Collaborative Influenza Vaccine Innovation Centers

STATISTICAL ANALYSIS PLAN

for

DMID Protocol: 20-0005

Study Title:

A Multicenter, Blinded, Randomized, Placebo-Controlled, Dose-Ranging Influenza Challenge Study in Healthy Adult Volunteers to Determine the Optimal Infection Dose and Safety of a Recombinant H3N2 (A/Texas/71/2017 (H3N2), clade 3C3a) Influenza Challenge Virus

NCT04978454

Version 1.0

DATE: 11 July-2023

RESTRICTED

STUDY TITLE

Protocol Number Code:	**DMID Protocol:** 20-0005
Development Phase:	Phase 1
Products:	Live Influenza Virus RG-A/Texas/71/2017 H3N2 or Sham (SPG) inoculum
Form/Route:	Intranasal by atomizer delivery
Indication Studied:	N/A
Sponsor:	Division of Microbiology and Infectious Diseases Division of Allergy, Immunology, and Transplantation National Institute of Allergy and Infectious Diseases National Institutes of Health
Clinical Trial Initiation Date:	August 19, 2021
Clinical Trial Completion Date:	September 22, 2022
Date of the Analysis Plan:	July 11, 2023
Version Number:	1.0

This study was performed in compliance with Good Clinical Practice.

VERSION HISTORY

SAP Version	Approval Date	Change	Rationale
1.0	14JUN2023	Not Applicable	Original version. Based on v8.0 of the protocol.
[Additional versions]			

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LIST OF ABBREVIATIONS

AE	Adverse Event
ALC	Absolute Lymphocyte Count
ALT	Alanine Aminotransferase
AR	Attack Rate
AUC	Area Under Curve
BP	Blood Pressure
C	Celsius
CI	Confidence Interval
CRF	Case Report Form
CSR	Clinical Study Report
CXR	Chest X-Ray
DMID	Division of Microbiology and Infectious Diseases
EDC	Electronic Data Capture
ER	Emergency Room
F	Fahrenheit
GMT	Geometric Mean Titer
GMFR	Geometric Mean Fold-Rise
HAI	Hemagglutination Inhibition
HIV	Human Immunodeficiency Virus
ICH	International Conference on Harmonisation
IRB	Institutional Review Board
ITT	Intention to Treat
L	Liter
LLN	Lower Limit of Normal
LOD	Limit of Detection
mcg	Microgram
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligram
MJS	Modified Jackson Score
mL	Milliliter
MMID	Mild-to-Moderate Influenza Disease

List of Abbreviations *(continued)*

N	Number (typically refers to participants)
NAI	Neuraminidase Inhibition
NIH	National Institutes of Health
NLF	Nasal Lavage Fluid
NP	Nasopharyngeal
PI	Principal Investigator
PP	Per Protocol
PT	Preferred Term
RCD	Reverse Cumulative Distribution
RT-PCR	Reverse Transcription-Polymerase Chain Reaction
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SDMCC	Statistical and Data Management Coordination Center
SMC	Safety Monitoring Committee
SOC	System Organ Class
SOP	Standard Operating Procedures
$TCID_{50}$	Median Tissue Culture Infectious Dose
ULN	Upper Limit of Normal
WBC	White Blood Cell
WHO	World Health Organization

1. PREFACE

The Statistical Analysis Plan (SAP) for DMID Protocol 20-0005, A Multicenter, Blinded, Randomized, Placebo Controlled, Dose-Ranging Influenza Challenge Study in Healthy Adult Volunteers to Determine the Optimal Infection Dose and Safety of a Recombinant H3N2 (A/Texas/71/2017 (H3N2), clade 3C3a) Influenza Challenge Virus, 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, listings, and figures planned for the final analyses. Regarding the final analyses and Clinical Study Report (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).

This document contains four overarching sections: (1) a review of the study design, (2) general statistical considerations, (3) comprehensive statistical analysis methods for safety, efficacy, and immunological or other biomarker outcomes, and (4) a list of proposed tables and figures. Any deviation from this SAP will be described and justified in future amendments and/or in the CSR, as appropriate. 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

Despite current vaccination strategies and the availability of antivirals, influenza remains a leading cause of mortality, hospitalizations, missed work, missed school and economic disruption across the globe. Improved prevention and management approaches for seasonal and pandemic influenza across all populations are urgently needed, including the development of new universal vaccines that offer broad and robust protection. The human challenge model is a powerful tool for efficiently and safely determining the effectiveness of prevention and treatment options for influenza in a shorter timeframe and with a smaller number of participants compared to typical clinical trials, using a well-characterized virus strain. DMID Protocol 20-0005: A/Texas/71/2017 (H3N2) Dose-ranging Challenge Study is designed to determine the optimal infectious dose of the H3N2 (A/Texas/71/2017 (H3N2), clade 3C3a) influenza virus challenge strain for use in future Phase I clinical trials evaluating vaccine candidates. The study was designed to enroll and challenge up to 106 healthy adult volunteers with the H3N2 (A/Texas/71/2017 (H3N2), clade 3C3a) influenza virus challenge strain, plus approximately 8 participants receiving sham inoculum (saline) to allow for blinding. Participants were pre-screened for study inclusion to ensure enrolled participants have serological HAI antibody titers of ≤1:40 against the clinical challenge strain. Eligible participants were to be enrolled sequentially into dosing cohorts and randomly assigned to receive a single dose of either sham inoculum or a virus dose between 10^4 to 10^6 $TCID_{50}$ (in an allocation of 1:12 for the two lower dose levels and 1:17 at the highest dose level). Dose titration was to be conducted under an adaptive escalation schedule (see Figure 1), with dosing starting at the lowest dose (10^4 $TCID_{50}$) and only escalating to the next dose if a pre-determined infection and symptomatic attack rate was not met and the dose was determined to be safe with no pre-defined halting rule met. The attack rate (AR), defined as the percentage of participants meeting shedding and symptom criteria for symptomatic influenza virus infection (see clinical case definition in Section 3), will be determined for each challenge dose group in order to identify the optimal infectious dose (with a targeted 55%-80% AR). This adaptive, dose-ranging approach allows adjustments to challenge dose group size and escalation dose schedule to be informed by the AR and safety results.

2.1. Purpose of the Analyses

This study was designed to find a safe but infectious dose of the H3N2 (A/Texas/71/2017 (H3N2), clade 3C3a) influenza virus challenge strain to utilize in future vaccine studies. In addition to determining the rate of symptomatic influenza infection in each challenge dose group, the goals of the study include further characterization of the viral shedding and symptoms post-infection, describing the safety profile of the challenge virus, and to assess the immune response to infection.

This analysis plan covers the primary and secondary objectives of the study, along with exploratory objectives relating to available clinical data, which will be reported in the Clinical Study Report (CSR). The remaining exploratory objectives utilizing additional immunological, genomic, and/or transcriptomic data that will not be available at the time of the compilation of the primary CSR will be addressed in addenda to this analysis plan and presented in CSR addenda or separate standalone reports for the development of manuscripts.

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives and Endpoints

The study objectives and endpoints addressed in this SAP are presented below. The remaining exploratory objectives not included this SAP will be addressed in addenda to this analysis plan.

OBJECTIVES	ENDPOINTS (OUTCOME MEASURES)
Primary	
1. To determine the optimal infectious dose[1] of a recombinant influenza virus (A/Texas/71/2017 (H3N2), clade 3C3a) to be used as a clinical challenge strain in future vaccine efficacy or intervention studies as assessed by viral shedding and clinical symptoms	a. Percentage of participants within a challenge dose group with detectable shedding in nasopharyngeal (NP) swab(s) by RT-PCR over any 2 days beginning 24 hours post challenge through Day 8 and with symptom scores that meet the clinical case definition for symptomatic infection (Modified Jackson score). *See Section 3.2 for the clinical case definition for symptomatic infection.*
2. To describe viral detection by quantitative and qualitative RT-PCR from study participants at baseline and post-challenge	a. Percentage of participants within a challenge dose group with detected viral shedding in NP swab(s) each day post-challenge from Day 2 through Day 8 using qualitative RT-PCR and quantitative RT-PCR b. Magnitude of virus shedding post-challenge in each participant defined as the peak viral load in NP swab(s) from day 2 through Day 8 post-challenge by quantitative RT-PCR c. Duration of viral shedding defined as the number of days from first positive RT-PCR to last positive RT-PCR where virus is detected in NP swab(s) by quantitative or qualitative RT-PCR post challenge day 1 for each participant
3. To document clinical symptoms from self-reported surveys and standardized symptom scales at baseline and post challenge	a. Computed total symptom score from modified Jackson score through Day 8 and at Day 15. b. Percentage of participants with total symptom scores that define symptomatic or asymptomatic categories based on modified Jackson score for each participant

OBJECTIVES	ENDPOINTS (OUTCOME MEASURES)
Secondary	
1. To assess the safety profile of a live recombinant influenza strain (A/Texas/71/2017 (H3N2), clade 3C3a) following challenge in healthy adult volunteers	a. Number of adverse events (AE) reported from challenge through Day 29 b. Percentage of participants reporting any AE from challenge through Day 29 c. Number of serious adverse events (SAE) from challenge through Day 57 d. Percentage of participants reporting an SAE at any time from challenge through Day 57
2. To describe the host serum antibody responses at baseline and post-challenge	a. Percentage of participants with serological conversion defined as a minimum 4-fold rise in post-challenge serum antibodies (HAI and MN) to influenza infection at Days 8, 15, and 29, or latest time point available, post challenge compared to baseline (Day -1). b. HAI and MN antibody geometric mean titers (GMTs) at baseline (Day -1) and GMTs and Geometric Mean Fold Rise (GMFR) post-challenge at Days 8, 15, and 29, or latest time point available
3. To describe anti-HA-stalk antibody titer at baseline and post-challenge	a. Percentage of participants with serological conversion defined as a minimum 4-fold rise in post-challenge HA-stalk specific serum antibody response to HA group 2 stem domains at any day up to Day 29, or latest time point available, post challenge compared to baseline (Day -1). b. For HA-stalk specific response, the GMTs to HA group 2 stem domains at baseline (Day -1), and GMTs and GMFR at approximately Days 8, 15, and 29, or latest time point available.
Exploratory	
1. To describe the host serum neuraminidase inhibiting antibody responses at baseline and post-challenge	a. Percentage of subjects with serological conversion defined as a minimum 4-fold rise in post-challenge serum antibodies (NAI) to influenza infection at Days 8, 15, and 29, or latest time point available, post challenge compared to baseline (Day -1).

OBJECTIVES	ENDPOINTS (OUTCOME MEASURES)
	b. NAI antibody geometric mean titers (GMTs) at baseline (Day -1) and GMTs and Geometric Mean Fold Rise (GMFR) post-challenge at Days 8, 15, and 29, or latest time point available
5. To compare the clinical features of symptomatic RT-PCR-positive and RT-PCR-negative illness post-challenge	a. Self- and investigator-solicited report of clinical symptoms and their severity as measured by component questions in FLU-PRO and Validation Diary and modified Jackson score by post-challenge Study Day 15 and qualitative RT-PCR positive status
6. To explore alternative case definitions (e.g., MMID or MMID-2) for symptomatic RT-PCR-positive influenza virus infection	a. The combination of symptoms and symptom severity as determined by report using the FLU-PRO and Validation Diary or modified Jackson score which optimize sensitivity and/or specificity for classifying influenza virus infection based on qualitative RT-PCR.
7. To determine the symptomatic background within uninfected participants and between sites	a. Compare symptoms from participants inoculated with shams to participants inoculated with virus

3.2. Study Definitions and Derived Variables

3.2.1. Symptomatic Influenza Virus Infection (Shorthand: Symptomatic Infection)

Symptomatic influenza virus infection (binary yes/no) is the primary outcome for the study and will be determined by the following protocol-defined criteria, with one change from the protocol as indicated in bolded text in #1 below:

1. Viral shedding detected in NP swab(s) by qualitative **and/or quantitative** RT-PCR on at least two days beginning 24 hours after challenge until Study Day 8.
2. A cumulative symptom score ≥ 6 from daily component symptoms, including documented fever, computed across any consecutive 5-day window through Day 8 beginning on Day 2 post challenge using a modified Jackson score. Highest point score per day per sign or symptom will be used. Component signs and symptoms include fever, lymphopenia (< 1000 cells/mL), runny nose, stuffy nose, sneezing, sore throat, headache, cough, malaise, body ache, chills, feverish, shortness of breath, and earache, all ranked on a 4-point severity scale (0-3). Temperature is measured three times a day and symptoms are collected twice daily as part of the modified Jackson score.

Feverishness from the Modified Jackson Score (MJS, #2 above) and fever (graded according to Table 5) as an assessment of vital signs contribute once to the computation; the maximum of the two severity scores will be used to compute the MJS. Lymphopenia is determined based on clinical safety laboratory assessments at Days 2, 4, and 8, and graded according to Table 4.

For the purposes of determining challenge virus dose escalation during the conduct of the study, only qualitative RT-PCR results were available, and those were utilized to determine the attack rate. For the final analysis described here, quantitative RT-PCR (qRT-PCR) results will also be available, and both qualitative and quantitative RT-PCR results will be utilized for the primary analysis. As a sensitivity analysis, the attack rate will also be computed using only qualitative RT-PCR results, to compare with the primary results based on both assays. See Section 3.2.3 below for how viral shedding will be determined on each study day during the challenge period.

3.2.2. Viral Shedding Status and Duration of Viral Shedding

Viral shedding status will be determined for each participant on each study day during the challenge period, classified as follows:

- **RT-PCR+** if a qualitative RT-PCR result from the Biofire or Luminex multiplex assay is reported to be positive for Influenza A or Influenza A H3, and/or if a quantitative RT-PCR is reported to have detectable H3N2 virus.
- **RT-PCR-** if the qualitative RT-PCR results for Influenza A and Influenza A H3 are negative and the quantitative RT-PCR result indicates undetectable quantities of virus.

Detectable virus for the quantitative RT-PCR assay will be defined as being any quantity above a lower limit of detection (LLOD) reported by the laboratory conducting the assay.

Duration of viral shedding will be defined as time from the initial positive NP swab until the day after the final positive NP swab, with positivity defined as above. Intermittent negative results will be ignored for this computation.

3.2.3. Infection Status

Infection status, independent of symptom status, will be defined at the participant level in two different ways:

- Participants are considered **Infected** if viral shedding is detected in NP swab(s) by qualitative and/or quantitative RT-PCR on at least two days beginning 24 hours after challenge until Study Day 8
- Participants are considered to be **Currently Infected** from their first through their last study days meeting the viral shedding definition above (and in Section 3.2.2), regardless of any intermittent negative results between those two study days.

Pre-infection and post-infection results will be determined based on the definition of Current Infection above. New-onset symptoms will be those with a maximum severity post-infection (starting on the day of first RT-PCR positivity) above that of baseline, for infected participants.

3.2.4. Peak and Total Viral Shedding

Viral copies/mL will be estimated as a mean across quantitative RT-PCR replicates. Some replicates may be dropped from the calculations if potential quality control issues are noted. Values below the lower limit of detection will first be imputed as LOD/2 prior to taking the mean of the replicates.

Peak viral shedding will be calculated as the maximum viral concentration (RNA copies/mL) recorded the duration of the inpatient study period for each individual.

Total viral shedding over the inpatient period will be summarized by the area under the curve (AUC), approximated via the linear trapezoidal method, where the trajectory of an individual's viral concentration is

partitioned into n-1 subareas until the last inpatient observation at time t_n. As the linear trapezoidal AUC method approximates the entire area by calculating the cumulative sum of the subareas, the formula that will be applied is:

$$\text{AUC}_i = \frac{1}{2} * \sum_{j=1}^{n-1}(t_{j+1} - t_j) * (C_{ij+1} + C_{ij})$$

where $(t_{j+1} - t_j)$ is the difference between the *j*th and *j*+1th time points within the inpatient period, and C_{ij} and C_{ij+1} are the viral concentrations measured at the *j*th and *j*+1th time points for the *i*th individual. Intermittent missing values are expected to be minimal, so no imputation is planned.

3.2.5. Symptom Scores

The cumulative Modified Jackson Score (MJS; see Figure 4) will be calculated as described in Section 3.2.1.

The area under the MJS curve will be calculated for each participant from Day 2 through Day 8, for uninfected participants (see Section 3.2.3), or from the first RT-PCR+ day through the last, for infected participants; this calculation will be made as described above in Section 3.2.4 for total viral shedding, except in this case scaled by the number of days over which symptoms are summed.

The FLU-PRO total severity score is defined as the mean score across all 32 items (see Figure 5), with component scores ranging from 0 to 4. Six domain scores are also computed as mean scores, representing symptom severity in each body system. Scores will be computed for each study day utilizing the maximum severity score per symptom, and cumulative FLU-PRO scores (for the total FLU-PRO score and component scores) will be computed as the sum of the daily scores over the relevant time period.

3.2.6. Mild-to-Moderate Influenza Disease (MMID-2)

In addition to the symptomatic influenza infection definition used for the primary analysis, MMID-2 will be computed based on the following criteria reported at any point during the challenge period:

1. Viral shedding detected on at least two study days by any approved positive RT-PCR assay (qualitative or quantitative, as described in Section 3.2.2) from a NP swab.
2. Any one or more of the following symptoms or signs or laboratory findings, as related to the study agent: Arthralgia, Chest tightness, Chills, Conjunctivitis, Nasal Congestion, Sinus Congestion, Coryza, Decreased Appetite, Diarrhea, Dry Cough, Dyspnea/Shortness of Breath, Fatigue/Tiredness, Fever (>38.0°C), Headache, Lymphopenia (<1000 cells/mL), Myalgia, Nausea, Oxygen Saturation Decrease by ≥ 3% from baseline, Productive Cough, Rhinorrhea, Sore throat, and Sweats.

Fever is determined based on temperature taken as part of vital signs assessments, and lymphopenia based on the absolute lymphocyte count assessed as part of the clinical safety labs. All other items are determined via the corresponding questions on the FLU-PRO questionnaire; component questions on FLU-PRO do not all match the language above exactly, but any reported FLU-PRO symptoms result in the threshold described in #2 being met.

3.2.7. Immunogenicity Variables

Baseline values for immunogenicity (antibody) will be the last pre-challenge results available.

For individual participants, fold-rise in antibody titers will be calculated as (post-challenge titer)/(pre-challenge titer), where the pre-challenge value is the result obtained at baseline.

Seroconversion for HAI, NAI, MN, and anti-HA stalk assays will be defined as a minimum 4-fold rise in antibody titer from baseline. This corresponds to either a pre-challenge titer < LOD and a post-challenge titer ≥ 4*LOD, or a pre-challenge titer ≥ LOD and a minimum four-fold rise in post-challenge titer.

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

This is an exploratory Phase 1, blinded, randomized, dose-finding influenza virus challenge study in approximately between 62-114 (targeted maximum sample size of 106 active challenge virus plus 8 shams) males and non-pregnant females, 18 to 45 years old, inclusive, who are in good health and meet all eligibility criteria. The clinical study is designed to determine the optimal infectious dose and safety profile of a recombinant influenza A/Texas/71/2017 (H3N2) clade 3C3a strain in healthy adult volunteers.

Potentially eligible study participants may be pre-screened under an active screening protocol (DMID 20-0004) to identify those with HAI antibody titers ≤1:40 specific to the challenge virus strain. During the study screening period of this protocol (Day -45 to Day -3), participants who have not received a seasonal influenza vaccine within the past 4 months and for whom there are no safety concerns from standard safety assessments and screening labs are eligible for enrollment to the study.

Safety assessments and safety labs include a medical history review, physical examination, ECG, a chest X-ray (CXR), HIV and hepatitis B/C testing, baseline SpO_2 saturation, and testing for WBCs, ALC, hemoglobin, platelets, ALT, and creatinine. Women of childbearing potential must have a negative serum pregnancy test at screening and a negative urine pregnancy test on Day -2. Likewise, participants must have a negative drug urine toxicology test (unless the drug is deemed acceptable by the Investigator), negative multiplex respiratory viral test, and a negative SARS-CoV-2 RT-PCR test at screening and on Day -2. After a standard physical exam to exclude active infection or other illness, participants began confinement on Day -2 and remain confined for up to 12 days (Days -2 to 10).

On Day 1, participants are randomized and administered a single challenge dose of either a sham inoculum or a virus dose between 10^4 and 10^6 $TCID_{50}$. The challenge inoculum is administered using the MAD Nasal Intranasal Mucosal Atomization Device (Teleflex, Morrisville NC) attached to a 1cc syringe. Approximately 500 µL of study product is delivered in each nostril with the participant in a recumbent position. The dosing plan follows an adaptive dose-escalation schedule (Figure 1) that includes up to 8 different challenge cohorts. This dosing plan was designed to optimize participant safety, starting with a low dose and allowing flexibility to make informed adjustments between challenge cohorts from outcome results of the previous challenge cohort. For the first exposure in humans, the initial low dose challenge is conducted in a group of a targeted total of 13 participants (including 1 sham) to assure the virus is safe with no study-related or unanticipated adverse events observed or reported before further use. Dose escalation to the next (higher) dose and subsequent higher doses, if necessary, is informed by both safety and AR outcomes given a pre-specified decision algorithm for dose-escalating.

Clinical outcomes (see below) and pre-defined halting criteria were used to determine whether the trial moves forward to the higher dose of the challenge strain.

Symptomatic influenza virus infection criteria is based on the virologic assessment and the modified Jackson score. A participant is defined as having symptomatic influenza virus infection if the following criteria are met:

- Viral shedding detected in NP swab(s) by qualitative RT-PCR on at least two days beginning 24 hours after challenge until Study Day 8.
- A cumulative symptom score ≥ 6 from daily component symptoms, including documented fever, computed across any consecutive 5-day window through Day 8 beginning on Day 2 post challenge

using a modified Jackson score. Highest point score per day per sign or symptom will be used. Component signs and symptoms include fever, lymphopenia (< 1000 cells/mL), runny nose, stuffy nose, sneezing, sore throat, headache, cough, malaise, body ache, chills, feverish, shortness of breath, and earache ranked on a 4-point severity scale (0-3). Temperature will be measured three times a day and symptoms will be collected twice daily on the modified Jackson score. A documented fever and feeling feverish will count as one point on the cumulative symptom score.

The study design is presented in Figure 1. The AR is measured as the proportion of participants meeting the criteria for symptomatic influenza infection described above (and in Section 3.2), and the safety threshold used to halt dose escalation is given by the halting rules described in Section 7.1.1 of the protocol. Note that the AR was determined across all participants in a challenge cohort, blinded to receipt of active challenge virus or sham inoculum.

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

Participants were randomized to receive either Live Influenza Virus RG-A/Texas/71/2017 (H3N2) challenge virus or sham inoculum within each challenge dose group. Participants received one of three doses of challenge virus depending upon the challenge cohort into which they enrolled using the adaptive trial design. The targeted ratios of participants randomized to receive either challenge virus or sham inoculum are given below.

Challenge Cohort	Challenge Dose Group	Challenge virus: Sham inoculum
1A, 1B, 1C	10^4 $TCID_{50}$	Targeted 12:1
2A, 2B, 2C	10^5 $TCID_{50}$	Targeted 12:1
3A, 3B	10^6 $TCID_{50}$	Targeted 17:1

Sham inoculum was included as a control primarily to maintain the blind of the study, so neither participants nor study staff assessing participants' symptoms could be certain of the study assignment and unintentionally introduce bias in determining the incidence of influenza symptoms.

4.3. Selection of Study Population

The study population consists of male and female adult volunteers aged 18-45 years, inclusive, and generally in good health. Inclusion and exclusion criteria are presented in Sections 5.1 and 5.2 of the protocol, respectively. Importantly, screening is conducted after admission to the site's confinement unit (and prior to administration of the study challenge) for active viral infections and recent exposures to vaccinations or viruses that might impact study assessments.

4.4. Statistical Considerations for the Study Design

The study is not designed to achieve predetermined levels of power or precision to address the primary, secondary, or exploratory objectives. The adaptive design was chosen to utilize more of the available sample size at higher doses, unless there is adequate evidence that one of the lower doses is sufficiently infectious.

4.4.1. Sample Size Considerations

Figure 2 shows the probability of meeting the infection threshold for further enrollment at a dose, given varying numbers of participants enrolled at that dose (10 enrolled in Cohorts 1A or 2A, 15 at Cohort 3A, or 20 in Cohorts 1A+1B or 2A+2B), varying true infection probabilities, and the thresholds for further enrollment. For illustration, with n=10 participants enrolled in Cohort 1A at 10^4 $TCID_{50}$, the probability of achieving 8 infections would be only 0.01 if the true infection probability were 0.4, compared to 0.38 if the true infection probability were 0.7.

Depending on the number of infections observed at each dose level, the final sample size for each dose group would be approximately 10, 15, 20 or 30. Figure 3 shows the estimated infection probabilities and associated exact 95% confidence intervals that would result from observing varying numbers of symptomatic influenza events at a given dose level. The maximum CI width occurs at 50% observed events. With 30 participants enrolled at the optimal dose, this would correspond to observing 15 symptomatic influenza events and an estimated CI of (31.3%, 68.7%).

Table 2 gives the probability of observing one or more safety events, such as a solicited symptom or an AE of a particular classification in varying total dose group sizes, given underlying true event probabilities.

4.4.2. Allocation of Participants to Study Arms (Randomization)

The list of randomized treatment assignments is prepared by the study statistical team at Emmes and included in the enrollment module of Emmes' Internet Data Entry System (IDES). IDES assigns each participant a treatment code from the list after demographic and eligibility data have been entered into the system. A designated individual at each site is provided with a treatment key, which links the treatment code to the actual study assignment, which is kept in a secure place. Manual back-up randomization procedures are provided in the manual of procedures (MOP) for use in the event that the site temporarily loses access to the internet or the online enrollment system is unavailable.

4.5. Study Products

4.5.1. Study Products Administered

Participants were administered 1.0 mL (0.5 mL per nostril) of live influenza virus RG-A/Texas/71/2017 H3N2 or sham inoculum intranasally via atomizer delivery on Day 1.

4.5.2. Identity of Investigational Product(s)

A GMP lot of reverse-genetics (RG) derived, recombinant influenza A/Texas/71/2017 (H3N2) virus for the purpose of conducting human influenza virus challenge studies has been manufactured by Charles River Laboratories (CRL), Malvern, PA.

Live Influenza Virus RG-A/Texas/71/2017 (H3N2)

The final product was vialed at approximately 1.86 X 10^6 $TCID_{50}$/mL of Influenza A Human Challenge Virus (H3N2) in 1X SPG (7.4% sucrose, 3.8 mM KH_2PO_4, 7.2 mM K_2HPO_4, 5.4 mM L-glutamic acid). Each vial has a fill volume of 0.6 mL.

Diluent and Sham Product

1X SPG (7.4% sucrose, 3.8 mM KH_2PO_4, 7.2 mM K_2HPO_4, 5.4 mM L-glutamic acid). Each vial has a fill volume of 1.2 mL. The diluent is also be used as a sham inoculum.

4.5.3. Selection of Doses in the Study

Participants are randomized to receive a single challenge dose of either sham inoculum or a virus dose between 10^4 and 10^6 $TCID_{50}$. Historically, a 10^4 $TCID_{50}$ has been safely used as the lowest dose tested in other influenza human challenge studies [1-3]. There was no indication from non-clinical studies of the recombinant influenza A/Texas/71/2017 (H3N2), clade 3C3a virus in mouse, hamster, and ferret models of infection that this virus would behave any differently in humans than the wild-type parent influenza virus.

The dosing plan will follow an adaptive dose escalation schedule (Figure 1) that will include up to three different challenge dosing groups. This dosing plan is designed to optimize participant safety, starting with a low dose and allowing flexibility to make informed adjustments between challenge cohorts from outcome results of the previous challenge cohort.

4.5.4. Selection and Timing of Dose for Each Participant

On Day 1, eligibility and clinical status are reviewed. If criteria for proceeding with challenge are met, participants receive live influenza virus RG-A/Texas/71/2017 H3N2 or sham inoculum intranasally.

4.5.5. Blinding

Study product is prepared by an unblinded pharmacist but administered by a blinded administrator. The participants, the study personnel who perform study assessments after administration, data entry personnel at the sites, and laboratory personnel performing immunologic assays are blinded to study assignment. The administered study products are visually indistinguishable to blinded staff and participants.

The nasal sample respiratory virus panel result only accessible by unblinded staff and is not shared or revealed to blinded staff. Except for the nasal sample respiratory virus panel result, all study assessments are performed by blinded study personnel. All other staff, as well as all participants, are blinded to study assignments.

The SMC receive data in aggregate by cohort and challenge dose group, and may be unblinded to individual study product assignments, as needed, to adequately assess safety issues.

