CLINICAL RESEARCH IN INFECTIOUS DISEASES

STATISTICAL ANALYSIS PLAN
for
DMID Protocol: 17-0010
Study Title:
A Phase 2A Partially-blind Placebo Controlled Trial to Evaluate the Safety and Immunogenicity of Live Attenuated, Intranasal *B. pertussis* vaccine (BPZE1) in Healthy Adults

NCT03541499

Version 1.0

DATE: 29-OCT-2019

STUDY TITLE

A Phase 2A Partially-blind Placebo Controlled Trial to Evaluate the Safety and Immunogenicity of Live Attenuated, Intranasal B. pertussis vaccine (BPZE1) in Healthy Adults

Protocol Number Code:	**DMID Protocol: 17-0010**
Development Phase:	Phase 2a
Products:	One dose (10^7 CFU or 10^9 CFU) of lyophilized, live-attenuated *Bordetella pertussis* vaccine (BPZE1) manufactured by [redacted]
Form/Route:	Intranasal
Indication Studied:	*B. pertussis*
Sponsor:	Division of Microbiology and Infectious Diseases National Institute of Allergy and Infectious Diseases National Institutes of Health
Clinical Trial Initiation Date:	14SEP2018
Clinical Trial Completion Date:	15MAY2020
Date of the Analysis Plan:	29OCT2019
Version Number:	1.0

This study was performed in compliance with Good Clinical Practice.

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LIST OF ABBREVIATIONS

AE	Adverse Event
AESI	Adverse Event of Special Interest
ALT	Alanine Aminotransferase
aPV	Acellular Pertussis Vaccine
BP	Blood Pressure
BPZE1	Live Attenuated, Intranasal B. pertussis vaccine
C	Celsius
CFU	Colony Forming Units
CI	Confidence Interval
CRF	Case Report Form
CSR	Clinical Study Report
Desc.	Description
dL	Deciliter
DMID	Division of Microbiology and Infectious Diseases
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
ELISA	Enzyme-linked Immunosorbent Assay
F	Fahrenheit
FHA	Filamentous Hemagglutinin
FIM	Fimbriae
GMT	Geometric Mean Titer
GMFR	Geometric Mean Fold Rise
Hgb	Hemoglobin
HIV	Human Immunodeficiency Virus
ICH	International Conference on Harmonisation
ITT	Intention to Treat
MedDRA	Medical Dictionary for Regulatory Activities
MedDRA PT	MedDRA Preferred Term
mg	Milligram
mL	Milliliter
N	Number (typically refers to subjects)

List of Abbreviations *(continued)*

NIH	National Institutes of Health
NOCMCs	New Onset Chronic Medical Conditions
PP	Per Protocol
PRN	Pertactin
PT	Pertussis Toxin
RCD	Reverse Cumulative Distribution
SAE	Serious Adverse Event
SD	Standard Deviation
SDCC	Statistical and Data Coordinating Center
SMC	Safety Monitoring Committee
SOC	System Organ Class
VUMC	Vanderbilt University Medical Center
U	Units
µL	Microliter
WBC	White Blood Cell
WHO	World Health Organization
wPV	Whole Cell Pertussis Vaccine

1. PREFACE

The Statistical Analysis Plan (SAP) for "A Phase 2A Partially-blind Placebo Controlled Trial to Evaluate the Safety and Immunogenicity of Live Attenuated, Intranasal *B. pertussis* vaccine (BPZE1) in Healthy Adults" (DMID Protocol 17-0010) describes and expands upon the statistical information presented in the protocol.

This document describes all planned analyses and provides reasons and justifications for these analyses. It also includes sample tables, listings, and figures planned for the final analyses. Regarding the final analyses and Clinical Study Report (CSR), this SAP follows the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Guidelines, as indicated in Topic E3 (Structure and Content of Clinical Study Reports), and more generally is consistent with Topic E8 (General Considerations for Clinical Trials) and Topic E9 (Statistical Principles for Clinical Trials). 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 a review of the study design, general statistical considerations, comprehensive statistical analysis methods for efficacy and safety outcomes, and a list of proposed tables and figures. Within the table, figure, and listing mock-ups (Appendices 1, 2, and 3), references to CSR sections are included. Any deviation from this SAP will be described and justified 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

Bordetella pertussis (*B. pertussis*) is a gram-negative bacterium and a causative agent of pertussis colonizing infection, a precursor to the disease more commonly known as whooping cough. A recent publication modeling pertussis cases and deaths estimated there were 24.1 million pertussis cases and 160,700 deaths in children younger than 5 years in 2014 worldwide.[1] Despite the dramatic decline in Whooping Cough cases and deaths in industrialized nations during the 20th Century due to public health vaccine initiatives, recent decades have witnessed a sharp increase in cases.

Two types of pertussis vaccines are available worldwide: whole cell Pertussis vaccine (wPV) and acellular Pertussis vaccine (aPV). Although aPV overcomes several potential adverse effects of wPV (e.g. fever and seizures) and is the only pertussis vaccine marketed in the U.S., the protective efficacy of aPV appears to be lower than wPV with induced immunity waning in about 4-12 years. Additionally, the high cost of aPV limits its use in developing countries.

Acellular pertussis vaccines (aPVs have several deficiencies that have contributed to pertussis outbreaks across the US and around the world. Young infants are especially vulnerable but are not fully protected until they complete a 3 dose aPV vaccination series, at about 7 months of age. Preclinical baboon studies suggest that aPV does not prevent nasopharyngeal colonization and, hence, does not prevent transmission from adults and adolescents to vulnerable infants.[2] Multiple published studies in various countries have demonstrated high rates of subclinical (asymptomatic) *B. pertussis* colonizing infections. [3-6]. Mathematical models predict that asymptomatic *B. pertussis* colonization is the most probable cause of the surge in pertussis rates. [7] Thus, a need exists for an adult and adolescent vaccine that induces potent and durable systemic immunity, but also mucosal immunity to prevent nasopharyngeal colonization and transmission to infants.

Since the best-known method of inducing both potent systemic and mucosal immunity is by natural *B. pertussis* infection, BPZE1 was constructed through [redacted]. Over 20 peer-reviewed publications have demonstrated the preclinical safety and efficacy of the live-attenuated vaccine [8-11], and two Phase 1 clinical studies [12, 13] have demonstrated safety and immunogenicity at various doses in healthy adults.

The investigational BPZE1 [redacted] Preclinical studies showed no safety concerns.[14] [redacted]

The main advantage of the lyophilized BPZE1 formulation over the liquid formulation is long-term stability and storage at refrigeration temperature instead of storage at very low freezing temperature. The primary purpose of this Phase 2a study is to evaluate the safety and immunogenicity of the lyophilized formulation. The hypothesis for this trial is that lyophilized BPZE1, administered intranasally, will be sufficiently safe and immunogenic.

2.1. Purpose of the Analyses

These analyses will assess the safety, tolerability, immunogenicity, and nasal clearance of a single intranasal dose of either 10^7 or 10^9 colony forming units (CFU) of lyophilized BPZE1 vaccine. The protocol for DMID 17-0010 calls for a planned preliminary analysis on safety, immunogenicity, and B. pertussis colonization data through Day 46 (or Day 29 if no subjects remain colonized with B. pertussis at the Day 29 visit). The preliminary report may be made available to DMID and the vaccine company partner and to the lead principal investigator for planning subsequent trials. Interim analyses will not be used to make any decisions concerning the conduct of this trial. This Statistical Analysis Plan encompasses the analyses to be included in the preliminary report and final CSR.

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives

3.1.1. Primary Objective

- To assess the safety and tolerability of a single intranasal dose of either 10^7 or 10^9 colony forming units (CFU) of lyophilized BPZE1 vaccine.

3.1.2. Secondary Objectives

- To assess the humoral immunogenicity of lyophilized BPZE1 vaccine at Day 15, Day 29 and Day 181 following receipt of one intranasal dose of 10^7 or 10^9 CFU of BPZE1.
- To assess mucosal immunogenicity of lyophilized BPZE1 vaccine at Day 29 and Day 181 following receipt of one intranasal dose of 10^7 or 10^9 CFU of BPZE1.
- To evaluate nasal clearance of BPZE1 by culture at Day 29 (and if still positive, at Day 46) following receipt of one intranasal dose of lyophilized BPZE1 vaccine of 10^7 or 10^9 CFU of BPZE1.

3.2. Endpoints

3.2.1. Primary Outcome Measures

- Occurrence of solicited local and systemic reactogenicity from the time of the study vaccination through 14 days post-vaccination
- Occurrence of unsolicited non-serious adverse events from the time of the study vaccination through 28 days post-vaccination
- Occurrence of serious adverse events (SAEs) and new onset chronic medical conditions (NOCMCs) from the time of the study vaccination through approximately Day 181 post vaccination
- Occurrence of adverse events of special interest through approximately Day 29 post vaccination

3.2.2. Secondary Outcome Measures

Humoral Immune Response

- Geometric mean titers (GMTs) by serum IgG and IgA ELISA to PT, FHA, PRN, FIM 2/3 on Days 1, 15, 29, and 181
- Geometric mean fold rise (GMFR) by serum IgG and IgA ELISA to PT, FHA, PRN, FIM 2/3 on Days 15, 29 and 181 relative to baseline (Day 1)
- The proportion of subjects that achieve seroconversion (defined as ≥2-fold rise from baseline) to individual pertussis antigens (PT, FHA, PRN, and FIM 2/3) by serum IgG or IgA ELISA at Days 15, 29, 181 or any time point relative to baseline (Day 1)
- Proportion of subjects achieving seroconversion (serum IgG or IgA ELISA) to one or more pertussis antigens at Days 15, 29, 181 or any time point, relative to baseline (Day 1)

- Proportion of subjects achieving seroconversion (serum IgG/IgA ELISA) to two or more pertussis antigens at Days 15, 29, 181 or any time point, relative to baseline (Day 1)

Mucosal Immune Response

- Geometric mean titer ratios (GMTRs) and ratio of antigen-specific IgA ELISA (PT-IgA, FHA-IgA, PRN-IgA, FIM-IgA) to total IgA by nasal aspirate at screening, and Days 29 and 181.
- Fold rise of the ratio of antigen-specific IgA (PT-IgA, FHA-IgA, PRN-IgA, FIM-IgA) to total IgA by nasal aspirate from the screening visit to Days 29 and 181
- The proportion of subjects that achieve seroconversion (defined as ≥2-fold rise of the ratio from baseline) to individual pertussis antigens (PT, FHA, PRN, and FIM 2/3) by nasal aspirate IgA ELISA at Days 29 and 181 or any time point relative to baseline (screening)
- Proportion of subjects that achieve seroconversion (≥2-fold rise of the ratio from baseline) to at least 1 antigen (PT, FHA, PRN, or FIM 2/3) by nasal aspirate IgA ELISA from the screening visit to Days 29 and/or 181.

Nasal Clearance

- Proportion of subjects with detectable B. pertussis from nasopharyngeal cultures at Day 29.
- For those who remain positive at Day 29, the subjects with detectable B. pertussis at Day 46 will also be evaluated and reported. Detection of B. pertussis in culture will be assumed to be due to study-product administration.

3.3. Study Definitions and Derived Variables

New Onset Chronic Medical Conditions (NOCMCs) will be defined as new medical conditions, not present at the time of screening or enrollment, that require ongoing medical care and intervention.

Achievement of seroconversion based on humoral response will be defined as a ≥2-fold rise from baseline. Achievement of seroconversion based on mucosal response will be defined as a ≥2-fold rise the ratio of antigen-specific IgA ELISA (PT-IgA, FHA-IgA, PRN-IgA, FIM-IgA) to total IgA by nasal aspirate from baseline.

Medically Significant Wheezing will be defined as clinician (licensed to make medical diagnoses) documented wheezing on PE accompanied by any one or more of the following: Respiratory distress (tachypnea, retractions or dyspnea), Hypoxemia (O2 saturation <95%), new prescription, or use of daily bronchodilator therapy (not on an “as needed” basis).

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

This is a phase 2a, single center, randomized, partially blind (i.e. the method of vaccination will be known), placebo controlled, clinical trial in which 50 healthy males and non-pregnant females 18-49 years of age who meet all eligibility criteria receive either BPZE1 10^7 CFU administered via VaxINator: BPZE1 10^9 CFU administered via VaxINator: placebo administered via VaxINator: BPZE1 10^9 CFU administered via Needleless Tuberculin Syringe, randomized in a 3:3:3:1 ratio. Subjects will be screened by medical history, physical exam, and clinical laboratory tests, including a urine or serum pregnancy test for women of childbearing potential. A schematic of the study design is presented in Figure 1.

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

This study is designed to obtain preliminary estimates of the safety and immune response induced by the BPZE1 lyophilized vaccine. Fifteen placebo recipients are included in order to partially blind the subjects and observer.

4.3. Selection of Study Population

The study population for DMID protocol 17-0010 is males and non-pregnant females, 18 to 49 years old, inclusive, who are in good health and meet all eligibility criteria. Potential subjects will be screened from the general population at VUMC by history, physical exam, clinical laboratory tests including White Blood Cells (WBC), Hemoglobin (Hgb), platelets, serum IgG antibodies, alanine aminotransferase (ALT), Creatinine, and Human Immunodeficiency Virus (HIV), and a urine or serum pregnancy test. Potential subjects with close contact, defined as sharing a household, serving as a healthcare worker, or working professionally in settings with repeated exposures, with children less than 1 year of age or with persons with known immunocompromising conditions will be excluded. Otherwise eligible potential subjects experiencing an acute illness, including temperature >100˚F, will be eligible for postponed enrollment within the screening window or rescreening once symptoms resolve.

4.4. Treatments

4.4.1. Treatments Administered

Subjects are administered one dose (either 10^7 CFU or 10^9 CFU) of lyophilized, live-attenuated *Bordetella pertussis* vaccine (BPZE1) or placebo.

4.4.2. Identity of Investigational Product(s)

The investigational BPZE1 lyophilized vaccine is for nasal administration and contains [redacted] The placebo consists of the same constituents in the same quantities as the BPZE1 investigational vaccines, absent the [redacted]. Both were provided by [redacted].

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

Enrollment/randomization will be performed through the enrollment module in the electronic data capture system, maintained by the SDCC. Eligible subjects will be randomized and assigned in a 3:3:3:1 ratio to BPZE1 10^7 CFU administered via VaxINator: BPZE1 10^9 CFU administered via VaxINator: placebo

administered via VaxINator: BPZE1 10^9 CFU administered via Needleless Tuberculin Syringe. The randomization is based on a block scheme to provide an approximately balanced allocation to the treatment groups during the study.

4.4.4. Selection of Doses in the Study

In a Phase 1a clinical study, a dose of 10^7 CFU of the liquid formulation of BPZE1 administered nasally resulted in colonization of the mucosal surface in 42% of subjects with no serious adverse events. [12] In a Phase 1b clinical study, also using the liquid formulation administered nasally, but in a greater volume (400 µL per nostril), doses of 10^7, 10^8, and 10^9 CFU all resulted in colonization in ≥75% of subjects with faster colonization rate and faster clearance rate being correlated with higher dosage. [13] No serious adverse events were observed in any of the dosage groups and there were no detectable differences in adverse events between dosage groups. The lyophilized formulation is hypothesized to share similar safety characteristics with the liquid formulation.

4.4.5. Selection and Timing of Dose for Each Subject

Subjects are assigned randomly to treatment groups in a 3:3:3:1 ratio (BPZE1 10^7 CFU administered via VaxINator: BPZE1 10^9 CFU administered via VaxINator: placebo administered via VaxINator: BPZE1 10^9 CFU administered via needleless tuberculin syringe). Each subject will receive a single intranasal dose in clinic on Day 1. Timing of dose is not specified.

4.4.6. Blinding

This is a partially-blind clinical trial as the method of immunization (i.e. VaxINator vs. needleless syringe) will be known. After reconstitution and transfer to a 1-mL syringe, the 10^7 CFU dose investigational vaccine and the placebo are transparent and indistinguishable while the 10^9 CFU dose can be discriminated from the placebo and the 10^7 CFU dose due to its opaque appearance. Therefore, syringes will be wrapped with a colored sleeve to avoid potential unblinding of study personnel or the subject. Investigators, the subject, and study personnel will remain blinded to allocation of BPZE1 or placebo.

The randomization scheme will be generated by the SDCC and provided to unblinded study personnel (i.e., research pharmacists performing study vaccination preparations and unblinded study vaccine administrators) at the participating VTEU site.

The unblinded study vaccine administrator is a study personnel member credentialed to administer vaccines and may also participate in dose preparation but will not be involved in study-related assessments or have subject contact for data collection following study vaccine administration. Laboratory personnel performing immunogenicity assays will be blinded to study assignment.

Upon request by the participating VTEU site, and at the discretion of DMID, unmasking may occur after all data have been locked at Day 181, analyzed, interpreted, and the final CSR has been completed. The Safety Monitoring Committee (SMC) may receive data in aggregate and presented by treatment arm. The SMC may also be provided with expected and observed rates of the expected AEs in an unblinded fashion and may request the treatment arm be unblinded for an individual subject if required for safety assessment. The SMC will review grouped and unblinded data in the closed session only.

4.4.7. Prior and Concomitant Therapy

Administration of medications, therapies, or vaccines will be recorded on the appropriate data collection form. Concomitant medications will include all current medications and medications taken within 30 days prior to

signing the informed consent form through approximately 28 days after study vaccination (or through the early termination visit if prior to that time). Prescription and over-the-counter drugs will be included, as well as herbals, vitamins and supplements. In addition, receipt of non-study vaccines will be solicited through approximately 181 days after study vaccination and reported in the eCRF.

4.4.8. Treatment Compliance

Subject compliance is not expected to be an issue because all subjects are to receive a single dose of study product administered in the clinic by a study personnel member who is unblinded to subject treatment assignment.

4.5. Efficacy (Immunogenicity) and Safety Variables

See Table 1 and Table 2for a schedule of study procedures.

4.5.1. Safety Variables

Safety will be assessed by the frequency and severity of:

1. Serious adverse events (SAE) occurring from the time of vaccination through approximately 6 months after vaccination.
2. Solicited Adverse Events – reactogenicity events occurring from the time of each study vaccination through 14 days after study vaccination:
   - **a.** Mucosal reactions including runny nose, stuffy nose/congestion, nasal pain/irritation, epistaxis, sneezing, sinus pressure/pain, sore throat, cough, and shortness of breath, cough, rhinorrhea, and sneezing
   - **b.** Systemic reactions including fever, chills, fatigue, malaise, myalgia, arthralgia, headache, and hypersensitivity.
3. Unsolicited Adverse Events – study vaccine-related non-serious adverse events occurring from the time of study vaccination through approximately 28 days after study vaccination.
4. New onset chronic medical conditions (NOCMCs) and adverse events of special interest (AESI) – NOCMC's will be assessed throughout the follow-up period, while medically attended wheezing events (an AESI) will be collected through Day 29 post-vaccination.

4.5.2. Immunogenicity Variables

Humoral immune response will be assessed from venous blood samples collected at screening and on Days 1, 15, 29, and 181

Mucosal immune response will be determined by ELISA on specimens collected by nasal wick at screening for baseline immunology and again on Day 29 and Day 181.

Immunogenicity will be assessed by the Vanderbilt Vaccine Research Program Laboratory.

4.5.3. Nasal Clearance Variables

Nasal clearance of *B. pertussis* will be determined by culture on specimens collected by nasal swab. The nasopharyngeal culture result will be reported as a binary outcome (i.e. bacteria detected / no bacteria detected) at Day 29 and Day 46 for subjects who remained positive at Day 29.

5. SAMPLE SIZE CONSIDERATIONS

This study is planned to enroll approximately 50 healthy adults randomized into four treatment groups in a 3:3:3:1 ratio, as described in Section 4.4.3. Table 3 and Table 4 in the appendices describe the probability of observing safety events and the minimum detectable difference in seroconversion rates for the planned sample size.

Table 3 indicates the probability of observing one or more safety events (such as solicited local or systemic reactogenicity events, or an unsolicited non-serious AE of a particular type) for a treatment arm with the assumed event frequency and for the given sample size. For example, for any of the treatment arms with a sample size of 15 subjects, there is a 79.4% probability of detecting an AE that occurs at a frequency of 10%, and a 14% probability if the AE occurs at a rate of 1%.

One of the secondary outcome measures is the proportion of subjects that achieve seroconversion to individual pertussis antigens (PT, FHA, PRN, and FIM 2/3) by serum IgG or IgA ELISA at Days 15, 29 and 181 for humoral immune response. Table 4 shows the minimum detectable differences with 80% power between the proportion of subjects attaining seroconversion in the BPZE1 by VaxINator group versus Placebo using a two-sided Fisher's Exact test and alpha = 0.05.

6. GENERAL STATISTICAL CONSIDERATIONS

6.1. General Principles

Unless otherwise noted, all continuous variables will be summarized using the following descriptive statistics: n (non-missing sample size), mean, standard deviation, median, maximum and minimum. The frequency and percentages (based on the non-missing sample size) of observed levels will be reported for all categorical measures. In general, all data will be listed, sorted by treatment group and subject, and when appropriate by visit number within subject. All summary tables will be structured with a column for each treatment in the order (BPZE1 10^7 CFU administered via VaxINator, BPZE1 10^9 CFU administered via VaxINator, BPZE1 10^9 CFU administered via needleless tuberculin syringe, placebo administered via VaxINator) and will be annotated with the total population size relevant to that table/treatment, including any missing observations.

