CLINICAL RESEARCH IN INFECTIOUS DISEASES

STATISTICAL ANALYSIS PLAN
for
DMID Protocol: 16-0024

Study Title:
A Phase II Double-blind Trial to Evaluate the Safety, Immunogenicity and Effect on Infant Immune Responses of a Single Dose of Tdap in Pregnant Women in Mali

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Version 1.0

DATE: 31-MAR-2021

A Phase II Double-blind Trial to Evaluate the Safety, Immunogenicity and Effect on Infant Immune Responses of a Single Dose of Tdap in Pregnant Women in Mali

Protocol Number Code:	**DMID Protocol: 16-0024**
Development Phase:	Phase II
Products:	BOOSTRIX/Td Control Vaccine
Form/Route:	Administered intramuscularly as a single 0.5 mL dose.
Indication Studied:	Pertussis
Sponsor:	Division of Microbiology and Infectious Diseases National Institute of Allergy and Infectious Diseases National Institutes of Health
Clinical Trial Initiation Date:	20 DECEMBER 2018
Clinical Trial Completion Date:	01 JULY 2020
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Version Number:	1.0

This study was performed in compliance with Good Clinical Practice.

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LIST OF ABBREVIATIONS

°C	Degrees Celsius
°F	Degrees Fahrenheit
ACIP	Advisory Committee on Immunization Practices, CDC
ACOG	American College of Obstetrics and Gynecology
AE	Adverse Event
ATC	Anatomical Therapeutic Classification
BP	Blood Pressure
BSE	Bovine Spongiform Encephalopathy
bpm	Beats per Minute
CBC	Complete Blood Count
CI	Confidence Interval
CRF	Case Report Form
CS	Cesarean Section
CSR	Clinical Study Report
D	Day
DMID	Division of Microbiology and Infectious Diseases
DSMB	Data and Safety Monitoring Board
DTwP	Diphtheria, Tetanus, and whole-cell Pertussis Vaccine
EBL	Estimated Blood Loss
eCRF	Electronic Case Report Form
EGA	Estimated Gestational Age
ELISA	Enzyme-Linked Immunosorbent Assay
FDA	Food and Drug Administration
FHA	Filamentous Hemagglutinin
FIM 2	Fimbriae 2
FIM 3	Fimbriae 3
GA	Gestational Age
gDM	Gestational Diabetes Mellitus
GMC	Geometric Mean Concentration
GMR	Geometric Mean Ratio
GSK	GlaxoSmithKline Biologicals
HEENT	Head, Eyes, Ears, Nose, and Throat
HELLP	Hemolysis, Elevated Liver enzymes, Low Platelet count
HIV	Human Immunodeficiency Virus
ICF	Informed Consent Form
ICH	International Council for Harmonisation
IFN	Interferon

List of Abbreviations *(continued)*

IgA	Immunoglobulin A
IgG	Immunoglobulin G
IL	Interleukin
ITT	Intent-to-Treat
LMP	Last Menstrual Period
MedDRA®	Medical Dictionary for Regulatory Activities
mg	Milligram(s)
mL	Milliliter(s)
mm	Millimeter(s)
mm Hg	Millimeters of Mercury
MOP	Manual of Procedures
N	Number of Subjects
NCPAP	Nasal Continuous Positive Airway Pressure
NICU	Neonatal intensive care unit
NIH	National Institutes of Health
PBMC	Peripheral Blood Mononuclear Cells
PP	Per Protocol
PRN	Pertactin
PT	Pertussis Toxin
RCD	Reverse Cumulative Distribution
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SCN	Special Care Nursery
SD	Standard Deviation
SDCC	Statistical and Data Coordinating Center
Td	Tetanus Diphtheria Toxoid
Tdap	Tetanus Diphtheria Acellular Pertussis Vaccine
TNF	Tumor Necrosis Factor
TOA	Tubo-ovarian abscess
TT	Tetanus Toxoid
US	United States
USDA	United States Department of Agriculture
USP	United States Pharmacopeial Convention
V	Visit
VTEU	Vaccine and Treatment Evaluation Unit
WHO	World Health Organization

1. PREFACE

The Statistical Analysis Plan (SAP) for "A Phase II Double-blind Trial to Evaluate the Safety, Immunogenicity and Effect on Infant Immune Responses of a Single Dose of Tdap in Pregnant Women in Mali" (DMID Protocol 16-0024) 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 Council 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 protocol amendments and/or in the CSR, as appropriate. The reader of this SAP is encouraged to also review the study protocol for details on conduct of the study and the operational aspects of clinical assessments.

2. INTRODUCTION

Pertussis, or whooping cough, is a disease of the upper and lower respiratory tract caused by Bordetella pertussis (B. pertussis), a Gram-negative bacterium that lives in the upper respiratory tract. Pertussis is highly contagious. The bacteria attach to the cilia that line part of the upper respiratory system and release toxins which damage the cilia and inflame the airways. While disease usually starts with cold-like symptoms and maybe a mild cough or fever, it may progress to paroxysms of coughing, post-tussive vomiting, and exhaustion. Pertussis is particularly dangerous in young infants, in whom it may lead to pneumonia, pulmonary hypertension, convulsions, apnea, encephalopathy, and death.

The introduction of pertussis vaccination in the past century has led to dramatic decreases in pertussis disease throughout the world. Nevertheless, pertussis burden remains high globally, as an estimated 16 million cases of pertussis occurred worldwide as recently as 2008. [1] Moreover, there has been a resurgence in pertussis disease in industrialized countries in recent years, with over 48,000 cases reported in the US alone for 2012. [2] This rise is likely due to a combination of factors, including improved diagnostics, heightened awareness of the disease, a decrease in natural immunity due to low circulation, and decreased duration of protection from acellular pertussis vaccines. [3]

Even in settings where vaccination coverage is high, the highest incidence of serious disease and mortality occurs in infants under two months of age, as they are too young to receive protection through current pertussis vaccines. In the US, this age group accounts for 57% of all infant pertussis hospitalizations. [4, 5]

In the US, the Advisory Committee on Immunization Practices, CDC (ACIP) states that the optimal timing for Tdap administration is between 27 and 36 weeks gestation although Tdap may be given at any time during pregnancy.[6] Two recent studies support that earlier vaccination may be more beneficial. In Israel, a prospective study that included women in their 20th week of pregnancy or later demonstrated that Immunoglobulin G (IgG) geometric mean concentrations (GMCs) to pertussis toxin (PT) were higher in newborn cord sera when women were immunized at 27-30 weeks compared with 31-36 weeks of gestation. [7] Likewise, in a prospective observation cohort study in Geneva, Switzerland, early second-trimester maternal Tdap immunization significantly increased neonatal antibodies compared to later dosing. [8]

In Mali, and elsewhere in Africa, tetanus-containing vaccines are recommended to be given at the first pregnancy encounter. The rationale for this recommendation is that many women in Mali will not present for multiple, regular prenatal visits, as is done in the United States. Thus, the recommendation for first encounter vaccination ensures that a woman receives the vaccine and has adequate time to develop immunity and transfer antibody to her unborn child. Delaying the administration of tetanus-containing vaccines until the third trimester of pregnancy would be a deviation from standard of care and would likely be unacceptable to the community. Therefore, second trimester vaccination may be the best option in this trial for consistency with local practices.

Existing antenatal tetanus immunization programs have been successful worldwide and may serve as a platform for pertussis vaccine introduction as Tdap combinations could be substituted for Td or tetanus toxoid (TT). In Mali, standard of care is to administer Td to pregnant women during their first contact with the health care system, which for most women is in the second trimester.

Realizing the importance of pertussis prevention in infants too young to receive vaccine, and the lack of data on the impact of maternal vaccination on infant responses in developing country settings where whole-cell vaccines are used, a study is necessary to examine the safety, immunogenicity, and effect on infant antibody responses of a Tdap vaccine administered during pregnancy among women in Mali.

2.1. Purpose of the Analyses

These analyses will assess the immunogenicity and safety of BOOSTRIX in comparison with Td and will be included in the clinical study report. An interim safety review will occur when safety data collected through Day 8 is available for 25% of pregnant study subjects. Reports for interim safety reviews will include data for pregnant participants, and any infants born at the time of data cutoff. Summaries may include enrollment and demographic information, medical history, concomitant medications, physical assessments, and solicited and unsolicited adverse events (AEs)/serious adverse events (SAEs).

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives

3.1.1. Primary

Safety and Tolerability:

- To assess the safety and tolerability of a single 0.5 mL intramuscular injection of BOOSTRIX in pregnant women.
- To assess the safety of a single maternal BOOSTRIX vaccination on the fetus and infant.

Immunogenicity:

- To assess the level of PT antibody at birth among infants whose mothers received a single dose of BOOSTRIX or Td while pregnant.

3.1.2. Secondary

Immunogenicity:

- To assess the antibody response to BOOSTRIX vaccine antigens in pregnant women one month after receipt of BOOSTRIX, at the time of delivery, and at 6 months after delivery.
- To compare the antibody levels of BOOSTRIX vaccine antigens at birth (cord blood) and 6 weeks of age (before receiving any infant doses of Diphtheria, Tetanus, and whole-cell Pertussis (DTwP)) in infants whose mothers received BOOSTRIX or Td during pregnancy.
- To assess placental antibody transfer by determining the ratio of maternal and infant BOOSTRIX - specific antibody responses at delivery.
- To assess interference with infant antibody responses to DTwP either prior to the second dose of the primary DTwP series, at approximately 10 weeks of age (in ½ of subjects), or approximately one month after the third dose of the primary DTwP series, at approximately 18 weeks of age (in ½ of subjects), and at 6 months of age (all subjects).

3.1.3. Exploratory

Immunogenicity:

- To assess the effects of maternal age, parity, gestational age (GA) at which the vaccine is given, GA at delivery, and infant birthweight on antibody responses to BOOSTRIX in pregnant women at time of delivery, and in their newborn infants at birth.
- To assess maternal secretory immunity through measurement of breast milk antibodies to Tdap vaccine antigens in women at the time of delivery, at 6 weeks postpartum, at 10 weeks (in ½ of women) or 18 weeks (in ½ of women) postpartum, and at 6 months after delivery.
- To assess the cytokine profile after stimulation in vitro with diphtheria, tetanus and pertussis antigens of peripheral blood mononuclear cells (PBMC) obtained from women before and one month after receiving Tdap or Td.

- To assess the cytokine profile after stimulation in vitro with diphtheria, tetanus, and pertussis antigens of PBMC obtained from infants before the first dose of DTwP (approximately 6 weeks of age) in all subjects, one month after the first dose of DTwP (approximately 10 weeks of age) in ½ of infants, one month after the last dose of DTwP (approximately 18 weeks of age) in ½ of infants, and at 6 months of age in all infants.

3.2. Endpoints

3.2.1. Primary

Safety and Tolerability:

- Safety in pregnant women: Frequency and severity of study vaccine-related serious adverse events, and all SAEs in pregnant women from study vaccination through 6 months postpartum, description and comparison between those receiving BOOSTRIX and Td.
- Safety in pregnant women and fetuses/infants: Frequency and severity of adverse events specific to pregnancy, in pregnant women and their infants (as delineated in Section 4.5.1), description and comparison between those receiving BOOSTRIX and Td.
- Tolerability in pregnant women: Frequency and severity of solicited injection site and systemic reactogenicity events from study vaccination until 7 days following vaccination (Day 8).
- Tolerability in pregnant women: Frequency and severity of all unsolicited non-serious AEs from day of study vaccination to Day 31, description and comparison between those receiving BOOSTRIX and Td.
- Safety in the infants: Frequency and severity of study vaccine-related serious adverse events, and all SAEs in infants from birth through 6 months of age, description and comparison between infants born to women vaccinated with BOOSTRIX and Td.

Immunogenicity:

- Infant humoral immunity: GMC of serum IgG antibodies to PT as measured by Enzyme-Linked Immunosorbent Assay (ELISA) at birth between infants born to women vaccinated with BOOSTRIX and Td.

3.2.2. Secondary

Immunogenicity:

- Maternal humoral immunity: GMC of serum IgG antibodies to Tdap vaccine antigens (PT, FHA (Filamentous Hemagglutinin), PRN (Pertactin), tetanus, diphtheria) as measured by ELISA in pregnant women one month after receipt of BOOSTRIX or Td, at the time of delivery, and 6 months after delivery.
- Infant humoral immunity: GMC of serum IgG antibodies to Tdap vaccine antigens (PT, FHA, PRN, tetanus, diphtheria) as measured by ELISA at birth and prior to receipt of first DTwP (approximately 6 weeks of age) among infants born to women vaccinated with BOOSTRIX compared to Td.

- Placental antibody transfer: The geometric mean ratio (GMR) of maternal and infant-specific Tdap-specific antibodies (PT, FHA, PRN, tetanus, diphtheria) as measured by ELISA at delivery after intrapartum receipt of BOOSTRIX versus Td.
- Interference with infant responses among infants whose mothers received intrapartum BOOSTRIX compared to Td: GMC of antibodies to DTwP vaccine antigens (PT, FHA, PRN, Fimbriae 2 (FIM2), Fimbriae 3 (FIM3), tetanus, diphtheria) as measured by ELISA one month after the first dose of DTwP (~10 weeks of age, ½ of infants), one month after the third dose of DTwP vaccine (~18 weeks of age, ½ of infants), and at 6 months of age.

3.2.3. Exploratory

Immunogenicity:

- Maternal immunogenicity cofactors for maternal and neonatal anti-PT antibody responses following intrapartum BOOSTRIX: Maternal age (18-29, 30-39 years old), parity (primiparous vs. multiparous), GA at time of vaccination (14-17, 18-21, 22-26 weeks), GA at time of delivery (28-32, 33-36, 37 or more weeks), and infant birthweight as potential independent associations with PT GMC.
- Maternal secretory immunity: GMC of breast milk IgG and Immunoglobulin A (IgA) antibodies to Tdap vaccine antigens (PT, FHA, PRN, tetanus, diphtheria) as measured by ELISA in women at the time of delivery, at 6 weeks after deliver, at 10 weeks (in ½ of women) or 18 weeks (in ½ of women) after delivery, and 6 months after delivery after intrapartum receipt of BOOSTRIX versus Td.
- Maternal cytokine responses: Cytokines produced by peripheral blood cells stimulated with DTwP vaccine antigens, as measured by multiplex assays, in women before and one month after receiving Tdap or Td. Cytokines measured will include: Interferon (IFN)-γ, Inerleukin (IL)-10, IL-12p70, IL-12/IL-23p40, IL-13, IL-15, IL-16, IL-17A, IL-1α, IL-1β, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, Tumor Necrosis Factor (TNF)-α, and TNF-β.
- Infant cytokine responses: Cytokines produced by infant peripheral blood cells stimulated with DTwP antigens from infants whose mothers received intrapartum BOOSTRIX versus Td, measured by multiplex assays before the first dose (or umbilical cord blood), one month after the first dose of DTwP (~10 weeks of age, ½ of subjects), one month after the last dose of study vaccine (approximately 18 weeks, ½ of subjects), and at 6 months of age. Cytokines measured will include: IFN-γ, IL-10, IL-12p70, IL-12/IL-23p40, IL-13, IL-15, IL-16, IL-17A, IL-1α, IL-1β, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, TNF-α, and TNF-β.

3.3. Study Definitions and Derived Variables

- An adverse event is considered “life-threatening” if, in the view of either the site principal investigator or sponsor, its occurrence places the patient or subject at immediate risk of death. It does not include an adverse event that, had it occurred in a more severe form, might have caused death.
- Major congenital anomaly is defined as “defects that are present at birth and that have surgical, medical, or serious cosmetic significance.” [9]

- Oral temperature, pulse, and blood pressure assessed on Day 1 prior to study vaccination will be considered as baseline.
- HELLP syndrome: Group of symptoms that occur in pregnant women who have hemolysis (H); elevated liver enzymes (EL); low platelet count (LP).

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

This is a phase II, single center, randomized, double-blind, active-controlled study in which 200 healthy pregnant women, ages 18 through 39 years, inclusive, will be randomly allocated in a 2:1 ratio to receive either Tdap (BOOSTRIX*)* or Td at 14 0/7 weeks through 26 6/7 weeks estimated gestational age. After signing an informed consent form (ICF), all subjects will undergo a review of current and past medical history, current and prior medication use, and recent vaccination history. A physical examination performed as part of routine antenatal care or a study-specific brief exam may be used to determine eligibility. For the fetuses of pregnant subjects, GA will be established by ultrasound, whenever possible, in combination with date of last menstrual period (LMP), when available, and fundal height.

Eligibility will be confirmed, and the subject will be enrolled in the study. Each subject will receive prenatal care consistent with national guidelines and with local standards as practiced by clinicians caring for pregnant women and delivering neonates in the study area. In Mali, this includes complete blood count (CBC), glucose, HIV, syphilis, toxoplasmosis, and rubella serology at the first presentation for antenatal care.

At the time of randomization to vaccine allocation, women will also be randomized to a schedule of postpartum visits for specimen collection. All women-infant pairs will have specimens collected at birth, at 6 weeks after delivery, and at 6 months after delivery. In addition, women-infant pairs will be allocated in a 1:1 ratio to have specimen collections at one month following the first dose of DTwP (approximately 10 weeks of age), or at one month following the third dose of DTwP (approximately 18 weeks of age). Thus, pregnant subjects will typically have 7 clinic visits (only 6 if delivery occurs before the first visit after vaccination, on Day 31): 3 antenatal visits (Screening Visit, Study Day 1 and Study Day 31, unless delivery occurs first), 1 visit at the time of delivery, and 3 postpartum visits – at 6 weeks, at 10 or 18 weeks postpartum, and a final visit 6 months postpartum. The maternal subject will also undergo 2 home visits after vaccination to assess her health status (Days 4 and 8).

Infants born to the pregnant subjects will have 4 study visits: at birth, at approximately 6 weeks of age (day of first DTwP), at approximately 10 or 18 weeks of age (one month after first or third dose of DTwP, respectively), and at 6 months of age.

Blood and colostrum/breast milk samples for immunologic assessments will be collected as described below:

- Pregnant subject: approximately 20 mL of blood will be collected on Study Day 1 (prior to vaccination), Study Day 31 (one month after vaccination), at delivery, and at 6 months postpartum in all women.
- Infants: up to 30 mL of umbilical cord blood will be collected at delivery and 5 mL peripheral blood will be collected at 6 weeks (prior to first dose of DTwP), either the 10-week or 18-week (per randomized study schedule), and 6 months of age in all infants. If cord blood cannot be obtained, 2-5 mL of peripheral blood will be collected by venipuncture within 72 hours of birth, before discharge, when possible. Cord blood is preferred over venipuncture.
- At delivery, and at the 6-week, either the 10-week or 18-week (per randomized study schedule), and the 6-month postpartum visit, a 10-20 mL sample of colostrum or breast milk will be collected. When possible, the first breast milk or colostrum collection will occur while the mother and baby are admitted for delivery and postpartum care. When not possible, it may be collected any time within the first 4 days of life.

Safety will be monitored from the time of signing of the ICF until trial termination.

See Table 1 and Figure 1 for study design.

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

The study was designed to compare safety, immunogenicity, and effect on infant immune responses between BOOSTRIX (Tdap) and Td. Td was chosen as the control group because it is the standard of care in Mali.

4.3. Selection of Study Population

4.3.1. Study Inclusion Criteria

Prospective subjects must meet all of the following inclusion criteria to be considered eligible for enrollment:

1. Healthy pregnant woman 18-39 years of age, inclusive.
2. Singleton fetus, with estimated gestational age of 14 0/7 through 26 6/7 weeks gestation, inclusive, on the day of study vaccination.
3. Provide written consent after the nature of the study has been explained according to local regulatory requirements and prior to any study procedures.[1]
4. In good health as determined by medical history, targeted physical examination[2,3], vital signs[4,5,6], and clinical judgment of the investigator.
5. Ability to comprehend and comply with all study procedures, as determined by the investigator determining eligibility, and availability for follow-up.
6. Willing to allow study staff to gather pertinent medical information, including pregnancy outcome data and medical information about her infant.

[1] Prior to obtaining individual informed consent for each subject, the investigators will obtain community consent by discussing the trial with all the appropriate local groups, as necessary, to obtain permission to approach the subjects. Written, informed consent for participation in the trial will be obtained by the investigators from all individual subjects. The consent forms will be written in French, the official language of Mali, and will be translated into Bambara, the most prevalent of the local languages, and recorded on audiotape.