4.5.6. Prior and Concomitant Therapy

All concomitant medications taken within 90 days prior to signing the ICF are reviewed with participants to determine stability of chronic diseases and eligibility. Medications reported in the eCRF are limited to those taken within 30 days prior to challenge. Concomitant medications are reviewed at every study visit through the end of the study. Women of childbearing potential in a heterosexual relationship must agree to use true abstinence or use at least one acceptable primary form of contraception through the end of the study. Receipt of any influenza vaccine during the 2019/2020 and/or 2020/2021 influenza vaccine seasons, regardless of the date of receipt, are documented. Prior participation in any influenza challenge study will be documented. Prior enrollment in any influenza challenge study within the prior two years and/or receipt of any influenza vaccine four months prior to challenge is exclusionary. Participants should not have received any investigational drug/investigational vaccine/licensed vaccine within 30 days prior to the planned date of challenge, with the exception of an EUA authorized or licensed COVID-19 vaccine product ≥ two weeks prior to admission. The following prescription or over-the-counter medications cannot be used within 7 days prior to admission to and through the confinement period, unless approved by the investigator: oseltamivir, zanamivir, peramivir, baloxavir marboxil, amantadine (generic) and rimantadine (Flumadine and generic), aspirin, intranasal steroids, decongestants, antihistamines, and other non-steroidal anti-inflammatory drugs (NSAIDs). Participants who use asthma medications including inhaled, oral, or IV corticosteroids, leukotriene

modifiers, long and short acting beta agonists, theophylline, ipratropium, biologics, will be excluded from the study. Any medications that may be associated with impaired immune responsiveness including, but not limited to, corticosteroids exceeding 10 mg/day of prednisone equivalent, allergy injections, immunoglobulin, interferon, immunomodulators, cytotoxic drugs, or systemic corticosteroids or other similar or toxic drugs cannot be used during the preceding 12-month period prior to screening. Low dose topical and intranasal steroid preparations used for a discrete period of time are permitted. Participants should not have received blood or blood products during the six months prior to the planned date of challenge.

4.5.7. Study Product Compliance

All participants are directly observed at the time of dosing by a member of the clinical research team licensed to administer the study product at the clinical site.

4.6. Clinical, Safety, and Immunogenicity Variables

The Schedule of Activities (SoA) describes the planned visits and assessments at each visit and is presented in Table 1.

4.6.1. Clinical Variables

Clinical variables such as viral detection, viral shedding, and solicited symptoms and laboratory findings that are a part of the definition of symptomatic influenza virus infection, are assessed at each study day during the confinement period, after the day of study challenge. Symptoms are also assessed in the clinic visit on Day 15.

Virologic assessments are done at screening (Days -45 to -3), baseline (Days -2 and -1), and then repeated daily from Days 2-8 during the confinement period or for a longer period if still RT-PCR positive for influenza on Days 7 or 8 until two negative swabs are confirmed, at least 12 hours apart, consecutively. Only qualitative RT-PCR is performed at the screening visit, but subsequently nasopharyngeal (NP) swab samples are collected for quantitative RT-PCR as well. Quantitative RT-PCR (qRT-PCR) will be conducted by a research laboratory at Duke University. Qualitative RT-PCR is conducted via multiplex respiratory virus assay (BIOFIRE® FILMARRAY® respiratory panel by bioMérieux or Luminex xTAG®) on NP swabs at the local clinical site. Qualitative and quantitative RT-PCR for influenza from NLF specimens and quantitative viral culture from NP swabs and/or NLF specimens may be performed as well; these would be analyzed subsequently to compilation of the primary CSR, if the assays are performed.

Symptomatic influenza infection is assessed using a Modified Jackson score (MJS) collected by study staff twice a day (approximately 8 AM and after 3 PM) from Day -2 until the time of discharge, and again at the Day 15 visit to assess any ongoing symptoms. Figure 4 displays the MJS investigator tool for assessing symptoms. Fever and lymphopenia, both included among the MJS symptoms for determining the symptomatic influenza attack rate, are assessed separately from the MJS form.

An additional validated, patient-reported outcome (PRO) measure to standardize assessment of influenza symptoms in clinical research (i.e., FLU-PRO Survey Instrument and Validation Diary) is to be completed by participants once a day (after 3:00 PM) from Day -2 through Day 15. The investigators review the FLU-PRO and Validation Diary at the Day 15 visit to assess any ongoing symptoms. The FLU-PRO questionnaire is presented in Figure 5 for reference.

4.6.2. Safety Variables

Safety is assessed by the incidence, frequency, and severity of:

1. Study product-related serious adverse events occurring from the time of the challenge through the end of the study (approximately 2 months post-challenge).
2. Clinical safety laboratory adverse events occurring from the time of challenge through Study Day 8. Parameters to be evaluated include: white blood cells (WBCs), absolute lymphocyte count, hemoglobin, platelets, and alanine transaminase (ALT), and creatinine (Cr).
3. Adverse Events (AEs) – non-serious adverse events occurring from the time of challenge through approximately 28 days post-challenge.

Unsolicited Adverse Events

The FDA defines an AE as any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related (21 CFR 312.32 (a)). An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of medicinal (investigational) product.

In this study, solicited symptoms of symptomatic influenza infection are collected from the time of challenge through 7 days post-challenge and will not be considered adverse events. Objective clinical examination findings consistent with the solicited symptom, such as oropharyngeal erythema or lymphadenopathy, will also not be considered AEs. Any influenza signs, symptoms or lab findings determined by the clinician to have exceeded the expected severity or any moderate or severe complications, as listed in Section 2.3.1 of the protocol, are considered unsolicited adverse events. Events that are not consistent with illness due to influenza, and events that occur after administration of antivirals, are considered unsolicited AEs as well. Note that there are no solicited AEs for this study.

AEs, along with severity, relatedness to study challenge, duration, and outcome, are assessed at every study visit. Additionally, a physical exam is conducted at screening (Day -45 to -3), and a more targeted physical examination is conducted at pre-challenge screen (Day -2), pre-challenge baseline (Day -1), viral challenge (Days 1-8), and at follow-up visits (Days 15, 29, 57). The targeted physical exam includes evaluation of the oral/pharyngeal, neck, lung, and heart exams. An otoscopic exam is performed as part of the targeted physical exam at baseline (Day -1) and as needed. Additional clinical evaluations are performed if clinically indicated.

Unsolicited AEs are graded according to the following severity scale:

- Mild (Grade 1): Events that are usually transient and may require only minimal or no treatment or therapeutic intervention and generally do not interfere with the participant's usual activities of daily living.
- Moderate (Grade 2): Events that are usually alleviated with additional specific therapeutic intervention. The event interferes with usual activities of daily living, causing discomfort but poses no significant or permanent risk of harm to the research participant.
- Severe (Grade 3): Events interrupt usual activities of daily living, or significantly affect clinical status, or may require intensive therapeutic intervention. Severe events are usually incapacitating.

Vital Signs

Vital signs are assessed at screening (Day -45 to -3), pre-challenge screen (Day -2), pre-challenge baseline (Day -1), pre-challenge baseline (Day 1 prior to challenge), post-challenge (Days 1-8) approximately within each 8-hour period (i.e., three times per day), and at follow-up visits (Days 15, 29, 57). Vital signs assessed include pulse, systolic blood pressure, diastolic blood pressure, respiratory rate, and oral temperature. SpO_2 is assessed at screening (Day -45 to -3), pre-challenge screen (Day -2), pre-challenge baseline (Day -1), pre-challenge baseline (Day 1 prior to challenge), post-challenge (Days 1-8) approximately within each 8-hour period (i.e., three times per day) and follow-up (Days 15, 29, 57).

Vital signs are graded for severity according to the scales presented in Table 5.

Clinical Laboratory Evaluations

Laboratory assessments for safety include:

- Serology at screening: HIV, Hepatitis B surface antigen, Hepatitis C antibody, and HAI titer
- Hematology (at screening and study Days 2, 4, and 8): white blood cells (WBCs), absolute lymphocyte count, hemoglobin, and platelets
- Chemistry at (as screening and study Days 2, 4, and 8): alanine transaminase (ALT) and creatinine (Cr)
- A urine toxicology test (amphetamines, cocaine, and opiates,) at screening and on the day of admission to the confinement unit (amphetamines, cocaine, and opiates)
- Serum HCG pregnancy test at screening
- Urine HCG pregnancy test (for female participants of childbearing potential) to be done before the baseline CXR (if > 7 days have passed since the negative serum pregnancy test was drawn) and on Day -2, to be performed locally.
- Qualitative multiplex respiratory virus assay (BIOFIRE® FILMARRAY® respiratory panel by bioMérieux or Luminex xTAG®), including SARS-CoV-2 RT-PCR, on NP swab(s) at screening and on Day -2 and Day -1 in order to remain on the unit for challenge and daily from Day 2 through the confinement period.

Safety laboratory values are graded according to the severity scales presented in Table 4.

Other Safety Evaluations

Additional assessments are made at screening to help determine eligibility for the study challenge, and some are also conducted post-challenge to determine potential unsolicited adverse events.

SpO_2 is assessed at screening (Day -45 to -3), pre-challenge screen (Day -2), pre-challenge baseline (Day -1), pre-challenge baseline (Day 1 prior to challenge), post-challenge (Days 1-8) approximately within each 8-hour period (i.e., three times per day), and at follow-up visits (Days 15, 29, 57).

A 12-lead ECG is performed at screening (Day -45 to -3), post-challenge (Day 6), and as clinically indicated and confirmed by the PI or designated clinician licensed to make medical diagnoses and listed on Form FDA 1572. Screening ECGs must be within normal reference ranges or deemed not clinically significant. A PA and lateral chest x-ray (CXR) is performed at screening (Day -45 to -3).

4.6.3. Immunogenicity Variables

Individual hemagglutinin inhibition (HAI) and microneutralization (MN) antibody results will be reported by the research laboratory at Duke University. Neuraminidase inhibition (NAI) and anti-HA stalk antibody results will be reported by the research laboratory at the University of Maryland. Assay results are reported as endpoint titers, with values of 10*2k, where k=0, 1, 2, etc., or are reported to be below the lower limit of detection (LOD). See Section 3.2 for definitions of derived variables for the analysis of HAI, MN, NAI, and anti-HA stalk assay data.

All immunogenicity data will be uploaded into the SDMCC's electronic data capture system. Data for the remaining exploratory assays and the corresponding analyses not covered in this document will be described in a separate analysis plan addendum(a).

4.7. Genomics and Transcriptomics

Objectives relating to genomics and transcriptomics endpoints will be addressed in a separate analysis plan.

5. GENERAL STATISTICAL CONSIDERATIONS

5.1. General Principles

The challenge period is defined as the day of study challenge (Day 1) through discharge from the confinement period (Day 8 or later).

Continuous variables will generally be summarized using the following descriptive statistics: non-missing sample size (denoted by "n"), mean or geometric mean, standard deviation, minimum, median, and maximum. Titers will be summarized with geometric means, first across replicates to compute one value for each individual sample and then across participants within clinical outcome groups. The frequencies and percentages (based on the non-missing sample size) of observed levels will be reported for categorical measures. Data listings will typically be sorted by site or other grouping variable (e.g. infection status), participant, and by visit number within participant, where appropriate. All tables will be annotated with the total population size relevant to that table, including any missing observations.

For continuous variables, confidence intervals will be computed based on the t-distribution, unless the data appear especially non-normal and the sample sizes for the analysis are insufficient to apply the central limit theorem. Bootstrap confidence intervals may be calculated instead if the t-distribution is determined to be unsuitable. For binary variables, confidence intervals will be computed using the exact Clopper-Pearson method.

5.2. Timing of Analyses

The adaptive study design is based on periodic analysis of symptoms and infection status to determine whether dose escalation criteria have been met. These analyses are blinded, assessing the attack rate across all participants at a given dose level, regardless of receipt of active challenge virus or sham inoculum.

The CSR will be completed when all primary and secondary safety, clinical, and immunological endpoint data are available. Any available data from the exploratory endpoints may also be included. Additional exploratory endpoint data would be included in an addendum to the CSR or standalone analysis report(s) to be incorporated into manuscripts.

A topline report to facilitate timely reporting of primary and secondary objective analysis results will be generated prior to the compilation of the CSR. This will consist of a select portion of tables, which are indicated in Appendix 1 with asterisks alongside titles. These results will be final and will be included in the CSR as well. A portion of these analyses will be presented at the CIVICs network's 2023 annual meeting, prior to publishing the results in the National Library of Medicine (clinicaltrials.gov).

5.3. Analysis Populations

Analyses will be conducted within one of the following populations, or in subsets of these populations, such as infected participants, or those receiving what is determined to be the optimal dose.

5.3.1. Safety (SA) Population

The Safety population will include all participants who received study influenza challenge or sham inoculum.

5.3.2. Intent-to-Treat (ITT) Population

The Intent-to-Treat population will consist of all enrolled participants.

5.3.3. Per Protocol (PP) Population

The Per-Protocol population will include participants in the ITT population with the following exclusions of data:

- All data from any participants who withdraw prior to the end of the challenge period
- Data from any visit that occurs substantially out of window
- Data from all visits subsequent to major protocol deviations that could impact the validity of later data, such as:
  - Study ineligibility at enrollment (determined thereafter)
  - Receipt of immunosuppression or any medications that may be associated with impaired responsiveness
  - Receipt of any investigational drug/investigational vaccine/licensed vaccine
  - Receipt of blood or blood products, or blood donation

5.4. Covariates and Subgroups

Exploratory analysis will include an assessment of the association between the following covariates and development of symptomatic influenza illness: age (continuous), sex (male, female), prior receipt of seasonal influenza vaccine(s) or viral challenge (yes/no), and clinical site (DU or UMD).

The protocol does not define any formal subgroup analyses, and the study was not powered to perform subgroup analyses.

5.5. Missing Data and Outliers

All attempts are made to collect all data per protocol, and missing data are expected to be minimal due to the nature of the study, with participants in confinement units for much of the follow-up period. No imputation is planned for missing data.

Any data point that appears to be erroneous or inexplicable based on the observed data distribution and the statistical team's understanding of the analysis variables will be investigated as a possible outlier. If data points are identified as outliers, sensitivity analyses may be performed to examine the impact of including or excluding the outliers. Any substantive differences in these analyses will be reported.

5.6. Interim Analyses and Data Monitoring

No formal interim analysis is planned., but analysis of symptoms and infection status is performed after completion of the confinement period for each dosing cohort to determine whether dose escalation criteria have been met.

A safety monitoring committee (SMC) meets to review safety and disposition data at scheduled time points or ad hoc as needed during this study, as delineated in the SMC charter.

5.7. Multicenter Studies

For most analyses, data will be pooled across both clinical sites. While the two sites use standardized procedures and rely on central laboratories for the assessment of immunogenicity and clinical endpoints, some exploratory analysis will be conducted within site-specific subgroups.

5.8. Multiple Comparisons/Multiplicity

Analysis will be primarily descriptive, but hypothesis testing results will be reported for regression models and some other selected comparisons of interest. No adjustments for multiplicity are planned, but the number of comparisons made will be factored into the interpretation of results, as appropriate.

6. STUDY PARTICIPANTS

6.1. Demographic and Other Baseline Characteristics

Sex, race, ethnicity, age, and BMI will be summarized by site in Table 9 and Table 10 and by challenge dose group Table 11 and Table 12. Age will be summarized as both a categorical and continuous variable. Baseline characteristics will be detailed per participant in Listing 6.

6.2. Disposition of Participants

Screening failures will be summarized in Table 8. A summary of participant disposition will be presented in Table 6, including the total number of participants screened, enrolled, challenged, terminated early, and having completed the last follow-up visit.

The number and percentage of enrolled participants excluded from each analysis population are presented in Table 7. A listing of participants excluded from each analysis population will be presented in Listing 5.

A flowchart showing the disposition of study participants, adapted from the CONSORT Statement, will be included and will present the number of participants screened, challenged, lost to follow up, and analyzed (Figure 6).

A listing of participants who discharged early or terminated from study follow-up and the reason will be included in Listing 2, where details about missed follow-up visits related to the Coronavirus Disease 2019 (COVID-19) pandemic will be included.

6.3. Prior and Concurrent Medical Conditions

All current illnesses and past or pre-existing medical conditions will be coded using Medical Dictionary for Regulatory Activities (MedDRA®) version 25.1 or higher.

Summaries of participants' prior and concurrent medical conditions will be presented by challenge dose group and MedDRA system organ class in Table 13.

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

6.4. Prior and Concomitant Medications

Prior (within 90 days of enrollment) and concomitant medications will be coded to the Anatomical Therapeutic Classification (ATC) using the WHO Drug Dictionary. The use of concomitant medications during the study will be summarized by ATC1 and ATC2 code, as well as challenge dose group, for the Safety population in Table 79.

A listing of concomitant medications will be presented in Listing 17.

6.5. Measurements of Study Product Compliance

Participants are directly observed at the time of dosing by a member of the clinical research team licensed to administer the study product. The number of participants receiving the challenge virus or sham inoculum will be presented as part of the participant disposition table (Table 6). The timing of challenge and study assignment will be presented for all challenged participants in Listing 1.

6.6. Protocol Deviations

A summary of participant-specific protocol deviations will be presented by the reason for the deviation and the deviation category for all enrolled participants (Table 3). All participant-specific protocol deviations and non-participant-specific protocol deviations will be included in Listing 3 and Listing 4, respectively.

7. CLINICAL EVALUATIONS

Analysis of clinical endpoints that do not involve immunoassays will be done in the Safety population. Analyses involving immune responses will be conducted using the ITT population. If at least 10% of analysis data would be excluded by the reasons given in Section 5.3.3, some analyses may be conducted in the PP population as well, as a sensitivity analysis.

7.1. Primary Clinical Analysis

7.1.1. Symptomatic Influenza Attack Rate

The primary objectives of the study include determining the optimal dose of the study challenge virus, for future use as a clinical challenge strain in vaccine efficacy or intervention studies. This evaluation includes an objective assessment of the AR for symptomatic influenza infection (as defined in Section 3.2.1), with additional primary objectives to further describe the symptoms and the viral detection via RT-PCR (qualitative and quantitative) for each challenge dose group and cross-tabulated by the other related outcomes.

The symptomatic influenza AR will be analyzed by challenge dose group in Table 14, along with component outcomes and a summary of the per-participant maximum cumulative MJS score during the challenge period, and the total MJS score at Day 15.

7.1.2. Influenza Symptoms

The maximum severity of influenza symptoms during the challenge period, reported as part of the Modified Jackson Score and used to determine the AR, will be summarized by challenge dose group in Table 15, and separately by infection status (see Section 3.2.3) in Table 16 and Figure 7 (infected participants) and Table 17 and Figure 8 (uninfected participants). Symptoms reported on Study Day 15 will be presented similarly in Table 18 and Table 19. Symptoms over the challenge period will also be summarized by infection status, independent of challenge dose group, in Table 20, and Day 15 symptoms will be presented in Table 21.

New-onset symptoms (see Section 3.2.3) among infected participants will be summarized in Figure 9, and the maximum severity of symptoms will be summarized by concurrent infection status in Table 26. Wilcoxon signed rank tests will be used to compare maximum severities among infected participants: pre-infection to during infection, post-infection to during infection, and pre-infection to post-infection, in Table 27. No p-value adjustment is planned for multiple comparisons, but the number of comparisons made will be considered when interpreting the results. Current/concurrent infection status is defined in Section 3.2.3.

The maximum symptom severities reported for each study day during the challenge period and at any point post-challenge will be summarized for currently infected participants, separately by challenge dose group in Table 22 through Table 25. At baseline and Day 1, all participants will be included in these summaries, as a comparison for post-infection symptoms.

Total MJS scores during the challenge period will be presented by study day and challenge group in Figure 10, with RT-PCR+ study days indicated with annotation in the given cell.

MJS symptoms will be presented in detail in Listing 8.

7.1.3. Viral Shedding – Timing, Duration, and Magnitude

Viral shedding is measured by qualitative and quantitative RT-PCR, which are both incorporated into determining viral shedding status (binary yes/no) for a given day, as described in Section 3.2.2.

Qualitative RT-PCR status will be cross-tabulated with RT-qPCR status (RT-PCR+/undetectable) by challenge dose group in Table 28. Qualitative RT-PCR results will be summarized for all targets of the multiplex assays for each study day during the challenge period in Table 29 through Table 32. An overall comparison of qualitative and quantitative RT-PCR results will be presented in Table 33, to assess the agreement of the two assays.

The number of days to first detected viral shedding will be summarized by challenge dose group in Table 34. The median number of days to infection and corresponding 95% CI will be estimated for each group via the Kaplan-Meier method, in order to account for the censoring of participants who never tested RT-PCR+ throughout the challenge period.

The number of total days with RT-PCR+ results will be summarized by challenge dose group in Table 35. A summary of peak viral shedding, total viral shedding (via AUC), and the duration of viral shedding (from first positive through last positive) will be presented in Table 36.

7.2. Exploratory Clinical Analyses

7.2.1. Comparisons of MJS to FLU-PRO

Total FLU-PRO scores will be presented by study day and challenge group in Figure 11, with RT-PCR+ study days annotated on the heatmap, for comparison to Figure 10 for MJS scores.

FLU-PRO symptoms will be summarized by study day for currently infected participants (similarly to MJS symptoms in Table 19 through Table 22) in Table 37 through Table 40, for a qualitative comparison between the two symptom scoring tools. The maximum severities of symptoms reported during the challenge period will be cross-tabulated between MJS and FLU-PRO in Table 41 (infected participants) and Table 42 (uninfected participants). Cumulative FLU-PRO scores will be summarized by challenge dose group and infection status in Table 43, with maximum cumulative MJS scores (already analyzed as part of the primary endpoint in Table 14) included for reference.

Scatterplots of each symptom score by total viral shedding (log-10 AUC) will be presented in Figure 12, along with Spearman rank correlation coefficient estimates between each score and the area under the viral shedding curve. Mean total MJS and FLU-PRO scores will be presented by challenge dose group, viral shedding status, and study day during the challenge period, in Figure 13; the entire distributions of symptom scores will be presented in boxplots in Figure 14.

FLU-PRO symptoms will be detailed in Listing 9, and answers to additional FLU-PRO questions will be presented in Listing 10.

7.2.2. Comparisons of Symptoms Between Clinical Sites

To compare symptom background signals, as well as post-infection symptoms, between clinical sites, MJS Symptoms will be summarized by site, for infected participants in Table 44 and uninfected participants in Table 45.

7.2.3. Alternative Definitions of Symptomatic Influenza Infection

While the study was not powered to establish a predictive signature of symptoms for influenza infection, exploratory analysis will be conducted to determine a predictive multi-symptom model to validate in an independent influenza challenge study.

To predict infection status, as defined by two or more days with RT-PCR+ results, the maximum severity of each symptom reported during current infection (for infected participants) or across the entire challenge period (for uninfected participants) will be included as candidate predictors in a penalized logistic regression model (lasso) [4]. The penalization parameter will be selected based on 10-fold cross-validation. The resultant model will be refit without penalization to remove the bias in estimation of the coefficients caused by the penalization parameter, with estimated odds ratios presented in Table 46. The internal performance of the model in the training set will be shown in the receiver operating characteristic (ROC) curve in Figure 15. The optimal cutpoint from the model, as determined by Youden's J statistic [5], will be used in a future validation of these results.

Additionally, the MMID-2 outcome will be compared with the primary symptomatic influenza infection outcome in Table 47. Sensitivity analyses will also be conducted to assess varying thresholds for MJS scores and, separately, for the number of days of detectable viral shedding (Table 14).

7.2.4. Other Exploratory Clinical Analyses

An exploratory logistic regression model will be fit to assess the associations between baseline characteristics and the development of symptomatic influenza infection post-challenge, in Table 48. Challenge virus dose will be included as a continuous covariate, with sham inoculum being assigned a $TCID_{50}$ value of zero. Age at baseline (in years), sex (male vs. female), prior receipt of seasonal influenza vaccine or viral challenge (yes vs. no), and clinical site (UMD vs. DU) will be included as other covariates.

8. IMMUNOLOGICAL EVALUATION

8.1. Secondary Immunogenicity Analyses

Only secondary immunogenicity analysis of HAI, MN, NAI, and anti-HA stalk assay data will be included in the interim CSR. Exploratory immunogenicity analysis not included in this SAP will be planned in a separate SAP addenda to this analysis plan and presented in an addendum to the CSR or one or more separate reports for the purposes of manuscript development.

Immunogenicity analyses are planned in the ITT population. If 10% or more of the timepoints utilized in the immunogenicity analyses would be excluded by the list given in Section 5.3.3 to define the Per Protocol population, the secondary immunogenicity analyses will be conducted in the PP population as a sensitivity analysis.

HAI, MN, and anti-HA stalk antibody titers against the challenge strain will be analyzed by time point, challenge dose group, and infection status in Table 49, Table 50, and Table 52, respectively. Geometric mean titers (GMTs) will be computed at each time point for each group, as well as geometric mean fold-rise (GMFR) and seroconversion (as defined in Section 3.2.7) at each post-challenge time point. Associated 95% CIs will be presented as well. GMTs and 95% CIs will be presented graphically in Figure 16 and Figure 18, and the entire distribution of titers reported at each visit will be presented in reverse cumulative distribution (RCD) curves in Figure 19, Figure 20, and Figure 22.

The assays will be analyzed similarly by symptomatic infection status in Table 53, Table 54, and Table 56.

Antibody titers will be listed, by assay, in Listing 11.

8.2. Exploratory Immunogenicity Analyses

NAI antibody titers will be analyzed similarly to HAI, MN, and anti-HA stalk antibody titers (see Section 8.1), in Table 51, Table 55, Figure 17, and Figure 21. These will be included in the primary CSR if the data are available at the time of non-clinical database lock for the analysis; otherwise, they will be included in an addendum report.

9. GENOMIC AND/OR OTHER BIOMARKERS EVALUATIONS

All genomic endpoints will be addressed in a separate SAP addendum(a).

10. SAFETY EVALUATION

All summaries and analysis of safety data will be presented for the Safety population. The denominator for the percentages may be based on the number of non-missing observations for an assessment or based on the number of participants in a population. This will be described for each table.

10.1. Adverse Events

For this study, only unsolicited AEs and severe influenza complications were considered to be adverse events. An overall summary of all AEs will be presented in Table 57. A summary of AEs occurring in at least 5% or more of participants will be presented in Table 58.

10.1.1. Solicited Events

No solicited adverse events were collected for this study.

10.1.2. Unsolicited Adverse Events

The incidence and frequency of unsolicited AEs occurring post-challenge will be summarized by MedDRA System Organ Class (SOC) and Preferred Term (PT), time post-challenge, and challenge dose group in Table 59. The incidence of unsolicited AEs will be further cross-tabulated by relatedness to study challenge in Table 60. The frequency of related unsolicited AEs will be displayed graphically in Figure 23 and the incidence in Figure 24.

All unsolicited AEs will be detailed in Listing 12.

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

A listing of serious adverse events (SAEs), including any deaths reported during the study, will be presented in Table 61. Severe influenza complications reported as adverse events will be reported in Table 62.

10.3. Pregnancies

Pregnancies occurring in study participants are reported via Advantage electronic data capture system (Advantage eClinical) on the Pregnancy Report form. Efforts are made to follow all pregnancies reported throughout the course this study to pregnancy outcome pending the participant's permission.

Details of any pregnancies and their outcomes are presented in Listing 18 through Listing 22.

10.4. Clinical Laboratory Evaluations

Chemistry parameters assessed as part of clinical safety evaluations include creatinine and alanine aminotransferase (ALT). Hematology parameters assessed include white blood cells, absolute lymphocyte count, hemoglobin, and platelets. These are graded according to the protocol-defined toxicity table (Table 4). Abnormal values are listed in Table 63 and Table 64 and summarized by parameter and challenge dose group in Table 65 through Table 72. Clinical laboratory assessments are listed in full in Listing 13 (Chemistry) and Listing 14 (Hematology).

10.5. Vital Signs and Physical Evaluations

Vital signs, including pulse, systolic blood pressure, diastolic blood pressure, respiratory rate, oxygen saturation and oral temperature, were assessed at each study visit, including multiple times per day during the

challenge period. Fever was assessed as part of the evaluation of the primary symptomatic influenza infection endpoint.

Maximum severity of heart rate, systolic blood pressure, diastolic blood pressure, oxygen saturation and respiratory rate are summarized by time point and challenge dose group in Table 73 through Table 78.

Vital signs are detailed in Listing 15. Physical exam findings are presented in Listing 16.

11. OTHER ANALYSES

Analysis of physiological data from wearable devices will be planned in a separate SAP.