6.2. Timing of Analyses

- The preliminary safety and immunogenicity analysis will be performed when all safety, reactogenicity, immunogenicity and *B. pertussi*s colonization data through Day 46 (or Day 29 if no subjects remain colonized with *B. pertussis* at Day 29) are available.
- The final analysis will be performed after all clinical, safety, and reactogenicity data through approximately 180 days after the study vaccination are available. Once the last subject completes the last visit, the final clinical database will be cleaned, monitored and locked. Unblinded analyses of safety, reactogenicity, colonization, and available immunogenicity data will then be performed by the SDCC and will be included in the CSR.

6.3. Analysis Populations

Summaries and analysis of safety data will be presented for the Safety Population. Summaries and analysis of immunogenicity data will be presented for the Immunogenicity Population. If there are major protocol deviations, a per-protocol (PP) analysis may also be performed. Summaries and analysis of nasal colonization data will be presented for the PP Population. A tabular listing of all subjects, visits, and observations excluded from the analysis populations will be provided in the CSR (Listing 4, Appendix 16.2.3).

6.3.1. Safety Population

The Safety Population will consist of all subjects who have received the study vaccine and for whom any data on safety are available. Subjects will be classified according to the treatment received. The primary safety analysis will be done on this population.

6.3.2. Immunogenicity Population

The Immunogenicity Population will include all subjects who have received the study vaccination and contributed both pre-vaccination samples and either at least one post vaccination sample for humoral immunogenicity testing for which valid results were reported, or at least one post vaccination nasal sample for which valid results were reported. Subjects will be classified according to the treatment received.

6.3.3. Per Protocol Population

The Per Protocol (PP) Population will include all subjects in the immunogenicity population, with the following exclusions:

- Data from all available visits for subjects found to be ineligible at baseline.
- Data from all visits subsequent to major protocol deviations, such as:
  - Receipt of non-study licensed live vaccine within 30 days before or after the study vaccination,
  - Receipt of non-study licensed inactivated vaccine within 14 days before or after the study vaccination,
  - Receipt of immunosuppressive therapy (e.g., corticosteroids) within 30 days before or after the study vaccination.
- Data from any visit that occurs substantially out of window. Whether a visit that occurs substantially out of window will be determined jointly by the principal investigator, the Sponsor, and the SDCC.

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

6.4. Covariates and Subgroups

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

6.5. Missing Data

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

6.6. Interim Analyses and Data Monitoring

Interim analyses would only be used to terminate this trial in the event that unanticipated safety events deemed to be of sufficient concern require such action by the sponsor. These interim assessments will not be made based on testing a formal statistical hypothesis; therefore, p-value adjustment will not be made to any analyses.

6.6.1. Interim Safety Review

An ISM and SMC will be convened by DMID to review study progress and participant, clinical, safety, and reactogenicity data. An interim safety review may include enrollment and demographic information, medical history, concomitant medications, physical assessments, clinical laboratory values, dosing compliance, solicited and unsolicited AE/SAEs, and *B. pertussis* colonization data. Additional data may be requested by the SMC, and interim statistical reports may be generated as deemed necessary and appropriate by DMID. The SMC may receive data in aggregate and presented by treatment arm, including expected and observed rates of the expected AEs. The SMC will review grouped data in the closed session only. The SMC will meet and review this data at scheduled time points or ad hoc as needed during this trial as defined in the SMC charter. As an outcome of each review/meeting, the SMC will make a recommendation as to the advisability of proceeding with study vaccinations (as applicable), and to continue, modify, or terminate this trial.

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

A preliminary report prepared with data through Day 46 (or Day 29 if no subjects remain colonized with *B. pertussis* at the Day 29 visit) will be prepared. This report will include analyses of safety and immunogenicity data.

6.6.2. Interim Immunogenicity Review

A preliminary report of safety and immunogenicity and *B. pertussis* colonization data through Day 46 (or Day 29 if no subjects remain colonized with *B. pertussis* at the Day 29 visit) will be prepared. The analyses presented in this report will be released while subjects remain in the trial for long-term safety and immunogenicity follow-up and will be included in the final analysis of these data.

6.7. Multicenter Studies

Not applicable. This study will take place at a single VTEU site.

6.8. Multiple Comparisons/Multiplicity

This study was not designed to test any specific null hypothesis, and as such no adjustments for multiple testing are planned.

7. STUDY SUBJECTS

7.1. Disposition of Subjects

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

The composition of analysis populations, including reasons for subject exclusion, by treatment arm, is presented in Table 11. A listing of subjects excluded from each analysis population will be presented in Listing 4.

The disposition of subjects in the study will be tabulated by treatment group (Table 10). The table shows the total number of subjects screened, enrolled, receiving study product, completing the Day 8 visit, completing the Day 15 reactogenicity period, completing the Day 29 blood draw, terminated from study follow-up, and the number who completed the study.

A flowchart showing the disposition of study subjects, adapted from the CONSORT Statement [15] will be included (Figure 2). This figure will present the number of subjects screened, enrolled, lost to follow-up, and analyzed, by treatment arm.

A listing of subjects who terminated from study follow-up and the reason will be included in Listing 1.

7.2. Protocol Deviations

A summary of subject-specific protocol deviations will be presented by the deviation category, deviation type, and treatment group for all enrolled subjects (Table 5.) Deviations that are considered major deviations that will be reviewed for possible subject exclusion from the per protocol population include: deviations related to eligibility/enrollment, treatment administration schedule, follow-up visit schedule, and study product or specimen temperature excursions. All subject-specific protocol deviations and non-subject specific protocol deviations will be included in Appendix 3 as data listings (Listing 2 and Listing 3, respectively.)

8. EFFICACY EVALUATION

This study was not designed to test a specific null hypothesis, rather the primary objectives included assessing the safety and tolerability of lyophilized BPZE1 vaccine.

8.1. Secondary Immunogenicity Analysis

Summaries and analysis of immunogenicity data will be presented for the immunogenicity and PP populations by treatment group.

Immune responses in terms of toxin-specific serum IgG and IgA antibody titers (PT, FHA, PRN, FIM 2/3) will be summarized at each time point. Analyses will include the Geometric Mean Titers (GMTs) along with corresponding 95% confidence intervals (Table 17, Table 18, Table 19, and Table 20) and Geometric Mean Fold Rise (GMFR) (Table 21, Table 22, Table 23, and Table 24), as well as the proportion of subjects achieving seroconversion (defined as 2-fold increase over baseline of GMT) for each antigen (PT, FHA, PRN, and FIM 2/3) and the proportion of subjects that achieved seroconversion for ≥ 1 (Table 25 and Table 26) and ≥ 2 (Table 27 and Table 28) antigens (PT, FHA, PRN, and FIM 2/3.) Rates of seroconversion will be compared using Barnard's exact test. Reverse cumulative distributions (RCD) curves will also be presented for PT, FHA, PRN, and FIM 2/3 antibody titers. Plots for each assay will be generated with four panels (pre-vaccination, Day 15, Day 29, and Day 181), and separate curves within each panel for each treatment group, as shown in Figure 3, Figure 4, Figure 5, and Figure 6. Individual immunogenicity response data will also be presented (Listing 7 and Listing 8.)

Immune responses in terms of the ratio of toxin-specific (PT, FHA, PRN, FIM 2/3) nasal mucosal IgA antibody to total nasal mucosal IgA antibody will be summarized at each time point (Table 29 and Table 30.) Analyses will include the geometric mean titer ratios (GMTR) of antigen-specific IgA to total IgA and corresponding 95% confidence intervals, along with fold change of the GMTR from baseline. The proportion of subjects achieving seroconversion, defined as ≥2-fold rise of the GMTR from baseline, to each antigen (PT, FHA, PRN, and FIM 2/3) will be reported (Table 29 and Table 30) as well as the proportion of subjects that achieve seroconversion by nasal aspirate ELISA to one or more (Table 31 and Table 32) antigens (PT, FHA, PRN, and FIM 2/3) at either or both of Day 29 and Day 181. Rates of seroconversion will be compared using Barnard's exact test. Reverse cumulative distributions (RCD) curves will also be presented for mucosal PT, FHA, PRN, and FIM 2/3 antibody titers. Plots for each assay will be generated with three panels (pre-vaccination, Day 15, Day 29, and Day 181), and separate curves within each panel for each treatment group, as shown in Figure 7 and Figure 8. Individual immunogenicity response data will also be presented (Listing 9.)

Subjects will be tested for *B. pertussis* colonization by culture at Day 29 and, if positive, again at Day 46. The proportion of subjects with positive *B. pertussis* culture will be reported for the PP population at each time point with corresponding 95% confidence intervals (Table 33.) Individual nasal colonization data will also be presented (Listing 13.)

No formal hypothesis testing is planned.

9. SAFETY EVALUATION

All summaries and analysis of safety data will be presented for the Safety Analysis Population. Safety summaries will be presented overall and by treatment group.

Listings will be sorted by treatment group, subject ID, parameter (if applicable), and visit.

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

9.1. Demographic and Other Baseline Characteristics

Summaries of age, sex, ethnicity, and race will be presented by treatment group and overall (Table 14 and Table 15.) Ethnicity is categorized as Hispanic or Latino, or not Hispanic and not Latino. In accordance with NIH reporting policy, subjects may self-designate as belonging to more than one race or may refuse to identify a race, the latter reflected in the CRF as "No" to each racial option.

Individual subject listings (Appendix 3) will be presented for all demographics (Listing 5;) pre-existing medical conditions (Listing 6;) vital signs and oral temperature (Listing 16;) and concomitant medications (Listing 18.)

9.1.1. Prior and Concurrent Medical Conditions

All current illnesses and pre-existing medical conditions will be MedDRA® coded using MedDRA dictionary version 21.0 or higher. Summaries of subjects' pre-existing medical conditions will be presented by treatment group (Table 16.) Individual subject listings will be presented for all medical conditions (Listing 6.)

9.1.2. Prior and Concomitant Medications

During screening, medications and vaccines used up to 30 days prior will be solicited. Any medications used within 30 days prior to signing the informed consent form through 28 days after study vaccination (or early termination if prior to 28 days after study vaccination) will be recorded in the eCRFs. In addition, receipt of non-study vaccines will be solicited through approximately 28 days after study vaccination and recorded in the eCRFs.

Summaries of medications that were started prior to dosing and continuing at the time of dosing will be presented by WHO Drug Terms 2 and 3 and treatment group (Table 80.)

Individual subject listings will be presented for all concomitant medications (Listing 18.)

9.2. Measurements of Treatment Compliance

Any subjects who are enrolled but not vaccinated will be presented by treatment group as part of the subject disposition table (Table 10.) Dates of treatment administration by treatment arm are presented in Table 12.)

9.3. Adverse Events

When calculating the incidence of adverse events (i.e., on a per subject basis), each subject will only be counted once and any repetitions of adverse events within a subject will be ignored; the denominator will be

the total number of subjects in the safety population. All adverse events reported will be included in the summaries and analyses.

An overall summary of adverse events is presented in Table 34. Unsolicited adverse events occurring in more than 5% of subjects in any treatment group are presented in Table 35.

9.3.1. Solicited Events and Symptoms

Systemic and mucosal (local) solicited adverse events will be collected from the time of study vaccination through 14 days after study vaccination. Systemic events include: fever, chills, fatigue, malaise, myalgia, arthralgia, headache, and hypersensitivity. Mucosal events include: runny nose, stuffy nose/congestion, nasal pain/irritation, epistaxis, sneezing, sinus pressure/pain, sore throat, cough, and shortness of breath. Solicited AEs will be summarized by severity for each day after the study vaccination (Days 1-14 post study vaccination) and as the maximum severity over all 15 days (Table 38, Table 40, Table 41, Table 42, Table 43, Table 44, Table 45, Table 46, Table 47, Table 48, Table 49, Figure 9, Figure 10, Figure 11, and Figure 12.) Severity will be graded on a scale of 0 (absent), 1 (mild), 2 (moderate) and 3 (severe). Grading scales for mucosal and systemic solicited adverse events are presented in Table 6, Table 7, and Table 8, respectively. Additionally, solicited AEs will be analyzed by taking the most severe response over the follow-up period, dichotomizing into a binary variable (none versus mild, moderate, or severe) and using standard techniques, such as exact confidence intervals, to summarize the proportion of subjects reporting each symptom, any local symptom, and any systemic symptom (Table 39.) Summaries of solicited AEs will be presented by treatment arm (Table 36.) The proportion of subjects reporting symptoms will be compared between treatment arms using Chi-square or Fisher's exact test (Table 37.) Solicited adverse events by subject will be presented in Listing 10 and Listing 11.

9.3.2. Unsolicited Adverse Events

Unsolicited AEs will be coded by Medical Dictionary for Regulatory Activities (MedDRA) for preferred term and system organ class (SOC). Unsolicited SAEs will be collected from the time of study vaccination through approximately 6 months after study vaccination and reported by detailed listings showing the event description, MedDRA preferred term and SOC, relevant dates (study vaccinations and AEs), severity, relatedness, and outcome for each event (Listing 12). Non-serious unsolicited AEs will be collected from time of study vaccination through approximately 28 days after study vaccination and summarized as number and percentage of subjects reporting at least one event in each MedDRA preferred term and SOC, cross tabulated by severity and relationship to study product (Table 51, Table 52, Table 53, Table 54, Table 55, and Figure 13) and listed in Table 56. Additionally, the proportion of subjects and exact 95% confidence intervals of AEs in aggregate and by MedDRA categories will be computed (Table 50.)

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

The following listings will be presented including Subject ID, Adverse Event Description, Number of Days Post Dose (Duration), Reason Reported as an SAE, Relationship to Treatment, Alternate Etiology if not Related, and Outcome:

- Deaths and Serious Adverse Events (Table 56)
- Non-Serious Adverse Events (Table 57)
- New Onset Chronic Medical Conditions and Adverse Events of Special Interest (Table 58)

9.5. Pregnancies

Safety population who become pregnant during the study, every attempt will be made to follow these subjects to completion of pregnancy to document the outcome, including information regarding any complications with pregnancy and/or delivery. A listing of pregnancies and outcomes will be presented (Listing 19, Listing 20, Listing 21, Listing 22, and Listing 23.)

9.6. Clinical Laboratory Evaluations

Clinical safety laboratory adverse events will be collected at the time of study vaccination through approximately 7 days after study vaccination (Day 8). Any clinical laboratory parameter that is abnormal at Day 8 will be repeated at the next study visit (or sooner if medically indicated) and followed until normal or stabilization. Parameters to be evaluated include white blood cell count, platelet count, hemoglobin concentration, alanine aminotransferase (ALT), and creatinine. Grading scales for safety laboratory parameters are presented in Table 9.

The number and percentage of subjects with at least one clinical safety laboratory abnormality through Day 8 is presented in the overall summary of adverse events (Table 34.)

The distribution of chemistry results by severity, time point, and treatment group will be presented in Table 61, Table 62, Table 63, Table 64, Table 65, Table 66, and Figure 14. The distribution of hematology results by severity, time point, and treatment group will be presented in Table 69, Table 70, Table 71, Table 72, Table 73, Table 74, Table 75, Table 76, and Figure 15. Descriptive statistics including mean, standard deviation, median, minimum and maximum values by time point, for each laboratory parameter, will be summarized in Table 67 and Table 68 (chemistry) and Table 77, Table 78, and Table 79 (hematology). Changes in laboratory values will be presented in Figure 16, Figure 17, Figure 18, Figure 19, and Figure 20.

Subject visits with abnormal laboratory results, Grade 1 severity or higher, will be presented in Table 59 and Table 60.

Listing 14 and Listing 15 will provide complete listings of individual clinical laboratory results with applicable reference ranges.

9.7. Vital Signs and Physical Evaluations

Vital sign measurements will include systolic blood pressure, diastolic blood pressure, oral temperature, and, pulse. Vital signs will be assessed at screening and at baseline prior to study vaccination. As abnormal vital signs are not expected, these will be listed by subject and time point (Listing 16.)

Full Physical Examinations will be performed at screening. Limited physical examinations focused on the nasopharynx, oropharynx, and lungs will be performed at Day 1, Day 8, and Day 15. If indicated based on review of interim medical history, a targeted physical examination will be performed at each in-clinic visit. A listing of physical exam findings will be presented (Listing 17.)

9.8. Concomitant Medications

Concomitant medications will be coded to the Anatomical Therapeutic Classification using the WHO Drug Dictionary. The use of prior and concomitant medications taken during the study will be recorded on the CRFs. A by-subject listing of concomitant medication use will be presented in Listing 18. The use of concomitant medications during the study will be summarized by ATC1, ATC2 code and treatment group for the Safety population (Table 80.)

9.9. Other Safety Measures

Not applicable.

10. PHARMACOKINETICS

Not applicable.

11. IMMUNOGENICITY

See Section 8.

12. OTHER ANALYSES

Not applicable.

13. 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.

14. TECHNICAL DETAILS

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

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

Not applicable.

16. REFERENCES

1. Yeung, K.H.T., et al., An update of the global burden of pertussis in children younger than 5 years: a modelling study. Lancet Infect Dis, 2017. 17(9): p. 974-980.
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3. Zhang, Q., et al., Prevalence of asymptomatic Bordetella pertussis and Bordetella parapertussis infections among school children in China as determined by pooled real-time PCR: a cross-sectional study. Scand J Infect Dis, 2014. 46(4): p. 280-7.
4. Ward, J.I., et al., Efficacy of an acellular pertussis vaccine among adolescents and adults. N Engl J Med, 2005. 353(15): p. 1555-63.
5. de Greeff, S.C., et al., Seroprevalence of pertussis in The Netherlands: evidence for increased circulation of Bordetella pertussis. PLoS One, 2010. 5(12): p. e14183.
6. Palazzo, R., et al., Evidence of increased circulation of Bordetella pertussis in the Italian adult population from seroprevalence data (2012-2013). J Med Microbiol, 2016.
7. Althouse, B.M. and S.V. Scarpino, Asymptomatic transmission and the resurgence of Bordetella pertussis. BMC Med, 2015. 13: p. 146.
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10. Skerry, C.M., et al., A live attenuated Bordetella pertussis candidate vaccine does not cause disseminating infection in gamma interferon receptor knockout mice. Clin Vaccine Immunol, 2009. 16(9): p. 1344-51.
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13. Thorstensson, R., et al., A phase Ib (high dose), double-blind, single center, dose-escalating, placebocontrolled, randomized study of a live attenuated B. pertussis strain given as a single intranasal dose to healthy adult volunteers. 2017: on file at ILiAD Biotechnologies.
14. Locht, C., et al., Live attenuated pertussis vaccine BPZE1 protects baboons against B. pertussis disease and infection. J Infect Dis, 2017.
15. Drummond R. CONSORT Revised: Improving the Reporting of Randomized Clinical Trials. JAMA. 2001; 285(15):2006-2007.

17. LISTING OF TABLES, FIGURES, AND LISTINGS

Table, figure, and listing shells are presented in Appendix 1, Appendix 2, and Appendix 3, respectively. Please note that items marked with an asterisk (*) are included in Preliminary Report.

APPENDICES

APPENDIX 1. TABLE MOCK-UPS

Tables that will be included in the Preliminary Report are indicated with an asterisk (*) in the title.

