Against A/Shanghai/2/2013 (H7N9) by Study Day and Study Arm - Per-Protocol Population

[Implementation Note: A generic sample figure is shown below. The scatter plots should be presented in a single figure with separate panels for each visit (Baseline, D8, D22, D29, D43, D202. Visit labels should be included in the panel header. Within each panel distinct marker types and colors should be used to indicate the study arms, with treatment group labels included in a legend. Each study arm should have a unique color and marker shape. The spearman correlation should be calculated over all subjects and annotated within each panel as "Spearman Correlation (r=0.xx, p=0.xx)".]

[Implementation Note: repeat for all heterologous strains]



Figures with similar format (may repeat as needed for additional strains):

Figure 21: Correlation of Hemagglutination Inhibition Antibody and Neutralizing Antibody Against A/Guangdong/17SF003/2016 (H7N9) by Study Day and Study Arm - Per-Protocol Population

Figure 22: Correlation of Hemagglutination Inhibition Antibody Against 2017 A/H7N9 and A/Shanghai/2/2013 (H7N9) by Study Day and Study Arm - Per-Protocol Population

14.3.1 Safety Figures

14.3.1.1 Solicited Adverse Events

Figure 26: Maximum Severity of Solicited Systemic Symptoms per Subject by Day Post Study Vaccination – Safety Population

[Implementation Note: A Generic figure is shown below. A ***vertical*** bar chart should be presented ***in 3 image files*** with separate panels for each study arm and study vaccination (4 rows (study arms) x 2 columns (vaccination #)). Axes should be labeled as follows: x-axis label: Study Day, y-axis label: Percentage of Subjects (%). The study arms should be indicated in the panel headers including "(N=X)", where N = the number of subjects in the in the Safety Population who received the relevant dose. Subjects are counted at most once at the maximum severity across all systemic events reported for the specified time point]

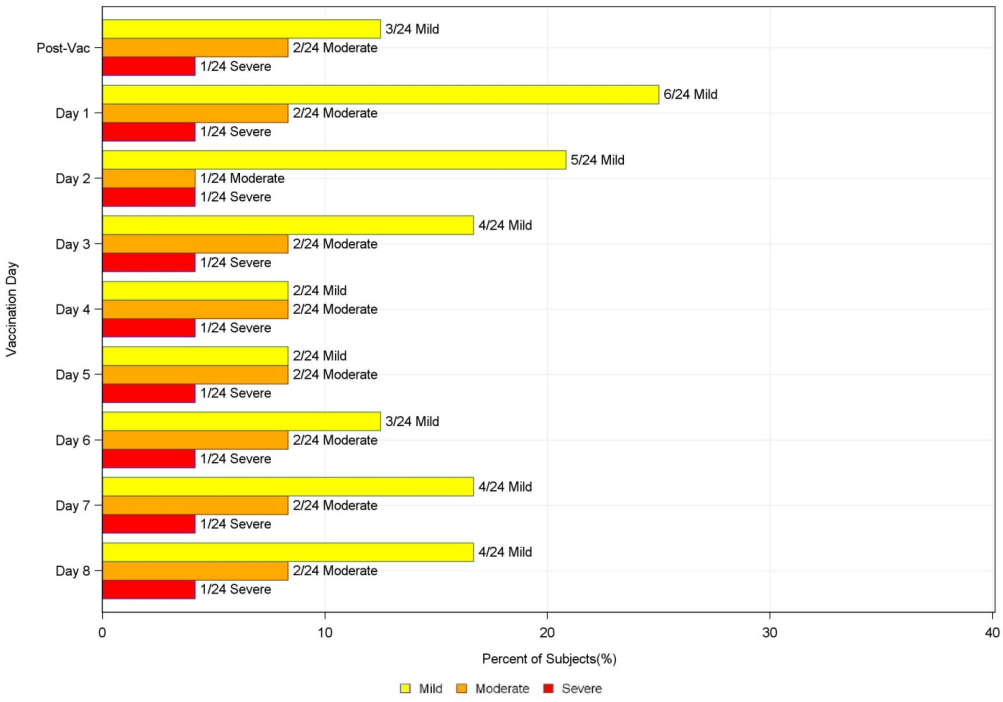


Figure with similar format:

Figure 27: Maximum Severity of Solicited Injection Site Symptoms per Subject by Day Post Study Vaccination – Safety Population

14.3.1.2 Unsolicited Adverse Events

Figure 28: Frequency of Unsolicited Adverse Events by MedDRA® System Organ Class and Severity – Safety Population