12. 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" The mean, standard deviation, and other statistics will be reported to 1 decimal place greater than the original data. The minimum and maximum will use the same number of decimal places as the original data. Proportions will be presented as 2 decimal places; values greater than zero but <0.01 will be presented as "<0.01". Percentages will be reported to the nearest whole number; values greater than zero but <1% will be presented as "<1"; values greater than 99% but less than 100% will be reported as >99%. Estimated parameters, not on the same scale as raw observations (e.g., regression coefficients) will be reported to 3 significant figures.

13. TECHNICAL DETAILS

SAS version 9.4 or above, or R version 4.2 or above, will be used to generate all tables, figures and listings.

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

No substantive changes to the analysis planned in the protocol have been made.

15. REFERENCES

1. Carrat, F., et al., Time lines of infection and disease in human influenza: a review of volunteer challenge studies. American Journal of Epidemiology, 2008. 167(7): p. 775-785.
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3. Han, A., et al., A Dose-finding Study of a Wild-type Influenza A(H3N2) Virus in a Healthy Volunteer Human Challenge Model. Clin Infect Dis, 2019. 69(12): p. 2082-2090.
4. Friedman, J., Hastie, T., Tibshirani, R. (2010). Regularization Paths for Generalized Linear Models via Coordinate Descent. Journal of Statistical Software, 33(1), 1-22. URL https://www.jstatsoft.org/v33/i01/.
5. Youden, W. J. (1950). Index for rating diagnostic tests. Cancer, 3(1), 32–35.

16. LISTING OF TABLES, FIGURES, AND LISTINGS

Table, figure, and listing shells are presented in Appendices 1, 2, and 3.

APPENDICES

APPENDIX 1. TABLE MOCK-UPS

This document includes examples mock-ups of tables to present clinical, immunogenicity, and safety data.

Instructional text is included in brackets [Instruction or Implementation Note:].

Note that the section headings in the appendices are taken from the ICH E3 guidance on clinical study reports.

LIST OF TABLES

9.5.1 Clinical, Safety, and Immunogenicity Measurements Assessed and Flow Chart

Table 1: Schedule of Activities

	Study Screening	Pre-Challenge		Viral Challenge	Post-Challenge												
		Confinement period											Follow-up[29]				
Study Days	D -45 to -3	D -2	D -1	D1	D2	D3	D4	D5	D6	D7	D8	D9+	D15 ± 3	D29 ± 5	D57 ± 7	E[1]	U[2]
Visit Number	00A	00B	00C	1	2	3	4	5	6	7	8		9	10	11		
Type of Visit[3]	C	I	I	I	I	I	I	I	I	I	I	I	C	C	C	C	C
Clinical Procedures																	
Informed consent	X																
Review/confirm eligibility criteria[4]	X	X	X	X													
Review/confirm informed consent[5]		X		X													
Confinement begins		X[6]															
Confinement period		X	X	X	X	X	X	X	X	X	X	X					
Discharge from confinement unit											X[7]	X					
Initiate treatment course with antiviral											X[8]					X[8]	
Demographics	X																
Medical History	X	X															
Height[9]	X																
Weight[9]	X																
Concomitant medications[10]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Physical exam	X																
Targeted physical exam[11]		X	X	X	X	X	X	X	X	X	X	X[24]	X	X	X	X[24]	X[24]
Vital signs[12]	X	X	X	X	X	X	X	X	X	X	X	X[24]	X	X	X	X[24]	X[24]
SpO_2[13]	X	X	X	X	X	X	X	X	X	X	X	X[24]	X	X	X		
Influenza challenge				X													
FLU-PRO survey instrument PM[14]		X	X	X	X	X	X	X	X	X	X	X	X				
Modified Jackson Score AM and PM[15]		X	X	X	X	X	X	X	X	X	X	X	X				
Adverse event review[16]				X	X	X	X	X	X	X	X	X[24]	X	X		X[24]	X[24]
SAE review				X	X	X	X	X	X	X	X	X	X	X	X	X	X

	Study Screening	**Pre-Challenge**		**Viral Challenge**	**Post-Challenge**												
		Confinement period											**Follow-up[29]**				
Study Days	D -45 to -3	D -2	D -1	D1	D2	D3	D4	D5	D6	D7	D8	D9+	D15 ± 3	D29 ± 5	D57 ± 7	E[1]	U[2]
Visit Number	00A	00B	00C	1	2	3	4	5	6	7	8		9	10	11		
Type of Visit[3]	C	I	I	I	I	I	I	I	I	I	I	I	C	C	C	C	C
ECG (12 lead)	X[17]								X[17]								
Chest X-Ray[18]	X																
Blood for HIV, HBV, and HCV	X																
Serum HCG	X																
Urine HCG[18]		X															
Urine toxicology[19]	X	X															
Safety screening labs[20]	X																
HAI Serology screen	X																
Safety follow-up labs[21]					X		X				X	X[24]				X[25]	X[24]
Research Laboratory Procedures																	
Blood - for plasma and PBMC for T- and B- cell immunology			X								X[24]		X	X	X	X[26]	X[26]
Blood - Serum for antibody and cytokine assays[22]		X	X		X	X	X	X	X	X	X		X	X	X	X[26]	
Plasmablasts											X						
Blood – PBMC for immunophenotyping[31]			X		X		X		X		X			X			
Blood - RNA transcriptomics		X	X		X	X	X	X	X	X	X	X[24]	X			X[26]	X[26]
Blood – DNA – collected for genetic testing			X														
Nasopharyngeal swab(s) for viral culture and/or Qualitative[23] and quantitative RT-PCR	X	X	X		X	X	X	X	X	X	X	X					
Nasal absorptive matrices and nasal lavage for antibody and other assays		X	X		X	X	X	X	X	X	X		X	X	X	X[26]	X[26]

	Study Screening	Pre-Challenge		Viral Challenge	Post-Challenge											
		Confinement period											Follow-up[29]			
Study Days	D -45 to -3	D -2	D -1	D1	D2	D3	D4	D5	D6	D7	D8	D9+	D15 ± 3	D29 ± 5	D57 ± 7	E[1]	U[2]
Visit Number	00A	00B	00C	1	2	3	4	5	6	7	8		9	10	11		
Type of Visit[3]	C	I	I	I	I	I	I	I	I	I	I	I	C	C	C	C	C
Curettage – nasal mucosa for T cell activation[30]		X											X	X	X	X[26]	X[26]
Wearable Devices																	
Garmin and/or Oura Ring[27]	X[28]	X	X	X	X	X	X	X	X	X	X	X					
Faros device[27]		X	X	X	X	X	X	X	X	X	X	X					

1. E=Early termination visit
2. U=Unscheduled visit
3. Visit type: C = Clinic, I = Inpatient
4. Eligibility criteria may change from the day of screening to Study Day -3. To avoid admitting participants to confinement with new exclusion criteria, the eligibility criteria will be reviewed and confirmed before the confinement stay.
5. Participants will have approximately a 48-hour window to decide if they would like to drop out of the study and leave the confinement unit before challenge virus is administered.
6. Eligible participants will be confined under respiratory isolation beginning on Study Day -2 (which is two days prior to the planned challenge).
7. Participants will remain in the confinement unit for a minimum of seven days after the date of challenge. Participants will leave the unit after they meet the following discharge criteria: two consecutive negative NP swabs collected 12 hours apart (that are performed on Study Day 6 or thereafter) for influenza A by qualitative RT-PCR performed by the local clinical laboratory, are afebrile (< 100.6°F/38.1°C), have $SpO_2 \geq$ 95% on room air, show no moderate or severe influenza signs or symptoms by clinical evaluation, and are clinically and hemodynamically stable for 48 hours. Participants who do not meet discharge criteria on Study Day 8 will remain in the confinement unit until the criteria are met. Study procedures for the confinement unit will be the same as on Study Day 8, except for no NLF collection or additional blood draws unless clinically indicated.
8. A treatment course of oseltamivir phosphate or baloxavir marboxil will be provided to all participants who do not have two consecutive negative NP swabs by qualitative RT-PCR for influenza by Study Day 6. Treatment will begin as early as Study Day 6, or thereafter if indicated, or earlier if terminates study prior to Study Day 8.
9. Height and weight will be measured at Screening.
10. Concomitant medications taken within 90 days prior to signing the ICF are collected.
11. Clinical evaluation (including oral/pharyngeal, neck, lung and heart exam), and symptom evaluation daily while in the confinement unit. An otoscopic exam will be performed at baseline and as needed.
12. Oral temperature, blood pressure, pulse, and respiratory rate will be assessed approximately every 8 hours while in the confinement unit (from 12:00AM – 11:59PM), while the participants are awake, and as clinically indicated.
13. Peripheral oxygen saturation (SpO_2) on room air at screening, on admission, and when oral temperature, blood pressure, pulse, and respiratory rate are assessed through the confinement period and at follow-up visits.
14. Self-assessment using FLU-PRO and Validation Diary to be performed after 3:00 pm on the Day -2 and after 3:00 pm each day of confinement and through Day
15. Modified Jackson Score to be obtained on the evening of Day -2 and in the morning and afternoon of each day of confinement (Approximately at 8:00 AM and after 3:00 PM) and on Day 15 during visit. Assure AM assessment on Study Day 1 is performed pre-challenge.
16. Unsolicited AEs will be monitored for approximately 28 days post challenge. Review of FLU-PRO for indicators of possible severe influenza associated illness (signs, symptoms, or lab findings).
17. ECG to be performed at screening, on Study Day 6, and as clinically indicated. Sites will consult a cardiologist if ECG is abnormal to determine clinically necessary work up.
18. Among female participants of childbearing potential, a repeat urine pregnancy test will be performed locally before CXR performed if > 7 days have passed since the negative serum pregnancy test was drawn.
19. Negative drug urine toxicology result (amphetamines, cocaine, and opiates) required on screening and (amphetamines, cocaine, opiates) on admission to the challenge unit, unless the drug is deemed acceptable by the Investigator.

	Study Screening	Pre-Challenge		Viral Challenge	Post-Challenge											
		Confinement period										Follow-up[29]				
Study Days	D -45 to -3	D -2	D -1	D1	D2	D3	D4	D5	D6	D7	D8	D9+	D15 ± 3	D29 ± 5	D57 ± 7	E[1]	U[2]
Visit Number	00A	00B	00C	1	2	3	4	5	6	7	8		9	10	11		
Type of Visit[3]	C	I	I	I	I	I	I	I	I	I	I	I	C	C	C	C	C

20. Screening Safety/Eligibility Labs: white blood cells (WBCs), absolute lymphocyte count, hemoglobin, platelets, alanine transaminase (ALT), and creatinine (Cr).
21. Follow-Up Safety Labs: Study Days 2, 4, and 8, and as clinically indicated: white blood cells (WBCs), absolute lymphocyte count, hemoglobin, platelets, and alanine transaminase (ALT), and creatinine (Cr).
22. Including HAI, MN and NAI antibody titers on Visits 00C (Day -1) 8, 9, 10 and 11.
23. Multiplex respiratory virus assay to include SARS-CoV-2 to be performed at each site at the time points listed above. Positive results prior to influenza virus challenge will result in subject exclusion from the study. No respiratory virus testing will be done on the day of challenge. Quantitative PCR will not be done at screening.
24. If indicated.
25. If terminates study < Study Day 8 and procedure not performed on day study terminated.
26. If terminates study early and procedure not scheduled to be performed on day study terminated or if missed study procedure on scheduled day.
27. To achieve baseline data for physiological biomarkers (e.g., heartrate variability, sleep patterns, etc.).
28. If the Garmin and/or Oura ring is not able to be distributed at screening this will not be a protocol deviation.
29. Follow-up visits can be conducted by phone if in-person visit is not feasible.
30. Nasal curettage will be an optional procedure.
31. At UMB, on Study Days -1, 2, 4, 6 and 8, $1x10^6$ freshly isolated PBMCs will be used to stain by mass cytometry. These specimens will be stained in conjunction with NLF cells isolated from individuals whose NLF cell counts trigger mass cytometry staining (>50,000 cells). No additional blood volumes or additional blood draws will be required.

9.7.1 Sample Size

Table 2: Probability (%) of observing at least one safety event, given varying underlying event probabilities and challenge dose group sizes

True Event Probability	Dose group Size			
	N=10	N=15	N=20	N=30
0.01 (Rare)	0.1	0.15	0.2	0.3
0.1 (Uncommon)	0.996	1.49	1.98	2.96
1 (Common)	9.56	14	18.2	26
10 (Very Common)	65.1	79.4	87.8	95.8

10.2 Protocol Deviations

Table 3: Distribution of Protocol Deviations by Category, Type, and Challenge Dose Group

Category	Deviation Type	10^4 $TCID_{50}$ Challenge Virus (N=X)		10^5 $TCID_{50}$ Challenge Virus (N=X)		10^6 $TCID_{50}$ Challenge Virus (N=X)		Sham Inoculum (N=X)		All Participants (N=X)	
		No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.
Eligibility/enrollment	Any type	x	x	x	x	x	x	x	x	x	x
	Did not meet inclusion criterion	x	x	x	x	x	x	x	x	x	x
	Met exclusion criterion	x	x	x	x	x	x	x	x	x	x
	ICF not signed prior to study procedures	x	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x	x
Treatment administration schedule	Any type	x	x	x	x	x	x	x	x	x	x
	Out of window visit	x	x	x	x	x	x	x	x	x	x
	Missed visit/visit not conducted	x	x	x	x	x	x	x	x	x	x
	Missed treatment administration	x	x	x	x	x	x	x	x	x	x
	Delayed treatment administration	x	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x	x
Follow-up visit schedule	Any type	x	x	x	x	x	x	x	x	x	x
	Out of window visit	x	x	x	x	x	x	x	x	x	x
	Missed visit/visit not conducted	x	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x	x
Protocol procedure/ assessment	Any type	x	x	x	x	x	x	x	x	x	x
	Incorrect version of ICF signed	x	x	x	x	x	x	x	x	x	x
	Blood not collected	x	x	x	x	x	x	x	x	x	x
	Urine not collected	x	x	x	x	x	x	x	x	x	x
	Stool not collected	x	x	x	x	x	x	x	x	x	x
	Other specimen not collected	x	x	x	x	x	x	x	x	x	x
	Too few aliquots obtained	x	x	x	x	x	x	x	x	x	x
	Specimen result not obtained	x	x	x	x	x	x	x	x	x	x
	Required procedure not conducted	x	x	x	x	x	x	x	x	x	x

Category	Deviation Type	10^4 $TCID_{50}$ Challenge Virus (N=X)		10^5 $TCID_{50}$ Challenge Virus (N=X)		10^6 $TCID_{50}$ Challenge Virus (N=X)		Sham Inoculum (N=X)		All Participants (N=X)	
		No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.
	Required procedure done incorrectly	x	x	x	x	x	x	x	x	x	x
	Study product temperature excursion	x	x	x	x	x	x	x	x	x	x
	Specimen temperature excursion	x	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x	x
Treatment administration	Any type	x	x	x	x	x	x	x	x	x	x
	Required procedure done incorrectly	x	x	x	x	x	x	x	x	x	x
	Study product temperature excursion	x	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x	x
Blinding policy/procedure	Any type	x	x	x	x	x	x	x	x	x	x
	Treatment unblinded	x	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x	x

Note: N = Number of enrolled participants

12.4.1 Individual Laboratory Measurements and Abnormal Laboratory Values

Table 4: Laboratory Adverse Event Grading Scales

Hematology	**Mild (Grade 1)**	**Moderate (Grade 2)**	**Severe (Grade 3)**
WBC x10^3/µL (Decrease)	2.50 – <LLN	1.50 – 2.49	<1.50
WBC x10^3/µL (Increase)	>ULN – 15.09	15.10 – 20.00	>20.00
Absolute Lymphocyte count x 10^3/µL (Decrease)	0.50 – <LLN	0.40 - 0.49	<0.40
Hgb g/dL (Decrease) (Female)	10.1 – <LLN	8.5 – 10.0	<8.5
Hgb g/dL (Decrease) (Male)	11.0 – <LLN	9.5 – 10.9	<9.5
Platelets cell x 10^3/µL (Decrease) EDTA	120 – <LLN	100 – 119	<100
Platelets x 10^3/µL (Increase) EDTA	>ULN – 550	551– 750	>750
Chemistry	**Mild (Grade 1)**	**Moderate (Grade 2)**	**Severe (Grade 3)**
ALT IU/L (Increase) (Female)	>ULN – 100	101 – 200	>200
ALT IU/L (Increase) (Male)	>ULN – 138	139 – 275	>275
Creatinine mg/dL (Increase)	>ULN – 1.8	1.9 – 2.2	>2.2

12.5 Vital Signs, Physical Findings, and Other Observations Related to Safety

Table 5: Vital Signs Grading Scales

Systemic (Quantitative)	**Mild (Grade 1)**	**Moderate (Grade 2)**	**Severe (Grade 3)**
Fever* - oral†	**38.1°C – 38.4°C** **100.6°F – 101.1°F**	**38.5°C – 38.9°C** **101.2°F – 102.0°F**	**>38.9°C** **>102.0°F**
**A fever can be considered not related to the study product if an alternative etiology can be documented.* *†Participants must not eat or drink anything hot or cold, or smoke within 10 minutes prior to taking oral temperature*			
Physiologic Parameter	**Mild (Grade 1)**	**Moderate (Grade 2)**	**Severe (Grade 3)**
Bradycardia – beats per minute	45 – 46	40 – 44	<40
Tachycardia – beats per minute	100 – 130	131 – 155	>155
Hypotension (systolic) mmHg	80 – 84	75 – 79	<75
Hypotension (diastolic) mmHg	50 – 54	45 – 49	<45
Hypertension (systolic) mmHg	140 – 155	156 – 160	>160
Hypertension (diastolic) mmHg	90 – 100	101 – 110	>110
SpO_2 (%)	92-94	89-91	<89
RR (increase) (bpm)	21-24	25-29	≥30
RR (decrease) (bpm)	9-11	6-8	<6

14.1 Description of Study Participants

14.1.1 Disposition of Participants

Table 6: Participant Disposition by Challenge Dose Group*

Participant Disposition	10^4 $TCID_{50}$ Challenge Virus (N=X)		10^5 $TCID_{50}$ Challenge Virus (N=X)		10^6 $TCID_{50}$ Challenge Virus (N=X)		Sham Inoculum (N=X)		All Participants (N=X)	
	n	%	n	%	n	%	n	%	n	%
Screened	--	--	--	--	x	--	--	--	--	--
Eligible but Not Enrolled	--	--	--	--	x	--	--	--	--	--
Enrolled/Randomized	x	100	x	100	x	100	x	100	x	100
Received Study Challenge	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Completed Challenge Period	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Completed Follow-up (Study Day 57)[a]	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Completed Per Protocol[b]	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

Note: N = Number of enrolled participants
[a] Refer to Listing 16.2.1 for reasons participants discontinued or terminated early.
[b] Refer to Listing 16.2.3 for reasons participants are excluded from the analysis populations.

Table 7: Analysis Populations by Challenge Dose Group

Analysis Populations	Reason Participants Excluded	10^4 $TCID_{50}$ Challenge Virus (N=X)		10^5 $TCID_{50}$ Challenge Virus (N=X)		10^6 $TCID_{50}$ Challenge Virus (N=X)		Sham Inoculum (N=X)		All Participants (N=X)	
		n	%	n	%	n	%	n	%	n	%
Safety/ITT Populations	No study challenge received										
Per Protocol, Challenge Period	Any reason										
	No study challenge received										
	Ineligible at enrollment										
	Early termination										
Per Protocol, Day 15	Any reason										
	No study challenge received										
	Ineligible at enrollment										
	Early termination										
	Receipt of non-study vaccination										
	Receipt of immunosuppressive medication										
	Receipt of blood or blood products, or blood donation										
	Study Day 15 visit out of window										
Per Protocol, Day 29	Any reason										
	No study challenge received										
	Ineligible at enrollment										
	Early termination										
	Receipt of non-study vaccination										
	Receipt of immunosuppressive medication										
	Receipt of blood or blood products, or blood donation										
	Study Day 29 visit out of window										
Per Protocol, Day 57	Any reason										
	No study challenge received										
	Ineligible at enrollment										
	Early termination										
	Receipt of non-study vaccination										
	Receipt of immunosuppressive medication										
	Receipt of blood or blood products, or blood donation										
	Study Day 57 visit out of window										

Table 8: Ineligibility Summary of Screen Failures

[Implementation Note: All I/E criteria reported to not have been met by screen failures will be included.]

Inclusion/Exclusion Category	Inclusion/Exclusion Criterion	n[a]	%[b]
Inclusion and Exclusion	Number of participants failing any eligibility criterion	x	x.x
Inclusion	Any inclusion criterion	x	x.x
	[inclusion criterion 1]	x	x.x
	[inclusion criterion 2]	x	x.x
	[inclusion criterion 3]	x	x.x
Exclusion	Any exclusion criterion	x	x.x
	[exclusion criterion 1]	x	x.x
	[exclusion criterion 2]	x	x.x
	[exclusion criterion 3]	x	x.x
Other Reasons	Any other reason	x	x.x
	[reason 1, if applicable]	x	x.x

[a] More than one criterion may be marked per individual.
[b] Denominator for percentages is the total number of screen failures.

14.1.2 Demographic Data

Table 9: Summary of Categorical Demographic and Baseline Characteristics by Site

Variable	Characteristic	Duke University (N = X)		University of Maryland (N = X)		All Participants (N = X)	
		n	%	n	%	n	%
Sex	Male	x	x.x	x	x.x	x	x.x
	Female	x	x.x	x	x.x	x	x.x
Ethnicity	Not Hispanic or Latino	x	x.x	x	x.x	x	x.x
	Hispanic or Latino	x	x.x	x	x.x	x	x.x
	Not Reported	x	x.x	x	x.x	x	x.x
	Unknown	x	x.x	x	x.x	x	x.x
Race	American Indian or Alaska Native	x	x.x	x	x.x	x	x.x
	Asian	x	x.x	x	x.x	x	x.x
	Native Hawaiian or Other Pacific Islander	x	x.x	x	x.x	x	x.x
	Black or African American	x	x.x	x	x.x	x	x.x
	White	x	x.x	x	x.x	x	x.x
	Multi-Racial	x	x.x	x	x.x	x	x.x
	Unknown	x	x.x	x	x.x	x	x.x

Note: N = Number of enrolled participants

Table 10: Summary of Continuous Demographic and Baseline Characteristics by Site

Variable	Statistic	Duke University (N = X)	University of Maryland (N = X)	All Participants (N = X)
Age (years)	Mean	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x
	Median	x	x	x
	Minimum	x	x	x
	Maximum	x	x	x
BMI	Mean	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x
	Median	x	x	x
	Minimum	x	x	x
	Maximum	x	x	x

Note: N = Number of enrolled participants

Table 11: Summary of Categorical Demographic and Baseline Characteristics by Challenge Dose Group, All Randomized Participants*

Variable	Characteristic	10^4 $TCID_{50}$ Challenge Virus (N=X)		10^5 $TCID_{50}$ Challenge Virus (N=X)		10^6 $TCID_{50}$ Challenge Virus (N=X)		Sham Inoculum (N=X)		All Participants (N=X)	
		n	%	n	%	n	%	n	%	n	%
Sex	Male	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Female	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Ethnicity	Not Hispanic or Latino	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Hispanic or Latino	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Not Reported	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Unknown	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Race	American Indian or Alaska Native	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Asian	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Native Hawaiian or Other Pacific Islander	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Black or African American	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	White	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Multi-Racial	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Unknown	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

Note: N = Number of enrolled participants

Table 12: Summary of Continuous Demographic and Baseline Characteristics by Study Group, All Randomized Participants*

Variable	Statistic	10^4 $TCID_{50}$ Challenge Virus (N=X)	10^5 $TCID_{50}$ Challenge Virus (N=X)	10^6 $TCID_{50}$ Challenge Virus (N=X)	Sham Inoculum (N=X)	All Participants (N=X)
Age (years)	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.x	x.x	x.x
	Minimum	x.x	x.x	x.x	x.x	x.x
	Maximum	x.x	x.x	x.x	x.x	x.x

Note: N = Number of enrolled participants

14.1.3 Prior and Concurrent Medical Conditions

Table 13: Summary of Participants with Pre-Existing Medical Conditions by MedDRA System Organ Class and Challenge Dose Group

[Implementation Note: SOCs will be sorted by frequency across all participants, most to least common.]

MedDRA System Organ Class	10^4 $TCID_{50}$ Challenge Virus (N=X)		10^5 $TCID_{50}$ Challenge Virus (N=X)		10^6 $TCID_{50}$ Challenge Virus (N=X)		Sham Inoculum (N=X)		All Participants (N=X)	
	n	%	n	%	n	%	n	%	n	%
Any SOC										
[SOC 1]										
[SOC 2]										

Note: N = Number of enrolled participants; n = Number of participants reporting medical history within the specified SOC. A participant is only counted once per SOC.

14.2 Clinical and Immunogenicity Data

14.2.1 Clinical Data Summary Tables

Table 14: Symptomatic Influenza Infection Post-Challenge with 95% Confidence Intervals by Challenge Dose Group, Safety Population*

Variable	Statistic	10^4 $TCID_{50}$ Challenge Virus (N=X)		10^5 $TCID_{50}$ Challenge Virus (N=X)		10^6 $TCID_{50}$ Challenge Virus (N=X)		Sham Inoculum (N=X)	
		Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI
Primary Analysis									
Viral shedding detected in NP swab(s) by qualitative and/or quantitative RT-PCR on at least two days (Day 2 through Day 8)	n (%)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
Cumulative MJS >= 6 across Days 2 through 6, Days 3 through 7, or Days 4 through 8	n (%)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
Symptomatic Influenza Infection: Viral shedding (by qualitative and/or quantitative RT-PCR) on at least two days and cumulative MJS >= 6 across Days 2 through 6, Days 3 through 7, or Days 4 through 8	n (%)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
Maximum cumulative MJS across Days 2 through 6, Days 3 through 7, or Days 4 through 8	Mean	x.x	(x.x, x.x)	x.x	(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	-
	Median	x	-	x	-	x	-	x	-
	Minimum	x	-	x	-	x	-	x	-
	Maximum	x	-	x	-	x	-	x	-
Total MJS at Day 15	Mean	x.x	(x.x, x.x)	x.x	(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	-
	Median	x	-	x	-	x	-	x	-
	Minimum	x	-	x	-	x	-	x	-
	Maximum	x	-	x	-	x	-	x	-

Variable	Statistic	10^4 $TCID_{50}$ Challenge Virus (N=X)		10^5 $TCID_{50}$ Challenge Virus (N=X)		10^6 $TCID_{50}$ Challenge Virus (N=X)		Sham Inoculum (N=X)	
		Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI
Sensitivity Analysis – Qualitative RT-PCR Only									
Viral shedding detected in NP swab(s) by qualitative RT-PCR on at least two days (Day 2 through Day 8)	n (%)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
Symptomatic Influenza Infection: Viral shedding (by qualitative RT-PCR) on at least two days and cumulative MJS >= 6 across Days 2 through 6, Days 3 through 7, or Days 4 through 8	n (%)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
Sensitivity Analysis – Varying MJS Thresholds									
Cumulative MJS >= 10 across Days 2 through 6, Days 3 through 7, or Days 4 through 8	n (%)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
Symptomatic Influenza Infection: Viral shedding (by qualitative and/or quantitative RT-PCR) on at least two days and **cumulative MJS >= 10** across Days 2 through 6, Days 3 through 7, or Days 4 through 8	n (%)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
Cumulative MJS >= 15 across Days 2 through 6, Days 3 through 7, or Days 4 through 8	n (%)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
Symptomatic Influenza Infection: Viral shedding (by qualitative and/or quantitative RT-PCR) on at least two days and **cumulative MJS >= 15** across Days 2 through 6, Days 3 through 7, or Days 4 through 8	n (%)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
Sensitivity Analysis – Varying the Number of Days of Viral Shedding									
Symptomatic Influenza Infection: Viral shedding (by qualitative and/or quantitative RT-PCR) on **at least one day** and cumulative MJS >= 6 across Days 2 through 6, Days 3 through 7, or Days 4 through 8	n (%)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
Symptomatic Influenza Infection: Viral shedding (by qualitative and/or quantitative RT-PCR) on **at least three days** and cumulative MJS >= 6 across Days 2 through 6, Days 3 through 7, or Days 4 through 8	n (%)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)

Notes: N = Number of participants in the Safety population, n = Number of participants meeting the given criteria during the challenge period. Confidence intervals for the probability of meeting the given criteria computed via the exact Clopper-Pearson method. Confidence intervals for the mean computed via the t-distribution. MJS = Modified Jackson Score.