LIST OF TABLES

List of Tables *(continued)*

List of Tables *(continued)*

List of Tables *(continued)*

List of Tables *(continued)*

9.5.1 Efficacy/Immunogenicity and Safety Measurements Assessed and Flow Chart

Table 1: Schedule of Study Procedures*

Study Visit Number	**V00**	**V01**	**V02**	**V03**	**V04****	**V05**	**Early Termination (if needed)**	**Unscheduled (if needed)**
Study Day post study vaccination	**Screening (D-30 to D-1)**	**Enrollment and Dose 1 D1**	**D8±2d**	**D15±3d**	**D29±3d**	**D181±21d**		
Obtain Informed Consent∞	X	X†¬						
Collect Demographic Information	X							
Review Eligibility Criteria	X	X†¬						
Medical History@	X	X†¬	X	X	X	X	X	X
Concomitant Medications	X√	X√†¬	X	X	X		X (if prior to 28 days after study vaccination)	X (if prior to 28 days after study vaccination)
Vital Signs$ (Oral Temperature%, Pulse, and BP)	X	X†					X (may be obtained if indicated)	X (may be obtained if indicated)
Physical Examination!	X	X†1	X1	X1	(X)	(X)	(X)	(X)
Urine or Serum Pregnancy Test	X^	X^						
Venous Blood Collection for Screening Laboratory Assays2	X							
Venous Blood Collection for Safety Laboratory Assays			X					
Venous Blood Collection for Serum Antibody Assays-	X	X†		X	X	X	XΩ	
Venous Blood Collection for PBMC isolation and Future Research		X†	X		X	X	XΩ	
Nasal Sample Collection for Mucosal Antibody Assays	X				X	X		
Nasal Sample Collection for *B. pertussis* Culture					X*			
Enrollment in AdvantageEDC℠ and Randomization		X†						

Table 1: Schedule of Study Procedures *(continued)*

Study Visit Number	**V00**	**V01**	**V02**	**V03**	**V04****	**V05**	**Early Termination (if needed)**	**Unscheduled (if needed)**
Study Day post study vaccination	**Screening (D-30 to D-1)**	**Enrollment and Dose 1 D1**	**D8±2d**	**D15±3d**	**D29±3d**	**D181±21d**		
Pre-Administration Reactogenicity Assessments		X†						
Study Vaccination		X						
2-hour Evaluation After Study Vaccination		X						
Post-Administration Reactogenicity Assessments		X					X (if within 15 days after study vaccination)	X (if within 15 days after study vaccination)
Distribute Memory Aid and Study-Related Materials		X						
Review Memory Aid for Reactogenicity			X	X			X (if within 15 days after study vaccination)	X (if within 15 days after study vaccination)
AE/SAE Assessment		X&	X&	X&	X	X***	X***(AEs if prior to 28 days after study vaccination)	X*** (AEs if prior to 28 days after study vaccination)

∞ Prior to study procedures.
† Prior to study vaccination.
¬ Review/confirm information or activity in subjects previously consented and screened.
@ Complete medical history will be obtained by interview of the subjects at the screening visit and will be updated on Day 1 prior to study vaccination and interim medical history will be obtained by interview of the subjects at follow-up visits after study vaccination.
√ All concomitant medications taken, and vaccines received within 30 days prior to signing the informed consent and/or prior to study vaccination. Medications reported in the eCRF for this visit are limited to those taken within 30 days prior to signing the informed consent and/or prior to study vaccination.
$ Vital signs assessed on Day 1 prior to study vaccination will be considered as baseline.
% Subjects must not eat or drink anything hot or cold, or smoke within 10 minutes prior to taking oral temperature.
! A physical examination will be performed by a study clinician licensed to make medical diagnoses and listed on the Form FDA 1572 as the site principal investigator or sub-investigator.
1 limited physical examination will be performed, focused on the nasopharynx, oropharynx, and lungs; in addition, a targeted physical examination will be performed, if indicated, based on review of interim medical history, by a study clinician.
() Targeted physical examination if indicated based on review of complete and any updates obtained by interview of subjects since the screening visit, by a study clinician licensed to make medical diagnoses and listed on the Form FDA 1572 as the site principal investigator or sub-investigator.

Table 1: Schedule of Study Procedures *(continued)*

^ Will be performed on all women of childbearing potential at screening and within 24 hours prior to study vaccination and results must be negative and known prior randomization and study vaccination.
- PT and pertactin serum IgG
& Inclusive of reactogenicity assessments performed on the day of study vaccination through 14 days after study vaccination.
*** Assessment of AE/SAE limited to new-onset chronic medical conditions, AESI, and SAEs if after 28 days following the study vaccination.
2 To be performed locally by the site, and will include white blood cell count, hemoglobin, platelet count, alanine aminotransferase, serum creatinine, and HIV screening
Ω Venous blood will only be obtained if the early termination visit occurs: 1) prior to Visit 2, 2) after day 14 post-vaccination but before Visit 3, or 3) at least 28 days following Visit 3.
** See Schedule of Events secondary table for Visits 4a and 4b.

Table 2: Schedule of Study Procedures Secondary Table for Visits 4a and 4b*

Study Visit Number	**V4a****	**V4b*** (Phone call)**
Study Day post study vaccination	**D46±3d**	**Day 50 ± 3 days**
Nasal Sample Collection for *B. pertussis* Culture and immunological assays	X	
Prescription of Azithromycin 500 mg by mouth once daily		X
Interim Medical History	X	
SAE Assessment	X	
Targeted Physical Examination, if indicated	X	

**Study visit only if nasal sample is positive for *B. pertussis* at Day 29
***Study visit only if nasal sample is positive for *B. pertussis* at Day 46

9.7.1 Sample Size

Table 3: Probability (%) of Observing at Least One Adverse Event*

Event Frequency	N = 5	N=15
≥0.01% Rare	<0.1	<0.1
≥0.1% Uncommon	0.5	1.5
≥1% Common	4.9	14.0
≥10% Very Common	41.0	79.4

Table 4: Minimum Detectable Difference in Proportion of Subjects Attaining Seroconversion comparing Placebo versus the BPZE1 (10^7 or 10^9 CFU)*

Placebo by VaxINator	BPZE1 (10^7 or 10^9 CFU) by VaxINator	Assumed Proportion of Subjects Attaining Seroconversion (Placebo)	Proportion of Subjects Attaining Seroconversion (BPZE1)	Minimum Detectable Difference (Treatment – Placebo)
N=15	N=15	0.00	0.41	0.41
		0.01	0.43	0.42
		0.05	0.54	0.49
		0.10	0.63	0.53
		0.20	0.76	0.56

10.2 Protocol Deviations

Table 5: Distribution of Protocol Deviations by Category, Type, and Treatment Group

Category	Deviation Type	BPZE1 10^7 CFU by VaxINator (N=X)		BPZE1 10^9 CFU by VaxINator (N=X)		BPZE1 10^9 CFU by Syringe (N=X)		Placebo by VaxINator (N=X)		All Subjects (N=X)	
		# of Subj.	# of Dev.	# of Subj.	# of Dev.	# of Subj.	# of Dev.	# of Subj.	# of Dev.	# of Subj.	# of Dev.
Eligibility/enrollment	Any type										
	Did not meet inclusion criterion	x	x	x	x	x	x	x	x	x	x
	Met exclusion criterion										
	ICF not signed prior to study procedures										
	Other										
Treatment administration schedule	Any type										
	Out of window visit										
	Missed visit/visit not conducted										
	Missed treatment administration										
	Delayed treatment administration										
	Other										
Follow-up visit schedule	Any type										
	Out of window visit										
	Missed visit/visit not conducted										
	Other										
Protocol procedure/assessment	Any type										
	Incorrect version of ICF signed										
	Blood not collected										
	Nasal mucus not collected										
	Other specimen not collected										
	Too few aliquots obtained										
	Specimen result not obtained										
	Required procedure not conducted										

Table 5: Distribution of Protocol Deviations by Category, Type, and Treatment Group *(continued)*

Category	Deviation Type	BPZE1 10^7 CFU by VaxINator (N=X)		BPZE1 10^9 CFU by VaxINator (N=X)		BPZE1 10^9 CFU by Syringe (N=X)		Placebo by VaxINator (N=X)		All Subjects (N=X)	
		# of Subj.	# of Dev.	# of Subj.	# of Dev.	# of Subj.	# of Dev.	# of Subj.	# of Dev.	# of Subj.	# of Dev.
	Required procedure done incorrectly										
	Study product temperature excursion										
	Specimen temperature excursion										
	Other										
Treatment administration	Any type										
	Required procedure done incorrectly										
	Study product temperature excursion										
	Other										
Blinding policy/procedure	Any type										
	Treatment unblinded										
	Other										
Note: N= Number of subjects in the Safety Population											

12.2.2 Displays of Adverse Events

Table 6: Mucosal Reactogenicity Grading Scale*

Local Reaction	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
Runny nose	Noticeable but does not interfere with daily activity	Moderate discomfort that interferes with daily activity	Significant discomfort/prevents daily activity or seeks medical care
Stuffy nose/congestion	Noticeable but does not interfere with daily activity	Moderate discomfort that interferes with breathing from nose	Unable to breathe through nose or seeks medical care
Nasal pain/Irritation	Noticeable but does not interfere with daily activity	Moderate discomfort that interferes with daily activity	Significant discomfort that prevents daily activity or seeks medical care
Epistaxis	Total duration of all episodes in a 24-hour period <30 minutes	Total duration of all episodes in a 24-hour period >30 minutes	Any bleeding that required visit for medical encounter
Sneezing	Noticeable but does not interfere with daily activity	Moderate discomfort that interferes with daily activity	Significant discomfort; prevents daily activity
Sinus pressure/pain	Noticeable but does not interfere with daily activity	Moderate discomfort that interferes with daily activity	Significant discomfort that prevents daily activity or seeks medical care
Sore/irritated throat	Noticeable but does not interfere with eating or drinking	Moderate discomfort that interferes with eating or drinking	Significant discomfort that prevents eating or drinking or seeks medical care
Cough	Noticeable but does not interfere with daily activity or sleeping	Frequent cough that interferes with daily activity or sleeping	Prevents daily activity, prevents sleep, or seeks medical care
Shortness of breath/wheezing	Noticeable but does not interfere with daily activity	Moderate discomfort that interferes with daily activity	Significant discomfort/ prevents daily activity or seeks medical encounter

Table 7: Subjective Systemic Reactogenicity Grading Scale*

Systemic (Subjective)	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
Feverishness (Chills/Shivering/Sweating)	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Fatigue (Tiredness)	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Malaise (General Unwell Feeling)	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Myalgia (Body Aches/Muscular Pain)	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Arthralgia (Joint Pain)	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Headache	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Rash/Hypersensitivity	Pruritus with or without rash	Localized urticaria	Generalized urticaria, anaphylaxis, or angioedema or localized urticaria that requires medical encounter.

Table 8: Quantitative Systemic Reactogenicity Grading Scale*

Systemic (Quantitative)	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
Fever[$] - oral[†]	38.0°C – 38.4°C 100.4°F – 101.1°F	38.5°C – 38.9°C 101.2°F – 102.0°F	>38.9°C >102.0°F

Oral temperature assessed on Day 1 prior to the first study vaccination will be considered as baseline.
[$] A fever can be considered not related to the study product if an alternative etiology can be documented.
† Subjects must not eat or drink anything hot or cold, or smoke within 10 minutes prior to taking oral temperature

12.4.1 Individual Laboratory Measurements and Abnormal Laboratory Values

Table 9: Laboratory Adverse Event Grading Scale

Hematology	Protocol Range	Reference Range	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
WBC 10^3/µL (Decrease)	≥3.9	3.9 – 10.7	2.5 – 3.8	1.5 – 2.4	<1.5
WBC 10^3/µL (Increase)	≥3.9	3.9 – 10.7	10.8 – 15.0	15.1 – 20.0	>20.0
Hemoglobin g/dL (Decrease, Male)	≥13.0	13.0 – 18.1	11.0 – 12.9	9.5 – 10.9	<9.5
Hemoglobin g/dL (Decrease, Female)	≥11.8	11.8 – 16.0	10.1 – 11.7	8.5 – 10.0	<8.5
Platelet count 10^3/µL (Decrease)	≥135	135 – 371	125 – 134	100 – 124	<100
Platelet count 10^3/µL (Increase)	≥135	135 – 371	372 – 550	551 – 750	>750

Chemistry	Protocol Range	Reference Range	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
ALT U/L (Increase, Female)	<45	0-44	45 – 100	101 – 200	>200
ALT U/L (Increase, Male)	<62	0-61	62 – 138	139 – 275	>275
Creatinine mg/dL (Increase, Female)	≤1.11	0.57-1.11	1.12 – 1.60	1.61 – 2.00	>2.00 or requires dialysis
Creatinine mg/dL (Increase, Male)	≤1.25	0.72-1.25	1.26 – 1.70	1.71 – 2.00	>2.00 or requires dialysis

14.1 Description of Study Subjects

14.1.1 Disposition of Subjects

Table 10: Subject Disposition by Treatment Group*

Subject Disposition	BPZE1 10^7 CFU by VaxINator (N=X)		BPZE1 10^9 CFU by VaxINator (N=X)		BPZE1 10^9 CFU by Syringe (N=X)		Placebo by VaxINator (N=X)		All Subjects (N=X)	
	n	%	n	%	n	%	n	%	n	%
Screened	--	--	--	--	--	--	--	--	x	--
Enrolled/Randomized	x	100	x	100	x	100	x	100	x	100
Received Treatment	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Day 8 Visit	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Day 15 Reactogenicity Period	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Day 29 Blood Draw	x	xx	x	xx	x	xx	x	xx	x	xx
Early Termination [a]	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Follow-up (Study Day 181)[b]	x	xx	x	xx	x	xx	x	xx	x	xx

Note: N=Number of subjects enrolled
[a] Refer to Listing 1 (Appendix section 16.2.1) for reasons subjects terminated early.
[b] Refer to Listing 4 (Appendix section 16.2.3) for reasons subjects are excluded from the Analysis populations.

Table 11: Analysis Populations by Treatment Group*

Analysis Populations	Reason Subjects Excluded	BPZE1 10^7 CFU by VaxINator (N=X)		BPZE1 10^9 CFU by VaxINator (N=X)		BPZE1 10^9 CFU by Syringe (N=X)		Placebo by VaxINator (N=X)		All Subjects (N=X)	
		%	n	%	n	%	n	%	n	%	n
Safety Population	Any Reason	x	xx	x	xx	x	xx	x	xx	x	xx
	[Reason 1, for example: Did not meet eligibility criteria]										
	[Reason 2]										
	[Reason 3]										
	[Reason 4]										
Immunogenicity Population	Any Reason										
	[Reason 1]										
	[Reason 2]										
	[Reason 3]										
	[Reason 4]										
Per Protocol Population	Any Reason										
	[Reason 1]										
	[Reason 2]										
	[Reason 3]										
	[Reason 4]										
Note: N=Number of subjects enrolled											

Table 12: Dates of First Treatment by Treatment Group

Dates of Dosing	BPZE1 10^7 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by Syringe (N=X)	Placebo by VaxINator (N=X)	All Subjects (N=X)
Total (Entire period of enrollment)					
DDMMMYYYY-DDMMMYYYY	x	x	x	x	x
Note: N= Number of subjects in the Safety Population					

Table 13: Ineligibility Summary of Screen Failures

Inclusion/Exclusion Category	Inclusion/Exclusion Criterion	n[a]	%[b]
Inclusion and Exclusion	Number of subjects failing any eligibility criterion	x	100
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

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

14.1.2 Demographic Data by Study Group

Table 14 Summary of Categorical Demographic and Baseline Characteristics by Treatment Group, All Enrolled Subjects*

		BPZE1 10^7 CFU by VaxINator (N=X)		BPZE1 10^9 CFU by VaxINator (N=X)		BPZE1 10^9 CFU by Syringe (N=X)		Placebo by VaxINator (N=X)		All Subjects (N=X)	
Variable	**Characteristic**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Sex	Male	x	xx	x	xx	x	xx	x	xx	x	xx
	Female										
Ethnicity	Not Hispanic or Latino	x	xx	x	xx	x	xx	x	xx	x	xx
	Hispanic or Latino										
	Not Reported										
	Unknown										
Race	American Indian or Alaska Native	x	xx	x	xx	x	xx	x	xx	x	xx
	Asian										
	Native Hawaiian or Other Pacific Islander										
	Black or African American										
	White										
	Multi-Racial										
	Unknown										

Note: N=All subjects enrolled

Table 15: Summary of Continuous Demographic and Baseline Characteristics by Treatment Group, All Enrolled Subjects*

Variable	Statistic	BPZE1 10^7 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by Syringe (N=X)	Placebo by VaxINator (N=X)	All Subjects (N=X)
Age (Years)	Mean	xx	xx	xx	xx	xx
	Standard Deviation	xx	xx	xx	xx	xx
	Median	x	x	x	x	x
	Minimum	x	x	x	x	x
	Maximum	x	x	x	x	x
Note: N=All subjects enrolled						

14.1.3 Prior and Concurrent Medical Conditions

Table 16: Summary of Subjects with Pre-Existing Medical Conditions by MedDRA System Organ Class and Treatment Group

	BPZE1 10^7 CFU by VaxINator (N=X)		BPZE1 10^9 CFU by VaxINator (N=X)		BPZE1 10^9 CFU by Syringe (N=X)		Placebo by VaxINator (N=X)		All Subjects (N=X)	
MedDRA System Organ Class	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Any SOC	x	xx	x	xx	x	xx	x	xx	x	xx
[SOC 1]										
[SOC 2]										
Note: N= Number of subjects in the Safety Population; n = Number of subjects reporting medical history within the specified SOC. A subject is only counted once per SOC.										

14.2 Efficacy/Immunogenicity Data

Table 17: Serum IgA ELISA Geometric Mean Titer (GMT) Results with 95% Confidence Intervals by Time Point and Treatment Group, Immunogenicity Population*

Antigen	Time Point	Statistic	BPZE1 10^7 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by Syringe (N=X)	Placebo by VaxINator (N=X)
Pertussis Toxin (PT)						
	Day 1 Pre-Vaccination	n	x	x	x	x
		GMT	x.x	x x	x x	x x
		95% CI	x x, x.x	x x, x x	x x, x x	x x, x.x
	Day 15 Post-Vaccination	n	x	x	x	x
		GMT	x.x	x x	x x	x x
		95% CI	x x, x.x	x x, x x	x x, x x	x x, x.x
	Day 29 Post-Vaccination	n	x	x	x	x
		GMT	x.x	x x	x x	x x
		95% CI	x x, x.x	x x, x x	x x, x x	x x, x.x
	Day 181 Post-Vaccination	n	x	x	x	x
		GMT	x.x	x x	x x	x x
		95% CI	x x, x.x	x x, x x	x x, x x	x x, x.x
Filamentous Hemagglutinin (FHA)						
	Day 1 Pre-Vaccination	n	x	x	x	x
		GMT	x.x	x x	x x	x x
		95% CI	x x, x.x	x x, x x	x x, x x	x x, x.x
	Day 15 Post-Vaccination	n	x	x	x	x
		GMT	x.x	x x	x x	x x
		95% CI	x x, x.x	x x, x x	x x, x x	x x, x.x
	Day 29 Post-Vaccination	n	x	x	x	x
		GMT	x.x	x x	x x	x x
		95% CI	x x, x.x	x x, x x	x x, x x	x x, x.x
	Day 181 Post-Vaccination	n	x	x	x	x
		GMT	x.x	x x	x x	x x
		95% CI	x x, x.x	x x, x x	x x, x x	x x, x.x
Pertactin (PRN)						
	Day 1 Pre-Vaccination	n	x	x	x	x
		GMT	x.x	x x	x x	x x
		95% CI	x x, x.x	x x, x x	x x, x x	x x, x.x

Table 17: Serum IgA ELISA Geometric Mean Titer (GMT) Results with 95% Confidence Intervals by Time Point and Treatment Group, Immunogenicity Population *(continued)*

Antigen	Time Point	Statistic	BPZE1 10^7 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by Syringe (N=X)	Placebo by VaxINator (N=X)
	Day 15 Post-Vaccination	n	x	x	x	x
		GMT	x.x	x x	x x	x x
		95% CI	x x, x.x	x x, x x	x x, x x	x x, x.x
	Day 29 Post-Vaccination	n	x	x	x	x
		GMT	x.x	x x	x x	x x
		95% CI	x x, x.x	x x, x x	x x, x x	x x, x.x
	Day 181 Post-Vaccination	n	x	x	x	x
		GMT	x.x	x x	x x	x x
		95% CI	x x, x.x	x x, x x	x x, x x	x x, x.x
Fimbriae (FIM)						
	Day 1 Pre-Vaccination	n	x	x	x	x
		GMT	x.x	x x	x x	x x
		95% CI	x x, x.x	x x, x x	x x, x x	x x, x.x
	Day 15 Post-Vaccination	n	x	x	x	x
		GMT	x.x	x x	x x	x x
		95% CI	x x, x.x	x x, x x	x x, x x	x x, x.x
	Day 29 Post-Vaccination	n	x	x	x	x
		GMT	x.x	x x	x x	x x
		95% CI	x x, x.x	x x, x x	x x, x x	x x, x.x
	Day 181 Post-Vaccination	n	x	x	x	x
		GMT	x.x	x x	x x	x x
		95% CI	x x, x.x	x x, x x	x x, x x	x x, x.x

Note: N=Number of subjects in the Immunogenicity Population
n=Number of subjects with results available at time point

*Day 181 time point will not be presented in Preliminary Analysis

Tables with similar format:

Table 18: Serum IgA ELISA Geometric Mean Titer (GMT) Results with 95% Confidence Intervals by Time Point and Treatment Group, Per Protocol Population*

Table 19: Serum IgG ELISA Geometric Mean Titer (GMT) Results with 95% Confidence Intervals by Time Point and Treatment Group, Immunogenicity Population*

Table 20: Serum IgG ELISA Geometric Mean Titer (GMT) Results with 95% Confidence Intervals by Time Point and Treatment Group, Per Protocol Population*

Table 21: Serum IgA ELISA Geometric Mean Fold Rise (GMFR) and Seroconversion (2-Fold Rise) Results by Time Point and Treatment Group, Immunogenicity Population*

Antigen	Time Point	Statistic	BPZE1 10^7 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by Syringe (N=X)	Placebo by VaxINator (N=X)
Pertussis Toxin (PT)						
	Day 15 Post-Vaccination	n	x	x	x	x
		GMFR[a]	x x	x.x	x.x	x x
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x
		2-Fold Rise[b]	x x	x.x	x.x	x x
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x
		Difference[c]	x x	x.x	N/A	N/A
		95% CI of Difference	x x, x x	x.x, x x	N/A	N/A
		p-value[d]	0 xx	0.xx	N/A	N/A
	Day 29 Post-Vaccination	n	x	x	x	x
		GMFR[a]	x x	x.x	x.x	x x
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x
		2-Fold Rise[b]	x x	x.x	x.x	x x
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x
		Difference[c]	x x	x.x	N/A	N/A
		95% CI of Difference	x x, x x	x.x, x x	N/A	N/A
		p-value[d]	0 xx	0.xx	N/A	N/A
	Day 181 Post-Vaccination	n	x	x	x	x
		GMFR[a]	x x	x.x	x.x	x x
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x
		2-Fold Rise[b]	x x	x.x	x.x	x x
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x
		Difference[c]	x x	x.x	N/A	N/A
		95% CI of Difference	x x, x x	x.x, x x	N/A	N/A
		p-value[d]	0 xx	0.xx	N/A	N/A
	Any Time Point	n	x	x	x	x
		2-Fold Rise[b]	x x	x.x	x.x	x x
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x
		Difference[c]	x x	x.x	N/A	N/A
		95% CI of Difference	x x, x x	x.x, x x	N/A	N/A