[Implementation Note: A Generic figure is shown below. This figure includes all unsolicited events across all vaccinations. A ***horizontal*** bar chart should be presented ***in 3 image files*** with separate panels for each study arm (4 columns (study arms)). Axes should be labeled as follows: y-axis label: System Organ Class, x-axis label: Number of Events. The study arms should be indicated in the panel headers including "(N=X)", where N = the number of subjects in the in the Safety Population. The y-axis should present all SOCs reported by at least 1 subject and an "All Events" category. Y-axis should be sorted with "All Events first, then in decreasing order of total incidence]

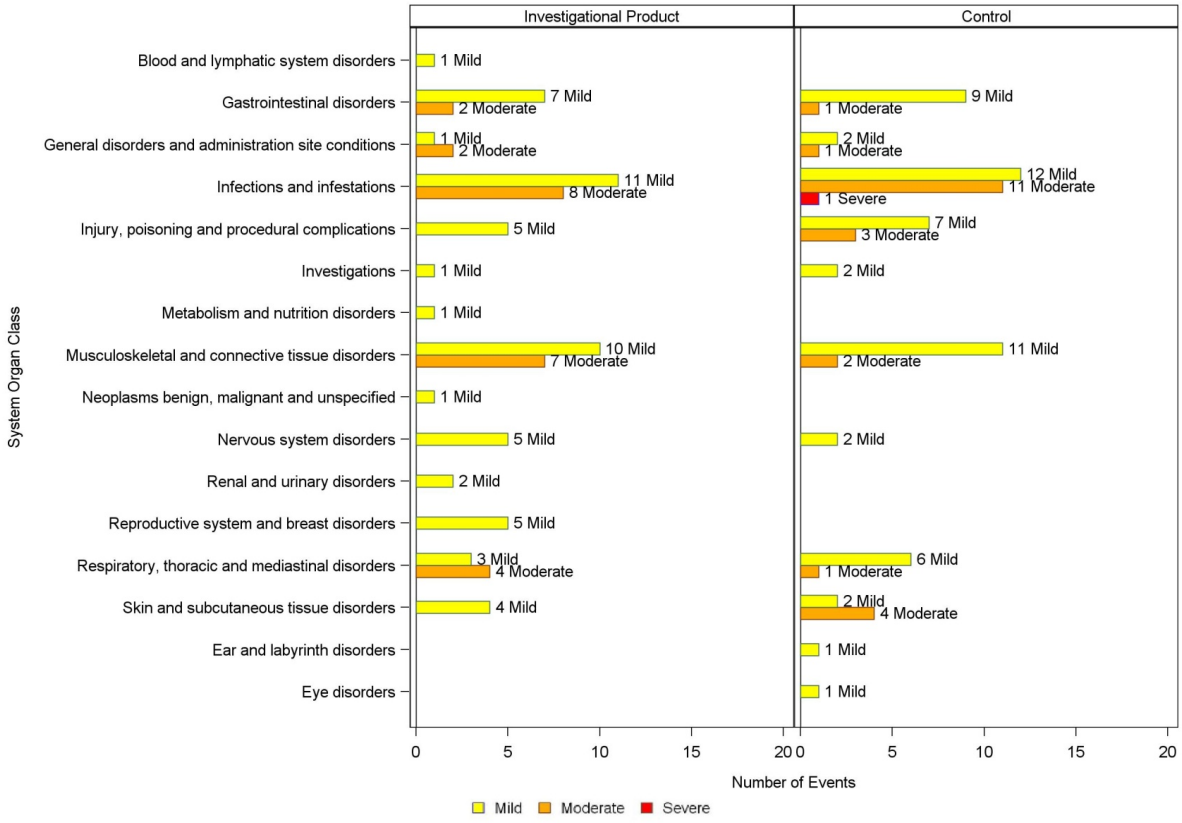


Figure 29: Incidence of Unsolicited Adverse Events by MedDRA® System Organ Class and Severity – Safety Population

[Implementation Note: A Generic figure is shown below. This figure includes all unsolicited events across all vaccinations. A ***horizontal*** bar chart should be presented ***in 2 image files*** per each vaccination with separate panels for each study arm (4 columns). Axes should be labeled as follows: y-axis label: System Organ Class, x-axis label: Percentage of Subjects (%). The study arms should be indicated in the panel headers including "(N=X)", where N = the number of subjects in the in the Safety Population. Subjects are counted at most once at the maximum severity across for any events in the applicable SOC. The y-axis should present all SOCs reported by at least 1 subject and an "All Events" category. Y-axis should be sorted with "All Events" first then in decreasing order of total incidence]

