CLINICAL RESEARCH IN INFECTIOUS DISEASES

STATISTICAL ANALYSIS PLAN
for
DMID Protocol: 17-0112
Study Title:
A Double-Blind Placebo Controlled, Randomized Phase 2 Trial to Evaluate the Safety, Reactogenicity and Immunogenicity of a Live-Attenuated *Shigella sonnei* Vaccine, WRSs2 and Determine its Efficacy in a Challenge Model of *S. sonnei* 53G in Healthy Adults

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RESTRICTED

A DOUBLE-BLIND PLACEBO CONTROLLED, RANDOMIZED PHASE 2 TRIAL TO EVALUATE THE SAFETY, REACTOGENICITY AND IMMUNOGENICITY OF A LIVE-ATTENUATED *SHIGELLA SONNEI* VACCINE, WRSS2 AND DETERMINE ITS EFFICACY IN A CHALLENGE MODEL OF *S. SONNEI* 53G IN HEALTHY ADULTS

Protocol Number Code:	**DMID Protocol: 17-0112**
Development Phase:	Phase 2
Products:	WRSs2, *S. sonnei* 53G
Form/Route:	Oral
Indication Studied:	Shigellosis
Sponsor:	Division of Microbiology and Infectious Diseases National Institute of Allergy and Infectious Diseases National Institutes of Health
Clinical Trial Initiation Date:	11OCT2022
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This study was performed in compliance with Good Clinical Practice.

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LIST OF ABBREVIATIONS

AE	Adverse Event
ALT	Alanine Aminotransferase
ANC	Absolute Neutrophil Count
ASC	Antibody Secreting Cells
BUN	Blood Urea Nitrogen
C	Celsius
CCHMC	Cincinnati Children's Hospital Medical Center
CFU	Colony Forming Unit
CI	Confidence Interval
CRF	Case Report Form
CSR	Clinical Study Report
DMID	Division of Microbiology and Infectious Diseases
DSMB	Data and Safety Monitoring Board
eCRF	Electronic Case Report Form
ELISA	Enzyme-linked Immunosorbent Assay
ELISpot	Enzyme-linked Immunosorbent Spot
ER	Emergency Room
ERC	Endpoint Review Committee
F	Fahrenheit
FDA	Food and Drug Administration
gm	Grams
GMT	Geometric Mean Titer
GMFR	Geometric Mean Fold Rise
HBsAg	Hepatitis B Surface Antigen
HCV	Hepatitis C Virus
HEA	Hektoen Enteric Agar
HEENT	Head, Ears, Eyes, Nose, Oral, and Throat Examination
Hgb	Hemoglobin
HIV	Human Immunodeficiency Virus
HLA-B27	Human Leukocyte Antigen B27
ICH	International Conference on Harmonisation

List of Abbreviations *(continued)*

IDES	Internet Data Entry System
IgA	Immunoglobulin A
IgG	Immunoglobulin G
L	Liter
LPS	Lipopolysaccharides
MCB	Master Cell Bank
µm	Micrometer
MedDRA	Medical Dictionary for Regulatory Activities
mEq	Milliequivalent
mg	Milligram
mL	Milliliter
MOP	Manual of Procedures
N	Number (typically refers to participants)
NaCl	Sodium Chloride
NaHCO3	Sodium Bicarbonate
NPO	Nothing By Mouth
PBF	Pilot Bioproduction Facility
PBMC	Peripheral Blood Mononuclear Cells
PBS	Phosphate Buffered Saline
PCB	Production Cell Bank
PCR	Polymerase Chain Reaction
PI	Principal Investigator
PP	Per-Protocol
PT	Preferred Term
RCD	Reverse Cumulative Distribution
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SD	Standard Deviation
SDCC	Statistical and Data Coordinating Center
SOC	System Organ Class

List of Abbreviations *(continued)*

ULN	Upper Limit of Normal
USP	United States Pharmacopeia
WBC	White Blood Cell Count
WHO	World Health Organization
WRAIR	Walter Reed Army Institute of Research
WRSs1	Live-attenuated *S. sonnei* vaccine candidate derived from "Moseley"
WRSs2	WRSs1 with deletions in the genes *virG(icsA)*, *senA,* and *senB*
WRSs3	WRSs2 with deletion of *msbB2* gene
VE	Vaccine Efficacy

1. PREFACE

The Statistical Analysis Plan (SAP) for "A Double-Blind Placebo Controlled, Randomized Phase 2 Trial to Evaluate the Safety, Reactogenicity and Immunogenicity of a Live-Attenuated *Shigella sonnei* Vaccine, WRSs2 and Determine its Efficacy in a Challenge Model of *S. sonnei* 53G in Healthy Adults" (DMID Protocol 17-0112) 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. The analyses planned in this document do not encompass the secondary research described in the protocol. 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). The structure and content of the SAP provides sufficient detail to meet the requirements identified by the FDA and ICH, while all work planned and reported for this SAP will follow internationally accepted guidelines published by the American Statistical Association and the Royal Statistical Society for statistical practice.

This document contains four sections: (1) a review of the study design, (2) general statistical considerations, (3) comprehensive statistical analysis methods for efficacy and safety outcomes, and (4) a list of proposed tables and figures. Within the table, figure, and listing mock-ups (**Appendix 1**, **Appendix 2**, and **Appendix 3**), references to CSR sections are included. Any deviation from this SAP will be described and justified in protocol 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

Diarrheal disease poses a major public health threat to human populations with diarrhea being a leading cause of death and disability among all ages. The *Shigella* virus is one of the leading causes of diarrheal death especially in children < 5 years of age in developing countries where malnutrition, unsafe water, and sanitation concerns lead risk factors. The mainstays against Shigella are prevention means such as sanitation and education about improved hygienic practices and treatment of infections using antimicrobial therapy. However, due to limitations in resources and multidrug-resistant *Shigella* strains complicating treatment, vaccines are critically needed to prevent infection. Of the four species of *Shigella* (*S. dysenteriae*, *S. flexneri*, *S. boydii* and *S. sonnei*), *S. flexneri* is the most common species found in developing countries and *S. sonnei* is the most common in developed countries. A virulent strain of *Shigella,* known as *S. sonnei* 53G, is the species that will be the focus of this study.

A Phase 1 trial in the US (inpatient) and in Israeli adults (outpatient) led to the development of a highly immunogenic but unacceptably reactogenic vaccine to combat Shigellosis (WRSS1). This led to the development of more attenuated vaccine candidates (WRSs2 and WRSs3). WRSs2 has two additional deletions in the genes *senA* and *senB* that are present on the virulence plasmid while WRSs3 includes the added deletion of the virulence plasmid-based *msbB2* gene. Animal safety, immunogenicity, and efficacy studies have shown that WRSs2 and WRSs3 compare favorably with WRSs1. WRSs2 is the vaccine candidate that will be the focus of this study.

The original goal of this clinical trial was to assess in healthy males and non-pregnant females, 18-49 years of age, the safety, reactogenicity, immunogenicity, and efficacy of 1 and 2 doses 10^6 CFU oral live-attenuated *Shigella sonnei* vaccine (WRSs2) to protect against shigellosis after a targeted oral challenge with a virulent strain of *S. sonnei* (*S. sonnei* 53G). After the initiation of the study using 10^6 CFU, two participants had Grade 3 diarrhea and/or vomiting in the days following vaccination. This triggered a halting rule. To meet the recommendations of the Data and Safety Monitoring Board (DSMB) and evaluate the safety and efficacy signal of a lower dose, several changes to the protocol were made. The vaccination dose was reduced to $5x10^5$ CFU, enrollment was changed to 2 arms and randomized 2:1 (vaccine:placebo). Furthermore, participants with morbid obesity were excluded and weight loss medication prohibited.

This analysis plan has been drafted based on Version 8.0 of the protocol, and any future amendments to the protocol that substantially impact the planned analyses would be addressed in amendments to this SAP.

2.1. Purpose of the Analyses

These analyses will assess the safety, reactogenicity, immunogenicity, and efficacy of two oral doses (10^6 CFU or $5x10^5$ CFU) of a live attenuated *Shigella sonnei* vaccine (WRSs2) in comparison with a 0.9% sterile normal saline (used as the placebo) against a targeted oral challenge of $1.5x10^3$ CFU of wild type *Shigella sonnei* 53G and will be included in the clinical study report.

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives

3.1.1. Primary Objective

- (Efficacy): Estimate combined vaccine efficacy of 2 doses of WRSs2 (10^6 cfu or $5x10^5$ cfu) in preventing shigellosis following challenge with *S. sonnei* strain 53G.

3.1.2. Secondary Objectives

- (Efficacy): Estimate vaccine efficacy of 1 dose of 10^6 cfu, 2 doses of 10^6 cfu, and 2 doses of $5x10^5$ cfu of WRSs2 in preventing shigellosis following challenge with *S. sonnei* 53G
- (Safety): Safety evaluations of WRSs2.
- (Immunogenicity): Evaluate immune responses following vaccination (immunogenicity) with WRSs2 and after challenge with *S. sonnei* strain 53G by serum anti-LPS and anti-Invaplex IgG and IgA by ELISA.
- (Efficacy): Determine fecal shedding of *S. sonnei* after WRSs2 vaccination and 53G challenge by qualitative stool culture.

3.1.3. Exploratory Objectives

- (Efficacy): Evaluate fecal shedding of *S. sonnei* post vaccination and post challenge by colony immunoblot and PCR.
- (Immunogenicity): Evaluate *S. sonnei* antigen (LPS and Invaplex) specific IgG and IgA-ASC following vaccination and challenge.
- (Immunogenicity): Evaluate fecal IgA following vaccination and challenge.

3.1.4. Secondary Research

- Blood and stool samples will be collected and stored to characterize in depth innate and acquired immune response to WRSs2 and *Shigella* infection.

3.2. Endpoints

3.2.1. Primary Endpoint

- (Efficacy): The occurrence of shigellosis (as outlined in **Table 1**) following challenge with *S. sonnei* strain 53G through Day 63 in the pooled group of participants receiving two doses of 10^6 cfu or $5x10^5$ cfu of WRSs2 compared to participants receiving two doses of placebo

3.2.2. Secondary Endpoints

- (Efficacy): The occurrence of shigellosis following challenge with *S. sonnei* strain 53G through Day 63 in participants receiving 1 dose of 10^6 cfu, 2 doses of 10^6 cfu, or 2 doses of $5x10^5$ cfu of WRSs2 compared to participants receiving two doses of placebo

- (Safety): Occurrence of solicited systemic AEs through 7 days after each study vaccination
- (Safety): Occurrence of vaccine-related unsolicited AEs through 28 days post last vaccination
- (Safety): Occurrence of SAEs through Study Day 180 or until resolution or stabilization even if this extends beyond the study-reporting period
- **Pre-Challenge Immunogenicity**
  - (Immunogenicity): Number of participants with ≥ 4-fold rise from pre-vaccination in *S. sonnei* LPS-specific and Invaplex-specific serum IgG and IgA by ELISA at Study Days 15, 29, 43, and 56
  - (Immunogenicity): Maximum *S. sonnei* LPS-specific and Invaplex-specific serum IgG and IgA titer by ELISA post-vaccination through Study Day 56.
  - (Immunogenicity): Peak fold-rise in *S. sonnei* LPS-specific and Invaplex-specific serum IgG and IgA titer by ELISA from pre-vaccination through Study Day 56.
- **Post-Challenge Immunogenicity**
  - (Immunogenicity): Number of participants with ≥ 4-fold rise from pre-challenge (Study Day 56) in *S. sonnei* LPS-specific and Invaplex-specific serum IgG and IgA by ELISA at Study Days 64, 71, 85, and 113.
  - (Immunogenicity): Maximum *S. sonnei* LPS-specific and Invaplex-specific serum IgG and IgA titer by ELISA post-challenge through Study Day 113.
  - (Immunogenicity): Peak fold-rise in *S. sonnei* LPS-specific and Invaplex-specific serum IgG and IgA titer by ELISA from pre-challenge through Study Day 113.
- (Efficacy): Number of participants shedding vaccine strain in their stool by culture pre-vaccination as well as at Study Days 4, 8, 15, 29, 32, 34, 36, and 43.
- (Efficacy): Duration of shedding *S. sonnei* post-vaccination through Study Day 56 by culture.
- (Efficacy): Number of participants shedding 53G in their stool by culture post-challenge through Study Day 65.
- (Efficacy): Duration of shedding 53G post-challenge through Study Day 65 by culture.

3.2.3. Exploratory Endpoints

- (Efficacy): Duration of *S. sonnei* shedding post-vaccination through Study Day 56 by immunoblot and PCR.
- (Efficacy): Maximum *S. sonnei* CFU per gram of stool post-vaccination through Study Day 56 by immunoblot.
- (Efficacy): Duration of shedding 53G post-challenge through Study Day 65 by immunoblot and PCR.
- (Efficacy): Maximum *S. sonnei* CFU per gram of stool post-challenge through Study Day 65 by immunoblot.
- (Immunogenicity): Number of *S. sonnei* LPS-specific and Invaplex-specific IgG and IgA ASCs per 10^6 PBMCs by ELISpot pre-vaccination and at Study Day 8, 29, 36, 56, 60, and 64.

- (Immunogenicity): Number of participants with ≥10 IgG or IgA ASCs per 10^6 PBMCs (*S. sonnei* LPS-specific and Invaplex-specific) by ELISpot at any time post-vaccination through Study Day 56.
- (Immunogenicity): Number of participants with ≥10 IgG or IgA ASCs per 10^6 PBMCs (*S. sonnei* LPS-specific and Invaplex-specific) by ELISpot at any time post-challenge through Study Day 64.
- (Immunogenicity): Number of participants with ≥ 4-fold rise from pre-vaccination in *S. sonnei* LPS-specific and Invaplex-specific fecal IgA and total fecal IgA by ELISA at Study Day 8, 15, 29, 36, 43, 56, 61, 64, 71, and 85.
- (Immunogenicity): Maximum fold rise post-vaccination of *S. Sonnei* LPS-specific and Invaplex-specific fecal IgA and total fecal IgA by ELISA through Study Day 56.

3.3. Study Definitions and Derived Variables

3.3.1. Study Definitions

The primary shigellosis endpoint will be defined as described in **Table 1.** To assess diarrhea, study personnel will use the definitions outlined in **Table 4** for classification of stool samples. The qualitative (consistency) and quantitative (count and weight of stools) assessment of participant stool samples collected through Day 63 after challenge administration will be used to define the primary endpoint of occurrence of shigellosis. For the shigellosis endpoint, a rolling 24-hour period will be utilized to identify stools and vomiting episodes meeting the definitions described in **Table 1**. A participant should have met each of the criteria at any time during the inpatient period through Day 63. The SDCC will programmatically determine whether each participant has met the shigellosis endpoint. This determination along with all data points necessary for the determination of endpoint status will be provided to an Endpoint Review Committee (ERC) who will make the final determination used in the primary efficacy analysis.

AEs will be assessed by the investigator using a protocol-defined grading system (**Table 8**, **Table 9**, and **Table 10**). For solicited reactogenicity, diarrhea and vomiting will consider a 24-hour period as a calendar day for consistency with the solicited events collection.

For events not included in the protocol-defined grading system, the following guidelines will be used to quantify severity:

- 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 affects clinical status, or may require intensive therapeutic intervention. Severe events are usually incapacitating.

The following guidelines will be used to assess the relationship of an AE to the administration of study product:

- Related – There is a reasonable possibility that the study product caused the AE. Reasonable possibility means that there is evidence to suggest a causal relationship between the study product and the AE.
- Not Related – There is not a reasonable possibility that the administration of the study product caused the event.

3.3.2. Derived Variables

The baseline value will be defined as the last value obtained prior to the first vaccination/dose of study product.

For individual participants, fold rise will be calculated as the ratio of $\frac{follow-up\ titer}{baseline\ titer}$, where baseline value is the result obtained prior to the first vaccination dose, or challenge administration, as appropriate.

The duration of viral shedding will be evaluated from the day of the initial positive result to the day of the last positive qualitative or quantitative culture, immunoblot, or PCR result, regardless of intermittent negative results.

A result is considered culture positive if the culture and agglutination assay results are positive.

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

This is a phase 2 randomized, double-blind, placebo-controlled, clinical trial to evaluate the safety, reactogenicity, efficacy and immunogenicity of up to a 10^6 CFU dose of an oral live-attenuated *S. sonnei* vaccine candidate, WRSs2, in males and non-pregnant females aged 18-49 inclusive at the time of the first vaccination. This study is conducted in two phases, an outpatient WRSs2 vaccination phase and an inpatient *S. sonnei* 53G challenge phase.

Up to 120 participants will be enrolled and randomized 1:1:1 into 3 vaccination arms. Arm 1 received 2 doses of WRSs2, Arm 2 received placebo followed by WRSs2, and Arm 3 received 2 doses of placebo. Twenty-eight ($\pm$2) days after the second dose of study agent, participants are admitted to the inpatient unit and given an oral challenge of approximately 1500 CFU of 53G. The goal is to have 90 participants (30 per group) receive a challenge dose of 53G.

After the initiation of the study, two participants had Grade 3 diarrhea and/or vomiting in the days following vaccination. This triggered a halting rule. To meet the recommendations of the DSMB and evaluate the safety and efficacy signal of a lower dose, several changes to the protocol were made. The vaccination dose was reduced to $5x10^5$, enrollment was changed to 2 arms and randomized 2:1 (vaccine: placebo). Furthermore, participants with morbid obesity were excluded and weight loss medications prohibited. No changes in sample collection or challenge phase were made. The original study design is found in **Table 2** and the corresponding schematic in **Figure 1** and the changes to the study design are found in **Table 3** and the corresponding schematic in **Figure 2**.

The two phases of the study are conducted as follows:

Vaccination phase (Outpatient)

Participants are randomized to a vaccination arm per the Internet Data Entry System (IDES) in a 1:1:1 ratio. The possible arms that a participant can be randomized to are either WRSs2+WRSs2, Placebo+WRSs2, or Placebo+Placebo. All participants enrolled after protocol V8.0 will be randomized 2:1 in vaccine or placebo groups.

Participants return for follow-up at time points defined in section 3.1 of the protocol to be assessed for immunogenicity, vaccine fecal shedding, and safety outcomes during the vaccination phase.

Challenge phase (Inpatient)

Participants are scheduled for admission to the inpatient unit for approximately 9 days to be challenged with live *S. sonnei* 53G 28 ($\pm$ 2) days after the second dose of study agent. Blood and stool samples are collected to evaluate safety and immunogenicity outcomes at pre-challenge. Participants remain in the inpatient unit for a minimum of 8 days post-challenge.

Assessments and symptom-directed physical examinations are performed daily, or more often as clinically indicated, by qualified medical staff. Stool samples are collected daily and used for immunological outcome assessments. Vital signs are obtained and assessed for safety outcomes at least daily. If gastrointestinal illness occurs, intake and output are recorded and assessed.

Antibiotic treatment with ciprofloxacin begins on the 5th day after challenge.

Upon discharge from the inpatient facility, participants are provided with verbal and written instructions, a memory aid, and digital thermometer to take home and record symptoms and body temperature daily for 5 days. Following discharge, participants return to the outpatient clinic on Study Days 71, 85, and 113 for assessment of safety and immunogenicity outcomes.

On Study Day 180, participants complete a final safety contact by phone or email to assess for occurrence of pregnancy and SAEs.

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

This is a phase 2 randomized, double-blind, placebo-controlled study in which males and non-pregnant females aged 18-49 are challenged with *S. sonnei* strain 53G approximately 28 days after one or two doses of vaccination with WRSs2 or sterile saline (used as placebo). Participants are randomized to one of three study arms; two doses of WRSs2, a single dose of WRSs2 and a single dose of placebo, or two doses of placebo in a 1:1:1 ratio. All participants enrolled after protocol V8.0 will be randomized 2:1 to two doses of $5x10^5$ cfu WRSs2 or two doses of placebo. The placebo group provides a control in evaluating the safety and efficacy of one and two doses of WRSs2.

4.3. Selection of Study Population

The study population for this protocol is approximately 120 healthy male and non-pregnant female volunteers between the ages of 18 to 49 from the general population of the participating VTEU sites. Each participant is enrolled regardless of religion, sex, or ethnic background and meet all of the inclusion and none of the exclusion criteria.

Inclusion and exclusion criteria for enrollment in the study are detailed in protocol section 5.1.

4.4. Treatments

4.4.1. Treatments Administered

WRSs2 is a live-attenuated vaccine candidate derived from a virulent strain of *S. sonnei.* The principal attenuating feature is the loss of the virulence plasmid encoded protein *virG(icsA)*, as well as deletions in the genes *sen4* and *senB*. The loss of these 3 genes is expected to make this strain, when administered orally, safe, immunogenic, and protective against challenge in participants. The strain is also sensitive to tetracycline and other commonly used antibiotics. The administration schedule for WRSs2, along with the placebo and challenge strain, is outlined for each study arm in **Table 2** and **Table 3**.

4.4.2. Identity of Investigational Product(s)

WRSs2, *S. sonnei* vaccine candidate

The wild type *S. sonnei* strain was isolated from a laboratory worker "Moseley", accidentally infected in 1975 with laboratory *S. sonnei* strain obtained from an infected monkey. A vial (#56) of Moseley strain [redacted], received in July 2004 was the starting material for the construction of WRSs2. Specific gene deletion was carried out to obtain the research seed of WRSs2. The method of lambda red recombineering was used to sequentially delete the entire open reading frames (ORFs) of *senA*, *senB*, and *virG(icsA)*. Finally, the strain was made tetracycline sensitive (tet-S) by growth on fusaric acid. The loss of these 3 genes is expected to

make this strain when given orally, safe, immunogenic and protective against challenge in volunteers. It is also sensitive to tetracycline and other commonly used antibiotics. The strain constructed was named WRSs2.

The research seed of WRSs2 was used to manufacture the lyophilized WRSs2 vaccine products for clinical use. Master Cell Bank (MCB) seeds and Production Cell Bank (PCB) seeds were manufactured and stored at [redacted]. A single vial of PCB was used to [redacted]. The product WRSs2 [redacted], was lyophilized in 2 mL aliquots (4.8×10^8 CFU/mL) and is stored at -80ºC ± 10ºC under continuous temperature monitoring at the Walter Reed Army Institute of Research (WRAIR), Pilot Bioproduction Facility (PBF). All vials were inspected under extra light and magnification and [redacted].

Placebo (0.9% Sterile Normal Saline, USP)

0.9% sterile normal saline for human use will be used as the placebo for this trial. The USP grade 0.9% sodium chloride (normal saline) is a sterile, nonpyrogenic, isotonic solution; each mL of fluid contains 9 mg of sodium chloride. It contains no bacteriostatic agent, antimicrobial agent, preservatives, or added buffer and is supplied only in single-dose containers. The solution may contain hydrochloric acid and/or sodium hydroxide for pH adjustment (pH 5.3, range 4.5-7.0).

0.9% sterile normal saline will be stored at 20ºC to 25ºC (68°F to 77ºF) [See USP Controlled Room Temperature]. Study product will remain on site stored as indicated until final accountability is completed. Used and unused product vials will remain on site stored as indicated until final accountability is completed. At study completion the site is given direction from DMID regarding disposition of the product.

The study product will be labeled according to manufacturer or regulatory specifications and include the statement "Caution: New Drug – Limited by Federal Law to Investigational Use."

Challenge (*S. sonnei* 53G)

53G is a virulent *S. sonnei* strain that was initially isolated from a child with diarrhea in Tokyo in 1954. The seed was maintained at the Center for Vaccine Development (CVD), University of Maryland. In Sep 1998, a research seed vial was streaked out on a [redacted] plate at the CVD and transferred to WRAIR PBF for the purpose of manufacturing a MCB ([redacted]) and PCB ([redacted]) under cGMP. The MCB and PCB are 1 mL glycerol cultures that are stored at -80ºC ±10ºC and in liquid nitrogen at the WRAIR PBF. In 2013, one vial of the PCB ([redacted]) was plated [redacted] and the contents harvested and lyophilized as 2 mL aliquots [redacted]. This standardized, lyophilized lot of *S. sonnei* 53G [redacted].

The *S. sonnei* 53G [redacted] and content of the vials appears as [redacted].

4.4.3. Method of Assigning Participants to Study Arms (Randomization)

Up to 120 participants were planned to be randomized to three vaccination arms (Arm 1: WRSs2/WRSs2, Arm 2: Placebo/WRSs2, and Arm 3: Placebo/Placebo) in a 1:1:1 ratio. Based on recommendations of the DSMB, the dose of study vaccine was decreased to $5x10^5$ cfu WRSs2 and the design modified to 2 arms with a randomization scheme of 2:1 (vaccine:placebo). Randomization is stratified by site. A permuted block randomization scheme was developed to avoid the potential for serious imbalance in the number of participants assigned to each arm, an imbalance that can occur in the simple randomization procedures. Participants who withdraw, or are withdrawn from the study, or are lost to follow-up after randomization were not replaced. The list of randomized treatment assignments was prepared by the statisticians at the SDCC and included in the enrollment module internet data entry system (IDES) for the trial. IDES assigned each participant a sequence number and treatment number after demographic and eligibility data were entered into the system. A designated individual at the site was provided with a treatment key, which links the treatment number to the actual treatment assigned, which was kept in a secure place.

It is likely that a larger number of participants were vaccinated than challenged. This was to ensure that there was an adequate number of participants who continued to qualify for the inpatient challenge portion of the study. If there were more vaccinated participants than space available in the inpatient challenge, participants were consecutively selected for inpatient challenge based on sequence number (NOT treatment number) that is displayed when a participant is randomized.

4.4.4. Selection of Doses in the Study

Vaccine WRSs2

A Phase 1 trial evaluating the safety and immunogenicity of WRSs2 and WRSs3 was recently completed. Healthy adults 18-45 years of age, assigned to 5 cohorts of 18 subjects each (WRSs2 (n=8), WRSs3 (n=8) or placebo (n=2) were housed in an inpatient facility and administered a single oral dose of study agent 5 minutes after ingestion of oral bicarbonate. Ascending dosages of vaccine (from 10^3 cfu to 10^7 cfu) were evaluated. On day 8, treatment with ciprofloxacin (500 mg BID for 3 days) was initiated and subjects were discharged home 2 days after completing antibiotics. Subjects returned for outpatient visits on day 14, 28 and 56 post-vaccination for monitoring and collection of stool and blood samples.

Both WRSs2 and WRSs3 were generally well-tolerated and safe over the entire dose range. Among the 80 vaccinees, 11 subjects developed diarrhea, 8 of which were mild and did not affect daily activities. At the 10^7 cfu dose, moderate diarrhea occurred in one subject receiving WRSs2 while at the same dose of WRSs3, two subjects had moderate to severe diarrhea (see Risk Section for more detailed description of AEs associated with WRSs2). As predicted, doses of WRSs2 and WRSs3 that were 2 logs higher than what was overly reactogenic for WRSS1 were well-tolerated by subjects. Additionally, the attenuation of both WRSs2 and WRSs3 was demonstrated by the fact that despite close housing for 9 days with subjects who received and excreted either WRSs2 or WRSs3, none of the 9 placebo subjects shed the vaccine candidate nor did placebo recipients develop any symptoms during the inpatient stay.

Based on the safety and immunological profile of WRSs2 and the availability of a robust challenge model, the study originally planned to evaluate the safety, immunogenicity and protective efficacy of 1 and 2 doses of WRSs2 (10^6 cfu) in a human challenge model in protecting subjects against shigellosis after challenge with a targeted approximately 1.5 $x10^3$ cfu dose of *S. sonnei* 53G ([redacted]). After the initiation of the study using $1x10^6$ (see protocol version 7.0 for prior study design), two participants had Grade 3 diarrhea and/or vomiting in the days following receipt of study product. This triggered a halting rule. To meet the recommendations of

the DSMB and evaluate the safety and efficacy signal of a lower dose, several changes to the protocol were made. The vaccination dose was reduced to $5x10^5$, enrollment was changed to only two arms and randomized 2:1 (vaccine: placebo). Furthermore, participants with morbid obesity were excluded and weight loss medications prohibited.

One mL of 0.9% saline containing 10^6 CFU of WRSs2 vaccine is added to 30 L of sterile normal saline (0.9% NaCl) and placed in a container. 150 mL of sodium bicarbonate solution (2 grams of sodium bicarbonate, NaHCO3, in 150 mL of sterile water for injection) is placed in a second container. Placebo consists of 30 mL of sterile normal saline.

Challenge *S. sonnei* 53G

A Phase 1 study recently completed, established a controlled human infection model (CHIM) for *S. sonnei* using a lyophilized, standardized inoculum of strain 53G to address some of the concerns raised about earlier studies. The lot of 53G used in the study ([redacted]) was grown, harvested and lyophilized at the WRAIR PBF under conditions of cGMP. The study was designed as an ascending dose study with the goal to identify the dose of 53G that would induce shigellosis in approximately 60% of subjects. Overall, of subjects receiving the 1.1-1.7 $x10^3$ cfu of 53G, approximately 63% developed one of the primary endpoints of shedding *Shigella* and either having mod-severe diarrhea and fever or mod-severe diarrhea and dysentery with more than one constitutional symptom of at least moderate severity. Therefore, a targeted approximately 1.5 $x10^3$ cfu dose of *S. sonnei* 53G was determined to be the optimal dose to be used in future CHIM studies. Based on the availability of a robust challenge model, the study planned to administer challenge with a targeted approximately 1.5 $x10^3$ cfu dose of *S. sonnei* 53G ([redacted]).

One mL of prepared challenge was added to 30 mL of sterile United States Pharmacopeia (USP) 0.9% saline in a plastic drinking cup. The maximum hold time for placebo is 2 hours.

4.4.5. Selection and Timing of Dose for Each Participant

Vaccine WRSs2

Participants were designated “nothing by mouth” (NPO) for 90 minutes prior to and after receiving the vaccine. Participants were to drink approximately 150 mL of sodium bicarbonate buffer solution to neutralize gastric acidity prior to administration of vaccine or placebo. After consuming the buffer solution, participants then were to drink approximately 30 mL of saline suspended vaccine or placebo within 5 minutes. Care was taken to ensure that a minimum amount of time, not exceeding 2 hours, was spent between the reconstitution of the vaccine and the oral administration of the vaccine to the participants.

If a participant vomited the vaccine (WRSs2 or placebo) within 5 minutes of ingestion, the participant could be re-dosed once and allowed to remain in the study.

Challenge *S. sonnei* 53G

Participants were NPO for 90 minutes prior to receiving approximately 120 mL solution of bicarbonate buffer (2 gm bicarbonate in 120 mL water). Within 5 minutes of the buffer, participants were to drink approximately 31 mL of saline containing approximately $1.5x10^3$ CFU of the *S. sonnei* 53G suspension.