[2] if indicated based on medical history, to evaluate acute or currently ongoing chronic medical diagnoses or conditions that would affect the assessment of eligibility and safety of subjects. Chronic medical diagnoses or conditions being actively managed must be within acceptable limits in the last 180 days. Any prescription change that is due to change of health care provider, insurance company, etc., or that is done for financial reasons, as long as in the same class of medication, will not be considered a deviation of this inclusion criterion. Any change in prescription medication due to improvement of a disease outcome, as determined by the site principal investigator or appropriate sub-investigator, will not be considered a deviation of this inclusion criterion. Subjects may be on chronic or as needed (prn) medications if, in the opinion of the site principal investigator or appropriate sub-investigator, they pose no additional risk to subject safety or assessment of reactogenicity and immunogenicity and do not indicate a worsening of medical diagnosis or condition. Similarly, medication changes subsequent to enrollment and the study vaccination are acceptable provided the subject is asymptomatic, condition stable, and there is no additional risk to the subject or interference with the evaluation of responses to the study vaccination.

[3] Physical examination performed as part of routine antenatal care of a study-specific brief exam may be used to determine eligibility.

[4] Oral temperature less than 37.8°C.

[5] Pulse 55 to 100 bpm, inclusive.

[6] Systolic blood pressure 90 to 140 mm Hg, inclusive. Diastolic blood pressure 55 to 90 mm Hg, inclusive.

4.3.2. Study Exclusion Criteria

Prospective subjects must not meet any of the following exclusion criteria to be considered eligible for enrollment:

1. History of illness or an ongoing illness that, in the opinion of the investigator, may pose additional risk to the subject or her fetus if she participates in the study.

2. Infection requiring systemic antibiotics or antiviral treatment within the 7 days prior to study vaccination.

3. Fever (oral temperature ≥ 37.8°C/100.0°F) or other acute illness within 3 days prior to study vaccination.[7]

4. Known active neoplastic disease[8], anticancer chemotherapy, or radiation therapy (cytotoxic) within 3 years prior to study vaccination.

5. History of any hematologic malignancy at any time.

6. A history of a serious adverse event following previous immunizations (e.g., Bell's Palsy, Guillain-Barre Syndrome, encephalopathy), or history of progressive neurologic disorders.

7. Known or suspected disease that impairs the immune system including known or suspected HIV infection or HIV-related disease.

8. Receipt of immunosuppressive therapy.[9]

9. Known hepatitis B or hepatitis C infection, by history or medical record.

10. Behavioral or cognitive impairment or psychiatric disease[10] that, in the opinion of the investigator, may interfere with the subject's ability to participate in the trial.

11. Have a history of alcohol or drug abuse within 5 years prior to study vaccination.[11]

12. Known hypersensitivity or allergy to any component of the study vaccine (formaldehyde, alum).

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[7] An acute illness which is nearly resolved with only minor residual symptoms remaining is allowable if, in the opinion of the site principal investigator or appropriate sub-investigator, the residual symptoms will not interfere with the ability to assess safety parameters as required by the protocol.

[8] excluding non-melanoma skin cancer.

[9] including long-term use of glucocorticoids: oral, inhaled, intranasal or parenteral prednisone ≥ 20 mg/day or equivalent for more than 2 weeks within the 30 days prior to enrollment. Use of topical corticosteroids is allowed.

[10] includes hospitalization for psychiatric illness, suicide attempt, or confinement for danger to self or others within 10 years prior to study vaccination.

[11] that is believed by the site investigator to potentially interfere with the subject's ability to participate in the study.

13. History of severe allergic reaction (e.g., anaphylaxis) after a previous dose of BOOSTRIX or any other vaccine directed against tetanus, diphtheria, or pertussis.

14. Receipt or planned receipt of any live licensed vaccine within 30 days before or after vaccination or any inactivated licensed vaccine within 14 days before or after vaccination.

15. Receipt of immunoglobulin (except RhoGAM, which is allowed) or other blood products within 90 days prior to study vaccination.

16. Receipt of an experimental agent or device within 30 days prior to vaccination, or the expected receipt of an experimental agent[12] (other than BOOSTRIX) during this trial-reporting period.

17. High risk for serious obstetrical complication (refer to ACOG Practice Bulletins for definitions, as necessary).[13]

18. Pregnant with a fetus with a known or suspected major congenital[14] anomaly or genetic abnormality.

19. Study personnel or immediate family members (brother, sister, child, parent) or the spouse of study personnel.

4.3.3. Reasons for Withdrawal and Discontinuation of Study Product Administration

Subjects may voluntarily withdraw their consent for study participation at any time without penalty or loss of benefits to which they are otherwise entitled.

An investigator may also withdraw a subject from receiving the study product for any reason. Follow-up safety evaluations will be conducted, if the subject agrees. If a subject withdraws or is withdrawn prior to completion of the study, the reason for this decision must be recorded in the data collection forms.

The reasons, might include, but are not limited to the following:

- Subject no longer meets eligibility criteria
- Subject meets individual halting criteria (reference to Section 9.5 of the protocol)

[12] Experimental agents include vaccines, drugs, biologics, devices, blood products, and medications. Subjects who have received a licensed product, as a subject in a clinical trial, within 30 days prior to vaccination or who are expecting to enroll in such a trial during the study period will also be excluded. Observational studies, surveys, and other studies that do not involve experimental agents or devices are allowed.

[13] including the following: (a)gestational hypertension (well controlled history of essential or gestational hypertension, as evidenced by normal BPs as defined above, is allowed), (b)gestational diabetes not controlled by diet and exercise (the use of insulin or glyburide to control gDM, at the time of enrollment, is exclusionary), (c)current pre-eclampsia or eclampsia, (d)known current multiple gestation, (e)history of preterm delivery before EGA 35 weeks 0 days or current preterm labor, and/or (f)known intrauterine fetal growth restriction (defined as ultrasound confirmation of an estimated fetal weight that is less than the 10th percentile for gestational age).

[14] Congenital anomalies and definitions of major congenital anomalies are discussed in detail in Section 9.1 of the protocol under Assessment of Safety.

- Subject becomes noncompliant
- Medical disease or condition, or new clinical finding(s) for which continued participation, in the opinion of the investigator might compromise the safety of the subject, interfere with the subject's successful completion of this study, or interfere with the evaluation of responses
- Subject lost to follow-up
- Determined by a physician's discretion to require additional therapy not indicated in the protocol to ensure subject's health and well-being (or treatment failure, if applicable)
- New information becomes available that makes further participation unsafe or unwarranted.
- Termination of this trial
- Subject withdrawal of consent

4.4. Treatments

4.4.1. Treatments Administered

Subjects are administered one dose (0.5mL administered intramuscularly) of BOOSTRIX or Td (control).

4.4.2. Identity of Investigational Product(s)

BOOSTRIX

BOOSTRIX (Tetanus Toxoid, Reduced Diphtheria Toxoid, and Acellular Pertussis Vaccine, Adsorbed) is a noninfectious, sterile, vaccine for intramuscular administration. It contains tetanus toxoid, diphtheria toxoid, and pertussis antigens (inactivated PT, formaldehyde-treated FHA, and PRN). The antigens are the same as those in INFANRIX, but BOOSTRIX is formulated with reduced quantities of these antigens.

Tetanus toxin is produced by growing *Clostridium tetani* in a modified Latham medium derived from bovine casein. The diphtheria toxin is produced by growing *Corynebacterium diphtheriae* in Fenton medium containing a bovine extract. The bovine materials used in these extracts are sourced from countries which the United States Department of Agriculture (USDA) has determined neither have nor are at risk of bovine spongiform encephalopathy (BSE). Both toxins are detoxified with formaldehyde, concentrated by ultrafiltration, and purified by precipitation, dialysis, and sterile filtration.

The acellular pertussis antigens (PT, FHA, and PRN) are isolated from *Bordetella pertussis* culture grown in modified Stainer-Scholte liquid medium. PT and FHA are isolated from the fermentation broth; PRN is extracted from the cells by heat treatment and flocculation. The antigens are purified in successive chromatographic and precipitation steps. PT is detoxified using glutaraldehyde and formaldehyde. FHA and PRN are treated with formaldehyde.

Tetanus and diphtheria toxoid potency is determined by measuring the amount of neutralizing antitoxin in previously immunized guinea pigs. The potency of the acellular pertussis components (inactivated PT, formaldehyde-treated FHA, and PRN) is determined by ELISA on sera from previously immunized mice.

BOOSTRIX is manufactured by GSK and is approved for use in the US in persons 10 years and older and by the WHO for persons 4 years and older. In Mali, the vaccine is not approved by the national drug authority.

Tetanus and Diphtheria Toxoids Adsorbed (Td) Control Vaccine

The Td control vaccine is used for the active immunization of adults and children 7 years of age and older against diphtheria and tetanus manufactured by Biological E. Limited in Hyderabad, India.

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

Enrollment/randomization will be performed through the enrollment module in the electronic data capture system, maintained by the statistical and data coordinating center (SDCC).

Eligible subjects will be randomized based on Tdap (BOOSTRIX) or Td at 14 0/7 weeks through 26 6/7 weeks estimated GA and the study schedule for the third specimen collection after delivery/birth for mother/infant pairs at either one month following the first dose of DTwP (approximately 10 weeks of age) or one month following the third dose of DTwP (approximately 18 weeks of age). Subjects will be randomized in 1:2:2:1 ratio to Td:10 weeks collection, BOOSTRIX:18 weeks collection, BOOSTRIX:10 weeks collection or Td:18 weeks collections using a block scheme to provide an approximately balanced allocation.

4.4.4. Selection of Doses in the Study

The doses for BOOSTRIX and Td are standard approved doses. However, both will be administered during non-standard timeframes.

In the US, the ACIP states that the optimal timing for Tdap administration is between 27 and 36 weeks gestation although Tdap may be given at any time during pregnancy. [6] Two recent studies support that earlier vaccination may be more beneficial. In Israel, a prospective study that included women in their 20th week of pregnancy or later demonstrated that IgG GMCs to PT were higher in newborn cord sera when women were immunized at 27-30 weeks compared with 31-36 weeks of gestation. [7] Likewise, in a prospective observation cohort study in Geneva, Switzerland, early second-trimester maternal Tdap immunization significantly increased neonatal antibodies compared to later dosing. [8]

In Mali, and elsewhere in Africa, tetanus-containing vaccines are recommended to be given at the first pregnancy encounter. The rationale for this recommendation is that many women in Mali will not present for multiple, regular prenatal visits, as is done in the United States. Thus, the recommendation for first encounter vaccination ensures that a woman receives the vaccine and has adequate time to develop immunity and transfer antibody to her unborn child. Delaying the administration of tetanus-containing vaccines until the third trimester of pregnancy would be a deviation from standard of care and would likely be unacceptable to the community. Therefore, second trimester vaccination may be the best option in this trial for consistency with local practices. Any pregnant women who presents in the first trimester and wishes to participate in the study will be asked to return during the second trimester for randomization and receipt of a tetanus-containing vaccine.

4.4.5. Selection and Timing of Dose for Each Subject

Eligible subjects will be randomized and assigned in a 2:1 ratio to either Tdap (BOOSTRIX) or Td at 14 0/7 weeks through 26 6/7 weeks estimated GA.

4.4.6. Blinding

The vaccine/control will be prepared by the licensed pharmacist and administered by an unblinded study nurse. All follow-up safety and efficacy evaluations will be performed by blinded clinic staff.

The pharmacist at each site will refer to the Treatment Key provided for the trial by the SDCC to determine the treatment for the subjects. The pharmacist will maintain an open label code (provided by the SDCC) under locked/secured conditions and will follow the randomization code. The study products are identical in appearance.

The protocol contains no explicit provisions for emergency unblinding. According to DMID policy, the study medical monitor responds to requests for emergency unblinding and instructs the SDCC to release treatment codes only if necessary to ensure that the subject receives appropriate clinical care.

4.4.7. Prior and Concomitant Therapy

Subject receipt of any medications, therapies, or vaccines will be recorded on the appropriate data collection form. Concomitant medications will include all current medications and medications taken within the 90 days prior to signing the informed consent form until discharge after delivery for pregnant women. For infants, concomitant medications will be recorded from birth until the day of life 180 visit.

Medications/vaccinations reported in the electronic case report form (eCRF) are limited to those taken within 30 days prior to study vaccination through discharge after delivery for pregnant women and the day of life 180 visit for infants. Participants cannot plan to receive a live vaccine within 30 days following study vaccination, nor should they plan to receive an inactivated vaccine within 14 days following study vaccination. Prescription medications, vaccinations, over-the-counter drugs, herbals, vitamins, and supplements will be recorded. Use of any new post-study vaccination medication that is not considered standard of care for conditions associated with pregnancy should prompt evaluation for the presence of a new diagnosis or condition.

Medications that might interfere with the evaluation of the investigational product should be avoided unless necessary. Medications in this category include the prohibited medications per the Subject Exclusion Criteria (see Section 4.3.2). In addition, the site principal investigator or sub-investigator may identify other medications that should not be used due to a risk to subject safety or assessment of reactogenicity and immunogenicity.

4.4.8. Treatment Compliance

All subjects are to receive a single dose of study product administered in the clinic.

4.5. Immunogenicity and Safety Variables

See Table 2 for a schedule of study procedures.

4.5.1. Safety Variables

Safety will be assessed by the frequency and severity of the following:

1) Study vaccine-related Serious Adverse Events occurring from the time of the study vaccination through the visit 6 months postpartum (180 days of life for the infant visit) for pregnant subjects and infants. All SAEs during this timeframe will be assessed and documented.
2) Adverse Events related to pregnancy and the infant (Table 8). For the pregnant woman/mother: pregnancy loss, vaginal bleeding (antepartum or postpartum), post-abortal endometritis/salpingitis, preterm rupture of membranes, preterm contractions/labor/delivery, poor fetal growth, hypertension/pre-eclampsia/eclampsia, chorioamnionitis, postpartum endometritis, gestational diabetes

mellitus. For the infant: preterm birth, low birth weight, neonatal complications, and congenital anomalies.

3) Solicited Adverse Events – reactogenicity events occurring from the time of study vaccination through 7 days after study vaccination (Day 8) or until resolution.
    a. Injection site reactions including ecchymosis (bruising), erythema (redness), induration (hardness)/edema(swelling), pain, and tenderness.
    b. Systemic reactions including fever (days 4 and 8 only during home visits), feverishness (chills/shivering/sweating), fatigue (tiredness), malaise (general unwell feeling), myalgia (body aches/muscular pain exclusive of the injection site), arthralgia (joint pain exclusive of the injection site), headache, nausea, and allergic reaction (pruritus/urticaria).
4) Unsolicited Non-Serious Adverse Events – all non-serious unsolicited adverse events will be assessed and documented, and all study vaccine-related non-serious adverse events occurring from the time of study vaccination through approximately 30 days after study vaccination (the Day 31 visit). For pregnant women who deliver before Day 31, unsolicited adverse events will be recorded until delivery.
5) Major Congenital Anomalies

    Congenital Anomalies: In this study, we will report as SAEs all major congenital anomalies known prior to a mother/infant dyad completing the study. These outcomes must occur following maternal vaccination during gestation or the perinatal period (within the first 5 days after delivery) but the diagnosis may be confirmed anytime during participation. We define "major congenital anomaly" as "defects that are present at birth and that have surgical, medical, or serious cosmetic significance." [9]

    The following list of problems are among the conditions reported in the US National Birth Defects registry and would be deemed as examples of major congenital anomalies: anencephaly, spina bifida, encephalocele, anophthalmia, microphthalmia, cyanotic congenital heart diseases, cleft lip or palate, tracheoesophageal fistula, rectal stenosis, major limb deformities including shortening, gastroschisis, omphalocele, and diaphragmatic hernia. Some problems that are congenital anomalies but would be considered minor include most simple birthmarks, single transverse palmar creases, clinodactyly, umbilical hernias, post-axial polydactyly, ankyloglossia, and epicanthal folds.

    Positional deformations, such as molding or overriding cranial sutures, metatarsus adductus, tibial torsion, and genu varum are not to be recorded as major congenital anomalies. Normal variants, such as minor anomalies of the pinna, supernumerary nipples, and penile torsion are also not major congenital anomalies. If major congenital anomalies are found prenatally, before enrollment, women will be excluded from participation. Many minor congenital anomalies will typically only be noted at or soon after birth.

4.5.2. Immunogenicity Variables

Infant humoral immune response will be measured using ELISA and assessed from umbilical cord blood at delivery. If cord blood cannot be obtained, then peripheral blood by phlebotomy will be used. Venous blood will be collected at 6-weeks postpartum (prior to receipt of first DTwP vaccine).

Maternal humoral immunity will be measured using ELISA and assessed from venous blood at approximately one month post vaccination, at delivery, and at 6 months post- delivery.

Placental antibody transfer will be assessed using venous blood taken from the mother at delivery and cord blood (peripheral blood if necessary) taken from the infant at delivery as measured by ELISA.

Interference with infant responses will be assessed from venous blood taken at one month after the first dose of DTwP or one month after the third dose of DTwP (depending on which group the subject is randomized to), and at 6-months of age as measured by ELISA.

Maternal secretory immunity will be assessed from breast (or colostrum) milk collected at delivery (or within 4 days of delivery), at 10 weeks or 18 weeks (depending to which group the subject is randomized) post-delivery, and 6 months post-delivery as measured by ELISA.

Maternal cytokine responses will be measured from venous blood taken prior to vaccination and one month after receiving Tdap or Td.

Infant cytokine responses will be measured from venous blood (or cord blood) taken before the first dose of DTwP, one month after the first dose or one month after the last dose (depending on which group the subject is randomized to), and at 6 months of age.

5. SAMPLE SIZE CONSIDERATIONS

Based on the accrual rate for similar studies, it seems reasonable to expect that the sites will be able to enroll this study in a timely fashion. Prior experience suggests up to 15% of subjects may be excluded from the per protocol analysis for the primary immunogenicity outcome either because they were lost-to-follow-up or otherwise do not have data available following the study vaccination, or because they had a protocol deviation requiring their exclusion from the per protocol analysis.

The study is planned to enroll 200 pregnant women (133 BOOSTRIX, 67 Td) and their infants.

This will be one of the first studies of maternal Tdap vaccination in an African, low resource setting, and where infants received whole cell, rather than acellular pertussis vaccinations. Thus, this study is intended to obtain preliminary estimates of immune response in this setting; it is not designed to test a specific null hypothesis.

Table 3 indicates the probability of observing one or more safety event, such as solicited injection site or systemic symptom, or an unsolicited adverse event of a particular type within a treatment arm.

In addition to safety, as a co-primary objective, the study will assess serum PT antibody at birth among infants whose mothers received a single dose of BOOSTRIX or Td, and as secondary and exploratory objectives, the study will assess maternal and infant humoral response to all vaccine antigens. Immune response will be measured by ELISA. Table 4 presents the precision (95% confidence interval (CI)) available for estimating GMC of ELISA titers against the vaccine component using assumptions for GMC and standard deviation (SD) for maternal and infant response to Tdap from Munoz et al. [10] and infant response post third dose of primary DTwP vaccine series from Ladhani et al. [11]

Table 5 presents the minimum difference in infant PT antibody GMC at birth between the Td and Tdap (BOOSTRIX) vaccination arms that would be detectable with 80% power. The assumed GMC and SD used for these calculations are based on the PT antibody GMC and SD observed at birth in infants whose mother received either Tdap or placebo vaccination during pregnancy, reported in Munoz et al. [10] The calculations are based on a two-sided two sample T-test to compare means, with alpha = 0.05.

6. GENERAL STATISTICAL CONSIDERATIONS

6.1. General Principles

All continuous variables will be summarized using the following descriptive statistics: n (non-missing sample size), mean, standard deviation, median, maximum, and minimum. The frequency and percentages (based on the non-missing sample size) of observed levels will be reported for all categorical measures. In general, all data will be listed, sorted by treatment group and subject, and when appropriate by visit number within subject. All summary tables will be structured with a column or row for each treatment in the order (BOOSTRIX, Td) and will be annotated with the total population size relevant to that table/treatment, including any missing observations.

6.2. Timing of Analyses

- The interim safety review will occur when safety data collected through Day 8 is available for 25% of pregnant study subjects. Reports for interim safety reviews will include data for pregnant participants, and any infants born at the time of data cutoff.
- The final analysis will be performed after database lock.

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 and Per-Protocol (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).

In the case of mis-randomization, subjects will be analyzed according to the study product actually received for all analysis populations.

6.3.1. Intention-to-Treat Analysis (ITT) Population

The maternal intent-to-treat (ITT) population for immunogenicity analyses includes all pregnant women who received the study vaccination.

The infant ITT population for immunogenicity analyses includes all infants born to women who received the study vaccination.