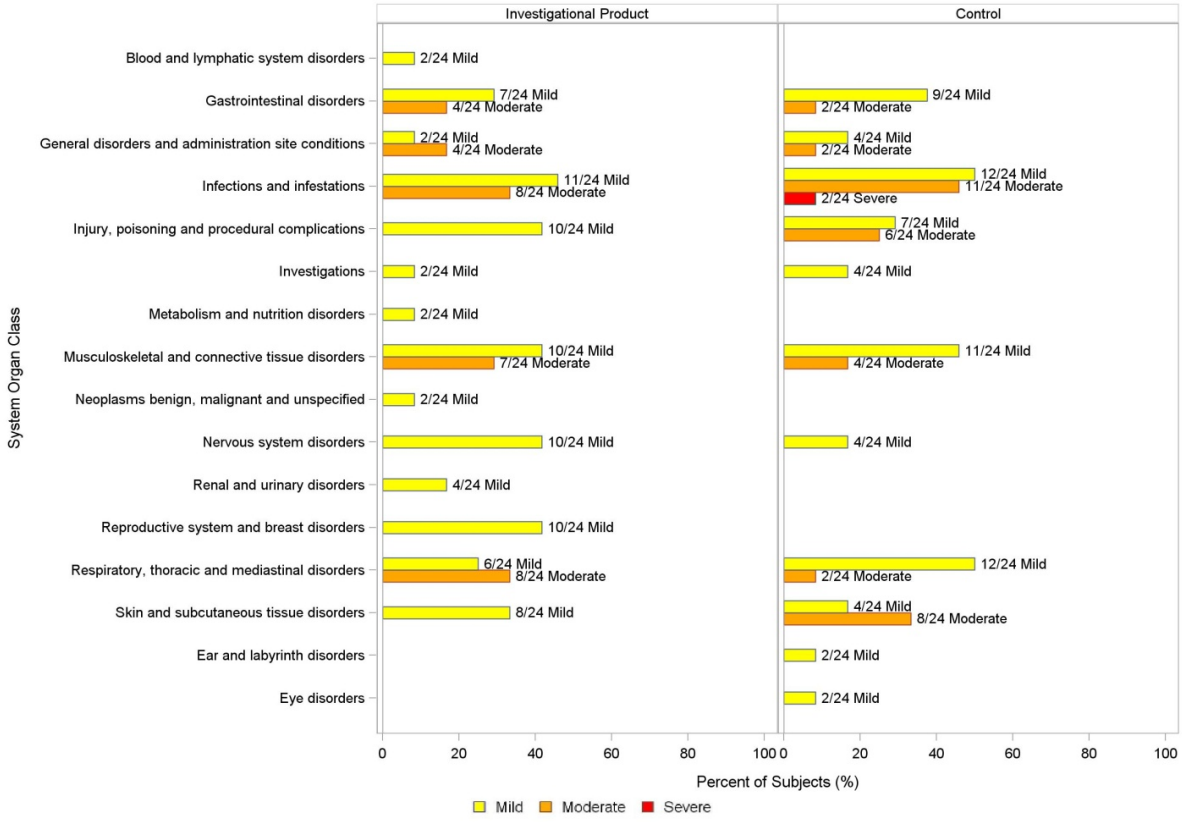


Figure 30: Frequency of Adverse Events by MedDRA® System Organ Class and Relationship to Treatment – Safety Population

[Implementation Note: A generic sample figure is shown below. This figure includes all unsolicited events across all vaccinations. A ***horizontal*** bar chart should be presented ***in 2 image files*** per each vaccination with separate panels for each study arm (4 columns). Axes should be labeled as follows: y-axis label: System Organ Class, x-axis label: Number of Events. The study arms should be indicated in the panel headers including "(N=X)", where N = the number of subjects in the in the Safety Population. The y-axis should present all SOCs reported by at least 1 subject and an "All Events" category. Y-axis should be sorted with "All Events first then in decreasing order of total frequency]