Table 15: Maximum Severity of Influenza Symptoms Reported During the Challenge Period by Challenge Dose Group, Safety Population

Symptom	Maximum Severity	10^4 $TCID_{50}$ Challenge Virus (N=X)		10^5 $TCID_{50}$ Challenge Virus (N=X)		10^6 $TCID_{50}$ Challenge Virus (N=X)		Sham Inoculum (N=X)	
		n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
Any Symptom	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	Mild or Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	Moderate or Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	Severe or Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Runny Nose[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Stuffy Nose[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Sneezing[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Sore Throat[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-

Symptom	Maximum Severity	10^4 $TCID_{50}$ Challenge Virus (N=X)		10^5 $TCID_{50}$ Challenge Virus (N=X)		10^6 $TCID_{50}$ Challenge Virus (N=X)		Sham Inoculum (N=X)	
		n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Headache[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Cough[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Malaise (tiredness)[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Body Ache[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Chills[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-

Symptom	Maximum Severity	10^4 $TCID_{50}$ Challenge Virus (N=X)		10^5 $TCID_{50}$ Challenge Virus (N=X)		10^6 $TCID_{50}$ Challenge Virus (N=X)		Sham Inoculum (N=X)	
		n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Feverish[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Fever[b]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	Mild	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	Moderate	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	Severe	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Shortness of Breath[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Earache[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Lymphopenia[c]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)

Symptom	Maximum Severity	10^4 $TCID_{50}$ Challenge Virus (N=X)		10^5 $TCID_{50}$ Challenge Virus (N=X)		10^6 $TCID_{50}$ Challenge Virus (N=X)		Sham Inoculum (N=X)	
		n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	Mild	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	Moderate	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	Severe	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-

Notes: N = Number of participants in the Safety population; n = Number of participants reporting each symptom.
[a.] As reported on the Modified Jackson Score (MJS) tool; maximum severity across the challenge period reported.
[b.] As part of vital signs assessments, with temperature collected three times daily during the challenge period. Fever and feverishness (from MJS) contribute as one item towards the Modified Jackson Score.
[c.] As part of clinical safety laboratory assessments, on Study Days 2, 4, 8, and any supplemental visits during the challenge period.

Table 16: Maximum Severity of Influenza Symptoms Reported During the Challenge Period by Challenge Dose Group, Infected Participants in the Safety Population

		10^4 $TCID_{50}$ Challenge Virus, RT-PCR+ (N=X)		10^5 $TCID_{50}$ Challenge Virus, RT-PCR+ (N=X)		10^6 $TCID_{50}$ Challenge Virus, RT-PCR+ (N=X)		Any Active Challenge Virus Dose, RT-PCR+ (N=X)		Sham Inoculum, RT-PCR+ (N=X)	
Symptom	**Maximum Severity**	**n (%)**	**95% CI**	**n (%)**	**95% CI**	**n (%)**	**95% CI**	**n (%)**	**95% CI**	**n (%)**	**95% CI**
Any Symptom	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	Mild or Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	Moderate or Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	Severe or Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Runny Nose[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Stuffy Nose[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Sneezing[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-

Symptom	Maximum Severity	10^4 $TCID_{50}$ Challenge Virus, RT-PCR+ (N=X)		10^5 $TCID_{50}$ Challenge Virus, RT-PCR+ (N=X)		10^6 $TCID_{50}$ Challenge Virus, RT-PCR+ (N=X)		Any Active Challenge Virus Dose, RT-PCR+ (N=X)		Sham Inoculum, RT-PCR+ (N=X)	
		n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
Sore Throat[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Headache[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Cough[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Malaise (tiredness)[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Body Ache[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-

Symptom	Maximum Severity	10^4 $TCID_{50}$ Challenge Virus, RT-PCR+ (N=X)		10^5 $TCID_{50}$ Challenge Virus, RT-PCR+ (N=X)		10^6 $TCID_{50}$ Challenge Virus, RT-PCR+ (N=X)		Any Active Challenge Virus Dose, RT-PCR+ (N=X)		Sham Inoculum, RT-PCR+ (N=X)	
		n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Chills[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Feverish[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Fever[b]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	Mild	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	Moderate	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	Severe	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Shortness of Breath[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Earache[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-

Symptom	Maximum Severity	10^4 $TCID_{50}$ Challenge Virus, RT-PCR+ (N=X)		10^5 $TCID_{50}$ Challenge Virus, RT-PCR+ (N=X)		10^6 $TCID_{50}$ Challenge Virus, RT-PCR+ (N=X)		Any Active Challenge Virus Dose, RT-PCR+ (N=X)		Sham Inoculum, RT-PCR+ (N=X)	
		n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Lymphopenia[c]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	Mild	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	Moderate	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	Severe	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-

Notes: N = Number of participants in the Safety population with at least two days with positive qualitative and/or quantitative results; n = Number of participants reporting each symptom.
[a]As reported on the Modified Jackson Score (MJS) tool; maximum severity across the challenge period reported.
[b]As part of vital signs assessments, with temperature collected three times daily during the challenge period. Fever and feverishness (from MJS) contribute as one item towards the Modified Jackson Score.
[c]As part of clinical safety laboratory assessments, on Study Days 2, 4, 8, and any supplemental visits during the challenge period.

Similar Tables:

Table 17: Maximum Severity of Influenza Symptoms Reported During the Challenge Period by Challenge Dose Group, Uninfected Participants in the Safety Population

[Implementation note: Update Table 16 to include only participants testing RT-PCR+ once or never during the challenge period and update the headers and footnotes to match.]

Table 18: Maximum Severity of Influenza Symptoms Reported on Study Day 15 by Challenge Dose Group, Infected Participants in the Safety Population

Table 19: Maximum Severity of Influenza Symptoms Reported on Study Day 15 by Challenge Dose Group, Uninfected Participants in the Safety Population

[Implementation note: Update Table 16 to include only participants testing RT-PCR+ once or never during the challenge period and update the headers and footnotes to match.]

Table 20: Maximum Severity of Influenza Symptoms Reported During the Challenge Period by Infection Status, Safety Population

		RT-PCR+ at Least Twice (N=X)		RT-PCR+ Less than Twice (N=X)	
Symptom	**Severity**	**n (%)**	**95% CI**	**n (%)**	**95% CI**
Any Symptom	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-
	Mild or Just Noticeable	x (x.x)	-	x (x.x)	-
	Moderate or Bothersome from Time to Time	x (x.x)	-	x (x.x)	-
	Severe or Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-
Runny Nose[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-
Stuffy Nose[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-
Sneezing[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-
Sore Throat[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-
Headache[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-
Cough[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-

Symptom	Severity	RT-PCR+ at Least Twice (N=X)		RT-PCR+ Less than Twice (N=X)	
		n (%)	95% CI	n (%)	95% CI
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-
Malaise (tiredness)[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-
Body Ache[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-
Chills[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-
Feverish[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-
Fever[b]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-
	Mild	x (x.x)	-	x (x.x)	-
	Moderate	x (x.x)	-	x (x.x)	-
	Severe	x (x.x)	-	x (x.x)	-
Shortness of Breath[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-
Earache[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-

Symptom	Severity	RT-PCR+ at Least Twice (N=X)		RT-PCR+ Less than Twice (N=X)	
		n (%)	95% CI	n (%)	95% CI
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-
Lymphopenia[c]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-
	Mild	-	-	-	-
	Moderate	-	-	-	-
	Severe	-	-	-	-

Notes: N = Number of participants in the Safety population with the given infection status; n = Number of participants reporting each symptom, regardless of timing with respect to RT-PCR positivity.
[a]As reported on the Modified Jackson Score (MJS) tool; maximum severity across the challenge period reported.
[b]As part of vital signs assessments, with temperature collected three times daily during the challenge period. Fever and feverishness (from MJS) contribute as one item towards the Modified Jackson Score.
[c]As part of clinical safety laboratory assessments, on Study Days 2, 4, 8, and any supplemental visits during the challenge period.

Similar Table:

Table 21: Maximum Severity of Influenza Symptoms Reported on Study Day 15 by Infection Status, Safety Population

Table 22: Maximum Severity of Influenza Symptoms by Study Day, 10^4 $TCID_{50}$ Challenge Virus Group, Currently Infected Participants in the Safety Population

[Implementation note: Table will be generated in landscape format with larger font.]

		Baseline (N=XX)		Day 1 (Post-Challenge) (N=XX)		Day 2: RT-PCR+ (N=XX)		Day 3: RT-PCR+ (N=XX)		Day 4: RT-PCR+ (N=XX)		Day 5: RT-PCR+ (N=XX)		Day 6: RT-PCR+ (N=XX)		Day 7: RT-PCR+ (N=XX)		Day 8: RT-PCR+ (N=XX)		Days 9 through Discharge: RT-PCR+ (N=XX)		Anytime Post-Challenge[a]: RT-PCR+ (N=XX)	
Symptom	**Maximum Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Any Symptom	Any Severity	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	None	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Mild or Just Noticeable	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Moderate or Bothersome from Time to Time	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Severe or Bothersome Most or All of the Time	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Runny Nose[a]	Any Severity	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	0: None	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1: Just Noticeable	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2: Bothersome from Time to Time	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3: Bothersome Most or All of the Time	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Stuffy Nose[a]	Any Severity	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	0: None	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1: Just Noticeable	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

		Baseline (N=XX)		Day 1 (Post-Challenge) (N=XX)		Day 2: RT-PCR+ (N=XX)		Day 3: RT-PCR+ (N=XX)		Day 4: RT-PCR+ (N=XX)		Day 5: RT-PCR+ (N=XX)		Day 6: RT-PCR+ (N=XX)		Day 7: RT-PCR+ (N=XX)		Day 8: RT-PCR+ (N=XX)		Days 9 through Discharge: RT-PCR+ (N=XX)		Anytime Post-Challenge[a]: RT-PCR+ (N=XX)	
Symptom	**Maximum Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	2: Bothersome from Time to Time	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3: Bothersome Most or All of the Time	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Sneezing[a]	Any Severity	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	0: None	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1: Just Noticeable	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2: Bothersome from Time to Time	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3: Bothersome Most or All of the Time	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Sore Throat[a]	Any Severity	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	0: None	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1: Just Noticeable	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2: Bothersome from Time to Time	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3: Bothersome Most or All of the Time	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Headache[a]	Any Severity	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	0: None	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1: Just Noticeable	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2: Bothersome from Time to Time	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

		Baseline (N=XX)		Day 1 (Post-Challenge) (N=XX)		Day 2: RT-PCR+ (N=XX)		Day 3: RT-PCR+ (N=XX)		Day 4: RT-PCR+ (N=XX)		Day 5: RT-PCR+ (N=XX)		Day 6: RT-PCR+ (N=XX)		Day 7: RT-PCR+ (N=XX)		Day 8: RT-PCR+ (N=XX)		Days 9 through Discharge: RT-PCR+ (N=XX)		Anytime Post-Challenge[a]: RT-PCR+ (N=XX)	
Symptom	**Maximum Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	3: Bothersome Most or All of the Time	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Cough[a]	Any Severity	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	0: None	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1: Just Noticeable	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2: Bothersome from Time to Time	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3: Bothersome Most or All of the Time	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Malaise (tiredness)[a]	Any Severity	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	0: None	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1: Just Noticeable	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2: Bothersome from Time to Time	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3: Bothersome Most or All of the Time	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Body Ache[a]	Any Severity	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	0: None	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1: Just Noticeable	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2: Bothersome from Time to Time	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

		Baseline (N=XX)		Day 1 (Post-Challenge) (N=XX)		Day 2: RT-PCR+ (N=XX)		Day 3: RT-PCR+ (N=XX)		Day 4: RT-PCR+ (N=XX)		Day 5: RT-PCR+ (N=XX)		Day 6: RT-PCR+ (N=XX)		Day 7: RT-PCR+ (N=XX)		Day 8: RT-PCR+ (N=XX)		Days 9 through Discharge: RT-PCR+ (N=XX)		Anytime Post-Challenge[a]: RT-PCR+ (N=XX)	
Symptom	**Maximum Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	3: Bothersome Most or All of the Time	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Chills[a]	Any Severity	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	0: None	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1: Just Noticeable	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2: Bothersome from Time to Time	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3: Bothersome Most or All of the Time	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Feverish[a]	Any Severity	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	0: None	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1: Just Noticeable	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2: Bothersome from Time to Time	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3: Bothersome Most or All of the Time	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Fever[b]	Any Severity	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	None	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Mild	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Moderate	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Severe	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

		Baseline (N=XX)		Day 1 (Post-Challenge) (N=XX)		Day 2: RT-PCR+ (N=XX)		Day 3: RT-PCR+ (N=XX)		Day 4: RT-PCR+ (N=XX)		Day 5: RT-PCR+ (N=XX)		Day 6: RT-PCR+ (N=XX)		Day 7: RT-PCR+ (N=XX)		Day 8: RT-PCR+ (N=XX)		Days 9 through Discharge: RT-PCR+ (N=XX)		Anytime Post-Challenge[a]: RT-PCR+ (N=XX)	
Symptom	**Maximum Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Shortness of Breath[a]	Any Severity	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	0: None	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1: Just Noticeable	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2: Bothersome from Time to Time	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3: Bothersome Most or All of the Time	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Earache[a]	Any Severity	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	0: None	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1: Just Noticeable	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2: Bothersome from Time to Time	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3: Bothersome Most or All of the Time	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Lymphopenia[c]	Any Severity	-	-	-	-	x	x.x	-	-	x	x.x	-	-	-	-	-	-	x	x.x	x	x.x	x	x.x
	None	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Mild	-	-	-	-	x	x.x	-	-	x	x.x	-	-	-	-	-	-	x	x.x	x	x.x	x	x.x
	Moderate	-	-	-	-	x	x.x	-	-	x	x.x	-	-	-	-	-	-	x	x.x	x	x.x	x	x.x
	Severe	-	-	-	-	x	x.x	-	-	x	x.x	-	-	-	-	-	-	x	x.x	x	x.x	x	x.x

		Baseline (N=XX)		Day 1 (Post-Challenge) (N=XX)		Day 2: RT-PCR+ (N=XX)		Day 3: RT-PCR+ (N=XX)		Day 4: RT-PCR+ (N=XX)		Day 5: RT-PCR+ (N=XX)		Day 6: RT-PCR+ (N=XX)		Day 7: RT-PCR+ (N=XX)		Day 8: RT-PCR+ (N=XX)		Days 9 through Discharge: RT-PCR+ (N=XX)		Anytime Post-Challenge[a]: RT-PCR+ (N=XX)	
Symptom	**Maximum Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Notes: N = Number of participants in the Safety population RT-PCR+ on the given study day; n = Number of participants reporting each symptom. **Prior to Day 2, all participants included as symptom background.** [a] As reported on the Modified Jackson Score (MJS) tool. [b] As part of vital signs assessments, with temperature collected three times daily during the challenge period. Fever and feverishness (from MJS) contribute as one item towards the Modified Jackson Score. [c] As part of clinical safety laboratory assessments, on Study Days 2, 4, 8, and any supplemental visits during the challenge period.																						

Similar Tables:

Table 23: Maximum Severity of Participant-Reported Influenza Symptoms by Study Day, 10^5 $TCID_{50}$ Challenge Virus Group, Currently Infected Participants in the Safety Population

Table 24: Maximum Severity of Participant-Reported Influenza Symptoms by Study Day, 10^6 $TCID_{50}$ Challenge Virus Group, Currently Infected Participants in the Safety Population

Table 25: Maximum Severity of Participant-Reported Influenza Symptoms by Study Day, Sham Inoculum Group, Currently Infected Participants in the Safety Population

Table 26: Maximum Severity of Influenza Symptoms Reported During the Challenge Period by Current Infection Status, Safety Population

Symptom	Severity	Pre-Infection (N=X)		Current Infection (N=X)		Post-Infection (N=X)		Uninfected (N=X)	
		n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
Any Symptom	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	Mild or Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	Moderate or Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	Severe or Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Runny Nose[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Stuffy Nose[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Sneezing[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-

Symptom	Severity	Pre-Infection (N=X)		Current Infection (N=X)		Post-Infection (N=X)		Uninfected (N=X)	
		n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Sore Throat[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Headache[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Cough[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Malaise (tiredness)[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-

Symptom	Severity	Pre-Infection (N=X)		Current Infection (N=X)		Post-Infection (N=X)		Uninfected (N=X)	
		n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Body Ache[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Chills[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Feverish[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Fever[b]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	Mild	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	Moderate	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-

Symptom	Severity	Pre-Infection (N=X)		Current Infection (N=X)		Post-Infection (N=X)		Uninfected (N=X)	
		n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
	Severe	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Shortness of Breath[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Earache[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
Lymphopenia[c]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-	x (x.x)	-	x (x.x)	-
	Mild	-	-	-	-	-	-	-	-
	Moderate	-	-	-	-	-	-	-	-
	Severe	-	-	-	-	-	-	-	-

Notes: N = Number of participants in the Safety population reporting symptoms relevant to the given subgroup; n = Number of participants reporting each symptom, regardless of timing with respect to RT-PCR positivity. Uninfected participants include all those RT-PCR+ on no more than one study day.

[a]As reported on the Modified Jackson Score (MJS) tool; maximum severity across the challenge period reported.

[b]As part of vital signs assessments, with temperature collected three times daily during the challenge period. Fever and feverishness (from MJS) contribute as one item towards the Modified Jackson Score.

[c]As part of clinical safety laboratory assessments, on Study Days 2, 4, 8, and any supplemental visits during the challenge period.

Table 27: Paired Comparisons of Influenza Symptoms Reported Before, During, and After Infection, Infected Participants in the Safety Population

Symptom	Severity	Pre-Infection n (%)	Current Infection n (%)	Post-Infection n (%)	Pre-Infection vs. Current Infection p-value[d]	Pre-Infection vs. Post-Infection p-value[d]	Current Infection vs. Post-Infection p-value[d]
Any Symptom	None	x (x.x)	x (x.x)	x (x.x)	0.xx	0.xx	0.xx
	Mild or Just Noticeable	x (x.x)	x (x.x)	x (x.x)	-	-	-
	Moderate or Bothersome from Time to Time	x (x.x)	x (x.x)	x (x.x)	-	-	-
	Severe or Bothersome Most or All of the Time	x (x.x)	x (x.x)	x (x.x)	-	-	-
Runny Nose[a]	0: None	x (x.x)	x (x.x)	x (x.x)	0.xx	0.xx	0.xx
	1: Just Noticeable	x (x.x)	x (x.x)	x (x.x)	-	-	-
	2: Bothersome from Time to Time	x (x.x)	x (x.x)	x (x.x)	-	-	-
	3: Bothersome Most or All of the Time	x (x.x)	x (x.x)	x (x.x)	-	-	-
Stuffy Nose[a]	0: None	x (x.x)	x (x.x)	x (x.x)	0.xx	0.xx	0.xx
	1: Just Noticeable	x (x.x)	x (x.x)	x (x.x)	-	-	-
	2: Bothersome from Time to Time	x (x.x)	x (x.x)	x (x.x)	-	-	-
	3: Bothersome Most or All of the Time	x (x.x)	x (x.x)	x (x.x)	-	-	-
Sneezing[a]	0: None	x (x.x)	x (x.x)	x (x.x)	0.xx	0.xx	0.xx
	1: Just Noticeable	x (x.x)	x (x.x)	x (x.x)	-	-	-
	2: Bothersome from Time to Time	x (x.x)	x (x.x)	x (x.x)	-	-	-
	3: Bothersome Most or All of the Time	x (x.x)	x (x.x)	x (x.x)	-	-	-
Sore Throat[a]	0: None	x (x.x)	x (x.x)	x (x.x)	0.xx	0.xx	0.xx
	1: Just Noticeable	x (x.x)	x (x.x)	x (x.x)	-	-	-

Symptom	Severity	Pre-Infection n (%)	Current Infection n (%)	Post-Infection n (%)	Pre-Infection vs. Current Infection p-value[d]	Pre-Infection vs. Post-Infection p-value[d]	Current Infection vs. Post-Infection p-value[d]
	2: Bothersome from Time to Time	x (x.x)	x (x.x)	x (x.x)	-	-	-
	3: Bothersome Most or All of the Time	x (x.x)	x (x.x)	x (x.x)	-	-	-
Headache[a]	0: None	x (x.x)	x (x.x)	x (x.x)	0.xx	0.xx	0.xx
	1: Just Noticeable	x (x.x)	x (x.x)	x (x.x)	-	-	-
	2: Bothersome from Time to Time	x (x.x)	x (x.x)	x (x.x)	-	-	-
	3: Bothersome Most or All of the Time	x (x.x)	x (x.x)	x (x.x)	-	-	-
Cough[a]	0: None	x (x.x)	x (x.x)	x (x.x)	0.xx	0.xx	0.xx
	1: Just Noticeable	x (x.x)	x (x.x)	x (x.x)	-	-	-
	2: Bothersome from Time to Time	x (x.x)	x (x.x)	x (x.x)	-	-	-
	3: Bothersome Most or All of the Time	x (x.x)	x (x.x)	x (x.x)	-	-	-
Malaise (tiredness)[a]	0: None	x (x.x)	x (x.x)	x (x.x)	0.xx	0.xx	0.xx
	1: Just Noticeable	x (x.x)	x (x.x)	x (x.x)	-	-	-
	2: Bothersome from Time to Time	x (x.x)	x (x.x)	x (x.x)	-	-	-
	3: Bothersome Most or All of the Time	x (x.x)	x (x.x)	x (x.x)	-	-	-
Body Ache[a]	0: None	x (x.x)	x (x.x)	x (x.x)	0.xx	0.xx	0.xx
	1: Just Noticeable	x (x.x)	x (x.x)	x (x.x)	-	-	-
	2: Bothersome from Time to Time	x (x.x)	x (x.x)	x (x.x)	-	-	-
	3: Bothersome Most or All of the Time	x (x.x)	x (x.x)	x (x.x)	-	-	-
Chills[a]	0: None	x (x.x)	x (x.x)	x (x.x)	0.xx	0.xx	0.xx

Symptom	Severity	Pre-Infection	Current Infection	Post-Infection	Pre-Infection vs. Current Infection	Pre-Infection vs. Post-Infection	Current Infection vs. Post-Infection
		n (%)	n (%)	n (%)	p-value[d]	p-value[d]	p-value[d]
	1: Just Noticeable	x (x.x)	x (x.x)	x (x.x)	-	-	-
	2: Bothersome from Time to Time	x (x.x)	x (x.x)	x (x.x)	-	-	-
	3: Bothersome Most or All of the Time	x (x.x)	x (x.x)	x (x.x)	-	-	-
Feverish[a]	0: None	x (x.x)	x (x.x)	x (x.x)	0.xx	0.xx	0.xx
	1: Just Noticeable	x (x.x)	x (x.x)	x (x.x)	-	-	-
	2: Bothersome from Time to Time	x (x.x)	x (x.x)	x (x.x)	-	-	-
	3: Bothersome Most or All of the Time	x (x.x)	x (x.x)	x (x.x)	-	-	-
Fever[b]	None	x (x.x)	x (x.x)	x (x.x)	0.xx	0.xx	0.xx
	Mild	x (x.x)	x (x.x)	x (x.x)	-	-	-
	Moderate	x (x.x)	x (x.x)	x (x.x)	-	-	-
	Severe	x (x.x)	x (x.x)	x (x.x)	-	-	-
Shortness of Breath[a]	0: None	x (x.x)	x (x.x)	x (x.x)	0.xx	0.xx	0.xx
	1: Just Noticeable	x (x.x)	x (x.x)	x (x.x)	-	-	-
	2: Bothersome from Time to Time	x (x.x)	x (x.x)	x (x.x)	-	-	-
	3: Bothersome Most or All of the Time	x (x.x)	x (x.x)	x (x.x)	-	-	-
Earache[a]	0: None	x (x.x)	x (x.x)	x (x.x)	0.xx	0.xx	0.xx
	1: Just Noticeable	x (x.x)	x (x.x)	x (x.x)	-	-	-
	2: Bothersome from Time to Time	x (x.x)	x (x.x)	x (x.x)	-	-	-
	3: Bothersome Most or All of the Time	x (x.x)	x (x.x)	x (x.x)	-	-	-

Symptom	Severity	Pre-Infection n (%)	Current Infection n (%)	Post-Infection n (%)	Pre-Infection vs. Current Infection p-value[d]	Pre-Infection vs. Post-Infection p-value[d]	Current Infection vs. Post-Infection p-value[d]
Lymphopenia[c]	None	x (x.x)	x (x.x)	x (x.x)	0.xx	0.xx	0.xx
	Mild	-	-	-	-	-	-
	Moderate	-	-	-	-	-	-
	Severe	-	-	-	-	-	-

Notes: N = XX participants in the Safety population tested RT-PCR+ on at least two study days; n = Number of participants reporting each symptom within each timing category.
[a]As reported on the Modified Jackson Score (MJS) tool; maximum severity across the challenge period reported.
[b]As part of vital signs assessments, with temperature collected three times daily during the challenge period. Fever and feverishness (from MJS) contribute as one item towards the Modified Jackson Score.
[c]As part of clinical safety laboratory assessments, on Study Days 2, 4, 8, and any supplemental visits during the challenge period.
[d]Wilcoxon signed rank tests used to compare paired severities for each symptom, for infected participants.

Table 28: Qualitative and Quantitative RT-PCR Status During the Challenge Period by Study Day and Challenge Dose Group, Safety Population*

Study Day	Quantitative RT-PCR (RT-qPCR) Status	10^4 $TCID_{50}$ Challenge Virus (N=X)		10^5 $TCID_{50}$ Challenge Virus (N=X)		10^6 $TCID_{50}$ Challenge Virus (N=X)		Sham Inoculum (N=X)	
		Qualitative RT-PCR+ n (%)	Qualitative RT-PCR- n (%)	Qualitative RT-PCR+ n (%)	Qualitative RT-PCR- n (%)	Qualitative RT-PCR+ n (%)	Qualitative RT-PCR- n (%)	Qualitative RT-PCR+ n (%)	Qualitative RT-PCR- n (%)
Day 1 (Baseline)	RT-qPCR+	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	Undetectable Virus	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Day 2	RT-qPCR+	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	Undetectable Virus	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Day 3	RT-qPCR+	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	Undetectable Virus	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Day 4	RT-qPCR+	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	Undetectable Virus	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Day 5	RT-qPCR+	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	Undetectable Virus	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Day 6	RT-qPCR+	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	Undetectable Virus	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Day 7	RT-qPCR+	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	Undetectable Virus	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Day 8+	RT-qPCR+	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	Undetectable Virus	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Anytime Post-Challenge[a]	RT-qPCR+	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	Undetectable Virus	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)

Note: N = Number of participants in the Safety population with available results.
[a] The number of participants with viral shedding reported at any time point within the challenge period (Days 2 to 8+).

Table 29: Multiplex Respiratory Virus Assay Results by Virus, Subtype, and Study Day, 10^4 $TCID_{50}$ Challenge Virus Group, Safety Population

Virus	Subtype[a]	Day 2 (N=X)		Day 3 (N=X)		Day 4 (N=X)		Day 5 (N=X)		Day 6 (N=X)		Day 7 (N=X)		Day 8 (N=X)		Days 9+ (N=X)		Anytime Post-Challenge (N=X)	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Influenza	Any Subtype	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Influenza A[a]	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Influenza A 2009 H1N1	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Influenza A H1	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Influenza A H3[a]	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Influenza B	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Other	Any Subtype	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Adenovirus	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Bocavirus	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Bordetella Pertussis	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Coronavirus 229E	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Coronavirus HKU1	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Coronavirus NL63	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Coronavirus OC43	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Human Metapneumovirus	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Mycoplasma Pneumoniae	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Parainfluenza Virus 1	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Parainfluenza Virus 2	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Parainfluenza Virus 3	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Parainfluenza Virus 4	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Respiratory Syncytial Virus (unspecified)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Rhinovirus/Enterovirus	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

Virus	Subtype[a]	Day 2 (N=X)		Day 3 (N=X)		Day 4 (N=X)		Day 5 (N=X)		Day 6 (N=X)		Day 7 (N=X)		Day 8 (N=X)		Days 9+ (N=X)		Anytime Post-Challenge (N=X)	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	SARS-CoV-2	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Bordatella Parapertussis	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Chlamydia Pneumonia	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

Note: N = Number of participants in the Safety population with available data; n = Number of participants in the Safety population reporting positive results.
[a] Used in part to determine viral shedding positivity.

Similar Tables:

Table 30: Multiplex Respiratory Virus Assay Results by Virus, Subtype, and Study Day, 10^5 $TCID_{50}$ Challenge Virus Group, Safety Population

Table 31: Multiplex Respiratory Virus Assay Results by Virus, Subtype, and Study Day, 10^6 $TCID_{50}$ Challenge Virus Group, Safety Population

Table 32: Multiplex Respiratory Virus Assay Results by Virus, Subtype, and Study Day, Sham Inoculum Group, Safety Population

Table 33: Comparison of Qualitative and Quantitative RT-PCR Results, Safety Population

Quantitative RT-PCR (copies/mL)	Qualitative RT-PCR+	Qualitative RT-PCR-
n	x	x
Minimum	xx	xx
Median	xx.x	xx.x
Mean	xx.x	xx.x
Maximum	xx	xx
# Above LOD (%)	xx (x.x)	xx (x.x)
# Below LOD (%)	xx (x.x)	xx (x.x)

Notes: n = Number of samples across all participants in the Safety population and all study days during the challenge period; row percentages presented.