6.3.2. Per Protocol (PP) Population

The maternal per-protocol (PP) population for immunogenicity analyses includes all subjects in the ITT subset with the following exclusions:

- Data from all available visits for subjects:
  - Found to be ineligible at baseline.
  - Without results from the baseline visits.
  - Without results from at least one post-vaccination visit.
- Data from all visits subsequent to major protocol deviations, such as:
  - Receipt of non-study licensed vaccine within the pre-specified exclusion windows (Section 4.3.2).

- Receipt of immunosuppressive therapy (e.g., corticosteroids) within 30 days prior to or after study vaccination.
- Data from any visit that occurs substantially out of window.

The infant PP population for *primary and secondary* immunogenicity analyses includes all infants in the ITT subset who have a blood sample from the perinatal period (cord blood or drawn blood within the 72 hours after birth).

The infant PP population for *exploratory* immunogenicity analyses includes all infants in the ITT subset with the following exclusions:

- Infants who did not receive DTwP within appropriate window.
- Infants who received any product that would impact immune response.
- Infants with blood samples captured substantially out of window.

6.3.3. Safety Population

The Safety Analysis population includes all pregnant women who received the study vaccination, and all infants born during the study.

6.3.4. Immunogenicity Population

The immunogenicity population will be the ITT population and PP population as described in Section 6.3.1 and Section 6.3.2.

6.4. Covariates and Subgroups

This study is not powered for formal subgroup analyses; however, immunogenicity subgroups will be explored.

To evaluate the association with maternal immunogenicity cofactors, maternal and infant anti-PT ELISA response will be summarized stratified by maternal age (18-29, 30-39 years old), parity (primiparous vs. multiparous), GA at time of vaccination (14-17, 18-21, 22-26 weeks), GA at time of delivery (28-32, 33-36, 37 or more weeks), and infant birthweight. These cofactors will be evaluated in regression modeling.

6.5. Missing Data and Outliers

All attempts will be made to collect all data per protocol. As missing data are expected to be minimal, no imputation will be performed for missing values. Any data point that appears to be erroneous or inexplicable based on clinical 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 to require such action by the sponsor. A DSMB will be convened by DMID to review study progress and subject, clinical, safety, and reactogenicity data.

Cumulative safety information, study status, and primary endpoint results may be presented at a public forum in a blinded manner or presented as summaries aggregated by study arm at the discretion of the sponsor while the primary study is ongoing. While the primary study is ongoing no data will be released that is unblinding at an individual subject level, and caution will be taken to ensure that data summarized by treatment arm does not identify the treatment assignment of any individual subject. Any ad-hoc analyses, jointly developed by the SDCC and/or University of Maryland, will be executed by the SDCC as needed. None of the interim analyses will include any formal statistical hypothesis testing; therefore, pvalue adjustment will not be made to any analyses

An interim safety review will occur when safety data collected through Day 8 is available for 25% of pregnant study subjects. Reports for interim safety reviews will include data for pregnant participants, and any infants born at the time of data cutoff. Summaries may include enrollment and demographic information, medical history, concomitant medications, physical assessments, and solicited and unsolicited AE/SAEs. Additional data may be requested by the DSMB. This trial will be monitored to determine if any of the halting rules are met.

An interim immunogenicity review is not planned.

6.7. Multicenter Studies

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

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 14 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 for maternal subjects and Table 12 for infant subjects.

The disposition of subjects in the study will be tabulated by treatment group (Table 9 and Table 10). Table 9 shows the total number of maternal subjects screened, enrolled, receiving treatment, and completing the study. Table 10 shows the number of infant subjects enrolled, completing the birth visit blood draw, and completing the study.

A flowchart showing the disposition of study subjects, adapted from the Consort Statement [12] 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 reason for the deviation, the deviation category, and treatment group for all enrolled mothers and infants (Table 6 and Table 7, respectively). Deviations that are considered major deviations that will be reviewed for possible subject exclusion from the per protocol population include: mother receipt of non-study licensed vaccine, mother receipt of immunosuppressive therapy, infant did not receive DTwP within window, infant received product that would impact immune response and infant blood samples captured substantially out of window. 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. IMMUNOGENICITY EVALUATION

This study was not designed to test a specific null hypothesis, rather the primary objectives included assessing the safety and tolerability of BOOSTRIX compared to Td and assessing infant humoral immunity between maternal subjects that received BOOSTRIX or Td.

Immunogenicity data summaries and analysis for maternal subjects will be presented for the maternal ITT and the maternal PP populations. Immunogenicity data summaries and analysis for infants will be presented for the infant ITT and infant PP populations.

Listing 8 (antibody) and Listing 9 (cytokine) will present individual immunogenicity results.

8.1. Primary Immunogenicity Analysis

The primary immunogenicity analysis will assess the level of PT antibody at birth among infants whose mothers received a single dose of BOOSTRIX or Td while pregnant. Summaries and analysis of serum IgG antibody concentrations to PT at birth will be presented. Analysis will include GMCs along with corresponding 95% confidence intervals. The GMC between treatment groups will be compared using a t-test on log-transformed ELISA titers (Table 21 and Table 22).

Reverse cumulative distributions (RCD) curves will be presented for serum IgG antibody concentrations to PT. Plots will be generated with two panels (Birth and Prior to Receipt of First dose of DTwP), and separate curves within each panel for each treatment group, as shown in Figure 3 and Figure 4 . Log-transformed serum IgG antibodies to PT will be plotted by treatment group along with the geometric mean (Figure 57 and Figure 58). The GMCs and 95% confidence intervals of log-transformed serum IgG antibodies to PT will be plotted with panels for each treatment group (Figure 111 and Figure 112).

8.2. Secondary Immunogenicity Analyses

8.2.1. Maternal humoral immunity

Summaries and analysis of maternal humoral immunogenicity data will be presented by treatment group at one month after receipt of BOOSTRIX or Td, time of delivery, and 6 months after delivery. Serum IgG antibody concentrations to PT, FHA, PRN, tetanus and diphtheria will be summarized. Analysis will include GMCs along with corresponding 95% confidence intervals. The GMC between treatment groups will be compared using a t-test on log-transformed ELISA titers (Table 25 and Table 26).

RCD curves for maternal subjects will be presented for serum IgG antibody concentrations to PT, FHA, PRN, tetanus and diphtheria. Plots will be generated with three panels (One Month After Vaccination, At Delivery, and 6 Months After Delivery), and separate curves within each panel for each treatment group, as shown in Figure 27, Figure 28, Figure 29, Figure 30, Figure 31, Figure 32, Figure 33, Figure 34, Figure 35, and Figure 36.

Log-transformed serum IgG antibody concentrations to PT, FHA, PRN, tetanus and diphtheria for maternal subjects will be plotted over time by treatment group along with the geometric mean at each time point (Figure 81, Figure 82, Figure 83, Figure 84, Figure 85, Figure 86, Figure 87, Figure 88, Figure 89, and Figure 90). The GMCs and 95% confidence intervals of log-transformed serum IgG antibodies to each antigen will be plotted over time by treatment group in Figure 135, Figure 136, Figure 137, Figure 138, Figure 139, Figure 140, Figure 141, Figure 142, Figure 143, and Figure 144.

8.2.2. Infant humoral immunity

Summaries and analysis of infant humoral immunogenicity data will be presented by treatment group at birth and prior to receipt of first DTwP. Serum IgG antibody concentrations to PT, FHA, PRN, tetanus, and diphtheria will be summarized. Analysis will include GMCs along with corresponding 95% confidence intervals. The GMC between treatment groups will be compared using a t-test on log-transformed ELISA titers (Table 23 and Table 24).

RCD curves for infants will be presented for serum IgG antibody concentrations to PT, FHA, PRN, tetanus and diphtheria. Plots will be generated with two panels (Birth and Prior to Receipt of First Dose of DTwP), and separate curves within each panel for each treatment group, as shown in Figure 3, Figure 4, Figure 5, Figure 6, Figure 7, Figure 8, Figure 9, Figure 10, Figure 11, and Figure 12.

Log-transformed serum IgG antibody concentrations to PT, FHA, PRN, tetanus and diphtheria for infants will be plotted over time by treatment group along with the geometric mean at each time point (Figure 57, Figure 58, Figure 59, Figure 60, Figure 61, Figure 62, Figure 63, Figure 64, Figure 65, and Figure 66). The GMCs and 95% confidence intervals of log-transformed serum IgG antibodies to each antigen will be plotted over time by treatment group in Figure 111, Figure 112, Figure 113, Figure 114, Figure 115, Figure 116, Figure 117, Figure 118, Figure 119, and Figure 120.

8.2.3. Placental antibody transfer

Summaries and analysis of immunogenicity data will be presented by treatment group for placental antibody transfer where data is available for both mother and child at delivery/birth. Serum IgG antibody concentrations to PT, FHA, PRN, tetanus and diphtheria will be summarized. Analysis will include Geometric Mean Ratios (GMRs) along with corresponding 95% confidence intervals (Table 27 and Table 28).

8.2.4. Inference with infant responses among infants whose mothers received intrapartum BOOSTRIX compared to Td

Summaries and analysis of immunogenicity data will be presented by treatment group at one month after receipt of first DTwP, one month after receipt of third DTwP, and at 6 months of age. DTwP antibody concentrations to PT, FHA, PRN, FIM2, FIM3, tetanus and diphtheria, will be summarized. Analysis will include GMCs along with corresponding 95% confidence intervals. The GMC between treatment groups will be compared using a t-test on log-transformed ELISA titers (Table 23 and Table 24).

RCD curves for infants will be presented for DTwP antibody concentrations to PT, FHA, PRN, FIM2, FIM3, tetanus and diphtheria. Plots will be generated with three panels (One Month After Receipt of First Dose of DTwP, One Month After Receipt of Last Dose of DTwP, and 6 Months of Age), and separate curves within each panel for each treatment group, as shown in Figure 13, Figure 14, Figure 15, Figure 16, Figure 17, Figure 18, Figure 19, Figure 20, Figure 21, Figure 22, Figure 23, Figure 24, Figure 25, and Figure 26.

Log-transformed DTwP antibody concentrations for infants to PT, FHA, PRN, FIM2, FIM3, tetanus and diphtheria will be plotted over time by treatment group along with the geometric mean at each time point (Figure 67, Figure 68, Figure 69, Figure 70, Figure 71, Figure 72, Figure 73, Figure 74, Figure 75, Figure 76, Figure 77, Figure 78, Figure 79, and Figure 80). The GMCs and 95% confidence intervals of log-transformed serum IgG antibodies to each antigen will be plotted over time by treatment group in Figure 121, Figure 122, Figure 123, Figure 124, Figure 125, Figure 126, Figure 127, Figure 128, Figure 129, Figure 130, Figure 131, Figure 132, Figure 133, and Figure 134.

8.3. Exploratory Immunogenicity Analyses

8.3.1. Maternal immunogenicity cofactors for maternal and neonatal anti-PT antibody responses following intrapartum BOOSTRIX

Summaries and analysis of immunogenicity data will be presented for maternal and infant subjects in the BOOSTRIX group for anti-PT antibody responses at time of delivery or birth, as applicable. Serum IgG antibody concentrations to PT will be summarized by maternal age (18-29, 30-39 years old), parity (primiparous vs multiparous), GA at time of vaccination (14-17, 18-21, 22-26 weeks), GA at time of delivery (28-32, 33-36, 37+ weeks), and infant birthweight. Analysis will include GMCs along with corresponding 95% confidence intervals (Table 37, Table 38, Table 39, and Table 40).

Additionally, regression modelling will be employed to evaluate the association of log-transformed anti-PT antibody response with each of the stratified maternal cofactors defined previously, as well as with infant birthweight as a continuous variable. Separate models will be used for each analysis population and each cofactor. The analysis of variance model for a stratified cofactors is as follows,

$$ln(titer) = \beta_0 + \beta_{1i}x_i + \varepsilon;$$

where β_0 is the intercept, x_i is a categorical variable with i levels for a cofactor with $i+1$ levels, β_{1i} is the regression coefficient for each level of the covariate x_i, and ε is random error assumed to be normally distributed. The model will be constructed using reference cell coding; a single level of each cofactor will be used as the reference level and the parameter β_{1i} will be estimated for the remaining levels.

The model for the continuous cofactor of infant birthweight is as follows,

$$ln(titer) = \alpha_0 + \alpha_1 z + \varepsilon;$$

where α_0 is the intercept, α_1 is the regression coefficient, z is the continuous covariate, and ε is random error assumed to be normally distributed.

The models will be produced using PROC GLM or equivalent in SAS. All assumptions for regression models will be assessed by viewing diagnostic plots such as residual plots and QQ plots. The sample sizes, parameter estimates, and parameter standard errors will be presented in Table 41, Table 42, Table 43, and Table 44. For the analysis of variance models of categorical cofactors, the ratio of the GMC of each non-reference level with respect to the GMCs of the reference level will be computed and displayed along with the 95% confidence interval. These values are calculated by exponentiating the level-specific parameter estimate $\hat{\beta}_{1i}$ and its 95% confidence interval.

8.3.2. Maternal secretory immunity

Summaries and analysis of immunogenicity data will be presented by treatment group for maternal secretory immunity at time of delivery, at 6 weeks after delivery, at 10 weeks (in half of women) or 18 weeks (in half of women) after delivery, and 6 months after delivery. Immune responses to breast milk IgG and IgA antibodies to Tdap vaccine antigens (PT, FHA, PRN, tetanus, and diphtheria) as measured by ELISA will be summarized. Analysis will include GMCs along with corresponding 95% confidence intervals. The GMC between treatment groups will be compared using a t-test on log-transformed ELISA titers (Table 29, Table 30, Table 31, and Table 32).

RCD curves for maternal subjects will be presented for Breast Milk IgG and IgA antibody concentrations to PT, FHA, PRN, tetanus, and diphtheria. Plots will be generated with five panels (At Delivery, 6 Weeks After Delivery, 10 Weeks After Delivery, 18 Weeks After Delivery, and 6 Months After Delivery), and separate

curves within each panel for each treatment group, as shown in Figure 37, Figure 38, Figure 39, Figure 40, Figure 41, Figure 42, Figure 43, Figure 44, Figure 45, Figure 46, Figure 47, Figure 48, Figure 49, Figure 50, Figure 51, Figure 52, Figure 53, Figure 54, Figure 55, and Figure 56.

Log-transformed Breast Milk IgG and IgA concentrations to PT, FHA, PRN, tetanus and diphtheria for maternal subjects will be plotted over time by treatment group along with the geometric mean at each time point (Figure 91, Figure 92, Figure 93, Figure 94, Figure 95, Figure 96, Figure 97, Figure 98, Figure 99, Figure 100, Figure 101, Figure 102, Figure 103, Figure 104, Figure 105, Figure 106, Figure 107, Figure 108, Figure 109, and Figure 110.) The GMCs and 95% confidence intervals of log-transformed serum IgG and IgA antibodies to each antigen will be plotted over time by treatment group in Figure 145, Figure 146, Figure 147, Figure 148, Figure 149, Figure 150, Figure 151, Figure 152, Figure 153, Figure 154, Figure 155, Figure 156, Figure 157, Figure 158, Figure 159, Figure 160, Figure 161, Figure 162, Figure 163, and Figure 164.

8.3.3. Maternal cytokine responses

Summaries and analysis of immunogenicity data will be presented by treatment group for maternal cytokine responses at one month before and after receiving Tdap or Td. Cytokines produced by peripheral blood stimulated with DTwP vaccine antigens will be measured by multiplex assays. Cytokines measured will include Interferon (IFN)-γ, Interleukin (IL)-10, IL-12p70, IL-12/IL-23p40, IL-13, IL-15, IL-16, IL-17A, IL-1α, IL-1β, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, Tumor Necrosis Factor (TNF)-α, and TNF-β. Analysis will include GMCs and corresponding 95% confidence intervals, median, first quartile (Q1), third quartile (Q3), minimum, and maximum for each cytokine at each time point as well as for the change in cytokine concentration between the time points (Table 33 and Table 34).

Concentrations of each cytokine will be plotted over time by treatment group in Figure 175, Figure 176, Figure 177, Figure 178, Figure 179, Figure 180, Figure 181,, Figure 182 Figure 183, and Figure 184. The GMCs and 95% confidence intervals of the concentrations of each cytokine will be presented over time by treatment group in Figure 195, Figure 196, Figure 197, Figure 198, Figure 199, Figure 200, Figure 201, Figure 202, Figure 203, and Figure 204. The change in cytokine concentration will be plotted for the post-baseline time point by treatment group in Figure 215 Figure 216 Figure 217, Figure 218, Figure 219, Figure 220, Figure 221, Figure 222, Figure 223, and Figure 224.

8.3.4. Infant cytokine responses

Summaries and analysis of immunogenicity data will be presented by treatment group for infant cytokine responses prior to first dose of DTwP (or umbilical cord blood), one month after the first dose of DTwP (half of subjects), one month after last dose of study vaccine (half of subjects), and at 6 months of age. Cytokines produced by peripheral blood stimulated with DTwP vaccine antigens will be measured by multiplex assays. Cytokines measured will include IFN-γ, IL-10, IL-12p70, IL-12/IL-23p40, IL-13, IL-15, IL-16, IL-17A, IL-1α, IL-1β, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, TNF-α, and TNF-β. Analysis will include GMCs and corresponding 95% confidence intervals, median, Q1, Q3, minimum, and maximum for each cytokine at each time point as well as the change in cytokine concentration from baseline to each time point (Table 35 and Table 36).

Concentrations of each cytokine will be plotted over time by treatment group in Figure 165, Figure 166, Figure 167, Figure 168, Figure 169, Figure 170, Figure 171, Figure 172, Figure 173, and Figure 174. The GMCs and 95% confidence intervals of the concentrations of each cytokine will be presented over time by treatment group in Figure 185, Figure 186, Figure 187, Figure 188, Figure 189, Figure 190, Figure 191, Figure 192, Figure 193, and Figure 194. The change in cytokine concentration will be plotted for each post-

baseline time point by treatment group in Figure 205, Figure 206, Figure 207, Figure 208, Figure 209, Figure 210, Figure 211, Figure 212, Figure 213, and Figure 214.

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 maternal or infant, 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 maternal age, ethnicity, other ethnic group, race, maternal age, and GA at vaccination will be presented by treatment group and overall in Table 15 (categorical characteristics) and Table 16 (continuous characteristics). Summaries of infant, sex, ethnicity, other ethnic group, race, GA at birth, delivery, Apgar score (1, 5 and 10 minutes), birth weight, length at birth, and head circumference at birth, will be presented by treatment group and overall in Table 17 (categorical characteristics) and Table 18 (continuous characteristics). 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 case report form (CRF) as "No" to each racial option.

Individual subject listings (Appendix 3) will be presented for all demographics (Listing 5 and Listing 6).

9.1.1. Prior and Concurrent Medical Conditions

Complete medical history will be obtained by interview of subjects at the screening visit and will be reviewed and/or updated on Day 1 prior to study vaccination. Subjects will be queried regarding a history of significant medical disorders of the head, eyes, ears, nose, throat, mouth, cardiovascular system, lungs, gastrointestinal tract, liver, pancreas, kidney, urologic system, nervous system, blood, lymph nodes, endocrine system, musculoskeletal system, skin, and genital/reproductive tract. A history of any allergies, cancer, immunodeficiency, psychiatric illness, substance abuse, and autoimmune disease will be solicited.

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 19 and Table 20).

Individual subject listings will be presented for all medical conditions (Listing 7).

9.1.2. Prior and Concomitant Medications

During screening, medications used up to 90 days prior to signing informed consent will be solicited. Any medications used within 30 days prior to vaccination through discharge after delivery for pregnant women and the day of life 180 visit for infants (or early termination if prior) will be 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 Anatomical Therapeutic Classification (ATC) Levels 1 and 2 and treatment group (Table 73 and Table 74).

Individual subject listings will be presented for all concomitant medications (Listing 17).

9.2. Measurements of Treatment Compliance

Any subjects who were enrolled but not vaccinated will be presented by treatment group as part of the maternal subject disposition table (Table 9).

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 size of the specified population being analyzed. All adverse events reported will be included in the summaries and analyses.

An overall summary of adverse events is presented in Table 45 and Table 46.

Adverse events occurring in 5% of subjects in either treatment group will be presented in Table 47 and Table 48.

9.3.1. Solicited Events and Symptoms

Systemic solicited adverse events will be collected in maternal subjects pre-vaccination, and systemic and local solicited adverse events will be collected 30 minutes post-vaccination and then daily for 7 days after vaccination and graded on a scale of 0 (absent), 1 (mild), 2 (moderate) and 3 (severe). Systemic events include fatigue, headache, nausea, allergic reaction, myalgia, malaise, arthralgia, feverishness and fever. Local events include pain at injection site, tenderness, ecchymosis, erythema, induration, and measurements of ecchymosis, erythema, and induration (Table 8).