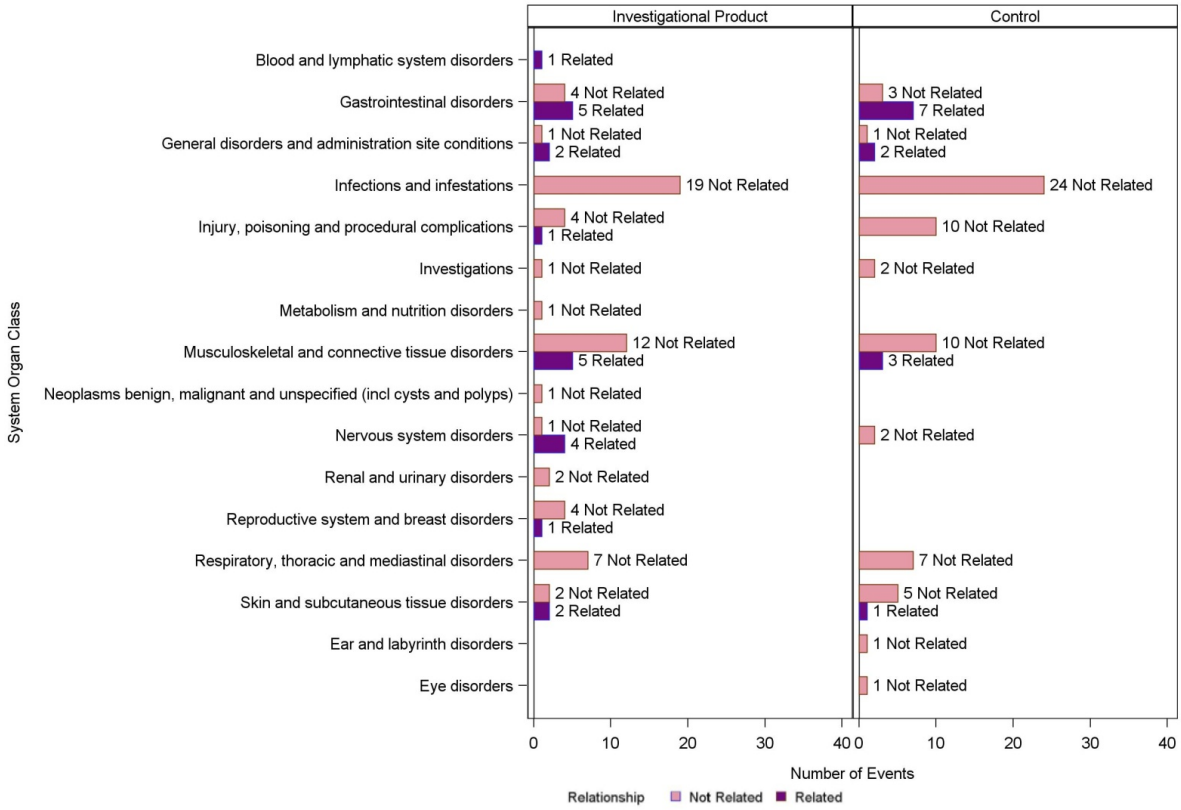
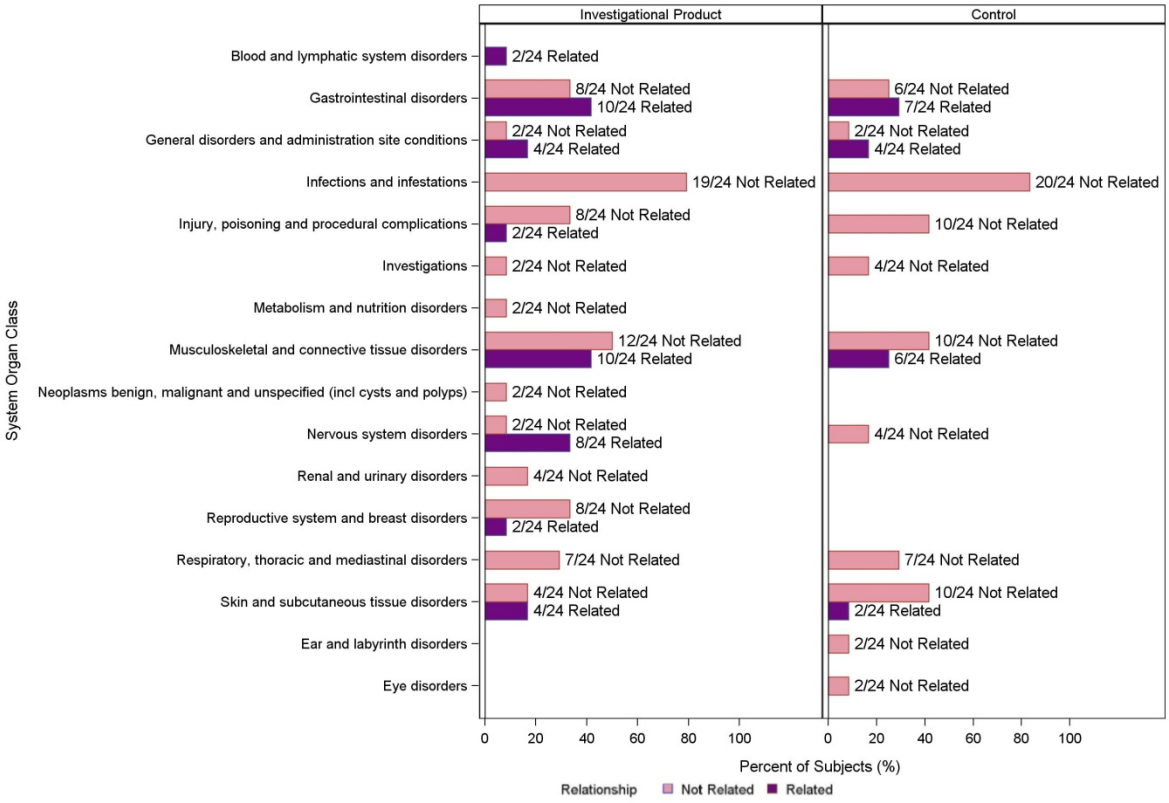