Table 34: Days to First RT-PCR-Positive Result by Challenge Dose Group and Subgroup, Safety Population

Subgroup	Statistic	10^4 $TCID_{50}$ Challenge Virus (N=X)	10^5 $TCID_{50}$ Challenge Virus (N=X)	10^6 $TCID_{50}$ Challenge Virus (N=X)	Sham Inoculum (N=X)
All Challenged Participants	Median (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
All Infected Participants[b]	n (%)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	Mean	x.x	x.x	x.x	x.x
	Minimum	x	x	x	x
	Maximum	x	x	x	x

Notes: N = Number of participants in the Safety population; n = Number of participants reporting at least one positive qualitative or quantitative RT-PCR result.
[a] Kaplan-Meier estimate among all challenged participants, accounting for censoring of participants who never tested positive.
[b] Estimated in participants reporting RT-PCR+ results on at least two study days during the challenge period.

Table 35: Number of Total Days of RT-PCR Positivity by Challenge Dose Group, Safety Population

Number of Days Testing RT-PCR+	10^4 $TCID_{50}$ Challenge Virus (N=X)		10^5 $TCID_{50}$ Challenge Virus (N=X)		10^6 $TCID_{50}$ Challenge Virus (N=X)		Sham Inoculum (N=X)	
	n	%	n	%	n	%	n	%
0	x	x.x	x	x.x	x	x.x	x	x.x
1	x	x.x	x	x.x	x	x.x	x	x.x
2	x	x.x	x	x.x	x	x.x	x	x.x
3-6	x	x.x	x	x.x	x	x.x	x	x.x
7+	x	x.x	x	x.x	x	x.x	x	x.x

Notes: N = Number of participants in the Safety population; n = Number of participants reporting a given number of days of positive qualitative and/or quantitative RT-PCR results.

Table 36: Summary of Peak, Total, and Duration of Viral Shedding by Challenge Dose Group, Safety Population*

Variable	Statistic	10^4 $TCID_{50}$ Challenge Virus (N=X)	10^5 $TCID_{50}$ Challenge Virus (N=X)	10^6 $TCID_{50}$ Challenge Virus (N=X)	Sham Inoculum (N=X)
Peak viral load (log-10 copies/mL)	Mean (95% CI)	x.x (x.x, x.x)	x.x (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
	Minimum	x.x	x.x	x.x	x.x
	Median	x.x	x.x	x.x	x.x
	Maximum	x.x	x.x	x.x	x.x
AUC (log-10 copies/mL)[a]	Mean (95% CI)	x.x (x.x, x.x)	x.x (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
	Minimum	x.x	x.x	x.x	x.x
	Median	x.x	x.x	x.x	x.x
	Maximum	x.x	x.x	x.x	x.x
Duration of Viral Shedding[b]	Mean (95% CI)	x.x (x.x, x.x)	x.x (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
	Minimum	x.x	x.x	x.x	x.x
	Median	x.x	x.x	x.x	x.x
	Maximum	x.x	x.x	x.x	x.x

Note: N = Number of participants in the Safety population followed for the entire challenge period.
[a]Area under the curve calculated using raw viral copies/mL through discharge from the challenge unit, then log-10 transformed.
[b]Duration measured as the number of days between the first positive and last negative RT-PCR results, inclusive, regardless of any intermittent negative results.

Table 37: Maximum Severity of Participant-Reported FLU-PRO Symptoms by Study Day, 10^4 $TCID_{50}$ Challenge Virus Group, Currently Infected Participants in the Safety Population

		Baseline (N=XX)		Day 1 (Post-Challenge) (N=XX)		Day 2: RT-PCR+ (N=XX)		Day 3: RT-PCR+ (N=XX)		Day 4: RT-PCR+ (N=XX)		Day 5: RT-PCR+ (N=XX)		Day 6: RT-PCR+ (N=XX)		Day 7: RT-PCR+ (N=XX)		Day 8: RT-PCR+ (N=XX)		Days 9+[a]: RT-PCR+ (N=XX)		Anytime Post-Challenge[a]: RT-PCR+	
Symptom	**Extent**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Any Symptom	0	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Nose																							
Any Symptom	0	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Running or Dripping Nose	0 (Not at all)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (A little bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Somewhat)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Quite a bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Very much)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Congested or Stuffy Nose	0 (Not at all)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (A little bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Somewhat)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Quite a bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Very much)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

		Baseline (N=XX)		Day 1 (Post-Challenge) (N=XX)		Day 2: RT-PCR+ (N=XX)		Day 3: RT-PCR+ (N=XX)		Day 4: RT-PCR+ (N=XX)		Day 5: RT-PCR+ (N=XX)		Day 6: RT-PCR+ (N=XX)		Day 7: RT-PCR+ (N=XX)		Day 8: RT-PCR+ (N=XX)		Days 9+[a]: RT-PCR+ (N=XX)		Anytime Post-Challenge[a]: RT-PCR+	
Symptom	**Extent**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Sinus Pressure	0 (Not at all)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (A little bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Somewhat)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Quite a bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Very much)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Sneezing	0 (Never)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (Rarely)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Sometimes)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Often)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Always)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Throat																							
Any Symptom	0	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Scratchy or Itchy Throat	0 (Not at all)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (A little bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Somewhat)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Quite a bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Very much)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Sore or Painful Throat	0 (Not at all)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (A little bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Somewhat)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

		Baseline (N=XX)		Day 1 (Post-Challenge) (N=XX)		Day 2: RT-PCR+ (N=XX)		Day 3: RT-PCR+ (N=XX)		Day 4: RT-PCR+ (N=XX)		Day 5: RT-PCR+ (N=XX)		Day 6: RT-PCR+ (N=XX)		Day 7: RT-PCR+ (N=XX)		Day 8: RT-PCR+ (N=XX)		Days 9+[a]: RT-PCR+ (N=XX)		Anytime Post-Challenge[a]: RT-PCR+	
Symptom	**Extent**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	3 (Quite a bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Very much)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Difficulty Swallowing	0 (Not at all)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (A little bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Somewhat)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Quite a bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Very much)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Eyes																							
Any Symptom	0	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Teary or Watery Eyes	0 (Not at all)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (A little bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Somewhat)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Quite a bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Very much)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Sore or Painful Eyes	0 (Not at all)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (A little bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Somewhat)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Quite a bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Very much)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Eyes Sensitive to Light	0 (Not at all)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

		Baseline (N=XX)		Day 1 (Post-Challenge) (N=XX)		Day 2: RT-PCR+ (N=XX)		Day 3: RT-PCR+ (N=XX)		Day 4: RT-PCR+ (N=XX)		Day 5: RT-PCR+ (N=XX)		Day 6: RT-PCR+ (N=XX)		Day 7: RT-PCR+ (N=XX)		Day 8: RT-PCR+ (N=XX)		Days 9+[a]: RT-PCR+ (N=XX)		Anytime Post-Challenge[a]: RT-PCR+	
Symptom	**Extent**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	1 (A little bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Somewhat)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Quite a bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Very much)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Chest/Respiratory																							
Any Symptom	0	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Trouble Breathing	0 (Not at all)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (A little bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Somewhat)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Quite a bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Very much)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Chest Congestion	0 (Not at all)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (A little bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Somewhat)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Quite a bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Very much)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Chest Tightness	0 (Not at all)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (A little bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Somewhat)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Quite a bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

		Baseline (N=XX)		Day 1 (Post-Challenge) (N=XX)		Day 2: RT-PCR+ (N=XX)		Day 3: RT-PCR+ (N=XX)		Day 4: RT-PCR+ (N=XX)		Day 5: RT-PCR+ (N=XX)		Day 6: RT-PCR+ (N=XX)		Day 7: RT-PCR+ (N=XX)		Day 8: RT-PCR+ (N=XX)		Days 9+[a]: RT-PCR+ (N=XX)		Anytime Post-Challenge[a]: RT-PCR+	
Symptom	**Extent**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	4 (Very much)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Dry or Hacking Cough	0 (Not at all)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (A little bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Somewhat)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Quite a bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Very much)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Wet or Loose Cough	0 (Not at all)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (A little bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Somewhat)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Quite a bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Very much)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Coughing	0 (Never)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (Rarely)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Sometimes)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Often)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Always)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Coughing Up Mucus or Phlegm	0 (Never)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (Rarely)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Sometimes)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Often)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Always)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Body/Systemic																							
Any Symptom	0	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

		Baseline (N=XX)		Day 1 (Post-Challenge) (N=XX)		Day 2: RT-PCR+ (N=XX)		Day 3: RT-PCR+ (N=XX)		Day 4: RT-PCR+ (N=XX)		Day 5: RT-PCR+ (N=XX)		Day 6: RT-PCR+ (N=XX)		Day 7: RT-PCR+ (N=XX)		Day 8: RT-PCR+ (N=XX)		Days 9+[a]: RT-PCR+ (N=XX)		Anytime Post-Challenge[a]: RT-PCR+	
Symptom	**Extent**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	2	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Felt Dizzy	0 (Not at all)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (A little bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Somewhat)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Quite a bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Very much)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Head Congestion	0 (Not at all)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (A little bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Somewhat)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Quite a bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Very much)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Headache	0 (Not at all)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (A little bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Somewhat)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Quite a bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Very much)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Lack of Appetite	0 (Not at all)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (A little bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Somewhat)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Quite a bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Very much)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Sleeping More Than Usual	0 (Not at all)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

		Baseline (N=XX)		Day 1 (Post-Challenge) (N=XX)		Day 2: RT-PCR+ (N=XX)		Day 3: RT-PCR+ (N=XX)		Day 4: RT-PCR+ (N=XX)		Day 5: RT-PCR+ (N=XX)		Day 6: RT-PCR+ (N=XX)		Day 7: RT-PCR+ (N=XX)		Day 8: RT-PCR+ (N=XX)		Days 9+[a]: RT-PCR+ (N=XX)		Anytime Post-Challenge[a]: RT-PCR+	
Symptom	**Extent**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	1 (A little bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Somewhat)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Quite a bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Very much)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Body Aches or Pains	0 (Not at all)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (A little bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Somewhat)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Quite a bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Very much)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Weak or Tired	0 (Not at all)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (A little bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Somewhat)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Quite a bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Very much)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Chills or Shivering	0 (Not at all)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (A little bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Somewhat)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Quite a bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Very much)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Felt Cold	0 (Not at all)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (A little bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Somewhat)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Quite a bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Very much)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

		Baseline (N=XX)		Day 1 (Post-Challenge) (N=XX)		Day 2: RT-PCR+ (N=XX)		Day 3: RT-PCR+ (N=XX)		Day 4: RT-PCR+ (N=XX)		Day 5: RT-PCR+ (N=XX)		Day 6: RT-PCR+ (N=XX)		Day 7: RT-PCR+ (N=XX)		Day 8: RT-PCR+ (N=XX)		Days 9+[a]: RT-PCR+ (N=XX)		Anytime Post-Challenge[a]: RT-PCR+	
Symptom	**Extent**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Felt Hot	0 (Not at all)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (A little bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Somewhat)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Quite a bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Very much)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Sweating	0 (Not at all)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (A little bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Somewhat)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Quite a bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Very much)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Gastrointestinal																							
Any Symptom	0	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Felt Nauseous	0 (Not at all)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (A little bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Somewhat)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (Quite a bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Very much)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Stomachache	0 (Not at all)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (A little bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (Somewhat)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

		Baseline (N=XX)		Day 1 (Post-Challenge) (N=XX)		Day 2: RT-PCR+ (N=XX)		Day 3: RT-PCR+ (N=XX)		Day 4: RT-PCR+ (N=XX)		Day 5: RT-PCR+ (N=XX)		Day 6: RT-PCR+ (N=XX)		Day 7: RT-PCR+ (N=XX)		Day 8: RT-PCR+ (N=XX)		Days 9+[a]: RT-PCR+ (N=XX)		Anytime Post-Challenge[a]: RT-PCR+	
Symptom	**Extent**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	3 (Quite a bit)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (Very much)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Vomit	0 (0 times)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (1 time)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (2 times)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (3 times)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (4 or more times)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Diarrhea	0 (0 times)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	1 (1 time)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	2 (2 times)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	3 (3 times)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	4 (4 or more times)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

Notes: N = Number of participants in the Safety population RT-PCR+ on the given study day; n = Number of participants reporting each symptom. **Prior to Day 2, all participants included as symptom background.**

[a]As reported on the FLU-PRO tool.

Similar tables:

Table 38: Maximum Severity of Participant-Reported FLU-PRO Symptoms by Study Day, 10^5 $TCID_{50}$ Challenge Virus Group, Currently Infected Participants in the Safety Population

Table 39: Maximum Severity of Participant-Reported FLU-PRO Symptoms by Study Day, 10^6 $TCID_{50}$ Challenge Virus Group, Currently Infected Participants in the Safety Population

Table 40: Maximum Severity of Participant-Reported FLU-PRO Symptoms by Study Day, Sham Inoculum Group, Currently Infected Participants in the Safety Population

Table 41: Cross-Tabulation of the Maximum Severity of Solicited Influenza Symptoms and Participant-Reported FLU-PRO Symptoms During the Challenge Period, Infected Participants in the Safety Population

Symptom (Modified Jackson Score)	Maximum Severity	FLU-PRO Symptom and Maximum Extent n (%)				
		Any Symptom				
		Extent: 0	1	2	3	4
Any Symptom	Any Severity	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	None	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Mild or Just Noticeable	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Moderate or Bothersome from Time to Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Severe or Bothersome Most or All of the Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Running or Dripping Nose				
		Extent: 0 (Not at all)	1 (A little bit)	2 (Somewhat)	3 (Quite a bit)	4 (Very much)
Runny Nose	Any Severity	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	0: None	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	1: Just Noticeable	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	2: Bothersome from Time to Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	3: Bothersome Most or All of the Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Congested or Stuffy Nose				
		Extent: 0 (Not at all)	1 (A little bit)	2 (Somewhat)	3 (Quite a bit)	4 (Very much)
Stuffy Nose	Any Severity	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	0: None	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	1: Just Noticeable	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	2: Bothersome from Time to Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	3: Bothersome Most or All of the Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Sneezing				

Symptom (Modified Jackson Score)	**Maximum Severity**	**FLU-PRO Symptom and Maximum Extent n (%)**				
		Extent: 0 (Never)	1 (Rarely)	2 (Sometimes)	3 (Often)	4 (Always)
Sneezing	Any Severity	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	0: None	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	1: Just Noticeable	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	2: Bothersome from Time to Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	3: Bothersome Most or All of the Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Sore or Painful Throat				
		Extent: 0 (Not at all)	1 (A little bit)	2 (Somewhat)	3 (Quite a bit)	4 (Very much)
Sore Throat	Any Severity	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	0: None	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	1: Just Noticeable	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	2: Bothersome from Time to Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	3: Bothersome Most or All of the Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Headache				
		Extent: 0 (Not at all)	1 (A little bit)	2 (Somewhat)	3 (Quite a bit)	4 (Very much)
Headache	Any Severity	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	0: None	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	1: Just Noticeable	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	2: Bothersome from Time to Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	3: Bothersome Most or All of the Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Dry or Hacking Cough				
		Extent: 0 (Not at all)	1 (A little bit)	2 (Somewhat)	3 (Quite a bit)	4 (Very much)
Cough	Any Severity	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	0: None	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	1: Just Noticeable	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	2: Bothersome from Time to Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Symptom (Modified Jackson Score)	**Maximum Severity**	**FLU-PRO Symptom and Maximum Extent n (%)**				
	3: Bothersome Most or All of the Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Wet or Loose Cough				
		Extent: 0 (Not at all)	1 (A little bit)	2 (Somewhat)	3 (Quite a bit)	4 (Very much)
Cough	Any Severity	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	0: None	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	1: Just Noticeable	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	2: Bothersome from Time to Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	3: Bothersome Most or All of the Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Coughing				
		Extent: 0 (Never)	1 (Rarely)	2 (Sometimes)	3 (Often)	4 (Always)
Cough	Any Severity	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	0: None	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	1: Just Noticeable	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	2: Bothersome from Time to Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	3: Bothersome Most or All of the Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Coughing Up Mucus or Phlegm				
		Extent: 0 (Never)	1 (Rarely)	2 (Sometimes)	3 (Often)	4 (Always)
Cough	Any Severity	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	0: None	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	1: Just Noticeable	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	2: Bothersome from Time to Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	3: Bothersome Most or All of the Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Sleeping More Than Usual				
		Extent: 0 (Not at all)	1 (A little bit)	2 (Somewhat)	3 (Quite a bit)	4 (Very much)
Malaise (tiredness)	Any Severity	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	0: None	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Symptom (Modified Jackson Score)	**Maximum Severity**	**FLU-PRO Symptom and Maximum Extent n (%)**				
	1: Just Noticeable	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	2: Bothersome from Time to Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	3: Bothersome Most or All of the Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Weak or Tired				
		Extent: 0 (Not at all)	1 (A little bit)	2 (Somewhat)	3 (Quite a bit)	4 (Very much)
Malaise (tiredness)	Any Severity	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	0: None	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	1: Just Noticeable	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	2: Bothersome from Time to Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	3: Bothersome Most or All of the Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Body Aches or Pains				
		Extent: 0 (Not at all)	1 (A little bit)	2 (Somewhat)	3 (Quite a bit)	4 (Very much)
Body Ache	Any Severity	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	0: None	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	1: Just Noticeable	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	2: Bothersome from Time to Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	3: Bothersome Most or All of the Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Chills or Shivering				
		Extent: 0 (Not at all)	1 (A little bit)	2 (Somewhat)	3 (Quite a bit)	4 (Very much)
Chills	Any Severity	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	0: None	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	1: Just Noticeable	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	2: Bothersome from Time to Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	3: Bothersome Most or All of the Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Felt Cold				
		Extent: 0 (Not at all)	1 (A little bit)	2 (Somewhat)	3 (Quite a bit)	4 (Very much)

Symptom (Modified Jackson Score)	Maximum Severity	FLU-PRO Symptom and Maximum Extent n (%)				
Chills	Any Severity	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	0: None	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	1: Just Noticeable	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	2: Bothersome from Time to Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	3: Bothersome Most or All of the Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Felt Hot				
		Extent: 0 (Not at all)	1 (A little bit)	2 (Somewhat)	3 (Quite a bit)	4 (Very much)
Feverish	Any Severity	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	0: None	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	1: Just Noticeable	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	2: Bothersome from Time to Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	3: Bothersome Most or All of the Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
		Trouble Breathing				
		Extent: 0 (Not at all)	1 (A little bit)	2 (Somewhat)	3 (Quite a bit)	4 (Very much)
Shortness of Breath	Any Severity	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	0: None	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	1: Just Noticeable	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	2: Bothersome from Time to Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	3: Bothersome Most or All of the Time	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Notes: N = Number of infected participants in the Safety population; n = Number of participants reporting each symptom. Earache from Modified Jackson Score tool not included, with no corresponding FLU-PRO data for comparison.

Similar Table:

Table 42: Cross-Tabulation of the Maximum Severity of Solicited Influenza Symptoms and Participant-Reported FLU-PRO Symptoms During the Challenge Period, Uninfected Participants in the Safety Population

[Implementation Note: Update the footnote from the shell above for uninfected participants.]

Table 43: Summary of Symptom Scores by Challenge Dose Group and Infection Status, Safety Population

Symptom Score	Statistic	10^4 $TCID_{50}$ Challenge Virus (N=X)			10^5 $TCID_{50}$ Challenge Virus (N=X)			10^6 $TCID_{50}$ Challenge Virus (N=X)			Sham Inoculum (N=X)		
		Infected[a]	Uninfected	All Participants in Dose Group	Infected[a]	Uninfected	All Participants in Dose Group	Infected[a]	Uninfected	All Participants in Dose Group	Infected[a]	Uninfected	All Participants in Dose Group
Maximum Cumulative Modified Jackson Score (Total)	Mean (95% CI)[b]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Minimum	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
	Median	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
	Maximum	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
Area Under the Modified Jackson Score Curve per Day (Days 2 through 8 for uninfected participants, or during infection for infected participants)	Mean (95% CI)[b]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Minimum	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
	Median	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
	Maximum	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
Modified Jackson Score (Total), Study Day 15	Mean (95% CI)[b]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Minimum	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
	Median	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
	Maximum	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
Cumulative FLU-PRO Score (Total)	Mean (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Minimum	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
	Median	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx

Symptom Score	Statistic	10^4 $TCID_{50}$ Challenge Virus (N=X)			10^5 $TCID_{50}$ Challenge Virus (N=X)			10^6 $TCID_{50}$ Challenge Virus (N=X)			Sham Inoculum (N=X)		
		Infected[a]	Uninfected	All Participants in Dose Group	Infected[a]	Uninfected	All Participants in Dose Group	Infected[a]	Uninfected	All Participants in Dose Group	Infected[a]	Uninfected	All Participants in Dose Group
	Maximum	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
Cumulative FLU-PRO (Nose)	Mean (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Minimum	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
	Median	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
	Maximum	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
Cumulative FLU-PRO (Throat)	Mean (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Minimum	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
	Median	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
	Maximum	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
Cumulative FLU-PRO (Eyes)	Mean (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Minimum	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
	Median	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
	Maximum	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
Cumulative FLU-PRO (Chest/Respiratory)	Mean (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Minimum	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
	Median	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
	Maximum	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
Cumulative FLU-PRO (Body/Systemic)	Mean (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Minimum	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
	Median	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx

Symptom Score	Statistic	10^4 $TCID_{50}$ Challenge Virus (N=X)			10^5 $TCID_{50}$ Challenge Virus (N=X)			10^6 $TCID_{50}$ Challenge Virus (N=X)			Sham Inoculum (N=X)		
		Infected[a]	Uninfected	All Participants in Dose Group	Infected[a]	Uninfected	All Participants in Dose Group	Infected[a]	Uninfected	All Participants in Dose Group	Infected[a]	Uninfected	All Participants in Dose Group
	Maximum	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
Cumulative FLU-PRO (Gastrointestinal)	Mean (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Minimum	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
	Median	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
	Maximum	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx

Notes: N = Number of participants in the Safety population; GMT = Geometric Mean Titer; GMFR = Geometric Mean Fold-Rise. Cumulative FLU-PRO scores are the sum of the daily scores (based on maximum severity per question) across the entire challenge period.

[a] RT-PCR+ results reported on at least two days during the challenge period (Days 2 to 8).

[b] Confidence interval calculated based on the Student's t-distribution.

Table 44: Maximum Severity of Influenza Symptoms Reported During the Challenge Period by Clinical Site, Infected Participants in the Safety Population

Symptom	Severity	Duke University (N=X)		University of Maryland (N=X)	
		n (%)	95% CI	n (%)	95% CI
Any Symptom	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-
	Mild or Just Noticeable	x (x.x)	-	x (x.x)	-
	Moderate or Bothersome from Time to Time	x (x.x)	-	x (x.x)	-
	Severe or Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-
Runny Nose[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-
Stuffy Nose[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-
Sneezing[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-
Sore Throat[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-
Headache[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)

Symptom	Severity	Duke University (N=X)		University of Maryland (N=X)	
		n (%)	95% CI	n (%)	95% CI
	0: None	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-
Cough[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-
Malaise (tiredness)[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-
Body Ache[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-
Chills[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-
Feverish[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-

Symptom	Severity	Duke University (N=X)		University of Maryland (N=X)	
		n (%)	95% CI	n (%)	95% CI
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-
Fever[b]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-
	Mild	x (x.x)	-	x (x.x)	-
	Moderate	x (x.x)	-	x (x.x)	-
	Severe	x (x.x)	-	x (x.x)	-
Shortness of Breath[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-
Earache[a]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	0: None	x (x.x)	-	x (x.x)	-
	1: Just Noticeable	x (x.x)	-	x (x.x)	-
	2: Bothersome from Time to Time	x (x.x)	-	x (x.x)	-
	3: Bothersome Most or All of the Time	x (x.x)	-	x (x.x)	-
Lymphopenia[c]	Any Severity	x (x.x)	(x.x, x.x)	x (x.x)	(x.x, x.x)
	None	x (x.x)	-	x (x.x)	-
	Mild	x (x.x)	-	x (x.x)	-
	Moderate	x (x.x)	-	x (x.x)	-
	Severe	x (x.x)	-	x (x.x)	-

Notes: N = Number of participants in the Safety population with RT-PCR+ results on at least two study days; n = Number of participants reporting each symptom, regardless of timing with respect to RT-PCR positivity.

[a] As reported on the Modified Jackson Score (MJS) tool; maximum severity across the challenge period reported.

[b] As part of vital signs assessments, with temperature collected three times daily during the challenge period. Fever and feverishness (from MJS) contribute as one item towards the Modified Jackson Score.

[c] As part of clinical safety laboratory assessments, on Study Days 2, 4, 8, and any supplemental visits during the challenge period.

Similar Table:

Table 45: Maximum Severity of Influenza Symptoms Reported During the Challenge Period by Clinical Site, Uninfected Participants in the Safety Population

Table 46: Symptoms Predicting Infection Status Lasso Logistic Regression Model to Predict Infection Status, Safety Population

Model Parameter	Parameter Estimate	SE	p-value	Odds Ratio	95% CI
Intercept	x.xx	x.xx	x.xxx	-	-
[Symptom x]	x.xx	x.xx	x.xxx	x.xx	(x.xx, x.xx)
[Symptom y]	x.xx	x.xx	x.xxx	x.xx	(x.xx, x.xx)
[Repeat for any additional symptom(s) selected in lasso procedure]					

Notes: XX participants in the Safety population included in the model; the infection outcome is defined as two or more study days with RT-PCR+ tests at any point during the challenge period. The maximum severity of each MJS symptom during the infection period, or across the challenge period for the uninfected participants, is utilized in the set of candidate predictors.
The optimal value for the penalization parameter determined using10-fold cross-validation .
Unbiased coefficient estimates obtained by refitting selected covariates in logistic regression model.
Hosmer and Lemeshow Goodness of Fit p-value = 0.xxx.

Table 47: Comparison of Symptomatic Influenza Infection to Mild-to-Moderate Influenza Disease, Safety Population

Variable	10^4 $TCID_{50}$ Challenge Virus (N=X)		10^5 $TCID_{50}$ Challenge Virus (N=X)		10^6 $TCID_{50}$ Challenge Virus (N=X)		Sham Inoculum (N=X)		All Participants (N=X)	
	MMID-2 n (%)	No MMID-2 n (%)	MMID-2 n (%)	No MMID-2 n (%)	MMID-2 n (%)	No MMID-2 n (%)	MMID-2 n (%)	No MMID-2 n (%)	MMID-2 n (%)	No MMID-2 n (%)
Symptomatic Influenza Infection	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
No Symptomatic Influenza Infection	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)

Notes: N = Number of participants in the Safety population; n = Number of participants reporting the given combination of Symptomatic Influenza Infection and MMID-2 outcomes after challenge.

Table 48: Logistic Regression Model to Assess the Associations Between Baseline Characteristics and Development of Symptomatic Influenza Infection, Safety Population

Model Parameter	Parameter Estimate	SE	p-value	Odds Ratio	95% CI
Intercept	x.xx	x.xx	x.xxx	-	-
Challenge Virus Dose ($TCID_{50}$)	x.xx	x.xx	x.xxx	x.xx	(x.xx, x.xx)
Age at Baseline (Years)	x.xx	x.xx	x.xxx	x.xx	(x.xx, x.xx)
Sex (Male vs. Female)	x.xx	x.xx	x.xxx	x.xx	(x.xx, x.xx)
Prior Receipt of Seasonal Influenza Vaccine or Viral Challenge (Yes vs. No)	x.xx	x.xx	x.xxx	x.xx	(x.xx, x.xx)
Clinical Site (UMD vs. DU)	x.xx	x.xx	x.xxx	x.xx	(x.xx, x.xx)

Notes: XX participants in the Safety population included in the model; the symptomatic influenza infection outcome is defined as two or more study days with RT-PCR+ tests and, separately, a cumulative Modified Jackson Score of at least 6 over any 5-day window during the challenge period. Hosmer and Lemeshow Goodness of Fit p-value = 0.xxx.