Table 21: Serum IgA ELISA Geometric Mean Fold Rise (GMFR) and Seroconversion (2-Fold rise) by Time Point and Treatment Group, Immunogenicity Population *(continued)*

Antigen	Time Point	Statistic	BPZE1 10^7 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by Syringe (N=X)	Placebo by VaxINator (N=X)
		p-value[d]	0 xx	0.xx	N/A	N/A
Filamentous Hemagglutinin (FHA)						
	Day 15 Post-Vaccination	n	x	x	x	x
		GMFR[a]	x x	x.x	x.x	x x
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x
		2-Fold Rise[b]	x x	x.x	x.x	x x
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x
		Difference[c]	x x	x.x	N/A	N/A
		95% CI of Difference	x x, x x	x.x, x x	N/A	N/A
		p-value[d]	0 xx	0.xx	N/A	N/A
	Day 29 Post-Vaccination	n	x	x	x	x
		GMFR[a]	x x	x.x	x.x	x x
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x
		2-Fold Rise[b]	x x	x.x	x.x	x x
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x
		Difference[c]	x x	x.x	N/A	N/A
		95% CI of Difference	x x, x x	x.x, x x	N/A	N/A
		p-value[d]	0 xx	0.xx	N/A	N/A
	Day 181 Post-Vaccination	n	x	x	x	x
		GMFR[a]	x x	x.x	x.x	x x
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x
		2-Fold Rise[b]	x x	x.x	x.x	x x
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x
		Difference[c]	x x	x.x	N/A	N/A
		95% CI of Difference	x x, x x	x.x, x x	N/A	N/A
		p-value[d]	0 xx	0.xx	N/A	N/A
	Any Time Point	n	x	x	x	x
		2-Fold Rise[b]	x x	x.x	x.x	x x
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x
		Difference[c]	x x	x.x	N/A	N/A

Table 21: Serum IgA ELISA Geometric Mean Fold Rise (GMFR) and Seroconversion (2-Fold rise) by Time Point and Treatment Group, Immunogenicity Population *(continued)*

Antigen	Time Point	Statistic	BPZE1 10^7 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by Syringe (N=X)	Placebo by VaxINator (N=X)
		95% CI of Difference	x x, x x	x.x, x x	N/A	N/A
		p-value[d]	0 xx	0.xx	N/A	N/A
Pertactin (PRN)						
	Day 15 Post-Vaccination	n	x	x	x	x
		GMFR[a]	x x	x.x	x.x	x x
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x
		2-Fold Rise[b]	x x	x.x	x.x	x x
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x
		Difference[c]	x x	x.x	N/A	N/A
		95% CI of Difference	x x, x x	x.x, x x	N/A	N/A
		p-value[d]	0 xx	0.xx	N/A	N/A
	Day 29 Post-Vaccination	n	x	x	x	x
		GMFR[a]	x x	x.x	x.x	x x
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x
		2-Fold Rise[b]	x x	x.x	x.x	x x
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x
		Difference[c]	x x	x.x	N/A	N/A
		95% CI of Difference	x x, x x	x.x, x x	N/A	N/A
		p-value[d]	0 xx	0.xx	N/A	N/A
	Day 181 Post-Vaccination	n	x	x	x	x
		GMFR[a]	x x	x.x	x.x	x x
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x
		2-Fold Rise[b]	x x	x.x	x.x	x x
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x
		Difference[c]	x x	x.x	N/A	N/A
		95% CI of Difference	x x, x x	x.x, x x	N/A	N/A
		p-value[d]	0 xx	0.xx	N/A	N/A
	Any Time Point	n	x	x	x	x
		2-Fold Rise[b]	x x	x.x	x.x	x x
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x

Table 21: Serum IgA ELISA Geometric Mean Fold Rise (GMFR) and Seroconversion (2-Fold rise) by Time Point and Treatment Group, Immunogenicity Population *(continued)*

Antigen	Time Point	Statistic	BPZE1 10^7 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by Syringe (N=X)	Placebo by VaxINator (N=X)
		Difference[c]	x x	x.x	N/A	N/A
		95% CI of Difference	x x, x x	x.x, x x	N/A	N/A
		p-value[d]	0 xx	0.xx	N/A	N/A
Fimbriae (FIM)	**Day 15 Post-Vaccination**	n	x	x	x	x
		GMFR[a]	x x	x.x	x.x	x x
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x
		2-Fold Rise[b]	x x	x.x	x.x	x x
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x
		Difference[c]	x x	x.x	N/A	N/A
		95% CI of Difference	x x, x x	x.x, x x	N/A	N/A
		p-value[d]	0 xx	0.xx	N/A	N/A
	Day 29 Post-Vaccination	n	x	x	x	x
		GMFR[a]	x x	x.x	x.x	x x
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x
		2-Fold Rise[b]	x x	x.x	x.x	x x
		Difference[c]	x x	x.x	N/A	N/A
		95% CI of Difference	x x, x x	x.x, x x	N/A	N/A
		p-value[d]	0 xx	0.xx	N/A	N/A
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x
	Day 181 Post-Vaccination	n	x	x	x	x
		GMFR[a]	x x	x.x	x.x	x x
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x
		2-Fold Rise[b]	x x	x.x	x.x	x x
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x
		Difference[c]	x x	x.x	N/A	N/A
		95% CI of Difference	x x, x x	x.x, x x	N/A	N/A
		p-value[d]	0 xx	0.xx	N/A	N/A
	Any Time Point	n	x	x	x	x
		2-Fold Rise[b]	x x	x.x	x.x	x x
		95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x

Table 21: Serum IgA ELISA Geometric Mean Fold Rise (GMFR) and Seroconversion (2-Fold rise) by Time Point and Treatment Group, Immunogenicity Population *(continued)*

Antigen	Time Point	Statistic	BPZE1 10^7 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by Syringe (N=X)	Placebo by VaxINator (N=X)
		Difference[c]	x x	x.x	N/A	N/A
		95% CI of Difference	x x, x x	x.x, x x	N/A	N/A
		p-value[d]	0 xx	0.xx	N/A	N/A

Note: N=Number of subjects in the Immunogenicity Population
n=Number of subjects with results available at time point
[a] GMFR represents the geometric mean fold rise in antibody titer compared to pre-dose 1.
[b] 2-Fold Rise represents the percentage of subjects with at least a 2-Fold Rise in antibody compared to pre-dose 1.
[c] vs. placebo
[d]Barnard's Exact test

*Day 181 time point will not be presented in Preliminary Analysis

Tables with similar format:

Table 22: Serum IgA ELISA Geometric Mean Fold Rise (GMFR) and Seroconversion (2-Fold Rise) Results by Time Point and Treatment Group, Per Protocol Population*

Table 23: Serum IgG ELISA Geometric Mean Fold Rise (GMFR) and Seroconversion (2-Fold Rise) Results by Time Point and Treatment Group, Immunogenicity Population*

Table 24: Serum IgG ELISA Geometric Mean Fold Rise (GMFR) and Seroconversion (2-Fold Rise) Results by Time Point and Treatment Group, Per Protocol Population*

Table 25: Any One or More Serum Pertussis Antigens Seroconversion (2-Fold Rise) Results by Time Point and Treatment Group, Immunogenicity Population*

Time Point	Statistic	BPZE1 10^7 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by Syringe (N=X)	Placebo by VaxINator (N=X)
Day 15 Post-Vaccination	n	x	x	x	x
	2-Fold Rise[a]	x x	x x	x x	x.x
	95% CI	x x, x x	x.x, x x	x.x, x x	x.x, x x
	Difference[b]	x x	x x	N/A	N/A
	95% CI of Difference	x x, x x	x.x, x x	N/A	N/A
	p-value[c]	0 xx	0 xx	N/A	N/A
Day 29 Post-Vaccination	n	x	x	x	x
	2-Fold Rise[a]	x x	x x	x x	x.x
	95% CI	x x, x x	x.x, x x	x.x, x x	x.x, x x
	Difference[b]	x x	x x	N/A	N/A
	95% CI of Difference	x x, x x	x.x, x x	N/A	N/A
	p-value[c]	0 xx	0 xx	N/A	N/A
Day 181 Post-Vaccination	n	x	x	x	x
	2-Fold Rise[a]	x x	x x	x x	x.x
	95% CI	x x, x x	x.x, x x	x.x, x x	x.x, x x
	Difference[b]	x x	x x	N/A	N/A
	95% CI of Difference	x x, x x	x.x, x x	N/A	N/A
	p-value[c]	0 xx	0 xx	N/A	N/A
Any Time Point	n	x	x	x	x
	2-Fold Rise[a]	x x	x x	x x	x.x
	95% CI	x x, x x	x.x, x x	x.x, x x	x.x, x x
	Difference[b]	x x	x x	N/A	N/A
	95% CI of Difference	x x, x x	x.x, x x	N/A	N/A
	p-value[c]	0 xx	0 xx	N/A	N/A

Note: N=Number of subjects in the Immunogenicity Population
n=Number of subjects with results available at time point
[a] 2-Fold Rise represents the percentage of subjects with at least a 2-Fold Rise in one or more antibodies compared to pre-dose 1.
[b] vs. placebo
[c]Barnard's Exact test

*Day 181 time point will not be presented in Preliminary Analysis

Tables with similar format:

Table 26: Any One or More Serum Pertussis Antigens Seroconversion (2-Fold Rise) Results by Time Point and Treatment Group, Per Protocol Population*

Table 27: Any Two or More Serum Pertussis Antigens Seroconversion (2-Fold Rise) Results by Time Point and Treatment Group, Immunogenicity Population*

Table 28: Any Two or More Serum Pertussis Antigens Seroconversion (2-Fold Rise) Results by Time Point and Treatment Group, Per Protocol Population*

Table 29: Mucosal Ratio of PT-IgA to Total IgA ELISA Geometric Mean Titer Ratio (GMTR) and Seroconversion (2-Fold Rise) Results by Time Point and Treatment Group, Immunogenicity Population*

Antigen	Time Point	Statistic	BPZE1 10^7 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by Syringe (N=X)	Placebo by VaxINator (N=X)
Pertussis Toxin (PT)						
	Day 29 Post-Vaccination	n	x	x	x	x
		GMTR[a]	x x	x x	x.x	x x
		95% CI	x x, x x	x x, x x	x x, x.x	x.x, x x
		2-Fold Rise[b]	x x	x x	x.x	x x
		95% CI	x x, x x	x x, x x	x x, x.x	x.x, x x
		Difference[c]	x x	x x	N/A	N/A
		95% CI of Difference	x x, x x	x x, x x	N/A	N/A
		p-value[d]	0 xx	0 xx	N/A	N/A
	Day 181 Post-Vaccination	n	x	x	x	x
		GMTR[a]	x x	x x	x.x	x x
		95% CI	x x, x x	x x, x x	x x, x.x	x.x, x x
		2-Fold Rise[b]	x x	x x	x.x	x x
		95% CI	x x, x x	x x, x x	x x, x.x	x.x, x x
		Difference[c]	x x	x x	N/A	N/A
		95% CI of Difference	x x, x x	x x, x x	N/A	N/A
		p-value[d]	0 xx	0 xx	N/A	N/A
	Any Time Point	n	x	x	x	x
		2-Fold Rise[b]	x x	x x	x.x	x x
		95% CI	x x, x x	x x, x x	x x, x.x	x.x, x x
		Difference[c]	x x	x x	N/A	N/A
		95% CI of Difference	x x, x x	x x, x x	N/A	N/A
		p-value[d]	0 xx	0 xx	N/A	N/A
Filamentous Hemagglutinin (FHA)						
	Day 29 Post-Vaccination	n	x	x	x	x
		GMTR[a]	x x	x x	x.x	x x
		95% CI	x x, x x	x x, x x	x x, x.x	x.x, x x
		2-Fold Rise[b]	x x	x x	x.x	x x
		95% CI	x x, x x	x x, x x	x x, x.x	x.x, x x
		Difference[c]	x x	x x	N/A	N/A

Table 29: Mucosal Ratio of PT-IgA to Total IgA ELISA Geometric Mean Titer Ratio (GMTR) and Seroconversion (2-Fold Rise) Results by Time Point and Treatment Group, Immunogenicity Population *(continued)*

Antigen	Time Point	Statistic	BPZE1 10^7 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by Syringe (N=X)	Placebo by VaxINator (N=X)
		95% CI of Difference	x x, x x	x x, x x	N/A	N/A
		p-value[d]	0 xx	0 xx	N/A	N/A
	Day 181 Post-Vaccination	n	x	x	x	x
		GMTR[a]	x x	x x	x.x	x x
		95% CI	x x, x x	x x, x x	x x, x.x	x.x, x x
		2-Fold Rise[b]	x x	x x	x.x	x x
		95% CI	x x, x x	x x, x x	x x, x.x	x.x, x x
		Difference[c]	x x	x x	N/A	N/A
		95% CI of Difference	x x, x x	x x, x x	N/A	N/A
		p-value[d]	0 xx	0 xx	N/A	N/A
	Any Time Point	n	x	x	x	x
		2-Fold Rise[b]	x x	x x	x.x	x x
		95% CI	x x, x x	x x, x x	x x, x.x	x.x, x x
		Difference[c]	x x	x x	N/A	N/A
		95% CI of Difference	x x, x x	x x, x x	N/A	N/A
		p-value[d]	0 xx	0 xx	N/A	N/A
Pertactin (PRN)						
	Day 29 Post-Vaccination	n	x	x	x	x
		GMTR[a]	x x	x x	x.x	x x
		95% CI	x x, x x	x x, x x	x x, x.x	x.x, x x
		2-Fold Rise[b]	x x	x x	x.x	x x
		95% CI	x x, x x	x x, x x	x x, x.x	x.x, x x
		Difference[c]	x x	x x	N/A	N/A
		95% CI of Difference	x x, x x	x x, x x	N/A	N/A
		p-value[d]	0 xx	0 xx	N/A	N/A
	Day 181 Post-Vaccination	n	x	x	x	x
		GMTR[a]	x x	x x	x.x	x x
		95% CI	x x, x x	x x, x x	x x, x.x	x.x, x x
		2-Fold Rise[b]	x x	x x	x.x	x x
		95% CI	x x, x x	x x, x x	x x, x.x	x.x, x x

Table 29: Mucosal Ratio of PT-IgA to Total IgA ELISA Geometric Mean Titer Ratio (GMTR) and Seroconversion (2-Fold Rise) Results by Time Point and Treatment Group, Immunogenicity Population *(continued)*

Antigen	Time Point	Statistic	BPZE1 10^7 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by Syringe (N=X)	Placebo by VaxINator (N=X)
		Difference[c]	x x	x x	N/A	N/A
		95% CI of Difference	x x, x x	x x, x x	N/A	N/A
		p-value[d]	0 xx	0 xx	N/A	N/A
	Any Time Point	n	x	x	x	x
		2-Fold Rise[b]	x x	x x	x.x	x x
		95% CI	x x, x x	x x, x x	x x, x.x	x.x, x x
		Difference[c]	x x	x x	N/A	N/A
		95% CI of Difference	x x, x x	x x, x x	N/A	N/A
		p-value[d]	0 xx	0 xx	N/A	N/A
Fimbriae (FIM)						
	Day 29 Post-Vaccination	n	x	x	x	x
		GMTR[a]	x x	x x	x.x	x x
		95% CI	x x, x x	x x, x x	x x, x.x	x.x, x x
		2-Fold Rise[b]	x x	x x	x.x	x x
		95% CI	x x, x x	x x, x x	x x, x.x	x.x, x x
		Difference[c]	x x	x x	N/A	N/A
		95% CI of Difference	x x, x x	x x, x x	N/A	N/A
		p-value[d]	0 xx	0 xx	N/A	N/A
	Day 181 Post-Vaccination	n	x	x	x	x
		GMTR[a]	x x	x x	x.x	x x
		95% CI	x x, x x	x x, x x	x x, x.x	x.x, x x
		2-Fold Rise[b]	x x	x x	x.x	x x
		95% CI	x x, x x	x x, x x	x x, x.x	x.x, x x
		Difference[c]	x x	x x	N/A	N/A
		95% CI of Difference	x x, x x	x x, x x	N/A	N/A
		p-value[d]	0 xx	0 xx	N/A	N/A
	Any Time Point	n	x	x	x	x
		2-Fold Rise[b]	x x	x x	x.x	x x
		95% CI	x x, x x	x x, x x	x x, x.x	x.x, x x
		Difference[c]	x x	x x	N/A	N/A

Table 29: Mucosal Ratio of PT-IgA to Total IgA ELISA Geometric Mean Titer Ratio (GMTR) and Seroconversion (2-Fold Rise) Results by Time Point and Treatment Group, Immunogenicity Population *(continued)*

Antigen	Time Point	Statistic	BPZE1 10^7 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by Syringe (N=X)	Placebo by VaxINator (N=X)
		95% CI of Difference	x x, x x	x x, x x	N/A	N/A
		p-value[d]	0 xx	0 xx	N/A	N/A

Note: N=Number of subjects in the Immunogenicity Population
n=Number of subjects with results available at time point
[a] GMTR represents the geometric mean titer ratio to total IgA
[b] 2-Fold Rise represents the percentage of subjects with at least a 2-Fold Rise in antibody compared to pre-dose 1.
[c] vs. placebo
[d]Barnard's Exact test
*Day 181 time point will not be presented in Preliminary Analysis

Tables with similar format:

Table 30: Mucosal IgA to Total IgA ELISA Geometric Mean Titer Ratio (GMTR) and Seroconversion (2-Fold Rise) Results by Time Point and Treatment Group, Per Protocol Population*

Table 31: Any One or More Mucosal Pertussis Antigens Seroconversion (2-Fold Rise) Results by Time Point and Treatment Group, Immunogenicity Population*

Time Point	Statistic	BPZE1 10^7 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by Syringe (N=X)	Placebo by VaxINator (N=X)
Day 29 Post-Vaccination	N	x	x	x	x
	2-Fold Rise[a]	x x	x x	x x	x.x
	95% CI	x x, x x	x.x, x x	x.x, x x	x.x, x x
	Difference[b]	x x	x x	N/A	N/A
	95% CI of Difference	x x, x x	x.x, x x	N/A	N/A
	p-value[c]	0 xx	0 xx	N/A	N/A
Day 181 Post-Vaccination	N	x	x	x	x
	2-Fold Rise[a]	x x	x x	x x	x.x
	95% CI	x x, x x	x.x, x x	x.x, x x	x.x, x x
	Difference[b]	x x	x x	N/A	N/A
	95% CI of Difference	x x, x x	x.x, x x	N/A	N/A
	p-value[c]	0 xx	0 xx	N/A	N/A

Note: N=Number of subjects in the Immunogenicity Population
[a] 2-Fold Rise represents the percentage of subjects with at least a 2-Fold Rise in one or more antibodies compared to pre-dose 1.
[b] vs. placebo
[c]Barnard's Exact test

*Day 181 time point will not be presented in Preliminary Analysis

Tables with similar format:

Table 32: Any One or More Mucosal Pertussis Antigens Seroconversion (2-Fold Rise) Results by Time Point and Treatment Group, Per Protocol Population*

Table 33: Nasal Colonization Results by Time Point and Treatment Group, Per Protocol Population*

Time Point	Statistic	BPZE1 10^7 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by Syringe (N=X)	Placebo by VaxINator (N=X)
Day 29 Post-Vaccination	Subjects with detectable *B. pertussis*, n	x	x	x	x
	Proportion of subjects with detectable *B. pertussis*	xx	xx	xx	xx
	95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x
Day 46 Post-Vaccination	Subjects with detectable *B. pertussis*, n	x	x	x	x
	Proportion of subjects with detectable *B. pertussis*	xx	xx	xx	xx
	95% CI	x x, x x	x.x, x x	x x, x.x	x x, x x

Note: N=Number of subjects in the Per Protocol Population

14.3 Safety Data

14.3.1 Displays of Adverse Events

Table 34: Overall Summary of Adverse Events*

	BPZE1 10^7 CFU by VaxINator (N=X)		BPZE1 10^9 CFU by VaxINator (N=X)		BPZE1 10^9 CFU by Syringe (N=X)		Placebo by VaxINator (N=X)		All Subjects (N=X)	
Subjects[a] with	n	%	n	%	n	%	n	%	n	%
At least one local solicited adverse event	x	x	x	x	x	x	x	x	x	x
At least one systemic solicited adverse event	x	x	x	x	x	x	x	x	x	x
At least one unsolicited adverse event	x	x	x	x	x	x	x	x	x	x
At least one unsolicited non-serious adverse event through Day 29	x	x	x	x	x	x	x	x	x	x
At least one related unsolicited adverse event	x	x	x	x	x	x	x	x	x	x
Mild (Grade 1)	x	x	x	x	x	x	x	x	x	x
Moderate (Grade 2)	x	x	x	x	x	x	x	x	x	x
Severe (Grade 3)	x	x	x	x	x	x	x	x	x	x
Not yet assessed										
At least one severe (Grade 3) unsolicited adverse event	x	x	x	x	x	x	x	x	x	x
Related	x	x	x	x	x	x	x	x	x	x
Unrelated	x	x	x	x	x	x	x	x	x	x

Table 34: Overall Summary of Adverse Events *(continued)*

	BPZE1 10^7 CFU by VaxINator (N=X)		**BPZE1 10^9 CFU by VaxINator (N=X)**		**BPZE1 10^9 CFU by Syringe (N=X)**		**Placebo by VaxINator (N=X)**		**All Subjects (N=X)**	
Subjects[a] with	n	%	n	%	n	%	n	%	n	%
At least one serious adverse event[b]	x	x	x	x	x	x	x	x	x	x
At least one related, serious adverse event	x	x	x	x	x	x	x	x	x	x
At least one adverse event leading to early termination[c]	x	x	x	x	x	x	x	x	x	x
At least one medically attended adverse event	x	x	x	x	x	x	x	x	x	x
At least one new onset chronic medical condition	x	x	x	x	x	x	x	x	x	x
At least one potentially immune mediated medical condition	x	x	x	x	x	x	x	x	x	x

N = Number of subjects in the Safety Population
[a] Subjects are counted once for each category regardless of the number of events.
[b] A listing of Serious Adverse Events is included in Table 56.
[c] As reported on the Adverse Event eCRF.