Figure 31: Incidence of Adverse Events by MedDRA® System Organ Class and Relationship to Treatment – Safety Population

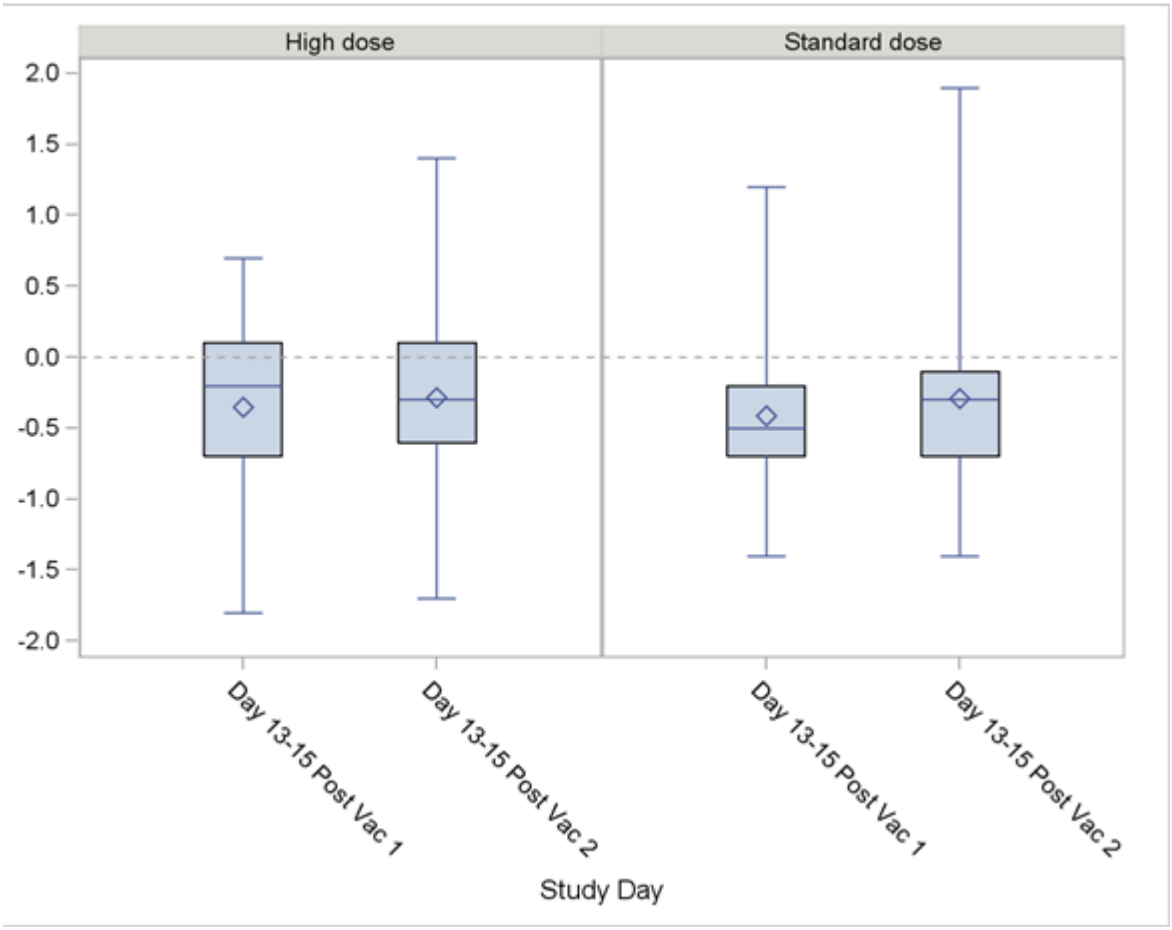
[Implementation Note: A Generic figure is shown below. This figure includes all unsolicited events across all vaccinations. A ***horizontal*** bar chart should be presented ***in 2 image files*** per each vaccination with separate panels for each study arm (4 columns). Axes should be labeled as follows: y-axis label: System Organ Class, x-axis label: Percentage of Subjects (%). The study arms should be indicated in the panel headers including "(N=X)", where N = the number of subjects in the in the Safety Population. Subjects are counted at most once at the maximum relationship (related >not-related) across for any events in the applicable SOC. The y-axis should present all SOCs reported by at least 1 subject and an "All Events" category. Y-axis should be sorted with "All Events first, then in decreasing order of total incidence across groups]