14.2.2 Immunogenicity Data Summary Tables

Table 49: Summary of Hemagglutination Inhibition Antibody Titers Against A/Texas/71/2017 (H3N2), clade 3C3a Virus, by Challenge Dose Group, Infection Status, and Study Day, ITT Population*

Study Day	Statistic	10^4 $TCID_{50}$ Challenge Virus (N=X)		10^5 $TCID_{50}$ Challenge Virus (N=X)		10^6 $TCID_{50}$ Challenge Virus (N=X)		Sham Inoculum (N=X)	
		Infected[a]	Uninfected	Infected[a]	Uninfected	Infected[a]	Uninfected	Infected[a]	Uninfected
Baseline	n	x	x	x	x	x	x	x	x
	GMT (95% CI)[b]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Day 8	n	x	x	x	x	x	x	x	x
	GMT (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	GMFR (95% CI)[b]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroconversion - % (95% CI)[c]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Day 15	n	x	x	x	x	x	x	x	x
	GMT (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	GMFR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroconversion - % (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Day 29	n	x	x	x	x	x	x	x	x
	GMT (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	GMFR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroconversion - % (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Day 57	n	x	x	x	x	x	x	x	x
	GMT (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	GMFR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroconversion % (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)

Notes: n = Number of participants in the Intent-to-Treat population with available results; GMT = Geometric Mean Titer; GMFR = Geometric Mean Fold-Rise.
[a] RT-PCR+ results reported on at least two days during the challenge period (Days 2 to 8).
[b] Confidence Interval calculated based on the Student's t-distribution.
[c] Exact binomial confidence interval calculated using the Clopper-Pearson methodology.

Similar Tables:

Table 50: Summary of Microneutralization Antibody Titers Against A/Texas/71/2017 (H3N2), clade 3C3a Virus, by Challenge Dose Group, Infection Status, and Study Day, ITT Population*

Table 51: Summary of Neuraminidase Inhibition Antibody Titers Against A/Texas/71/2017 (H3N2), clade 3C3a Virus, by Challenge Dose Group, Infection Status, and Study Day, ITT Population

Table 52: Summary of Anti-Hemagglutination Stalk Antibody Titers Against A/Texas/71/2017 (H3N2), clade 3C3a Virus, by Challenge Dose Group, Infection Status, and Study Day, ITT Population*

Table 53: Summary of Hemagglutination Inhibition Antibody Titers Against A/Texas/71/2017 (H3N2), clade 3C3a Virus, by Symptomatic Infection Status, and Study Day, ITT Population

Study Day	Statistic	Symptomatic and Infected (N=X)	Asymptomatic and Infected (N=X)	Symptomatic and Uninfected (N=X)	Asymptomatic and Uninfected (N=X)
Baseline	n	x	x	x	x
	GMT (95% CI)[b]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Day 8	n	x	x	x	x
	GMT (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	GMFR (95% CI)[b]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroconversion - % (95% CI)[c]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Day 15	n	x	x	x	x
	GMT (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	GMFR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroconversion - % (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Day 29	n	x	x	x	x
	GMT (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	GMFR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroconversion - % (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Day 57	n	x	x	x	x
	GMT (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	GMFR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroconversion % (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)

Similar Tables:

Table 54: Summary of Microneutralization Antibody Titers Against A/Texas/71/2017 (H3N2), clade 3C3a Virus, by Symptomatic Infection Status, and Study Day, ITT Population

Table 55: Summary of Neuraminidase Inhibition Antibody Titers Against A/Texas/71/2017 (H3N2), clade 3C3a Virus, by Symptomatic Infection Status, and Study Day, ITT Population

Table 56: Summary of Anti-Hemagglutination Stalk Antibody Titers Against A/Texas/71/2017 (H3N2), clade 3C3a Virus, by Symptomatic Infection Status, and Study Day, ITT Population

14.3 Safety Data

14.3.1 Displays of Adverse Events

Table 57: Overall Summary of Adverse Events*

Participants[a] with	10^4 $TCID_{50}$ Challenge Virus (N=X)		10^5 $TCID_{50}$ Challenge Virus (N=X)		10^6 $TCID_{50}$ Challenge Virus (N=X)		Sham Inoculum (N=X)		All Participants (N=X)	
	n	%	n	%	n	%	n	%	n	%
At least one unsolicited adverse event	x	x.x	x	x.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	x.x	x	x.x
Mild (Grade 1)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Moderate (Grade 2)	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Severe (Grade 3)	x	x.x	x	x.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	x.x	x	x.x
Related	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Unrelated	x	x.x	x	x.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	x.x	x	x.x
At least one related, serious adverse event	x	x.x	x	x.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	x.x	x	x.x

N = Number of participants in the Safety population; n = Number of participants meeting the given criterion.
[a] Participants are counted once for each category regardless of the number of events.
[b] A listing of Serious Adverse Events is included in Table 61.
[c] As reported on the Adverse Event eCRF.

Table 58: Adverse Events Occurring in 5% of Participants in Any Study Group by MedDRA System Organ Class and Preferred Term, and Study Group - Safety Population*

[Implementation Note: This table should include a row for any PT/SOC reported by ≥5% participants in any group.]

MedDRA System Organ Class	Preferred Term	10^4 $TCID_{50}$ Challenge Virus (N=X)		10^5 $TCID_{50}$ Challenge Virus (N=X)		10^6 $TCID_{50}$ Challenge Virus (N=X)		Sham Inoculum (N=X)		All Participants (N=X)	
		n (%)	# Events	n (%)	# Events	n (%)	# Events	n (%)	# Events	n (%)	# Events
SOC1	PT1										
Etc.	Etc.										

Notes: N = Number of participants in the Safety population (number of participants at risk); n= number of participants reporting event.

14.3.1.1 Unsolicited Adverse Events

Table 59: Summary of Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Time Post-Challenge, and Challenge Dose Group*

[Implementation note: If any unsolicited AEs are reported during supplemental challenge period visits (e.g., Visits 08S, 08T, etc.), include in the Day 1-8 portion of the table and add a footnote to clarify how many AEs of that nature occurred.]

MedDRA System Organ Class	MedDRA Preferred Term	Day 1-8 (Challenge Period)				Day 9+ (Post-Discharge)				Any Time Post-Challenge			
		n	%	95% CI	# Events	n	%	95% CI	# Events	n	%	95% CI	# Events
10^4 $TCID_{50}$ Challenge Virus (N=X)													
Any SOC	Any PT	x	x.x	x.x, x.x	x	x	x.x	x.x, x.x	x	x	x.x	xx, xx	x
[SOC 1]	Any PT	x	x.x	x.x, x.x	x	x	x.x	x.x, x.x	x	x	x.x	xx, xx	x
	[PT 1]	x	x.x	x.x, x.x	x	x	x.x	x.x, x.x	x	x	x.x	xx, xx	x
	[PT 2]	x	x.x	x.x, x.x	x	x	x.x	x.x, x.x	x	x	x.x	xx, xx	x
[SOC 2]	Any PT	x	x.x	x.x, x.x	x	x	x.x	x.x, x.x	x	x	x.x	xx, xx	x
	[PT 1]	x	x.x	x.x, x.x	x	x	x.x	x.x, x.x	x	x	x.x	xx, xx	x
	[PT 2]	x	x.x	x.x, x.x	x	x	x.x	x.x, x.x	x	x	x.x	xx, xx	x
[Repeat for all SOC/PTs reported and for other challenge dose groups]													

Notes: N = Number of participants in the Safety population; n = Number of participants reporting each SOC/PT. A participant is only counted once per PT/time point. Confidence intervals for the probability of reporting a given event are calculated via the exact Clopper-Pearson method.

Table 60: Incidence of Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, Relationship, and Challenge Dose Group

MedDRA System Organ Class	Preferred Term	Severity	10^4 $TCID_{50}$ Challenge Virus (N = X)				10^4 $TCID_{50}$ Challenge Virus (N = X)				10^4 $TCID_{50}$ Challenge Virus (N = X)				Sham Inoculum (N=X)				All Participants Receiving Active Challenge Virus (N=X)			
			Related		Not Related		Related		Not Related		Related		Not Related		Related		Not Related		Related		Not Related	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Any SOC	Any PT	Any Severity	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
		Mild	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
		Moderate	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
		Severe	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
[SOC 1]	[PT 1]	Any Severity	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
		Mild	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
		Moderate	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
		Severe	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	[PT 2]	Any Severity	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
		Mild	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
		Moderate	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
		Severe	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

Note: N = Number of participants in the Safety Population; n = Number of participants reporting each SOC/PT.

14.3.1.2 Solicited Adverse Events

This is just a placeholder for the CSR. No solicited AEs are collected for the 20-0005 study.

14.3.2 Listing of Deaths, Other Serious and Significant Adverse Events

Table 61: Listing of Serious Adverse Events

[Implementation Notes: If the event is ongoing (no stop date), indicate "ongoing" for the "Duration". If more than one reason is selected for the reason reported as an SAE, list all reasons in the column, separated by commas. In the "If Not Related, Alternate Etiology" column, merge the 2 data fields for collecting alternate etiology, separate by a colon. If there are no comments for an event, populate 'Comments' row with 'None'. Participant ID should be USUBJID (not PATID) for purposes of de-identification. Listing should be sorted by Challenge Dose Group, Participant ID, Associated with Dose No., and No. of Days Post Associated Dose.]

Adverse Event	No. of Days Post Challenge (Duration)	No. of Days Post Challenge the Event Became Serious	Reason Reported as an SAE	Severity	Relationship to Study Challenge	If Not Related, Alternative Etiology	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Participant ID: , Challenge Dose Group: , AE Number:									
Comments:									
Participant ID: , Challenge Dose Group: , AE Number:									
Comments:									

Table 62: Listing of Severe Influenza Complications Reported as Adverse Events

[Implementation Note: 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. If there are no comments for an event, populate 'Comments' row with 'None'. Participant ID should be USUBJID (not PATID) for purposes of de-identification. Listing should be sorted by Challenge Dose Group, Participant ID, and No. of Days Post Challenge.]

Adverse Event	No. of Days Post Challenge (Duration)		Severity	Relationship to Study Challenge	If Not Related, Alternative Etiology	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Participant ID: , Challenge Dose Group: , AE Number:								
Comments:								
Participant ID: , Challenge Dose Group: , AE Number:								
Comments:								

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 Abnormal Laboratory Value Listings (by Participant)

Table 63: Listing of Abnormal Laboratory Results - Chemistry

[Implementation Note: A complete listing of all laboratory results is included separately. In the Laboratory Parameter column, indicate the units after the parameter, e.g., Hemoglobin (g/dL).This listing is not color-coded, but the severity should be included in parentheses after the result, e.g., 16.2 (mild).In the "If Not Related, Alternate Etiology" column, merge the 2 data fields for collecting alternate etiology, separate by a colon. Participant ID should be USUBJID (not PATID) for purposes of de-identification.]

Participant ID	Challenge Dose Group	Sex	Age (years)	Planned Study Day	Actual Study Day	Laboratory Parameter (Units)	Result (Severity)	Relationship to Study Challenge	If Not Related, Alternate Etiology

Table 64: Listing of Abnormal Laboratory Results - Hematology

[Implementation Note: A complete listing of all laboratory results is included separately. In the Laboratory Parameter column, indicate the units after the parameter, e.g., Hemoglobin (g/dL). This listing is not color-coded, but the severity should be included in parentheses after the result, e.g., 16.2 (mild).In the "If Not Related, Alternate Etiology" column, merge the 2 data fields for collecting alternate etiology, separate by a colon. Participant ID should be USUBJID (not PATID) for purposes of de-identification.]

Participant ID	Challenge Dose Group	Sex	Age (years)	Planned Study Day	Actual Study Day	Laboratory Parameter (Units)	Result (Severity)	Relationship to Study Challenge	If Not Related, Alternate Etiology

14.3.5 Displays of Laboratory Results

14.3.5.1 Chemistry Results

Table 65: Laboratory Results by Parameter, Maximum Severity, Time Point, and Challenge Dose Group – Any Chemistry Parameter

[Implementation Note: If results are available for all participants at all timepoints, remove the Missing column.]

Time Point	Challenge Dose Group	N	None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%
Baseline	10^4 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^5 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^6 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Sham Inoculum	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Day 2	10^4 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^5 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^6 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Sham Inoculum	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Day 4	10^4 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^5 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^6 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Sham Inoculum	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Day 8	10^4 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^5 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^6 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Sham Inoculum	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Max Severity Post Baseline	10^4 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^5 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^6 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Sham Inoculum	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

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

Similar Tables:

Table 66: Laboratory Results by Parameter, Maximum Severity, Time Point, and Challenge Dose Group – Creatinine

Table 67: Laboratory Results by Parameter, Maximum Severity, Time Point, and Challenge Dose Group – Alanine Aminotransferase (ALT)

14.3.5.2 Hematology Results

Table 68: Laboratory Results by Parameter, Maximum Severity, Time Point, and Challenge Dose Group – Any Hematology Parameter

[Implementation Note: If results are available for all participants at all timepoints, remove the Missing column. For parameters with both a gradable increase and a gradable decrease (WBC and Platelets), collapse into one severity for display in the Any Hematology Parameter table. For WBC and Platelets tables, include columns for both increases and decreases (e.g., "Mild/Grade 1 (Low)" and "Mild/Grade 1 (High)".]

Time Point	Challenge Dose Group	N	None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%
Baseline	10^4 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^5 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^6 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Sham Inoculum	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Day 2	10^4 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^5 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^6 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Sham Inoculum	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Day 4	10^4 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^5 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^6 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Sham Inoculum	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Day 8	10^4 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^5 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^6 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Sham Inoculum	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Max Severity Post Baseline	10^4 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^5 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

Time Point	Challenge Dose Group	N	None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%
	10^6 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Sham Inoculum	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Max Severity Post Infection	10^4 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^5 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^6 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Sham Inoculum	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

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

Similar Tables:

Table 69: Laboratory Results by Parameter, Maximum Severity, Time Point, and Challenge Dose Group – White Blood Cells

Table 70: Laboratory Results by Parameter, Maximum Severity, Time Point, and Challenge Dose Group – Absolute Lymphocyte Count

Table 71: Laboratory Results by Parameter, Maximum Severity, Time Point, and Challenge Dose Group – Hemoglobin

Table 72: Laboratory Results by Parameter, Maximum Severity, Time Point, and Challenge Dose Group – Platelets

14.3.6 Displays of Vital Signs

Table 73: Vital Signs by Maximum Severity, Time Point, and Challenge Dose Group – Any Assessment

[Implementation Note: If results are available for all participants at all timepoints, remove the Missing column. For the heart rate, blood pressure (each of systolic and diastolic), and respiratory rate tables, include columns for both increases and decreases (e.g., "Mild/Grade 1 (Low)" and "Mild/Grade 1 (High)".]

Time Point	Challenge Dose Group	N	None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%
Baseline	10^4 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^5 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^6 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Sham Inoculum	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Max Severity During the Challenge Period	10^4 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^5 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^6 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Sham Inoculum	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Day 15	10^4 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^5 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^6 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Sham Inoculum	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Max Severity Post Baseline	10^4 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^5 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^6 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Sham Inoculum	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Max Severity Post Infection	10^4 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	10^5 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

Time Point	Challenge Dose Group	N	None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%
	10^6 $TCID_{50}$ Challenge Virus	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Sham Inoculum	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

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

Similar Tables:

Table 74: Vital Signs by Maximum Severity, Time Point, and Challenge Dose Group – Heart Rate

Table 75: Vital Signs by Maximum Severity, Time Point, and Challenge Dose Group – Blood Pressure (Systolic)

Table 76: Vital Signs by Maximum Severity, Time Point, and Challenge Dose Group – Blood Pressure (Diastolic)

Table 77: Vital Signs by Maximum Severity, Time Point, and Challenge Dose Group – SpO_2

Table 78: Vital Signs by Maximum Severity, Time Point, and Challenge Dose Group – Respiratory Rate

14.4 Summary of Concomitant Medications

Table 79: Number and Percentage of Participants Reporting Concomitant Medications by WHO Drug Classification and Challenge Dose Group

WHO Drug Code Level 1, Anatomic Group	WHO Drug Code Level 2, Therapeutic Subgroup	10^4 $TCID_{50}$ Challenge Virus (N=X)		10^5 $TCID_{50}$ Challenge Virus (N=X)		10^6 $TCID_{50}$ Challenge Virus (N=X)		Sham Inoculum (N=X)		All Participants (N=X)	
		n	%	n	%	n	%	n	%	n	%
Any Level 1 Codes	Any Level 2 Codes	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
[ATC Level 1 - 1]	Any [ATC 1 – 1]	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	[ATC 2 - 1]	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	[ATC 2 - 2]	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	[ATC 2 - 3]	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
[ATC Level 1 – 2]	[ATC 2 - 1]	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	[ATC 2 - 2]	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	[ATC 2 - 3]	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

Notes: N = Number of challenged participants; n = Number of participants reporting taking at least one medication in the specific WHO Drug Class.

APPENDIX 2. FIGURE MOCK-UPS

This document includes examples mock-ups of figures to present clinical, immunogenicity, and safety data. General conventions for figures, unless stated otherwise: Include N and study group in figure; e.g., Group A (N = X) at top of panel.Utilize pattern-coding, when possibleOutput figures in PNG format

LIST OF FIGURES

9.1 Overall Study Design and Plan Description

Figure 1: Adaptive Dosing Schedule

9.7.1 Sample Size

Figure 2: Probabilities of further enrollment at the current dose, given varying true infection probabilities, numbers of participants enrolled at the current dose, and decision thresholds

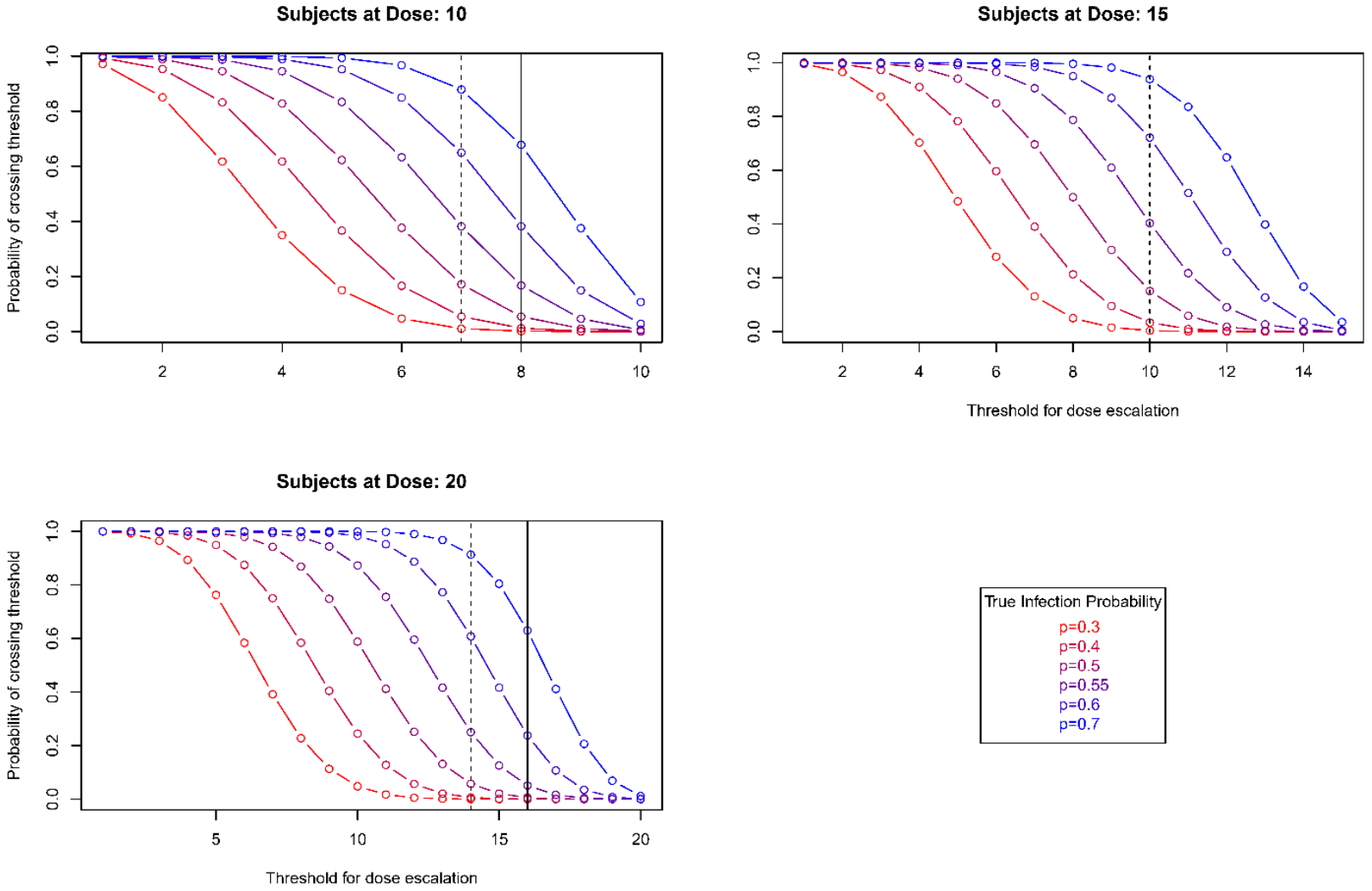


Figure 3: Estimated symptomatic influenza probabilities and associated exact 95% CIs, given varying numbers of symptomatic influenza events observed and varying sample sizes

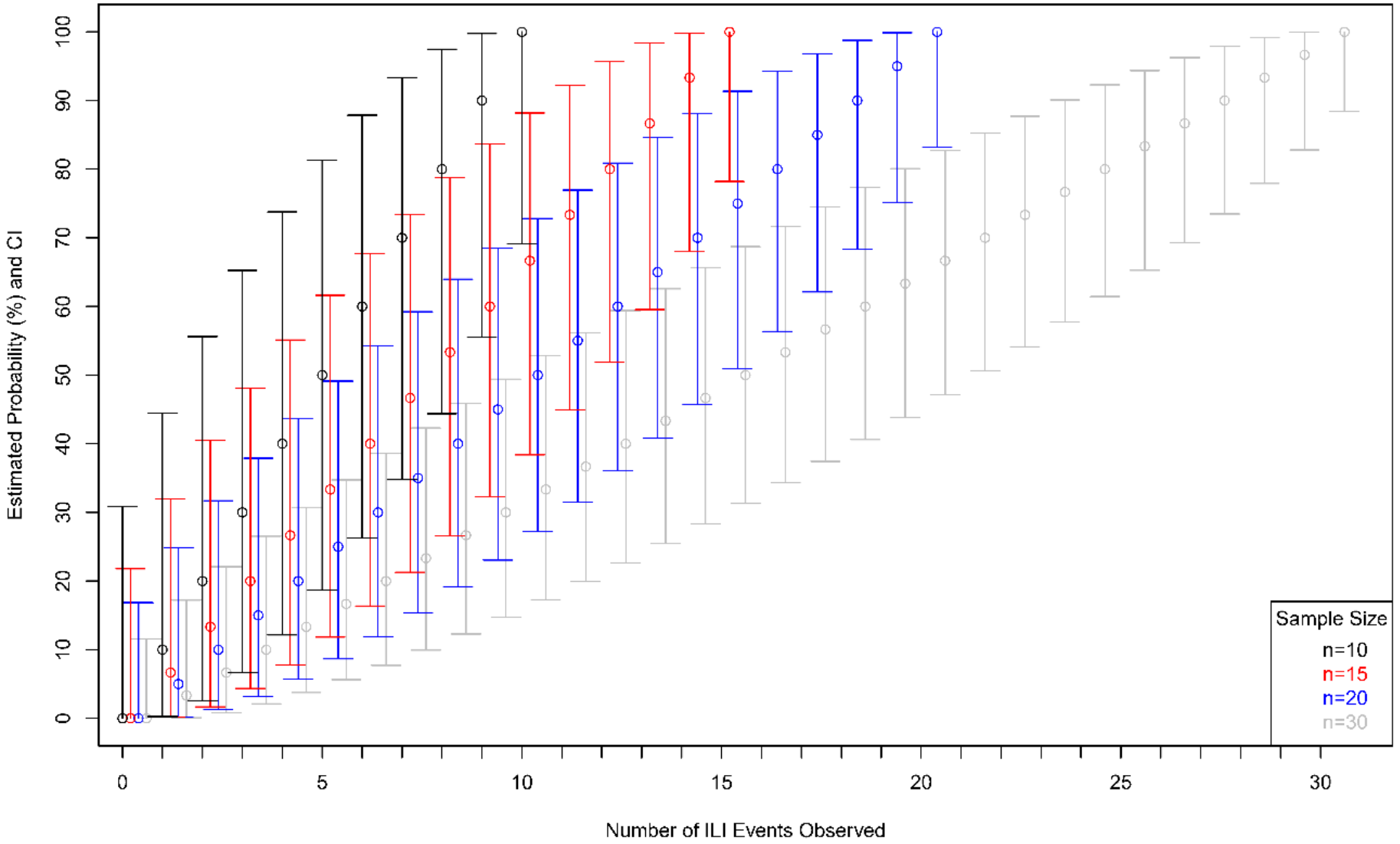


Figure 4: Modified Jackson Score – Investigator Assessment Tool

MODIFIED JACKSON SCORE – INVESTIGATOR ASSESSMENT TOOL

Protocol Number: 20-0005
Study Day:__ __
Form Number: ☐001(AM) ☐ 002 (PM) Other __ __ __

Subject ID ☐☐☐☐☐☐☐☐ Today's Date D D M M M Y Y Y Y Current Time 2 4 : 0 0

Symptom Form	0 = absent, 1 = mild, 2 = moderate, 3 = severe			
Severity Level	**0**	**1**	**2**	**3**
Symptoms *As reported by subject*	**Subject has NO symptoms**	**Just noticeable**	**Bothersome from time to time, but doesn't prevent me from doing activities**	**Bothersome most or all the time, and prevents me from doing activities**
Runny Nose *(check with an X)*	0 ☐	1 ☐	2 ☐	3 ☐
Stuffy Nose *(check with an X)*	0 ☐	1 ☐	2 ☐	3 ☐
Sneezing *(check with an X)*	0 ☐	1 ☐	2 ☐	3 ☐
Sore Throat *(check with an X)*	0 ☐	1 ☐	2 ☐	3 ☐
Headache *(check with an X)*	0 ☐	1 ☐	2 ☐	3 ☐
Cough *(check with an X)*	0 ☐	1 ☐	2 ☐	3 ☐
Malaise (tiredness) *(check with an X)*	0 ☐	1 ☐	2 ☐	3 ☐
Body Ache *(check with an X)*	0 ☐	1 ☐	2 ☐	3 ☐
Chills *(check with an X)*	0 ☐	1 ☐	2 ☐	3 ☐
Feverish *(check with an X)*	0 ☐	1 ☐	2 ☐	3 ☐
Shortness of Breath *(check with an X)*	0 ☐	1 ☐	2 ☐	3 ☐
Earache *(check with an X)*	0 ☐	1 ☐	2 ☐	3 ☐
TOTAL SCORE				

Administered by: _____ Date (ddMMMyyyy): ___ ___ ___ ___ ___ ___ ___ ___ ___

DMID 20-0005 V3.0 24FEB2022

Figure 5: FLU-PRO – Participant Reported Tool

Participant ID: _____ Participant Initials:_____Date:_____/_____/_____

FLU-PRO©

People experience the flu in different ways. We would like to know about the symptoms you have been experiencing during the past 24 hours. For each symptom, please mark one box ☐ under the response that best matches your experience. Mark the "Not at all" box, if you did not have that symptom in the past 24 hours.

What time is it?_____AM / PM (please circle)

Please rate the extent to which you had each symptom during the past 24 hours.

	Not at all	A little bit	Somewhat	Quite a bit	Very much
Runny or dripping nose	☐	☐	☐	☐	☐
Congested or stuffy nose	☐	☐	☐	☐	☐
Sinus pressure	☐	☐	☐	☐	☐
Scratchy or itchy throat	☐	☐	☐	☐	☐
Sore or painful throat	☐	☐	☐	☐	☐
Difficulty swallowing	☐	☐	☐	☐	☐
Teary or watery eyes	☐	☐	☐	☐	☐
Sore or painful eyes	☐	☐	☐	☐	☐
Eyes sensitive to light	☐	☐	☐	☐	☐
Trouble breathing	☐	☐	☐	☐	☐
Chest congestion	☐	☐	☐	☐	☐
Chest tightness	☐	☐	☐	☐	☐
Dry or hacking cough	☐	☐	☐	☐	☐
Wet or loose cough	☐	☐	☐	☐	☐
Felt nauseous (feeling like you wanted to throw-up)	☐	☐	☐	☐	☐
Stomachache	☐	☐	☐	☐	☐
Felt dizzy	☐	☐	☐	☐	☐
Head congestion	☐	☐	☐	☐	☐
Headache	☐	☐	☐	☐	☐

Participant ID: _____ **Participant Initials:**_____**Date:**_____/_____/_____

Please rate the extent to which you had each symptom during the past 24 hours.