Table 35: Adverse Events Occurring in 5% of Subjects in Any Treatment Group by MedDRA System Organ Class and Preferred Term, and Treatment Group - Safety Population*

Preferred Term	MedDRA System Organ Class	BPZE1 10^7 CFU by VaxINator (N=X)			BPZE1 10^9 CFU by VaxINator (N=X)			BPZE1 10^9 CFU by Syringe (N=X)			Placebo by VaxINator (N=X)			All Subjects (N=X)		
		n	%	Events	n	%	Events	n	%	Events	n	%	Events	n	%	Events
Serious Adverse Events																
All	All	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
PT1	SOC1	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Etc.	Etc.															
Other (Non-serious) Adverse Events																
All	All	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
PT1	SOC1	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Etc.	Etc.															

N = number of subjects in the Safety Population (number of subjects at risk).
n= number of subjects reporting event.
Events= total frequency of events reported.

14.3.1.1 Solicited Adverse Events

Table 36: Number and Percentage of Subjects Experiencing Solicited Events with 95% Confidence Intervals by Symptom and Treatment Group*

	BPZE1 10^7 CFU by VaxINator (N=X)			BPZE1 10^9 CFU by VaxINator (N=X)			BPZE1 10^9 CFU by Syringe (N=X)			Placebo by VaxINator (N=X)			All Subjects (N=X)		
Symptom	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Any Symptom	x	xx	x x, x x	x	xx	x.x, x x	x	xx	x x, x.x	x	xx	x x, x.x	x	xx	x x, x.x
Any Systemic Symptom															
Fever															
Feverishness															
Fatigue (tiredness)															
Malaise (general unwell feeling)															
Myalgia (body aches /muscular pain)															
Arthralgia (joint pain)															
Headache															
Rash / hypersensitivity															
Any Local Symptom															
Runny nose															
Stuffy nose/congestion															
Nasal pain/ Irritation															
Epistaxis															
Sneezing															
Sinus pressure/pain															
Sore/irritated throat															
Cough															
Shortness of breath/wheezing															
Note: N= Number of subjects in the Safety Population															

Table 37: Comparison of the Proportion of Subjects Experiencing Solicited Events by Treatment Group*

Symptom	Statistic	BPZE1 10^7 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by VaxINator (N=X)	BPZE1 10^9 CFU by Syringe (N=X)	Placebo by VaxINator (N=X)
Any Symptom	Proportion	x.xx	x.xx	x.xx	x xx
	95% CI (for proportion)	x xx, x.xx	x xx, x.xx	x xx, x.xx	x xx, x xx
	Difference[a]	x.xx	x.xx	N/A	N/A
	95% CI (for difference)	x xx, x.xx	x xx, x.xx	N/A	N/A
[Symptom 1]	Proportion	x.xx	x.xx	x.xx	x xx
	95% CI (for proportion)	x xx, x.xx	x xx, x.xx	x xx, x.xx	x xx, x xx
	Difference[a]	x.xx	x.xx	N/A	N/A
	95% CI (for difference)	x xx, x.xx	x xx, x.xx	N/A	N/A

Note: N = Number of subjects in the Safety Population who received at least one dose
[a] vs. placebo

Table 38: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, and Treatment Group*

Symptom	Severity	BPZE1 10^7 CFU by VaxINator (N=X)			BPZE1 10^9 CFU by VaxINator (N=X)			BPZE1 10^9 CFU by Syringe (N=X)			Placebo by VaxINator (N=X)			All Subjects (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
Any Symptom	None	x	xx	x.x, x x	x	xx	x x, x.x	x	xx	x.x, x x	x	xx	x x, x.x	x	xx	x x, x.x
	Mild															
	Moderate															
	Severe															
Systemic Symptoms																
Any Systemic Symptom	None	x	xx	x.x, x x	x	xx	x x, x.x	x	xx	x.x, x x	x	xx	x x, x.x	x	xx	x x, x.x
	Mild															
	Moderate															
	Severe															
Fever	None															
	Mild															
	Moderate															
	Severe															
Feverishness	None															
	Mild															
	Moderate															
	Severe															
Fatigue (tiredness)	None															
	Mild															
	Moderate															
	Severe															

Table 38: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, and Treatment Group *(continued)*

Symptom	Severity	BPZE1 10^7 CFU by VaxINator (N=X)			BPZE1 10^9 CFU by VaxINator (N=X)			BPZE1 10^9 CFU by Syringe (N=X)			Placebo by VaxINator (N=X)			All Subjects (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
Malaise (general unwell feeling)	None															
	Mild															
	Moderate															
	Severe															
Myalgia (body aches /muscular pain)	None															
	Mild															
	Moderate															
	Severe															
Arthralgia (joint pain)	None															
	Mild															
	Moderate															
	Severe															
Headache	None															
	Mild															
	Moderate															
	Severe															
Rash / hypersensitivity	None															
	Mild															
	Moderate															
	Severe															

Table 38: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, and Treatment Group
(continued)

Symptom	Severity	BPZE1 10^7 CFU by VaxINator (N=X)			BPZE1 10^9 CFU by VaxINator (N=X)			BPZE1 10^9 CFU by Syringe (N=X)			Placebo by VaxINator (N=X)			All Subjects (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
Local Symptoms																
Any Local Symptom	None	x	xx	x.x, x x	x	xx	x x, x.x	x	xx	x.x, x x	x	xx	x x, x.x	x	xx	x x, x.x
	Mild															
	Moderate															
	Severe															
Runny nose	None															
	Mild															
	Moderate															
	Severe															
Stuffy nose/congestion	None															
	Mild															
	Moderate															
	Severe															
Nasal pain/ Irritation	None															
	Mild															
	Moderate															
	Severe															
Epistaxis	None															
	Mild															
	Moderate															
	Severe															

Table 38: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, and Treatment Group *(continued)*

Symptom	Severity	BPZE1 10^7 CFU by VaxINator (N=X)			BPZE1 10^9 CFU by VaxINator (N=X)			BPZE1 10^9 CFU by Syringe (N=X)			Placebo by VaxINator (N=X)			All Subjects (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
Sneezing	None															
	Mild															
	Moderate															
	Severe															
Sinus pressure/pain	None															
	Mild															
	Moderate															
	Severe															
Sore/irritated throat	None															
	Mild															
	Moderate															
	Severe															
Cough	None															
	Mild															
	Moderate															
	Severe															
Shortness of breath/wheezing	None															
	Mild															
	Moderate															
	Severe															

Note: N = Number of subjects in the Safety Population who received the specified dose. Severity is the maximum severity reported over all solicited symptoms post dosing for each subject.

Table 39: Maximum Severity of Solicited Symptoms Dichotomized, by Symptom and Treatment Group

Symptom	Severity	BPZE1 10^7 CFU by VaxINator (N=X)			BPZE1 10^9 CFU by VaxINator (N=X)			BPZE1 10^9 CFU by Syringe (N=X)			Placebo by VaxINator (N=X)			All Subjects (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
Any Symptom	None	x	xx	x.x, x x	x	xx	x x, x x	x	xx	x x, x x	x	xx	x x, x x	x	xx	x x, x.x
	Mild or Worse															
	Moderate or Worse															
	Severe or Worse															
Systemic Symptoms																
Any Systemic Symptom	None															
	Mild or Worse															
	Moderate or Worse															
	Severe or Worse															
Fever	None															
	Mild or Worse															
	Moderate or Worse															
	Severe or Worse															
Feverishness	None															
	Mild or Worse															
	Moderate or Worse															
	Severe or Worse															

Table 39: Maximum Severity of Solicited Symptoms Dichotomized, by Symptom and Treatment Group *(continued)*

Symptom	Severity	BPZE1 10^7 CFU by VaxINator (N=X)			BPZE1 10^9 CFU by VaxINator (N=X)			BPZE1 10^9 CFU by Syringe (N=X)			Placebo by VaxINator (N=X)			All Subjects (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
Fatigue (tiredness)	None															
	Mild or Worse															
	Moderate or Worse															
	Severe or Worse															
Malaise (general unwell feeling)	None															
	Mild or Worse															
	Moderate or Worse															
	Severe or Worse															
Myalgia (body aches /muscular pain)	None															
	Mild or Worse															
	Moderate or Worse															
	Severe or Worse															
Arthralgia (joint pain)	None															
	Mild or Worse															
	Moderate or Worse															
	Severe or Worse															

Table 39: Maximum Severity of Solicited Symptoms Dichotomized, by Symptom and Treatment Group *(continued)*

Symptom	Severity	BPZE1 10^7 CFU by VaxINator (N=X)			BPZE1 10^9 CFU by VaxINator (N=X)			BPZE1 10^9 CFU by Syringe (N=X)			Placebo by VaxINator (N=X)			All Subjects (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
Headache	None															
	Mild or Worse															
	Moderate or Worse															
	Severe or Worse															
Rash / hypersensitivity	None															
	Mild or Worse															
	Moderate or Worse															
	Severe or Worse															
Local Symptoms																
Any Local Symptom	None															
	Mild or Worse															
	Moderate or Worse															
	Severe or Worse															
Runny nose	None															
	Mild or Worse															
	Moderate or Worse															
	Severe or Worse															

Table 39: Maximum Severity of Solicited Symptoms Dichotomized, by Symptom and Treatment Group *(continued)*

Symptom	Severity	BPZE1 10^7 CFU by VaxINator (N=X)			BPZE1 10^9 CFU by VaxINator (N=X)			BPZE1 10^9 CFU by Syringe (N=X)			Placebo by VaxINator (N=X)			All Subjects (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
Stuffy nose/congestion	None															
	Mild or Worse															
	Moderate or Worse															
	Severe or Worse															
Nasal pain/ Irritation	None															
	Mild or Worse															
	Moderate or Worse															
	Severe or Worse															
Epistaxis	None															
	Mild or Worse															
	Moderate or Worse															
	Severe or Worse															
Sneezing	None															
	Mild or Worse															
	Moderate or Worse															
	Severe or Worse															

Table 39: Maximum Severity of Solicited Symptoms Dichotomized, by Symptom and Treatment Group *(continued)*

Symptom	Severity	BPZE1 10^7 CFU by VaxINator (N=X)			BPZE1 10^9 CFU by VaxINator (N=X)			BPZE1 10^9 CFU by Syringe (N=X)			Placebo by VaxINator (N=X)			All Subjects (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
Sinus pressure/pain	None															
	Mild or Worse															
	Moderate or Worse															
	Severe or Worse															
Sore/irritated throat	None															
	Mild or Worse															
	Moderate or Worse															
	Severe or Worse															
Cough	None															
	Mild or Worse															
	Moderate or Worse															
	Severe or Worse															
Shortness of breath/wheezing	None															
	Mild or Worse															
	Moderate or Worse															
	Severe or Worse															

Note: N = Number of subjects in the Safety Population. Severity is the maximum severity reported over all solicited symptoms post dosing for each subject.

Table 40: Number and Percentage of Subjects Experiencing Systemic Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group - BPZE1 10^7 CFU by VaxINator *

BPZE1 10^7 CFU by VaxINator (N=X)																							
		Pre-Dose (N=X)		**Post-Dose (N=X)**		**Day 1-2 (N=X)**		**Day 3-4 (N=X)**		**Day 5-6 (N=X)**		**Day 7-8 (N=X)**		**Day 9-10 (N=X)**		**Day 11-12 (N=X)**		**Day 13-14 (N=X)**		**Day 15+ (N=X)**		**Any Post-Dose[a]**	
Symptom	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**
Any Systemic Symptom	None	x	x x	x	x.x	x	x x	x	x.x	x	x x	x	x x	x	x x	x	x x	x	x x	x	x x	x	x x
	Mild																						
	Moderate																						
	Severe																						
	Not Reported																						
Fever	None																						
	Mild																						
	Moderate																						
	Severe																						
	Not Reported																						
Feverishness	None																						
	Mild																						
	Moderate																						
	Severe																						
	Not Reported																						
Fatigue (tiredness)	None																						
	Mild																						
	Moderate																						
	Severe																						
	Not Reported																						

Table 40: Number and Percentage of Subjects Experiencing Systemic Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group - BPZE1 10^7 CFU by VaxINator *(continued)*

BPZE1 10^7 CFU by VaxINator (N=X)																							
		Pre-Dose (N=X)		**Post-Dose (N=X)**		**Day 1-2 (N=X)**		**Day 3-4 (N=X)**		**Day 5-6 (N=X)**		**Day 7-8 (N=X)**		**Day 9-10 (N=X)**		**Day 11-12 (N=X)**		**Day 13-14 (N=X)**		**Day 15+ (N=X)**		**Any Post-Dose[a]**	
Symptom	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**
Malaise (general unwell feeling)	None																						
	Mild																						
	Moderate																						
	Severe																						
	Not Reported																						
Myalgia (body aches / muscular pain)	None																						
	Mild																						
	Moderate																						
	Severe																						
	Not Reported																						
Arthralgia (joint pain)	None																						
	Mild																						
	Moderate																						
	Severe																						
	Not Reported																						
Headache	None																						
	Mild																						
	Moderate																						
	Severe																						
	Not Reported																						

Table 40: Number and Percentage of Subjects Experiencing Systemic Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group - BPZE1 10^7 CFU by VaxINator *(continued)*

BPZE1 10^7 CFU by VaxINator (N=X)																							
		Pre-Dose (N=X)		**Post-Dose (N=X)**		**Day 1-2 (N=X)**		**Day 3-4 (N=X)**		**Day 5-6 (N=X)**		**Day 7-8 (N=X)**		**Day 9-10 (N=X)**		**Day 11-12 (N=X)**		**Day 13-14 (N=X)**		**Day 15+ (N=X)**		**Any Post-Dose[a]**	
Symptom	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**
Rash / hypersensitivity	None																						
	Mild																						
	Moderate																						
	Severe																						
	Not Reported																						

Severity is the maximum severity reported post dosing for each subject for each day.
[a]Indicates how many subjects had "None", "Mild", "Moderate", "Severe", or "Not Reported" as the maximum severity for any day.

Tables with similar format:

Table 41: Number and Percentage of Subjects Experiencing Systemic Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group - BPZE1 10^9 CFU by VaxINator *

Table 42: Number and Percentage of Subjects Experiencing Systemic Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group - BPZE1 10^9 CFU by Syringe *

Table 43: Number and Percentage of Subjects Experiencing Systemic Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group - Placebo by VaxINator *

Table 44: Number and Percentage of Subjects Experiencing Systemic Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group - All Subjects *

Table 45: Number and Percentage of Subjects Experiencing Local Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group - BPZE1 10^7 CFU by VaxINator *

BPZE1 10^7 CFU by VaxINator (N=X)																							
		Pre-Dose (N=X)		**Post-Dose (N=X)**		**Day 1-2 (N=X)**		**Day 3-4 (N=X)**		**Day 5-6 (N=X)**		**Day 7-8 (N=X)**		**Day 9-10 (N=X)**		**Day 11-12 (N=X)**		**Day 13-14 (N=X)**		**Day 15+ (N=X)**		**Any Post- Dose[a]**	
Symptom	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**
Any Local Symptom	None	x	x x	x	x.x	x	x x	x	x x	x	x x	x	x x	x	x x	x	x.x	x	x x	x	x x	x	x x
	Mild																						
	Moderate																						
	Severe																						
	Not Reported																						
Runny nose	None																						
	Mild																						
	Moderate																						
	Severe																						
	Not Reported																						
Stuffy nose/congestion	None																						
	Mild																						
	Moderate																						
	Severe																						
	Not Reported																						
Nasal pain/irritation	None																						
	Mild																						
	Moderate																						
	Severe																						
	Not Reported																						
Epistaxis	None																						
	Mild																						
	Moderate																						
	Severe																						
	Not Reported																						

Table 45: Number and Percentage of Subjects Experiencing Local Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group -- BPZE1 10^7 CFU by VaxINator *(continued)*

BPZE1 10^7 CFU by VaxINator (N=X)																							
		Pre-Dose (N=X)		**Post-Dose (N=X)**		**Day 1-2 (N=X)**		**Day 3-4 (N=X)**		**Day 5-6 (N=X)**		**Day 7-8 (N=X)**		**Day 9-10 (N=X)**		**Day 11-12 (N=X)**		**Day 13-14 (N=X)**		**Day 15+ (N=X)**		**Any Post- Dose[a]**	
Symptom	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**
Sneezing	None																						
	Mild																						
	Moderate																						
	Severe																						
	Not Reported																						
Sinus pressure/pain	None																						
	Mild																						
	Moderate																						
	Severe																						
	Not Reported																						
Sore/irritated throat	None																						
	Mild																						
	Moderate																						
	Severe																						
	Not Reported																						
Cough	None																						
	Mild																						
	Moderate																						
	Severe																						
	Not Reported																						

Table 45: Number and Percentage of Subjects Experiencing Local Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group -- BPZE1 10^7 CFU by VaxINator *(continued)*

BPZE1 10^7 CFU by VaxINator (N=X)																							
		Pre-Dose (N=X)		**Post-Dose (N=X)**		**Day 1-2 (N=X)**		**Day 3-4 (N=X)**		**Day 5-6 (N=X)**		**Day 7-8 (N=X)**		**Day 9-10 (N=X)**		**Day 11-12 (N=X)**		**Day 13-14 (N=X)**		**Day 15+ (N=X)**		**Any Post- Dose[a]**	
Symptom	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**
Shortness of breath/wheezing	None																						
	Mild																						
	Moderate																						
	Severe																						
	Not Reported																						

Severity is the maximum severity reported post dosing for each subject for each day.
[a]Indicates how many subjects had "None", "Mild", "Moderate", "Severe", or "Not Reported" as the maximum severity for any day.

Tables with Similar Format:

Table 46: Number and Percentage of Subjects Experiencing Local Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group - BPZE1 109 CFU by VaxINator *

Table 47: Number and Percentage of Subjects Experiencing Local Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group - BPZE1 109 CFU by Syringe *

Table 48: Number and Percentage of Subjects Experiencing Local Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group - Placebo by VaxINator *

Table 49: Number and Percentage of Subjects Experiencing Local Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group - All Subjects *

14.3.1.2 Unsolicited Adverse Events

Table 50: Summary of Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, and Treatment Group*

MedDRA System Organ Class	MedDRA Preferred Term	BPZE1 10^7 CFU by VaxINator (N=X)				BPZE1 10^9 CFU by VaxINator (N=X)				BPZE1 10^9 CFU by Syringe (N=X)				Placebo by VaxINator (N=X)				All Subjects (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																				
	[PT 1]																				
	[PT 2]																				
[SOC 2]	Any PT																				
	[PT 1]																				
	[PT 2]																				

Note: N = number of subjects in the Safety Population who received the specified dose. This table presents number and percentage of subjects. A subject is only counted once per PT.

Table 51: Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, Relationship, and Treatment Group - BPZE1 10^7 CFU by VaxINator*

MedDRA System Organ Class	Preferred Term	Severity	BPZE1 10^7 CFU by VaxINator (N = X)					
			Related		Not Related		Total	
			n	%	n	%	n	%
Any SOC	Any PT	Any Severity	x	xx	x	xx	x	xx
		Mild	x	xx	x	xx	x	xx
		Moderate	x	xx	x	xx	x	xx
		Severe	x	xx	x	xx	x	xx
SOC 1	Any PT	Any Severity	x	xx	x	xx	x	xx
		Mild	x	xx	x	xx	x	xx
		Moderate	x	xx	x	xx	x	xx
		Severe	x	xx	x	xx	x	xx
	PT 1	Any Severity	x	xx	x	xx	x	xx
		Mild	x	xx	x	xx	x	xx
		Moderate	x	xx	x	xx	x	xx
		Severe	x	xx	x	xx	x	xx
Note: N = Number of subjects in the Safety Population.								