The proportion of subjects reporting at least one solicited adverse event will be summarized for each solicited adverse event, any systemic symptom, any local symptom, and any symptoms. The 95% CI calculated using Clopper-Pearson methodology from a binomial distribution (SAS Proc Freq with a binomial (exact) option) will be presented and a Fisher's exact test will be performed to test for the difference in the proportion of subjects reporting a solicited adverse event (Table 49 and Table 50).

For each systemic and local event, any systemic event, any local event, and any solicited event, the maximum severity over 7 days after vaccination will be summarized for the Safety population. The number and percentage of subjects reporting each event will be summarized by the maximum severity and treatment group (Table 51).

The number of subjects reporting a solicited adverse event will be summarized for each day post vaccination by treatment group in a summary table (Table 52, Table 53, and Table 54) and graphically in a bar chart (Figure 225 and Figure 226).

Solicited adverse events by subject will be presented in Listing 10 and Listing 11.

9.3.2. Unsolicited Adverse Events

The proportion of subjects reporting at least one unsolicited adverse event will be summarized by MedDRA system organ class (SOC) and preferred term (PT).

Unsolicited adverse events by subject will be presented in Listing 12.

The following summaries for unsolicited adverse events will be presented:

- Subject incidence and total frequency of adverse events over time by MedDRA SOC, PT, and treatment group with 95% CI (Days 1-8 Days > 8) (Table 55, Table 56, Table 57, and. Table 58);

- Summary of severity and relationship to study product by MedDRA SOC, PT and treatment group (Table 59 and Table 60);
- Subject incidence and total frequency of pregnancy-or infancy related adverse events by treatment group with 95% CI (Table 77 and Table 78);
- Subject listing of non-serious adverse events of moderate or greater severity by MedDRA SOC, PT, and treatment group (Table 63);
- Listing of new onset chronic medical conditions by MedDRA SOC, PT, and treatment group (Table 64);
- Bar chart of the frequency of serious and non-serious related adverse events by severity, MedDRA SOC, and treatment group (Figure 227);
- Bar chart of the incidence of serious and non-serious related adverse events by maximum severity, MedDRA SOC, and treatment group (Figure 228)

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

The following listing will be presented including Subject ID, Gestational Age/Infant Age, Adverse Event, Number of days post dose (duration), Reason Reported as an SAE, Relationship to Treatment, Alternate Etiology if not Related, and Outcome:

- Serious Adverse Events (Table 61);
- Major Congenital Anomalies (Table 62);
- Non-Serious, Unsolicited, Moderate or Severe Adverse Events (Table 63);
- New Onset Chronic Medical Conditions (Table 64)

9.5. Pregnancies

Every attempt was made to follow subjects to completion of pregnancy to document the outcome, including information regarding any complications with pregnancy and/or delivery. A table summarizing the total pregnancies, number of live births, and number of spontaneous abortions, elective abortions or still births by treatment group will be presented (Table 75). In addition, a listing of pregnancies and outcomes will be presented (Listing 18, Listing 19, Listing 20, and Listing 21). A summary of infant size for gestational age at birth by treatment group will be presented in Table 76 and Figure 233.

Pregnancy related adverse events will be collected throughout the study and graded on a scale of 0 (absent), 1 (mild), 2 (moderate) and 3 (severe). Pregnancy related maternal events include pregnancy loss, bleeding during pregnancy or labor, postpartum hemorrhage, postabortal endometritis/salpingitis, preterm rupture of membranes, preterm contractions/labor/delivery, poor fetal growth, hypertension/preeclampsia/eclampsia, chorioamnionitis, postpartum endometritis, gestational diabetes and other pregnancy related AE. Infant events include preterm birth, birth weight, neonatal complications in a term infant, other AE in newborn and congenital abnormality/birth defect (Table 8).

The proportion of subjects reporting at least one pregnancy related adverse event will be summarized for each pregnancy related adverse event, any maternal symptom, and any infant symptom. The 95% CI will be calculated using Clopper-Pearson methodology from a binomial distribution (SAS Proc Freq with a binomial

(exact) option) will be presented (Table 77 and Table 78). A Fisher's exact test w the difference in the proportion of subjects reporting a pregnancy related adverse event (Table 79 and Table 80).

For each pregnancy related event, any maternal event, and any infant event, the maximum severity will be summarized for the maternal and infant Safety populations. The number and percentage of subjects reporting each event will be summarized by the maximum severity and treatment group. (Table 81 and Table 82). The frequency of pregnancy- and infancy-related adverse events are presented in a bar chart in Figure 229 and Figure 231. The incidence of pregnancy- and infancy-related AEs are presented in Figure 230 and Figure 232.

A listing of all pregnancy or infancy related adverse events will be presented in Listing 13.

9.6. Clinical Laboratory Evaluations

Not applicable. Clinical laboratory tests will not be done as a part of this study.

9.7. Vital Signs and Physical Evaluations

Vital sign measurements collected for maternal subjects include systolic blood pressure, diastolic blood pressure, oral temperature and pulse. Vital signs will be assessed in maternal subjects at baseline, Day 1, Day 31, and at delivery Table 65, Table 66, Table 67, Table 68, and Listing 14). Vital sign measurements collected for infant subjects at birth, including axillary temperature, heart rate, and respiratory rate. Vital signs will be tabulated by visit and treatment group. (Table 69, Table 70, Table 71, Table 72, and Listing 15).

Physical Examinations will be performed in maternal subjects at baseline and Day 31, and in both infants and maternal subjects at birth, Day 70 or Day 130, and Day 180. The following body systems will be assessed: Abdomen, Cardiovascular/heart Extremities, General Appearance, HEENT, Lymph nodes, Musculoskeletal, Neck, Neurological, Pulmonary/Chest, and Skin (Listing 16).

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 (Listing 17). The use of concomitant medications during the study will be summarized by ATC1, ATC2 code and treatment group for the maternal and infant safety populations (Table 73 and Table 74).

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 9.3 or above or R language and environment for statistical computing 3.4.2 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. Pertussis vaccines: WHO position paper. Wkly Epidemiol Rec **2010**; 85(40): 385-400.
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5. Tanaka M, Vitek CR, Pascual FB, Bisgard KM, Tate JE, Murphy TV. Trends in pertussis among infants in the United States, 1980-1999. JAMA **2003**; 290(22): 2968-75.
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8. Eberhardt CS, Blanchard-Rohner G, Lemaitre B, et al. Maternal Immunization Earlier in Pregnancy Maximizes Antibody Transfer and Expected Infant Seropositivity Against Pertussis. Clin Infect Dis **2016**; 62(7): 829-36.
9. Rasmussen SA, Hernandez-Diaz S, Abdul-Rahman OA, et al. Assessment of congenital anomalies in infants born to pregnant women enrolled in clinical trials. Clin Infect Dis **2014**; 59 Suppl 7: S428-36.
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11. Ladhani SN, Andrews NJ, Southern J, et al. Antibody responses after primary immunization in infants born to women receiving a pertussis-containing vaccine during pregnancy: single arm observational study with a historical comparator. Clin Infect Dis **2015**; 61(11): 1637-44. Erratum in: Clin Infect Dis. 2016 Jun 15;62(12):1621.
12. Rennie D. 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 Appendices 1, 2, and 3.

APPENDICES

APPENDIX 1. TABLE MOCK-UPS

LIST OF TABLES

9.1 Overall Study Design and Plan Description

Table 1: Study Design

	Treatment Arm		
Subject Group	BOOSTRIX	Td	Total
Pregnant women	133	67	200

9.5.1 Immunogenicity and Safety Measurements Assessed and Flow Chart

Table 2: Schedule of Study Procedures

Study Visit Type	**Recruitment**	**Screening**	**Enrollment/ Vaccination**	**Clinic or Home Visit**	**Clinic or Home Visit**	**Follow-up**	**Follow-up**	**Follow-up**	**Follow-up**	**Follow-up**	**Early Termination**	**Unscheduled**
Study Visit Number	**R˜**	**VOO**	**V01**	**V02**	**V03**	**V04**	**V05**	**V06**	**V07**	**V08**		
Study Day	**1st & 2nd Trimesters**	**-30 to 1**	**D1**	**D4±1**	**D8±3d**	**D31±4d**	**Birth + 3d**	**Birth + 42d±5d**	**Birth + 70d±5d or 130d±5d**	**Birth + 180d ±7d**		
EGA or Infant Age	**10-26 weeks**	**14-26 weeks**	**14-26 weeks**	**15-27 weeks**	**15-27 weeks**	**19-31 weeks**	**Birth**	**1.5 months**	**2.5 or 4.5 months**	**6 months**		
Introduction to Study, Recruiting	X	X[m]	X[m]									
Obtain Informed Consent∞		X	X[m¬]									
Review Eligibility Criteria		X	X[m¬]			X¬						
Medical History[@]		X	X[m¬]	X¬	X¬	X¬	X¬	X¬˜	X¬˜	X¬˜	X¬	X¬
Concomitant Medications[√@]		X	X[m¬]	X¬	X¬	X¬	X[!]	X˜	X˜	X˜	X[!]	X[!]
Vaccination History[@]		X	X[m¬]	X¬	X¬	X¬	X[!]					
Vital Signs[$] (Oral Temperature[%], Pulse, and BP)		X	X[†]			X	X				X	X
Height and Weight		X	X[m]									
Targeted Physical Exam {}		X	X [m¬†#]			X	X	X	X	X	X	X
Ultrasound to Date Pregnancy		X										
Venous Blood Collection from Mother (30 mL)			X[†]			X	X			X		
Cord Blood (up to 30 mL)							X					
Venous Blood from Infant (5 mL)							X[&]	X	X	X		
Obtain Breastmilk Sample from Mother (10-20 mL)							X[ψ]	X	X	X		
Pre-Administration Solicited Event Assessments			X[†]									
Randomize and Vaccinate Mother			X									
30-minute Evaluation After Study Vaccination			X									
Subject AE instruction			X									
Examine Study Vaccination Site			X			X					X[!]	X[m!]
Post-Administration Solicited Event Assessments			X	X	X						X[×]	X[×]

Table 2: Schedule of Study Procedures (continued)

Study Visit Type	**Recruitment**	**Screening**	**Enrollment/ Vaccination**	**Clinic or Home Visit**	**Clinic or Home Visit**	**Follow-up**	**Follow-up**	**Follow-up**	**Follow-up**	**Follow-up**	**Early Termination**	**Unscheduled**
Study Visit Number	**R~**	**V00**	**V01**	**V02**	**V03**	**V04**	**V05**	**V06**	**V07**	**V08**		
Study Day	**1st & 2nd Trimesters**	**-30 to 1**	**D1**	**D4±1**	**D8±3d**	**D31±4d**	**Birth + 3d**	**Birth + 42d±5d**	**Birth + 70d±5d or 130d±5d**	**Birth + 180d ±7d**		
EGA or Infant Age	**10-26 weeks**	**14-26 weeks**	**14-26 weeks**	**15-27 weeks**	**15-27 weeks**	**19-31 weeks**	**Birth**	**1.5 months**	**2.5 or 4.5 months**	**6 months**		
Record Mother AEs and SAEs			X/	X	X	X	X*	X*	X*	X*	X*	X*
Record Infant AEs and SAEs+							X	X	X	X	X	X
Record Birth Outcomes							X	X	X	X	X	X
Infant Vital Signs°, Head Circumference, Length, and Weight							XΨ	XΩ	XΩ	XΩ	XΩ	XΩ
Infant Targeted Physical Exam, if indicated							X	X	X	X	X	X

~Recruitment and screening visits are not entered into Advantage eClinical.
∞Prior to study procedures. In Mali, a research ID card with photo may be given to subjects.
&Venous blood for infant within 72 hrs. of birth only if no cord blood obtained.
ᵂIf not obtained in previous visit.
†Prior to study vaccination.
¬Review/confirm information or activity in subjects previously consented and screened/enrolled. This includes review of the pregnant woman's medical chart to obtain information about this pregnancy that may be relevant to the conduct of this study.
^Review results of all clinical screening or safety laboratory evaluations.
@Complete medical history, medication use, and vaccination history by medical record review and interview of subjects to be obtained prior to study vaccination (screening or Day 1) and interim medical history, medication use, and vaccination history by interview of subjects to be obtained at follow-up visits.
√All current medications and vaccinations taken within 90 days prior to vaccination will be reviewed, but only those taken within 30 days prior to vaccination and through discharge after delivery for pregnant women will be recorded in Advantage eClinical.
%Subjects must not eat or drink anything hot or cold, or smoke within 10 minutes prior to taking oral temperature.
/If AE or SAE occurs post-vaccination.
{}Targeted physical examination, if indicated based on review of complete or interim medical history. An examination performed by a pregnant woman's own obstetrical clinician may also provide data when a targeted exam is called for. An exam should be performed for both the mother and infant if indicated for pregnant women on and after birth.
$Vital signs assessed on Day 1 (Visit 01) prior to the study vaccination will be considered as baseline and used to determine eligibility. For the birth visit, vital signs recorded for the mother as part of her delivery record may be used in lieu of study personnel performing vital sign measurements.
#A physical examination performed as part of routine antenatal care or a study-specific brief exam may be used.
!If within 30 days post vaccination.
× If within 8 days post vaccination.
*SAEs and new-chronic onset medical conditions only after Day 31 or delivery, whichever occurs earlier.
+Only medically attended AEs will be recorded.
Ψ The first colostrum collection may occur within the first 4 days of life of the infant.
° Infant vital signs will include axillary temperature, heart rate, and respiratory rate.
ʸ If not performed as routine care, these measurements, except for weight, may be taken by qualified members of the research team within 7 days of infant life. Weights will only be recorded when obtained at birth.
~ Procedures will be performed on both mother and infant.
Ω Only infant height, weight, and head circumference will be recorded at these visits.

9.7.1 Sample Size

Table 3: Power (%) to Detect Safety Events

Event Frequency	N = 133	N = 67
≥0.01% Rare	1.3	<1
≥0.1% Uncommon	12.5	6.5
≥1% Common	73.7	49.0
≥10% Very Common	100.0	99.9

Table 4: Precision for Estimating GMC of ELISA Antibody Response

	GMC	SD (log-scale)	95% CI Estimate			
			N = 133		N=67	
Maternal ELISA Antibodies at Delivery following maternal Tdap						
PT	51	0.90	43.7	59.5	41.0	63.5
FHA	184.8	0.73	163.1	209.3	154.8	220.6
PRN	184.5	1.45	143.8	236.7	129.5	262.9
FIM	1485.7	1.17	1214.8	1817.0	1115.8	1978.2
Infant ELISA Antibodies at Birth following maternal Tdap						
PT	68.8	0.78	60.2	78.7	56.8	83.3
FHA	234.2	0.67	208.7	262.8	198.8	276.0
PRN	219	1.38	172.9	277.4	156.5	306.5
FIM	1867	1.22	1514.7	2301.3	1386.7	2513.7
Infant Response post 3rd Dose DTwP following maternal Tdap						
PT	28.8	0.68	25.6	32.3	24.4	34.0
FHA	25.5	0.60	23.0	28.3	22.0	29.5
FIM	113.9	0.81	99.1	130.9	93.5	138.8
Infant Response post 3rd Dose DTwP (no maternal vaccination)						
PT	43.2	0.65	38.6	48.3	36.9	50.6
FHA	41.1	0.66	36.7	46.1	35.0	48.3
FIM	224.9	0.97	190.2	265.9	177.2	285.4

Table 5: Minimum Detectable Difference in Infant PT Antibody GMC at Birth Comparing Infants Born to Mothers Vaccinated with BOOSTRIX versus Td

Td	Tdap (BOOSTRIX)	Assumed GMC (BOOSTRIX)	Maximum GMC Detectable with Power = 0.8 (Td)	Minimum Detectable Difference (BOOSTRIX - Td)
N=67	N=133	50.0	33.1	16.9
		60.0	40.4	19.6
		70.0	44.7	25.3
		80.0	49.4	30.6
		90.0	60.3	29.7

10.2 Protocol Deviations

Table 6: Distribution of Protocol Deviations by Category, Type, and Treatment Group – Maternal Subjects

Category	Deviation Type	BOOSTRIX (N=X)		Td (N=X)		All Subjects (N=X)	
		No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.
Eligibility/enrollment	Any type	x	x	x	x	x	x
	Did not meet inclusion criterion						
	Met exclusion criterion						
	ICF not signed prior to study procedures						
	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						
	Breast Milk not collected						
	Too few aliquots obtained						
	Specimen result not obtained						
	Required procedure not conducted						
	Required procedure done incorrectly						
	Study product temperature excursion						
	Specimen temperature excursion						
	Other						
Treatment administration	Any type						
	Required procedure done incorrectly						
	Study product temperature excursion						
	Other						
Blinding policy/procedure	Any type						
	Treatment unblinded						
	Other						
Note: N=Maternal ITT population							

Table 7: Distribution of Protocol Deviations by Category, Type, and Treatment Group – Infant Subjects

Category	Deviation Type	BOOSTRIX (N=X)		Td (N=X)		All Subjects (N=X)	
		No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.
Eligibility/enrollment	Any type	x	x	x	x	x	x
	Did not meet inclusion criterion						
	Met exclusion criterion						
	ICF not signed prior to study procedures						
	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						
	Breast Milk not collected						
	Too few aliquots obtained						
	Specimen result not obtained						
	Required procedure not conducted						
	Required procedure done incorrectly						
	Study product temperature excursion						
	Specimen temperature excursion						
	Other						
Treatment administration	Any type						
	Required procedure done incorrectly						
	Study product temperature excursion						
	Other						
Blinding policy/procedure	Any type						
	Treatment unblinded						
	Other						

Note: N=Infant ITT population

12.2.2 Displays of Adverse Events

Table 8: Solicited Adverse Event Grading Scale

	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
Local (Injection Site) Reaction			
Pain	Does not interfere with daily activity	Repeated use of non-narcotic pain reliever > 24 hours or interferes with daily activity	Any use of narcotic pain reliever or prevents daily activity
Tenderness	Discomfort only to deep palpation	Discomfort to light palpation or movement	Significant discomfort to any touch or movement
Ecchymosis (Bruising)^	No interference with daily activity	Some interference with daily activity not requiring medical intervention	Prevents daily activity and requires medical intervention
Erythema (Redness)^	Does not interfere with daily activity	Interferes with daily activity	Prevents daily activity
Induration (Hardness)/Edema (Swelling)^	Does not interfere with daily activity	Interferes with daily activity	Prevents daily activity
Ecchymosis (Bruising) Measurement^	1-50 mm	51-100 mm	> 100 mm
Erythema (Redness) Measurement^	1-50 mm	51-100 mm	> 100 mm
Induration (Hardness)/Edema (Swelling) Measurement^	1-50 mm	51-100 mm	> 100 mm
Systemic (Subjective)			
Feverishness (Chills/Shivering/Sweating)	No interference with daily activity	Some interference with daily activity not requiring medical intervention	Prevents daily activity and requires medical intervention
Fatigue (Tiredness)	No interference with daily activity	Some interference with daily activity	Significant; prevents daily activity
Malaise (General Unwell Feeling)	No interference with daily activity	Some interference with daily activity not requiring medical intervention	Prevents daily activity and requires medical intervention
Myalgia (Body Aches/Muscular Pain)*	No interference with daily activity	Some interference with daily activity	Significant; prevents daily activity
Arthralgia (Joint Pain)*	No interference with daily activity	Some interference with daily activity not requiring medical intervention	Prevents daily activity and requires medical intervention
Headache	No interference with daily activity	Repeated use of non-narcotic pain reliever > 24 hours or some interference with daily activity	Significant; any use of narcotic pain reliever or prevents daily activity
Nausea	No interference with daily activity	Some interference with daily activity	Prevents daily activities

Table 8: Solicited Adverse Event Grading Scale (continued)