If a participant vomited after receipt of the challenge dose of 53G, then they are not to be re-dosed due to safety concerns for potentially administering higher than intended dose of virulent *Shigella.*

4.4.6. Blinding

The *Shigella* vaccine and placebo were prepared by the unblinded site pharmacist and administered by unblinded study staff on Day 1 and Day 29. The participants, the study personnel who performed any study-related assessments after administration, data entry personnel at the sites, and laboratory personnel performing immunologic assays were blinded to treatment assignment.

Unblinded investigational pharmacy staff at the study site provided the investigator/study coordinator with the list of Participant ID #s for participants who had completed vaccination that could potentially receive challenge. Other than the unblinded study member(s), no member of the research team or study participants knew the vaccination arm of the participants. The role of the unblinded pharmacy staff was limited to preparation and accountability of the vaccination doses, preparation and accountability of the challenge administration, and the development of the list of participants proceeding on to receive the challenge strain to maintain study blind.

The DSMB received data in aggregate and presented by study arm, but without the study arm identified. The DSMB could be unblinded to individual study treatment assignments, as needed to adequately assess safety issues. In the case of a medical emergency, the PI could deem it medically necessary to unblind the participant's treatment assignment. If the PI believed that unblinding the individual would benefit the medical care of the participant and time permits, DMID was consulted prior to unblinding, and concurrence obtained. After DMID approved the unblinding, an appropriate designee at the site, who is not the principal investigator or blinded staff, would contact the SDCC. If the designee couldn't contact Emmes staff, and/or time did not permit, the unblinding process could occur on-site by contacting the unblinded pharmacist.

4.4.7. Prior and Concomitant Therapy

Administration of any medications or vaccines were documented in the appropriate electronic Case Report Form (eCRF). All concomitant medications, taken in the 30 days prior to study enrollment through Day 28 following challenge or early termination, whichever occurs first, were recorded. All prescription and over-the-counter medications as well as vitamins and supplements were also recorded.

Medications that could interfere with the evaluation of the investigational product were not to be used unless absolutely necessary. Assessment of whether the participant qualified to receive the second dose or challenge product included a review of permitted and prohibited medications.

If a participant was noted to have any disease or medical condition that, in the opinion of the site principal investigator or appropriate sub-investigator, was a contraindication to further study participation, Dose 2 was not given. In addition, a participant was not given Dose 2 if any of the following were noted:

- Have diarrhea within 14 days before Dose 2
- Use of immunosuppressive/immunomodulating disease therapy since enrollment
- Received or plan to receive a licensed live vaccine within 30 days prior to Dose 2
- Received or plan to receive a licensed, inactivated vaccine, COVID-19 vaccine or an influenza vaccine +/- 7 days of Dose 2.
- Received Ig or other blood products (with exception of Rho D Ig) since enrollment
- Have taken oral or parenteral (including intra-articular) corticosteroids of any dose, or high-dose inhaled corticosteroids within 30 days before Dose 2

- Have taken systemic antibiotics within 7 days before Dose 2
- Have taken prescription and/or OTC medication containing loperamide, acetaminophen, aspirin, ibuprofen, or other non-steroidal anti-inflammatory <48 hours prior to Dose 2
- Have fever or an acute illness within 72 hours before Dose 2.
- Received an investigational agent (including vaccine, drug, biologic, device, blood product, or medication outside of the current study) since enrollment which might affect safety or assessment of study endpoints.

If a previous AE was ongoing at dose 2, the participant could be vaccinated if the AE did not exceed the definition of AE Grade 1 and the AE was considered to be stable by a study investigator. If a Grade 2 or Grade 3 AE occurred between vaccine dose 1 and 2 and was determined not to be related to investigational product and returned to Grade 1 or lower before the next dose, the participant could receive the second dose.

If the participant was noted to have any disease or medical condition that, in the opinion of the site principal investigator or appropriate sub-investigator, was a contraindication to further study participation, challenge was not given. In addition, a participant was not given the challenge product if any of the following are noted:

- Have diarrhea within 14 days before Dose 2
- Use of immunosuppressive/immunomodulating disease therapy since Dose 2
- Received or plan to receive a licensed live vaccine within 30 days prior to challenge
- Received or plan to receive a licensed, inactivated vaccine, COVID-19 vaccine or an influenza vaccine within 7 days of challenge.
- Received Ig or other blood products (with exception of Rho D Ig) since Dose 2
- Have taken oral or parenteral (including intra-articular) corticosteroids of any dose, or high-dose inhaled corticosteroids within 30 days before challenge
- Have taken systemic antibiotics within the past 7 days before challenge
- Have taken prescription and/or OTC medication containing loperamide, acetaminophen, aspirin, ibuprofen, or other non-steroidal anti-inflammatory <48 hours prior to challenge
- Have fever or an acute illness within the past 72 hours before challenge
- Have a positive SARS-CoV-2 test at the time of admission to the inpatient unit
- Received an investigational agent (including vaccine, drug, biologic, device, blood product, or medication outside of the current study) since Dose 2 which might affect safety or assessment of study endpoints.
- Work or plan to work in either a health care setting, day care center, or as a food handler, or have known daily contact with individuals with possible increased susceptibility[$] to *Shigella* within 14 days after discharge from inpatient challenge

[$]Immunocompromised, elderly persons aged 70 years or more, diapered individuals, persons with disabilities, children <2 years old, a woman known to be pregnant or nursing, or anyone with diminished immunity. Known daily contact includes contact at home, school, day-care, nursing home, or similar places.

Any medications considered for treatment of fever, AE, or reactogenicity were given only at the discretion of a study investigator. If a previous AE was ongoing at the time of challenge, the participant could be given the challenge dose if the AE did not exceed the definition of AE Grade 1 and the AE was considered to be stable by a study investigator. If a Grade 2 or Grade 3 AE occurred between vaccine dose 2 and challenge and was determined not to be related to investigational product and returned to Grade 1 or lower before the challenge, the participant could receive the challenge dose.

4.4.8. Treatment Compliance

All participants were to receive two doses of study product administered in the clinic followed by an oral challenge 28 (±2) days following second vaccination. Any participants who receive an incorrect vaccination will be noted in the CSR.

4.5. Efficacy, Safety, and Immunogenicity Variables

The following sections describe the collection of efficacy, safety, and immunogenicity variables. See **Table 5** for the screening and vaccination schedule of study procedures and **Table 6** for the inpatient challenge and follow-up schedule of study procedures.

4.5.1. Efficacy Variables

The primary efficacy outcome is occurrence of shigellosis (as outlined in **Table 1**) following challenge with *S. sonnei* strain 53G through Day 63. Assessment of symptoms (e.g., fever, headache, arthralgia, nausea, pain/abdominal cramps, myalgia, malaise/fatigue, anorexia/loss of appetite, chills) will be completed once in the evening of challenge administration and then at least daily until discharge and 5 days after discharge. Vomiting (number of episodes per day and weights), and diarrhea with stool consistency, number of stools per day, and stool weights during the inpatient stay will be recorded. All stools classified as consistency 3-5 (i.e., those that conform to the shape of the container) will be weighed and visually assessed for gross blood. Samples with gross blood will be confirmed by a hemoccult test. For each participant, at least one stool sample per day will be saved for testing (the first stool produced each 24-hour period) and up to two stools with blood present by visual inspection in a 24- hour period will be tested by Hemoccult.

Additionally, stool will be collected for *Shigella* detection. The local laboratory at each study site will assay for the presence of *S. sonnei* using fresh stool samples. The first procedure is qualitative and involves streaking swabs containing fecal material to Hektoen Enteric Agar (HEA) plates. Up to two blue-green (non-lactose fermenting) colonies will be selected from swab-streaked HEA plates and tested for agglutination by *S. sonnei* polyvalent Group D antiserum for each participant. Colonies that agglutinate will be recorded as potential positive for presence of *S. sonnei*. The second procedure is conducted at WRAIR and is quantitatively assessed by immunoblot. This procedure involves plating serial dilutions of frozen-thawed stool suspensions (in buffered glycerol saline (BGS)) to HEA plates used for the serial dilutions that contain blue-green colonies. These plates will be processed using a colony blot procedure specific for the detection of *S. sonnei*. The number of positive colonies for each dilution will be recorded and used to calculate the CFU per gram of stool. These procedures will follow the MOP for culture isolation, immunoblot, and identification for *S. sonnei* from stool specimens. Stool will be analyzed at WRAIR by PCR to detect WRSs2 vaccine and challenge strain *S. sonnei* 53G.

4.5.2. Safety Variables

Safety will be assessed by:

1) SAEs – serious adverse events occurring from the time of the first study vaccination through Study Day 180.
    a) SAEs that extend beyond the study-reporting period will continue to be monitored until resolution or stabilization.
2) Solicited AEs – reactogenicity events occurring from the time of each study vaccination through 7 days following vaccination doses:
    a) Systemic reaction events following vaccination to include: headache, arthralgia, nausea, vomiting, diarrhea, pain/abdominal cramps, myalgia (body aches, muscular pain), malaise/fatigue, anorexia/loss of appetite, chills, and fever.
3) Unsolicited AEs – non-serious AEs occurring from the time of each study vaccination and challenge through approximately 28 days post vaccination doses and challenge administration.
4) Clinical safety laboratory AEs occurring from the time of each study vaccination through 7 days following vaccination doses and challenge administration, respectively:
    a) Clinical chemistry parameters to be evaluated include sodium, potassium, creatinine, alanine aminotransferase (ALT), and total bilirubin.
    b) Clinical hematology parameters to be evaluated include white blood cell count (WBC), absolute neutrophil count (ANC), hemoglobin (Hgb), and platelet count.

Clinical safety laboratory evaluations will be performed by the local lab of the performance site and sites will follow the laboratory event grading scale located in Appendix B of the protocol (**Table 10**) to assess the severity of any abnormal laboratory values.

Vital sign measurements of oral temperature, pulse, systolic blood pressure, and diastolic blood pressure will be assessed prior to study vaccination on Day 1, pre-vaccination, post-vaccination, daily during the inpatient challenge, and at other time points of interest.

Grading scales for systemic solicited reactogenicity events, clinical laboratory parameters, and vital signs are provided in **Table 8**, **Table 9**, and **Table 10** respectively.

4.5.3. Immunogenicity Variables

Blood will be collected for IgA and IgG assays by ELISA. The serum will be separated and stored frozen for determination of specific antibody responses against *S. sonnei* LPS and Invaplex antigens. The serum IgA and IgG ELISA assays will be performed at Cincinnati Children's Hospital Medical Center (CCHMC).

At times specified in the schedule of study procedures, the peripheral blood mononuclear cells (PBMCs) will be isolated from whole blood and cryopreserved to be used in antibody secreting cells (ASC). An ELISpot assay will be used to enumerate *S. sonnei* LPS and *S. sonnei* Invaplex specific IgA and IgG ASCs per 10^6 PBMC. Total IgA and IgG ASCs per 10^6 PBMC will also be enumerated by an ELISpot assay. The IgA and IgG ASC assays will be performed at Cincinnati Children's Hospital Medical Center (CCHMC).

Stool will be collected for fecal IgA at times specified in the schedule of study procedures. The stool sample (4-5gm) will be placed in a 30 mL Oakridge tube and frozen at -70ºC or colder until ready for extraction using

soybean trypsin inhibitor-edetic acid procedure. Total and *Shigella*-antigen specific IgA will be measured in stool extracts using ELISA procedures. Fecal total and antigen-specific IgA ELISA assays will be performed at CCHMC.

Biosamples (serum, PBMCs, stool) for immunological assays will be collected, processed, and performed in batches after all samples have been collected for a given assay. To minimize variability, all pre- and post-vaccination/challenge samples of a participant will be assayed on the same day as detailed in the MOP.

5. SAMPLE SIZE CONSIDERATIONS

Assuming a rate of 70% in the placebo arm with shigellosis after challenge, and that the expected vaccine efficacy is 57%, this corresponds to an expected rate of 30% in a WRSs2 group.

The study was originally designed with three arms (one dose of WRSs2, two doses of WRSs2, and placebo) with two primary hypotheses comparing each vaccine arm to placebo. It was determined that 120 randomized participants would be required to ensure at least 90 participants were challenged, assuming approximately 25% of participants who are randomized would drop-out or no longer qualify to receive challenge. Thirty (30) participants per arm provided a power of ~82% for each hypothesis test, using a two-sided Chi-square test at alpha=0.025 (equivalent to a one-sided test at alpha=0.0125) utilizing a Bonferroni correction to adjust for the increase in Type I error due to having two primary hypotheses.

After the study accrued with 69 participants, the DSMB recommended lowering the dose due to a halting event. To meet the recommendation of the DSMB and evaluate the safety and efficacy signal, the decision was made to amend the protocol to discontinue further enrollment in the one dose vaccine arm and proceed with two arms (two lower doses of WRSs2 or two doses of placebo). It is anticipated that approximately 43 participants will be randomized to either two administrations of the lower dose or placebo to achieve approximately 30 participants challenged.

The primary objective was modified to estimate the combined vaccine efficacy of two doses of WRSs2 at either the higher or lower dose in order to have enough power to detect vaccine efficacy with a smaller sample size than planned. Given the following assumptions:

- 70% Shigellosis rate in placebo arm
- 57% true vaccine efficacy of WRSs2
- One hypothesis test for the combined vaccine efficacy of 2 doses of WRSs2 (eliminating the one dose arm from the primary analysis), with the following null and alternative hypothesis:
  - Null hypothesis: vaccine efficacy = 0
  - Alternative hypothesis: vaccine efficacy > 0
- Placebo arm sample size: 25 (~15 from prior to study halt + ~10 after protocol amendment)
- Combined 2 dose WRSs2 arm sample size: 35 (~15 from prior to study halt + ~20 after protocol amendment)

A two-sided Chi-squared test at alpha=0.05 provides approximately 89% power to detect a combined vaccine efficacy greater than zero.

6. GENERAL STATISTICAL CONSIDERATIONS

6.1. General Principles

In general, all data listings will be sorted by study arm, participant ID, and when appropriate, by time point within participant. All summary tables will be structured with a column for each study arm in the order WRSs2 + WRSs2 (10^6 cfu), WRSs2 + WRSs2 ($5x10^5$ cfu), Placebo + WRSs2 (10^6 cfu), Placebo + Placebo and will be annotated with the total population size relevant to that table, including any missing observations.

Continuous variables will be summarized using the following descriptive statistics: n (non-missing sample size), mean, standard deviation, median, maximum, and minimum. The frequency and percentages (based on the non-missing sample size) of observed levels will be reported for all categorical measures.

6.2. Timing of Analyses

The final analysis will be performed, and clinical study report completed and distributed when all primary, secondary, and exploratory endpoint data are available.

No formal interim analysis involving the testing of a hypothesis is planned.

6.3. Analysis Populations

6.3.1. Full Analysis Population

The Full Analysis Population includes all randomized participants with complete data for the primary efficacy endpoint. Participants will be analyzed according to the study arm to which they were randomized.

6.3.2. Per-Protocol Population

The Per-Protocol (PP) Population includes all participants in the Full Analysis Population with the following exclusions:

- Participants found to be ineligible at baseline
- Participants who received an incorrect study vaccination
- Participants with second study vaccination or challenge received out of window
- Participants who received any of the following outside the acceptable parameters outlined in the protocol:
    - Non-study vaccines (live vaccines received within 30 days prior to Dose 2 or Challenge or inactivated vaccines, COVID-19 vaccine, or influenza vaccine received within +/- 7 days of Dose 2 or Challenge)
    - Antibiotics (within 7 days before Dose 2 or Challenge)
    - Oral, Parenteral, or high-dose inhaled steroids (within 30 days before Dose 2 or Challenge)
    - Prescription and/or over-the-counter medication containing loperamide, acetaminophen, aspirin, ibuprofen, or other non-steroidal anti-inflammatory (≤ 48 hours prior to Dose 2 or Challenge)
    - Immunosuppressive or cytotoxic therapy (since enrollment)

- Blood products or immunoglobulins (since enrollment)
- Experimental products (since enrollment)

In the case of mis-randomization, participants in the PP population will be analyzed according to the study product actually received.

The SDCC will prepare a list of population eligibilities for each analysis population. The principal investigator (PI) and DMID scientific lead (SL) will review and confirm all analysis population eligibilities prior to database lock and unblinding.

6.3.3. Safety Population

The Safety Population includes all participants who received at least one dose of study vaccination. Participants will be analyzed according to the study product they actually received, not necessarily the study product to which a participant was randomized.

6.3.4. Immunogenicity Population

The Immunogenicity Population consists of all participants who received any study product and for whom immunogenicity endpoint data are available. Participants will be analyzed according to the study product actually received, not necessarily the study product to which a participant was randomized.

6.3.5. Shedding Analysis Population

The Shedding Analysis Population consists of all participants who received any study product. Participants will be analyzed according to the study product they actually received, not necessarily the study product to which a participant was randomized.

6.4. Missing Data and Outliers

All attempts will be made to collect all data per-protocol. As missing data are expected to be minimal, no imputation will be performed for missing values. Any data point that appears to be erroneous or inexplicable based on clinical judgement 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.

Sensitivity analyses may be performed to assess the impact of protocol non-compliance, based on the Per-Protocol population (defined in **Section 6.3.2**).

The number of non-missing values in each analysis group will be described for all analyses. Prior to participants receiving the challenge administration, a negative SAR-CoV-2 result must be obtained to allow the participant to continue the study. The impact of missing data due to COVID-19 will be discussed in the CSR.

6.5. Interim Analyses and Data Monitoring

There are no formal interim analyses or hypothesis testing planned for interim data.

A DSMB will review safety data after all challenge cohorts have been completed, ad hoc when a halting rule is met or as needed, and at least annually. The final review meeting will occur 6 to 8 months after clinical database lock to review the cumulative unblinded safety data for the study.

6.6. Multicenter Studies

Data will be pooled across all clinical sites. Center effects are not anticipated because the sites are using standardized procedures for vaccination, challenge, and assessment of adverse events and clinical efficacy endpoints, and the study relies on central laboratories for the assessment of immunogenicity. Nevertheless, to guard against the potential for site differences, the primary analysis will be repeated stratified by site as outlined in **Section 8.1.2**.

6.7. Multiple Comparisons/Multiplicity

As the primary efficacy endpoint involves only one hypothesis, there are no planned adjustments for multiple comparisons in any primary, secondary, or exploratory analyses.

7. STUDY PARTICIPANTS

7.1. Disposition of Participants

A summary of the reasons why participants were screened but not enrolled will be presented in **Table 14**.

The composition of analysis populations, including reasons for participant exclusion, by study arm, is presented in **Table 12**. A listing of participants excluded from analysis populations will be presented in **Listing 5**.

The disposition of participants in the study will be tabulated by study arm for all enrolled participants and presented in **Table 11**. The table displays the total number of participants screened, randomized, receiving the first study vaccination, receiving the second study vaccination, receiving the study challenge, and completing the last visit.

A flowchart showing the disposition of study participants, adapted from the CONSORT Statement will be included in **Figure 3**. This figure will present the number of participants screened, enrolled, randomized, lost to follow-up, and analyzed, by study arm.

A listing of participants who discontinued study product or terminated from the study follow-up and the reason will be included in **Listing 2**.

7.2. Protocol Deviations

A summary of participant-specific protocol deviations will be presented by the deviation category, the deviation type, and study arm for participants in the safety population (**Table 7**). Listings of all deviations with initial classifications of major or minor will be provided to DMID to make the final determinations prior to database lock. Deviations that are considered major deviations that will be reviewed for possible participant exclusion from the PP population include, but are not limited to, deviations related to eligibility/enrollment, treatment administration schedule, follow-up visit schedule, and study product or specimen temperature excursions. All participant-specific protocol deviations and non-participant-specific protocol deviations will be included as data listings in **Listing 3** and **Listing 4,** respectively.

8. EFFICACY EVALUATION

Efficacy data summaries will be presented for the Full Analysis and Per-Protocol populations. Analyses will be presented by study arm where the primary efficacy analysis is performed on pooled data across all sites and a secondary supporting efficacy analysis stratified by site as outlined in **Section 8.1.2.**

8.1. Primary Efficacy Analysis

8.1.1. Primary Analyses

The study was designed to test the hypothesis comparing the combined two doses of 10^6 or $5x10^5$ of WRSs2 to placebo. The null hypothesis is that the absolute vaccine efficacy (VE) of preventing shigellosis is zero. The one-sided alternative hypothesis is that the absolute VE is greater than zero.

Vaccine efficacy (VE) will be estimated by the prevention of shigellosis, as defined in **Table 1**, among vaccine recipients compared to placebo recipients through Study Day 63 after receipt of challenge. This will be defined mathematically as follows:

$$\widehat{VE} = \frac{P_0 - P_1}{P_0}$$

P_1 is the observed proportion of shigellosis among participants receiving 2 doses of WRSs2. P_0 is the observed proportion of shigellosis among participants receiving placebo.

The primary efficacy analysis will test the null hypothesis that the absolute vaccine efficacy is zero using a two-sided Chi-squared test within the Full Analysis population. If the p-value is <0.05 and the lower limit of the 95% confidence interval for VE is above zero, then we can conclude that the combined VE of two doses of WRSs2 is greater than zero.

The primary endpoint to assess the estimated vaccine efficacy of two doses of WRSs2 in preventing shigellosis will be determined by the occurrence of shigellosis following challenge with *S. sonnei* strain 53G through Day 63 as determined by the Endpoint Review Committee (ERC). For all enrolled participants, all available clinical trial data necessary for determination of primary endpoint status (shigellosis) will be reviewed by a blinded ERC. This committee will be comprised primarily of independent *Shigella* experts, the study PI, and the SDCC. The ERC will be responsible for making a final determination of endpoint status for each participant prior to database lock and study unblinding.

The number and percentage of participants with any occurrence of shigellosis, as determined by the ERC, associated two-sided Wilson 95% confidence intervals, estimated vaccine efficacy, and associated Wilson 95% confidence intervals will be presented by study arm in **Table 22** for the Full Analysis population. The two-sided Chi-squared p-value will be presented for the combined two-dose WRSs2 group as well. The percentage of participants with any occurrence of shigellosis, as determined by the ERC, will be presented by study arm graphically in **Figure 4** for the Full Analysis population.

8.1.2. Supplemental and Sensitivity Analyses

The interpretation of the efficacy results will focus on the primary analysis described in **Section 8.1.1**, however, supplementary analyses and sensitivity analyses will aim to provide additional insights into the understanding of the vaccine effect and underlying assumptions of the primary analysis.

The primary efficacy analysis will be repeated in the Per Protocol population in **Table 22** and **Figure 5** as a supplementary analysis.

The primary efficacy analysis will also be repeated using a programmatic determination of shigellosis using the definition found in **Table 1**. Note that if no participants are classified differently between the ERC and programmatic determinations, this analysis will not be performed as it will be identical to the primary efficacy analysis. The number and percentage of participants with any occurrence of shigellosis, as programmatically determined by the definition in **Table 1**, associated two-sided Wilson 95% confidence intervals, estimated vaccine efficacy, and associated Wilson 95% confidence intervals will be presented by study arm in **Table 22** for the Full Analysis population and the Per Protocol population. The percentage of participants with any occurrence of shigellosis as programmatically determined will be presented graphically by study arm in **Figure 6** for the Full Analysis population and **Figure 7** for the Per-Protocol Population.

The primary efficacy analysis will also be repeated requiring a culture or PCR positive result for *S. sonnei* in addition to the Endpoint Review Committee and programmatically determined definitions of shigellosis. The number and percentage of participants with any occurrence of shigellosis, including a culture or PCR positive result for *S. sonnei*, associated two-sided Wilson 95% confidence intervals, estimated vaccine efficacy, and associated Wilson 95% confidence intervals will be presented by study arm in **Table 23** for the Full Analysis population and the Per Protocol population.

The descriptive statistics of number and proportion of participants with any occurrence of shigellosis using the programmatic determination post-challenge will be presented by study arm and cohort in **Table 25**. Solicited symptoms of shigellosis (fever, headache, arthralgia, nausea, pain/abdominal cramps, fatigue/malaise, myalgia, anorexia/loss of appetite, chills, vomiting, and diarrhea) were collected following challenge administration through the inpatient period and for 5 days after discharge and graded on a scale of 0 (none), 1 (mild), 2 (moderate) and 3 (severe). The number, percentage, and two-sided Wilson 95% confidence interval will be displayed for participants through the inpatient period in **Table 26** and will also be summarized by event, maximum severity, and study arm in **Table 27**. Solicited symptoms of shigellosis collected through the inpatient period and 5 days after discharge by study arm and participant ID will be presented in **Listing 8**, **Listing 9**, and **Listing 10**.

The primary efficacy analysis will also be presented for the Full Analysis population and Per Protocol population stratified by site to evaluate the association between study arm and occurrence of shigellosis while adjusting for the effects of study sites. The Cochran Mantel-Haenszel (CMH) statistic will be used to assess the overall association between study arm and the occurrence of shigellosis while taking into account the potential differences between the study sites (Hope Clinic of the Emory Vaccine Center and CCHMC) with the goal of determining if we have consistent vaccine efficacy across the sites. The results of the CMH analysis will be presented in **Table 24**. To test the assumption that the relative risk is the same for each site, the Breslow-Day test will be used. The null hypothesis of the Breslow-Day test is that the relative risks are equivalent across the different sites. The results of the Breslow-Day test will be presented in **Table 24** for the Full Analysis and Per-Protocol populations.

8.2. Secondary Efficacy Analysis

Secondary efficacy analyses to estimate the vaccine efficacy of the individual vaccine arms (1 dose of 10^6 cfu, 2 doses of 10^6 cfu, and 2 doses of $5x10^5$ cfu) are presented along with 95% confidence intervals in **Table 22**. As the study is not powered for these individual comparisons to placebo, no formal hypothesis tests are planned, and no p-values will be presented.

The duration of viral shedding will be evaluated from the day of the initial positive result to the day of the last positive qualitative or quantitative PCR result, regardless of intermittent negative results.

The number of participants shedding WRSs2 vaccine strain pre-challenge and the duration participants experience shedding of *S. sonnei* post-vaccination by culture will be described as an indicator of the efficacy of vaccine uptake. The number and percentage of participants experiencing *S. sonnei* viral shedding by culture will be tabulated by study day and study arm pre-challenge in **Table 28** with summary statistics of the duration (in days) of shedding by culture presented by study arm in **Table 29**. **Figure 8** will display the proportion of participants with pre-challenge *S. sonnei* viral shedding by culture by study day and study arm in the Shedding Analysis population.

The number of participants shedding 53G post-challenge and the duration participants experience shedding of 53G post-challenge by culture will be described across all participants who were followed for the entire inpatient period. The number and percentage of participants experiencing *S. sonnei* 53G viral shedding by culture will be presented by study day and study arm post-challenge in **Table 31** with summary statistics of the duration (in days) of shedding by culture presented by study arm in **Table 32**. **Figure 9** will display the proportion of participants with post-challenge 53G viral shedding by culture by study day and study arm in the Full Analysis population.

8.3. Exploratory Efficacy Analysis

The exploratory endpoints assessing maximum *S. sonnei* CFU per gram of stool post-vaccination by immunoblot, along with the duration participants experience shedding of *S. sonnei* post-vaccination by immunoblot and PCR will be described as an indicator of the efficacy of vaccine uptake. Summary statistics will be used to report the duration (in days) of *S. sonnei* shedding by immunoblot and PCR by study arm pre-challenge in **Table 29**. The maximum CFU per gram of *S. sonnei* during the pre-challenge period will be summarized by study arm using immunoblot and PCR in **Table 30**.

The exploratory endpoints assessing maximum *S. sonnei* CFU per gram of post-challenge by immunoblot, along with the duration participants experience of shedding *S. sonnei* 53G post-challenge by immunoblot and PCR will be described. Summary statistics will be used to report the duration (in days) of 53G shedding by immunoblot and PCR by study arm post-challenge in **Table 32**. The maximum CFU per gram of *S. sonnei* during the post-challenge period will be summarized by study arm using immunoblot and PCR in **Table 33**.

9. SAFETY EVALUATION

9.1. Demographic and Other Baseline Characteristics

Categorical and continuous participant demographics and baseline characteristics will be summarized using the statistics described in **Section 6**.

Summaries of categorical demographic information such as sex, ethnicity, and race will be presented by site (**Table 15**) and by study arm (**Table 17**) for all enrolled participants. A similar summary of categorical demographic information will also be presented for the Full Analysis population (**Table 18**). Ethnicity is categorized as Hispanic or Latino, or not Hispanic and not Latino. In accordance with the National Institutes of Health reporting policy, participants may self-designate as belonging to more than one race or may refuse to identify a race, the latter reflected in the eCRF as "No" to each racial option. Summaries of continuous demographic information such as age and BMI will be presented by site (**Table 16**) and by study arm (**Table 19**) for all enrolled participants. A similar summary of continuous demographic information will also be presented for the Full Analysis population (**Table 20**). A listing of individual participants will be presented for all demographics (**Listing 6**).

9.1.1. Prior and Concurrent Medical Conditions

Any medical condition that is present at the time that the participant is screened is considered as baseline, documented as medical history, and not reported as an AE. However, if the severity of any pre-existing medical condition increases post-vaccination, according to the protocol-defined adverse event severity grading criteria found above in **Section 3.3.1**, it is then recorded as an AE.

All current illnesses and past pre-existing medical conditions will be coded using Medical Dictionary for Regulatory Activities (MedDRA) version 27.0 or higher. Summaries of participants' pre-existing medical conditions will be presented by MedDRA System Organ Class (SOC) and study arm for the Safety population (**Table 21**).

A listing of individual participants will be presented for all reported medical history events including prior and concurrent medical conditions (**Listing 7**).

9.1.2. Prior and Concomitant Medications

Concomitant medications will be coded to the Anatomical Therapeutic Classification (ATC) using the World Health Organization (WHO) Drug Dictionary. The use of concomitant medications during the study will be summarized by ATC1 and ATC2 code and study arm for the Safety population (**Table 120**).

A listing of individual participants will be presented for all prior and concomitant medications (**Listing 25**).

9.2. Measurements of Treatment Compliance

The number of participants receiving the first study vaccination by date of administration will be presented by study arm and site in **Table 13**. The number of participants receiving each study vaccination and challenge will also be presented by study arm as part of the participant disposition table in **Table 11**.