14.3.5 Displays of Laboratory Results

Figure 32: Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter and Study Arm – White Blood Cells - Safety Population

[Implementation note: A generic figure is shown below. Plot should be generated with all treatment groups in a single image file with panels for each study arm (4 rows) with a box plot shown for each post-baseline study day that labs are drawn (D8, D22, D29). Y-axis should be labeled "[Parameter] Change from baseline ([units]). Repeat for all clinical laboratory parameters: WBC, Hgb, PLT, ALT, T. Bili, Cr]



Figures with similar format:

Figure 33: Laboratory Summary Statistics of Change from Baseline by Parameter, Maximum Severity, Study Day, and Study Arm – Hemoglobin - Safety Population

Figure 34: Laboratory Summary Statistics of Change from Baseline Results by Parameter, Maximum Severity, Study Day, and Study Arm – Platelets - Safety Population

Figure 35: Laboratory Summary Statistics of Change from Baseline by Parameter, Maximum Severity, Study Day, and Study Arm – Alanine Aminotransferase (ALT) - Safety Population

APPENDIX 3. LISTINGS MOCK-UPS

LIST OF LISTINGS

16.1.6 Listing of Subjects Receiving Investigational Product

Listing 1: 16.1.6 - Listing of Subjects Receiving Investigational Product

Subject ID	Randomized Study Arm	Product Received Study Vaccination 1	Product Received Study Vaccination 2

16.2 Database Listings by Subject

16.2.1 Discontinued Subjects

Listing 2: 16.2.1 - Early Terminations or Discontinued Subjects

[Implementation Note: Category will be either "Early Termination" or "Treatment Discontinuation." In the "Reason" column, concatenate any "specify" fields, including AE number and DV number.]

Subject ID	Study Arm	Category	Reason for Early Termination or Treatment Discontinuation	Study Day

16.2.2 Protocol Deviations

Listing 3: 16.2.2.1 - Subject-Specific Protocol Deviations

[Implementation Note: In the "Deviation" column, concatenate any and all "specify" fields (including visit number, etc.). If "Reason for Deviation" is "Other," concatenate "specify" field, separate by a colon, e.g., "Other: Subject refusal."]

Subject ID	Study Arm	DV Number	Deviation	Deviation Category	Study Day	Reason for Deviation	Deviation Resulted in AE?	Deviation Resulted in Subject Termination?	Deviation Affected Product Stability?	Deviation Resolution	Comments

Listing 4: 16.2.2.2 - Non-Subject-Specific Protocol Deviations

[Implementation Note: In the "Deviation" column, concatenate any and all "specify" fields (including visit number, etc.). If "Reason for Deviation" is "Other," concatenate "specify" field, separate by a colon, e.g., "Other: Subject refusal."]

Site	Deviation	Start Date	End Date	Reason for Deviation	Deviation Resulted in Subject Termination ?	Deviation Affected Product Stability?	Deviation Category	Deviation Resolution	Comments

16.2.3 Subjects Excluded from the Analysis

Listing 5: 16.2.3 - Subjects Excluded from Analysis Populations

[Implementation Note: This data in this listing should be congruent with the "Analysis Populations by Treatment Group" table. The reasons included here should match the SAP text that describes who will be excluded from analyses.]

Study Arm	Subject ID	Analyses in which Subject is Included	Analyses from which Subject is Excluded	Results Available?	Reason Subject Excluded
		[e.g., Safety, ITT, PP]	[e.g., Safety, ITT, PP, Day x]		

Note: "Yes" in the "Results available" column indicates that available data were removed from the analysis. "No" indicates that no data were available for inclusion in the analysis.

16.2.4 Demographic Data

Listing 6: 16.2.4.1 - Demographics Data

[Implementation Note: If a subject is multi-racial, in "Race" column, note "Multiple: (list races, separated by a comma)."]