	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
Allergic Reaction	Pruritus without rash	Localized urticaria OR requires oral therapy	Generalized urticaria; angioedema OR anaphylaxis OR requires epinephrine
Systemic (Quantitative)			
Fever[%] - oral[#†]	38.0 – 38.4°C 100.4 – 101.1°F	38.5 – 38.9°C 101.2 – 102.0°F	> 38.9°C ≥ 102.1°F
Bradycardia - beats per minute	50 – 54 or 45-50 if baseline <60 bpm	45 – 49 or 40-44 if baseline <60 bpm	< 45 or <40 if baseline <60 bpm
Tachycardia - beats per minute	101 – 115	116 – 130	> 130 or ventricular dysrhythmias
Hypotension (systolic) mm Hg	85-89	80-84	< 80
Hypertension (systolic) mm Hg	141-150	151-160	> 160
Hypertension (diastolic) mm Hg	91-95	96-109	> 109
Maternal Adverse Events (Adverse Events During Pregnancy)			
Pregnancy loss[b] (Pregnancy does not result in a live birth) Spontaneous abortion or miscarriage in the first or second trimester of gestation Fetal death at or after 20 weeks of gestation (stillbirth)	N/A	N/A	Spontaneous abortion or miscarriage
Bleeding (vaginal) during pregnancy prior to the onset of labor	Spotting or bleeding less than menses	Bleeding like menses or heavier, no intervention indicated	Profuse bleeding with dizziness or orthostatic hypotension, transfusion indicated
Postpartum hemorrhage	EBL[c] 501-1000 for vaginal delivery or 1001-1500 for CS or reported as slightly increased	EBL >1000 for vaginal delivery or >1500 for CS, with or without mild dizziness, no transfusion required	Hemorrhage at a level for which transfusion of packed cells or any amount of other blood components is indicated
Postabortal endometritis/salpingitis	Low grade fever and uterine tenderness, resolved with oral antibiotics	Moderate symptoms, requiring ≤3 days of parenteral antibiotics	Severe symptoms requiring >3 days of IV antibiotics or development of TOA[d]
Preterm rupture of membranes	N/A	Preterm rupture but not resulting in delivery before 37 weeks gestation	Preterm rupture resulting in delivery before 37 weeks gestation
Preterm contractions /labor/delivery[e]	Preterm contractions which resolve without medical intervention	Preterm contractions with cervical change which result in medical intervention but not resulting in preterm delivery	Delivery before 37 weeks gestation

Table 8: Solicited Adverse Event Grading Scale (continued)

	Mild (Grade 1)	**Moderate (Grade 2)**	**Severe (Grade 3)**
Poor fetal growth If infant is small for gestational age on newborn exam: report as NEONATAL OUTCOME based on birth weight (see below)	Fetal growth <10th percentile but ≥3rd percentile for gestational age by ultrasound	N/A	Fetal growth <3rd percentile for gestational age by ultrasound
Hypertension, preeclampsia/eclampsia	Pregnancy induced hypertension	Preeclampsia	HELLP syndrome, or eclampsia,
Chorioamnionitis	Fever (38°C–38.4°C or 100.4°F–100.9°F) with two or more: FHR[e] >160 BPM[f], maternal HR >120, uterine tenderness between contractions or purulent AF or preterm labor	Same as Grade 1 plus fever 38.5°C–40°C or 101°F–104°	Criteria for Grade 2 plus fetal distress or fever >40°C or 104°F
Postpartum endometritis	Low grade fever and uterine tenderness, resolved with oral antibiotics	Moderate symptoms, treated by ≤3 days of parenteral antibiotics	Severe symptoms treated with >3 days of IV antibiotics, addition of heparin, or operative intervention
Gestational diabetes mellitus	New onset controlled by diet	New onset with initiation of medical therapy	Uncontrolled despite treatment modification
Clinical AE, pregnancy-related, NOT identified elsewhere in this AE Grading Table	Symptoms causing no or minimal interference with usual social & functional activitie	Symptoms causing greater than minimal interference with usual social & functional activities	Symptoms causing inability to perform usual social & functional activitie
Mode of delivery[f] (normal spontaneous vaginal delivery, induced delivery, assisted vaginal delivery, Caesarean Section)	**Not reported as AE/SAE**. Mode of delivery is a procedure and should not be reported or graded as an AE/SAE. The reason for selecting the mode of delivery (for example: Caesarean Section for **severe preeclampsia**) should be reported and graded as appropriate.		
Infant Adverse Events (Neonatal and Infant Events)			
Preterm birth[g]	Late preterm: 34 to 36 6/7 weeks gestation	Early preterm: 32 to 33 6/7 weeks gestation	Very or extremely preterm: ≤ 31 6/7 weeks gestation
Birth weight (grams)[g] (Small, appropriate, large for gestational age) Report separately poor fetal growth (as above)		Low birth weight: 1501-2500	Very low birth weight ≤1500
Neonatal complications in a term infant	Transient signs and symptoms requiring **no intervention**, and resolved spontaneously[h]	Signs/symptoms requiring **intervention**[i] but **discharged home with mother (± 2 days)**, or close to it	Required NICU for more than 1 week, and/or interventions (including surgery) leading to prolonged hospitalization (report SAE)[j]

Table 8: Solicited Adverse Event Grading Scale (continued)

	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
Clinical AE in the newborn NOT identified elsewhere in this AE Grading Table [k] (postmaturity[l])	Symptoms causing no or minimal interference with usual functional activities	Symptoms causing greater than minimal interference with function and activities	Symptoms causing inability to perform functions or activities
Congenital anomalies/ birth defects[m]	N/A	N/A	Major congenital anomalies are reported as SAEs.

^Will not be used as halting criteria.

*Not at injection site.

[#]Oral temperature assessed on Day 1 prior to 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.

[b] Even if pregnancy loss does not require obstetrical care, and is a natural outcome of non-viable conception, psychological events around the event require recognition especially in research subjects.

[c] EBL: Estimated blood loss.

[d] TOA: Tubo-ovarian abscess.

[e] For preterm delivery, report two AEs: one for mother and one for infant. Unless specified otherwise in the protocol, only one neonatal AE will be reported for all preterm birth-related problems. Additional AEs will be reported only if infant has unexpected AEs: surgery, congenital anomalies, etc.

[f] Examples of complications of delivery that would meet AE/SAE reporting are: maternal death, stillbirth, bleeding placenta previa or abruption that required emergency delivery, etc.

[g] Preterm birth and low birth weight carry different risks and will be reported separately (or twice if an infant is both preterm and low birth weight). If gestational age is not known, only birth weight will be reported. Infants will be plotted on the appropriate growth scale for the population being studied and percentage of 'appropriate', 'large', or 'small for gestational age' infants will be reported in the final study report.

[h] Examples: transient tachypnea, hypothermia, cephalo-hematoma, bruising. Admitted to normal nursery or observed for less than one day in NICU/SCN.

[i] Examples: admission to NICU/SCN for physiological causes like hyperbilirubinemia requiring phototherapy, hypoglycemia, suspected but ruled out congenial infection, oxygen via nasal cannula, or NCPAP.

[j] Examples: confirmed neonatal infection: bacterial, viral, fungal sepsis, meconium aspiration syndrome on respirator, severe laboratory, or/and clinical signs and symptoms.

[k] Examples: perinatal asphyxia: 10 min Apgar scores below 5, shock, critical neonatal laboratory values, etc.

[l] Post maturity carries unique, but still not clearly defined risks. Currently, this category should be used to evaluate signs and symptoms related to post-maturity.

[m] Investigators should consult the protocol and/or the MOP for a list of 'major congenital anomalies' and report them as SAE. Minor anomalies (also listed in the protocol and/or MOP) are structural findings that do not have surgical, medical or cosmetic importance. Minor physical features that typically occur in more than 4% of newborn infants are considered 'variants' of normal, while 'minor anomalies' occur in less than 4% of infants. If in doubt: review referenced articles in Rasmussen et al Clin Infect Dis 2014 p S 428ff [9] and/or consult DMID.

12.4.1 Individual Laboratory Measurements and Abnormal Laboratory Values

Not applicable.

14.1 Description of Study Subjects

14.1.1 Disposition of Subjects

Table 9: Subject Disposition by Treatment Group – Maternal Subjects

Subject Disposition	BOOSTRIX (N=X)		Td (N=X)		All Subjects (N=X)	
	n	%	n	%	n	%
Screened						
Enrolled/Randomized	x	100	x	100	x	100
Received Treatment						
Completed Follow-up (6-months postpartum)[a]						
Completed Per Protocol[b]						

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

Table 10: Subject Disposition by Treatment Group – Infant Subjects

Subject Disposition	BOOSTRIX (N=X)		Td (N=X)		All Subjects (N=X)	
	n	%	n	%	n	%
Enrolled	x	100	x	100	x	100
Completed Birth Visit Blood Draw						
Completed Follow-up (6-months of age)[a]						
Completed Per Protocol[b]						

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

Table 11: Analysis Populations by Treatment Group – Maternal Subjects

Analysis Populations	Reason Subjects Excluded	BOOSTRIX (N=X)		Td (N=X)		All Subjects (N=X)	
		n	%	n	%	%	n
Maternal Safety	Did not receive the study vaccination	x	xx	x	xx	x	xx
Maternal Intent-to-Treat	Did not receive the study vaccination						
Maternal Per Protocol	Any Reason						
	Found to be ineligible at baseline						
	Did not contribte valid results at baseline						
	Did not contribute any valid post-vaccination results						
	Major protocol deviations^						
	Visit occurred substantially out of window&						

Note: N= Number of maternal subjects enrolled; n=number of maternal subjects meeting the criterion
^Data from all visits subsequent to the major protocol will be excluded from Maternal Per Protocol analyses
&Data from the substantially out of window visit only will be excluded from Maternal Per Protocol analyses

Table 12: Analysis Populations by Treatment Group – Infant Subjects

Analysis Populations	Reason Subjects Excluded	BOOSTRIX (N=X)		Td (N=X)		All Subjects (N=X)	
		n	%	n	%	%	n
Infant Safety	Not born during the study period	x	xx	x	xx	x	xx
Infant Intent-to-Treat	Not born to a woman who received the study vaccination						
Infant Per Protocol	Any Reason						
	Did not contribute a valid perinatal blood sample*						
	Did not receive DTwP within appropriate window#						
	Received any product that would impact immune response#						
	Blood samples were captured substantially out of window#						

Note: N= Number of infant subjects enrolled; n=number of infant subjects meeting the criterion
*Exclusion only from the primary and secondary immunogenicity analysis Infant Per Protocol population
#Exclusion only from the exploratory immunogenicity analysis Infant Per Protocol population

Table 13: Dates of First Treatment by Treatment Group

Dates of Dosing	BOOSTRIX (N=X)	Td (N=X)	All Subjects (N=X)
Total (Entire period of enrollment)	x	x	x
DDMMMYYYY-DDMMMYYYY [categorize based on length of enrollment period]			
Note: N= Number of subjects in the Maternal Safety Population			

Table 14: 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	xx
Inclusion	Any inclusion criterion		
	Healthy pregnant woman 18-39 years of age, inclusive		
	Singleton fetus, with estimated gestational age of 14 0/7 through 26 6/7 weeks gestation, inclusive, on the day of study vaccination		
	Provide written consent after the nature of the study has been explained according to local regulatory requirements and prior to any study procedures		
	In good health as determined by medical history, targeted physical examination, vital signs, and clinical judgment of the investigator		
	Ability to comprehend and comply with all study procedures, as determined by the investigator determining eligibility, and availability for follow-up		
	Willing to allow study staff to gather pertinent medical information, including pregnancy outcome data and medical information about her infant		
Exclusion	Any exclusion criterion		
	History of illness or an ongoing illness that, in the opinion of the investigator, may pose additional risk to the subject or her fetus if she participates in the study		
	Infection requiring systemic antibiotics or antiviral treatment within the 7 days prior to study vaccination		
	Fever (oral temperature ≥ 37.8°C/100.0°F) or other acute illness within 3 days prior to study vaccination		
	Known active neoplastic disease, anticancer chemotherapy, or radiation therapy (cytotoxic) within 3 years prior to study vaccination		
	History of any hematologic malignancy at any time		
	A history of a serious adverse event following previous immunizations (e.g., Bell's Palsy, Guillain-Barre Syndrome, encephalopathy), or history of progressive neurologic disorders		
	Known or suspected disease that impairs the immune system including known or suspected HIV infection or HIV-related disease		
	Receipt of immunosuppressive therapy		
	Known hepatitis B or hepatitis C infection, by history or medical record		
	Behavioral or cognitive impairment or psychiatric disease that, in the opinion of the investigator, may interfere with the subject's ability to participate in the trial		
	Have a history of alcohol or drug abuse within 5 years prior to study vaccination		

Table 14: Ineligibility Summary of Screen Failures (continued)

Inclusion/Exclusion Category	Inclusion/Exclusion Criterion	N[a]	%[b]
	Known hypersensitivity or allergy to any component of the study vaccine (formaldehyde, alum)		
	History of severe allergic reaction (e.g., anaphylaxis) after a previous dose of BOOSTRIX or any other vaccine directed against tetanus, diphtheria, or pertussis		
	Receipt or planned receipt of any live licensed vaccine within 30 days before or after vaccination or any inactivated licensed vaccine within 14 days before or after vaccination		
	Receipt of immunoglobulin (except RhoGAM, which is allowed) or other blood products within 90 days prior to study vaccination		
	Receipt of an experimental agent or device within 30 days prior to vaccination, or the expected receipt of an experimental agent (other than BOOSTRIX) during this trial-reporting period		
	High risk for serious obstetrical complication		
	Pregnant with a fetus with a known or suspected major congenital anomaly or genetic abnormality		
	Study personnel or immediate family members (brother, sister, child, parent) or the spouse of study personnel		
Eligible but not enrolled	Any reason		

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

Table 14: Ineligibility Summary of Screen Failures (continued)

14.1.2 Demographic Data by Study Group

Table 15: Summary of Maternal Categorical Demographic and Baseline Characteristics by Treatment Group

Variable	Characteristic	BOOSTRIX (N=X)		Td (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%
Ethnicity	Not Hispanic or Latino	x	xx	x	xx	x	xx
	Hispanic or Latino						
	Not Reported						
	Unknown						
Other Ethnic Group	Bengali						
	Senoufo						
	Samogo						
	Mossi						
	Fulani						
	Bambara						
	Mandika/Malinke						
	Peulh						
	Sarahule/Sarakole						
	Minianka						
	Other						
Race	American Indian or Alaska Native						
	Asian						
	Native Hawaiian or Other Pacific Islander						
	Black or African American						
	White						
	Multiple						
	Unknown						
Maternal Age	18-29 years old						
	30-39 years old						
Gestational Age at Vaccination	14-17 weeks						
	18-21 weeks						
	22-26 weeks						
Note: N = Number of subjects in the Maternal Safety Population							

Table 16: Summary of Maternal Continuous Demographic and Baseline Characteristics by Treatment Group

Variable	Statistic	BOOSTRIX (N=X)	Td (N=X)	All Subjects (N=X)
Maternal Age (years)	Mean	xx.x	xx.x	xx.x
	Standard Deviation	xx.x	xx.x	xx.x
	Median	xx.x	xx.x	xx.x
	Minimum	xx	xx	xx
	Maximum	xx	xx	xx
Gestational Age at Vaccination (weeks)	Mean			
	Standard Deviation			
	Median			
	Minimum			
	Maximum			
Note: N= Number of subjects in the Maternal Safety Population				

Table 17: Summary of Infant Categorical Demographic and Baseline Characteristics by Treatment Group

Variable	Characteristic	BOOSTRIX (N=X)		Td (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%
Sex	Male	x	xx	x	xx	x	xx
	Female						
Ethnicity	Not Hispanic or Latino						
	Hispanic or Latino						
	Not Reported						
	Unknown						
Other Ethnic Group	Bengali						
	Senoufo						
	Samogo						
	Mossi						
	Fulani						
	Bambara						
	Mandika/Malinke						
	Peulh						
	Sarahule/Sarakole						
	Minianka						
	Other						
Race	American Indian or Alaska Native						
	Asian						
	Native Hawaiian or Other Pacific Islander						
	Black or African American						
	White						
	Multiple						
	Unknown						
Gestational Age at Delivery	28-32 weeks						
	33-36 weeks						
	37 or more weeks						
Delivery	Vaginal						
	Scheduled Cesarean Section						
	Emergency Cesarean Section						
Apgar Score, 1 Minute	0						

Table 17: Summary of Infant Categorical Demographic and Baseline Characteristics by Treatment Group (continued)

Variable	Characteristic	BOOSTRIX (N=X)		Td (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%
	1						
	2						
	3						
	4						
	5						
	6						
	7						
	8						
	9						
	10						
Apgar Score, 5 Minutes	0						
	1						
	2						
	3						
	4						
	5						
	6						
	7						
	8						
	9						
	10						
Apgar Score, 10 Minutes	0						
	1						
	2						
	3						
	4						
	5						
	6						
	7						
	8						
	9						
	10						

Note: N= Number of subjects in the Infant Safety Population

Table 18: Summary of Infant Continuous Demographic and Baseline Characteristics by Treatment Group

Variable	Statistic	BOOSTRIX (N=X)	Td (N=X)	All Subjects (N=X)
Gestational Age at Delivery (days)	Mean	xx.x	xx.x	xx.x
	Standard Deviation	xx.x	xx.x	xx.x
	Median	xx.x	xx.x	xx.x
	Minimum	xx	xx	xx
	Maximum	xx	xx	xx
Birth Weight (kg)	Mean			
	Standard Deviation			
	Median			
	Minimum			
	Maximum			
Length (cm) at Birth	Mean			
	Standard Deviation			
	Median			
	Minimum			
	Maximum			
Head Circumference (cm) at Birth	Mean			
	Standard Deviation			
	Median			
	Minimum			
	Maximum			
Note: N= Number of subjects in the Infant Safety Population				

14.1.3 Prior and Concurrent Medical Conditions

Table 19: Summary of Maternal Subjects with Pre-Existing Medical Conditions by MedDRA System Organ Class and Treatment Group

MedDRA System Organ Class	BOOSTRIX (N=X)		Td (N=X)		All Subjects (N=X)	
	n	%	n	%	n	%
Any SOC	x	xx	x	xx	x	xx
[SOC 1]						
[SOC 2]						

Note: N= Number of subjects in the Maternal Safety Population;
n = Number of subjects reporting medical history within the specified SOC. A subject is only counted once per SOC.

Table with Similar Format:

Table 20: Summary of Infant Subjects with Pre-Existing Medical Conditions by MedDRA System Organ Class and Treatment Group

14.2 Immunogenicity Data

Table 21: Serum IgG ELISA Geometric Mean Concentration (GMC) Results with 95% Confidence Intervals by Antigen, Time Point, and Treatment Group -- Infant Intent-to-Treat Population

Tdap Antigen	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
Pertussis Toxin (PT)					
	Birth	n	x	x	--
		GMC (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
		p-value*	--	--	0.xxx
	Prior to receipt of first dose of DTwP (approximately 6 weeks of age)	n			
		GMC (95% CI)			
		p-value*			
Filamentous Hemagglutinin (FHA)					
	Birth	n			
		GMC (95% CI)			
		p-value*			
	Prior to receipt of first dose of DTwP (approximately 6 weeks of age)	n			
		GMC (95% CI)			
		p-value*			
Pertactin (PRN)					
	Birth	n			
		GMC (95% CI)			
		p-value*			
	Prior to receipt of first dose of DTwP (approximately 6 weeks of age)	n			
		GMC (95% CI)			
		p-value*			
Tetanus					
	Birth	n			
		GMC (95% CI)			

Table 21: Serum IgG ELISA Geometric Mean Concentration (GMC) Results with 95% Confidence Intervals by Antigen, Time Point, and Treatment Group -- Infant Intent-to-Treat Population (continued)

Tdap Antigen	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
		p-value*			
	Prior to receipt of first dose of DTwP (approximately 6 weeks of age)	n			
		GMC (95% CI)			
		p-value*			
Diphtheria					
	Birth	n			
		GMC (95% CI)			
		p-value*			
	Prior to receipt of first dose of DTwP (approximately 6 weeks of age)	n			
		GMC (95% CI)			
		p-value*			

Note: N=Number of subjects in the Infant ITT Population
n=Number of subjects with results available at time point
*p-value is based on t-test on log-transformed ELISA titers.