9.3. Adverse Events

Post-vaccination, post-challenge, and exact dose periods will be used to aid in the presentation of timing for safety analyses as needed. The denominator for the percentages is based on the number of non-missing

observations for an assessment or based on the number of participants in the analysis population. This will be described for each exhibit. The binomial distribution will be assumed for binary endpoints such as the occurrence of safety events, and exact 95% Clopper-Pearson confidence intervals will be computed, where indicated.

Adverse events (AEs) will be reported in the Safety population according to vaccination(s) actually received. When calculating the incidence of AEs (i.e., on a per-participant basis), each participant will only be counted once and any repetitions of AEs within a participant will be ignored; the denominator will be the total population size. An overall summary of adverse events is presented by study arm in **Table 49**.

A summary of AEs that occurred in ≥ 5% of participants in any study arm by MedDRA SOC and preferred term (PT) is provided for the Safety population in **Table 50**.

9.3.1. Solicited Events and Symptoms

Systemic solicited AEs were collected pre-vaccination, 90 minutes post-vaccination, and then daily for 7 days after each vaccination using a memory aid and graded on a scale of 0 (none), 1 (mild), 2 (moderate) and 3 (severe). Solicited adverse reactions that continue beyond these periods will be followed until resolution or determined to be stable per investigator.

Systemic events include fever, headache, arthralgia, nausea, pain/abdominal cramps, fatigue/malaise, myalgia, anorexia/loss of appetite, chills, vomiting, and diarrhea.

The grading scale for solicited reactogenicity AEs, such as quantitative grading for fever, is included in **Table 8**.

The number, percentage, and exact two-sided 95% confidence interval (calculated using Clopper-Pearson methodology from a binomial distribution using SAS Proc Freq with a binomial option) will be displayed for participants in the Safety population reporting each solicited AE following each dose and will be summarized by symptom and study arm post-either vaccination dose in **Table 48**, post-vaccination dose 1 in **Table 52**, and post-vaccination dose 2 in **Table 53**. The number and percentage of participants in the Safety population experiencing solicited systemic (reactogenicity) adverse events will also be summarized by event, maximum severity, and study arm post-either vaccination dose in **Table 54**, post-vaccination dose 1 in **Table 55**, and post-vaccination dose 2 in **Table 56**. For each event, the denominator is the number of participants who received the respective dose with non-missing data for the specific event. Along with tabular displays of the systemic solicited AEs, the maximum severity of solicited events will be displayed graphically in bar charts by study day and study arm post-vaccination dose 1 in **Figure 16** and post-vaccination dose 2 in **Figure 17**.

The number and percentage of participants experiencing solicited events post each vaccination dose will also be summarized and displayed for each study arm by event, severity, and day post dosing starting with **Table 57** and concluding with **Table 65**.

The difference in proportions of participants experiencing solicited events between each study arm and the placebo group will be presented with 95% confidence intervals (**Table 66**).

A direct comparison using the number and percentage of participants experiencing solicited events after vaccination dose 1 to vaccination dose 2 will be displayed by study arm in **Table 67**.

Solicited systemic adverse events by study arm and participant ID will be presented in **Listing 16**, **Listing 17**, and **Listing 18**.

9.3.2. Unsolicited Adverse Events

All unsolicited AEs will be coded by MedDRA for PT and SOC. A listing of all reported unsolicited adverse events by study arm, participant ID, and AE number will be presented in **Listing 19**.

The following summaries for unsolicited adverse events will be presented by MedDRA SOC, PT, vaccination, and study arm:

Incidence and frequency of AEs over time with associated 95% confidence intervals post-first study vaccination (Days 1-8, Days 9-28, Days 29-37, Days 38-56, Days 57-69, Days 70-180) (**Table 68**, **Table 69**, **Table 70**, **Table 71**, **Table 72**, and **Table 73**).
Number and percentage of participants experiencing unsolicited AEs by maximum severity and relationship to study product post-any vaccination dose (**Table 74**, **Table 75**, **Table 76**, and **Table 77**).
Number and percentage of participants experiencing vaccine-related AEs within 28 days post-any vaccination dose (**Table 78**).
Participant listing of non-serious AEs of moderate or greater severity (**Table 81**).
Bar charts displaying the frequency of related AEs by MedDRA SOC, maximum severity, and study arm post-vaccination dose 1 (**Figure 19**) and post-vaccination dose 2 (**Figure 20**).
Bar chart displaying the incidence of related AEs by MedDRA SOC, maximum severity, and study arm post-vaccination dose 1 (**Figure 22**) and post-vaccination dose 2 (**Figure 23**).

9.4. Deaths and Serious Adverse Events

The following listing will be presented including Participant ID, Study Arm, Adverse Event Description, Associated Dose, Number of Days Post Associated Dose, Severity, Relationship to Treatment, Alternate Etiology if not Related, and Outcome:

- Deaths and Serious Adverse Events (**Table 79**)

The incidence and frequency of SAEs with associated 95% confidence intervals will be presented by MedDRA PT and SOC and study arm (**Table 80**).**Pregnancies**

For any participants in the Safety population who become pregnant during the study, every attempt will be made to follow these participants to completion of pregnancy to document the outcome, including information regarding any complications with pregnancy and/or delivery. Listings of pregnancies and outcomes will be presented as follows:

- Maternal Information (**Listing 26**)
- Gravida and Para (**Listing 27**)
- Live Birth Outcomes (**Listing 28**)
- Still Birth Outcomes (**Listing 29**)
- Spontaneous, Elective, or Therapeutic Abortion Outcomes (**Listing 30**)

9.6. Clinical Laboratory Evaluations

The distribution of laboratory chemistry results will be presented by parameter, maximum severity, time point, and study arm for any chemistry parameter in **Table 84**, sodium in **Table 85**, potassium in **Table 86**, creatinine in **Table 87**, alanine transaminase (ALT) in **Table 88**, and total bilirubin **Table 89**. Similarly, the

distribution of laboratory hematology results post-any vaccination dose will be presented by parameter, maximum severity, time point, and study arm for any hematology parameter in Table **101**, white blood cell count (WBC) in Table **102**, absolute neutrophil count (ANC) in Table **103**, hemoglobin (Hgb) in Table **104** and platelet count in Table **105**. Only a few blood urea nitrogen (BUN) results were reported in the study and summary tables will not be created for that parameter. BUN results will still be included in any laboratory listings.

Abnormal laboratory results related to study treatment will be presented by maximum severity, time point, and study arm for any chemistry parameter in Table **90**, sodium in Table **91**, potassium in Table **92**, creatinine in Table **93**, ALT in Table **94**, and total bilirubin in Table **95**. This will also be presented post baseline for hematology parameters in Table **106 ,** WBC in Table **107**, ANC in Table **108**, Hgb in Table **109** , and platelet count in Table **110**. Listings of participants with abnormal laboratory results, outside of the normal range or Grade 1 severity or higher, will be presented in Table **82** and Table **83** for chemistry and hematology parameters, respectively.

Descriptive statistics including mean, standard deviation, median, minimum and maximum values and change from baseline by time point and study arm, for each chemistry laboratory parameter, will be summarized for sodium in Table **96**, potassium in Table **97**, creatinine in Table **98**, alanine transaminase (ALT) in Table **99**, and total bilirubin in Table **100** as well as for each hematology laboratory parameter, will be summarized for white blood cell count (WBC) in Table **111** absolute neutrophil count (ANC) in Table **112**, hemoglobin (Hgb) in Table **113** and platelet count in Table **114**.

Listing 20, **Listing 21**, and **Listing 22** will provide complete listings of individual clinical laboratory results with applicable reference ranges for chemistry, hematology, and urinalysis parameters respectively sorted by study arm, participant ID, parameter, and study day.

9.7. Vital Signs and Physical Evaluations

Summaries of vital signs by maximum severity will be tabulated by time point and study arm for any vital sign parameter in Table **115**, oral temperature in Table **116**, pulse in Table **117**, systolic blood pressure in Table **118**, and diastolic blood pressure in Table **119**. A listing of vital signs will be presented by study arm, and participant ID in **Listing 23**. The baseline time point will be defined as the last measurement prior to first vaccination. For post-baseline time points, if assessments are repeated within 10 minutes, the repeat assessment will be used in analysis, otherwise all assessments will be taken into account in determining the maximum severity per time point and across time points. All assessments, including assessments that were repeated within 10 minutes will be presented in the listing.

Targeted physical examinations will be performed, pre-vaccination, post-vaccination, daily during the inpatient challenge, and at other time points of interest. The following body systems will be assessed: Abdomen, Cardiovascular/heart, Extremities, General Appearance, HEENT (head, ears, eyes, nose, oral, and throat examination), Lymph nodes, Musculoskeletal, Neck, Neurological, Pulmonary/Chest, and Skin. A listing of physical exam findings will be presented by study arm and participant ID in **Listing 24** along with any abnormal findings.

10. IMMUNOGENICITY

Immunogenicity data summaries and analysis for secondary and exploratory endpoints will be presented for the immunogenicity population. Descriptive summary statistics will be provided for all immunogenicity endpoint data using number and percentage of participants with non-missing results and, for assays in which the data are assumed to be log-normally distributed, geometric mean titers (GMTs) with corresponding 95% confidence intervals (based on Student's t-distribution), along with the minimum and maximum values. For assays assessing participants with greater or equal to 4-fold rise from pre-vaccination, results will be summarized using number and percentage of participants who meet the 4-fold rise threshold, the geometric mean fold rise (GMFR) along with associated 95% confidence intervals. Confidence intervals using the Score-Wilson method will be presented for proportional endpoints.

Each endpoint will be displayed at study days of interest outlined in **Section 3.2.2**.

Individual LPS-specific and Invaplex-specific ELISA results will be presented for IgG and IgA in **Listing 13** Individual LPS-specific and Invaplex-specific fecal IgA and total fecal IgA assay results will be presented in **Listing 14**. Individual exploratory assay results will be provided for immunoblot and PCR in **Listing 12**, for culture in **Listing 11,** and ELISpot in **Listing 15**. Total IgA and IgG ELISpot results will be included only in **Listing 15** and will not be summarized in tables.

10.1. Secondary Immunogenicity Analysis

The secondary immunogenicity endpoints of LPS-specific and Invaplex-specific IgG and IgA ≥ 4-fold rise, maximum titer, and peak fold-rise from pre-vaccination assessed pre-challenge and post-challenge will be summarized as described above in **Section 10**. LPS-specific IgG and IgA GMT and GMFR with associated 95% confidence intervals will be reported along with participants who achieve at least 4-fold rise pre-challenge by time point and by study arm in **Table 34** and Table **35**, respectively. Similarly, Invaplex-specific IgG and IgA GMT and GMFR results with associated 95% confidence intervals will be reported along with percentage of participants who achieve 4-fold rise pre-challenge by time point and by study arm in Table **36** and Table **37**. LPS-specific IgG and IgA GMT and GMFR with associated 95% confidence intervals as well as Invaplex-specific IgG and IgA GMT and GMFR results with associated 95% confidence intervals will also be reported with the same criteria for the post-challenge period in **Table 38**, **Table 39**, **Table 40**, and **Table 41** respectively. Each table will also report the peak-fold rise and geometric mean of the maximum result for LPS-specific immunoglobulins and Invaplex-specific immunoglobulins.

Reverse cumulative distribution (RCD) curves will be presented separately for pre-challenge and post-challenge time points for LPS-specific and Invaplex-specific IgG and IgA titers. Plots for each assay will be generated with separate panels for each time point of interest. For example, the RCD curve for LPS-specific IgG titers assessed pre-challenge will have panels for Day 1 (Baseline), Day 15, et cetera with separate curves within each panel for each study arm. RCD curves for LPS-specific IgG and IgA titers are presented pre-challenge in **Figure 4** and **Figure 5** and post-challenge in **Figure 8** and **Figure 9**. RCD curves for Invaplex-specific IgG and IgA titers are presented pre-challenge in **Figure 6** and **Figure 7** and post-challenge in **Figure 10** and **Figure 11**.

10.2. Exploratory Immunogenicity Analysis

The number of *S. sonnei* LPS-specific and Invaplex-specific IgG and IgA antibody secreting cells (ASCs) per 10^6 PBMCs by ELISpot will be summarized through Day 64 for each study arm and summarized for LPS-specific IgG ASC in Table **42**, LPS-specific IgA ASC in **Table 43**, Invaplex-specific IgG ASC in

Table 44, and Invaplex-specific IgA ASC in **Table 45**. Box plots will be used to illustrate the distribution of the results by time point and study arm in **Figure 12**, **Figure 13**, **Figure 14**, and **Figure 15**.The percentage of participants with ≥10 IgG or IgA ASCs per 10^6 PBMCs for both *S. sonnei* LPS-specific and Invaplex-specific results by ELISpot post-vaccination through Study Day 56 and post-challenge through Day 64 will also be reported. These results will be summarized and presented for LPS-specific IgG in **Table 42**, LPS-specific IgA ASC in **Table 43**, Invaplex-specific IgG ASC in **Table 44**, and Invaplex-specific IgA ASC in **Table 45**.

The number of participants with ≥ 4-fold rise in *S. sonnei* LPS-specific fecal IgA by ELISA will be assessed by calculating the percentage of participants and associated 95% CI by time point and study arm in **Table 46**. The GMT and GMFR and associated 95% confidence intervals will also be reported in the same table. This will also be displayed using similar criteria for *S. sonnei* Invaplex-specific fecal IgA in **Table 47** and for total fecal IgA in **Table 48**. Each table will also report the maximum fold rise post-vaccination of *S. sonnei* for LPS-specific and Invaplex-specific IgA by ELISA through Day 56 and the maximum fold-rise post-challenge through Day 85.

11. 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.

12. TECHNICAL DETAILS

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

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

As noted in other sections of the analysis plan, after the initiation of the study, two participants had Grade 3 diarrhea and/or vomiting in the days following vaccination. This triggered a halting rule. To meet the recommendations of the DSMB and evaluate the safety and efficacy signal of a lower dose, several changes to the protocol were made. The vaccination dose was reduced to $5x10^5$, enrollment was changed to 2 arms and randomized 2:1 (vaccine: placebo). Furthermore, participants with morbid obesity were excluded and weight loss medications prohibited. No changes in sample collection or challenge phase were made.

14. REFERENCES

15. 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

LIST OF TABLES

Table 1: Primary Endpoint

Shigellosis	**Definition**
1. Severe Diarrhea	≥6 stools classified as 3-5 in consistency in 24 hours **OR** >800 gm stool classified as 3-5 in 24 hours
2. Moderate Diarrhea with additional signs/symptoms	4-5 stools classified as 3-5 in consistency in 24 hours **OR** 400-800 gm stools classified as 3-5 in 24 hours **with one or more of the following:** oral temperature ≥38.0˚C[†]; ≥1 moderate constitutional/enteric symptom[‡]; ≥2 episodes of vomiting in 24 hours
3. Dysentery with additional signs/symptoms	≥2 stools classified as 3-5 in consistency with gross blood (hemoccult positive) in 24 hours **with one or more of the following:** oral temperature ≥38.0˚C; ≥1 moderate constitutional/enteric symptom; ≥2 episodes of vomiting in 24 hours

† Confirmed by two separate readings at least five minutes apart

‡ Moderate constitutional/enteric symptoms include nausea, abdominal pain/cramping, myalgia/arthralgia, malaise (does not include anorexia, chills, headache)

9.1 Overall Study Design and Plan Description

Table 2: Vaccine Administration, Challenge and Follow-up

Arm	Outpatient (Vaccination Phase)			Inpatient (CCHMC) (Challenge Phase)		Outpatient
	Study Day		Day 4-57 7 visits	Day 57 (±2)	Day 58-65 (planned discharge on study day 65)	Day 71-180 3 visits, final contact
	1	29 +2d				
1	WRSs2	WRSs2	Safety, vaccine fecal shedding, blood and stool collection for immunogenicity	challenge with *S. sonnei* 53G	Safety, challenge, fecal shedding, blood and stool collection for immune responses post challenge	Blood and stool collection for immune responses post challenge Final contact for safety
2	Placebo	WRSs2				
3	Placebo	Placebo				

Table 3: Amended Vaccine Administration, Challenge and Follow-up

<table>
<tr><td colspan="7">Amended Vaccine Administration</td></tr>
<tr><td rowspan="3">Arm</td><td colspan="3">Outpatient
(Vaccination Phase)</td><td colspan="2">Inpatient (CCHMC)
(Challenge Phase)</td><td>Outpatient</td></tr>
<tr><td colspan="2">Study Day</td><td rowspan="2">Day 4-57
7 visits</td><td rowspan="2">Day 57
(±2)</td><td rowspan="2">Day 58-65
(planned discharge on study day 65)</td><td rowspan="2">Day 71-180
3 visits, final contact</td></tr>
<tr><td>1</td><td>29 +2d</td></tr>
<tr><td>1</td><td>WRSs2</td><td>WRSs2</td><td rowspan="2">Safety, vaccine fecal shedding, blood, and stool collection for immunogenicity</td><td rowspan="2">challenge with S. sonnei 53G</td><td rowspan="2">Safety, challenge, fecal shedding, blood, and stool collection for immune responses post challenge</td><td rowspan="2">Blood and stool collection for immune responses post challenge
Final contact for safety</td></tr>
<tr><td>2</td><td>Placebo</td><td>Placebo</td></tr>
</table>

Table 4: Stool Sample Classification Criteria

Stool Classification	Consistency Grading	Description
Normal stool	1	Firm, tootsie roll consistency
Soft stool	2	Pudding consistency, not firm but holds some shape
Loose stool	3	Takes the shape of the container, thick gravy consistency/brown watery, opaque watery, chocolate milk consistency
Watery stool	4	Opaque colored, watery consistency
“Rice Water”	5	Soapy watery consistency

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

Table 5: Schedule of Study Procedures – Screening and Vaccination

Study Event										
Visit Number	00A	00B	01	03	05	06	07	09	11	12
Study Day	Screen -60 to-3	-3	1	4	8	15	29	32	36	43
Compliance range days		-2		±1	±1	±2	+2	±1	±1	±2
Day from Last vaccination			0	3	7	14	28	3	7	14
Vaccination WRSs2			X[5]				X[5]			
Contact Type	C	C	C	C	C	C	C	C	C	C
Inclusion / Exclusion Criteria review	✓		✓				✓			
Educational Materials, Written Test	✓	(✓)								
Informed Consent	✓									
Demographics	✓									
Abbreviated PE	✓									
Targeted PE			¶	¶	¶	¶	¶	¶	¶	¶
Vital Sign^[^,1,6]	✓		✓	¶	¶	¶	✓	¶	¶	¶
Concomitant Medication	✓		✓	¶	✓	✓	✓	¶	✓	✓
Medical History	✓									
Interim Medical History			✓	¶	✓	✓	✓	¶	✓	✓
Urine Pregnancy	✓		✓				✓			
Urine Dipstick, Opioid Testing	✓									
Screening health /safety blood[%], mL	11									
Safety Lab	6.5				6.5				6.5	
Reactogenicity Memory Aid			✓[2]	✓[3]	✓[3]		✓[2]	✓[3]	✓[3]	
Collection of AEs, SAEs, other illness, pregnancy			✓	✓	✓	✓	✓	✓	✓	✓
Serum IgA & IgG (mL blood)	5	10	(10)			10	10			10
ASC Whole Blood, mL		16	(16)		16		16		16	

Table 5: Schedule of Study Procedures – Screening and Vaccination *(continued)*

Study Event											
Visit Number	00A	00B	01	03	05	06	07	09	11	12	
Study Day	Screen -60 to-3	-3	1	4	8	15	29	32	36	43	
Compliance range days		-2		±1	±1	±2	+2	±1	±1	±2	
Day from Last vaccination			0	3	7	14	28	3	7	14	
Vaccination WRSs2			X[5]				X[5]				
Contact Type	C	C	C	C	C	C	C	C	C	C	
Stool collection for WRSs2 shedding		✓	(✓)	✓	✓	✓	✓	✓	✓	✓	
Stool for immunoblot and PCR		✓	(✓)	✓	✓	✓	✓	✓	✓	✓	
Stool for IgA		✓	(✓)		✓	✓	✓		✓	✓	
Samples for Secondary research[7]:											
Plasma		✓	(✓)	✓	✓	✓	✓	✓	✓	✓	
Whole Blood PBMC for Tfh (FACS T/B/IR Cell Panel) and Phenotyping, mL		16	(16)	16			16	16			
Paxgene Whole Blood, mL		2.5	(2.5)	2.5	2.5		2.5	2.5	2.5		
Blood for serum (IgG subclass, Avidity/affinity, Microarray)		5	(5)			5	5			5	
ALS whole blood		24	(24)		24		24		24		
Memory B cell Whole blood, mL		16	(16)				16				
SBA		✓	(✓)			✓	✓			✓	
Stool Microbiome		✓	(✓)	✓	✓	✓	✓	✓	✓	✓	
Estimated Total Blood Volume (Vaccination Phase) mL	22.5	89.5	(89.5)	18.5	49	15	89.5	18.5	49	15	366.5

Notes:

C = Clinic; SC = Contact;

¶ = if indicated

^ Vital signs include temperature, blood pressure, and pulse

% Screening health and safety labs include: hematology (white cell count, hemoglobin, platelets, absolute neutrophil count/ANC); chemistry (total bilirubin, ALT, creatinine, sodium, potassium); serology (HIV antibodies, HBsAg, and HCV antibodies, HLA-B27, *S. sonnei* LPS IgG (ELISA)).

+ Day 56 is admission to the inpatient isolation unit 1 day prior to challenge

Table 5: Schedule of Study Procedures – Screening and Vaccination *(continued)*

[#] All stools will be collected and visually assessed for consistency, blood or mucus. Stools that are classified as 3-5 consistency will be weighed, and if there is visible blood, a Hemoccult test will be performed to confirm presence of occult blood. Up to two stools with blood present by visual inspection in a 24- hour period will be tested by Hemoccult. Any remaining stool will be disinfected with bleach in the plastic stool collector and discarded in the hazardous waste.

[@] Discharge, continue daily protocol collections if participant does not meet discharge criteria and remains in inpatient isolation facility

* 65 mL: 5mL blood collected for secondary research; 60 mL blood will be collected to establish the repository for positive control for future assays.

! = On the 5th day after challenge (Day 62), participants will begin to receive 500 mg of ciprofloxacin twice daily for 3 days. Participants with contraindication to ciprofloxacin may receive as second-line treatment trimethoprim-sulfamethoxazole (160 mg/800 mg twice daily for 5 days), or any antibiotic that is deemed suitable according to local guidelines and the investigator's assessment can be used.

? = These are assays that may be performed.

( ) = collected on day of vaccination or second screening visit if not collected during initial screening visit

1 = Pre-vaccination vital signs and post vaccination dose if indicated

2 = review use of memory aid, provide thermometer and instruct to **contact** site for AEs, changes to health, emergency room visit or hospitalization, SAE, or pregnancy

3 = review and confirm information from memory aid

4 = **contact** by various methods, including email, text or phone call to remind participant to complete memory aid and instruct how to fill out memory aid

5 = vaccination assessment completed at least 90 minutes post dose

6 = Pre-challenge vital signs, post challenge dose per protocol +30 min and +60 min, daily and additional assessment as indicated

7 = Illness Labs collected per PI discretion include: serum chemistry, sodium, potassium, blood urea nitrogen/BUN, and creatinine. Urine dip for specific gravity, as indicated

8 = All emesis will be measured and recorded then disinfected with bleach and discarded in the hazardous waste

9 = A SARS-CoV-2 test will be performed on all participants upon entry into the challenge unit. Anyone with a positive test will be immediately escorted out of the challenge unit. In addition, a SARS-CoV-2 test will be performed 3 days post challenge as well as at any time a participant were to exhibit symptoms of COVID-19 illness during the inpatient stay.

10 = All concomitant medications, taken in the 30 days prior to study enrollment through Day 28 following challenge or early termination, whichever occurs first, will be Recorded.

Table 6: Schedule of Study Procedures – Inpatient Challenge and Follow-up

Study Event														
Visit Number	13	14	15	16	17	18	19	20	21	22	23	24	25	26
Study Day	56+	57	58	59	60	61	62	63	64	65	71	85	113	180
Compliance rage days	-	±2	-	-	-	-	-	-	-	-	±2	±2	±4	±14
Day from Last vaccination	27	28												
Day from Challenge			1	2	3	4	5	6	7	8	14	28	56	
Admission	✓	¶												
Challenge with 53G		✓												
Contact Type	Inpatient Period										C	C	C	SC
Assessing safety for challenge receipt	✓													Post-Study Safety Assessment, Clinical Phase study Completion
Dose Qualification	✓													
Medical Interview	✓													
Informed Consent														
Abbreviated PE	✓	¶												
Targeted PE			¶	¶	¶	¶	¶	¶	¶	¶	¶	¶	¶	
Vital Sign^,6 Body weight (pre-challenge and as indicated)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	¶	¶	¶	
Concomitant Medication[10]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		
Medical History	✓	¶	¶	¶	¶	¶	¶	¶	¶	¶	✓	✓	✓	
Urine Pregnancy	✓	¶												
SARS-CoV2 testing[9]	✓	¶	¶	¶	¶	¶	¶	¶	¶	¶				
Safety Lab	6.5								6.5		6.5	¶	¶	
Memory Aid										✓2	✓3			
Collection of AEs, SAEs, other illness, pregnancy	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	

Table 6: Schedule of Study Procedures – Inpatient Challenge and Follow-up *(continued)*

Study Event														
Visit Number	13	14	15	16	17	18	19	20	21	22	23	24	25	26
Study Day	56+	57	58	59	60	61	62	63	64	65	71	85	113	180
Compliance rage days	-	±2	-	-	-	-	-	-	-	-	±2	±2	±4	±14
Day from Last vaccination	27	28												
Day from Challenge			1	2	3	4	5	6	7	8	14	28	56	
Admission	✓	¶												
Challenge with 53G		✓												
Contact Type	Inpatient Period										C	C	C	SC
Reactogenicity assessment and Illness labs if needed[7],		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Post-Study Safety Assessment, Clinical Phase study Completion
Stool for classification of consistency, and hemoccult[#]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓				
Measure and Record emesis output[8]		✓	✓	✓	✓	✓	✓	✓	✓	✓				
Serum IgA & IgG, (mL Blood)	10								10		10	10	10	
Antibiotic Therapy[!] Day 62-64 and discharge[@] Day 65							✓	✓	✓	@				
ASC Whole Blood, mL	16				16				16					
Stool collection for shedding	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓				
Stool for immunoblot and PCR		✓	✓	✓	✓	✓	✓	✓	✓	✓				
Stool for IgA	✓					✓			✓		✓	✓		
Samples for Secondary research[7]														
Plasma	✓				✓				✓			✓	✓	
Whole Blood PBMC for Tfh (FACS T/B/IR Cell Panel) and Phenotyping, mL	16				16									
Paxgene whole blood, mL	2.5				2.5				2.5					

Study Event														
Visit Number	13	14	15	16	17	18	19	20	21	22	23	24	25	26

Table 6: Schedule of Study Procedures – Inpatient Challenge and Follow-up *(continued)*

Study Day	56+	57	58	59	60	61	62	63	64	65	71	85	113	180	
Compliance rage days	-	+2	-	-	-	-	-	-	-	-	±2	±2	±4	±14	
Day from Last vaccination	27	28													
Day from Challenge			1	2	3	4	5	6	7	8	14	28	56		
Admission	✓	¶													
Challenge with 53G		✓													
Contact Type	Inpatient Period										C	C	C	SC	
Blood for serum (IgG subclass, Avidity/affinity, Microarray)	5								5		5	65*	5		
ALS Whole blood	24				24				24						
Memory B-cell Whole blood, mL	16											16	16		
SBA	✓								✓		✓	✓	✓		
Stool Microbiome and Cytokine	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓		
Estimated Total Blood Volume (Challenge Phase), mL	96				58.5				64		21.5	91	31		759.5

Notes:

C = Clinic; SC = Contact;

¶ = if indicated

^ Vital signs include temperature, blood pressure, and pulse

% Screening health and safety labs include: hematology (white cell count, hemoglobin, platelets, absolute neutrophil count/ANC); chemistry (total bilirubin, ALT, creatinine, sodium, potassium); serology (HIV antibodies, HBsAg, and HCV antibodies, HLA-B27, *S. sonnei* LPS IgG (ELISA)).

+ Day 56 is admission to the inpatient isolation unit 1 day prior to challenge

All stools will be collected and visually assessed for consistency, blood or mucus. Stools that are classified as 3-5 consistency will be weighed, and if there is visible blood, a Hemoccult test will be performed to confirm presence of occult blood. Up to two stools with blood present by visual inspection in a 24- hour period will be tested by Hemoccult. Any remaining stool will be disinfected with bleach in the plastic stool collector and discarded in the hazardous waste.

@ Discharge, continue daily protocol collections if participant does not meet discharge criteria and remains in inpatient isolation facility

* 65 mL: 5mL blood collected for secondary research; 60 mL blood will be collected to establish the repository for positive control for future assays.

! = On the 5th day after challenge (Day 62), participants will begin to receive 500 mg of ciprofloxacin twice daily for 3 days. Participants with contraindication to ciprofloxacin may receive as second-line treatment trimethoprim-sulfamethoxazole (160 mg/800 mg twice daily for 5 days), or any antibiotic that is deemed suitable according to local guidelines and the investigator's assessment can be used.

? = These are assays that may be performed.

Table 6: Schedule of Study Procedures – Inpatient Challenge and Follow-up *(continued)*

( ) = collected on day of vaccination or second screening visit if not collected during initial screening visit

1 = Pre-vaccination vital signs and post vaccination dose if indicated

2 = review use of memory aid, provide thermometer and instruct to **contact** site for AEs, changes to health, emergency room visit or hospitalization, SAE, or pregnancy

3 = review and confirm information from memory aid

4 = **contact** by various methods, including email, text or phone call to remind participant to complete memory aid and instruct how to fill out memory aid

5 = vaccination assessment completed at least 90 minutes post dose

6 = Pre-challenge vital signs, post challenge dose per protocol +30 min and +60 min, daily and additional assessment as indicated

7 = Illness Labs collected per PI discretion include: serum chemistry, sodium, potassium, blood urea nitrogen/BUN, and creatinine. Urine dip for specific gravity, as indicated

8 = All emesis will be measured and recorded then disinfected with bleach and discarded in the hazardous waste

9 = A SARS-CoV-2 test will be performed on all participants upon entry into the challenge unit. Anyone with a positive test will be immediately escorted out of the challenge unit. In addition, a SARS-CoV-2 test will be performed 3 days post challenge as well as at any time a participant were to exhibit symptoms of COVID-19 illness during the inpatient stay.