Tables with similar format:

Table 52: Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, Relationship, and Treatment Group - BPZE1 10^9 CFU by VaxINator*

Table 53: Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, Relationship, and Treatment Group - BPZE1 10^9 CFU by Syringe*

Table 54: Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, Relationship, and Treatment Group – Placebo by VaxINator*

Table 55: Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, Relationship, and Treatment Group - All Subjects*

14.3.2 Listing of Deaths, Other Serious and Significant Adverse Events

Table 56: Listing of Serious Adverse Events*

Adverse Event	No. of Days Post 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	Subject Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Treatment Group: , Subject ID: , AE Number:											
Comments:											
Treatment Group: , Subject ID: , AE Number:											
Comments:											

Table 57: Listing of Unsolicited Non-Serious Adverse Events*

Adverse Event	No. of Days Post Dose (Duration)	Severity	Relationship to Study Treatment	If Not Related, Alternative Etiology	Action Taken with Study Treatment	Subject Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Treatment Group: , Subject ID: , AE Number:									
Comments:									
Treatment Group: , Subject ID: , AE Number:									
Comments:									

Table 58: Listing of New Onset Chronic Medical Conditions and Adverse Events of Special Interest*

Adverse Event	No. of Days Post Dose	Duration of Event	Severity	MedDRA System Organ Class	AESI?	NOCMC?	Relationship	Outcome
Treatment Group: , Subject ID: , AE Number:								
Comments:								
Treatment Group: , Subject ID: , 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 Subject)

Table 59: Listing of Abnormal Laboratory Results - Chemistry

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

Table 60: Listing of Abnormal Laboratory Results - Hematology

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

14.3.5 Displays of Laboratory Results

14.3.5.1 Chemistry Results

Table 61: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Chemistry Parameter

Any Chemistry Parameter			None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
Time Point	Treatment Group	N	n	%	n	%	n	%	n	%	n	%
Baseline	BPZE1 10^7 CFU by VaxINator	x	x	xx	x	xx	x	xx	x	xx	x	xx
	BPZE1 10^9 CFU by VaxINator											
	BPZE1 10^9 CFU by Syringe											
	Placebo by VaxINator											
	All Subjects											
Day 8	BPZE1 10^7 CFU by VaxINator											
	BPZE1 10^9 CFU by VaxINator											
	BPZE1 10^9 CFU by Syringe											
	Placebo by VaxINator											
	All Subjects											

Table 61: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Chemistry Parameter *(continued)*

Any Chemistry Parameter Time Point	Treatment Group	N	None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%
Max Severity Post Baseline	BPZE1 10^7 CFU by VaxINator											
	BPZE1 10^9 CFU by VaxINator											
	BPZE1 10^9 CFU by Syringe											
	Placebo by VaxINator											
	All Subjects											

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

Table 62: Laboratory Results by Parameter Time Point, and Treatment Group – ALT

Time Point	Treatment Group	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	BPZE1 10^7 CFU by VaxINator	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	BPZE1 10^9 CFU by VaxINator																	
	BPZE1 10^9 CFU by Syringe																	
	Placebo by VaxINator																	
	All Subjects																	
Day 8	BPZE1 10^7 CFU by VaxINator																	
	BPZE1 10^9 CFU by VaxINator																	
	BPZE1 10^9 CFU by Syringe																	
	Placebo by VaxINator																	
	All Subjects																	

Table 62: Laboratory Results by Parameter, Time Point, and Treatment Group – ALT *(continued)*

Time Point	Treatment Group	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	%
Max Severity Post Baseline	BPZE1 10^7 CFU by VaxINator																	
	BPZE1 10^9 CFU by VaxINator																	
	BPZE1 10^9 CFU by Syringe																	
	Placebo by VaxINator																	
	All Subjects																	

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

Table 63: Laboratory Results by Parameter Time Point, and Treatment Group – Creatinine

Time Point	Treatment Group	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	BPZE1 10^7 CFU by VaxINator	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	BPZE1 10^9 CFU by VaxINator																	
	BPZE1 10^9 CFU by Syringe																	
	Placebo by VaxINator																	
	All Subjects																	
Day 8	BPZE1 10^7 CFU by VaxINator																	
	BPZE1 10^9 CFU by VaxINator																	
	BPZE1 10^9 CFU by Syringe																	
	Placebo by VaxINator																	
	All Subjects																	

Table 63: Laboratory Results by Parameter, Time Point, and Treatment Group – Creatinine *(continued)*

Time Point	Treatment Group	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	%
Max Severity Post Baseline	BPZE1 10^7 CFU by VaxINator																	
	BPZE1 10^9 CFU by VaxINator																	
	BPZE1 10^9 CFU by Syringe																	
	Placebo by VaxINator																	
	All Subjects																	

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

Table 64: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Chemistry Parameter

Time Point	Treatment Group	N	Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%
Baseline	BPZE1 10^7 CFU by VaxINator	x	x	xx	x	xx	x	xx
	BPZE1 10^9 CFU by VaxINator							
	BPZE1 10^9 CFU by Syringe							
	Placebo by VaxINator							
	All Subjects							
Day 8	BPZE1 10^7 CFU by VaxINator							
	BPZE1 10^9 CFU by VaxINator							
	BPZE1 10^9 CFU by Syringe							
	Placebo by VaxINator							
	All Subjects							

Table 64: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Chemistry Parameter *(continued)*

Time Point	Treatment Group	N	Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%
Max Severity Post Baseline	BPZE1 10^7 CFU by VaxINator							
	BPZE1 10^9 CFU by VaxINator							
	BPZE1 10^9 CFU by Syringe							
	Placebo by VaxINator							
	All Subjects							

Note: The "Max Post Baseline" rows indicate the maximum severity of abnormal laboratory results related to study treatment experienced by each subject at any time point post baseline, including unscheduled assessments. N= Number of subjects in the Safety Population

Table 65: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – ALT

Time Point	Treatment Group	N	Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%
Baseline	BPZE1 10^7 CFU by VaxINator	x	x	xx	x	xx	x	xx
	BPZE1 10^9 CFU by VaxINator							
	BPZE1 10^9 CFU by Syringe							
	Placebo by VaxINator							
	All Subjects							
Day 8	BPZE1 10^7 CFU by VaxINator							
	BPZE1 10^9 CFU by VaxINator							
	BPZE1 10^9 CFU by Syringe							
	Placebo by VaxINator							
	All Subjects							

Table 65: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – ALT *(continued)*

Time Point	Treatment Group	N	Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%
Max Severity Post Baseline	BPZE1 10^7 CFU by VaxINator							
	BPZE1 10^9 CFU by VaxINator							
	BPZE1 10^9 CFU by Syringe							
	Placebo by VaxINator							
	All Subjects							

Note: The "Max Post Baseline" rows indicate the maximum severity of abnormal laboratory results related to study treatment experienced by each subject at any time point post baseline, including unscheduled assessments. N= Number of subjects in the Safety Population

Table 66: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Creatinine

Time Point	Treatment Group	N	Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%
Baseline	BPZE1 10^7 CFU by VaxINator	x	x	xx	x	xx	x	xx
	BPZE1 10^9 CFU by VaxINator							
	BPZE1 10^9 CFU by Syringe							
	Placebo by VaxINator							
	All Subjects							
Day 8	BPZE1 10^7 CFU by VaxINator							
	BPZE1 10^9 CFU by VaxINator							
	BPZE1 10^9 CFU by Syringe							
	Placebo by VaxINator							
	All Subjects							

Table 66: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Creatinine *(continued)*

Time Point	Treatment Group	N	Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%
Max Severity Post Baseline	BPZE1 10^7 CFU by VaxINator							
	BPZE1 10^9 CFU by VaxINator							
	BPZE1 10^9 CFU by Syringe							
	Placebo by VaxINator							
	All Subjects							

Note: The "Max Post Baseline" rows indicate the maximum severity of abnormal laboratory results related to study treatment experienced by each subject at any time point post baseline, including unscheduled assessments. N= Number of subjects in the Safety Population

Table 67: Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – ALT

Time Point	Treatment Group	N	Mean	Standard Deviation	Median	Min, Max
Baseline	BPZE1 10^7 CFU by VaxINator	x	xx x	xx x	xx x	xx x, xx x
	BPZE1 10^9 CFU by VaxINator					
	BPZE1 10^9 CFU by Syringe					
	Placebo by VaxINator					
	All Subjects					
Day 8	BPZE1 10^7 CFU by VaxINator					
	BPZE1 10^9 CFU by VaxINator					
	BPZE1 10^9 CFU by Syringe					
	Placebo by VaxINator					
	All Subjects					
Day 8, Change from Baseline	BPZE1 10^7 CFU by VaxINator					
	BPZE1 10^9 CFU by VaxINator					
	BPZE1 10^9 CFU by Syringe					
	Placebo by VaxINator					
	All Subjects					
Note: N= Number of subjects in the Safety Population						

Table 68: Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Creatinine

Time Point	Treatment Group	N	Mean	Standard Deviation	Median	Min, Max
Baseline	BPZE1 10^7 CFU by VaxINator	x	xx x	xx x	xx x	xx x, xx x
	BPZE1 10^9 CFU by VaxINator					
	BPZE1 10^9 CFU by Syringe					
	Placebo by VaxINator					
	All Subjects					
Day 8	BPZE1 10^7 CFU by VaxINator					
	BPZE1 10^9 CFU by VaxINator					
	BPZE1 10^9 CFU by Syringe					
	Placebo by VaxINator					
	All Subjects					
Day 8, Change from Baseline	BPZE1 10^7 CFU by VaxINator					
	BPZE1 10^9 CFU by VaxINator					
	BPZE1 10^9 CFU by Syringe					
	Placebo by VaxINator					
	All Subjects					
Note: N= Number of subjects in the Safety Population						

14.3.5.2 Hematology Results

Table 69: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Hematology Parameter

Any Hematology Parameter Time Point	Treatment Group	N	None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%
Baseline	BPZE1 10^7 CFU by VaxINator	x	x	xx	x	xx	x	xx	x	xx	x	xx
	BPZE1 10^9 CFU by VaxINator											
	BPZE1 10^9 CFU by Syringe											
	Placebo by VaxINator											
	All Subjects											
Day 8	BPZE1 10^7 CFU by VaxINator											
	BPZE1 10^9 CFU by VaxINator											
	BPZE1 10^9 CFU by Syringe											
	Placebo by VaxINator											
	All Subjects											

Table 69: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Hematology Parameter *(continued)*

Any Hematology Parameter Time Point	Treatment Group	N	None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%
Max Severity Post Baseline	BPZE1 10^7 CFU by VaxINator											
	BPZE1 10^9 CFU by VaxINator											
	BPZE1 10^9 CFU by Syringe											
	Placebo by VaxINator											
	All Subjects											

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

Table 70: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – White Blood Cell Count

Time Point	Treatment Group	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	BPZE1 10^7 CFU by VaxINator	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	BPZE1 10^9 CFU by VaxINator																	
	BPZE1 10^9 CFU by Syringe																	
	Placebo by VaxINator																	
	All Subjects																	
Day 8	BPZE1 10^7 CFU by VaxINator																	
	BPZE1 10^9 CFU by VaxINator																	
	BPZE1 10^9 CFU by Syringe																	
	Placebo by VaxINator																	
	All Subjects																	

Table 70: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – White Blood Cell Count *(continued)*

Time Point	Treatment Group	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	%
Max Severity Post Baseline	BPZE1 10^7 CFU by VaxINator																	
	BPZE1 10^9 CFU by VaxINator																	
	BPZE1 10^9 CFU by Syringe																	
	Placebo by VaxINator																	
	All Subjects																	

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

Table 71: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Platelet Count

Time Point	Treatment Group	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	BPZE1 10^7 CFU by VaxINator	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	BPZE1 10^9 CFU by VaxINator																	
	BPZE1 10^9 CFU by Syringe																	
	Placebo by VaxINator																	
	All Subjects																	
Day 8	BPZE1 10^7 CFU by VaxINator																	
	BPZE1 10^9 CFU by VaxINator																	
	BPZE1 10^9 CFU by Syringe																	
	Placebo by VaxINator																	
	All Subjects																	

Table 71: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Platelet Count *(continued)*

Time Point	Treatment Group	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	%
Max Severity Post Baseline	BPZE1 10^7 CFU by VaxINator																	
	BPZE1 10^9 CFU by VaxINator																	
	BPZE1 10^9 CFU by Syringe																	
	Placebo by VaxINator																	
	All Subjects																	

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

Table 72: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Hemoglobin

Time Point	Treatment Group	N	None		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%
Baseline	BPZE1 10^7 CFU by VaxINator	x	x	xx	x	xx	x	xx	x	xx	x	xx
	BPZE1 10^9 CFU by VaxINator											
	BPZE1 10^9 CFU by Syringe											
	Placebo by VaxINator											
	All Subjects											
Day 8	BPZE1 10^7 CFU by VaxINator											
	BPZE1 10^9 CFU by VaxINator											
	BPZE1 10^9 CFU by Syringe											
	Placebo by VaxINator											
	All Subjects											

Table 72: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Hemoglobin *(continued)*

Time Point	Treatment Group	N	None		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%
Max Severity Post Baseline	BPZE1 10^7 CFU by VaxINator											
	BPZE1 10^9 CFU by VaxINator											
	BPZE1 10^9 CFU by Syringe											
	Placebo by VaxINator											
	All Subjects											

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

Table 73: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Hematology Parameter

Time Point	Treatment Group	N	Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%
Day 8	BPZE1 10^7 CFU by VaxINator	x	x	xx	x	xx	x	xx
	BPZE1 10^9 CFU by VaxINator							
	BPZE1 10^9 CFU by Syringe							
	Placebo by VaxINator							
	All Subjects							
Max Severity Post Baseline	BPZE1 10^7 CFU by VaxINator							
	BPZE1 10^9 CFU by VaxINator							
	BPZE1 10^9 CFU by Syringe							
	Placebo by VaxINator							
	All Subjects							

Note: The "Max Post Baseline" rows indicate the maximum severity of abnormal laboratory results related to study treatment experienced by each subject at any time point post baseline, including unscheduled assessments. N = Number of subjects in the Safety Population

Table 74: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – White Blood Cell Count

Time Point	Treatment Group	N	Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%
Day 8	BPZE1 10^7 CFU by VaxINator	x	x	xx	x	xx	x	xx
	BPZE1 10^9 CFU by VaxINator							
	BPZE1 10^9 CFU by Syringe							
	Placebo by VaxINator							
	All Subjects							
Max Severity Post Baseline	BPZE1 10^7 CFU by VaxINator							
	BPZE1 10^9 CFU by VaxINator							
	BPZE1 10^9 CFU by Syringe							
	Placebo by VaxINator							
	All Subjects							

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

Table 75: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Platelet Count

Time Point	Treatment Group	N	Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%
Day 8	BPZE1 10^7 CFU by VaxINator	x	x	xx	x	xx	x	xx
	BPZE1 10^9 CFU by VaxINator							
	BPZE1 10^9 CFU by Syringe							
	Placebo by VaxINator							
	All Subjects							
Max Severity Post Baseline	BPZE1 10^7 CFU by VaxINator							
	BPZE1 10^9 CFU by VaxINator							
	BPZE1 10^9 CFU by Syringe							
	Placebo by VaxINator							
	All Subjects							

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

Table 76: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Hemoglobin

Time Point	Treatment Group	N	Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%
Day 8	BPZE1 10^7 CFU by VaxINator	x	x	xx	x	xx	x	xx
	BPZE1 10^9 CFU by VaxINator							
	BPZE1 10^9 CFU by Syringe							
	Placebo by VaxINator							
	All Subjects							
Max Severity Post Baseline	BPZE1 10^7 CFU by VaxINator							
	BPZE1 10^9 CFU by VaxINator							
	BPZE1 10^9 CFU by Syringe							
	Placebo by VaxINator							
	All Subjects							

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

Table 77: Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – White Blood Cell Count

Time Point	Treatment Group	N	Mean	Standard Deviation	Median	Min, Max
Baseline	BPZE1 10^7 CFU by VaxINator	x	xx x	xx x	xx x	xx x, xx x
	BPZE1 10^9 CFU by VaxINator					
	BPZE1 10^9 CFU by Syringe					
	Placebo by VaxINator					
	All Subjects					
Day 8	BPZE1 10^7 CFU by VaxINator					
	BPZE1 10^9 CFU by VaxINator					
	BPZE1 10^9 CFU by Syringe					
	Placebo by VaxINator					
	All Subjects					
Day 8, Change from Baseline	BPZE1 10^7 CFU by VaxINator					
	BPZE1 10^9 CFU by VaxINator					
	BPZE1 10^9 CFU by Syringe					
	Placebo by VaxINator					
	All Subjects					
Note: N = Number of subjects in the Safety Population						

Table 78: Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Platelet Count

Time Point	Treatment Group	N	Mean	Standard Deviation	Median	Min, Max
Baseline	BPZE1 10^7 CFU by VaxINator	x	xx x	xx x	xx x	xx x, xx x
	BPZE1 10^9 CFU by VaxINator					
	BPZE1 10^9 CFU by Syringe					
	Placebo by VaxINator					
	All Subjects					
Day 8	BPZE1 10^7 CFU by VaxINator					
	BPZE1 10^9 CFU by VaxINator					
	BPZE1 10^9 CFU by Syringe					
	Placebo by VaxINator					
	All Subjects					
Day 8, Change from Baseline	BPZE1 10^7 CFU by VaxINator					
	BPZE1 10^9 CFU by VaxINator					
	BPZE1 10^9 CFU by Syringe					
	Placebo by VaxINator					
	All Subjects					
Note: N = Number of subjects in the Safety Population						

Table 79: Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Hemoglobin

[Time Point	Treatment Group	N	Mean	Standard Deviation	Median	Min, Max
Baseline	BPZE1 10^7 CFU by VaxINator	x	xx x	xx x	xx x	xx x, xx x
	BPZE1 10^9 CFU by VaxINator					
	BPZE1 10^9 CFU by Syringe					
	Placebo by VaxINator					
	All Subjects					
Day 8	BPZE1 10^7 CFU by VaxINator					
	BPZE1 10^9 CFU by VaxINator					
	BPZE1 10^9 CFU by Syringe					
	Placebo by VaxINator					
	All Subjects					
Day 8, Change from Baseline	BPZE1 10^7 CFU by VaxINator					
	BPZE1 10^9 CFU by VaxINator					
	BPZE1 10^9 CFU by Syringe					
	Placebo by VaxINator					
	All Subjects					
Note: N = Number of subjects in the Safety Population						

14.4 Summary of Concomitant Medications

Table 80: Number and Percentage of Subjects with Prior and Concurrent Medications by WHO Drug Classification and Treatment Group

WHO Drug Code Level 1, Anatomic Group	WHO Drug Code Level 2, Therapeutic Subgroup	BPZE1 10^7 CFU by VaxINator (N=X)		BPZE1 10^9 CFU by VaxINator (N=X)		BPZE1 10^9 CFU by Syringe (N=X)		Placebo by VaxINator (N=X)		All Subjects (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]										
	[ATC 2 - 1]										
	[ATC 2 - 2]										
	[ATC 2 - 3]										
[ATC Level 1 – 2]	[ATC 2 - 1]										
	[ATC 2 - 2]										
	[ATC 2 - 3]										

N = Number of subjects in the Safety Population. n=Number of subjects reporting taking at least one medication in the specific WHO Drug Class.