Table with similar format:

Table 22: Serum IgG ELISA Geometric Mean Concentration (GMC) Results with 95% Confidence Intervals by Antigen, Time Point, and Treatment Group -- Infant Per Protocol Population

Table 23: ELISA Geometric Mean Concentration (GMC) Results of Antibodies to DTwP Antigens with 95% Confidence Intervals by Antigen, Time Point, and Treatment Group -- Infant Intent-to-Treat Population

DTwP Antigen	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
Pertussis Toxin (PT)					
	One month after receipt of first dose of DTwP (approximately 10 weeks of age)	n	x	x	--
		GMC (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
		p-value*	--	--	0.xxx
	One month after receipt of last dose of DTwP (approximately 18 weeks of age)	n			
		GMC (95% CI)			
		p-value*			
	At 6 months of age	n			
		GMC (95% CI)			
		p-value*			
Filamentous Hemagglutinin (FHA)					
	One month after receipt of first dose of DTwP (approximately 10 weeks of age)	n			
		GMC (95% CI)			
		p-value*			
	One month after receipt of last dose of DTwP (approximately 18 weeks of age)	n			
		GMC (95% CI)			
		p-value*			
	At 6 months of age	n			
		GMC (95% CI)			
		p-value*			
Pertactin (PRN)					
	One month after receipt of first dose of DTwP (approximately 10 weeks of age)	n			
		GMC (95% CI)			

Table 23: ELISA Geometric Mean Concentration (GMC) Results of Antibodies to DTwP Antigens with 95% Confidence Intervals by Antigen, Time Point, and Treatment Group -- Infant Intent-to-Treat Population (continued)

DTwP Antigen	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
		p-value*			
	One month after receipt of last dose of DTwP (approximately 18 weeks of age)	n			
		GMC (95% CI)			
		p-value*			
	At 6 months of age	n			
		GMC (95% CI)			
		p-value*			
Fimbriae 2 (FIM2)					
	One month after receipt of first dose of DTwP (approximately 10 weeks of age)	n			
		GMC (95% CI)			
		p-value*			
	One month after receipt of last dose of DTwP (approximately 18 weeks of age)	n			
		GMC (95% CI)			
		p-value*			
	At 6 months of age	n			
		GMC (95% CI)			
		p-value*			
Fimbriae 3 (FIM3)					
	One month after receipt of first dose of DTwP (approximately 10 weeks of age)	n			
		GMC (95% CI)			
		p-value*			
	One month after receipt of last dose of DTwP (approximately 18 weeks of age)	n			
		GMC (95% CI)			
		p-value*			

Table 23: ELISA Geometric Mean Concentration (GMC) Results of Antibodies to DTwP Antigens with 95% Confidence Intervals by Antigen, Time Point, and Treatment Group -- Infant Intent-to-Treat Population (continued)

DTwP Antigen	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
	At 6 months of age	n			
		GMC (95% CI)			
		p-value*			
Tetanus					
	One month after receipt of first dose of DTwP (approximately 10 weeks of age)	n			
		GMC (95% CI)			
		p-value*			
	One month after receipt of last dose of DTwP (approximately 18 weeks of age)	n			
		GMC (95% CI)			
		p-value*			
	At 6 months of age	n			
		GMC (95% CI)			
		p-value*			
Diphtheria					
	One month after receipt of first dose of DTwP (approximately 10 weeks of age)	n			
		GMC (95% CI)			
		p-value*			
	One month after receipt of last dose of DTwP (approximately 18 weeks of age)	n			
		GMC (95% CI)			
		p-value*			
	At 6 months of age	n			
		GMC (95% CI)			
		p-value*			

Note: N=Number of subjects in the Infant ITT Population
n=Number of subjects with results available at time point
*p-value is based on t-test on log-transformed ELISA titers.

Table with similar format:

Table 24: ELISA Geometric Mean Concentration (GMC) Results of Antibodies to DTwP Antigens with 95% Confidence Intervals by Antigen, Time Point, and Treatment Group -- Infant Per Protocol Population

Table 25: Serum IgG ELISA Geometric Mean Concentration (GMC) Results with 95% Confidence Intervals by Antigen, Time Point, and Treatment Group -- Maternal Intent-to-Treat Population

Antigen	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
Pertussis Toxin (PT)					
	One month after vaccination	n	x	x	--
		GMC (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
		p-value*	--	--	0.xxx
	At delivery	n			
		GMC (95% CI)			
		p-value*			
	6 months after delivery	n			
		GMC (95% CI)			
		p-value*			
Filamentous Hemagluttin (FHA)					
	One month after vaccination	n			
		GMC (95% CI)			
		p-value*			
	At delivery	n			
		GMC (95% CI)			
		p-value*			
	6 months after delivery	n			
		GMC (95% CI)			
		p-value*			
Pertactin (PRN)					
	One month after vaccination	n			
		GMC (95% CI)			
		p-value*			
	At delivery	n			
		GMC (95% CI)			
		p-value*			
	6 months after delivery	n			

Table 25: Serum IgG ELISA Geometric Mean Concentration (GMC) Results with 95% Confidence Intervals by Antigen, Time Point, and Treatment Group -- Maternal Intent-to-Treat Population (continued)

Antigen	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
		GMC (95% CI)			
		p-value*			
Tetanus					
	One month after vaccination	n			
		GMC (95% CI)			
		p-value*			
	At delivery	n			
		GMC (95% CI)			
		p-value*			
	6 months after delivery	n			
		GMC (95% CI)			
		p-value*			
Diphtheria					
	One month after vaccination	n			
		GMC (95% CI)			
		p-value*			
	At delivery	n			
		GMC (95% CI)			
		p-value*			
	6 months after delivery	n			
		GMC (95% CI)			
		p-value*			

Note: N=Number of subjects in the Maternal ITT Population
n=Number of subjects with results available at time point
*p-value is based on t-test on log-transformed ELISA titers.

Table with similar format:

Table 26: Serum IgG ELISA Geometric Mean Concentration (GMC) Results with 95% Confidence Intervals by Antigen, Time Point, and Treatment Group -- Maternal Per Protocol Population

Table 27: Geometric Mean Ratio (GMR) of Maternal and Infant-Specific Tdap-Specific Antibodies as Measured by ELISA with 95% Confidence Intervals by Antigen and Treatment Group -- Intent-to-Treat Population

Antigen	Statistic	BOOSTRIX	Td
Pertussis Toxin (PT)	N	x	x
	GMR[a] (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)
Filamentous Hemagluttin (FHA)	N		
	GMR[a] (95% CI)		
Pertactin (PRN)	N		
	GMR[a] (95% CI)		
Tetanus	N		
	GMR[a] (95% CI)		
Diphtheria	N		
	GMR[a] (95% CI)		

Note: N=Number of mother infant pairs in the intent-to-treat population with antibody levels available at delivery/birth.
[a] GMR represents the geometric mean ratio in maternal antibody concentration at delivery to infant antibody concentration at birth.

Table with similar format:

Table 28: Geometric Mean Ratio (GMR) of Maternal and Infant-Specific Tdap-Specific Antibodies as Measured by ELISA with 95% Confidence Intervals by Antigen and Treatment Group -- Per Protocol Population

Table 29: Breast Milk IgG ELISA Geometric Mean Concentration (GMC) Results with 95% Confidence Intervals by Antigen, Time Point, and Treatment Group -- Maternal Intent-to-Treat Population

Antigen	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
Pertussis Toxin (PT)					
	At delivery	n	x	x	--
		GMC (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x
		p-value*	--	--	0.xxx
	6 weeks after delivery	n			
		GMC (95% CI)			
		p-value*			
	10 weeks after delivery	n			
		GMC (95% CI)			
		p-value*			
	18 weeks after delivery	n			
		GMC (95% CI)			
		p-value*			
	6 months after delivery	n			
		GMC (95% CI)			
		p-value*			
Filamentous Hemagluttin (FHA)					
	At delivery	n			
		GMC (95% CI)			
		p-value*			
	6 weeks after delivery	n			
		GMC (95% CI)			
		p-value*			
	10 weeks after delivery	n			
		GMC (95% CI)			
		p-value*			
	18 weeks after delivery	n			

Table 29: Breast Milk IgG ELISA Geometric Mean Concentration (GMC) Results with 95% Confidence Intervals by Antigen, Time Point, and Treatment Group -- Maternal Intent-to-Treat Population (continued)

Antigen	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
		GMC (95% CI)			
		p-value*			
	6 months after delivery	n			
		GMC (95% CI)			
		p-value*			
Pertactin (PRN)					
	At delivery	n			
		GMC (95% CI)			
		p-value*			
	6 weeks after delivery	n			
		GMC (95% CI)			
		p-value*			
	10 weeks after delivery	n			
		GMC			
		95% CI			
		p-value*			
	18 weeks after delivery	n			
		GMC (95% CI)			
		p-value*			
	6 months after delivery	n			
		GMC (95% CI)			
		p-value*			
Tetanus					
	At delivery	n			
		GMC (95% CI)			
		p-value*			
	6 weeks after delivery	n			
		GMC (95% CI)			
		p-value*			
	10 weeks after delivery	n			

Table 29: Breast Milk IgG ELISA Geometric Mean Concentration (GMC) Results with 95% Confidence Intervals by Antigen, Time Point, and Treatment Group -- Maternal Intent-to-Treat Population (continued)

Antigen	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
		GMC (95% CI)			
		p-value*			
	18 weeks after delivery	n			
		GMC (95% CI)			
		p-value*			
	6 months after delivery	n			
		GMC (95% CI)			
		p-value*			
Diphtheria					
	At delivery	n			
		GMC (95% CI)			
		p-value*			
	6 weeks after delivery	n			
		GMC (95% CI)			
		p-value*			
	10 weeks after delivery	n			
		GMC (95% CI)			
		p-value*			
	18 weeks after delivery	n			
		GMC (95% CI)			
		p-value*			
	6 months after delivery	n			
		GMC (95% CI)			
		p-value*			

Note: N=Number of subjects in the Maternal ITT Population
n=Number of subjects with results available at time point
*p-value is based on t-test on log-transformed ELISA titers.

Tables with similar format:

Table 30: Breast Milk IgG ELISA GMC Results with 95% Confidence Intervals by Antigen, Time Point, and Treatment Group -- Maternal Per Protocol Population

Table 31: Breast Milk IgA ELISA GMC Results with 95% Confidence Intervals by Antigen, Time Point, and Treatment Group -- Maternal Intent-to-Treat Population

Table 32: Breast Milk IgA ELISA GMC Results with 95% Confidence Intervals by Antigen, Time Point, and Treatment Group -- Maternal Per Protocol Population

Table 33: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Maternal Intent-to-Treat Population

Cytokine	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
IFN-γ					
	Prior to vaccination	n	x	x	--
		GMC (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x, (x.x, x.x)
		Median (Q1, Q3)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
		Min, Max	x, x	x, x	x, x
	One month after vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to vaccination	n			
		Median (Q1, Q3)			
		Min, Max			
IL-10					
	Prior to vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to vaccination	n			
		Median (Q1, Q3)			
		Min, Max			
IL-12p70					
	Prior to vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			

Table 33: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Maternal Intent-to-Treat Population (continued)

Cytokine	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
		Min, Max			
	Change from prior to vaccination	n			
		Median (Q1, Q3)			
		Min, Max			
IL-12/IL-23p40					
	Prior to vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to vaccination	n			
		Median (Q1, Q3)			
		Min, Max			
IL-13					
	Prior to vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to vaccination	n			
		Median (Q1, Q3)			
		Min, Max			
IL-15					
	Prior to vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after vaccination	n			

Table 33: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Maternal Intent-to-Treat Population (continued)

Cytokine	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to vaccination	n			
		Median (Q1, Q3)			
		Min, Max			
IL-16					
	Prior to vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to vaccination	n			
		Median (Q1, Q3)			
		Min, Max			
IL-17A					
	Prior to vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to vaccination	n			
		Median (Q1, Q3)			
		Min, Max			
IL-1α					
	Prior to vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			

Table 33: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Maternal Intent-to-Treat Population (continued)

Cytokine	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
		Min, Max			
	One month after vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to vaccination	n			
		Median (Q1, Q3)			
		Min, Max			
IL-1β					
	Prior to vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to vaccination	n			
		Median (Q1, Q3)			
		Min, Max			
IL-2					
	Prior to vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to vaccination	n			
		Median (Q1, Q3)			
		Min, Max			
IL-4					
	Prior to vaccination	n			

Table 33: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Maternal Intent-to-Treat Population (continued)

Cytokine	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to vaccination	n			
		Median (Q1, Q3)			
		Min, Max			
IL-5					
	Prior to vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to vaccination	n			
		Median (Q1, Q3)			
		Min, Max			
IL-6					
	Prior to vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to vaccination	n			
		Median (Q1, Q3)			
		Min, Max			

Table 33: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Maternal Intent-to-Treat Population (continued)

Cytokine	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
IL-7					
	Prior to vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to vaccination	n			
		Median (Q1, Q3)			
		Min, Max			
IL-8					
	Prior to vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to vaccination	n			
		Median (Q1, Q3)			
		Min, Max			
TNF-α					
	Prior to vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to vaccination	n			

Table 33: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Maternal Intent-to-Treat Population (continued)

Cytokine	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
		Median (Q1, Q3)			
		Min, Max			
TNF-β					
	Prior to vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after vaccination	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to vaccination	n			
		Median (Q1, Q3)			
		Min, Max			

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

Table with similar format:

Table 34: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Maternal Per Protocol Population

Table 35: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Infant Intent-to-Treat Population

Cytokine	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
IFN-γ					
	Prior to receipt of first dose of DTwP (approximately 6 weeks of age)	n	x	x	--
		GMC (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
		Median (Q1, Q3)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
		Min, Max	x, x	x, x	x, x
	One month after receipt of first dose of DTwP (approximately 10 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post first dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of last dose of DTwP (approximately 18 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post last dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	6 months of age	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first dose of DTwP to 6 months of age	n			

Table 35: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Infant Intent-to-Treat Population (continued)

Cytokine	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
		Median (Q1, Q3)			
		Min, Max			
IL-10					
	Prior to receipt of first dose of DTwP (approximately 6 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of first dose of DTwP (approximately 10 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post first dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of last dose of DTwP (approximately 18 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post last dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	6 months of age	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			

Table 35: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Infant Intent-to-Treat Population (continued)

Cytokine	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
	Change from prior to first dose of DTwP to 6 months of age	n			
		Median (Q1, Q3)			
		Min, Max			
IL-12p70					
	Prior to receipt of first dose of DTwP (approximately 6 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of first dose of DTwP (approximately 10 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post first dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of last dose of DTwP (approximately 18 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post last dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	6 months of age	n			
		GMC (95% CI)			

Table 35: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Infant Intent-to-Treat Population (continued)

Cytokine	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first dose of DTwP to 6 months of age	n			
		Median (Q1, Q3)			
		Min, Max			
IL-12/IL-23p40					
	Prior to receipt of first dose of DTwP (approximately 6 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of first dose of DTwP (approximately 10 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post first dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of last dose of DTwP (approximately 18 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post last dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	6 months of age	n			

Table 35: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Infant Intent-to-Treat Population (continued)

Cytokine	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first dose of DTwP to 6 months of age	n			
		Median (Q1, Q3)			
		Min, Max			
IL-13					
	Prior to receipt of first dose of DTwP (approximately 6 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of first dose of DTwP (approximately 10 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post first dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of last dose of DTwP (approximately 18 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post last dose of DTwP	n			
		Median (Q1, Q3)			

Table 35: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Infant Intent-to-Treat Population (continued)

Cytokine	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
		Min, Max			
	6 months of age	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first dose of DTwP to 6 months of age	n			
		Median (Q1, Q3)			
		Min, Max			
IL-15					
	Prior to receipt of first dose of DTwP (approximately 6 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of first dose of DTwP (approximately 10 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post first dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of last dose of DTwP (approximately 18 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post last dose of DTwP	n			

Table 35: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Infant Intent-to-Treat Population (continued)

Cytokine	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
		Median (Q1, Q3)			
		Min, Max			
	6 months of age	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first dose of DTwP to 6 months of age	n			
		Median (Q1, Q3)			
		Min, Max			
IL-16					
	Prior to receipt of first dose of DTwP (approximately 6 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of first dose of DTwP (approximately 10 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post first dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of last dose of DTwP (approximately 18 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			

Table 35: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Infant Intent-to-Treat Population (continued)

Cytokine	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
	Change from prior to first to post last dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	6 months of age	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first dose of DTwP to 6 months of age	n			
		Median (Q1, Q3)			
		Min, Max			
IL-17A					
	Prior to receipt of first dose of DTwP (approximately 6 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of first dose of DTwP (approximately 10 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post first dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of last dose of DTwP (approximately 18 weeks of age)	n			
		GMC (95% CI)			

Table 35: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Infant Intent-to-Treat Population (continued)

Cytokine	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post last dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	6 months of age	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first dose of DTwP to 6 months of age	n			
		Median (Q1, Q3)			
		Min, Max			
IL-1α					
	Prior to receipt of first dose of DTwP (approximately 6 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of first dose of DTwP (approximately 10 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post first dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of last dose of DTwP (approximately 18 weeks of age)	n			

Table 35: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Infant Intent-to-Treat Population (continued)

Cytokine	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post last dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	6 months of age	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first dose of DTwP to 6 months of age	n			
		Median (Q1, Q3)			
		Min, Max			
IL-1β					
	Prior to receipt of first dose of DTwP (approximately 6 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of first dose of DTwP (approximately 10 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post first dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			

Table 35: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Infant Intent-to-Treat Population (continued)

Cytokine	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
	One month after receipt of last dose of DTwP (approximately 18 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post last dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	6 months of age	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first dose of DTwP to 6 months of age	n			
		Median (Q1, Q3)			
		Min, Max			
IL-2					
	Prior to receipt of first dose of DTwP (approximately 6 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of first dose of DTwP (approximately 10 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post first dose of DTwP	n			

Table 35: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Infant Intent-to-Treat Population (continued)

Cytokine	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of last dose of DTwP (approximately 18 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post last dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	6 months of age	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first dose of DTwP to 6 months of age	n			
		Median (Q1, Q3)			
		Min, Max			
IL-4					
	Prior to receipt of first dose of DTwP (approximately 6 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of first dose of DTwP (approximately 10 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			

Table 35: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Infant Intent-to-Treat Population (continued)

Cytokine	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
	Change from prior to first to post first dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of last dose of DTwP (approximately 18 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post last dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	6 months of age	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first dose of DTwP to 6 months of age	n			
		Median (Q1, Q3)			
		Min, Max			
IL-5					
	Prior to receipt of first dose of DTwP (approximately 6 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of first dose of DTwP (approximately 10 weeks of age)	n			
		GMC (95% CI)			

Table 35: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Infant Intent-to-Treat Population (continued)

Cytokine	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post first dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of last dose of DTwP (approximately 18 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post last dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	6 months of age	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first dose of DTwP to 6 months of age	n			
		Median (Q1, Q3)			
		Min, Max			
IL-6					
	Prior to receipt of first dose of DTwP (approximately 6 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of first dose of DTwP (approximately 10 weeks of age)	n			

Table 35: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Infant Intent-to-Treat Population (continued)

Cytokine	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post first dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of last dose of DTwP (approximately 18 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post last dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	6 months of age	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first dose of DTwP to 6 months of age	n			
		Median (Q1, Q3)			
		Min, Max			
IL-7					
	Prior to receipt of first dose of DTwP (approximately 6 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			

Table 35: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Infant Intent-to-Treat Population (continued)

Cytokine	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
	One month after receipt of first dose of DTwP (approximately 10 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post first dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of last dose of DTwP (approximately 18 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post last dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	6 months of age	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first dose of DTwP to 6 months of age	n			
		Median (Q1, Q3)			
		Min, Max			
IL-8					
	Prior to receipt of first dose of DTwP (approximately 6 weeks of age)	n			
		GMC (95% CI)			

Table 35: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Infant Intent-to-Treat Population (continued)

Cytokine	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of first dose of DTwP (approximately 10 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post first dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of last dose of DTwP (approximately 18 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post last dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	6 months of age	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first dose of DTwP to 6 months of age	n			
		Median (Q1, Q3)			
		Min, Max			
TNF-α					
	Prior to receipt of first dose of DTwP (approximately 6 weeks of age)	n			

Table 35: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Infant Intent-to-Treat Population (continued)

Cytokine	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of first dose of DTwP (approximately 10 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post first dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of last dose of DTwP (approximately 18 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post last dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	6 months of age	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first dose of DTwP to 6 months of age	n			
		Median (Q1, Q3)			
		Min, Max			
TNF-β					

Table 35: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Infant Intent-to-Treat Population (continued)

Cytokine	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
	Prior to receipt of first dose of DTwP (approximately 6 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of first dose of DTwP (approximately 10 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post first dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	One month after receipt of last dose of DTwP (approximately 18 weeks of age)	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first to post last dose of DTwP	n			
		Median (Q1, Q3)			
		Min, Max			
	6 months of age	n			
		GMC (95% CI)			
		Median (Q1, Q3)			
		Min, Max			
	Change from prior to first dose of DTwP to 6 months of age	n			
		Median (Q1, Q3)			

Table 35: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Infant Intent-to-Treat Population (continued)

Cytokine	Time Point	Statistic	BOOSTRIX (N=X)	Td (N=X)	Difference
		Min, Max			

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

Table with similar format:

Table 36: Multiplex Assays Stimulated Peripheral Blood Cells Results with 95% Confidence Intervals by Cytokine, Time Point, and Treatment Group -- Infant Per Protocol Population

Table 37: Serum IgG Anti-PT ELISA GMC Results with 95% Confidence Intervals at Delivery Stratified by Maternal Cofactors -- Maternal Intent-to-Treat Population

Cofactor	n	GMC	95% CI
Maternal Age			
18-29 years old	x	x.x	(x.x, x.x)
30-39 years old			
Parity			
Primiparous			
Multiparous			
GA at Time of Vaccination			
14-17 weeks			
18-21 weeks			
22-26 weeks			
GA at Time of Delivery			
28-32 weeks			
33-36 weeks			
37 or more weeks			

Tables with similar format:

Table 38: Serum IgG Anti-PT ELISA GMC Results with 95% Confidence Intervals at Delivery Stratified by Maternal Cofactors -- Maternal Per Protocol Population

Table 39: Serum IgG Anti-PT ELISAGMC Results with 95% Confidence Intervals at Birth Stratified by Maternal Cofactors -- Infant Intent-to-Treat Population

Table 40: Serum IgG Anti -PT ELISA GMC Results with 95% Confidence Intervals at Birth Stratified by Maternal Cofactors -- Infant Per Protocol Population

Table 41: Regression Analysis to Evaluate the Relationship of Anti-PT ELISA Response and Maternal Cofactors at Delivery -- Maternal Intent-to-Treat Population, BOOSTRIX

Model Parameter	n	Parameter Estimate	SE	p-value	Ratio*	95% CI of Ratio
Maternal Age						
Intercept	x	xxx.x	xxx.x	0.xxx	NA	NA
18-29 years old (reference)	x	NA	NA	NA	NA	NA
30-39 years old	x	xxx.x	xxx.x	0.xxx	xxx.x	(xxx.x, xxx.x)
Parity						
Intercept						
Primiparous (reference)						
Multiparous						
GA at Time of Vaccination						
Intercept						
14-17 weeks (reference)						
18-21 weeks						
22-26 weeks						
GA at Time of Delivery						
Intercept						
28-32 weeks (reference)						
33-36 weeks						
37 or more weeks						
Infant Birthweight (kg)						
Intercept	x	xxx.x	xxx.x	0.xxx	NA	NA
Infant Birthweight	n	xxx.x	xxx.x	0.xxx	NA	NA

*The ratio is the anti-PT antibody GMC of the relevant group divided by the GMC of the reference group.