10 = All concomitant medications, taken in the 30 days prior to study enrollment through Day 28 following challenge or early termination, whichever occurs first, will be recorded.

11= Height and weight collected to determine BMI at screening

10.2 Protocol Deviations

Table 7: Distribution of Protocol Deviations by Category, Type, and Study Arm – All Enrolled Participants

[Implementation Note: Only include the Deviation Types that were reported in the study. If the table will be multi-page, move the footnote/explanation to the footer so that it repeats for each page of the table.]

Category	Deviation Type	WRSs2 + WRSs2 (10^6 cfu) (N=X)			WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)			Placebo + WRSs2 (10^6 cfu) (N=X)			Placebo + Placebo (N=X)			All Participants (N=X)		
		No. of Part.	No. of Maj. Dev.	No. of Min. Dev.	No. of Part.	No. of Maj. Dev.	No. of Min. Dev.	No. of Part.	No. of Maj. Dev.	No. of Min. Dev.	No. of Part.	No. of Maj. Dev.	No. of Min. Dev.	No. of Part.	No. of Maj. Dev.	No. of Min. Dev.
Eligibility/enrollment	Any type	x	x	x	x	x	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	x	x	x	x	x
	Met exclusion criterion	x	x	x	x	x	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	x	x	x	x	x
	Other	x	x	x	x	x	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	x	x	x	x	x
	Out of window visit	x	x	x	x	x	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	x	x	x	x	x
	Missed treatment administration	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Delayed treatment administration	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	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	x	x	x	x	x
	Out of window visit	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

Table 7: Distribution of Protocol Deviations by Category, Type, and Study Arm – All Enrolled Participants *(continued)*

Category	Deviation Type	WRSs2 + WRSs2 (10^6 cfu) (N=X)			WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)			Placebo + WRSs2 (10^6 cfu) (N=X)			Placebo + Placebo (N=X)			All Participants (N=X)		
		No. of Part.	No. of Maj. Dev.	No. of Min. Dev.	No. of Part.	No. of Maj. Dev.	No. of Min. Dev.	No. of Part.	No. of Maj. Dev.	No. of Min. Dev.	No. of Part.	No. of Maj. Dev.	No. of Min. Dev.	No. of Part.	No. of Maj. Dev.	No. of Min. Dev.
	Missed visit/visit not conducted	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	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	x	x	x	x	x
	Incorrect version of ICF signed	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Blood not collected	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Urine not collected	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Stool not collected	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Other specimen not collected	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Too few aliquots obtained	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Specimen result not obtained	x	x		x	x	x	x	x	x	x	x	x	x	x	x
	Required procedure not conducted	x	x		x	x	x	x	x	x	x	x	x	x	x	x
	Required procedure done incorrectly	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Study product temperature excursion	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Specimen temperature excursion	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	[Insert other deviation types observed]	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

Table 7: Distribution of Protocol Deviations by Category, Type, and Study Arm – All Enrolled Participants *(continued)*

Category	Deviation Type	WRSs2 + WRSs2 (10^6 cfu) (N=X)			WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)			Placebo + WRSs2 (10^6 cfu) (N=X)			Placebo + Placebo (N=X)			All Participants (N=X)		
		No. of Part.	No. of Maj. Dev.	No. of Min. Dev.	No. of Part.	No. of Maj. Dev.	No. of Min. Dev.	No. of Part.	No. of Maj. Dev.	No. of Min. Dev.	No. of Part.	No. of Maj. Dev.	No. of Min. Dev.	No. of Part.	No. of Maj. Dev.	No. of Min. Dev.
	Other	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Treatment administration	Any type	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Required procedure done incorrectly	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Study product temperature excursion	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	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	x	x	x	x	x
	Treatment unblinded	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

Note: N = Number of enrolled participants randomized to the corresponding study arm.

12.2.2 Displays of Adverse Events

Table 8: Solicited Reactogenicity Adverse Event Grading Scale

Clinical Feature	Grade 0 (None)	Grade 1 (Mild)	Grade 2 (Moderate)	Grade 3 (Severe)
Fever	none	100.4 – 101.1 °F 38.0 – 38.4 °C	101.2 – 102.0 °F 38.5 – 38.9 °C	>102 °F/≥39.0 °C or ER visit or hospitalization
Headache	none	no pain medications taken	use of pain medication required	narcotic pain med required and/or prevents daily activity
Arthralgia	none	mild*	moderate**	severe***
Nausea	none	mild*	moderate**	severe***
Pain/Abdominal Cramps	none	mild*	moderate**	severe***
Myalgia	none	mild*	moderate**	severe***
Malaise, fatigue	none	mild*	moderate**	severe***
Anorexia, loss of appetite	none	mild*	moderate**	severe***
Chills	none	mild*	moderate**	severe***
Diarrhea	< 2 loose or watery stools of consistency 3-5	2-3 loose or watery stools consistency of 3-5 and < 400 gm per 24 hours	4-5 loose or watery stools consistency of 3-5 or 400-800 gm stools classified as consistency of 3-5 per 24 hours	≥ 6 loose or watery stools consistency of 3-5 or > 800 gm stools classified as consistency of 3-5 per 24 hours
Vomiting	none	1-2 episodes within 24-hour period	3-5 episodes within 24-hour period	>5 episodes within 24-hour period

Scoring guidelines:
***Mild**: aware of symptom, but easily tolerated
****Moderate**: discomfort enough to interfere with daily activities if at home
*****Severe**: incapacitating, unable to perform daily activities, would seek medical attention if at home

12.4.1 Individual Laboratory Measurements and Abnormal Laboratory Values

Table 9: Toxicity / Laboratory Adverse Event Grading Scale

	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
Serum			
Sodium – Hyponatremia mEq/L	132 – 134	130 – 131	<130
Sodium – Hypernatremia mEq/L	144 – 145	146 – 147	>147
Potassium – Hyperkalemia mEq/L	5.1 – 5.2	5.3 – 5.4	>5.4
Potassium – Hypokalemia mEq/L	3.5 – 3.6	3.3 – 3.4	< 3.3
Blood Urea Nitrogen BUN mg/dL	23 – 26	27 – 31	> 31
Creatinine – mg/dL	1.5 – 1.7	1.8 – 2.0	> 2.0
Liver Function Tests ALT increase by factor	1.1 – 2.5 x ULN**	2.6 – 5.0 x ULN	>5.0 x ULN
Bilirubin – when Liver Function Test is normal; increase by factor	1.1 – 1.5 x ULN	1.6 – 2.0 x ULN	>2.0 x ULN
Hematology			
Hemoglobin (Female) - gm/dL	11.0 – 12.0	9.5 – 10.9	< 9.5
Hemoglobin (Male) - gm/dL	12.5 – 13.5	10.5 – 12.4	< 10.5
WBC Increase - cell/mm^3	10,800 – 15,000	15,001 – 20,000	> 20, 000
WBC Decrease - cell/mm^3	2,500 – 3,500	1,500 – 2,499	< 1,500
Neutrophils Decrease - cell/mm^3	1,500 – 2,000	1,000 – 1,499	< 1,000
Platelets Decreased - cell/mm^3	125,000 – 140,000	100,000 – 124,000	< 100,000
Urine			
Protein	Trace	1+	2+
** ULN" is the upper limit of the normal range.			

Table 10: Vital Signs Adverse Event Grading Scale

AE	Severity	Parameter
Fever	1	38.0 – 38.4^{0}C 100.4 – 101.1^{0}F
	2	38.5 – 38.9^{0}C 101.2 – 102.0^{0}F
	3	≥39.0^{0}C >102^{0}F or ER visit or hospitalization
Hypertension (systolic)	1	141-150 mm Hg
	2	151-155 mm Hg
	3	>155mm Hg
Hypertension (diastolic)	1	91 – 95 mm Hg
	2	96-100 mm Hg
	3	>100 mm Hg
Hypotension (systolic)	1	85-89 mm Hg
	2	80-84 mm Hg
	3	<80 mm Hg
Hypotension (diastolic)	1	50-54 mm Hg
	2	45-49 mm Hg
	3	<45 mm Hg
Bradycardia	1	45-49 bpm
	2	40-44 bpm
	3	<40 bpm
Tachycardia	1	101-115 bpm
	2	116-130 bpm
	3	>130 bpm

14.1 Description of Study Participants

14.1.1 Disposition of Participants

Table 11: Participant Disposition by Study Arm, All Enrolled Participants

Participant Disposition	WRSs2 + WRSs2 (10^6 cfu) (N=X)		WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)		Placebo + WRSs2 (10^6 cfu) (N=X)		Placebo + Placebo (N=X)		All Participants (N=X)	
	n	%	n	%	n	%	n	%	n	%
Screening and Vaccination										
Screened	--	--	--	--	--	--	--	--	x	--
Enrolled/Randomized (Study Day 1)	x	100	x	100	x	100	x	100	x	100
Received First Study Vaccination (Study Day 1)	x	xx	x	xx	x	xx	x	xx	x	xx
Received Second Study Vaccination[a] (Study Day 29)	x	xx	x	xx	x	xx	x	xx	x	xx
Inpatient Challenge and Follow-up										
Received Study Challenge[a] (Study Day 57)	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Inpatient Period (Study Day 65)	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Follow-up (Study Day 180)[a]	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Per Protocol[b]	x	xx	x	xx	x	xx	x	xx	x	xx

Notes: N = Number of enrolled participants randomized to the corresponding study arm.
[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 12: Analysis Population Eligibilities by Study Arm, All Enrolled Participants

[Implementation Note: If at least one participant received an incorrect vaccination, then a footnote will be added which reads "XX participant(s) [was/were] randomized to [insert randomized study arm] but was administered [insert actual vaccination(s) received]."]

Analysis Population	Eligibility Category	Reason Participants Excluded	WRSs2 + WRSs2 (10^6 cfu) (N=X)		WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)		Placebo + WRSs2 (10^6 cfu) (N=X)		Placebo + Placebo (N=X)		All Participants (N=X)	
			n	%	n	%	n	%	n	%	n	%
Full Analysis Population	Eligible		x	xx	x	xx	x	xx	x	xx	x	xx
	Excluded	Any reason	x	xx	x	xx	x	xx	x	xx	x	xx
		Not challenged	x	xx	x	xx	x	xx	x	xx	x	xx
		Missing data for primary efficacy endpoint	x	xx	x	xx	x	xx	x	xx	x	xx
		[Other reason]	x	xx	x	xx	x	xx	x	xx	x	xx
Per Protocol Population	Eligible		x	xx	x	xx	x	xx	x	xx	x	xx
	Excluded	Any reason	x	xx	x	xx	x	xx	x	xx	x	xx
		Ineligible at baseline	x	xx	x	xx	x	xx	x	xx	x	xx
		Receipt of incorrect study vaccination	x	xx	x	xx	x	xx	x	xx	x	xx
		Receipt of second study vaccination or challenge out of window	x	xx	x	xx	x	xx	x	xx	x	xx
		Receipt of non-study vaccines, antibiotics, steroids, or immunosuppressive/cytotoxic therapy, blood products, immunoglobins, or experimental products prior to assessment of primary endpoint	x	xx	x	xx	x	xx	x	xx	x	xx
		[Other reason]	x	xx	x	xx	x	xx	x	xx	x	xx

Table 12: Analysis Population Eligibilities by Study Arm – All Enrolled Participants *(continued)*

Analysis Population	Eligibility Category	Reason Participants Excluded	WRSs2 + WRSs2 (10^6 cfu) (N=X)		WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)		Placebo + WRSs2 (10^6 cfu) (N=X)		Placebo + Placebo (N=X)		All Participants (N=X)	
			n	%	n	%	n	%	n	%	n	%
Safety Population	Eligible		x	xx	x	xx	x	xx	x	xx	x	xx
	Excluded	Any reason	x	xx	x	xx	x	xx	x	xx	x	xx
		Study product not received	x	xx	x	xx	x	xx	x	xx	x	xx
		[Other reason]	x	xx	x	xx	x	xx	x	xx	x	xx
Immunogenicity Population	Eligible		x	xx	x	xx	x	xx	x	xx	x	xx
	Excluded	Any reason	x	xx	x	xx	x	xx	x	xx	x	xx
		Study product not received	x	xx	x	xx	x	xx	x	xx	x	xx
		Immunogenicity endpoint data not available	x	xx	x	xx	x	xx	x	xx	x	xx
		[Other reason]	x	xx	x	xx	x	xx	x	xx	x	xx
Shedding Analysis Population	Eligible		x	xx	x	xx	x	xx	x	xx	x	xx
	Excluded	Any reason	x	xx	x	xx	x	xx	x	xx	x	xx
		Study product not received	x	xx	x	xx	x	xx	x	xx	x	xx
		[Other reason]	x	xx	x	xx	x	xx	x	xx	x	xx

Notes: N = Number of enrolled participants randomized to the corresponding study arm.

Table 13: Dates of First Administration by Site and Study Arm, All Enrolled Participants

	Cincinnati Children's Hospital					Hope Clinic of the Emory Vaccine Center				
Date of First Dose	**WRSs2 + WRSs2 (10^6 cfu) (N=X)**	**WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)**	**Placebo + WRSs2 (10^6 cfu) (N=X)**	**Placebo + Placebo (N=X)**	**All Participants (N=X)**	**WRSs2 + WRSs2 (10^6 cfu) (N=X)**	**WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)**	**Placebo + WRSs2 (10^6 cfu) (N=X)**	**Placebo + Placebo (N=X)**	**All Participants (N=X)**
Total (Entire period of enrollment)	x	x	x	x	x	x	x	x	x	x
DDMMMYYYY	x	x	x	x	x	x	x	x	x	x
Note: N=Number of participants randomized to the corresponding study arm who received the first study vaccination.										

Table 14: Ineligibility Summary of Screen Failures

Inclusion/Exclusion Category	Inclusion/Exclusion Criterion	n[a]	%[b]
Inclusion and Exclusion	Number of participants failing any eligibility criterion	x	xx
Inclusion	Any inclusion criterion	x	xx
	[inclusion criterion 1]	x	xx
	[inclusion criterion 2]	x	xx
	[inclusion criterion 3]	x	xx
Exclusion	Any exclusion criterion	x	xx
	[exclusion criterion 1]	x	xx
	[exclusion criterion 2]	x	xx
	[exclusion criterion 3]	x	xx
Eligible but Not Enrolled		x	xx

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

14.1.2 Demographic Data by Study Group

Table 15: Summary of Categorical Demographic and Baseline Characteristics by Site, All Enrolled Participants

Variable	Characteristic	Cincinnati Children's Hospital (N=X)		Hope Clinic of the Emory Vaccine Center (N=X)		All Participants (N=X)	
		n	%	n	%	n	%
Sex	Male	x	xx	x	xx	x	xx
	Female	x	xx	x	xx	x	xx
Ethnicity	Not Hispanic or Latino	x	xx	x	xx	x	xx
	Hispanic or Latino	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx
	Unknown	x	xx	x	xx	x	xx
Race	American Indian or Alaska Native	x	xx	x	xx	x	xx
	Asian	x	xx	x	xx	x	xx
	Native Hawaiian or Other Pacific Islander	x	xx	x	xx	x	xx
	Black or African American	x	xx	x	xx	x	xx
	White	x	xx	x	xx	x	xx
	Multi-Racial	x	xx	x	xx	x	xx
	Unknown	x	xx	x	xx	x	xx

Note: N = Number of participants enrolled in the study.

Table 16: Summary of Continuous Demographic and Baseline Characteristics by Site, All Enrolled Participants

Variable	Statistic	Cincinnati Children's Hospital (N=X)	Hope Clinic of the Emory Vaccine Center (N=X)	All Participants (N=X)
Age (years)	Mean	xx.x	xx.x	xx.x
	Standard Deviation	xx.x	xx.x	xx.x
	Median	xx.x	xx.x	xx.x
	Minimum	x	x	x
	Maximum	x	x	x
BMI[a]	Mean	xx.xx	xx.xx	xx.xx
	Standard Deviation	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x

Notes: N = Number of participants enrolled in the study.
[a] If height and/or weight were captured at baseline, BMI was calculated using these values. Otherwise, height and/or weight were captured at Visit 13 and used to calculate BMI.

Table 17: Summary of Categorical Demographic and Baseline Characteristics by Study Arm, All Enrolled Participants

Variable	Characteristic	WRSs2 + WRSs2 (10^6 cfu) (N=X)		WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)		Placebo + WRSs2 (10^6 cfu) (N=X)		Placebo + Placebo (N=X)		All Participants (N=X)	
		n	%	n	%	n	%	n	%	n	%
Sex	Male	x	xx	x	xx	x	xx	x	xx	x	xx
	Female	x	xx	x	xx	x	xx	x	xx	x	xx
Ethnicity	Not Hispanic or Latino	x	xx	x	xx	x	xx	x	xx	x	xx
	Hispanic or Latino	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx
	Unknown	x	xx	x	xx	x	xx	x	xx	x	xx
Race	American Indian or Alaska Native	x	xx	x	xx	x	xx	x	xx	x	xx
	Asian	x	xx	x	xx	x	xx	x	xx	x	xx
	Native Hawaiian or Other Pacific Islander	x	xx	x	xx	x	xx	x	xx	x	xx
	Black or African American	x	xx	x	xx	x	xx	x	xx	x	xx
	White	x	xx	x	xx	x	xx	x	xx	x	xx
	Multi-Racial	x	xx	x	xx	x	xx	x	xx	x	xx
	Unknown	x	xx	x	xx	x	xx	x	xx	x	xx

Note: N = Number of enrolled participants randomized to the corresponding study arm.

Table with similar format:

Table 18: Summary of Categorical Demographic and Baseline Characteristics by Study Arm, Full Analysis Population

Table 19: Summary of Continuous Demographic and Baseline Characteristics by Study Arm, All Enrolled Participants

Variable	Statistic	WRSs2 + WRSs2 (10^6 cfu) (N=X)	WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)	Placebo + WRSs2 (10^6 cfu) (N=X)	Placebo + Placebo (N=X)	All Participants (N=X)
Age (years)	Mean	xx.x	xx.x	xx.x	xx.x	xx.x
	Standard Deviation	xx.x	xx.x	xx.x	xx.x	xx.x
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Minimum	xx	xx	xx	xx	xx
	Maximum	xx	xx	xx	xx	xx
BMI[a]	Mean	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Standard Deviation	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Minimum	xx.x	xx.x	xx.x	xx.x	xx.x
	Maximum	xx.x	xx.x	xx.x	xx.x	xx.x

Notes: N = Number of enrolled participants randomized to the corresponding study arm.
[a] If height and/or weight were captured at baseline, BMI was calculated using these values. Otherwise, height and/or weight were captured at Visit 13 and used to calculate BMI.

Table with similar format:

Table 20: Summary of Continuous Demographic and Baseline Characteristics by Study Arm, Full Analysis Population

14.1.3 Prior and Concurrent Medical Conditions

Table 21: Summary of Participants with Pre-Existing or Concurrent Medical Conditions by MedDRA System Organ Class and Study Arm, All Enrolled Participants

MedDRA System Organ Class	WRSs2 + WRSs2 (10^6 cfu) (N=X)		WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)		Placebo + WRSs2 (10^6 cfu) (N=X)		Placebo + Placebo (N=X)		All Participants (N=X)	
	n	%	n	%	n	%	n	%	n	%
Any SOC	x	xx	x	xx	x	xx	x	xx	x	xx
[SOC 1]	x	xx	x	xx	x	xx	x	xx	x	xx
[SOC 2]	x	xx	x	xx	x	xx	x	xx	x	xx
…										

Notes: N = Number of enrolled participants randomized to the corresponding study arm.
n = Number of participants reporting medical history within the specified SOC. A participant is only counted once per SOC.

14.2 Efficacy and Immunogenicity Data

14.2.1 Efficacy Response Tabular Summaries by Measure, Study Arm, and Time Point

Table 22: Number and Proportion of Participants with Shigellosis and Estimated Vaccine Efficacy Post-Challenge by Shigellosis Determination Method, Analysis Population, and Study Arm

Shigellosis Determination Method	Population	Study Arm	Number of Participants with Any Occurrence of Shigellosis	Number of Participants	Proportion of Participants with Any Occurrence of Shigellosis (95% CI)[a]	Estimated Vaccine Efficacy (95% CI)[a]	P-Value[b]
Endpoint Review Committee	Full Analysis Population	WRSs2 + WRSs2 (10^6 cfu or $5x10^5$ cfu)	xxx	xxx	0.xx (0.xx, 0.xx)	x.xx (x.xx, x.xx)	0.xxx
		WRSs2 + WRSs2 (10^6 cfu)	xxx	xxx	0.xx (0.xx, 0.xx)	x.xx (x.xx, x.xx)	-
		WRSs2 + WRSs2 ($5x10^5$ cfu)	xxx	xxx	0.xx (0.xx, 0.xx)	x.xx (x.xx, x.xx)	-
		Placebo + WRSs2 (10^6 cfu)	xxx	xxx	0.xx (0.xx, 0.xx)	x.xx (x.xx, x.xx)	-
		Placebo + Placebo	xxx	xxx	0.xx (0.xx, 0.xx)	-	-
	Per-Protocol Population	WRSs2 + WRSs2 (10^6 cfu or $5x10^5$ cfu)	xxx	xxx	0.xx (0.xx, 0.xx)	x.xx (x.xx, x.xx)	-
		WRSs2 + WRSs2 (10^6 cfu)	xxx	xxx	0.xx (0.xx, 0.xx)	x.xx (x.xx, x.xx)	-
		WRSs2 + WRSs2 ($5x10^5$ cfu)	xxx	xxx	0.xx (0.xx, 0.xx)	x.xx (x.xx, x.xx)	-
		Placebo + WRSs2 (10^6 cfu)	xxx	xxx	0.xx (0.xx, 0.xx)	x.xx (x.xx, x.xx)	-
		Placebo + Placebo	xxx	xxx	0.xx (0.xx, 0.xx)	-	-

Table 22: Number and Proportion of Participants with Shigellosis and Estimated Vaccine Efficacy Post-Challenge by Shigellosis Determination Method, Analysis Population, and Study Arm *(continued)*

Shigellosis Determination Method	Population	Study Arm	Number of Participants with Any Occurrence of Shigellosis	Number of Participants	Proportion of Participants with Any Occurrence of Shigellosis (95% CI)[a]	Estimated Vaccine Efficacy (95% CI)[a]	P-Value[b]
Programmatic Definition	**Full Analysis Population**	**WRSs2 + WRSs2 (10^6 cfu or $5x10^5$ cfu)**	xxx	xxx	0.xx (0.xx, 0.xx)	x.xx (x.xx, x.xx)	-
		WRSs2 + WRSs2 (10^6 cfu)	xxx	xxx	0.xx (0.xx, 0.xx)	x.xx (x.xx, x.xx)	-
		WRSs2 + WRSs2 ($5x10^5$ cfu)	xxx	xxx	0.xx (0.xx, 0.xx)	x.xx (x.xx, x.xx)	-
		Placebo + WRSs2 (10^6 cfu)	xxx	xxx	0.xx (0.xx, 0.xx)	x.xx (x.xx, x.xx)	-
		Placebo + Placebo	xxx	xxx	0.xx (0.xx, 0.xx)	-	-
	Per-Protocol Population	**WRSs2 + WRSs2 (10^6 cfu or $5x10^5$ cfu)**	xxx	xxx	0.xx (0.xx, 0.xx)	x.xx (x.xx, x.xx)	-
		WRSs2 + WRSs2 (10^6 cfu)	xxx	xxx	0.xx (0.xx, 0.xx)	x.xx (x.xx, x.xx)	-
		WRSs2 + WRSs2 ($5x10^5$ cfu)	xxx	xxx	0.xx (0.xx, 0.xx)	x.xx (x.xx, x.xx)	-
		Placebo + WRSs2 (10^6 cfu)	xxx	xxx	0.xx (0.xx, 0.xx)	x.xx (x.xx, x.xx)	-
		Placebo + Placebo	xxx	xxx	0.xx (0.xx, 0.xx)	-	-

Notes: [a]The denominator for proportion is based on the number of participants enrolled in the specified study arm and analysis population. 95% CI = 95% Wilson Confidence Interval
[b] P-value is calculated using a two-sided Chi-squared test.

Table with a similar format:

Table 23: Number and Proportion of Participants with Culture- or PCR-Positive Shigellosis and Estimated Vaccine Efficacy Post-Challenge by Shigellosis Determination Method, Analysis Population, and Study Arm

Table 24: Site-Stratified Estimated Vaccine Efficacy Post-Challenge by Analysis Population

Population	Statistic Method	Statistic	Result
Full Analysis Population	**Cochran-Mantel-Haenszel**	**Vaccine Efficacy - CCHMC (95% CI)**	x.xx (x.xx, x.xx)
		Vaccine Efficacy – Hope Clinic of the Emory Vaccine Center (95% CI)	x.xx (x.xx, x.xx)
		Common Vaccine Efficacy[a] (95% CI)	x.xx (x.xx, x.xx)
	Breslow-Day Test for Homogeneity of the Odds Ratios	**Common Odds Ratio**	x.xx (x.xx, x.xx)
		P-value	0.xxx
Per-Protocol Population	**Cochran-Mantel-Haenszel**	**Vaccine Efficacy - CCHMC (95% CI)**	x.xx (x.xx, x.xx)
		Vaccine Efficacy – Hope Clinic of the Emory Vaccine Center (95% CI)	x.xx (x.xx, x.xx)
		Common Vaccine Efficacy[a] (95% CI)	x.xx (x.xx, x.xx)
	Breslow-Day Test for Homogeneity of the Odds Ratios	**Common Odds Ratio**	x.xx (x.xx, x.xx)
		P-value	0.xxx

Notes: Vaccine efficacy is calculated as (1 – relative risk).
[a] The denominator for proportion is based on the number of subjects enrolled in the specified study arm, site and analysis population. The numerator is the number of subjects who had shigellosis in the specified study arm, site and analysis population.

Table 25: Number and Proportion of Participants Meeting the Primary Endpoint Post-Challenge by Study Arm and Cohort, Full Analysis Population

Primary Endpoint	Site and Cohort	WRSs2 + WRSs2 (10^6 cfu)			WRSs2 + WRSs2 ($5x10^5$ cfu)			Placebo + WRSs2 (10^6 cfu)			Placebo + Placebo			All Participants		
		N	n	%	N	n	%	N	n	%	N	n	%	N	n	%
Any Occurrence of Shigellosis	Any	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	CCHMC – Cohort 1	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	CCHMC – Cohort 2	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	CCHMC – Cohort 3	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	Emory – Cohort 1	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	Emory – Cohort 2	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	Emory – Cohort 3	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	Emory – Cohort 4	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
Severe Shigellosis	Any	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	CCHMC – Cohort 1	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	CCHMC – Cohort 2	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	CCHMC – Cohort 3	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	Emory – Cohort 1	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	Emory – Cohort 2	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	Emory – Cohort 3	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	Emory – Cohort 4	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
Moderate Shigellosis	Any	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	CCHMC – Cohort 1	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	CCHMC – Cohort 2	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	CCHMC – Cohort 3	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	Emory – Cohort 1	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	Emory – Cohort 2	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	Emory – Cohort 3	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	Emory – Cohort 4	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx

Table 25: Number and Proportion of Participants Meeting the Primary Endpoint Post-Challenge by Study Arm and Cohort, Full Analysis Population *(continued)*

Primary Endpoint	Site and Cohort	WRSs2 + WRSs2 (10^6 cfu)			WRSs2 + WRSs2 ($5x10^5$ cfu)			Placebo + WRSs2 (10^6 cfu)			Placebo + Placebo			All Participants		
		N	n	%	N	n	%	N	n	%	N	n	%	N	n	%
Dysentery and/or Other Shigellosis Symptoms	Any	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	CCHMC – Cohort 1	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	CCHMC – Cohort 2	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	CCHMC – Cohort 3	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	Emory – Cohort 1	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	Emory – Cohort 2	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	Emory – Cohort 3	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx
	Emory – Cohort 4	x	x	xx	x	x	xx	x	x	xx	x	x	xx	x	x	xx

Notes: N = Number of participants in the Full Analysis Population.

n = Number of participants with shigellosis, as determined by programmatic definition.

Table 26: Number and Percentage of Participants Experiencing Symptoms of Shigellosis Post-Challenge Dose through Inpatient Challenge Period with 95% Confidence Intervals by Symptom and Study Arm – Full Analysis Population

	WRSs2 + WRSs2 (10^6 cfu) (N=X)			WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)			Placebo + WRSs2 (10^6 cfu) (N=X)			Placebo + Placebo (N=X)			All Participants (N=X)		
Symptom	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Any Symptom	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Anorexia/Loss of Appetite	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Arthralgia	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Chills	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Diarrhea	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Fever	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Headache	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Malaise/Fatigue	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Myalgia	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Nausea	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Pain/Abdominal Cramps	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Vomiting	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx

Notes: N = Number of participants in the Safety Population who received both vaccinations corresponding to the study arm.
n = Number of participants reporting each event.

Table 27: Number and Percentage of Participants Experiencing Symptoms of Shigellosis Post-Challenge Dose through Inpatient Challenge Period with 95% Confidence Intervals by Symptom, Maximum Severity, and Study Arm – Full Analysis Population

Symptom	Severity	WRSs2 + WRSs2 (10^6 cfu) (N=X)			WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)			Placebo + WRSs2 (10^6 cfu) (N=X)			Placebo + Placebo (N=X)			All Participants (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
Any Symptom	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Anorexia/Loss of Appetite	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Arthralgia	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Chills	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx

Table 27: Number and Percentage of Participants Experiencing Symptoms of Shigellosis Post-Challenge Dose through Inpatient Challenge Period with 95% Confidence Intervals by Symptom, Maximum Severity, and Study Arm – Full Analysis Population *(continued)*

Symptom	Severity	WRSs2 + WRSs2 (10^6 cfu) (N=X)			WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)			Placebo + WRSs2 (10^6 cfu) (N=X)			Placebo + Placebo (N=X)			All Participants (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
Diarrhea	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Fever	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Headache	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Malaise/Fatigue	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Myalgia	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Nausea	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx

Table 27: Number and Percentage of Participants Experiencing Symptoms of Shigellosis Post-Challenge Dose through Inpatient Challenge Period with 95% Confidence Intervals by Symptom, Maximum Severity, and Study Arm – Full Analysis Population *(continued)*

Symptom	Severity	WRSs2 + WRSs2 (10^6 cfu) (N=X)			WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)			Placebo + WRSs2 (10^6 cfu) (N=X)			Placebo + Placebo (N=X)			All Participants (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Pain/Abdominal Cramps	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Vomiting	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx

Notes: N = Number of participants in the Safety Population who received both vaccinations corresponding to the study arm.
n = Number of participants reporting each symptom.
Severity is the maximum severity reported post vaccination for each participant.