	Not at all	A little bit	Somewhat	Quite a bit	Very much
Lack of appetite	☐	☐	☐	☐	☐
Sleeping more than usual	☐	☐	☐	☐	☐
Body aches or pains	☐	☐	☐	☐	☐
Weak or tired	☐	☐	☐	☐	☐
Chills or shivering	☐	☐	☐	☐	☐
Felt cold	☐	☐	☐	☐	☐
Felt hot	☐	☐	☐	☐	☐
Sweating	☐	☐	☐	☐	☐

In the past 24 hours, how often have you had any of the following symptoms?

	Never	Rarely	Sometimes	Often	Always
Sneezing	☐	☐	☐	☐	☐
Coughing	☐	☐	☐	☐	☐
Coughed up mucus or phlegm	☐	☐	☐	☐	☐

	0 times	1 time	2 times	3 times	4 or more times
How many times did you vomit?	☐	☐	☐	☐	☐
How many times did you have diarrhea?	☐	☐	☐	☐	☐

Participant ID: _____ **Participant Initials:**_____ **Date:**_____/_____/_____

Items to be asked in the daily diary through to Day 15 along with the Flu-PRO items.

1. Overall, how severe were your flu symptoms today? (Please select one response only)
- ☐ 0 No flu symptoms today
- ☐ 1 Mild
- ☐ 2 Moderate
- ☐ 3 Severe
- ☐ 4 Very severe

2. [Skip this question if you answered 0 above]. Overall, how were your flu symptoms today compared to yesterday? (Please select one response only)
- ☐ 1 Much better
- ☐ 2 Somewhat better
- ☐ 3 A little better
- ☐ 4 About the same
- ☐ 5 A little worse
- ☐ 6 Somewhat worse
- ☐ 7 Much worse

3. [Skip this question if you answered 0 in Question #1]. How much did your flu symptoms interfere with your activities today? (Please select one response only)
- ☐ 1 Not at all
- ☐ 2 A little bit
- ☐ 3 Somewhat
- ☐ 4 Quite a bit
- ☐ 5 Very much

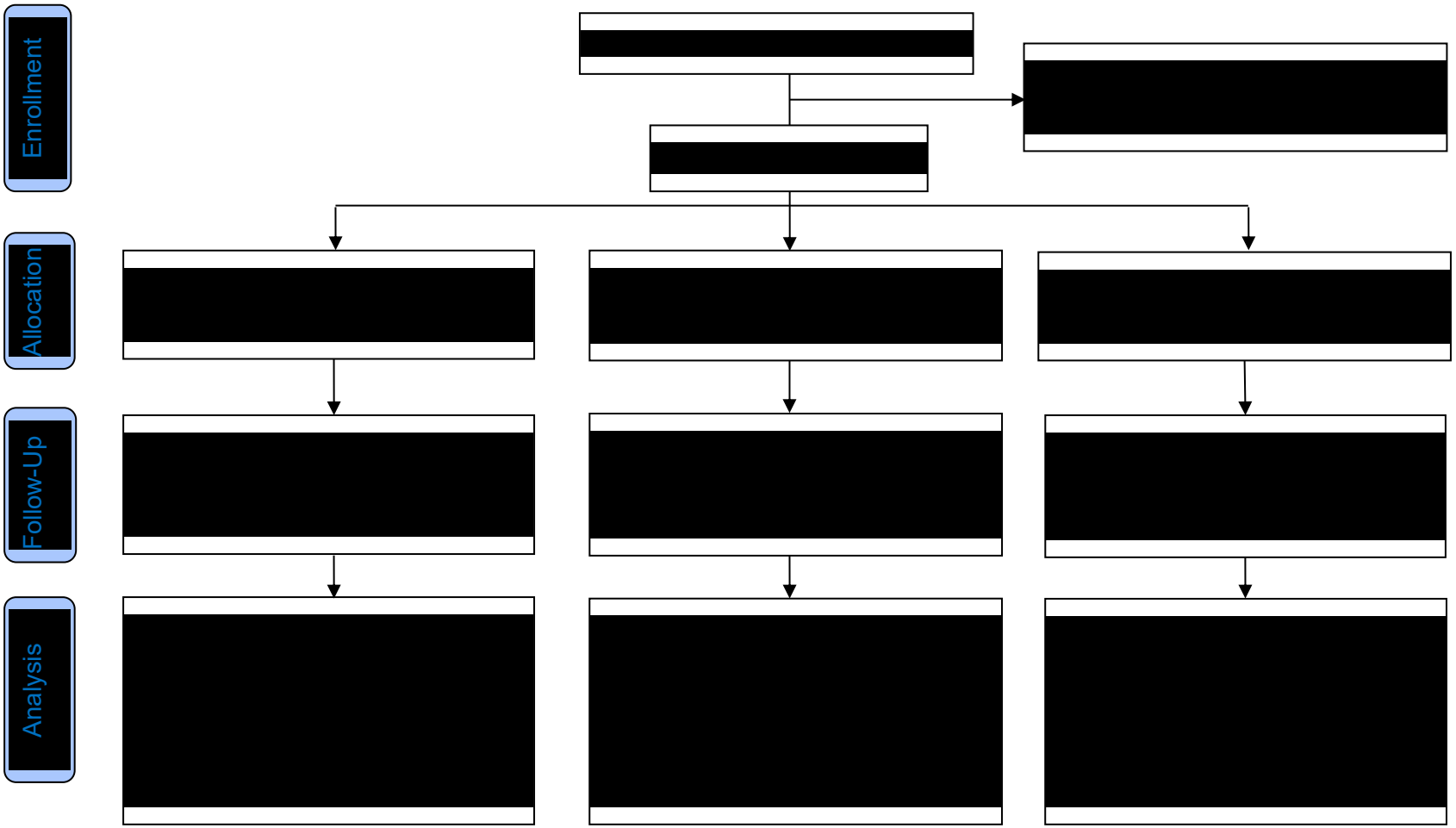
4. Have you returned to activities today?
- ☐ 0 No
- ☐ 1 Yes

5. In general, how would you rate your physical health today? (Please select one response only)
- ☐ 1 Poor
- ☐ 2 Fair
- ☐ 3 Good
- ☐ 4 Very Good
- ☐ 5 Excellent

6. Are you in your usual state of health today?
- ☐ 0 No
- ☐ 1 Yes

10.1 Disposition of Participants

Figure 6: CONSORT Flow Diagram

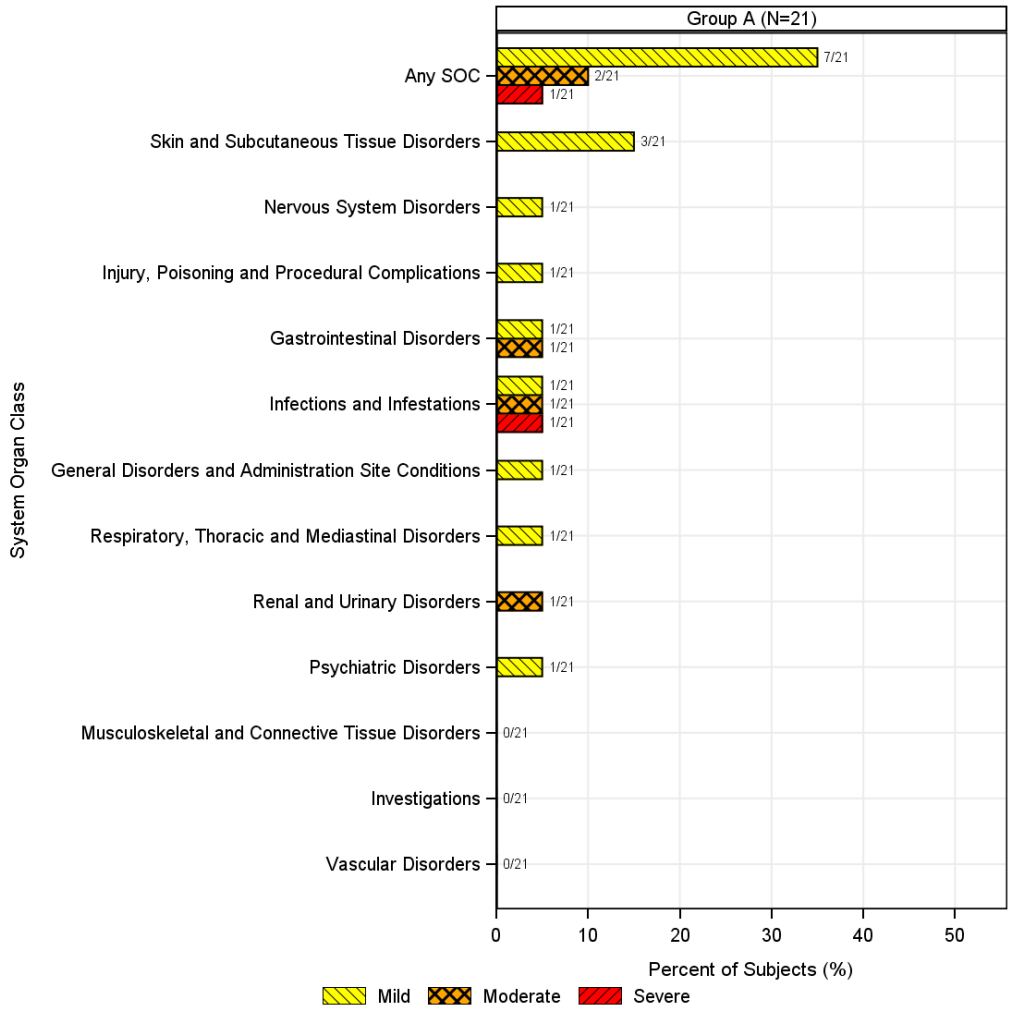


14.2 Clinical and Immunogenicity Response Figures

14.2.1 Clinical Response Figures

Figure 7: Maximum Severity of Influenza Symptoms During the Challenge Period by Challenge Dose Group, and Symptom – Infected Participants in the Safety Population

[Implementation Note: The figure shell below is a generic representation that will be updated for solicited influenza symptoms. This figure and the next one correspond to Table 16. All symptoms from MJS, plus fever and lymphopenia, should be included for each panel; Any Symptom will be presented on top. Four panels will include the infected participants from each of the 4 challenge dose groups. Y-axis label will be "Influenza Symptom" and x-axis label will be "Percentage of Participants".]



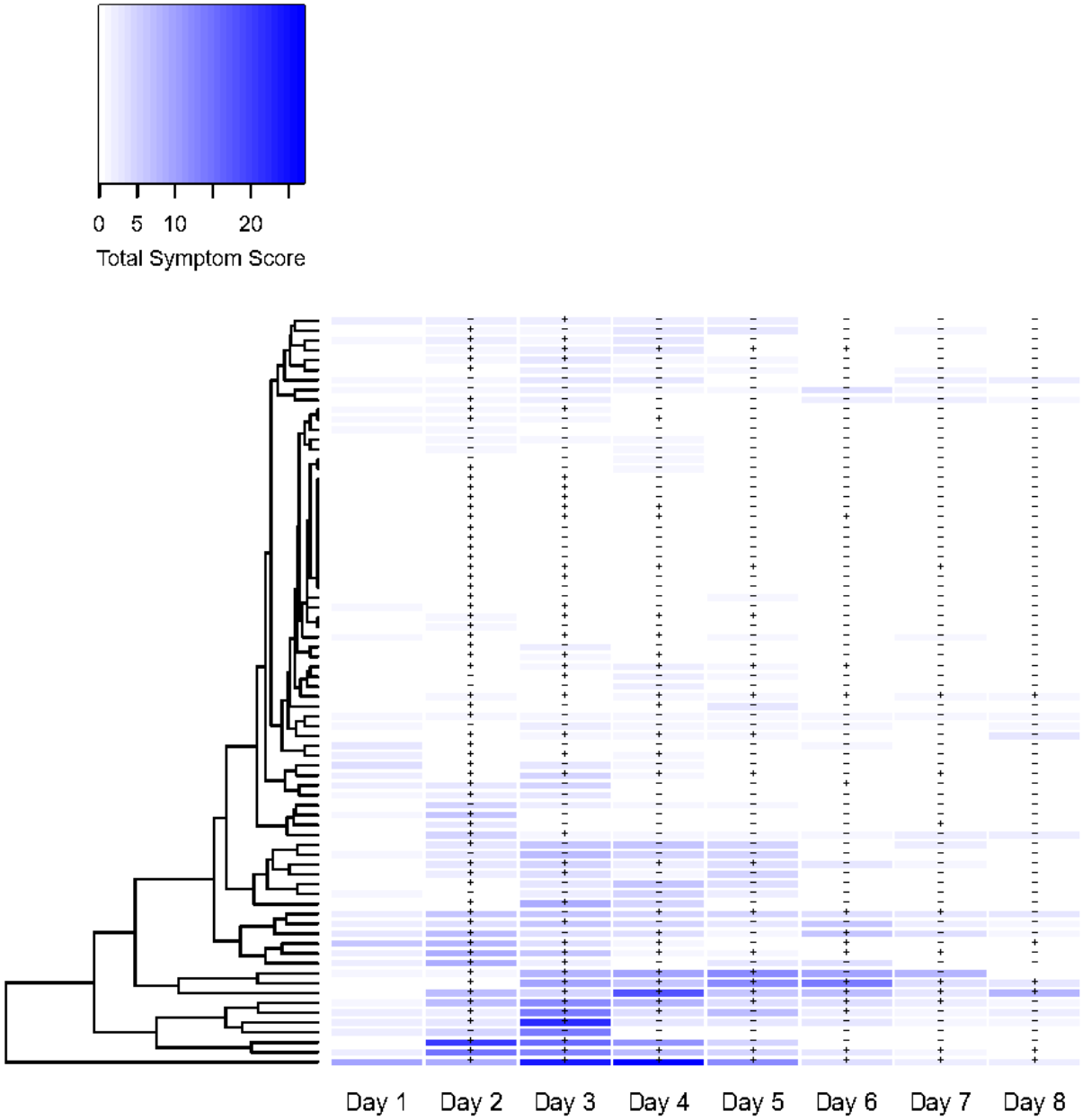
Similar Figures:

Figure 8: Maximum Severity of Influenza Symptoms During the Challenge Period by Challenge Dose Group, and Symptom – Uninfected Participants in the Safety Population

Figure 9: Maximum Severity of New-Onset Influenza Symptoms During the Challenge Period by Challenge Dose Group, and Symptom – Infected Participants in the Safety Population

Figure 10: Modified Jackson Scores by Study Day, Challenge Dose Group, and Viral Shedding Status – Safety Population

[Implementation note: Total MJS symptom scores will be presented on a by-day basis, sorted by and labeled with challenge dose group on the y-axis (instead of clustering) and with RT-PCR+ study days indicated by an overlaid "+".]



Similar Figure:

Figure 11: Total FLU-PRO Scores by Study Day, Challenge Dose Group, and Viral Shedding Status – Safety Population

Figure 12: Scatterplots of Maximum Cumulative Modified Jackson and FLU-PRO Scores by Total Viral Shedding – Safety Population

[Implementation note: This is an example figure, for illustration purposes. Only one y-axis and x-axis label will be included, and Spearman rank-order correlation will be estimated between each cumulative score and the log-10-transformed AUC and presented within the relevant figure panel.]

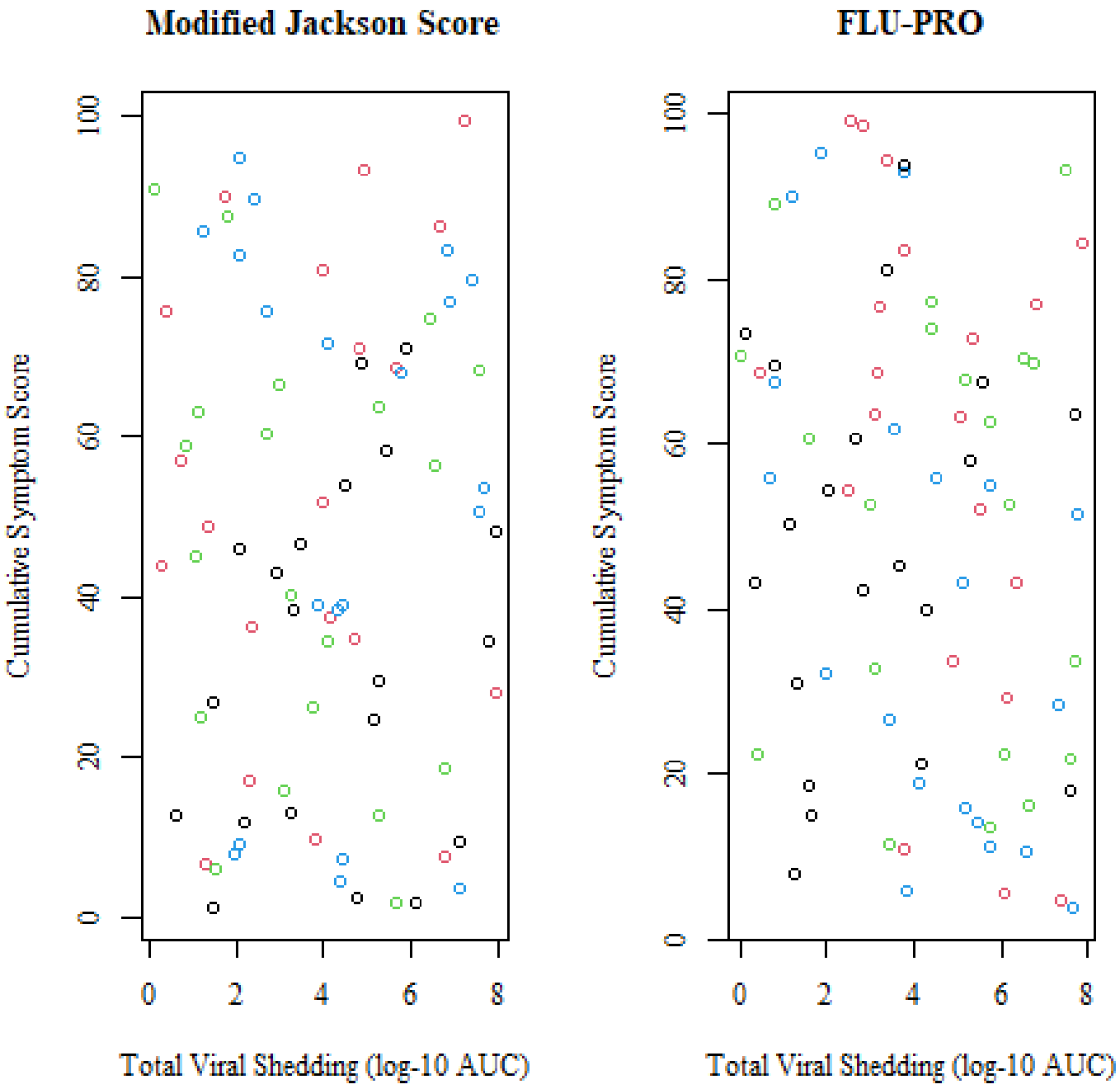


Figure 13: Mean Total Modified Jackson and FLU-PRO Scores by Study Day, Viral Shedding Status, and Challenge Dose Group – Safety Population

[Implementation note: This is an example figure, for illustration purposes. Mean total symptom scores will be computed for each study day and each viral shedding subgroup for the given day. A legend to define the groups will also be included.]

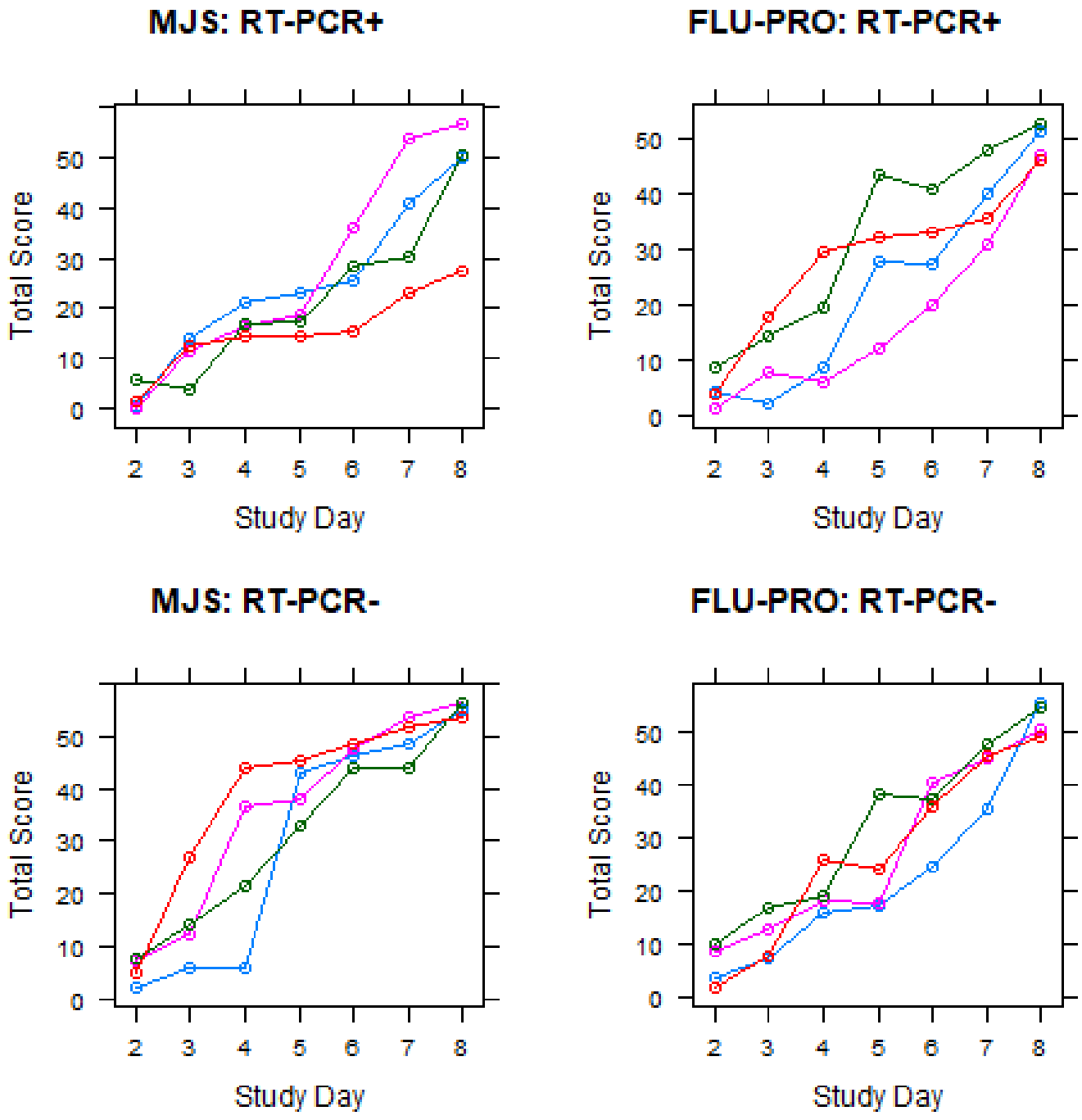


Figure 14: Maximum Cumulative Modified Jackson and FLU-PRO Scores by Infection Status and Challenge Dose Group – Safety Population

[Implementation note: This is an example figure, for illustration purposes. A legend to define the groups will also be included, and MJS will be presented on left with FLU-PRO on right.]

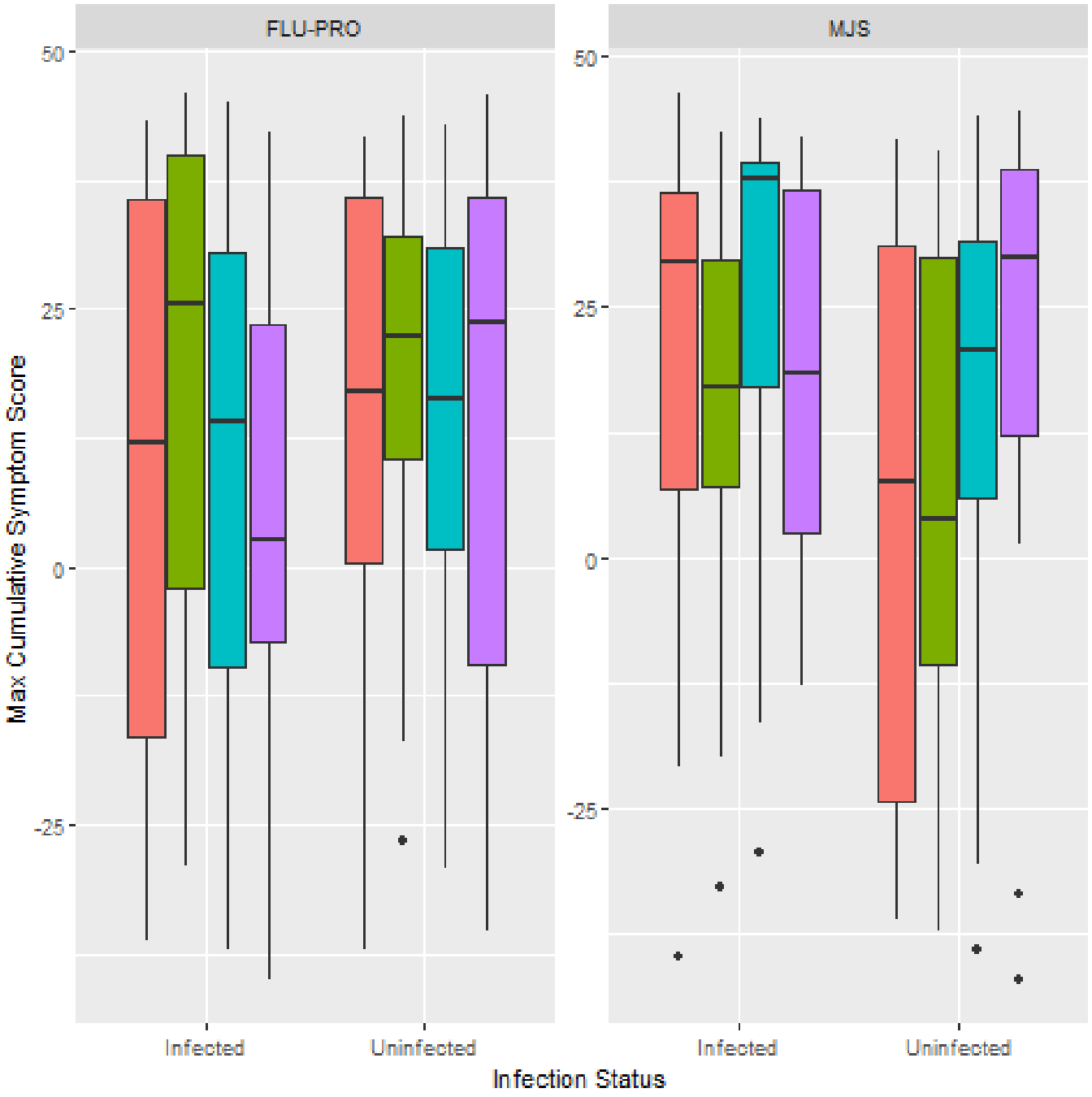
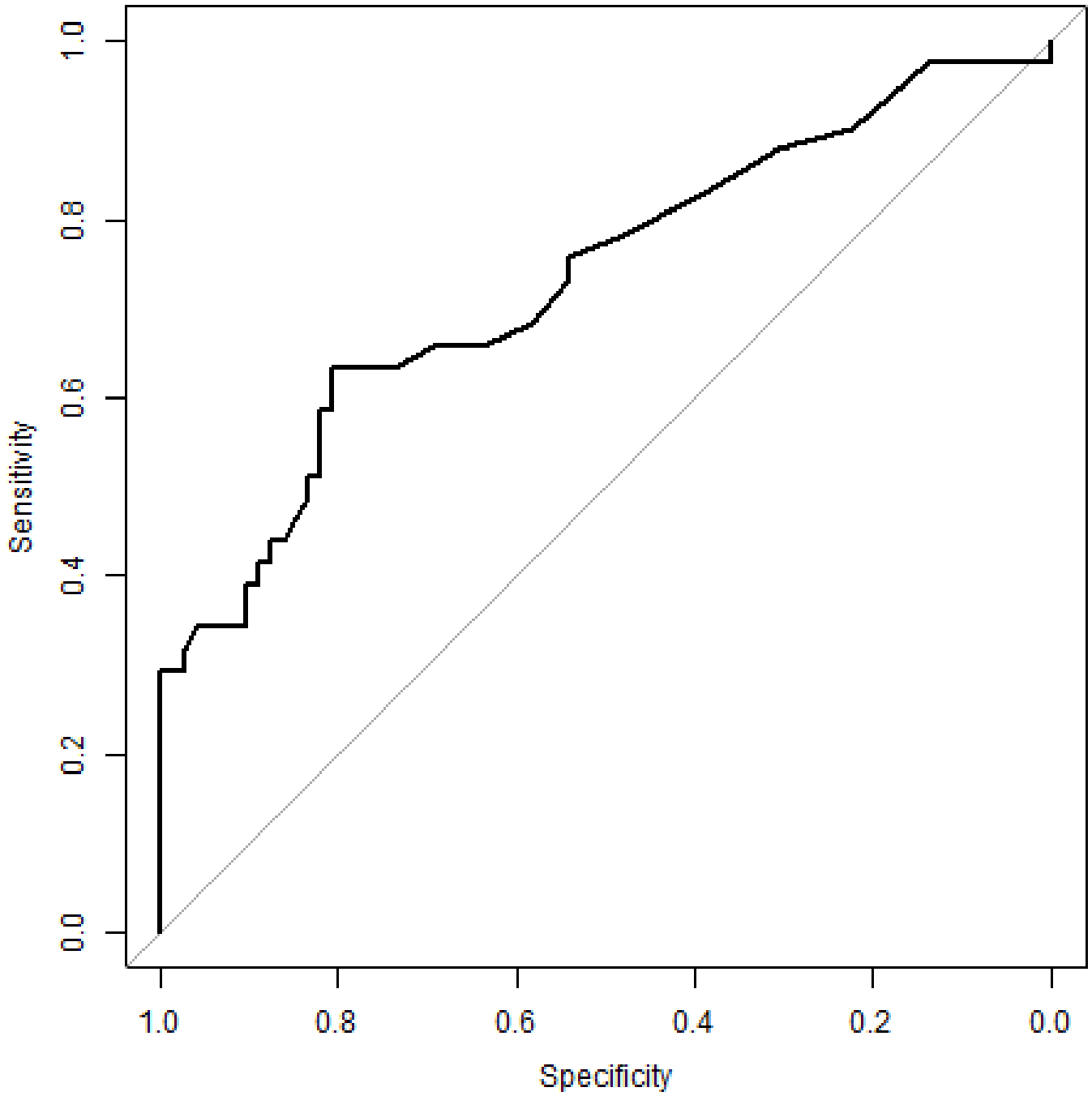