Tables with similar format:

Table 42: Regression Analysis to Evaluate the Relationship of Anti-PT ELISA Response and Maternal Cofactors at Delivery -- Maternal Per Protocol Population, BOOSTRIX

Table 43: Regression Analysis to Evaluate the Relationship of Anti-PT ELISA Response and Maternal Cofactors at Birth -- Infant Intent-to-Treat Population, BOOSTRIX

Table 44: Regression Analysis to Evaluate the Relationship of Anti-PT ELISA Response and Maternal Cofactors at Birth -- Infant Per Protocol Population, BOOSTRIX

14.3 Safety Data

14.3.1 Displays of Adverse Events

Table 45: Overall Summary of Adverse Events - Maternal Subjects

	BOOSTRIX (N=X)		Td (N=X)		All Subjects (N=X)	
Subjects[a] with	n	%	n	%	n	%
At least one local solicited adverse event	x	x	x	x	x	x
At least one systemic solicited adverse event						
At least one unsolicited adverse event						
At least one unsolicited non-serious adverse event through Day 31						
At least one related unsolicited adverse event						
Mild (Grade 1)						
Moderate (Grade 2)						
Severe (Grade 3)						
Not yet assessed						
At least one severe (Grade 3) unsolicited adverse event						
Related						
Unrelated						
At least one serious adverse event[b]						
At least one related, serious adverse event						
At least one adverse event leading to early termination[c]						
At least one new onset chronic medical condition						
At least one pregnancy-related adverse event[d]						
Mild (Grade 1)						
Moderate (Grade 2)						
Severe (Grade 3)						
Not yet assessed						

N = Number of subjects in the Maternal 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 61.
[c] As reported on the Adverse Event eCRF.
[d] As listed in section 9.2.4 in the protocol
Note: The difference in the percent of maternal subjects in the BOOSTRIX and Td groups reporting study vaccine-related SAEs is xx with 95% CI of (xx, xx). The difference in the percent of maternal subjects in the BOOSTRIX and Td groups reporting SAEs from study vaccination through 6 months postpartum is xx with 95% CI of (xx, xx).

Table 46: Overall Summary of Adverse Events - Infant Subjects

	BOOSTRIX (N=X)		Td (N=X)		All Subjects (N=X)	
Subjects[a] with	n	%	n	%	n	%
At least one unsolicited adverse event	x	x	x	x	x	x
At least one related unsolicited adverse event						
Mild (Grade 1)						
Moderate (Grade 2)						
Severe (Grade 3)						
Not yet assessed						
At least one severe (Grade 3) unsolicited adverse event						
Related						
Unrelated						
At least one serious adverse event[b]						
At least one related, serious adverse event						
At least one adverse event leading to early termination[c]						
At least one infancy related adverse event[d]						
Mild (Grade 1)						
Moderate (Grade 2)						
Severe (Grade 3)						
Not yet assessed						

N = Number of subjects in the Infant 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 61.
[c] As reported on the Adverse Event eCRF.
[d] As listed in section 9.2.4 in protocol
Note: The difference in the percent of infant subjects in the BOOSTRIX and Td groups reporting study vaccine-related SAEs is xx with 95% CI of (xx, xx). The difference in the percent of infant subjects in the BOOSTRIX and Td groups reporting SAEs from birth through 6 months of age is xx with 95% CI of (xx, xx).

Table 47: Adverse Events Occurring in 5% of Subjects in Any Treatment Group by MedDRA System Organ Class and Preferred Term, and Treatment Group – Maternal Subjects

MedDRA Preferred Term	MedDRA System Organ Class	BOOSTRIX (N=X)			Td (N=X)			All Subjects (N=X)		
		n	%	Events	n	%	Events	n	%	Events
Serious Adverse Events										
All	All	x	x	x	x	x	x	x	x	x
PT1	SOC1									
Etc.	Etc.									
Other (Non-serious) Adverse Events										
All	All									
PT1	SOC1									
Etc	Etc									

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

Table with similar format:

Table 48: Adverse Events Occurring in 5% of Subjects in Any Treatment Group by MedDRA System Organ Class and Preferred Term, and Treatment Group – Infant Safety Population

14.3.1.1 Solicited Adverse Events

Table 49: Number and Percentage of Maternal Subjects Experiencing Solicited Events with 95% Confidence Intervals by Symptom and Treatment Group

Symptom	BOOSTRIX (N=X)			Td (N=X)			All Subjects (N=X)		
	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
Any Systemic Symptom									
Feverishness									
Fatigue									
Malaise									
Myalgia									
Arthralgia									
Headache									
Nausea									
Allergic Reaction									
Fever									
Any Local Symptom									
Pain									
Tenderness									
Ecchymosis									
Erythema									
Induration									
Ecchymosis Measurement (mm)									
Erythema Measurement (mm)									
Induration Measurement (mm)									
Note: N= Number of subjects in the Maternal Safety Population									

Table 50: Comparison of the Proportion of Maternal Subjects Experiencing Solicited Events by Treatment Group

Symptom	Statistic	BOOSTRIX (N=X)	Td (N=X)
Any Symptom	Proportion (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
	Difference (95% CI)	NA	x.xx (x.xx, x.xx)
	p-value*	NA	0.xxx
Any Systemic Symptom	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Feverishness	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Fatigue	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Malaise	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Myalgia	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Arthralgia	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Headache	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Nausea	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Allergic Reaction	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Fever	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Any Local Symptom	Proportion (95% CI)		

Table 50: Comparison of the Proportion of Maternal Subjects Experiencing Solicited Events by Treatment Group (continued)

	Difference (95% CI)		
	p-value*		
Pain	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Tenderness	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Ecchymosis	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Erythema	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Induration	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Ecchymosis Measurement (mm)	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Erythema Measurement (mm)	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Induration Measurement (mm)	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		

Note: N = Number of subjects in the Maternal Safety Population.
*P-value is based on Fisher's exact test.

Table 51: Number and Percentage of Maternal Subjects Experiencing Solicited Events by Symptom, Maximum Severity, and Treatment Group

Symptom	Severity	BOOSTRIX (N=X)			Td (N=X)			All Subjects (N=X)		
		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
	Mild									
	Moderate									
	Severe									
Any Systemic Symptom	None									
	Mild									
	Moderate									
	Severe									
Feverishness	None									
	Mild									
	Moderate									
	Severe									
Fatigue	None									
	Mild									
	Moderate									
	Severe									
Malaise	None									
	Mild									
	Moderate									
	Severe									
Myalgia	None									
	Mild									
	Moderate									
	Severe									
Arthralgia	None									
	Mild									
	Moderate									
	Severe									
Headache	None									
	Mild									
	Moderate									
	Severe									

Table 51: Number and Percentage of Maternal Subjects Experiencing Solicited Events by Symptom, Maximum Severity, and Treatment Group (continued)

Symptom	Severity	BOOSTRIX (N=X)			Td (N=X)			All Subjects (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI
Nausea	None									
	Mild									
	Moderate									
	Severe									
Allergic Reaction	None									
	Mild									
	Moderate									
	Severe									
Fever	None									
	Mild									
	Moderate									
	Severe									
Any Local Symptom	None	x	xx		x	xx		x	xx	
	Mild									
	Moderate									
	Severe									
Pain	None									
	Mild									
	Moderate									
	Severe									
Tenderness	None									
	Mild									
	Moderate									
	Severe									
Ecchymosis	None									
	Mild									
	Moderate									
	Severe									
Erythema	None									
	Mild									
	Moderate									
	Severe									
Induration	None									

Table 51: Number and Percentage of Maternal Subjects Experiencing Solicited Events by Symptom, Maximum Severity, and Treatment Group (continued)

Symptom	Severity	BOOSTRIX (N=X)			Td (N=X)			All Subjects (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI
	Mild									
	Moderate									
	Severe									
Ecchymosis Measurement (mm)	None									
	Mild									
	Moderate									
	Severe									
Erythema Measurement (mm)	None									
	Mild									
	Moderate									
	Severe									
Induration Measurement (mm)	None									
	Mild									
	Moderate									
	Severe									

Note: N = Number of subjects in the Maternal Safety Population. The denominator for the percentages is the number of subjects with non-missing data for the specific event.

Table 52: Number and Percentage of Maternal Subjects Experiencing Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group – BOOSTRIX

BOOSTRIX (N=X)																			
		Pre-Dose		**Post-Dose**		**Day 2**		**Day 3**		**Day 4**		**Day 5**		**Day 6**		**Day 7**		**Day 8**	
Symptom	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Any Symptom	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild																		
	Moderate																		
	Severe																		
	Not Reported																		
Systemic Symptoms																			
Any Systemic Symptom	None																		
	Mild																		
	Moderate																		
	Severe																		
	Not Reported																		
Feverishness	None																		
	Mild																		
	Moderate																		
	Severe																		
	Not Reported																		
Fatigue	None																		
	Mild																		
	Moderate																		
	Severe																		
	Not Reported																		
Malaise	None																		
	Mild																		
	Moderate																		
	Severe																		

Table 52: Number and Percentage of Maternal Subjects Experiencing Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group – BOOSTRIX (continued)

BOOSTRIX (N=X)

Symptom	Severity	Pre-Dose		Post-Dose		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Not Reported																		
Myalgia	None																		
	Mild																		
	Moderate																		
	Severe																		
	Not Reported																		
Arthralgia	None																		
	Mild																		
	Moderate																		
	Severe																		
	Not Reported																		
Headache	None																		
	Mild																		
	Moderate																		
	Severe																		
	Not Reported																		
Nausea	None																		
	Mild																		
	Moderate																		
	Severe																		
	Not Reported																		
Allergic Reaction	None																		
	Mild																		
	Moderate																		
	Severe																		
	Not Reported																		
Fever	None																		
	Mild																		
	Moderate																		

Table 52: Number and Percentage of Maternal Subjects Experiencing Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group – BOOSTRIX (continued)

BOOSTRIX (N=X)

Symptom	Severity	Pre-Dose		Post-Dose		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Severe																		
	Not Reported																		
Local Symptoms																			
Any Local Symptom	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild																		
	Moderate																		
	Severe																		
	Not Reported																		
Pain	None																		
	Mild																		
	Moderate																		
	Severe																		
	Not Reported																		
Tenderness	None																		
	Mild																		
	Moderate																		
	Severe																		
	Not Reported																		
Ecchymosis	None																		
	Mild																		
	Moderate																		
	Severe																		
	Not Reported																		
Erythema	None																		
	Mild																		
	Moderate																		
	Severe																		

Table 52: Number and Percentage of Maternal Subjects Experiencing Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group – BOOSTRIX (continued)

BOOSTRIX (N=X)

Symptom	Severity	Pre-Dose		Post-Dose		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Not Reported																		
Induration	None																		
	Mild																		
	Moderate																		
	Severe																		
	Not Reported																		
Ecchymosis Measurement (mm)	None																		
	Mild																		
	Moderate																		
	Severe																		
	Not Reported																		
Erythema Measurement (mm)	None																		
	Mild																		
	Moderate																		
	Severe																		
	Not Reported																		
Induration Measurement (mm)	None																		
	Mild																		
	Moderate																		
	Severe																		
	Not Reported																		

Note: N = Number of subjects in the Maternal Safety Population randomized to receive intrapartum BOOSTRIX.
Severity is the maximum severity reported post dosing for each subject for each day.

Tables with Similar Format:

Table 53: Number and Percentage of Maternal Subjects Experiencing Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group – Td

Table 54: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, Day Post Dosing, and Treatment Group – All Subjects

14.3.1.2 Unsolicited Adverse Events

Table 55: Summary of Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, and Treatment Group – BOOSTRIX – Maternal Subjects

MedDRA System Organ Class	MedDRA Preferred Term	Day 1-8 Post Dose (N=X)				Days > 8 Post Dose (N=X)				Any Time (N=X)			
		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
[SOC 1]	Any PT												
	[PT 1]												
	[PT 2]												
[SOC 2]	Any PT												
	[PT 1]												
	[PT 2]												

Note: N = number of subjects in the Maternal Safety Population randomized to receive intrapartum BOOSTRIX. A subject is only counted once per PT/time point.

Tables with similar format:

Table 56: Summary of Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, and Treatment Group – Td – Maternal Subjects

Table 57: Summary of Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, and Treatment Group – All Subjects – Maternal Subjects

Table 58: Summary of Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, and Treatment Group —Infant Subjects

MedDRA System Organ Class	MedDRA Preferred Term	BOOSTRIX (N=X)				Td (N=X)				All Subjects (N=X)			
		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
[SOC 1]	Any PT												
	[PT 1]												
	[PT 2]												
[SOC 2]	Any PT												
	[PT 1]												
	[PT 2]												

Note: N = number of subjects in the Infant Safety Population. A subject is only counted once per PT.

Table 59: Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, Relationship, and Treatment Group -- Maternal Subjects

MedDRA System Organ Class	MedDRA Preferred Term	Severity	BOOSTRIX (N=X)						Td (N=X)						All Subjects (N=X)					
			Related		Not Related		Total		Related		Not Related		Total		Related		Not Related		Total	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Any SOC	Any PT	Any Severity	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Mild																		
		Moderate																		
		Severe																		
SOC 1	Any PT	Any Severity																		
		Mild																		
		Moderate																		
		Severe																		
	PT 1	Any Severity																		
		Mild																		
		Moderate																		
		Severe																		
	PT 2	Any Severity																		
		Mild																		
		Moderate																		
		Severe																		

Note: N = Number of subjects in the Maternal Safety Population.

Note: The difference in the percent of maternal subjects in the BOOSTRIX and Td groups reporting non-serious AEs from day of study vaccination to Day 31 is xx with 95% CI of (xx, xx).

Table with similar format:

Table 60: Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, Relationship, and Treatment Group- -- Infant Subjects

14.3.2 Listing of Deaths, Other Serious and Significant Adverse Events

Table 61: Listing of Serious Adverse Events

Maternal/Infant	Adverse Event	Estimated Gestational Age/Infant Age	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	Subject Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Subject ID: , Treatment Group: , AE Number:												
Comments:												
Subject ID: , Treatment Group: , AE Number:												
Comments:												

Table 62: Listing of Major Congenital Anomalies

Maternal/Infant	Adverse Event	Estimated Gestational Age/Infant Age	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	Subject Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Subject ID: Treatment Group: , AE Number:												
Comments:												
Subject ID: Treatment Group: , AE Number:												
Comments:												

Table 63: Listing of Non-Serious, Unsolicited, Moderate or Severe Adverse Events

Maternal/Infant	Adverse Event	Estimated Gestational Age/Infant Age	No. of Days Post Associated Dose (Duration)	Severity	Relationship to Study Treatment	If Not Related, Alternative Etiology	Subject Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Subject ID: , Treatment Group: , AE Number:										
Comments:										
Subject ID: , Treatment Group: , AE Number:										
Comments:										

Table 64: Listing of New Onset Chronic Medical Conditions

Maternal/Infant	Adverse Event	Estimated Gestational Age/ Infant Age	No. of Days Post Dose	Duration of Event	Severity	MedDRA System Organ Class	MedDRA Preferred Term	Relationship	Outcome
Subject ID: , Treatment Group: , AE Number:									
Comments:									
Subject ID: , Treatment Group: , AE Number:									
Comments:									

14.3.3 Narratives of Deaths, Other Serious and Significant Adverse Events

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

14.3.4 Abnormal Laboratory Value Listings (by Subject)

Not Applicable.

14.3.5 Displays of Laboratory Results

14.3.5.1 Chemistry Results

Not Applicable.

14.3.5.2 Hematology Results

Not Applicable.

14.3.5.3 Urinalysis Results

Not Applicable.