Table 28: Pre-Challenge *S. sonnei* Viral Shedding by Culture by Study Day and Study Arm, Shedding Analysis Population

[Implementation Note: For the participant who received the incorrect second vaccination, their shedding results post-first vaccination but prior to the second vaccination will be included in this table in the appropriate study arm column. Any shedding results post-second vaccination will be excluded.]

Time Point	Statistic	WRSs2 + WRSs2 (10^6 cfu or $5x10^5$ cfu) (N=X)	WRSs2 + WRSs2 (10^6 cfu) (N=X)	WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)	Placebo + WRSs2 (10^6 cfu) (N=X)	Placebo + Placebo (N=X)
Baseline	n	x	x	x	x	x
	Proportion (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)
Day 4 Post- Dose 1	n	x	x	x	x	x
	Proportion (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)
Day 8 Post-Dose 1	n	x	x	x	x	x
	Proportion (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)
Day 15 Post-Dose 1	n	x	x	x	x	x
	Proportion (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)
Day 29 Pre-Dose 2	n	x	x	x	x	x
	Proportion (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)
Day 32 Post-Dose 2	n	x	x	x	x	x
	Proportion (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)
Day 34 Post-Dose 2	n	x	x	x	x	x
	Proportion (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)
Day 36 Post-Dose 2	n	x	x	x	x	x
	Proportion (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)
Day 43 Post-Dose 2	n	x	x	x	x	x
	Proportion (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)
Anytime Pre-Challenge[a]	n	x	x	x	x	x
	Proportion (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)

Notes: N = Number of participants in the Shedding Analysis Population. The denominator for percentages post-dose 2 is the number of participants who received both vaccinations corresponding to the study arm.
[a] The number of participants with viral shedding reported at any time point prior to the inpatient challenge period (Baseline through Day 43).

Table 29: Summary of the Duration (Days) of *S. sonnei* Shedding Pre-Challenge by Study Arm, Shedding Analysis Population

[Implementation Note: The participant who received the incorrect second vaccination will be excluded from this table.]

Evaluation	Statistic	WRSs2 + WRSs2 (10^6 cfu or $5x10^5$ cfu) (N=X)	WRSs2 + WRSs2 (10^6 cfu) (N=X)	WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)	Placebo + WRSs2 (10^6 cfu) (N=X)	Placebo + Placebo (N=X)
Culture	n	x	x	x	x	x
	Mean[a]	x.x	x.x	x.x	x.x	x.x
	Standard Deviation (SD)[a]	x.x	x.x	x.x	x.x	x.x
	Median[a]	x.x	x.x	x.x	x.x	x.x
	IQR[a]	x.x	x.x	x.x	x.x	x.x
	Min, Max	x, x	x, x	x, x	x, x	x, x
Immunoblot	n	x	x	x	x	x
	Mean[a]	x.x	x.x	x.x	x.x	x.x
	Standard Deviation (SD)[a]	x.x	x.x	x.x	x.x	x.x
	Median[a]	x.x	x.x	x.x	x.x	x.x
	IQR[a]	x.x	x.x	x.x	x.x	x.x
	Min, Max	x, x	x, x	x, x	x, x	x, x
PCR	n	x	x	x	x	x
	Mean[a]	x.x	x.x	x.x	x.x	x.x
	Standard Deviation (SD)[a]	x.x	x.x	x.x	x.x	x.x
	Median[a]	x.x	x.x	x.x	x.x	x.x
	IQR[a]	x.x	x.x	x.x	x.x	x.x
	Min, Max	x, x	x, x	x, x	x, x	x, x

Notes: N = Number of participants in the Shedding Analysis Population who received both vaccinations corresponding to the study arm.
n = Number of participants with detected virus anytime post-vaccination but prior to challenge period (Days 1 to 56).
[a] Estimate among participants with detected virus anytime post-vaccination but prior to challenge period (Days 1 to 56).

Table 30: Summary of Maximum *S. sonnei* Colony Forming Units per Gram of Stool by Immunoblot and PCR Pre-Challenge by Study Arm, Shedding Analysis Population

[Implementation Note: The participant who received the incorrect second vaccination will be excluded from this table.]

Evaluation	Parameter	Statistic	WRSs2 + WRSs2 (10^6 cfu or $5x10^5$ cfu) (N=X)	WRSs2 + WRSs2 (10^6 cfu) (N=X)	WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)	Placebo + WRSs2 (10^6 cfu) (N=X)	Placebo + Placebo (N=X)
Immunoblot	Peak Virus Concentration (CFU/g) [a]	n	x	x	x	x	x
		Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
		95% CI	x.xxx, x.xxx	x.xxx, x.xxx	x.xxx, x.xxx	x.xxx, x.xxx	x.xxx, x.xxx
		Median	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx
		Min, Max	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx
	Day of Peak Virus Concentration	n	x	x	x	x	x
		Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
		Median (IQR)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
		Min, Max	x, x	x, x	x, x	x, x	x, x
PCR	Peak Virus Concentration (CFU/g) [a]	n	x	x	x	x	x
		Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
		95% CI	x.xxx, x.xxx	x.xxx, x.xxx	x.xxx, x.xxx	x.xxx, x.xxx	x.xxx, x.xxx
		Median	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx
		Min, Max	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx

Table 30: Summary of Maximum S. *sonnei* Colony Forming Units per Gram of Stool by Immunoblot and PCR Pre-Challenge by Study Arm, Shedding Analysis Population *(continued)*

Evaluation	Parameter	Statistic	WRSs2 + WRSs2 (10^6 cfu or $5x10^5$ cfu) (N=X)	WRSs2 + WRSs2 (10^6 cfu) (N=X)	WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)	Placebo + WRSs2 (10^6 cfu) (N=X)	Placebo + Placebo (N=X)
	Day of Peak Virus Concentration	n	x	x	x	x	x
		Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
		Median (IQR)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
		Min, Max	x, x	x, x	x, x	x, x	x, x

Notes: N = Number of participants in the Shedding Analysis Population who received both vaccinations corresponding to the study arm.
n = Number of participants with detected virus anytime post-vaccination but prior to challenge period (Days 1 to 56).
[a]Log_{10} transformation was used in calculating summary statistics.

Table 31: Post-Challenge 53G Viral Shedding by Culture by Study Day and Study Arm, Full Analysis Population

Time Point	Statistic	WRSs2 + WRSs2 (10^6 cfu or $5x10^5$ cfu) (N=X)	WRSs2 + WRSs2 (10^6 cfu) (N=X)	WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)	Placebo + WRSs2 (10^6 cfu) (N=X)	Placebo + Placebo (N=X)
Day 57 (Baseline)	n	x	x	x	x	x
	Proportion (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)
Day 58	n	x	x	x	x	x
	Proportion (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)
Day 59	n	x	x	x	x	x
	Proportion (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)
Day 60	n	x	x	x	x	x
	Proportion (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)
Day 61	n	x	x	x	x	x
	Proportion (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)
Day 62	n	x	x	x	x	x
	Proportion (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)
Day 63	n	x	x	x	x	x
	Proportion (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)
Day 64	n	x	x	x	x	x
	Proportion (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)
Day 65	n	x	x	x	x	x
	Proportion (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)
Anytime Post-Challenge[a]	n	x	x	x	x	x
	Proportion (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)

Notes: N = Number of participants in the Full Analysis population with non-missing results.

a The number of participants with viral shedding reported at any time point following the inpatient challenge period (Day 57 through Day 65).

Table 32: Summary of the Duration (Days) of 53G Shedding Post-Challenge by Culture, Immunoblot, and PCR by Study Arm, Full Analysis Population

Evaluation	Statistic	WRSs2 + WRSs2 (10^6 cfu or $5x10^5$ cfu) (N=X)	WRSs2 + WRSs2 (10^6 cfu) (N=X)	WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)	Placebo + WRSs2 (10^6 cfu) (N=X)	Placebo + Placebo (N=X)
Culture	n	x	x	x	x	x
	Mean[a]	x.x	x.x	x.x	x.x	x.x
	Standard Deviation (SD)[a]	x.x	x.x	x.x	x.x	x.x
	Median[a]	x.x	x.x	x.x	x.x	x.x
	IQR[a]	x.x	x.x	x.x	x.x	x.x
	Min, Max	x, x	x, x	x, x	x, x	x, x
Immunoblot	n	x	x	x	x	x
	Mean[a]	x.x	x.x	x.x	x.x	x.x
	Standard Deviation (SD)[a]	x.x	x.x	x.x	x.x	x.x
	Median[a]	x.x	x.x	x.x	x.x	x.x
	IQR[a]	x.x	x.x	x.x	x.x	x.x
	Min, Max	x, x	x, x	x, x	x, x	x, x
PCR	n	x	x	x	x	x
	Mean[a]	x.x	x.x	x.x	x.x	x.x
	Standard Deviation (SD)[a]	x.x	x.x	x.x	x.x	x.x
	Median[a]	x.x	x.x	x.x	x.x	x.x
	IQR[a]	x.x	x.x	x.x	x.x	x.x
	Min, Max	x, x	x, x	x, x	x, x	x, x

Notes: N = Number of participants in the Full Analysis population followed for the entire challenge period.
n = Number of participants with detected virus anytime post-challenge but prior to discharge (Days 56 to 65).
[a] Estimate among participants with detected virus anytime post-challenge but prior to discharge (Days 56 to 65).

Table 33: Summary of Maximum *S. sonnei* Colony Forming Units per Gram of Stool by Immunoblot and PCR Post-Challenge by Study Arm, Full Analysis Population

Evaluation	Parameter	Statistic	WRSs2 + WRSs2 (10^6 cfu or $5x10^5$ cfu) (N=X)	WRSs2 + WRSs2 (10^6 cfu) (N=X)	WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)	Placebo + WRSs2 (10^6 cfu) (N=X)	Placebo + Placebo (N=X)
Immunoblot	Peak Virus Concentration (CFU/g) [a]	n	x	x	x	x	x
		Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
		95% CI	x.xxx, x.xxx	x.xxx, x.xxx	x.xxx, x.xxx	x.xxx, x.xxx	x.xxx, x.xxx
		Median	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx
		Min, Max	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx
	Day of Peak Virus Concentration	n	x	x	x	x	x
		Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
		Median (IQR)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
		Min, Max	x, x	x, x	x, x	x, x	x, x
PCR	Peak Virus Concentration (CFU/g) [a]	n	x	x	x	x	x
		Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
		95% CI	x.xxx, x.xxx	x.xxx, x.xxx	x.xxx, x.xxx	x.xxx, x.xxx	x.xxx, x.xxx
		Median	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx
		Min, Max	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx
	Day of Peak Virus Concentration	n	x	x	x	x	x
		Mean (SD)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
		Median (IQR)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
		Min, Max	x, x	x, x	x, x	x, x	x, x

Notes: N = Number of participants in the Full Analysis population; n = Number of participants with detected virus anytime post-challenge but prior to discharge (Days 56 to 65).
[a] Log_{10} transformation was used in calculating summary statistics.

14.2.2 Immunogenicity Response Tabular Summaries by Measure, Study Arm, and Time Point

Table 34: Pre-Challenge LPS-specific IgG GMT, GMFR, and Seroresponse (≥ 4-Fold Rise) Results with 95% Confidence Intervals by Time Point and Study Arm, Immunogenicity Population

[Implementation Note: For the participant who received the incorrect second vaccination, their immunogenicity results post-first vaccination but prior to the second vaccination will be included in this table in the appropriate study arm column. Any immunogenicity results post-second vaccination will be excluded.]

Time Point	Statistic	WRSs2 + WRSs2 (10^6 cfu) (N=X)	WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)	Placebo + WRSs2 (10^6 cfu) (N=X)	Placebo + Placebo (N=X)	First Dose Placebo All Participants (N=X)
Baseline	n	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)
Day 15 Post-Dose 1	n	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)
	GMFR[a] (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)
	4-Fold Rise[b] (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)
Day 29 Pre-Dose 2	n	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)
	GMFR[a] (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)
	4-Fold Rise[b] (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)
Day 43 Post-Dose 2	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[a] (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)	-
	4-Fold Rise[b] (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)	-

Table 34: Pre-Challenge LPS-specific IgG GMT, GMFR, and Seroresponse (≥ 4-Fold Rise) Results with 95% Confidence Intervals by Time Point and Study Arm, Immunogenicity Population *(continued)*

Time Point	Statistic	WRSs2 + WRSs2 (10^6 cfu) (N=X)	WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)	Placebo + WRSs2 (10^6 cfu) (N=X)	Placebo + Placebo (N=X)	First Dose Placebo All Participants (N=X)
Day 56 Post-Dose 2	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[a] (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)	-
	4-Fold Rise[b] (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)	-
Maximum Titer Post-Vaccination	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[a] (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)	-
	4-Fold Rise[bc] (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)	-

Notes: N = Number of participants in the Immunogenicity Population. The denominator for percentages post-dose 2 is the number of participants who received both vaccinations corresponding to the study arm.
[a] GMFR represents the geometric mean fold rise in IgG antibody compared to pre-dose 1.
[b] 4-Fold Rise represents the percentage of participants with at least a 4-Fold Rise in IgG antibody compared to pre-dose 1.
[c] 4-Fold Rise at Maximum Titer Post-Vaccination represents the percentage of participants with at least a 4-Fold Rise in IgG antibody at the maximum titer value post-dose compared to pre-dose 1.

Tables with similar format:

Table 35: Pre-Challenge LPS-specific IgA GMT, GMFR, and Seroresponse (≥ 4-Fold Rise) Results with 95% Confidence Intervals by Time Point and Study Arm, Immunogenicity Population

Table 36: Pre-Challenge Invaplex-specific IgG GMT, GMFR, and Seroresponse (≥ 4-Fold Rise) Results with 95% Confidence Intervals by Time Point and Study Arm, Immunogenicity Population

Table 37: Pre-Challenge Invaplex-specific IgA GMT, GMFR, and Seroresponse (≥ 4-Fold Rise) Results with 95% Confidence Intervals by Time Point and Study Arm, Immunogenicity Population

Table 38: Post-Challenge LPS-specific IgG GMT, GMFR, and Seroresponse (≥ 4-Fold Rise) Results with 95% Confidence Intervals by Time Point and Study Arm, Immunogenicity Population

Time Point	Statistic	WRSs2 + WRSs2 (10^6 cfu) (N=X)	WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)	Placebo + WRSs2 (10^6 cfu) (N=X)	Placebo + Placebo (N=X)
Day 64	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[a] (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)
	4-Fold Rise[b] (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 71	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[a] (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)
	4-Fold Rise[b] (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 85	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[a] (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)
	4-Fold Rise[b] (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 113	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[a] (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)
	4-Fold Rise[b] (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)

Table 38: Post-Challenge LPS-specific IgG GMT, GMFR, and Seroresponse (≥ 4-Fold Rise) Results with 95% Confidence Intervals by Time Point and Study Arm, Immunogenicity Population *(continued)*

Time Point	Statistic	WRSs2 + WRSs2 (10^6 cfu) (N=X)	WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)	Placebo + WRSs2 (10^6 cfu) (N=X)	Placebo + Placebo (N=X)
Maximum Titer Post-Challenge	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)
Peak-Fold Rise	n	x	x	x	x
	GMFR[a] (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)
	4-Fold Rise[bc] (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)

Notes: N = Number of participants in the Immunogenicity Population who received challenge.
[a] GMFR represents the geometric mean fold rise in IgG antibody compared to pre-challenge (Day 56).
[b] 4-Fold Rise represents the percentage of participants with at least a 4-Fold Rise in IgG antibody compared to pre-challenge (Day 56).
[c] 4-Fold Rise at Peak-Fold Rise represents the percentage of participants with at least a 4-Fold Rise in IgG antibody at the maximum titer value post-dose compared to pre-challenge (Day 56).

Tables with similar format:

Table 39: Post-Challenge LPS-specific IgA GMT, GMFR, and Seroresponse (≥ 4-Fold Rise) Results with 95% Confidence Intervals by Time Point and Study Arm, Immunogenicity Population

Table 40: Post-Challenge Invaplex-specific IgG GMT, GMFR, and Seroresponse (≥ 4-Fold Rise) Results with 95% Confidence Intervals by Time Point and Study Arm, Immunogenicity Population

Table 41: Post-Challenge Invaplex-specific IgA GMT, GMFR, and Seroresponse (≥ 4-Fold Rise) Results with 95% Confidence Intervals by Time Point and Study Arm, Immunogenicity Population

Table 42: Summary Statistics of *S. sonnei* LPS-specific IgG ASCs per 10^6 PBMCs by Time Point and Study Arm, Immunogenicity Population

[Implementation Note: For the participant who received the incorrect second vaccination, their immunogenicity results post-first vaccination but prior to the second vaccination will be included in this table in the appropriate study arm column. Any immunogenicity results post-second vaccination will be excluded.]

Time Point	Statistic	WRSs2 + WRSs2 (10^6 cfu) (N=X)	WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)	Placebo + WRSs2 (10^6 cfu) (N=X)	Placebo + Placebo (N=X)	First Dose Placebo All Participants (N=X)
Baseline	n	x	x	x	x	x
	Mean (SD)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	Median	x.x	x.x	x.x	x.x	x.x
	Min, Max	x, x	x, x	x, x	x, x	x, x
Day 8 Post-Dose 1	n	x	x	x	x	x
	Mean (SD)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	Median	x.x	x.x	x.x	x.x	x.x
	Min, Max	x, x	x, x	x, x	x, x	x, x
	Response[a] - % (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)
Day 29 Pre-Dose 2	n	x	x	x	x	x
	Mean (SD)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	Median	x.x	x.x	x.x	x.x	x.x
	Min, Max	x, x	x, x	x, x	x, x	x, x
	Response[a] - % (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)
Day 36 Post-Dose 2	n	x	x	x	x	-
	Mean (SD)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	-
	Median	x.x	x.x	x.x	x.x	-
	Min, Max	x, x	x, x	x, x	x, x	-
	Response[a] - % (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)	-

Table 42: Summary Statistics of *S. sonnei* LPS-specific IgG ASCs per 10^6 PBMCs by Time Point and Study Arm, Immunogenicity Population *(continued)*

Time Point	Statistic	WRSs2 + WRSs2 (10^6 cfu) (N=X)	WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)	Placebo + WRSs2 (10^6 cfu) (N=X)	Placebo + Placebo (N=X)	First Dose Placebo All Participants (N=X)
Day 56 Post-Dose 2	n	x	x	x	x	-
	Mean (SD)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	-
	Median	x.x	x.x	x.x	x.x	-
	Min, Max	x, x	x, x	x, x	x, x	-
	Response[a] - % (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 60 Post-Challenge	n	x	x	x	x	-
	Mean (SD)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	-
	Median	x.x	x.x	x.x	x.x	-
	Min, Max	x, x	x, x	x, x	x, x	-
	Response[a] - % (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 64 Post-Challenge	n	x	x	x	x	-
	Mean (SD)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	-
	Median	x.x	x.x	x.x	x.x	-
	Min, Max	x, x	x, x	x, x	x, x	-
	Response[a] - % (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)	-
Anytime Post-Vaccination through Day 56	Response[a] - % (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)	-
Anytime Post-Challenge through Day 64	Response[a] - % (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)	-

Notes: N=Number of participants in the Immunogenicity Population. The denominator for percentages post-dose 2 is the number of participants who received both vaccinations corresponding to the study arm. The denominator for percentages post-challenge is the number of participants who received both vaccinations corresponding to the study arm and were challenged.
[a]Response represents the percentage of participants with ≥10 *S. sonnei* LPS-specific IgG ASCs.

Tables with similar format:

Table 43: Summary Statistics of *S. sonnei* LPS-specific IgA ASCs per 10^6 PBMCs by Study Day and Study Arm, Immunogenicity Population

Table 44: Summary Statistics of *S. sonnei* Invaplex-specific IgG ASCs per 10^6 PBMCs by Study Day and Study Arm, Immunogenicity Population

Table 45: Summary Statistics of *S. sonnei* Invaplex-specific IgA ASCs per 10^6 PBMCs by Study Day and Study Arm, Immunogenicity Population

Table 46: LPS-specific Fecal IgA GMT, GMFR, and Seroresponse (≥ 4-Fold Rise) Results by Time Point and Study Arm, Immunogenicity Population

[Implementation Note: For the participant who received the incorrect second vaccination, their immunogenicity results post-first vaccination but prior to the second vaccination will be included in this table in the appropriate study arm column. Any immunogenicity results post-second vaccination will be excluded.]

Time Point	Statistic	WRSs2 + WRSs2 (10^6 cfu) (N=X)	WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)	Placebo + WRSs2 (10^6 cfu) (N=X)	Placebo + Placebo (N=X)	First Dose Placebo All Participants (N=X)
Baseline	n	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)
Day 8 Post-Dose 1	n	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)
	GMFR[a] (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)
	4-Fold Rise[b] (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)
Day 15 Post-Dose 1	n	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)
	GMFR[a] (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)
	4-Fold Rise[b] (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)
Day 29 Pre-Dose 2	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[a] (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)	-
	4-Fold Rise[b] (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 36 Post-Dose 2	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[a] (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)	-
	4-Fold Rise[b] (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)	-

Table 46: LPS-specific Fecal IgA GMT, GMFR, and Seroresponse (≥ 4-Fold Rise) Results by Time Point and Study Arm, Immunogenicity Population *(continued)*

Time Point	Statistic	WRSs2 + WRSs2 (10^6 cfu) (N=X)	WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)	Placebo + WRSs2 (10^6 cfu) (N=X)	Placebo + Placebo (N=X)	First Dose Placebo All Participants (N=X)
Day 43 Post-Dose 2	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[a] (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)	-
	4-Fold Rise[b] (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 56 Post-Dose 2	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[a] (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)	-
	4-Fold Rise[b] (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 61 Post-Challenge	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[a] (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)	-
	4-Fold Rise[b] (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 64 Post-Challenge	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[a] (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)	-
	4-Fold Rise[b] (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 71 Post-Challenge	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[a] (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)	-
	4-Fold Rise[b] (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)	-

Table 46: LPS-specific Fecal IgA GMT, GMFR, and Seroresponse (≥ 4-Fold Rise) Results by Time Point and Study Arm, Immunogenicity Population *(continued)*

Time Point	Statistic	WRSs2 + WRSs2 (10^6 cfu) (N=X)	WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)	Placebo + WRSs2 (10^6 cfu) (N=X)	Placebo + Placebo (N=X)	First Dose Placebo All Participants (N=X)
Day 85 Post-Challenge	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[a] (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)	-
	4-Fold Rise[b] (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)	-
Maximum Post-Vaccination through Day 56	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[a] (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)	-
	4-Fold Rise[b] (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)	-
Maximum Post-Challenge through Day 85	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[a] (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)	-
	4-Fold Rise[b] (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)	-

Notes: N = Number of participants in the Immunogenicity Population. The denominator for percentages post-second dose 2 is the number of participants who received both vaccinations corresponding to the study arm. The denominator for percentages post-challenge is the number of participants who received both vaccinations and were challenged.
[a] GMFR represents the geometric mean fold rise in fecal IgA compared to pre-dose 1 for time points through Day 56 and represents the geometric mean fold rise in fecal IgA compared to pre-challenge (Day 56) for time points through Day 85.
[b] 4-Fold Rise represents the percentage of participants with at least a 4-fold rise in fecal IgA compared to pre-dose 1 for time points through Day 56 and represents the percentage of participants with at least a 4-fold rise in fecal IgA compared to pre-challenge (Day 56) for timepoints through Day 85.

Tables with similar format:

Table 47: Invaplex-specific Fecal IgA GMT, GMFR, and Seroresponse (≥ 4-Fold Rise) Results by Time Point and Study Arm, Immunogenicity Population

Table 48: Total Fecal IgA GMT, GMFR, and Seroresponse (≥ 4-Fold Rise) Results by Time Point and Study Arm, Immunogenicity Population

14.3 Safety Data

14.3.1 Displays of Adverse Events

Table 49: Overall Summary of Adverse Events by Study Arm, Safety Population

[Implementation Note: For the participant who received the incorrect second vaccination, solicited adverse events post-second vaccination will be excluded from counts and percentages in the table. A footnote will be added describing any unsolicited adverse events post-second vaccination.]

	WRSs2 + WRSs2 (10^6 cfu) (N = X)		**WRSs2 + WRSs2 ($5x10^5$ cfu) (N = X)**		**Placebo + WRSs2 (10^6 cfu) (N = X)**		**Placebo + Placebo (N = X)**		**All Participants (N = X)**	
Participants[a] with	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
At least one systemic solicited adverse event post-first vaccination	x	x	x	x	x	x	x	x	x	x
At least one systemic solicited adverse event post-second vaccination	x	x	x	x	x	x	x	x	x	x
At least one systemic solicited adverse event post-any vaccination	x	x	x	x	x	x	x	x	x	x
At least one unsolicited adverse event	x	x	x	x	x	x	x	x	x	x
At least one vaccine-related unsolicited adverse event through 28 days post-last vaccination	x	x	x	x	x	x	x	x	x	x
Mild (Grade 1)	x	x	x	x	x	x	x	x	x	x
Moderate (Grade 2)	x	x	x	x	x	x	x	x	x	x
Severe (Grade 3)	x	x	x	x	x	x	x	x	x	x
At least one severe (Grade 3) unsolicited adverse event post-vaccination	x	x	x	x	x	x	x	x	x	x
Related	x	x	x	x	x	x	x	x	x	x
Unrelated	x	x	x	x	x	x	x	x	x	x
At least one severe (Grade 3) unsolicited adverse event post-challenge	x	x	x	x	x	x	x	x	x	x
Related	x	x	x	x	x	x	x	x	x	x
Unrelated	x	x	x	x	x	x	x	x	x	x
At least one serious adverse event[b]	x	x	x	x	x	x	x	x	x	x
At least one related, serious adverse event	x	x	x	x	x	x	x	x	x	x

Table 49: Overall Summary of Adverse Events by Study Arm, Safety Population *(continued)*

	WRSs2 + WRSs2 (10^6 cfu) (N = X)		WRSs2 + WRSs2 ($5x10^5$ cfu) (N = X)		Placebo + WRSs2 (10^6 cfu) (N = X)		Placebo + Placebo (N = X)		All Participants (N = X)	
Participants[a] with	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
At least one adverse event leading to early termination[c]	x	x	x	x	x	x	x	x	x	x

Notes: N = Number of participants in the Safety Population. The denominator for percentages post-second vaccination is the number of participants who received both vaccinations corresponding to the study arm.

[a] Subjects are counted once for each category regardless of the number of events.

[b] A listing of Serious Adverse Events is included in Table X.

[c] As reported on the Adverse Event eCRF.

Table 50: Adverse Events Occurring in 5% of Participants in Any Study Arm by MedDRA System Organ Class and Preferred Term, and Study Arm - Safety Population

[Implementation Note: this table is used to complete the "Other Adverse Event Template" for clinicaltrials.gov reporting (See slide 6 in https://prsinfo.clinicaltrials.gov/trainTrainer/Adverse-Events-Module.pdf). Threshold value may be 0% to 5% (default 5). This includes all adverse events collected (e.g., solicited, unsolicited, laboratory adverse events, etc.), regardless of relationship to study product.

[Implementation Note: For the participant who received the incorrect second vaccination, solicited adverse events post-second vaccination will be excluded from counts and percentages in the table. A footnote will be added describing any unsolicited adverse events post-second vaccination.]

MedDRA System Organ Class	MedDRA Preferred Term	WRSs2 + WRSs2 (10^6 cfu) (N=X)			WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)			Placebo + WRSs2 (10^6 cfu) (N=X)			Placebo + Placebo (N=X)			All Participants (N=X)		
		N	%	Events	n	%	Events	n	%	Events	n	%	Events	n	%	Events
Serious Adverse Events																
All	All	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
SOC1	PT1	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Etc.	Etc.	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Other (Non-serious) Adverse Events																
All	All	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
SOC1	PT1	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Etc.	Etc.	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

Notes: N = Number of participants in the Safety Population (number of participants at risk).
n = Number of participants reporting event.
Events = Total frequency of events reported.

14.3.1.1 Solicited Adverse Events

Table 51: Number and Percentage of Participants Experiencing Solicited Events Post-Either Vaccination Dose with 95% Confidence Intervals by Symptom and Study Arm – Safety Population

[Implementation Note: For the participant who received the incorrect second vaccination, solicited adverse events post-second vaccination will be excluded from this table.]

	WRSs2 + WRSs2 (10^6 cfu) (N=X)			WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)			Placebo + WRSs2 (10^6 cfu) (N=X)			Placebo + Placebo (N=X)			All Participants (N=X)		
Symptom	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Any Symptom	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Anorexia/Loss of Appetite	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Arthralgia	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Chills	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Diarrhea	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Fever	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Headache	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Malaise/Fatigue	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Myalgia	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Nausea	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Pain/Abdominal Cramps	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Vomiting	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx

Notes: N = Number of participants in the Safety Population.
n = Number of participants reporting each event.

Table 52: Number and Percentage of Participants Experiencing Solicited Events Post-Vaccination Dose 1 with 95% Confidence Intervals by Symptom and Study Arm – Safety Population

	WRSs2 + WRSs2 (10^6 cfu) (N=X)			WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)			Placebo + WRSs2 (10^6 cfu) (N=X)			Placebo + Placebo (N=X)			First Dose Placebo All Participants (N=X)			All Participants (N=X)		
Symptom	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Any Symptom	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Anorexia/Loss of Appetite	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Arthralgia	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Chills	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Diarrhea	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Fever	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Headache	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Malaise/Fatigue	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Myalgia	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Nausea	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Pain/Abdominal Cramps	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Vomiting	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx

Notes: N = Number of participants in the Safety Population.
n = Number of participants reporting each event.

Table 53: Number and Percentage of Participants Experiencing Solicited Events Post-Vaccination Dose 2 with 95% Confidence Intervals by Symptom and Study Arm – Safety Population

[Implementation Note: The participant who received the incorrect second vaccination will be excluded from this table.]

	WRSs2 + WRSs2 (10^6 cfu) (N=X)			WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)			Placebo + WRSs2 (10^6 cfu) (N=X)			Placebo + Placebo (N=X)			All Participants (N=X)		
Symptom	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Any Symptom	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Anorexia/Loss of Appetite	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Arthralgia	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Chills	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Diarrhea	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Fever	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Headache	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Malaise/Fatigue	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Myalgia	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Nausea	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Pain/Abdominal Cramps	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Vomiting	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx

Notes: N = Number of participants in the Safety Population who received both vaccinations corresponding to the study arm.
n = Number of participants reporting each event.