APPENDIX 2. FIGURE MOCK-UPS

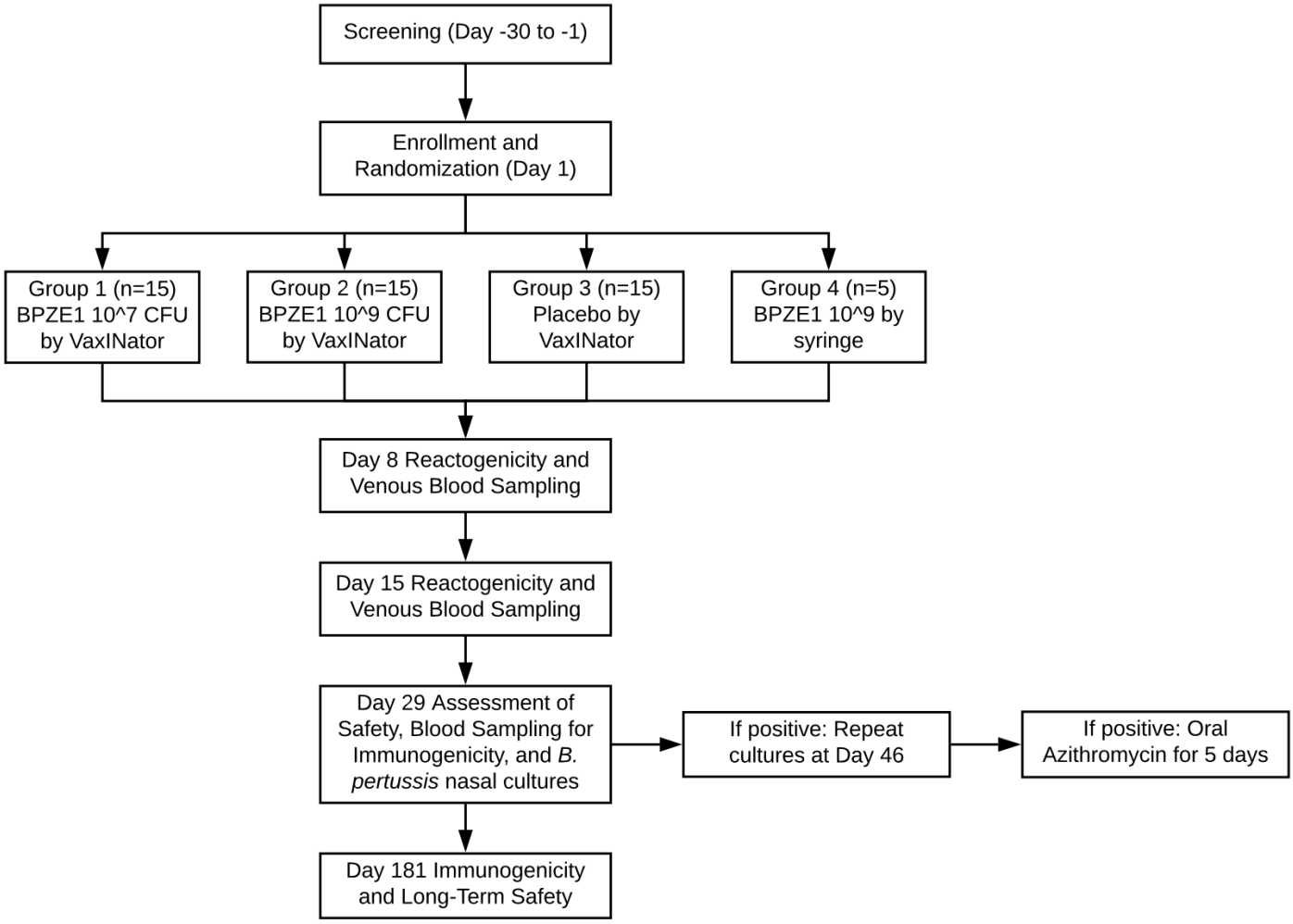
Figures that will be included in the Preliminary Report are indicated with an asterisk (*) in the title.

LIST OF FIGURES

List of Figures *(continued)*

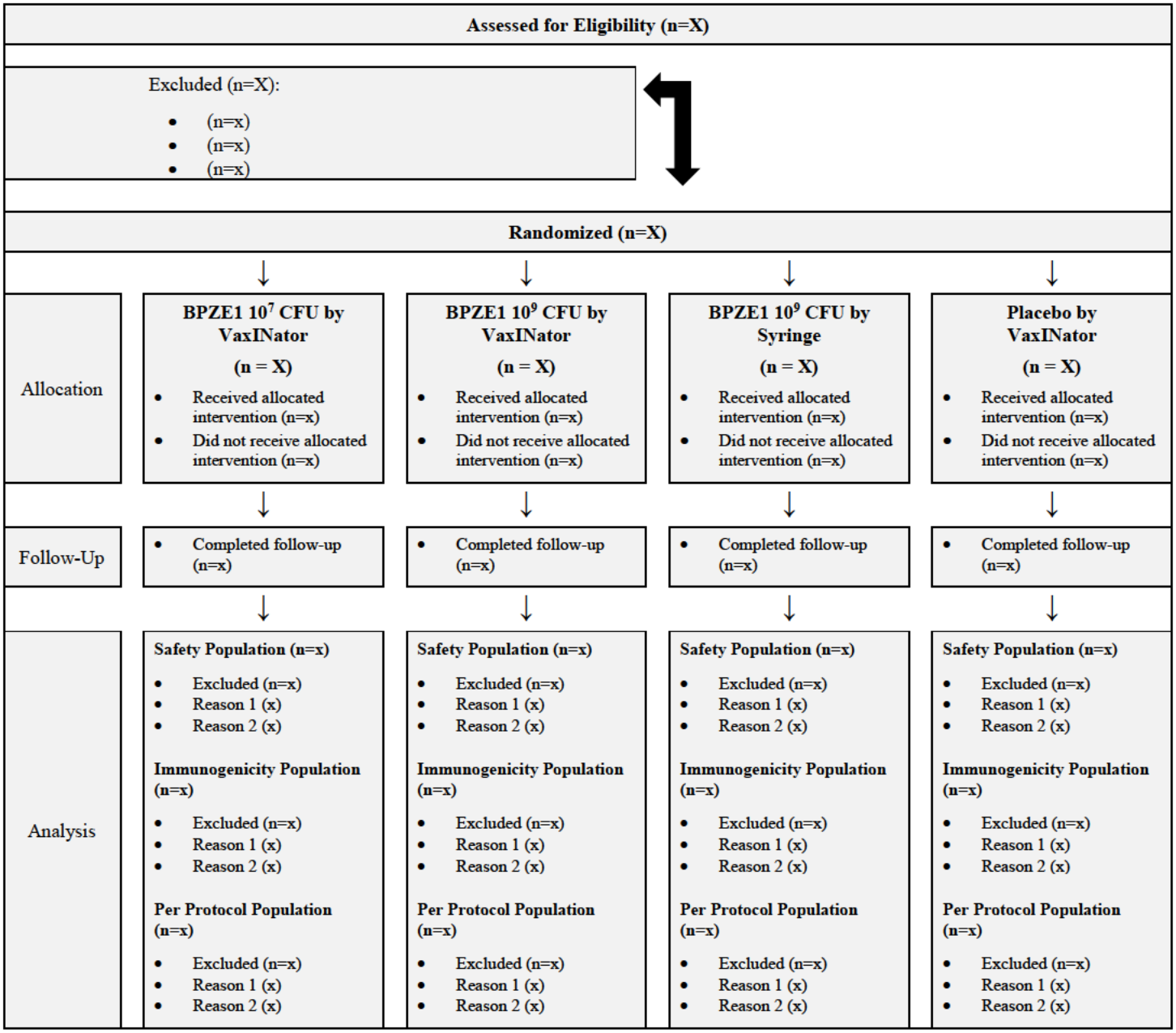
9.1 Overall Study Design and Plan Description

Figure 1 Schematic of Study Design*



10.1 Disposition of Subjects

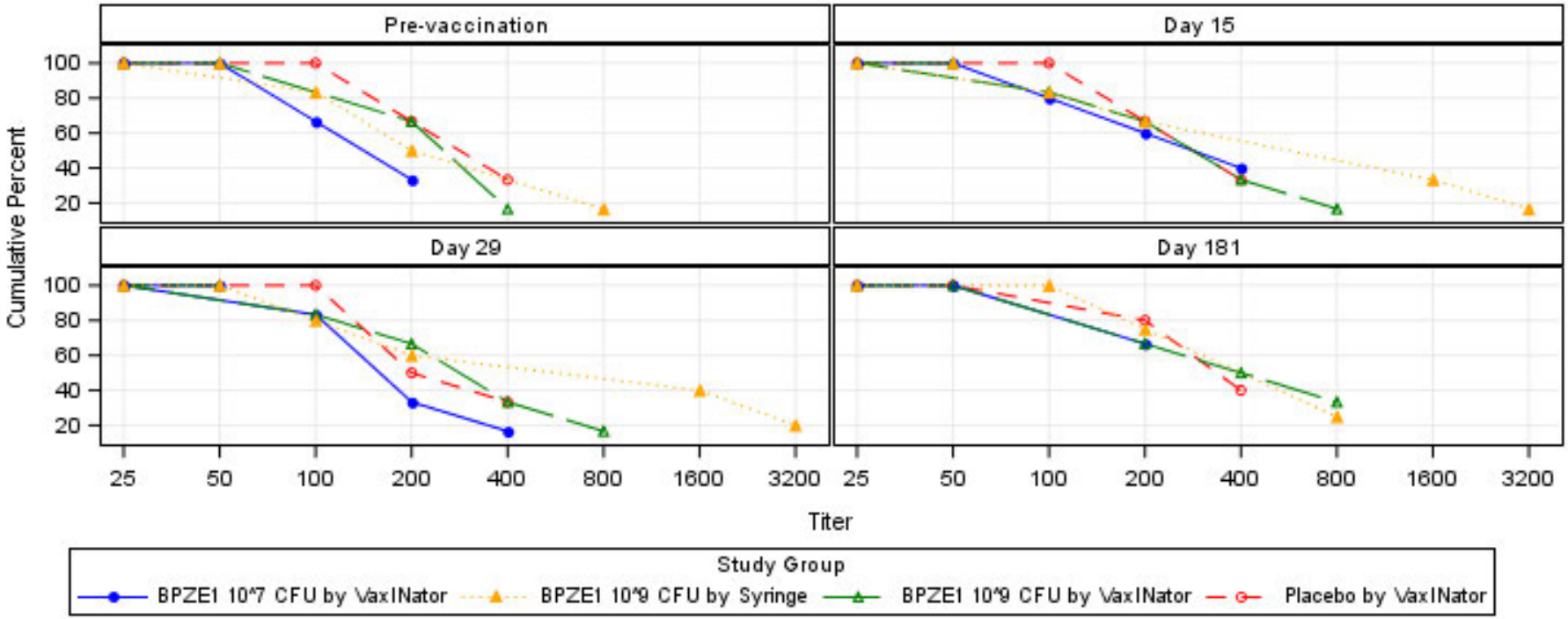
Figure 2: CONSORT Flow Diagram



14.2.2 Efficacy/Immunogenicity Response Figures by Measure, Treatment/Vaccination, and Time Point

Figure 3: Reverse Cumulative Distribution of Serum IgA Antibody Titers by Time Point and Treatment Group, Immunogenicity Population*

[Implementation Note: A sample figure is shown below. The legend order will be BPZE1 10^7 by VaxINator, BPZE1 10^9 by VaxINator, BPZE1 10^9 by Syringe and Placebo by VaxINator.]



Figures with similar format:

Figure 4: Reverse Cumulative Distribution of Serum IgA Antibody Titers by Time Point and Treatment Group, Per Protocol Population*

Figure 5: Reverse Cumulative Distribution of Serum IgG Antibody Titers by Time Point and Treatment Group, Immunogenicity Population*

Figure 6: Reverse Cumulative Distribution of Serum IgG Antibody Titers by Time Point and Treatment Group, Per Protocol Population*

Figure 7: Reverse Cumulative Distribution of Mucosal IgA Antibody Titers by Time Point and Treatment Group, Immunogenicity Population*

Figure 8: Reverse Cumulative Distribution of Mucosal IgA Antibody Titers by Time Point and Treatment Group, Per Protocol Population*

14.3.1.1 Solicited Adverse Events

Figure 9: Maximum Severity of Solicited Systemic Events (by Symptom)*

[Implementation Note: A sample figure is shown below. The following solicited events will be included: fever, feverishness, fatigue (tiredness), malaise (general unwell feeling), myalgia (body aches/muscular pain), arthralgia (joint pain), headache, rash/hypersensitivity and any systemic. The following five panels will be shown: BPZE1 10^7 by VaxINator, BPZE1 10^9 by VaxINator, BPZE1 10^9 by Syringe, Placebo by VaxINator and All Subjects.]

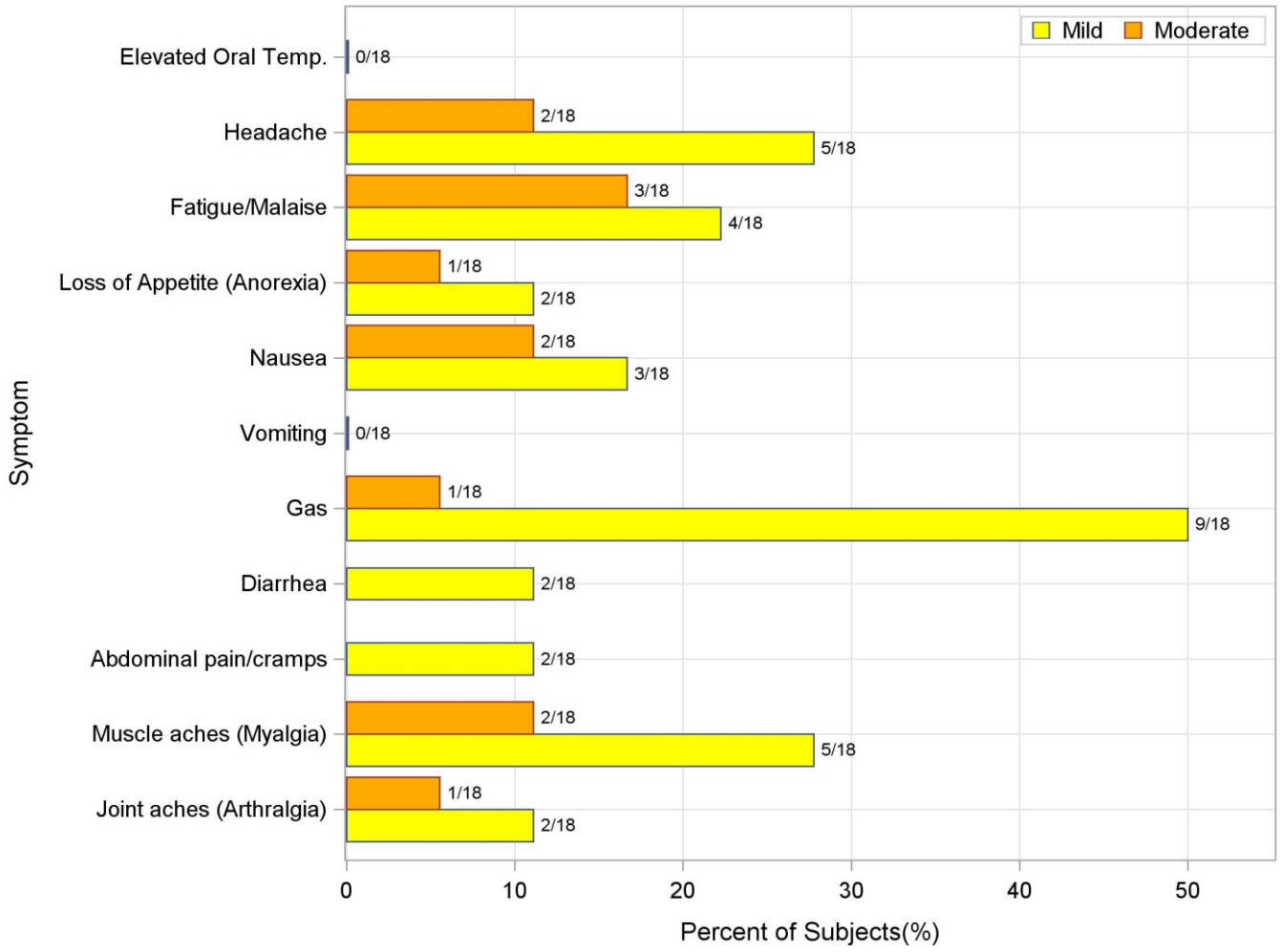


Figure with Similar Format:

Figure 10: Maximum Severity of Solicited Local Events (by Symptom)*

[Implementation Note: The following solicited events will be included: runny nose, stuffy nose/congestion, nasal pain/irritation, epistaxis, sneezing, sinus pressure/pain, sore/irritated throat, cough and shortness of breath/wheezing and any local. The following five panels will be shown: BPZE1 10^7 by VaxINator, BPZE1 10^9 by VaxINator, BPZE1 10^9 by Syringe, Placebo by VaxINator and All Subjects.]

Figure 11: Maximum Severity of Solicited Systemic Symptoms per Subject by Days Post Treatment*

[Implementation Note: A sample figure is shown below. The following timepoints will be presented; Post-vaccination, Days 1-2, Days 3-4, Days 5-6, Days 7-8, Days 9-10, Days 11-12, Days 13-14, and Days15+. The following five panels will be shown: BPZE1 10^7 by VaxINator, BPZE1 10^9 by VaxINator, BPZE1 10^9 by Syringe, Placebo by VaxINator and All Subjects.]

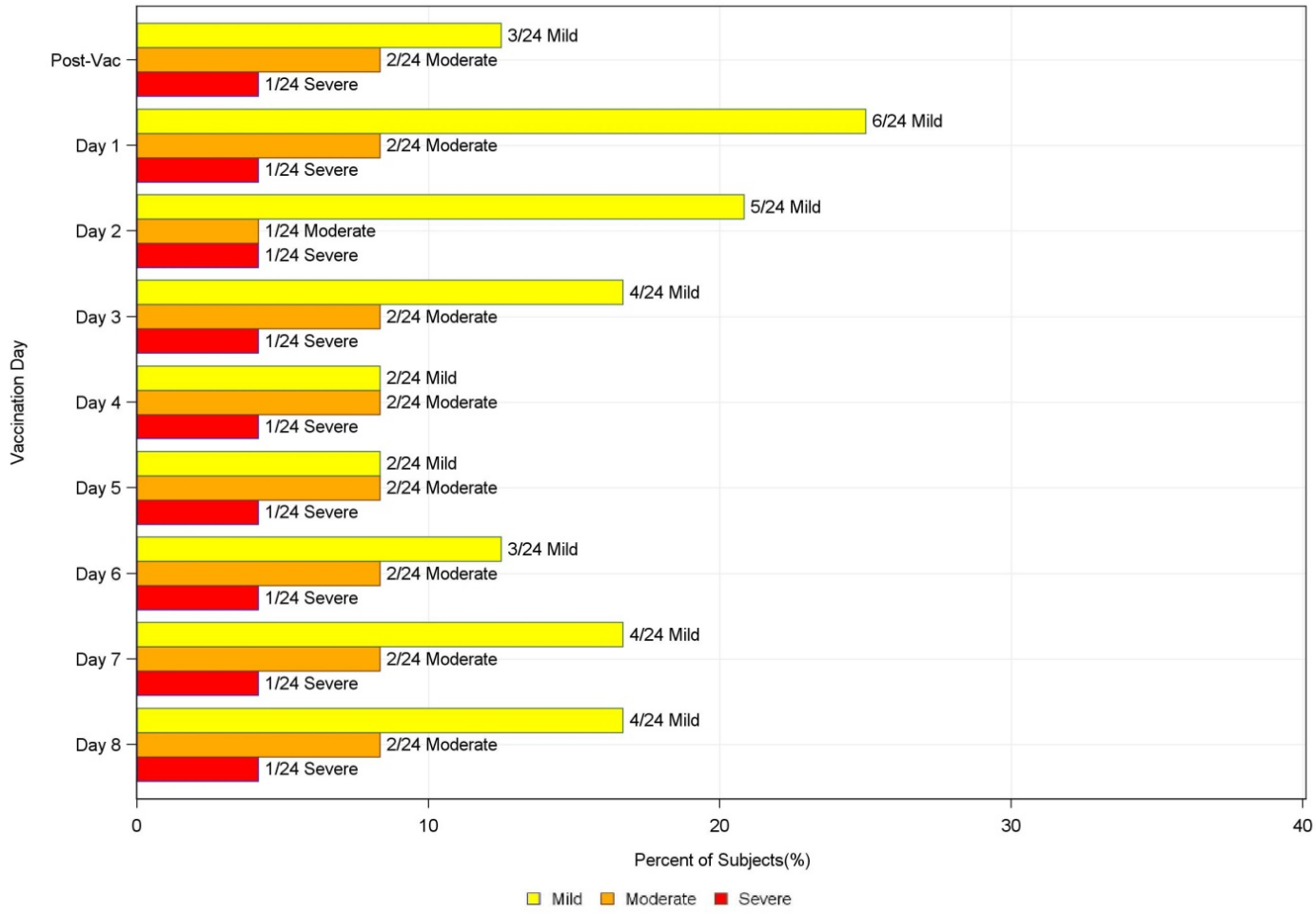


Figure with Similar Format:

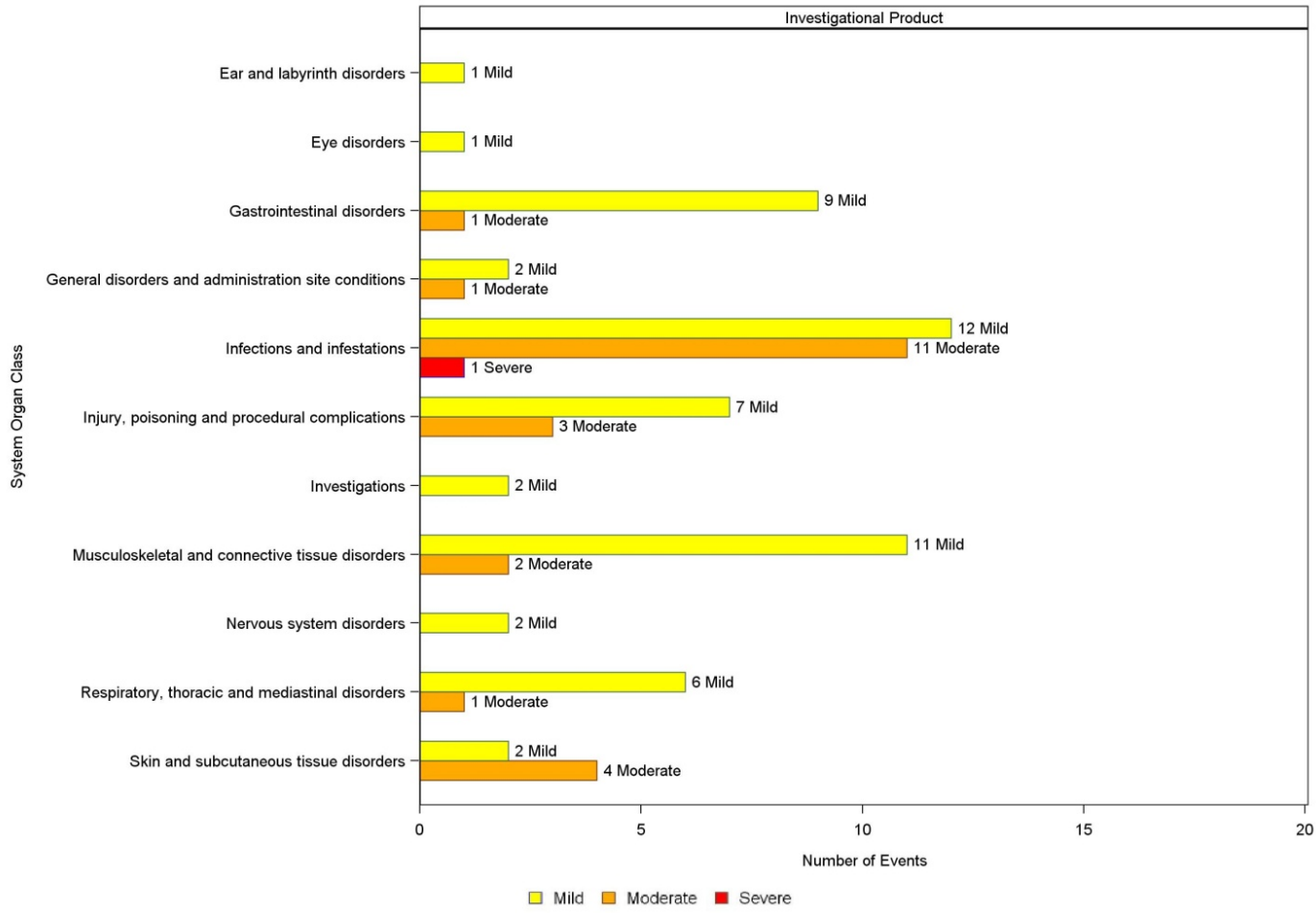
Figure 12: Maximum Severity of Solicited Local Symptoms by Days Post Treatment*

[Implementation Note: The following timepoints will be presented; Pre-vaccination, Post-vaccination, Days 1-2, Days 3-4, Days 5-6, Days 7-8, Days 9-10, Days 11-12, Days 13-14, and Days15+. The following five panels will be shown: BPZE1 10^7 by VaxINator, BPZE1 10^9 by VaxINator, BPZE1 10^9 by Syringe, Placebo by VaxINator and All Subjects.]