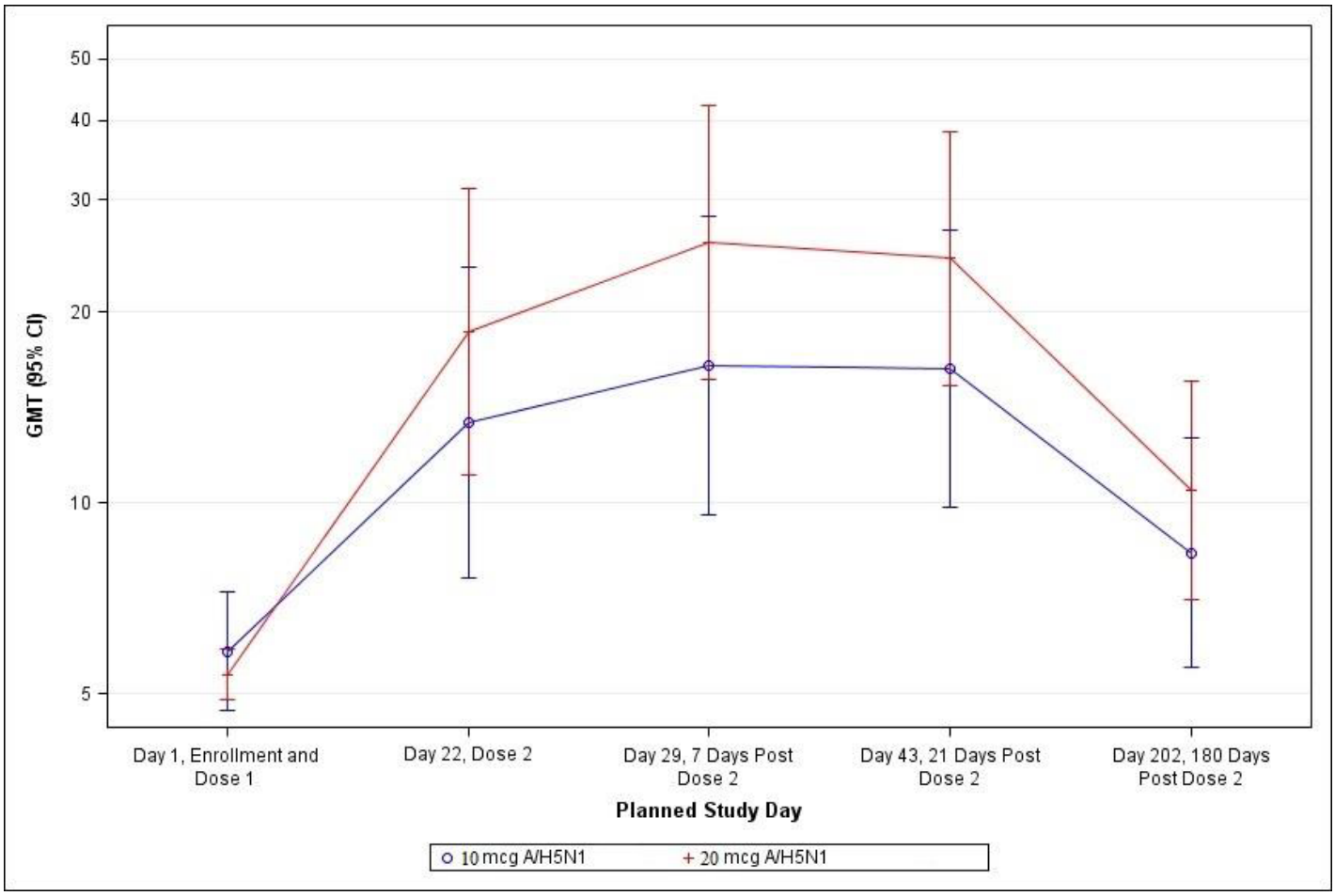
Figure 15: ROC Curve from Final Logistic Regression Predicting Influenza Infection Status with the Maximum Severity of Solicited Modified Jackson Score Symptoms, in the Training Data – Safety Population



14.2.1 Immunogenicity Response Figures

Figure 16: Geometric Mean Titers and 95% CI for Hemagglutination Inhibition and Microneutralization Antibodies Against A/Texas/71/2017 (H3N2), clade 3C3a Virus, by Study Visit and Challenge Dose Group – ITT Population

[Implementation note: There will be a separate panel for each combination of assay and infection status, with the 4 challenge dose groups in different colors with different line types within each panel. The paneling columns will be Infected and Uninfected, and the paneling rows will be HAI and MN.]



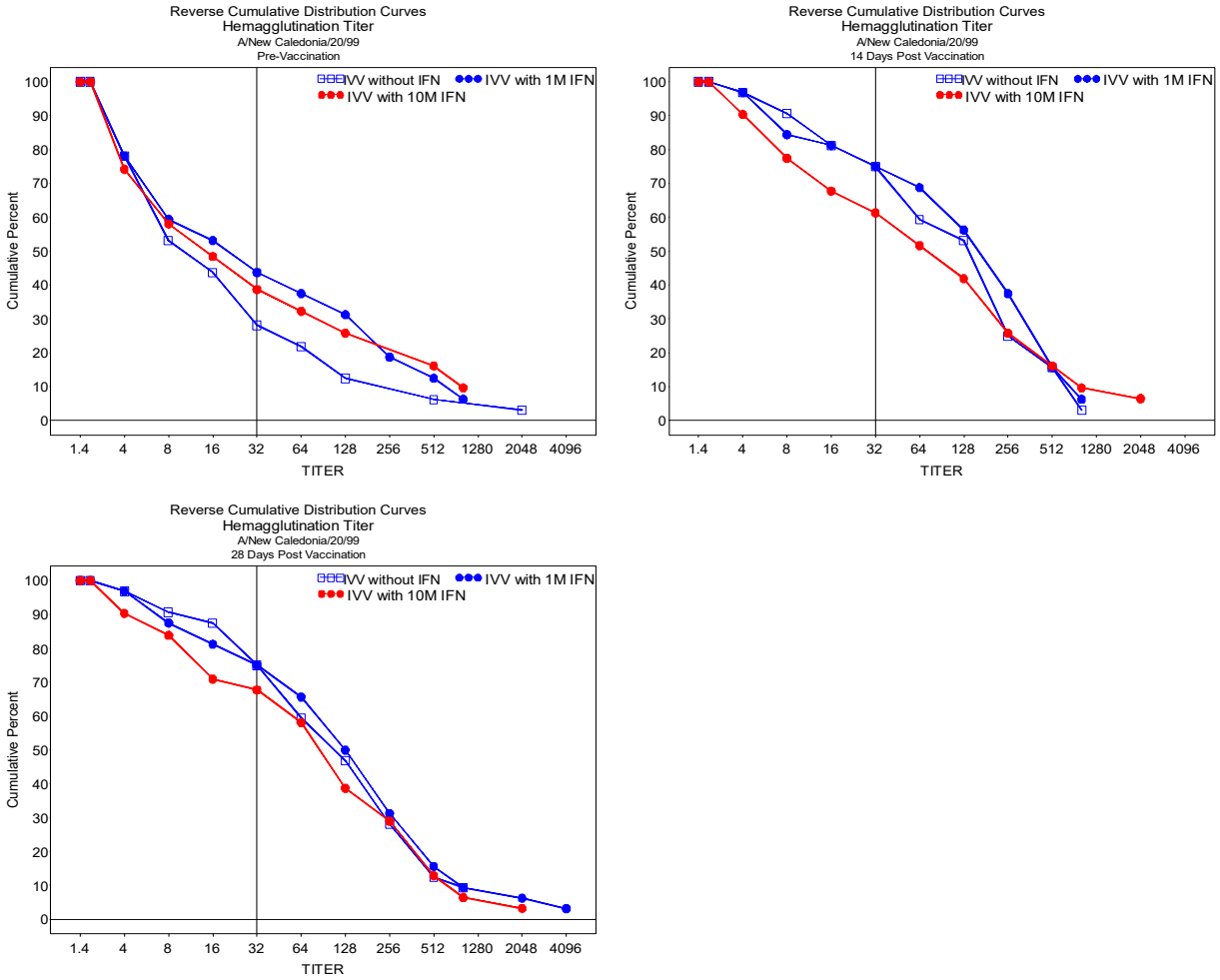
Similar Figures:

Figure 17: Geometric Mean Titers and 95% CI for Neuraminidase Inhibition Antibodies Against A/Texas/71/2017 (H3N2), clade 3C3a Virus, by Study Visit and Challenge Dose Group – ITT Population

Figure 18: Geometric Mean Titers and 95% CI for Anti-HA Stalk Antibodies Against A/Texas/71/2017 (H3N2), clade 3C3a Virus, by Study Visit and Challenge Dose Group – ITT Population

Figure 19: Reverse Cumulative Distribution of Hemagglutination Inhibition Antibody Titers Against A/Texas/71/2017 (H3N2), clade 3C3a Virus, by Study Visit and Challenge Dose Group

[Implementation note: There will be a separate panel for each combination of study day and infection status, with the 4 challenge dose groups in different colors with different line types within each panel. The paneling columns will be Infected and Uninfected, and the paneling rows will be study days.]



Similar Figures:

Figure 20: Reverse Cumulative Distribution of Microneutralization Antibody Titers Against A/Texas/71/2017 (H3N2), clade 3C3a Virus, by Study Visit and Challenge Dose Group

Figure 21: Reverse Cumulative Distribution of Neuraminidase Inhibition Antibody Titers Against A/Texas/71/2017 (H3N2), clade 3C3a Virus, by Study Visit and Challenge Dose Group

Figure 22: Reverse Cumulative Distribution of Hemagglutination Inhibition Antibody Titers Against A/Texas/71/2017 (H3N2), clade 3C3a Virus, by Study Visit and Challenge Dose Group

14.3.1.1 Unsolicited Adverse Events

Figure 23: Frequency of Related Adverse Events by MedDRA System Organ Class, Severity, and Challenge Dose Group

[Implementation Note: This figure includes serious and non-serious unsolicited adverse events deemed related to study challenge. The SOCs should be sorted in descending frequency; e.g., for this figure, "Infections and infestations" should be listed first. There will be separate panels for each challenge dose group.]

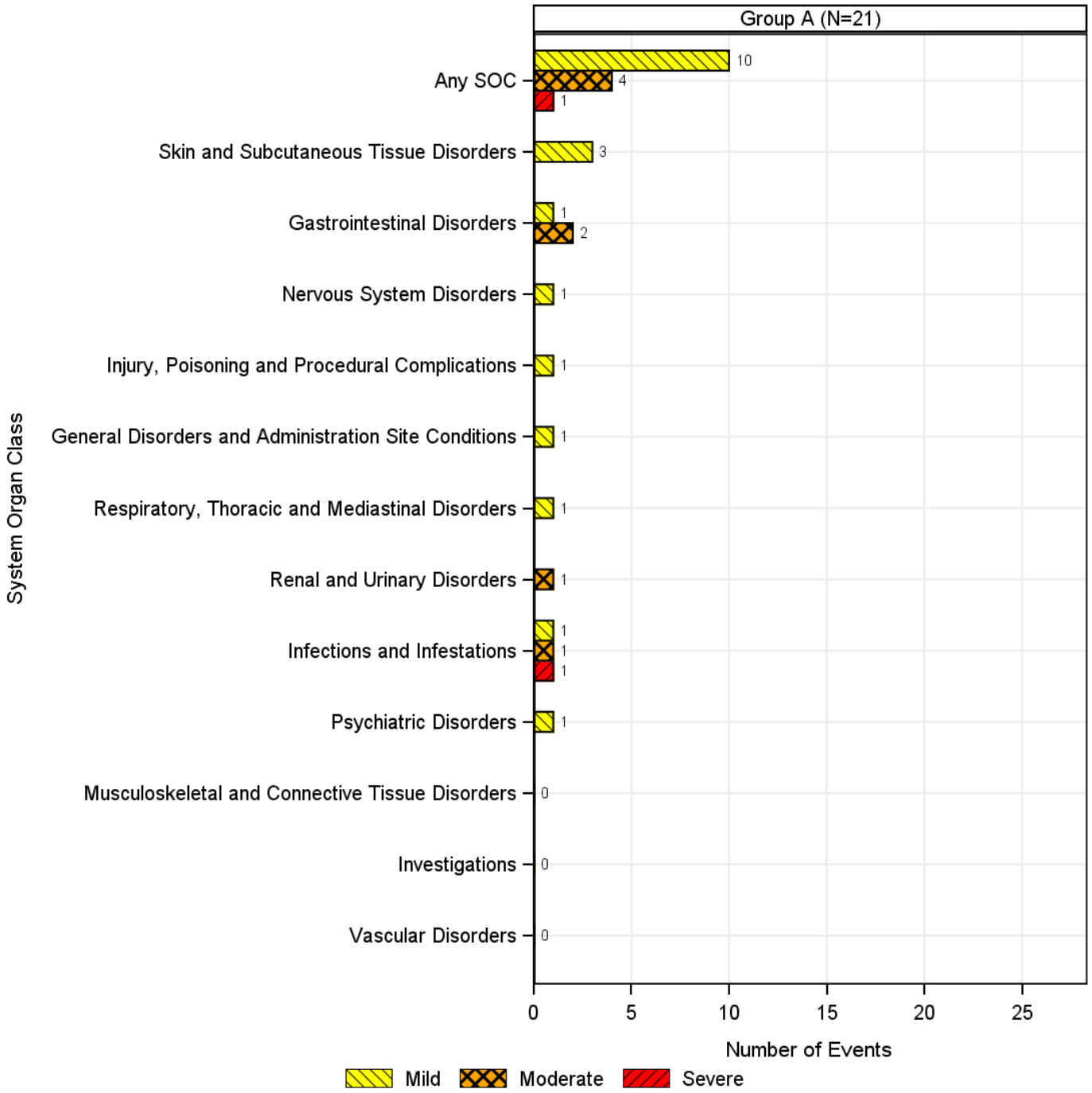
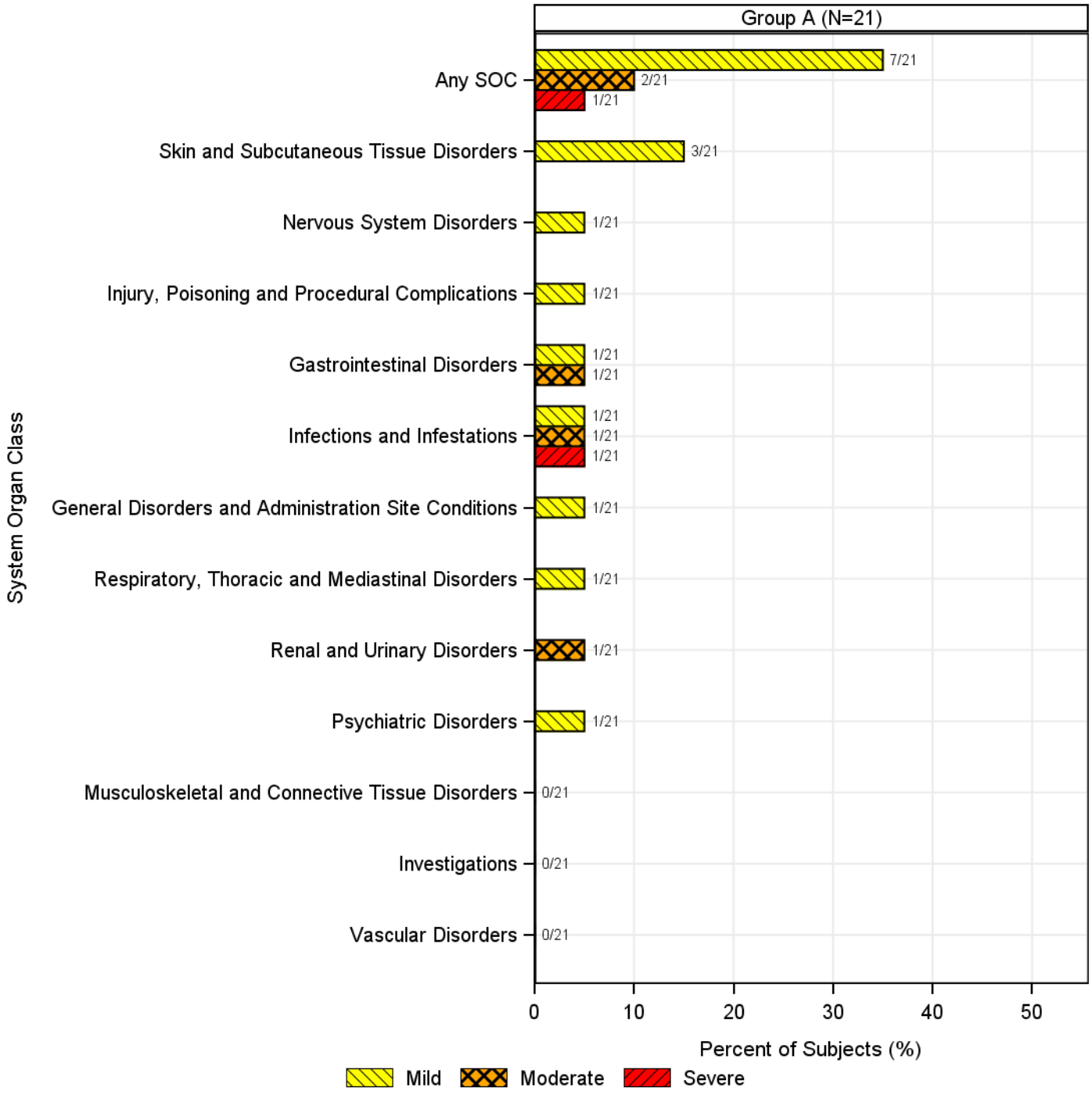


Figure 24: Incidence of Related Adverse Events by MedDRA® System Organ Class, Maximum Severity, and Challenge Dose Group

[Implementation Note: This figure includes serious and non-serious unsolicited adverse events deemed related to study product. The SOCs should be sorted in descending incidence; e.g., for this figure, "Infections and infestations" should be listed first. There will be separate panels for each challenge dose group.]



APPENDIX 3. LISTINGS MOCK-UPS

This appendix includes examples mock-ups of listings to present participant-level data.Instructional text is included in brackets [Instruction or Implementation Note:].General conventions for listings:If comments cause the table to be too wide, they can be moved to a merged row below the corresponding record (see AE listings for example).In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification.

LISTINGS

16.1.6: Listing of Participants Receiving Investigational Product

Listing 1: Listing of Participants Receiving Challenge Virus or Sham Inoculum

[Implementation Note: Listing will be sorted by cohort, then challenge dose group, then challenge date, and finally participant ID.]

Challenge Cohort	Challenge Dose Group	Participant ID	Challenge Date
[e.g., Cohort 1A, Cohort 2A]	[10^4 $TCID_{50}$ Challenge Virus, 10^5 $TCID_{50}$ Challenge Virus, 10^6 $TCID_{50}$ Challenge Virus, or Sham Inoculum]		

16.2 Database Listings by Participant

16.2.1 Discontinued Participants

Listing 2: Early Terminations

[Implementation note: Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Challenge Cohort, Participant ID.]

Challenge Cohort	Challenge Dose Group	Participant ID	Reason for Early Termination	Study Day
[e.g., Cohort 1A, Cohort 2A]				

16.2.2 Protocol Deviations

Listing 3: Participant-Specific Protocol Deviations

[Implementation Notes: 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: Participant refusal." Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Challenge Dose Group, Participant ID, DV Number.]

Challenge Dose Group	Participant ID	DV Number	Deviation	Deviation Category	Study Day	Reason for Deviation	Deviation Resulted in AE?	Deviation Resulted in Participant Termination?	Deviation Affected Product Stability?	Deviation Resolution	Comments

Listing 4: Non-Participant-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: Participant refusal." Sort order: Site, Start Date.]

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

16.2.3 Participants Excluded from Analysis

Listing 5: Participants Excluded from Analysis Populations

[Implementation Note: This data in this listing should be congruent with the "Analysis Populations by Challenge Dose Group" table. The reasons included here should match the SAP text that describes who will be excluded from analyses. Participant ID should be USUBJID (not PATID) for purposes of de-identification.] Sort order: Challenge Dose Group, Participant ID.]

Challenge Dose Group	Participant ID	Analyses in which Participant is Included	Analyses from which Participant is Excluded	Results Available?	Reason Participant 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: Demographic and Baseline Characteristics Data

[Implementation Note: If a participant is multi-racial, in "Race" column, note "Multiple: (list races, separated by a comma)."For studies in infants and young children, may be more appropriate to use weeks or months for age at enrollment. In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification.] Sort order: Study Group, Participant ID.]

Challenge Dose Group	Participant ID	Sex	Age at Enrollment (years)	Ethnicity	Race	BMI (kg/m^2)

Listing 7: 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). Rather than using exact study days, categorize as follows:5 years prior to enrollment1-5 years prior to enrollment1-12 months prior to enrollmentWithin 1 month of enrollmentDuring studyIf ongoing, display "Ongoing" in the "Condition End Day" columnWithin 1 month of enrollmentDuring studyIf ongoing, display "Ongoing" in the "Condition End Day" columnIt may be appropriate to add another category, based on exclusion criteria that restrict conditions within a particular time period (e.g., within 3 years prior to enrollment). Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Challenge Dose Group, Participant ID, MH Number.]

Challenge Dose Group	Participant ID	MH Number	Medical History Term	Condition Start Day	Condition End Day	MedDRA System Organ Class	MedDRA Preferred Term

16.2.6 Individual Clinical and Immunological Response Data

Listing 8: Individual Modified Jackson Score Symptoms

[Implementation Note: In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Listing should be sorted by Study Group, Participant ID, Planned Study Day, Form Number on Given Study Day, and Symptom. Fever and lymphopenia will be included as well, with footnotes indicated those are collected as part of vital signs and clinical labs assessments, respectively.]

Challenge Dose Group	Participant ID	Planned Study Day	Actual Study Day	Form Number on Given Study Day	Symptom	Severity
				[1st or 2nd]		

Listing 9: Individual FLU-PRO Symptoms

[Implementation Note: In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Listing should be sorted by Challenge Dose Group, Participant ID, Planned Study Day, Form Number on Given Study Day, and Symptom.]

Challenge Dose Group	Participant ID	Planned Study Day	Actual Study Day	Form Number on Given Study Day	Symptom	Extent
				[1st or 2nd]		

Listing 10: Individual FLU-PRO Additional Responses

[Implementation Note: This listing will present the responses from the additional FLU-PRO questions. In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification.] Listing should be sorted by Study Group, Participant ID, Planned Study Day.]

Challenge Dose Group	Participant ID	Planned Study Day	Actual Study Day	Form Number on Given Study Day	FLU-PRO Question	Response
				[1st or 2nd]		

Listing 11: Individual Immunogenicity Response Data

[Implementation Note: Update as appropriate for your study assay/strain and endpoints. In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Listing should be sorted by Challenge Dose Group, Participant ID, Planned Study Day.]

Challenge Dose Group	Participant ID	Planned Study Day	Actual Study Day	Assay	Assay Target	Response	Unit
				[e.g., HAI, MN, etc.]			[e.g., Titer]

16.2.7 Adverse Events

16.2.7.3: Unsolicited Adverse Events

Listing 12: Unsolicited Adverse Events

[Implementation Note: 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. If there are no comments for an event, populate 'Comments' row with 'None'. Participant ID should be USUBJID (not PATID) for purposes of de-identification. Listing should be sorted by Challenge Dose Group, Participant ID, and No. of Days Post Challenge.]

Adverse Event	No. of Days Post Challenge (Duration)	Severity	Relationship to Study Challenge	If Not Related, Alternative Etiology	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Participant ID: , Challenge Dose Group: , AE Number:							
Comments:							
Participant ID: , Challenge Dose Group: , AE Number:							
Comments:							

16.2.8 Individual Laboratory Measurements and Other Safety-Related Assessments

16.2.8.1: Clinical Laboratory Results – Chemistry

Listing 13: Clinical Laboratory Results – Chemistry

[Implementation Note: These listings (for hematology, chemistry, and urinalysis) 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). Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Challenge Dose Group, Participant ID, Planned Study Day, and Laboratory Parameter.]

Challenge Dose Group	Participant ID	Planned Study Day	Actual Study Day	Sex	Age (years)	Laboratory Parameter (Units)	Result (Severity Grade)	Reference Range Low	Reference Range High

16.2.8.2: Clinical Laboratory Results – Hematology

Listing 14: Clinical Laboratory Results – Hematology

Challenge Dose Group	Participant ID	Planned Study Day	Actual Study Day	Sex	Age (years)	Laboratory Parameter (Units)	Result (Severity Grade)	Reference Range Low	Reference Range High

16.2.8.3: Vital Signs

Listing 15: 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). Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Challenge Dose Group, Participant ID, Planned Study Day. Multiple assessments from the same day can be entered in one cell with semicolons between values.]

Challenge Dose Group	Participant ID	Planned Study Day	Actual Study Day	Temperature (°C)	Systolic Blood Pressure (mmHg)	Diastolic Blood Pressure (mmHg)	Heart Rate (beats/min)	Respiratory Rate (breaths/min)	Weight (kg)	Height (cm)

16.2.8.4: Physical Exam Findings

Listing 16: Physical Exam Findings

[Implementation Note: This listing includes all physical exam findings, scheduled and unscheduled. If a participant 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)". In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Challenge Dose Group, Participant ID, Planned Study Day.]

Challenge Dose Group	Participant ID	Planned Study Day	Actual Study Day	Body System	Abnormal Finding	Reported as an AE? (AE Description; Number)

16.2.8.5: Concomitant Medications

Listing 17: 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 enrollment1-5 years prior to enrollment1-12 months prior to enrollmentIf 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)". Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Challenge dose group, Participant ID, and CM Number.]

Challenge Dose Group	Participant ID	CM Number	Medication	Medication Start Day	Medication End Day	Indication	Taken for an AE? (AE Description; Number)	Taken for a condition on Medical History? (MH Description; Number)	ATC Level 1 (ATC Level 2)

16.2.8.6: Pregnancy Reports

Listing 18: Pregnancy Reports – Maternal Information

[Implementation Note: Only include the "Pregnancy Number" column if a participant 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. Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Challenge Dose Group, Participant ID, Pregnancy Number. These will be presented in landscape format for display purposes.]

Challenge Dose Group	Participant ID	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: Pregnancy Reports – Gravida and Para

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

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

Listing 20: Pregnancy Reports – Live Birth Outcomes

Participant 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: Pregnancy Reports – Still Birth Outcomes

Participant 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: Pregnancy Reports – Spontaneous, Elective, or Therapeutic Abortion Outcomes

Participant 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