Table 54: Number and Percentage of Participants Experiencing Solicited Events Post-Either Vaccination Dose with 95% Confidence Intervals by Symptom, Maximum Severity, and Study Arm – Safety Population

[Implementation Note: For the participant who received the incorrect second vaccination, solicited adverse events post-second vaccination will be excluded from this table.]

Symptom	Severity	WRSs2 + WRSs2 (10^6 cfu) (N=X)			WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)			Placebo + WRSs2 (10^6 cfu) (N=X)			Placebo + Placebo (N=X)			All Participants (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
Any Symptom	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Anorexia/Loss of Appetite	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Arthralgia	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Chills	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx

Table 54: Number and Percentage of Participants Experiencing Solicited Events Post-Either Vaccination Dose with 95% Confidence Intervals by Symptom, Maximum Severity, and Study Arm – Safety Population *(continued)*

Symptom	Severity	WRSs2 + WRSs2 (10^6 cfu) (N=X)			WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)			Placebo + WRSs2 (10^6 cfu) (N=X)			Placebo + Placebo (N=X)			All Participants (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
Diarrhea	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Fever	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Headache	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Malaise/Fatigue	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Myalgia	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Nausea	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx

Table 54: Number and Percentage of Participants Experiencing Solicited Events Post-Either Vaccination Dose with 95% Confidence Intervals by Symptom, Maximum Severity, and Study Arm – Safety Population *(continued)*

Symptom	Severity	WRSs2 + WRSs2 (10^6 cfu) (N=X)			WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)			Placebo + WRSs2 (10^6 cfu) (N=X)			Placebo + Placebo (N=X)			All Participants (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Pain/Abdominal Cramps	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Vomiting	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx

Notes: N = Number of participants in the Safety Population.
n = Number of participants reporting each symptom.
Severity is the maximum severity reported post vaccination for each participant.

Table 55: Number and Percentage of Participants Experiencing Solicited Reactogenicity Events Post-Vaccination Dose 1 with 95% Confidence Intervals by Symptom, Maximum Severity, and Study Arm– Safety Population

Symptom	Severity	WRSs2 + WRSs2 (10^6 cfu) (N=X)			WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)			Placebo + WRSs2 (10^6 cfu) (N=X)			Placebo + Placebo (N=X)			First Dose Placebo All Participants (N=X)			All Participants (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
Any Symptom	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Anorexia/Loss of Appetite	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Arthralgia	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Chills	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Diarrhea	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx

Table 55: Number and Percentage of Participants Experiencing Solicited Reactogenicity Events Post-Vaccination Dose 1 with 95% Confidence Intervals by Symptom, Maximum Severity, and Study Arm– Safety Population *(continued)*

Symptom	Severity	WRSs2 + WRSs2 (10^6 cfu) (N=X)			WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)			Placebo + WRSs2 (10^6 cfu) (N=X)			Placebo + Placebo (N=X)			First Dose Placebo All Participants (N=X)			All Participants (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
Fever	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Headache	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Malaise/Fatigue	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Myalgia	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Nausea	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx

Table 55: Number and Percentage of Participants Experiencing Solicited Reactogenicity Events Post-Vaccination Dose 1 with 95% Confidence Intervals by Symptom, Maximum Severity, and Study Arm– Safety Population *(continued)*

Symptom	Severity	WRSs2 + WRSs2 (10^6 cfu) (N=X)			WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)			Placebo + WRSs2 (10^6 cfu) (N=X)			Placebo + Placebo (N=X)			First Dose Placebo All Participants (N=X)			All Participants (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
Pain/Abdominal Cramps	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Vomiting	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx

Notes: N = Number of participants in the Safety Population.
n = Number of participants reporting each symptom.
Severity is the maximum severity reported post vaccination for each participant.

Table 56: Number and Percentage of Participants Experiencing Solicited Reactogenicity Events Post-Vaccination Dose 2 with 95% Confidence Intervals by Symptom, Maximum Severity, and Study Arm – Safety Population

[Implementation Note: The participant who received the incorrect second vaccination will be excluded from this table.]

Symptom	Severity	WRSs2 + WRSs2 (10^6 cfu) (N=X)			WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)			Placebo + WRSs2 (10^6 cfu) (N=X)			Placebo + Placebo (N=X)			All Participants (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
Any Symptom	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Anorexia/Loss of Appetite	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Arthralgia	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Chills	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx

Table 56: Number and Percentage of Participants Experiencing Solicited Reactogenicity Events Post-Vaccination Dose 2 with 95% Confidence Intervals by Symptom, Maximum Severity, and Study Arm – Safety Population *(continued)*

Symptom	Severity	WRSs2 + WRSs2 (10^6 cfu) (N=X)			WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)			Placebo + WRSs2 (10^6 cfu) (N=X)			Placebo + Placebo (N=X)			All Participants (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
jDiarrhea	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Fever	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Headache	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Malaise/Fatigue	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Myalgia	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Nausea	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx

Table 56: Number and Percentage of Participants Experiencing Solicited Reactogenicity Events Post-Vaccination Dose 2 with 95% Confidence Intervals by Symptom, Maximum Severity, and Study Arm – Safety Population *(continued)*

Symptom	Severity	WRSs2 + WRSs2 (10^6 cfu) (N=X)			WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)			Placebo + WRSs2 (10^6 cfu) (N=X)			Placebo + Placebo (N=X)			All Participants (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Pain/Abdominal Cramps	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
Vomiting	None	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Mild	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Moderate	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
	Severe	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx

Notes: N = Number of participants in the Safety Population who received both vaccinations corresponding to the study arm.
n = Number of participants reporting each symptom.
Severity is the maximum severity reported post vaccination for each participant.

Table 57: Number and Percentage of Participants Experiencing Solicited Events Post-Vaccination Dose 1 by Symptom, Severity, and Day Post Dosing - WRSs2 + WRSs2 (10^6 cfu) (N=X)

Symptom	Severity	Pre-Dose		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Any Symptom	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Anorexia/Loss of Appetite	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Arthralgia	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Chills	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Diarrhea	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

Table 57: Number and Percentage of Participants Experiencing Solicited Events Post-Vaccination Dose 1 by Symptom, Severity, and Day Post Dosing - WRSs2 + WRSs2 (10^6 cfu) (N=X) *(continued)*

Symptom	Severity	Pre-Dose		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Fever	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Headache	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Malaise/Fatigue	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Myalgia	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Nausea	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

Table 57: Number and Percentage of Participants Experiencing Solicited Events Post-Vaccination Dose 1 by Symptom, Severity, and Day Post Dosing - WRSs2 + WRSs2 (10^6 cfu) (N=X) *(continued)*

Symptom	Severity	Pre-Dose		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Pain/Abdominal Cramps	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Vomiting	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

Notes: N = Number of participants in the Safety Population who received the specified dose.
Severity is the maximum severity reported post dosing for each participant for each day.

Tables with similar format:

Table 58: Number and Percentage of Participants Experiencing Solicited Events Post-Vaccination Dose 2 by Symptom, Severity, and Day Post Dosing - WRSs2 + WRSs2 (10^6 cfu) (N=X)

Table 59: Number and Percentage of Participants Experiencing Solicited Events Post-Vaccination Dose 1 by Symptom, Severity, and Day Post Dosing – WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)

Table 60: Number and Percentage of Participants Experiencing Solicited Events Post-Vaccination Dose 2 by Symptom, Severity, and Day Post Dosing – WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)

Table 61: Number and Percentage of Participants Experiencing Solicited Events Post-Vaccination Dose 1 by Symptom, Severity, and Day Post Dosing - Placebo + WRSs2 (10^6 cfu) (N=X)

Table 62: Number and Percentage of Participants Experiencing Solicited Events Post-Vaccination Dose 2 by Symptom, Severity, and Day Post Dosing - Placebo + WRSs2 (10^6 cfu) (N=X)

Table 63: Number and Percentage of Participants Experiencing Solicited Events Post-Vaccination Dose 1 by Symptom, Severity, and Day Post Dosing - Placebo + Placebo (N=X)

Table 64: Number and Percentage of Participants Experiencing Solicited Events Post-Vaccination Dose 2 by Symptom, Severity, and Day Post Dosing - Placebo + Placebo (N=X)

Table 65: Number and Percentage of Participants Experiencing Solicited Events Post-Vaccination Dose 1 by Symptom, Severity, and Day Post Dosing – First Dose Placebo, All Participants (N=X)

Table 66: Difference in Proportion of Participants Experiencing Solicited Events Post-Either Vaccination Dose by Study Arm - Safety Population

[Implementation Note: For the participant who received the incorrect second vaccination, solicited adverse events post-second vaccination will be excluded from this table.]

Symptom	Statistic	WRSs2 + WRSs2 (10^6 cfu) (N=X)	WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)	Placebo + WRSs2 (10^6 cfu) (N=X)	Placebo + Placebo (N=X)
Any Symptom	Proportion (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
	Difference with Placebo + Placebo group (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	-
Fever	Proportion (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
	Difference with Placebo + Placebo group (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	-
Headache	Proportion (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
	Difference with Placebo + Placebo group (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	-
Arthralgia	Proportion (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
	Difference with Placebo + Placebo group (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	-
Nausea	Proportion (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
	Difference with Placebo + Placebo group (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	-
Pain/Abdominal Cramps	Proportion (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
	Difference with Placebo + Placebo group (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	-
Myalgia	Proportion (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
	Difference with Placebo + Placebo group (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	-
Malaise/Fatigue	Proportion (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
	Difference with Placebo + Placebo group (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	-

Table 66: Difference in Proportion of Participants Experiencing Solicited Events Post-Either Vaccination Dose by Study Arm - Safety Population *(continued)*

Symptom	Statistic	WRSs2 + WRSs2 (10^6 cfu) (N=X)	WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)	Placebo + WRSs2 (10^6 cfu) (N=X)	Placebo + Placebo (N=X)
Anorexia/Loss of Appetite	Proportion (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
	Difference with Placebo + Placebo group (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	-
Chills	Proportion (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
	Difference with Placebo + Placebo group (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	-
Vomiting	Proportion (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
	Difference with Placebo + Placebo group (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	-
Diarrhea	Proportion (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
	Difference with Placebo + Placebo group (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	-
Note: N = Number of participants in the Safety Population who received at least one dose.					

Table 67: Number and Percentage of Participants Experiencing Solicited Events for Dose 1 Compared with Dose 2 by Study Arm

Study Arm	Criteria	Dose 2 – Participants with No Events n (%)	Dose 2 – Participants with Mild or Greater Events n (%)	Dose 2 – Total Number of Participants n (%)
WRSs2 + WRSs2 (10^6 cfu)	Dose 1 - Participants with No Events	x (%)	x (%)	x (%)
	Dose 1 - Participants with Mild or Greater Events	x (%)	x (%)	x (%)
	Dose 1 - Total Number of Participants	x (%)	x (%)	x (100%)
WRSs2 + WRSs2 ($5x10^5$ cfu)	Dose 1 - Participants with No Events	x (%)	x (%)	x (%)
	Dose 1 - Participants with Mild or Greater Events	x (%)	x (%)	x (%)
	Dose 1 - Total Number of Participants	x (%)	x (%)	x (100%)
Placebo + WRSs2 (10^6 cfu)	Dose 1 - Participants with No Events	x (%)	x (%)	x (%)
	Dose 1 - Participants with Mild or Greater Events	x (%)	x (%)	x (%)
	Dose 1 - Total Number of Participants	x (%)	x (%)	x (100%)
Placebo + Placebo	Dose 1 - Participants with No Events	x (%)	x (%)	x (%)
	Dose 1 - Participants with Mild or Greater Events	x (%)	x (%)	x (%)
	Dose 1 - Total Number of Participants	x (%)	x (%)	x (100%)

Notes: Denominators for percentages are the number of participants in the Safety Population who received the first and second dose corresponding to the study arm.
[x] participant(s) did not get the second dose and are not included in this table.

14.3.1.2 Unsolicited Adverse Events

Table 68: Summary of Unsolicited Adverse Events for Study Day 1 – 8 by MedDRA System Organ Class, Preferred Term, and Study Arm – Safety Population

MedDRA System Organ Class	MedDRA Preferred Term	Day 1-8 Post Dose 1 WRSs2+ WRSs2 (10^6 cfu) (N=X)				Day 1-8 Post Dose 1 WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)				Day 1-8 Post Dose 1 Placebo + WRSs2 (10^6 cfu) (N=X)				Day 1-8 Post Dose 1 Placebo + Placebo (N=X)				Day 1-8 Post Dose 1 First Dose Placebo (N=X)				Day 1-8 Post Dose 1 All Participants (N=X)			
		n	%	95% CI	Events	n	%	95% CI	Events	n	%	95% CI	Events	n	%	95% CI	Events	n	%	95% CI	Events	n	%	95% CI	Events
Any SOC	Any PT	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x
[SOC 1]	Any PT	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x
	[PT 1]	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x
	[PT 2]	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x
[SOC 2]	Any PT	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x
	[PT 1]	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x
	[PT 2]	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x

Notes: N = Number of participants in the Safety Population who received the specified dose.
n = Number of participants reporting each SOC/PT.
This table presents number and percentage of participants. A participant is only counted once per PT/time point.

Tables with similar format:

Table 69: Summary of Unsolicited Adverse Events for Study Day 9 – 28 by MedDRA System Organ Class, Preferred Term, and Study Arm – Safety Population

[Implementation Note: Columns will be for Day 9-28 Post Dose 1]

Table 70: Summary of Unsolicited Adverse Events for Study Day 29-37 by MedDRA System Organ Class, Preferred Term, and Study Arm – Safety Population

[Implementation Note: Columns will be for Day 29-37 Post Dose 2; First Dose Placebo column will not be included.]

Similar Tables *continued*

Table 71: Summary of Unsolicited Adverse Events for Study Day 38-56 by MedDRA System Organ Class, Preferred Term, and Study Arm – Safety Population

[Implementation Note: Columns will be for Day 38-56 Post Dose 2; First Dose Placebo column will not be included.]

Table 72: Summary of Unsolicited Adverse Events for Study Day 57-69 by MedDRA System Organ Class, Preferred Term, and Study Arm – Safety Population

[Implementation Note: Columns will be for Day 57-69. First Dose Placebo column will not be included. Footnote will be updated to "N = Number of participants in the Safety Population who received at least the first dose of vaccination."]

Table 73: Summary of Unsolicited Adverse Events for Study Day 70-180 by MedDRA System Organ Class, Preferred Term, and Study Arm – Safety Population

[Implementation Note: Columns will be for Day 70-180. First Dose Placebo column will not be included. Footnote will be updated to "N = Number of participants in the Safety Population who received at least the first dose of vaccination."]

Table 74: Number and Percentage of Participants Experiencing Unsolicited Adverse Events Post-Any Vaccination Dose by MedDRA System Organ Class and Preferred Term, Maximum Severity, Relationship to Vaccination, and Study Arm– WRSs2 + WRSs2 (10^6 cfu), Safety Population, N=X

				Severity						Relationship to Treatment			
		Any Incidence		Mild		Moderate		Severe		Not Related		Related	
MedDRA System Organ Class	MedDRA Preferred Term	n	%	n	%	n	%	n	%	n	%	n	%
Any SOC	Any PT	x	x	x	x	x	x	x	x	x	x	x	x
[SOC 1]	[PT 1]	x	x	x	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x	x	x	x	x	x	x	x	x	x
[SOC 2]	[PT 1]	x	x	x	x	x	x	x	x	x	x	x	x

Notes: N = Number of subjects in the Safety Population.
n = Number of subjects reporting event. A subject is only counted once per PT/time point.

Tables with a similar format:

Table 75: Number and Percentage of Participants Experiencing Unsolicited Adverse Events Post-Any Vaccination Dose by MedDRA System Organ Class and Preferred Term, Maximum Severity, Relationship to Vaccination, and Study Arm – WRSs2 + WRSs2 ($5x10^5$ cfu), Safety Population, N=X

Table 76: Number and Percentage of Participants Experiencing Unsolicited Adverse Events Post-Any Vaccination Dose by MedDRA System Organ Class and Preferred Term, Maximum Severity, Relationship to Vaccination, and Study Arm – Placebo + WRSs2 (10^6 cfu), Safety Population, N=X

Table 77: Number and Percentage of Participants Experiencing Unsolicited Adverse Events Post-Any Vaccination Dose by MedDRA System Organ Class and Preferred Term, Maximum Severity, Relationship to Vaccination, and Study Arm – Placebo + Placebo, Safety Population, N=X

Table 78: Number and Percentage of Participants Experiencing Vaccine-Related Unsolicited Adverse Events Within 28 Days Post-Vaccination Dose by MedDRA System Organ Class and Preferred Term, Dose, and Study Arm – Safety Population

MedDRA System Organ Class	MedDRA Preferred Term	Day 1-28 Post First Dose		Day 1-28 Post Second Dose		Day 1-28 Post Either Dose	
		n	%	n	%	n	%
WRSs2 + WRSs2 (10^6 cfu) (N=X)							
Any SOC	Any PT	x	xx	x	xx	x	xx
[SOC 1]	Any PT	x	xx	x	xx	x	xx
	[PT 1]	x	xx	x	xx	x	xx
	[PT 2]	x	xx	x	xx	x	xx
[SOC 2]	Any PT	x	xx	x	xx	x	xx
	[PT 1]	x	xx	x	xx	x	xx
	[PT 2]	x	xx	x	xx	x	xx
WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)							
Any SOC	Any PT	x	xx	x	xx	x	xx
[SOC 1]	Any PT	x	xx	x	xx	x	xx
	[PT 1]	x	xx	x	xx	x	xx
	[PT 2]	x	xx	x	xx	x	xx
[SOC 2]	Any PT	x	xx	x	xx	x	xx
	[PT 1]	x	xx	x	xx	x	xx
	[PT 2]	x	xx	x	xx	x	xx

Table 78: Number and Percentage of Participants Experiencing Vaccine-Related Unsolicited Adverse Events Within 28 Days Post-Vaccination Dose by MedDRA System Organ Class and Preferred Term, Dose, and Study Arm – Safety Population *(continued)*

MedDRA System Organ Class	MedDRA Preferred Term	Day 1-28 Post First Dose		Day 1-28 Post Second Dose		Day 1-28 Post Either Dose	
		n	%	n	%	n	%
Placebo + WRSs2 (10^6 cfu) (N=X)							
Any SOC	Any PT	x	xx	x	xx	x	xx
[SOC 1]	Any PT	x	xx	x	xx	x	xx
	[PT 1]	x	xx	x	xx	x	xx
	[PT 2]	x	xx	x	xx	x	xx
[SOC 2]	Any PT	x	xx	x	xx	x	xx
	[PT 1]	x	xx	x	xx	x	xx
	[PT 2]	x	xx	x	xx	x	xx
Placebo + Placebo (N=X)							
Any SOC	Any PT	x	xx	x	xx	x	xx
[SOC 1]	Any PT	x	xx	x	xx	x	xx
	[PT 1]	x	xx	x	xx	x	xx
	[PT 2]	x	xx	x	xx	x	xx
[SOC 2]	Any PT	x	xx	x	xx	x	xx
	[PT 1]	x	xx	x	xx	x	xx
	[PT 2]	x	xx	x	xx	x	xx

Table 78: Number and Percentage of Participants Experiencing Vaccine-Related Unsolicited Adverse Events Within 28 Days Post-Vaccination Dose by MedDRA System Organ Class and Preferred Term, Dose, and Study Arm – Safety Population *(continued)*

MedDRA System Organ Class	MedDRA Preferred Term	Day 1-28 Post First Dose		Day 1-28 Post Second Dose		Day 1-28 Post Either Dose	
		n	%	n	%	n	%
First Dose Placebo (N=X)							
Any SOC	Any PT	x	xx	-	-	-	-
[SOC 1]	Any PT	x	xx	-	-	-	-
	[PT 1]	x	xx	-	-	-	-
	[PT 2]	x	xx	-	-	-	-
[SOC 2]	Any PT	x	xx	-	-	-	-
	[PT 1]	x	xx	-	-	-	-
	[PT 2]	x	xx	-	-	-	-

N = Number of participants in the Safety Population. The denominator for percentages post-second dose is the number of participants who received both vaccinations corresponding to the study arm.
Note: This table presents number and percentage of participants. For each time period, a participant is only counted once per PT.

14.3.2 Listing of Deaths, Other Serious and Significant Adverse Events

Table 79: Listing of Serious Adverse Events

[Implementation Note: If the event is ongoing (no stop date), indicate "ongoing" in the "Duration" column. If more than one reason is selected for the reason reported as an SAE, list all reasons in the column, separated by a comma. Listing should be sorted by Participant ID, Associated with Dose No., and No. of Days Post Associated Dose.]

Adverse Event	Associated with Dose No.	No. of Days Post Associated Dose (Duration)	No. of Days Post Dose the Event Became Serious	Reason Reported as an SAE	Severity	Relationship to Study Treatment	If Not Related, Alternative Etiology	Action Taken with Study Treatment	Participant Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Participant ID: , Randomized Study Arm: , Study Product(s) Received: , AE Number:												
Comments:												
Participant ID: , Randomized Study Arm: , Study Product(s) Received: , AE Number:												
Comments:												

Table 80: Summary of Serious Adverse Events by MedDRA System Organ Class, Preferred Term, and Study Arm – Safety Population

[Implementation Note: If there are no SAEs reported in the study, then the table will only consist of the first row (Any SOC, Any PT) with n and % equal to zero and appropriate 95% CIs.]

MedDRA System Organ Class	MedDRA Preferred Term	WRSs2+ WRSs2 (10^6 cfu) (N=X)				WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)				Placebo + WRSs2 (10^6 cfu) (N=X)				Placebo + Placebo (N=X)				All Participants (N=X)			
		n	%	95% CI	Events	n	%	95% CI	Events	n	%	95% CI	Events	n	%	95% CI	Events	n	%	95% CI	Events
Any SOC	Any PT	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x
[SOC 1]	Any PT	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x
	[PT 1]	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x
	[PT 2]	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x
[SOC 2]	Any PT	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x
	[PT 1]	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x
	[PT 2]	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x

Notes: This table presents number and percentage of participants. A participant is only counted once per PT.
N = Number of participants in the Safety Population.
n = Number of participants reporting each SOC/PT.

Table 81: Listing of Non-Serious, Unsolicited, Moderate or Severe Adverse Events

Adverse Event	Associated with Dose No.	No. of Days Post Associated Dose (Duration)	Severity	Relationship to Study Treatment	If Not Related, Alternative Etiology	Action Taken with Study Treatment	Participant Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Participant ID: , Randomized Study Arm: , Study Product(s) Received: , AE Number:										
Comments:										
Participant ID: , Randomized Study Arm: , Study Product(s) Received: , 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 82: Listing of Abnormal Laboratory Results - Chemistry

[Implementation Note: This listing should include all chemistry results for any participant that had at least one abnormal chemistry laboratory result post-vaccination. In the "If Not Related, Alternate Etiology" column, merge the two data fields for collecting alternate etiology, separated by a colon. Listing will be sorted by participant ID, laboratory parameter, and actual study day]

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

Table 83: Listing of Abnormal Laboratory Results – Hematology

[Implementation Note: This listing should include all hematology results for any participant that had at least one abnormal hematology laboratory result post-vaccination. In the "If Not Related, Alternate Etiology" column, merge the two data fields for collecting alternate etiology, separated by a colon. Listing will be sorted by participant ID, laboratory parameter, and actual study day]

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

14.3.5 Displays of Laboratory Results

14.3.5.1 Chemistry Results

Table 84: Laboratory Results by Parameter, Maximum Severity, Time Point, and Study Arm – Any Chemistry Parameter

Time Point	Study Arm	N	None		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%
Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx
	First Dose Placebo	x	x	xx	x	xx	x	xx	x	x	xx	x
Study Day 8	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	x	xx	x
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	x	xx	x
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	x	xx	x
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	x	xx	x
	First Dose Placebo	x	x	xx	x	xx	x	xx	x	x	xx	x
Study Day 36	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 56	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx

Table 84: Laboratory Results by Parameter, Maximum Severity, Time Point, and Study Arm – Any Chemistry Parameter *(continued)*

Time Point	Study Arm	N	None		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%
Study Day 64	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 71	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx
Max Severity Post Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx

Notes: The "Max Severity 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.

Table 85: Laboratory Results by Parameter, Maximum Severity, Time Point, and Study Arm – Sodium

Time Point	Study Arm	N	None		Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	First Dose Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 8	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	First Dose Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 36	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 56	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

Table 85: Laboratory Results by Parameter, Maximum Severity, Time Point, and Study Arm – Sodium *(continued)*

Time Point	Study Arm	N	None		Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Study Day 64	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 71	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Max Severity Post Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	Xx

Notes: The "Max Severity 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.

Tables with similar format:

Table 86: Laboratory Results by Parameter, Maximum Severity, Time Point, and Study Arm – Potassium

Table 87: Laboratory Results by Parameter, Maximum Severity, Time Point, and Study Arm – Creatinine

Table 88: Laboratory Results by Parameter, Maximum Severity, Time Point, and Study Arm – Alanine Aminotransferase (ALT)

Table 89: Laboratory Results by Parameter, Maximum Severity, Time Point, and Study Arm – Total Bilirubin

Table 90: Abnormal Laboratory Results Related to Study Vaccination or Challenge by Maximum Severity, Time Point, and Study Arm – Any Chemistry Parameter

Time Point	Study Arm	N	Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%
Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx
	First Dose Placebo	x	x	xx	x	xx	x	x
Study Day 8	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	x
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	x
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	x
	Placebo + Placebo	x	x	xx	x	xx	x	x
	First Dose Placebo	x	x	xx	x	xx	x	x
Study Day 36	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx
Study Day 56	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx

Table 90: Abnormal Laboratory Results Related to Study Vaccination or Challenge by Maximum Severity, Time Point, and Study Arm – Any Chemistry Parameter *(continued)*

Time Point	Study Arm	N	Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%
Study Day 64	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx
Study Day 71	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx
Max Severity Post Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx

Notes: The "Max Severity Post Baseline" rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments.
Time points following Study Day 64 are post-challenge and the abnormal results are likely related to the challenge.

N = Number of participants in the Safety Population.

Table 91: Abnormal Laboratory Results Related to Study Vaccination or Challenge by Maximum Severity, Time Point, and Study Arm – Sodium

Time Point	Study Arm	N	Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)	
			n	%	n	%	n	%	n	%	n	%	n	%
Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	First Dose Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 8	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	First Dose Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 36	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 56	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

Table 91: Abnormal Laboratory Results Related to Study Vaccination or Challenge by Maximum Severity, Time Point, and Study Arm – Sodium *(continued)*

Time Point	Study Arm	N	Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)	
			n	%	n	%	n	%	n	%	n	%	n	%
Study Day 64	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 71	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Max Severity Post Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

Notes: The "Max Severity Post Baseline" rows indicate the maximum severity of abnormal laboratory results related to study treatment experienced by each participant at any time point post baseline, including unscheduled assessments. Time points following Study Day 64 are post-challenge and the abnormal results are likely related to the challenge.

N = Number of participants in the Safety Population.

Tables with similar format:

Table 92: Abnormal Laboratory Results Related to Study Vaccination or Challenge by Maximum Severity, Time Point, and Study Arm – Potassium

Table 93: Abnormal Laboratory Results Related to Study Vaccination or Challenge by Maximum Severity, Time Point, and Study Arm – Creatinine

Table 94: Abnormal Laboratory Results Related to Study Vaccination or Challenge by Maximum Severity, Time Point, and Study Arm – Alanine Transaminase (ALT)

Table 95: Abnormal Laboratory Results Related to Study Vaccination or Challenge by Maximum Severity, Time Point, and Study Arm – Total Bilirubin

Table 96: Laboratory Summary Statistics by Time Point and Study Arm – Sodium (mmol/L)

Time Point	Study Arm	N	Mean	Standard Deviation	Median	Min, Max
Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x
	First Dose Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x
Study Day 8	WRSs2 + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x
	First Dose Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x
Study Day 8, Change from Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x
	First Dose Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x
Study Day 36	WRSs2 + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x

Table 96: Laboratory Summary Statistics by Time Point and Study Arm – Sodium (mmol/L) *(continued)*

Time Point	Study Arm	N	Mean	Standard Deviation	Median	Min, Max
Study Day 36, Change from Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x
Study Day 56	WRSs2 + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x
Study Day 56, Change from Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x
Study Day 64	WRSs2 + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x
Study Day 64, Change from Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x
Study Day 71	WRSs2 + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x

Table 96: Laboratory Summary Statistics by Time Point and Study Arm – Sodium (mmol/L) *(continued)*

Time Point	Study Arm	N	Mean	Standard Deviation	Median	Min, Max
Study Day 71, Change from Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x
Note: N = Number of participants in the Safety Population.						

Tables with similar format:

Table 97: Laboratory Summary Statistics by Time Point and Study Arm – Potassium (mmol/L)

Table 98: Laboratory Summary Statistics by Time Point and Study Arm – Creatinine (mg/dL)

Table 99: Laboratory Summary Statistics by Time Point and Study Arm – Alanine Aminotransferase (ALT) (unit/L)

Table 100: Laboratory Summary Statistics by Time Point and Study Arm – Total Bilirubin (mg/dL)

14.3.5.2 Hematology Results

Table 101: Laboratory Results by Parameter, Maximum Severity, Time Point, and Study Arm – Any Hematology Parameter

Time Point	Study Arm	N	None		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%
Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx
	First Dose Placebo	x	x	xx	x	xx	x	xx	x	x	xx	x
Study Day 8	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	x	xx	x
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	x	xx	x
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	x	xx	x
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	x	xx	x
	First Dose Placebo	x	x	xx	x	xx	x	xx	x	x	xx	x
Study Day 36	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 56	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx

Table 101: Laboratory Results by Parameter, Maximum Severity, Time Point, and Study Arm – Any Hematology Parameter *(continued)*

Time Point	Study Arm	N	None		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%
Study Day 64	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 71	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx
Max Severity Post Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx

Notes: The "Max Severity 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.

Table 102: Laboratory Results by Parameter, Maximum Severity, Time Point, and Study Arm – White Blood Cells (WBC)

Time Point	Study Arm	N	None		Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	First Dose Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 8	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	First Dose Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 36	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 56	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

Table 102: Laboratory Results by Parameter, Maximum Severity, Time Point, and Study Arm – White Blood Cells (WBC) *(continued)*

Time Point	Study Arm	N	None		Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Study Day 64	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 71	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Max Severity Post Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	Xx

Notes: The "Max Severity 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.