14.3.1.2 Unsolicited Adverse Events

Figure 13: Number and Severity of All Adverse Events by MedDRA® System Organ Class*

[Implementation Note: A sample figure is shown below. This will include NOCMC's and AESI's. The following five panels will be shown: BPZE1 10^7 by VaxINator, BPZE1 10^9 by VaxINator, BPZE1 10^9 by Syringe, Placebo by VaxINator and All Subjects.]



14.3.5 Displays of Laboratory Results

Figure 14: Clinical Laboratory Results by Severity – Hematology

[Implementation Note: A sample figure is shown below. White blood cell count increased/decreased, platelet count increased/decreased and hemoglobin decreased will be presented. The following five panels will be shown: BPZE1 10^7 by VaxINator, BPZE1 10^9 by VaxINator, BPZE1 10^9 by Syringe, Placebo by VaxINator and All Subjects.]

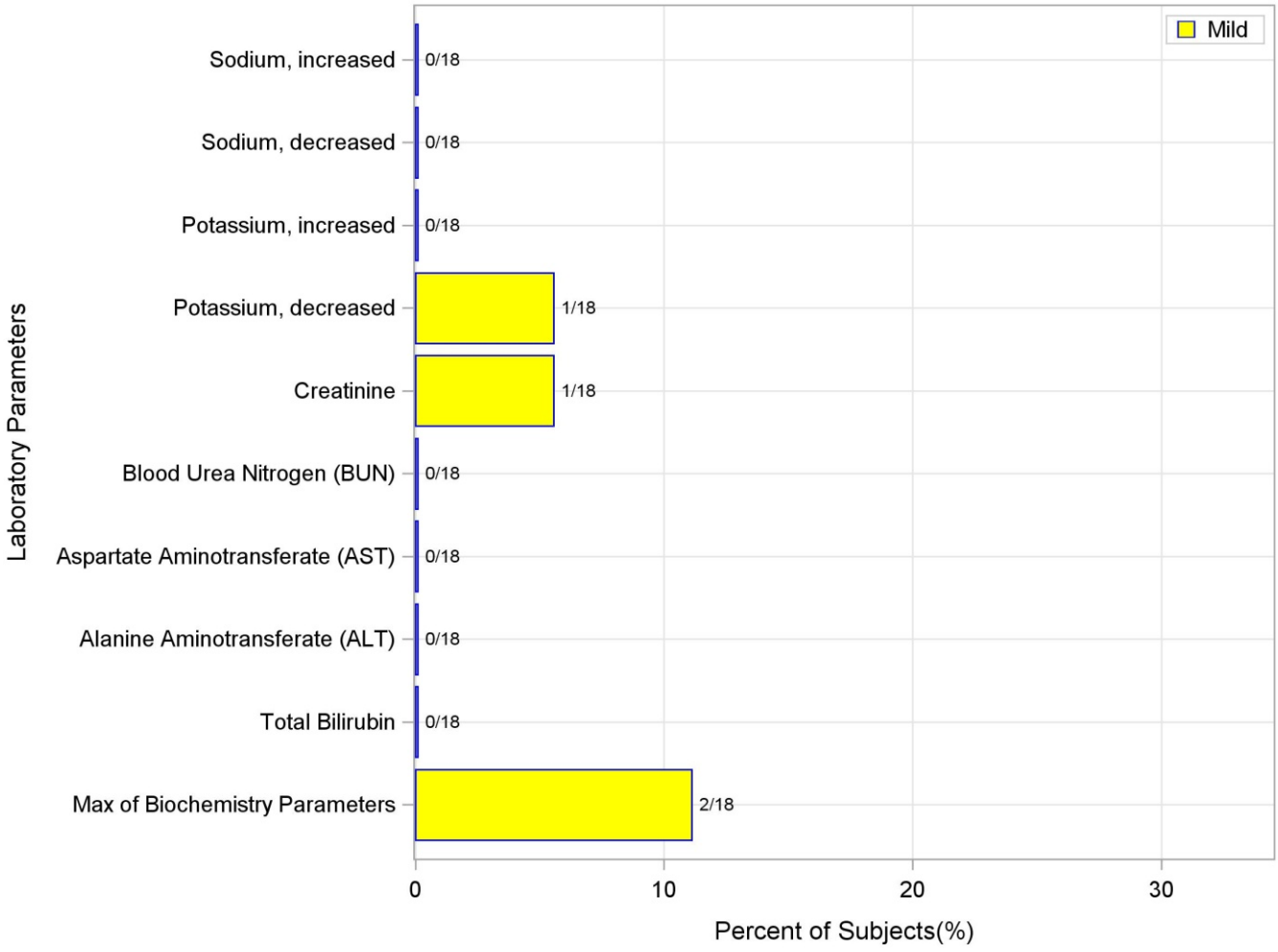


Figure 15: Clinical Laboratory Results by Severity – Chemistry

[Implementation Note: A sample figure is shown below. Only Creatinine and ALT will be presented. The following five panels will be shown: BPZE1 10^7 by VaxINator, BPZE1 10^9 by VaxINator, BPZE1 10^9 by Syringe, Placebo by VaxINator and All Subjects.]

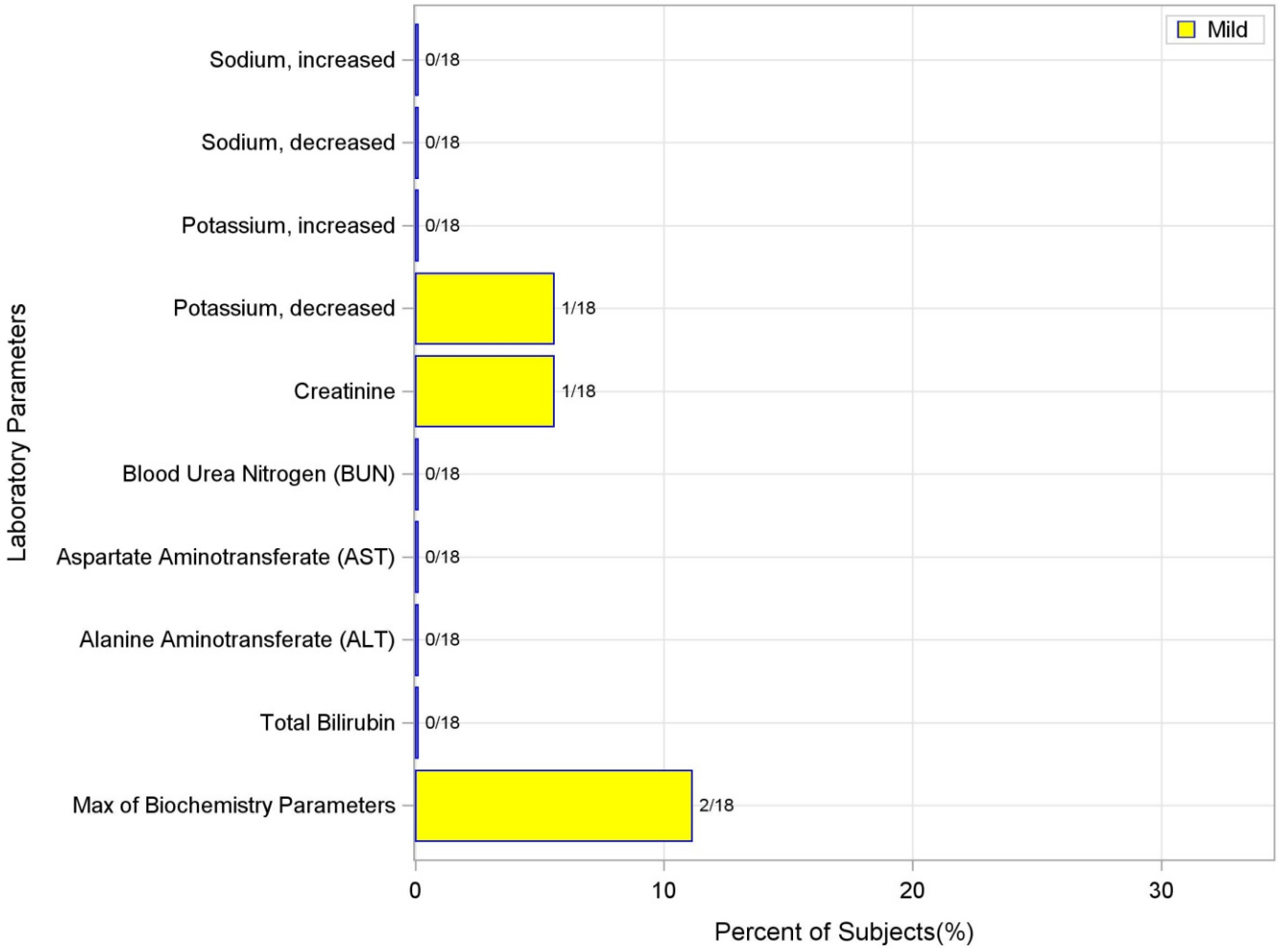
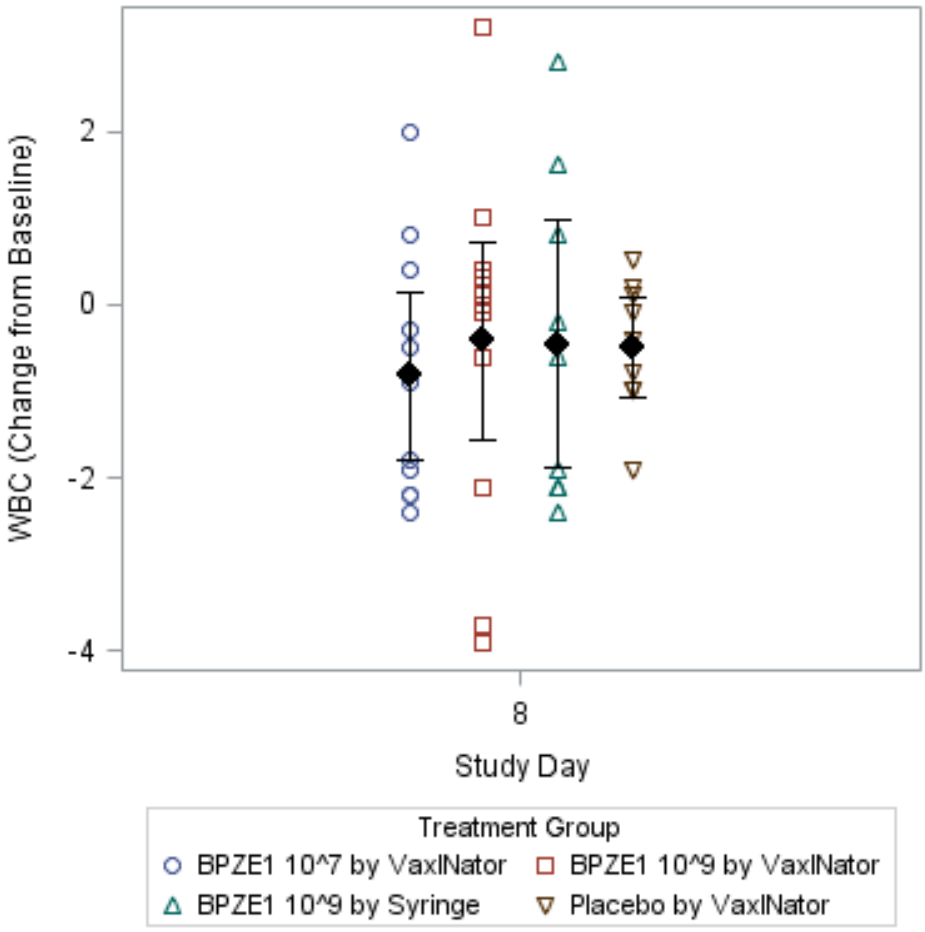


Figure 16: Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, and Treatment Group – White Blood Cell Count

[Implementation note: A sample figure is presented below. A scatter plot (dot plot) will be generated that displays each subject's change from baseline at Day 8 with the two treatment groups side by side. Overlaid on this plot will be the mean and standard deviation bars. Y-axis should be labeled "[Parameter] Change from Baseline ([units])"



Figures with similar format:

Figure 17: Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, and Treatment Group – Platelet Count

Figure 18: Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, and Treatment Group – Hemoglobin

Figure 19: Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, and Treatment Group – ALT

Figure 20: Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, and Treatment Group – Creatinine

APPENDIX 3. LISTINGS MOCK-UPS

Listings are not included in the Preliminary Report.

LISTINGS

16.1.6 Listing of Subjects Receiving Investigational Product

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

16.2 Database Listings by Subject

16.2.1 Discontinued Subjects

Listing 1: 16.2.1 Early Terminations

Treatment Group	Subject ID	Reason for Early Termination	Study Day

16.2.2 Protocol Deviations

Listing 2: 16.2.2.1: Subject-Specific Protocol Deviations

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

Listing 3: 16.2.2.2: Non-Subject-Specific Protocol Deviations

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

16.2.3 Subjects Excluded from Analysis

Listing 4: 16.2.3: Subjects Excluded from Analysis Populations

Treatment Group	Subject ID	Analyses in which Subject is Included	Analyses from which Subject is Excluded	Results Available?	Reason Subject Excluded
		[e.g., Safety, ITT, PP]	[e.g., Safety, ITT, PP, Day x]		
Note: "Yes" in the "Results available" column indicates that available data were removed from the analysis. "No" indicates that no data were available for inclusion in the analysis.					

16.2.4 Demographic Data

Listing 5: 16.2.4.1: Demographic Data

Treatment Group	Subject ID	Sex	Age at Enrollment (years)	Ethnicity	Race

Listing 6: 16.2.4.2: Pre-Existing and Concurrent Medical Conditions

Treatment Group	Subject ID	MH Number	Medical History Term	Condition Start Day	Condition End Day	MedDRA System Organ Class	MedDRA Preferred Term

16.2.6 Individual Immunogenicity Response Data

Listing 7: 16.2.6.1: Individual Immunogenicity Response Data – Serum IgA

				PT Antibody		FHA Antibody		PRN Antibody		FIM 2/3 Antibody	
Treatment Group	Subject ID	Planned Time Point	Actual Study Day	Titer	Fold-Rise	Titer	Fold-Rise	Titer	Fold-Rise	Titer	Fold-Rise

Listings with similar format:

Listing 8: 16.2.6.2: Individual Immunogenicity Response Data – Serum IgG

Listing 9: 16.2.6.3: Individual Immunogenicity Response Data –Mucosal IgA

16.2.7 Adverse Events

Listing 10: 16.2.7.1: Solicited Events – Systemic Symptoms

Treatment Group	Subject ID	Post Dose Day	Assessment[a]	Symptom	Severity	Attributed to Alternate Etiology?[b]	Alternate Etiology
			MA				
			Clinic				

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

Listing 11: 16.2.7.2: Solicited Events – Local Symptoms

Treatment Group	Subject ID	Post Dose Day	Assessment[a]	Symptom	Severity
			MA		
			Clinic		

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

Listing 12: 16.2.7.3: Unsolicited Adverse Events

Adverse Event	No. of Days Post Dose (Duration)	Severity	SAE?	Relationship to Study Treatment	In Not Related, Alternative Etiology	Action Taken with Study Treatment	Subject Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Treatment Group: , Subject ID: , AE Number:										
Comments:										
Treatment Group: , Subject ID: , AE Number:										
Comments:										
Note: For additional details about SAEs, see Table 56.										

Listing 13: 16.2.7.4: Individual Nasal Colonization Data

Treatment Group	Subject ID	Planned Time Point	Actual Study Day	*B. pertussis* Positive?

16.2.8 Individual Laboratory Measurements

Listing 14: 16.2.8.1: Clinical Laboratory Results – Chemistry

Treatment Group	Subject ID	Planned Time Point	Actual Study Day	Sex	Age (years)	Laboratory Parameter (Units)	Result (Severity Grade)	Reference Range Low	Reference Range High

Listing 15: 16.2.8.2: Clinical Laboratory Results – Hematology

Treatment Group	Subject ID	Planned Time Point	Actual Study Day	Sex	Age (years)	Laboratory Parameter (Units)	Result (Severity Grade)	Reference Range Low	Reference Range High

16.2.9 Vital Signs and Physical Exam Findings

Listing 16: 16.2.9.1: Vital Signs

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

Listing 17: 16.2.9.2: Physical Exam Findings

Treatment Group	Subject ID	Planned Time Point	Actual Study Day	Body System	Abnormal Finding	Reported as an AE? (AE Description; Number)	If Yes, Adverse Event
						No	
						Yes, Solicited	[Solicited AE]
						Yes, Unsolicited	[Unsolicited AE Desc.; Number]

16.2.10 Concomitant Medications

Listing 18: 16.2.10: Concomitant Medications

Treatment Group	Subject ID	CM Number	Medication	Medication Start Day	Medication End Day	Indication	Taken for an AE?	If Yes, Adverse Event	Taken for a condition on Medical History? (MH Description; Number)	ATC Level 1 (ATC Level 2)
							No			
							Yes, Solicited	[Solicited AE]		
							Yes, Unsolicited	[Unsolicited AE Desc.; Number]		

16.2.11 Pregnancy Reports

Listing 19: 16.2.11.1: Pregnancy Reports – Maternal Information

Treatment Group	Subject 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 20: 16.2.11.2: Pregnancy Reports – Gravida and Para

			Live Births												
Subject ID	Pregnancy Number	Gravida	Extremely PB[a]	Very Early PB[a]	Early PB[a]	Late PB[a]	Early TB[b]	Full TB[b]	Late TB[b]	Post TB[b]	Still Births	Spontaneous Abortion/ Miscarriage	Elective Abortions	Therapeutic Abortions	Major Congenital Anomaly with Previous Pregnancy?
Note: Gravida includes the current pregnancy, para events do not.															

a Preterm Birth
b Term Birth

Listing 21: 16.2.11.3: Pregnancy Reports – Live Birth Outcomes

Subject ID	Pregnancy Number	Fetus Number	Pregnancy Outcome (for this Fetus)	Fetal Distress During Labor and Delivery?	Delivery Method	Gestational Age at Live Birth	Size for Gestational Age	Apgar Score, 1 minute	Apgar Score, 5 minutes	Cord pH	Congenital Anomalies?	Illnesses/ Hospitalizations within 1 Month of Birth?
Note: Congenital Anomalies are included in the Adverse Event listing.												

Listing 22: 16.2.11.4: Pregnancy Reports – Still Birth Outcomes

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

Listing 23: 16.2.11.5: Pregnancy Reports – Spontaneous, Elective, or Therapeutic Abortion Outcomes

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