Subject ID	Study Arm	Sex	Age at Enrollment (years)	Ethnicity	Race	BMI	Seasonal Influenza Received (2016-2017)	Seasonal Influenza Received (2017-2018)	Seasonal Influenza Received (2018-2019)

Listing 7: 16.2.4.2 – Pre-Existing and Concurrent Medical Conditions

[Implementation Note: "Condition Start Day" and "Condition End Day" are relative to enrollment (which is Day 1, day before enrollment is Day -1). If ongoing, display "Ongoing" in the "Condition End Day" column

Subject ID	Study Arm	MH Number	Medical History Term	Condition Start Day	Condition End Day	MedDRA® System Organ Class	MedDRA® Preferred Term

16.2.5 Compliance and/or Drug Concentration Data (if available)

Not applicable for this study.

16.2.6 Individual Immunogenicity Response Data

Listing 8: 16.2.6.1 - Individual HAI Response Data

Subject ID	Study Arm	Planned Time Point	Actual Study Day	Assay	Strain	Titer Replicate 1	Titer Replicate 2

Listing 9: 16.2.6.2 - Individual Neut Antibody Response Data

Subject ID	Study Arm	Planned Time Point	Actual Study Day	Assay	Strain	Titer Replicate 1	Titer Replicate 2

16.2.7 Adverse Events

Listing 10: 16.2.7.1 - Solicited Events – Systemic Symptoms

Subject ID	Study Arm	Vac Number	Post Vac Day	Assessment[a]	Symptom	Severity	Attributed to Alternate Etiology?[b]	Alternate Etiology
				MA				
				Clinic				

[a] MA = Data reported by subject on the Memory Aid and reviewed by clinic staff and reported in Solicited Events eCRF.
Clinic = Data collected by clinic staff during physical exam or symptom assessment (treatment administration record, in-clinic assessment, etc.)
[b] Grade 3 events only.

Listing 11: 16.2.7.2 - Solicited Events – Injection Site Symptoms

Subject ID	Study Arm	Vac Number	Post Vac Day	Assessment[a]	Symptom	Severity
				MA		
				Clinic		

[a] MA = Data reported by subject on the Memory Aid and reviewed by clinic staff and reported in Solicited Events eCRF.
Clinic = Data collected by clinic staff during physical exam or symptom assessment (treatment administration record, in-clinic assessment, etc.)

Listing 12: 16.2.7.3 - Unsolicited Adverse Events

Adverse Event	Associated with Vac #	# of Days Post Associated Vac (Duration)	Severity	SAE? MAAE? PIMMC?	Relationship to Study Treatment	In Not Related, Alternative Etiology	Action Taken with Study Treatment	Subject Discontinued Due to AE	Outcome	MedDRA® System Organ Class	MedDRA® Preferred Term
Subject ID: , Study Arm: , AE Number:											
				SAE: No MAAE: Yes PIMMC: No							
Comments:											
Subject ID: , Study Arm: , AE Number:											
Comments:											
Note: For additional details about SAEs, see Section 14.3.3											

16.2.8 Individual Laboratory Measurements

Listing 13: 16.2.8.1 - Clinical Laboratory Results – Chemistry

[Implementation Note: These listings (for hematology and chemistry) include all laboratory results, scheduled and unscheduled. These listings are not color-coded, but the severity should be included in parentheses after the result for abnormal results, e.g., 16.2 (Mild). The "extra" fields that are completed for abnormal results are not included in this listing; they are included in the listing of abnormal laboratory results that is included in the table shells.]

Subject ID	Study Arm	Sex	Age (years)	Planned Time Point	Actual Study Day	Alanine aminotransferase (IU/L)	Total Bilirubin (mg/dL)	Creatinine (mg/dL)

Listing 14: 16.2.8.2 - Clinical Laboratory Results – Hematology

Subject ID	Study Arm	Sex	Age (years)	Planned Time Point	Actual Study Day	White Blood Cell (10^3/µL)	Hemoglobin (g/dL)	Platelets (10^3/µL)

16.2.9 Vital Signs and Physical Exam Findings

Listing 15: 16.2.9.1 - Vital Signs

[Implementation Note: This listing includes all vital sign assessments, scheduled and unscheduled. These listings are not color-coded, but the severity should be included in parentheses after the result for abnormal assessments, e.g., 100.7 (Mild).]

Subject ID	Study Arm	Planned Time Point	Actual Study Day	Temperature (°C)	Systolic Blood Pressure (mmHg)	Diastolic Blood Pressure (mmHg)	Pulse (beats/min)

Listing 16: 16.2.9.2 - Physical Exam Findings

[Implementation Note: This listing includes all physical exam findings, scheduled and unscheduled. If a subject does not have any findings upon examination, they will not be included in this listing. If reported as an AE, display "Yes" with the AE Number in parentheses, e.g., "Yes (7)".]