Tables with similar format:

Table 103: Laboratory Results by Parameter, Maximum Severity, Time Point, and Study Arm – Absolute Neutrophil Count (ANC)

Table 104: Laboratory Results by Parameter, Maximum Severity, Time Point, and Study Arm – Hemoglobin (Hgb)

Table 105: Laboratory Results by Parameter, Maximum Severity, Time Point, and Study Arm – Platelet Count

Table 106: Abnormal Laboratory Results Related to Study Vaccination or Challenge by Maximum Severity, Time Point, and Study Arm – Any Hematology Parameter

Time Point	Study Arm	N	Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%
Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx
	First Dose Placebo	x	x	xx	x	xx	x	x
Study Day 8	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	x
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	x
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	x
	Placebo + Placebo	x	x	xx	x	xx	x	x
	First Dose Placebo	x	x	xx	x	xx	x	x
Study Day 36	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx
Study Day 56	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx

Table 106: Abnormal Laboratory Results Related to Study Vaccination or Challenge by Maximum Severity, Time Point, and Study Arm – Any Hematology Parameter *(continued)*

Time Point	Study Arm	N	Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%
Study Day 64	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx
Study Day 71	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx
Max Severity Post Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	Xx

Notes: The "Max Severity Post Baseline" rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments. Time points following Study Day 64 are post-challenge and the abnormal results are likely related to the challenge.

N = Number of participants in the Safety Population.

Table 107: Abnormal Laboratory Results Related to Study Vaccination or Challenge by Maximum Severity, Time Point, and Study Arm – White Blood Cell Count (WBC)

Time Point	Study Arm	N	Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)	
			n	%	n	%	n	%	n	%	n	%	n	%
Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	First Dose Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 8	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	First Dose Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 36	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 56	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

Table 107: Abnormal Laboratory Results Related to Study Vaccination or Challenge by Maximum Severity, Time Point, and Study Arm – White Blood Cell Count (WBC) *(continued)*

Time Point	Study Arm	N	Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)	
			n	%	n	%	n	%	n	%	n	%	n	%
Study Day 64	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 71	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Max Severity Post Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	Xx

Notes: The "Max Severity Post Baseline" rows indicate the maximum severity of abnormal laboratory results related to study treatment experienced by each participant at any time point post baseline, including unscheduled assessments. Time points following Study Day 64 are post-challenge and the abnormal results are likely related to the challenge.

N = Number of participants in the Safety Population.

Tables with similar format:

Table 108: Abnormal Laboratory Results Related to Study Vaccination or Challenge by Maximum Severity, Time Point, and Study Arm – Absolute Neutrophil Count (ANC)

Table 109: Abnormal Laboratory Results Related to Study Vaccination or Challenge by Maximum Severity, Time Point, and Study Arm – Hemoglobin (Hgb)

Table 110: Abnormal Laboratory Results Related to Study Vaccination or Challenge by Maximum Severity, Time Point, and Study Arm – Platelet Count

Table 111: Laboratory Summary Statistics by Time Point and Study Arm – White Blood Cells (WBC) (10^3/mcL)

Time Point	Study Arm	N	Mean	Standard Deviation	Median	Min, Max
Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x
	First Dose Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x
Study Day 8	WRSs2 + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x
	First Dose Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x
Study Day 8, Change from Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x
	First Dose Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x
Study Day 36	WRSs2 + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x

Table 111: Laboratory Summary Statistics by Time Point and Study Arm – White Blood Cells (WBC) (10^3/mcL) *(continued)*

Time Point	Study Arm	N	Mean	Standard Deviation	Median	Min, Max
Study Day 36, Change from Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x
Study Day 56	WRSs2 + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x
Study Day 56, Change from Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x
Study Day 64	WRSs2 + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x

Table 111: Laboratory Summary Statistics by Time Point and Study Arm – White Blood Cells (WBC) (10^3/mcL) *(continued)*

Time Point	Study Arm	N	Mean	Standard Deviation	Median	Min, Max
Study Day 64, Change from Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x
Study Day 71	WRSs2 + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x
Study Day 71, Change from Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + WRSs2 (10^6 cfu)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Placebo + Placebo	x	xx.x	xx.x	xx.x	xx.x, xx.x
Note: N = Number of participants in the Safety Population.						

Tables with similar format:

Table 112: Laboratory Summary Statistics by Time Point and Study Arm – Absolute Neutrophil Count (ANC) (10^3/mcL)

Table 113: Laboratory Summary Statistics by Time Point and Study Arm – Hemoglobin (Hgb) (gm/dL)

Table 114: Laboratory Summary Statistics by Time Point and Study Arm – Platelet Count (10^3/mcL)

14.3.6 Displays of Vital Signs

Table 115: Vital Signs by Parameter, Maximum Severity, Time Point, and Study Arm – Any Vital Sign Parameter

Time Point	Study Arm	N	None		Mild		Moderate		Severe		Missing	
			n	%	n	%	n	%	n	%	n	%
Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx
	First Dose Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 29 Pre-Dose 2	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx
	First Dose Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 29 Post-Dose 2	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 56	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx

Table 115: Vital Signs by Parameter, Maximum Severity, Time Point, and Study Arm – Any Vital Sign Parameter *(continued)*

Time Point	Study Arm	N	None		Mild		Moderate		Severe		Missing	
			n	%	n	%	n	%	n	%	n	%
Study Day 57 Pre-Challenge	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 57 Post-Challenge	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 58	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 59	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 60	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx

Table 115: Vital Signs by Parameter, Maximum Severity, Time Point, and Study Arm – Any Vital Sign Parameter *(continued)*

Time Point	Study Arm	N	None		Mild		Moderate		Severe		Missing	
			n	%	n	%	n	%	n	%	n	%
Study Day 61	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 62	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 63	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 64	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 65	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx

Table 115: Vital Signs by Parameter, Maximum Severity, Time Point, and Study Arm – Any Vital Sign Parameter *(continued)*

Time Point	Study Arm	N	None		Mild		Moderate		Severe		Missing	
			n	%	n	%	n	%	n	%	n	%
Max Severity Post Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	Xx

Notes: The "Max Severity 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.

Table with similar format:

Table 116: Vital Signs by Parameter, Maximum Severity, Time Point, and Study Arm – Oral Temperature

Table 117: Vital Signs by Parameter, Maximum Severity, Time Point, and Study Arm – Pulse

Time Point	Study Arm	N	None		Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	First Dose Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 29 Pre-Dose 2	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	First Dose Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 29 Post-Dose 2	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 56	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

Table 117: Vital Signs by Parameter, Maximum Severity, Time Point, and Study Arm – Pulse *(continued)*

Time Point	Study Arm	N	None		Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Study Day 57 Pre-Challenge	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 57 Post-Challenge	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 58	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 59	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 60	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 61	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

Table 117: Vital Signs by Parameter, Maximum Severity, Time Point, and Study Arm – Pulse *(continued)*

Time Point	Study Arm	N	None		Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 62	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 63	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 64	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Study Day 65	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Max Severity Post Baseline	WRSs2 + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	WRSs2 + WRSs2 ($5x10^5$ cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + WRSs2 (10^6 cfu)	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo + Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	Xx

Table 117: Vital Signs by Parameter, Maximum Severity, Time Point, and Study Arm – Pulse *(continued)*

Time Point	Study Arm	N	None		Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Notes: The "Max Severity 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.																		

Tables with similar format:

Table 118: Vital Signs by Parameter, Maximum Severity, Time Point, and Study Arm – Systolic Blood Pressure

Table 119: Vital Signs by Parameter, Maximum Severity, Time Point, and Study Arm – Diastolic Blood Pressure

14.4 Summary of Concomitant Medications

Table 120: Number and Percentage of Participants with Prior and Concurrent Medications by WHO Drug Classification and Study Arm

WHO Drug Code Level 1, Anatomic Group	WHO Drug Code Level 2, Therapeutic Subgroup	WRSs2 + WRSs2 (10^6 cfu) (N=X)		WRSs2 + WRSs2 ($5x10^5$ cfu) (N=X)		Placebo + WRSs2 (10^6 cfu) (N=X)		Placebo + Placebo (N=X)		All Participants (N=X)	
		n	%	n	%	n	%	n	%	n	%
Any Level 1 Codes	Any Level 2 Codes	x	xx	x	xx	x	xx	x	xx	x	xx
[ATC Level 1 - 1]	Any [ATC 1 – 1]	x	xx	x	xx	x	xx	x	xx	x	xx
	[ATC 2 - 1]	x	xx	x	xx	x	xx	x	xx	x	xx
	[ATC 2 - 2]	x	xx	x	xx	x	xx	x	xx	x	xx
	[ATC 2 - 3]	x	xx	x	xx	x	xx	x	xx	x	xx
[ATC Level 1 – 2]	Any [ATC 1 – 2]	x	xx	x	xx	x	xx	x	xx	x	xx
	[ATC 2 - 1]	x	xx	x	xx	x	xx	x	xx	x	xx
	[ATC 2 - 2]	x	xx	x	xx	x	xx	x	xx	x	xx
	[ATC 2 - 3]	x	xx	x	xx	x	xx	x	xx	x	xx

Notes: N = Number of participants in the Safety Population who received at least the first vaccination corresponding to the study arm. n = Number of participants reporting taking at least one medication in the specific WHO Drug Class.

APPENDIX 2. FIGURE MOCK-UPS

LIST OF FIGURES

Figure 1: Schematic of Study Design

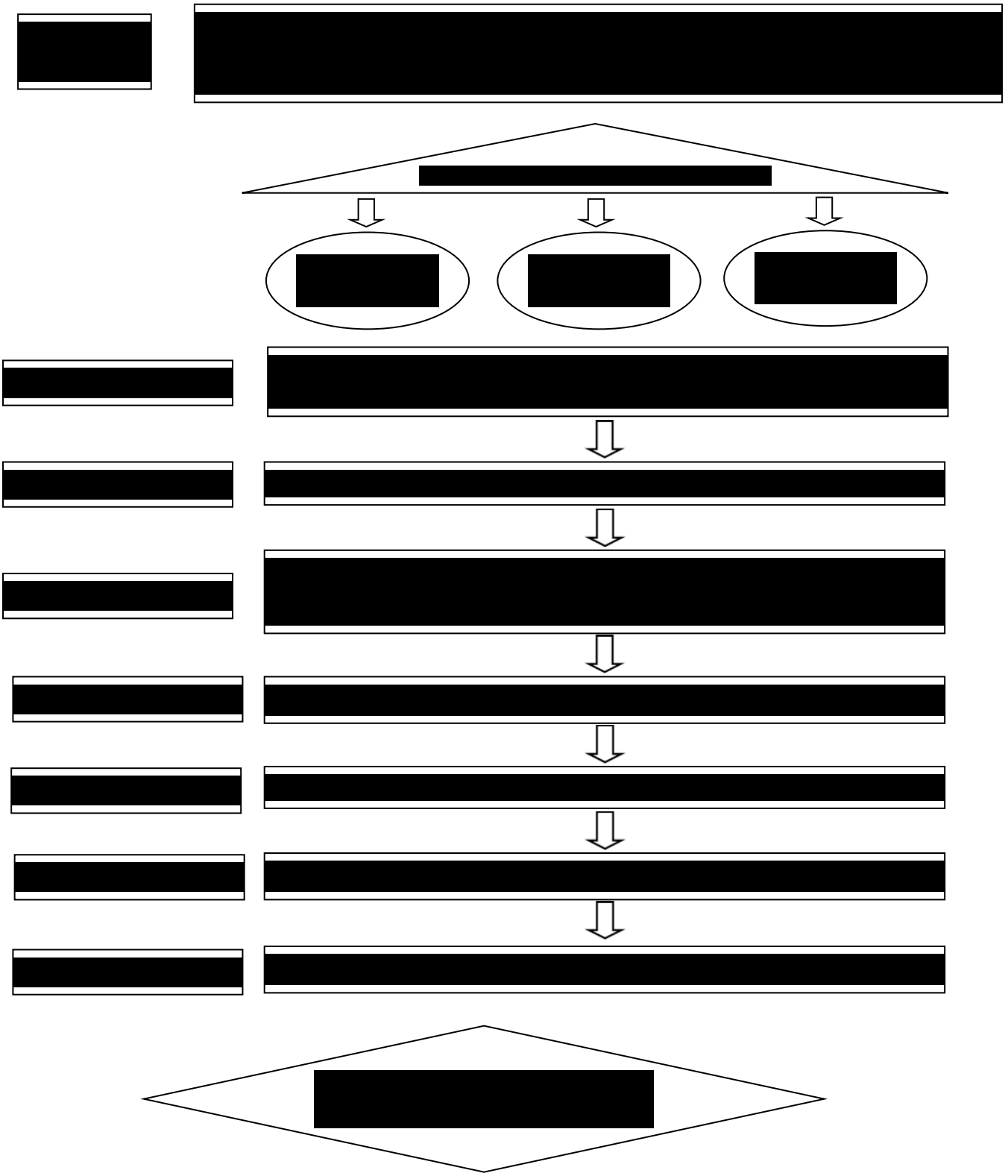
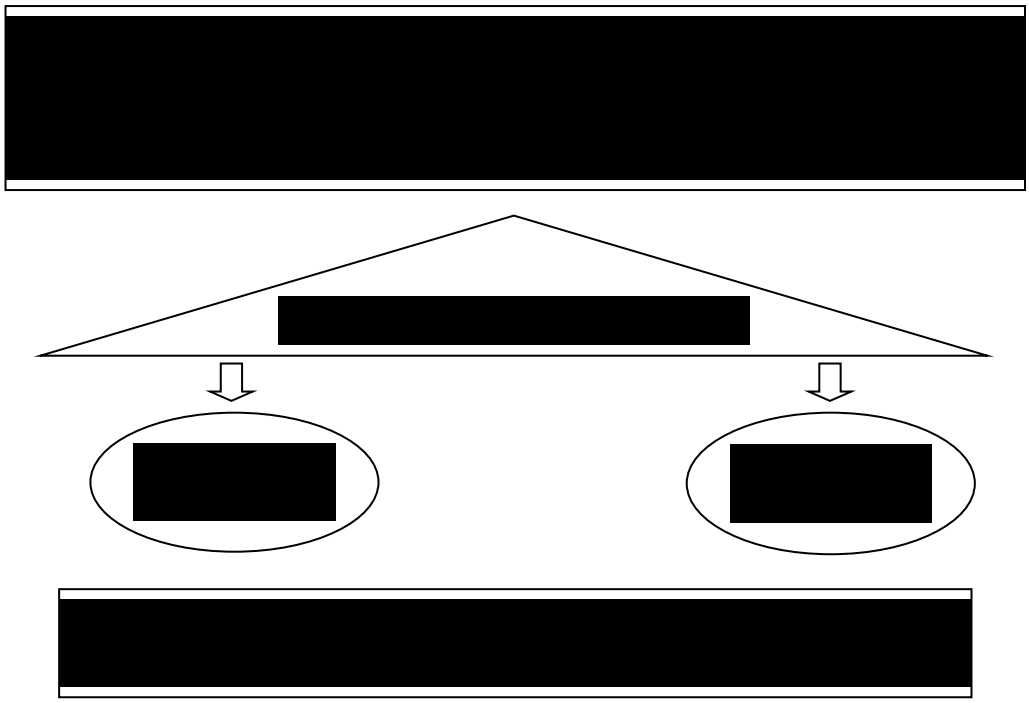


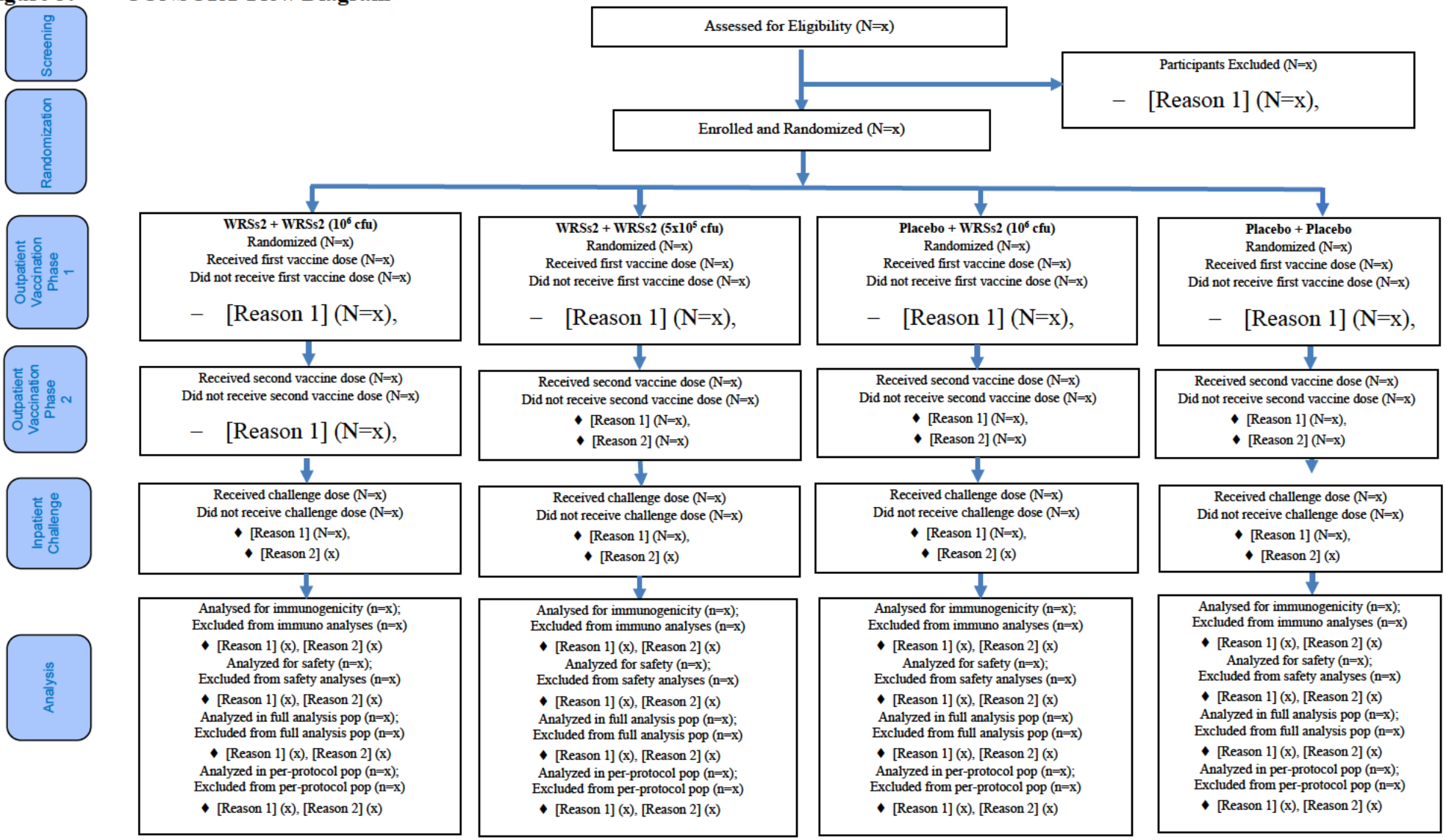
Figure 2: Change in Schematic of Study Design

Following changes were implemented in the schematic design of the study as described in Figure 1.



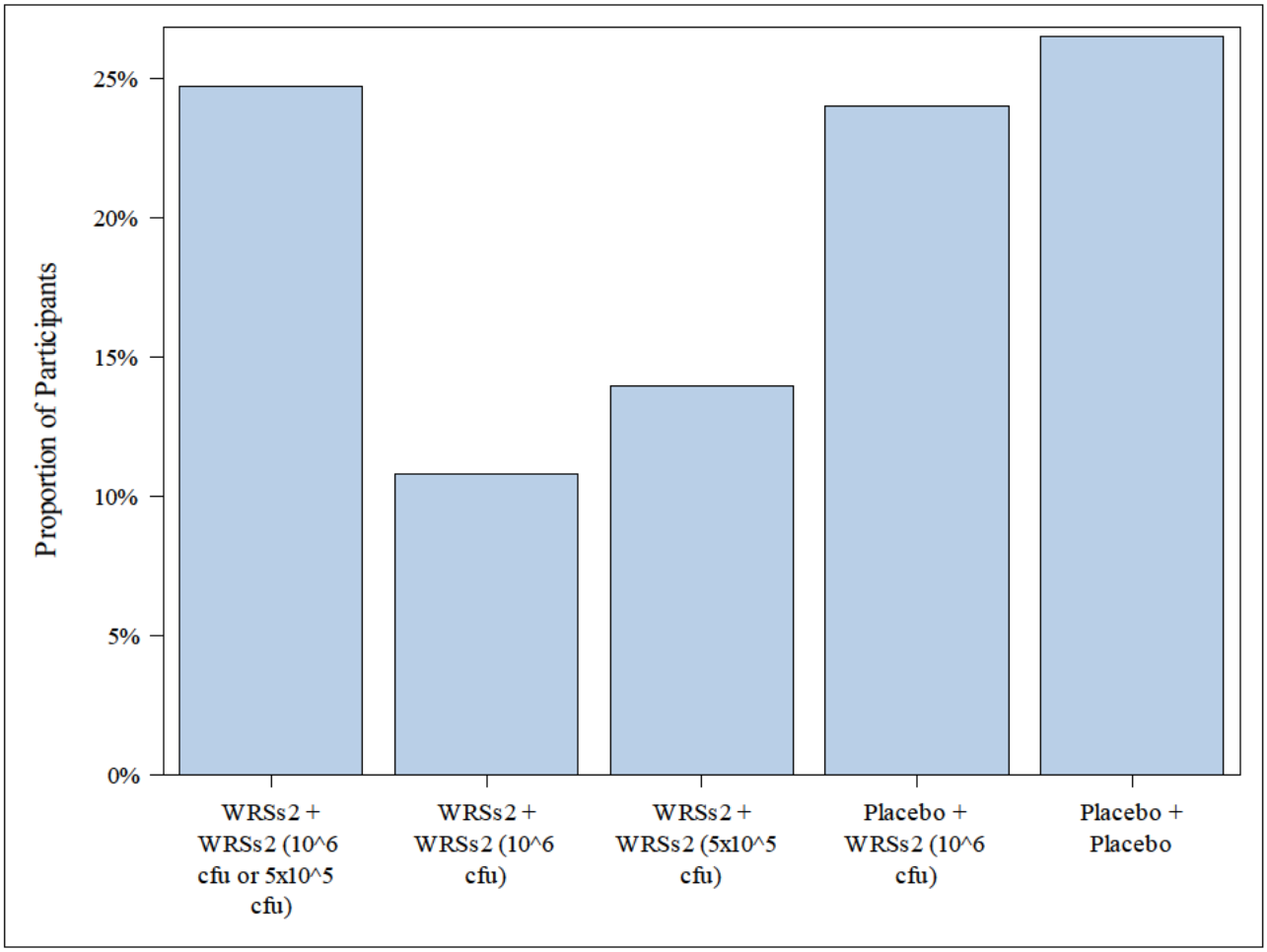
10.1 Disposition of Participants

Figure 3: CONSORT Flow Diagram



14.2.2 Efficacy Figures by Study Arm and Time Point

Figure 4: Proportion of Participants with Endpoint Review Committee-Determined Shigellosis by Study Arm, Full Analysis Population



Figures with a similar format:

Figure 5: Proportion of Participants with Endpoint Review Committee-Determined Shigellosis by Study Arm, Per-Protocol Population

Figure 6: Proportion of Participants with Programmatic Definition-Determined Shigellosis by Study Arm, Full Analysis Population

Figure 7: Proportion of Participants with Programmatic Definition-Determined Shigellosis by Study Arm, Per-Protocol Population

Figure 8: Proportion of Participants with Pre-Challenge *S. sonnei* Viral Shedding by Culture by Study Day and Study Arm, Shedding Analysis Population

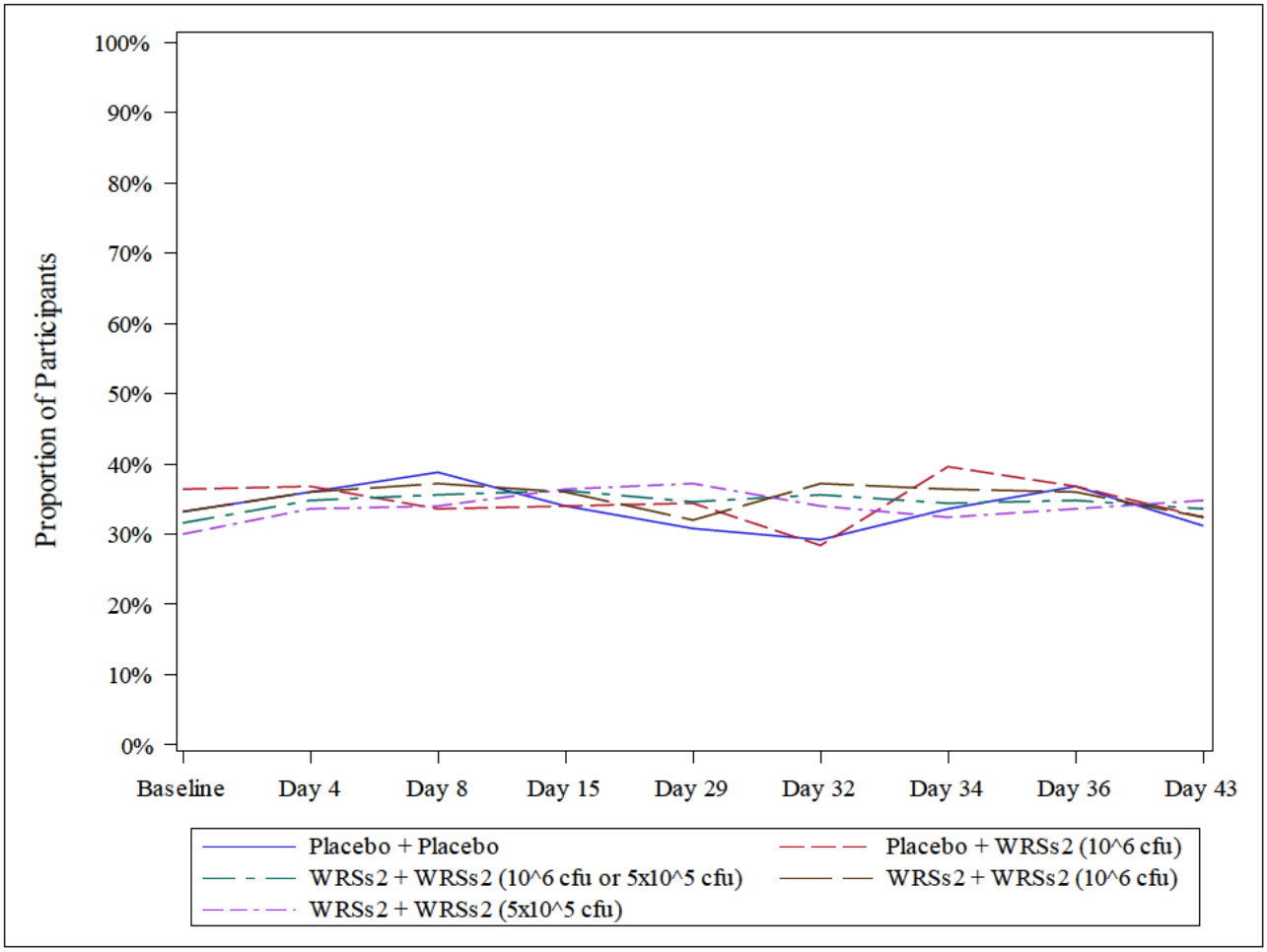


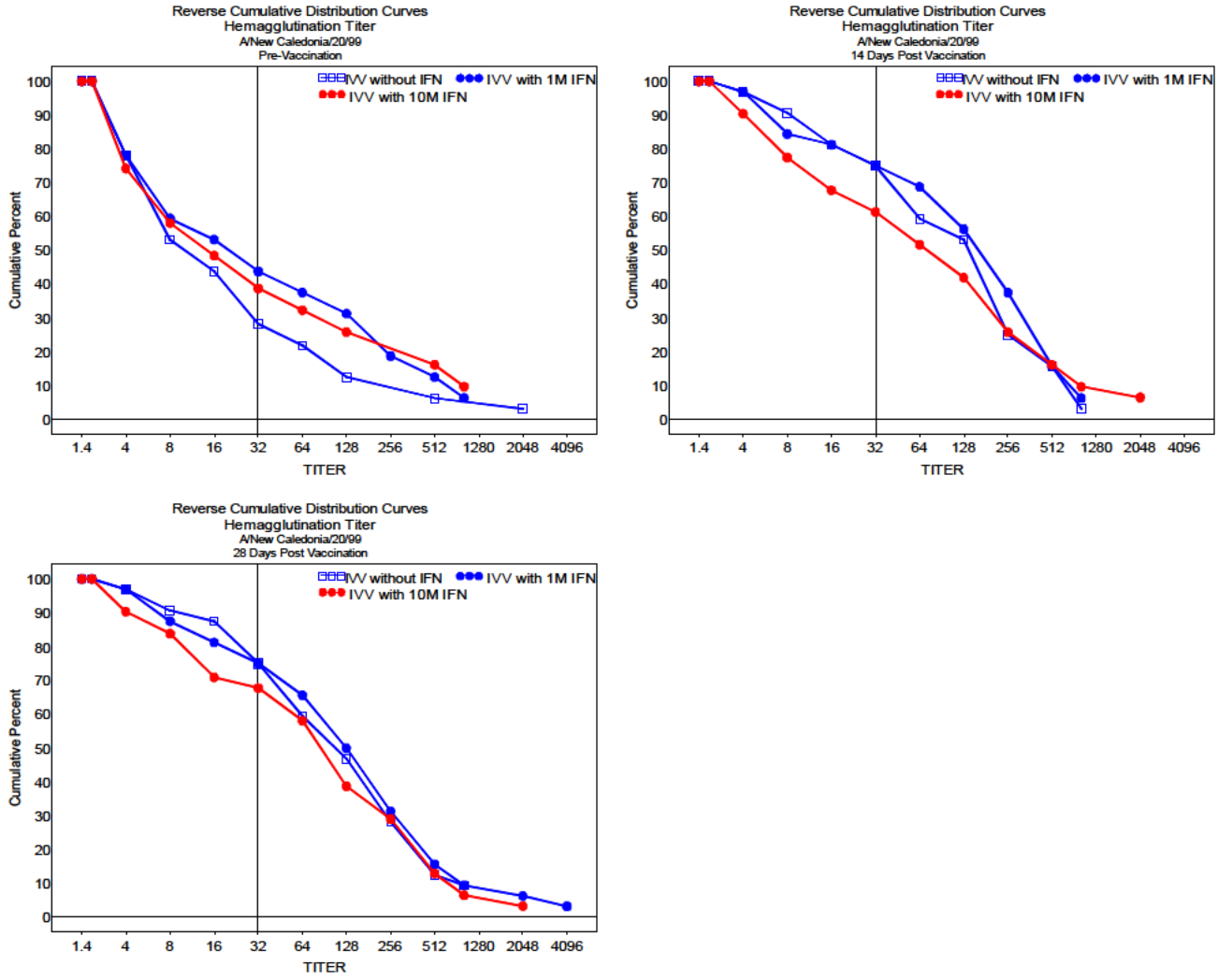
Figure with a similar format:

Figure 9: Proportion of Participants with Post-Challenge 53G Viral Shedding by Culture by Study Day and Study Arm, Full Analysis Population

14.2.4 Immunogenicity Response Figures by Measure, Study Arm, and Time Point

Figure 10: Reverse Cumulative Distribution of LPS-specific IgG Titers Pre-Challenge by Time Point and Study Arm, Immunogenicity Population

[Implementation Note: this is a generic plot. The final output should have one panel for each time point of interest: Days 1, 15, 29, 43, and 56 for Pre-Challenge figures; Days 64, 71, 85, and 113 for Post-Challenge figures. Each line in the graph will represent a study arm and will have a distinct color to distinguish the curve.]



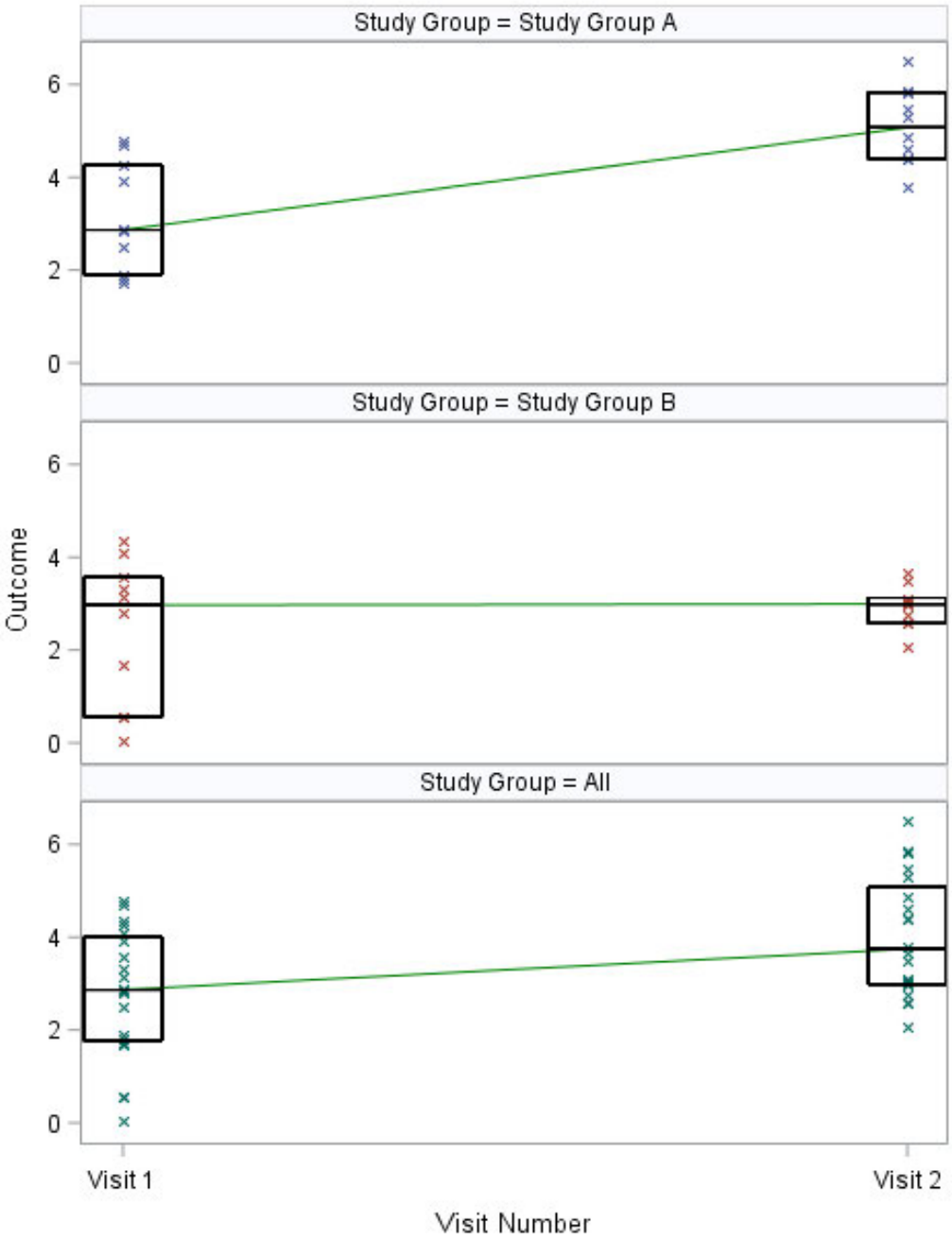
Figures with similar format:

Figure 11: Reverse Cumulative Distribution of LPS-specific IgA Titers Pre-Challenge by Time Point and Study Arm, Immunogenicity Population

Similar Figures *continued*

Figure 18: Box Plots of LPS-specific IgG ASC per 10^6 PBMC by Study Day and Study Arm, Immunogenicity Population

[Implementation Note: The GMT should be displayed in a single image file with separate panels for study arm. The x-axis should be labeled "Study Day" with measurements at baseline, and Day XX - XX. The y-axis should be labeled "Geometric Mean Titer". Include "[Outcome] assessed at any time prior to or during challenge period" footnote within image.]



Figures with similar format:

Figure 19: Box Plots of LPS-specific IgA ASC per 10^6 PBMC by Study Day and Study Arm, Immunogenicity Population

Figure 20: Box Plots of Invaplex-specific IgG ASC per 10^6 PBMC by Study Day and Study Arm, Immunogenicity Population

Figure 21: Box Plots of Invaplex-specific IgA ASC per 10^6 PBMC by Study Day and Study Arm, Immunogenicity Population

14.3.1.1 Solicited Adverse Events

Figure 22: Maximum Severity of Solicited Systemic Events Post-Vaccination Dose 1 per Participant by Study Day and Study Arm, Safety Population

[Implementation Note: A generic figure is shown below. A horizontal bar chart will be presented in 1 image file with separate panels for each study arm (5 panels for the post-vaccination dose 1 figure: one for each study arm and a combined group of all participants receiving placebo at the first product administration; 4 panels for all other figures; one for each study arm). Axes should be labeled as follows: y-axis label: Study Day, x-axis label: Percentage of Participants (%). The study arms should be indicated in the panel headers including "(N=X)", where N = the number of participants in the Safety Population who received the first study vaccination. Participants are counted at most once at the maximum severity across all systemic events reported for the specified time point]

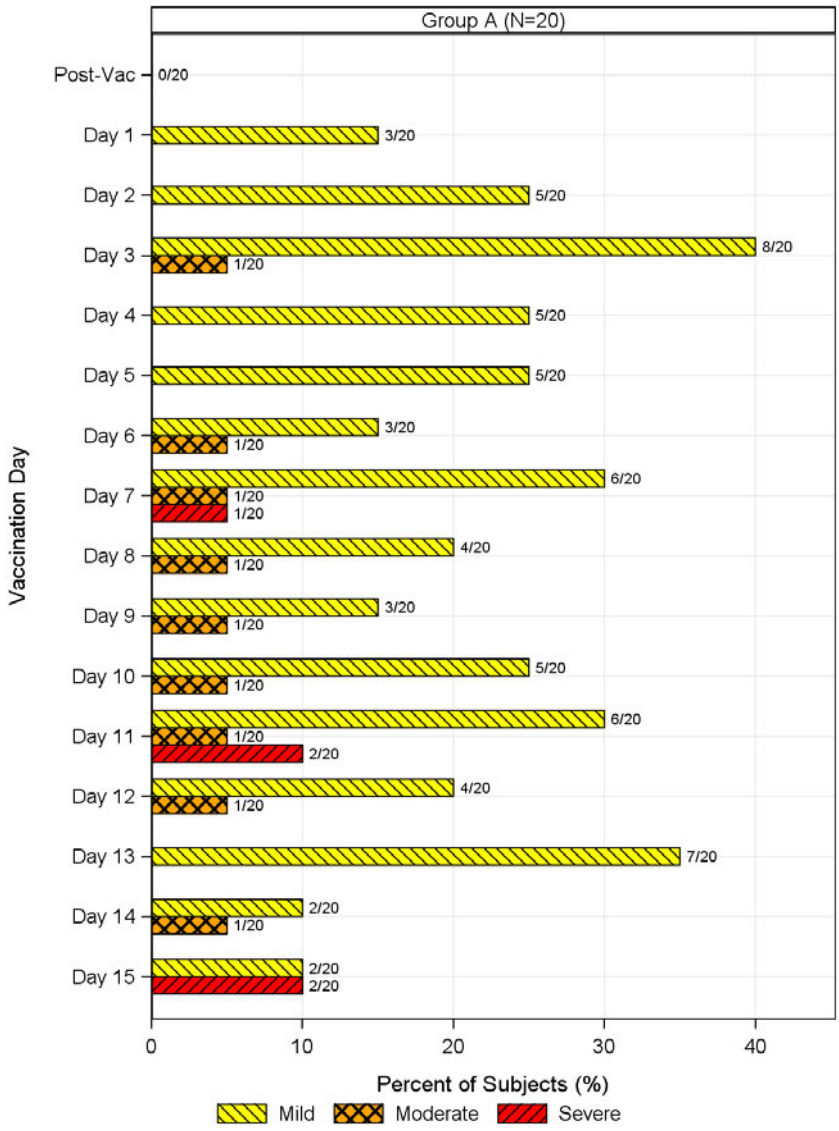


Figure with similar format:

Figure 23: Maximum Severity of Solicited Systemic Events Post-Vaccination Dose 2 per Participant by Study Day and Study Arm, Safety Population

14.3.1.2 Unsolicited Adverse Events

Figure 24: Frequency of Related Unsolicited Adverse Events Post-Vaccination Dose 1 by MedDRA System Organ Class, Maximum Severity, and Study Arm

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

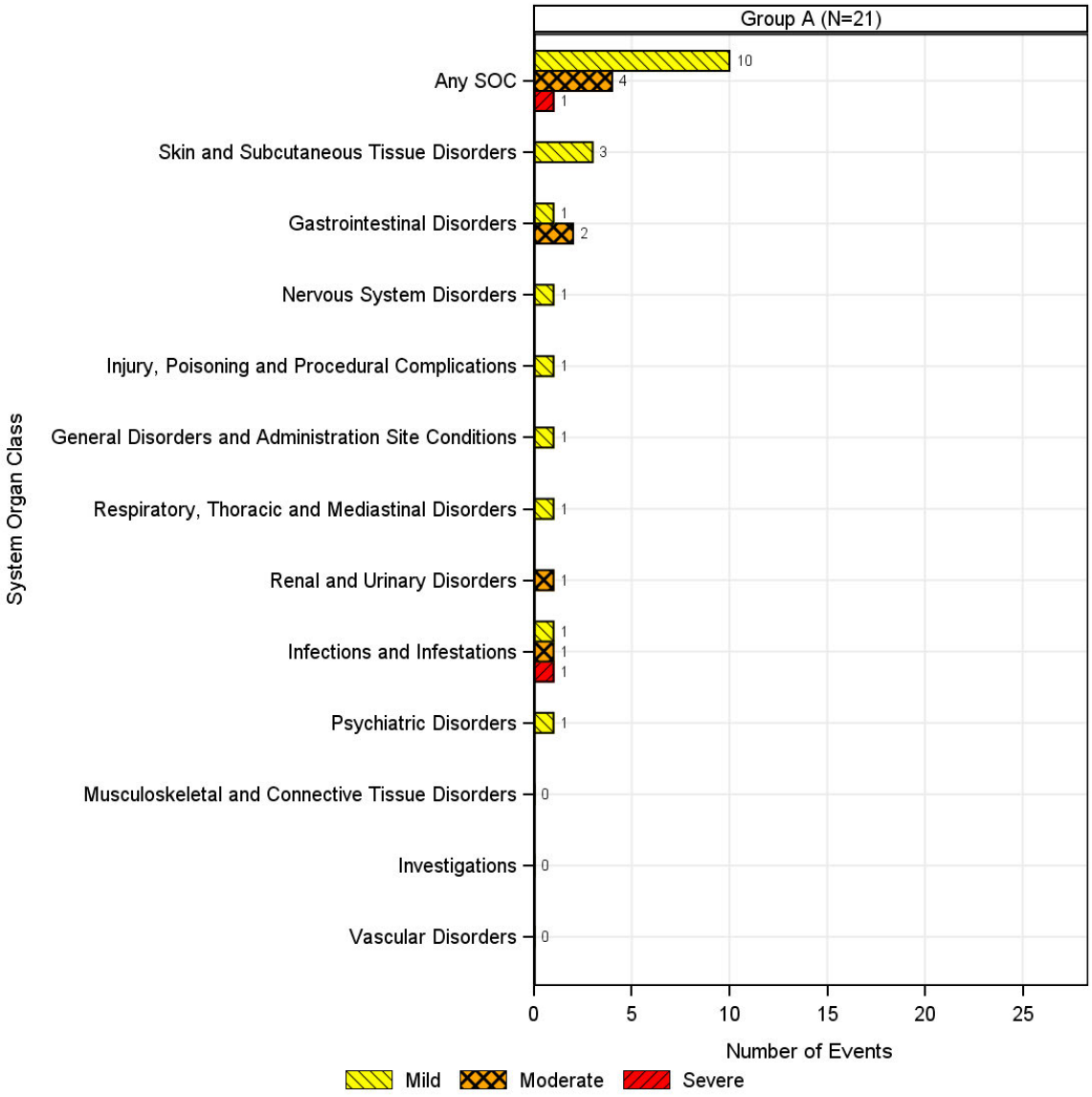


Figure with similar format:

Figure 25: Frequency of Related Unsolicited Adverse Events Post-Vaccination Dose 2 by MedDRA System Organ Class, Maximum Severity, and Study Arm

Figure 26: Incidence of Related Unsolicited Adverse Events Post-Vaccination Dose 1 by MedDRA System Organ Class, Maximum Severity, and Study Arm

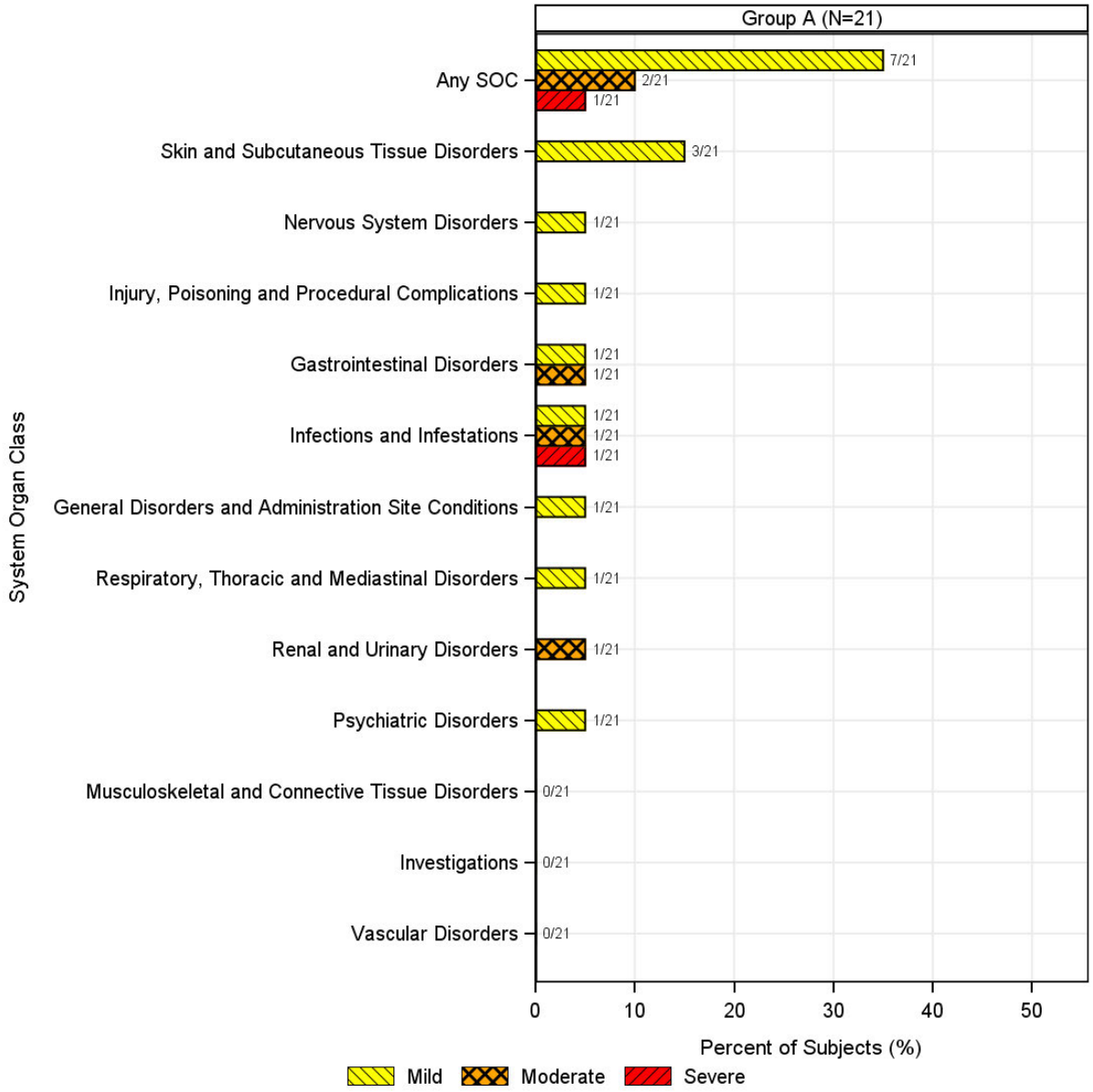


Figure with similar format:

Figure 27: Incidence of Related Unsolicited Adverse Events Post-Vaccination Dose 2 by MedDRA System Organ Class, Maximum Severity, and Study Arm

APPENDIX 3. LISTINGS MOCK-UPS

LIST OF LISTINGS

Listing 1: **16.1.6: Listing of Participants Receiving Investigational Product**

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

Randomized Study Arm	Participant ID	Study Vaccination 1 - Product Received	Study Vaccination 2 - Product Received

16.2 Database Listings by Participants

16.2.1 Discontinued Participants

Listing 2: 16.2.1: Early Terminations or Discontinued Participants

[Implementation Note: Category will be either "Early Termination" or "Treatment Discontinuation." In the "Reason" column, concatenate any "specify" fields, including AE number and DV number. In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Randomized Study Arm, Participant ID, alphabetically by Category (in the case a subject both terminates early and discontinues treatment).]

Randomized Study Arm	Study Product(s) Received	Participant ID	Category	Reason for Early Termination or Treatment Discontinuation	Study Day	Received Challenge?
			Early Termination			
			Treatment Discontinuation			

16.2.2 Protocol Deviations

Listing 3: 16.2.2.1: 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." The "Deviation Classification" column will contain values of "Major" or "Minor." In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Randomized Study Arm, Participant ID, DV Number.]

Randomized Study Arm	Study Product(s) Received	Participant ID	DV Number	Deviation	Deviation Category	Deviation Classification	Study Day	Reason for Deviation	Deviation Resulted in AE?	Deviation Resulted in Participant Termination?	Deviation Affected Product Stability?	Deviation Resolution	Comments

Listing 4: 16.2.2.2: 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." The "Deviation Classification" column will contain values of "Major" or "Minor." 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 Classification	Deviation Resolution	Comments

16.2.3 Participants Excluded from the Efficacy Analysis

Listing 5: 16.2.3: Participants Excluded from Analysis Populations

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

Randomized Study Arm	Study Product(s) Received	Participant ID	Analyses in which Participant is Included	Analyses from which Participant is Excluded	Results Available?	Reason Participant Excluded
			[e.g., Full, Safety, Immunogenicity Per Protocol]	[e.g., Full, Safety, Immunogenicity Per Protocol, Day x]		
Note: "Yes" in the "Results available" column indicates that available data were removed from the analysis. "No" indicates that no data were available for inclusion in the analysis.						

16.2.4 Demographic Data

Listing 6: 16.2.4.1: Demographics

[Implementation Note: If a participant is multi-racial, in "Race" column, note "Multiple: (list races, separated by a comma)." Sort order: Randomized Study Arm, Participant ID.]

Randomized Study Arm	Study Product(s) Received	Participant ID	Sex	Age at Enrollment (years)	Ethnicity	Race	BMI (kg/m^2)

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

[Implementation Note: "Condition Start Day" and "Condition End Day" are relative to enrollment (which is Day 1, day before enrollment is Day -1). If ongoing, display "Ongoing" in the "Condition End Day" column. Listing will be sorted by Randomized Study Arm, Participant ID, and MH Number]

Randomized Study Arm	Study Product(s) Received	Participant ID	MH Number	Medical History Term	Condition Start Day	Condition End Day	MedDRA System Organ Class	MedDRA Preferred Term

16.2.6 Individual Efficacy and Immunogenicity Response Data

Listing 8: 16.2.6.1: Solicited Symptoms of Shigellosis

[Implementation Note: To indicate severity for quantitative symptoms (e.g., temperature, measurements), include the grade in parentheses after the number, e.g., 100.7 (Mild). This listing includes baseline assessments in addition to post-treatment assessments. In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Randomized Study Arm, Participant ID, Dose Number, Post Challenge Day, Symptom.]

Randomized Study Arm	Study Product(s) Received	Participant ID	Post-Challenge Day	Symptom	Severity	Attributed to Alternate Etiology?[a]	Alternate Etiology

Notes:
[a] Grade 3 events only.

Listing 9: 16.2.6.2: Solicited Symptoms of Shigellosis – Stool Results

[Implementation Note: In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Listing should be sorted by Randomized Study Arm, Participant ID, Post- Challenge Day, Inpatient/Outpatient, Collection Time.]

Randomized Study Arm	Study Product(s) Received	Participant ID	Post-Challenge Day	Collection Time	Inpatient or Outpatient?	Consistency	Weight (g)	Visible Blood Present?	Comments

Listing 10: 16.2.6.3: Solicited Symptoms of Shigellosis – Emesis Results

[Implementation Note: In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Listing should be sorted by Study Arm, Participant ID, Post-Challenge Day, Inpatient/Outpatient, and Collection Time.]

Randomized Study Arm	Study Product(s) Received	Participant ID	Post-Challenge Day	Collection Time	Inpatient or Outpatient?	Volume (mL)	Comments

Listing 11: 16.2.6.4: Culture Results

[Implementation Note: Participant ID should be USUBJID (not PATID) for purposes of de-identification. Listing should be sorted by Randomized Study Arm, Participant ID, Planned Time Point.]

Randomized Study Arm	Study Product(s) Received	Participant ID	Planned Time Point	Actual Study Day	Hektoen Enteric Agar Culture Result	Slide Agglutination Assay Result

Listings with similar format:

Listing 12: 16.2.6.5: Immunoblot and PCR Assay Results

Listing 13: 16.2.6.6: LPS-specific and Invaplex-specific Serum IgG and IgA Assay Results

[Implementation Note: Participant ID should be USUBJID (not PATID) for purposes of de-identification. Listing should be sorted by Randomized Study Arm, Participant ID, Planned Time Point.]

Randomized Study Arm	Study Product(s) Received	Participant ID	Planned Time Point	Actual Study Day	LPS-specific				Invaplex-specific			
					IgG Titer	IgG Fold-Rise	IgA Titer	IgA Fold-Rise	IgG Titer	IgG Fold-Rise	IgA Titer	IgA Fold-Rise

Listings with similar format:

Listing 14: 16.2.6.7: LPS-specific and Invaplex-specific Fecal IgA and Total Fecal IgA Assay Results

Listing 15: 16.2.6.8: ELISpot Assay Results

[Implementation Note: Will include Total IgA and Total IgG assay results in addition to LPS-specific and Invaplex-specific results]

16.2.7 Adverse Events

Listing 16: 16.2.7.1: Solicited Events Post-Vaccination– Systemic Symptoms

[Implementation Note: To indicate severity for quantitative symptoms (e.g., temperature, measurements), include the grade in parentheses after the number, e.g., 100.7 (Mild). This listing includes baseline assessments in addition to post-treatment assessments. In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Randomized Study Arm, Participant ID, Dose Number, Post Dose Day, Symptom.]

Randomized Study Arm	Study Product(s) Received	Participant ID	Dose Number	Post-Dose Day	Assessment[a]	Symptom	Severity	Attributed to Alternate Etiology?[b]	Alternate Etiology
					MA				
					Clinic				

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

Listing 17: 16.2.7.2: Solicited Events Post-Vaccination – Stool Results

[Implementation Note: In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Listing should be sorted by Randomized Study Arm, Participant ID, Dose Number, Post-Dose Day, Collection Time.]

Randomized Study Arm	Study Product(s) Received	Participant ID	Dose Number	Post-Dose Day	Collection Time	Consistency	Weight (g)	Comments

Listing 18: 16.2.7.3: Solicited Events Post-Vaccination – Emesis Results

[Implementation Note: In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Listing should be sorted by Study Arm, Participant ID, Dose Number, Post-Dose Day, and Collection Time.]

Randomized Study Arm	Study Product(s) Received	Participant ID	Dose Number	Post-Dose Day	Collection Time	Volume (mL)	Comments

Listing 19: 16.2.7.4: 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. This listing includes all unsolicited adverse events. If there are no comments for an event, populate 'Comments' row with 'None'. In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Randomized Study Arm, Participant ID, Associated with Dose No., No. of Days Post Associated Dose. If the table will be multi-page, move the footnote/explanation to the footer so that it repeats for each page of the table.]

Adverse Event	Associated with Dose No.	No. of Days Post Associated Dose (Duration)	Severity	SAE?	Relationship to Study Treatment	In Not Related, Alternative Etiology	Action Taken with Study Treatment	Participant Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Randomized Study Arm: , Study Product(s) Received: , Participant ID: , AE Number:											
Comments:											
Randomized Study Arm: , Study Product(s) Received: , Participant ID: , AE Number:											
Comments:											
Note: For additional details about SAEs, see Section 14.3.2.											

16.2.8 Individual Laboratory Measurements

Listing 20: 16.2.8.1: Clinical Laboratory Results – Chemistry

[Implementation Note: These listings (for hematology and chemistry) include all laboratory results, scheduled and unscheduled. These listings are not color-coded, but the severity should be included in parentheses after the result for abnormal results, e.g., 16.2 (Mild). The "extra" fields that are completed for abnormal results are not included in this listing; they are included in the listing of abnormal laboratory results that is included in the table shells document. In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Randomized Study Arm, Participant ID, Laboratory Parameter, and Planned Time Point.]

Randomized Study Arm	Study Product(s) Received	Participant ID	Planned Time Point	Actual Study Day	Sex	Age (years)	Laboratory Parameter (Units)	Result (Severity Grade)	Reference Range Low	Reference Range High

Listing 21: 16.2.8.2: Clinical Laboratory Results – Hematology

Randomized Study Arm	Study Product(s) Received	Participant ID	Planned Time Point	Actual Study Day	Sex	Age (years)	Laboratory Parameter (Units)	Result (Severity Grade)	Reference Range Low	Reference Range High

Listing 22: 16.2.8.2: Clinical Laboratory Results – Urinalysis

Randomized Study Arm	Study Product(s) Received	Participant ID	Planned Time Point	Actual Study Day	Sex	Age (years)	Laboratory Parameter (Units)	Result (Severity Grade)

16.2.9 Vital Signs and Physical Exam Findings

Listing 23: 16.2.9.1: Vital Signs

[Implementation Note: This listing includes all vital sign assessments, scheduled and unscheduled. These listings are not color-coded, but the severity should be included in parentheses after the result for abnormal assessments, e.g., 100.7 (Mild). In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Randomized Study Arm, Participant ID, Vital Sign Parameter, Planned Time Point. Assessment Time.]

Randomized Study Arm	Study Product(s) Received	Participant ID	Planned Time Point	Actual Study Day	Assessment Time	Vital Sign Parameter (Units)	Result (Severity Grade)

Listing 24: 16.2.9.2: Physical Exam Findings

[Implementation Note: This listing includes all physical exam findings, scheduled and unscheduled. If a subject does not have any findings upon examination, they will not be included in this listing. If reported as an AE, display "Yes" with the AE Number in parentheses, e.g., "Yes (7)". In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Randomized Study Arm, Participant ID, Planned Time Point.]

Randomized Study Arm	Study Product(s) Received	Participant ID	Planned Time Point	Actual Study Day	Body System	Abnormal Finding	Reported as an AE? (AE Number)

16.2.10 Concomitant Medications

Listing 25: 16.2.10: Concomitant Medications

[Implementation Note: "Medication Start Day" and "Medication End Day" are relative to enrollment (which is Day 1, day before enrollment is Day -1). If ongoing, display "Ongoing" in the "Medication End Day" column. If taken for an AE or MH, display "Yes" with the AE or MH Number in parentheses, e.g., "Yes (5)". In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Randomized Study Arm, Participant ID, and CM Number.]

Randomized Study Arm	Study Product(s) Received	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)

16.2.11 Pregnancy Reports

Listing 26: 16.2.11.1: Pregnancy Reports – Maternal Information

[Implementation Note: Only include the "Pregnancy Number" column if a subject has more than 1 pregnancy. Date of Conception will be calculated based on estimated delivery date. BMI will be calculated based on pre-pregnancy height and weight. Mother's weight gain will be calculated based on pre-pregnancy weight and end of pregnancy weight. If a major congenital anomaly with previous pregnancy, display "Yes" and the text from the "specify" field, separated by a colon. If any substance use is reported, include a listing of substance use. If autopsy revealed an alternate etiology, display "Yes" and the text from the "specify" field, separated by a colon. If abnormality in product of conception, display "Yes" and the text from the "specify" field, separated by a colon. In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Study Arm, Participant ID, Pregnancy Number.]

Randomized Study Arm	Study Product(s) Received	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 27: 16.2.11.2: 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?**

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

Listing 28: 16.2.11.3: 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 29: 16.2.11.4: 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 30: 16.2.11.5: 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

APPENDIX 4. NCA TEMPLATE

Not applicable.