Subject ID	Study Arm	Planned Time Point	Actual Study Day	Body System	Abnormal Finding	Reported as an AE? (AE Number)

16.2.10 Concomitant Medications

Listing 17: 16.2.10 - Concomitant Medications

[Implementation Note: "Medication Start Day" and "Medication End Day" are relative to enrollment (which is Day 1, day before enrollment is Day -1). For medication start dates that are > 30 days prior to enrollment, rather than use exact study days, categorize as follows:

- > 5 years prior to enrollment
- 1-5 years prior to enrollment
- 1-12 months prior to enrollment

If ongoing, display "Ongoing" in the "Medication End Day" column. If taken for an AE or MH, display "Yes" with the AE or MH Number in parentheses, e.g., "Yes (7)".]

Subject ID	Study Arm	CM Number	Medication	Medication Start Day	Medication End Day	Indication	Taken for an AE? (AE Number)	Taken for a condition on Medical History? (MH Number)

16.2.11 Pregnancy Reports

[Implementation Note: Only include the "Pregnancy Number" column if a subject has more than 1 pregnancy. Date of Conception will be calculated based on estimated delivery date. BMI will be calculated based on pre-pregnancy height and weight. Mother's weight gain will be calculated based on pre-pregnancy weight and end of pregnancy weight. If a major congenital anomaly with previous pregnancy, display "Yes" and the text from the "specify" field, separated by a colon. If any substance use is reported, include a listing of substance use. If autopsy revealed an alternate etiology, display "Yes" and the text from the "specify" field, separated by a colon. If abnormality in product of conception, display "Yes" and the text from the "specify" field, separated by a colon.]

Listing 18: 16.2.11.1 - Pregnancy Reports – Maternal Information

Subject ID	Study Arm	Pregnancy Number	Study Day Corresponding to Estimated Date of Conception	Source of Maternal Information	Pregnancy Status	Mother's Pre-Pregnancy BMI	Mother's Weight Gain During Pregnancy	Tobacco, Alcohol, or Drug Use During Pregnancy?	Medications During Pregnancy?	Maternal Complications During Pregnancy?	Maternal Complications During Labor, Delivery, or Post-Partum?
Note: Maternal Complications are included in the Adverse Event listing. Medications taken during pregnancy are included in the Concomitant Medications Listing.											

Listing 19: 16.2.11.2 - Pregnancy Reports – Gravida and Para

			Live Births												
Subject ID	**Pregnancy Number**	**Gravida**	**Extremely PB[1]**	**Very Early PB[1]**	**Early PB[1]**	**Late PB[1]**	**Early TB[2]**	**Full TB[2]**	**Late TB[2]**	**Post TB[2]**	**Still Births**	**Spontaneous Abortion/ Miscarriage**	**Elective Abortions**	**Therapeutic Abortions**	**Major Congenital Anomaly with Previous Pregnancy?**

[1] Preterm Birth
[2] Term Birth
Note: Gravida includes the current pregnancy, para events do not.

Listing 20: 16.2.11.3 - Pregnancy Reports – Live Birth Outcomes

Subject ID	**Pregnancy Number**	**Fetus Number**	**Pregnancy Outcome (for this Fetus)**	**Fetal Distress During Labor and Delivery?**	**Delivery Method**	**Gestational Age at Live Birth**	**Size for Gestational Age**	**Apgar Score, 1 minute**	**Apgar Score, 5 minutes**	**Cord pH**	**Congenital Anomalies?**	**Illnesses/ Hospitalizations within 1 Month of Birth?**

Note: Congenital Anomalies are included in the Adverse Event listing.

Listing 21: 16.2.11.4 - Pregnancy Reports – Still Birth Outcomes

Subject ID	**Date of Initial Report**	**Fetus Number**	**Pregnancy Outcome (for this Fetus)**	**Fetal Distress During Labor and Delivery?**	**Delivery Method**	**Gestational Age at Still Birth**	**Size for Gestational Age**	**Cord pH**	**Congenital Anomalies?**	**Autopsy Performed?**	**If Autopsy, Etiology for Still Birth Identified?**

Listing 22: 16.2.11.5 - Pregnancy Reports – Spontaneous, Elective, or Therapeutic Abortion Outcomes

Subject ID	Date of Initial Report	Fetus Number	Pregnancy Outcome (for this Fetus)	Gestational Age at Termination	Abnormality in Product of Conception?	Reason for Therapeutic Abortion