14.3.6 Displays of Vital Signs

Table 65: Vital Signs in Maternal Subjects by Maximum Severity, Time Point, and Treatment Group – Any Assessment

Time Point	Treatment Group	N	None		Mild		Moderate		Severe		Missing	
			n	%	n	%	n	%	n	%	n	%
Baseline	BOOSTRIX	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Td											
Day 31	BOOSTRIX											
	Td											
Delivery	BOOSTRIX											
	Td											
Max Severity Post Baseline	BOOSTRIX											
	Td											

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 Maternal Safety Population

Tables with similar format:

Table 66: Vital Signs in Maternal Subjects by Maximum Severity, Time Point, and Treatment Group –Oral Temperature

Table 67: Vital Signs in Maternal Subjects by Maximum Severity, Time Point, and Treatment Group –Pulse

Table 68: Vital Signs in Maternal Subjects by Maximum Severity, Time Point, and Treatment Group –Blood Pressure

Table 69: Vital Signs in Infant Subjects by Maximum Severity and Treatment Group – Any Assessment

Time Point	Treatment Group	N	None		Mild		Moderate		Severe		Missing	
			n	%	n	%	n	%	n	%	n	%
Birth	BOOSTRIX	x	xx	xx	x	xx	xx	x	xx	xx	x	xx
	Td											
N = Number of subjects in the Infant Safety Population												

Tables with similar format:

Table 70: Vital Signs in Infant Subjects by Maximum Severity and Treatment Group – Axillary Temperature

Table 71: Vital Signs in Infant Subjects by Maximum Severity and Treatment Group – Heart Rate

Table 72: Vital Signs in Infant Subjects by Maximum Severity and Treatment Group – Respiratory Rate

14.4 Summary of Concomitant Medications

Table 73: Number and Percentage of Subjects with Prior and Concurrent Medications by WHO Drug Classification and Treatment Group – Maternal Subjects

WHO Drug Code Level 1, Anatomic Group	WHO Drug Code Level 2, Therapeutic Subgroup	BOOSTRIX (N=X)		Td (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%
Any Level 1 Codes	Any Level 2 Codes	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]	Any [ATC 1 – 2]–						
	[ATC 2 – 1]						
	[ATC 2 – 2]						

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

Table 74: Number and Percentage of Subjects with Prior and Concurrent Medications by WHO Drug Classification and Treatment Group – Infant Subjects

WHO Drug Code Level 1, Anatomic Group	WHO Drug Code Level 2, Therapeutic Subgroup	BOOSTRIX (N=X)		Td (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%
Any Level 1 Codes	Any Level 2 Codes	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]	Any [ATC 1 – 2]–						
	[ATC 2 – 1]						
	[ATC 2 – 2]						

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

14.5 Pregnancy Reports

Table 75: Summary of Pregnancy Outcomes by Treatment Group

Pregnancy Outcome	BOOSTRIX (N=X)			Td (N=X)			All Subjects (N=X)		
	n	%	95% CI	n	%	95% CI	n	%	95% CI
Live Births	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x
Spontaneous Abortions									
Elective Abortions or Still Births									
Note: N= Number of subjects in the Maternal Safety Population									

Table 76: Summary of Infant Size for Gestational Age at Birth

Size	BOOSTRIX (N=X)			Td (N=X)			All Subjects (N=X)		
	n	%	95% CI	n	%	95% CI	n	%	95% CI
Small for Gestational Age	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x
Appropriate for Gestational Age									
Large for Gestational Age									
Note: N= Number of subjects in the Infant Safety Population									

Table 77: Number and Percentage of Maternal Subjects Experiencing Pregnancy-Related Adverse Events with 95% Confidence Intervals by Symptom and Treatment Group

Symptom	BOOSTRIX (N=X)			Td (N=X)			All Subjects (N=X)		
	n	%	95% CI	n	%	95% CI	n	%	95% CI
Any Maternal Pregnancy Related Symptom	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x
Pregnancy Loss									
Bleeding									
Postpartum Hemorrhage									
Postabortal Endometritis/Salpingitis									
Preterm Rupture of Membranes									
Preterm Contractions/Labor/Delivery									
Poor Fetal Growth									
Hypertension, Preeclampsia/Eclampsia									
Chorioamnionitis									
Postpartum Endometritis									
Gestational Diabetes									
Other Pregnancy Related AE									

Note: N= Number of subjects in the Maternal Safety Population

Table 78: Number and Percentage of Infant Subjects Experiencing Infancy-Related Adverse Events with 95% Confidence Intervals by Symptom, and Treatment Group

	BOOSTRIX (N=X)			Td (N=X)			All Subjects (N=X)		
Symptom	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Any Neonatal and Infant Events	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x
Preterm Birth									
Birth Weight									
Neonatal Complications in a Term Infant									
Other AE in Newborn									
Congenital Abnormalities/Birth Defects									

Note: N= Number of subjects in the Infant Safety Population

Table 79: Comparison of the Proportion of Maternal Subjects Experiencing Pregnancy-Related Adverse Events by Symptom and Treatment Group

Symptom	Statistic	BOOSTRIX (N=X)	Td (N=X)
Any Maternal Pregnancy Related Symptom	Proportion (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
	Difference (95% CI)	NA	x.xx (x.xx, x.xx)
	p-value*	NA	0.xxx
Pregnancy Loss	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Bleeding	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Postpartum Hemorrhage	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Postabortal endometritis/salpingitis	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Preterm Rupture of Membranes	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Preterm Contractions/Labor/Delivery	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Poor Fetal Growth	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Hypertension, Preeclampsia/eclampsia	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Chorioamnionitis	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Postpartum Endometritis	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Gestational Diabetes	Proportion (95% CI)		

Table 79: Comparison of the Proportion of Maternal Subjects Experiencing Pregnancy-Related Adverse Events by Symptom and Treatment Group (continued)

Symptom	Statistic	BOOSTRIX (N=X)	Td (N=X)
	Difference (95% CI)		
	p-value*		
Other Pregnancy Related AE	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		

Note: N = Number of subjects in the Maternal Safety Population.

*P-value is based on Fisher's exact test.

Table 80: Comparison of the Proportion of Infant Subjects Experiencing Infancy-Related Adverse Events by Symptom and Treatment Group

Symptom	Statistic	BOOSTRIX (N=X)	Td (N=X)
Any Neonatal and Infant Event	Proportion (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
	Difference (95% CI)	NA	x.xx (x.xx, x.xx)
	p-value*	NA	0.xxx
Preterm Birth	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Birth Weight	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Neonatal Complications in a Term Infant	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Other AE in Newborn	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		
Congenital Abnormalities/Birth Defect	Proportion (95% CI)		
	Difference (95% CI)		
	p-value*		

Note: N = Number of subjects in the Infant Safety Population.
*P-value is based on Fisher's exact test.

Table 81: Number and Percentage of Maternal Subjects Experiencing Pregnancy-Related Events by Symptom, Maximum Severity, and Treatment Group

Symptom	Severity	BOOSTRIX (N=X)			Td (N=X)			All Subjects (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI
Any Maternal Pregnancy Related Symptom	None	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x
	Mild									
	Moderate									
	Severe									
Pregnancy Loss	None									
	Mild									
	Moderate									
	Severe									
Bleeding	None									
	Mild									
	Moderate									
	Severe									
Postpartum Hemorrhage	None									
	Mild									
	Moderate									
	Severe									
Postabortal endometritis/salpingitis	None									
	Mild									
	Moderate									
	Severe									
Preterm Rupture of Membranes	None									
	Mild									
	Moderate									

Table 81: Number and Percentage of Maternal Subjects Experiencing Pregnancy-Related Events by Symptom, Maximum Severity, and Treatment Group (continued)

Symptom	Severity	BOOSTRIX (N=X)			Td (N=X)			All Subjects (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI
	Severe									
Preterm Contractions/Labor/Delivery	None									
	Mild									
	Moderate									
	Severe									
Poor Fetal Growth	None									
	Mild									
	Moderate									
	Severe									
Hypertension, Preeclampsia/eclampsia	None									
	Mild									
	Moderate									
	Severe									
Chorioamnionitis	None									
	Mild									
	Moderate									
	Severe									
Postpartum Endometritis	None									
	Mild									
	Moderate									
	Severe									
Gestational Diabetes	None									
	Mild									
	Moderate									

Table 81: Number and Percentage of Maternal Subjects Experiencing Pregnancy-Related Events by Symptom, Maximum Severity, and Treatment Group (continued)

Symptom	Severity	BOOSTRIX (N=X)			Td (N=X)			All Subjects (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI
	Severe									
Other Pregnancy Related AE	None									
	Mild									
	Moderate									
	Severe									

Note: N = Number of subjects in the Maternal Safety Populations.

Table 82: Number and Percentage of Infant Subjects Experiencing Infancy-Related Events by Symptom, Maximum Severity, and Treatment Group

		BOOSTRIX (N=X)			Td (N=X)			All Subjects (N=X)		
Symptom	**Severity**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Any Neonatal and Infant Events	None	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x
	Mild									
	Moderate									
	Severe									
Preterm Birth	None									
	Mild									
	Moderate									
	Severe									
Birth Weight	None									
	Mild									
	Moderate									
	Severe									
Neonatal Complications in a Term Infant	None									
	Mild									
	Moderate									
	Severe									

Table 82: Number and Percentage of Infant Subjects Experiencing Infancy-Related Events by Symptom, Maximum Severity, and Treatment Group (continued)

Symptom	Severity	BOOSTRIX (N=X)			Td (N=X)			All Subjects (N=X)		
		n	%	95% CI	n	%	95% CI	n	%	95% CI
Other AE in Newborn	None									
	Mild									
	Moderate									
	Severe									
Congenital Abnormalities/Birth Defects	None									
	Mild									
	Moderate									
	Severe									

Note: N = Number of subjects in the Infant Safety Population.

APPENDIX 2. FIGURE MOCK-UPS

LIST OF FIGURES

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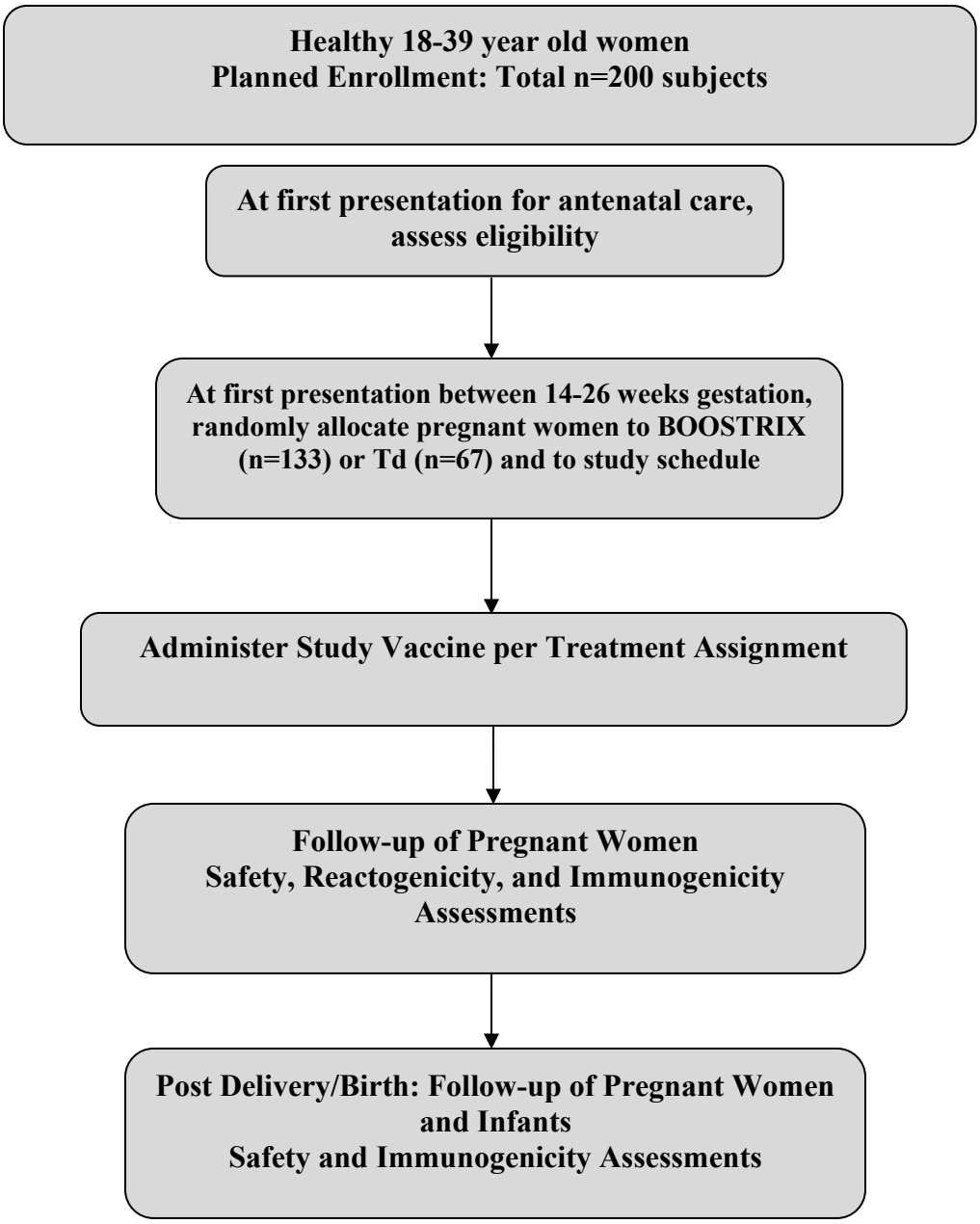
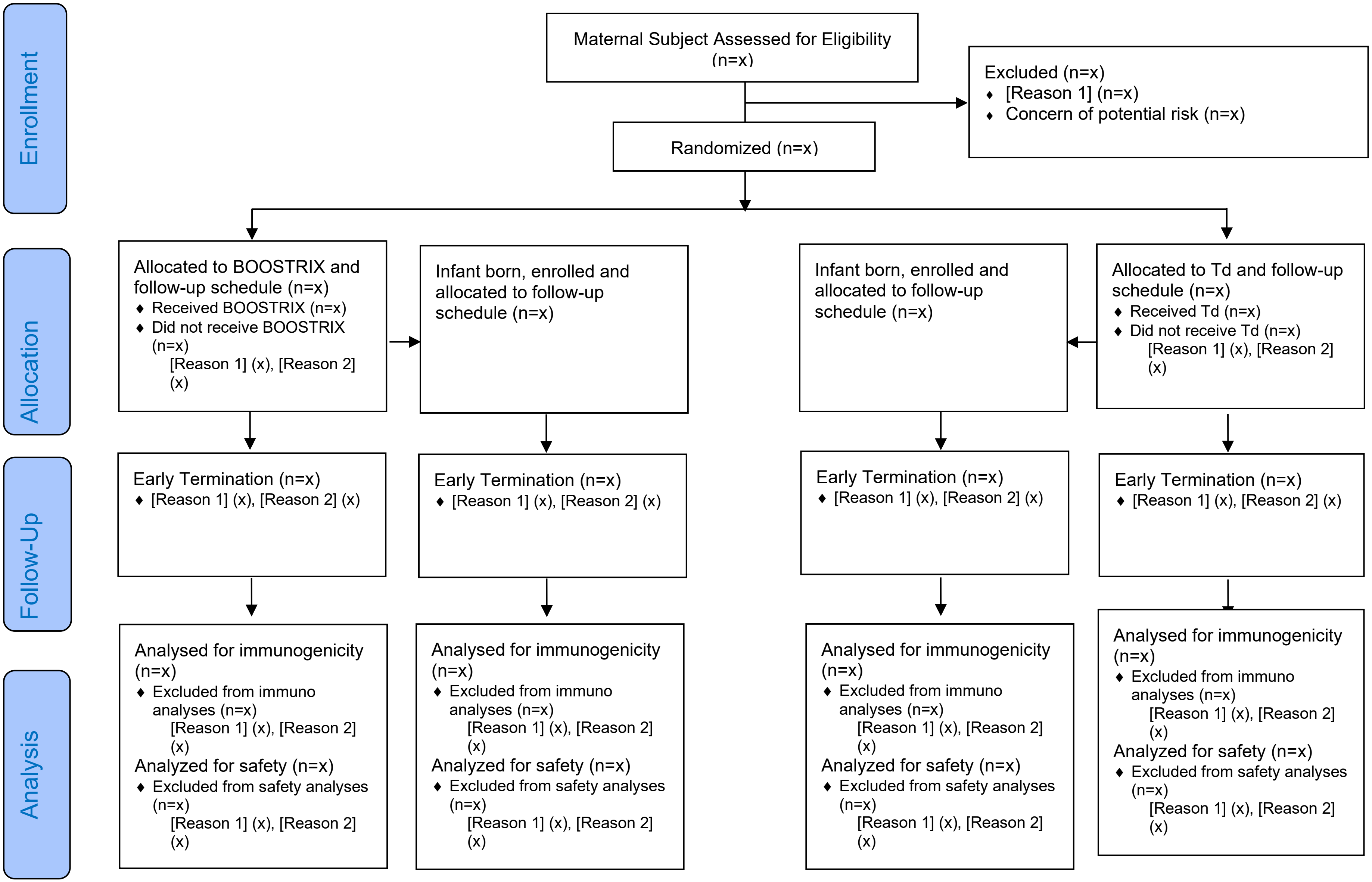
Figure 1: Study Schema



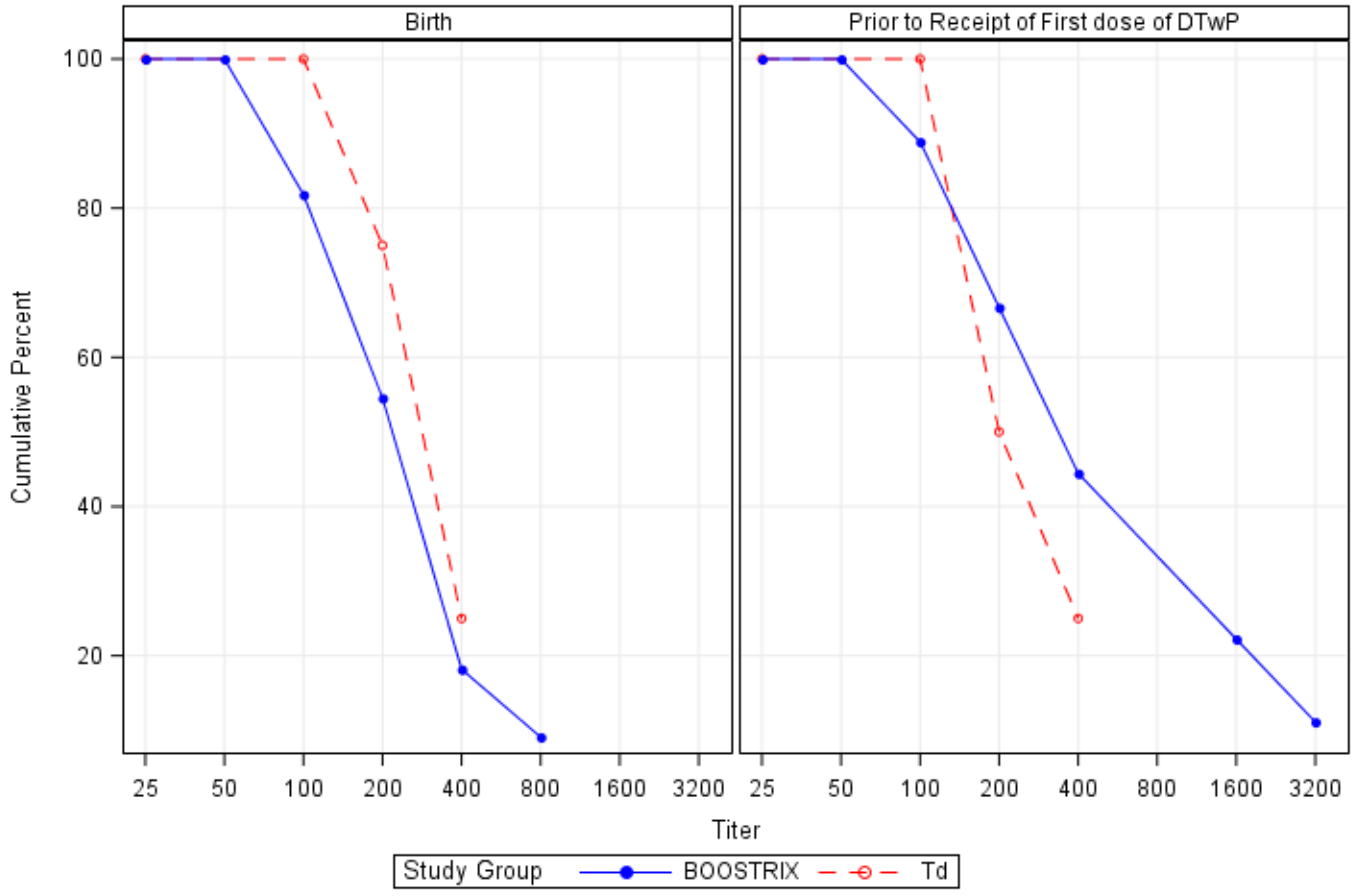
10.1 Disposition of Subjects

Figure 2: CONSORT Flow Diagram



14.2.2 Immunogenicity Response Figures by Measure, Vaccination, and Time Point

Figure 3: Reverse Cumulative Distribution of Serum IgG Antibody Titers to Pertussis Toxin by Time Point and Treatment Group - Infant Intent-to-Treat Population



Figures with similar format:

Figure 4: Reverse Cumulative Distribution of Serum IgG Antibody Titers to Pertussis Toxin by Time Point and Treatment Group - Infant Per Protocol Population

Figure 5: Reverse Cumulative Distribution of Serum IgG Antibody Titers to Filamentous Hemagglutinin by Time Point and Treatment Group - Infant Intent-to-Treat Population

Figure 6: Reverse Cumulative Distribution of Serum IgG Antibody Titers to Filamentous Hemagglutinin by Time Point and Treatment Group - Infant Per Protocol Population

Figure 7: Reverse Cumulative Distribution of Serum IgG Antibody Titers to Pertactin by Time Point and Treatment Group - Infant Intent-to-Treat Population

Figure 8: Reverse Cumulative Distribution of Serum IgG Antibody Titers to Pertactin by Time Point and Treatment Group - Infant Per Protocol Population

Figure 9: Reverse Cumulative Distribution of Serum IgG Antibody Titers to Tetanus by Time Point and Treatment Group - Infant Intent-to-Treat Population

Figure 10: Reverse Cumulative Distribution of Serum IgG Antibody Titers to Tetanus by Time Point and Treatment Group - Infant Per Protocol Population

Figure 11: Reverse Cumulative Distribution of Serum IgG Antibody Titers to Diphtheria by Time Point and Treatment Group - Infant Intent-to-Treat Population

Figure 12: Reverse Cumulative Distribution of Serum IgG Antibody Titers to Diphtheria by Time Point and Treatment Group - Infant Per Protocol Population

Figure 13: Reverse Cumulative Distribution of DTwP Antigens to Pertussis Toxin by Time Point and Treatment Group - Infant Intent-to-Treat Population

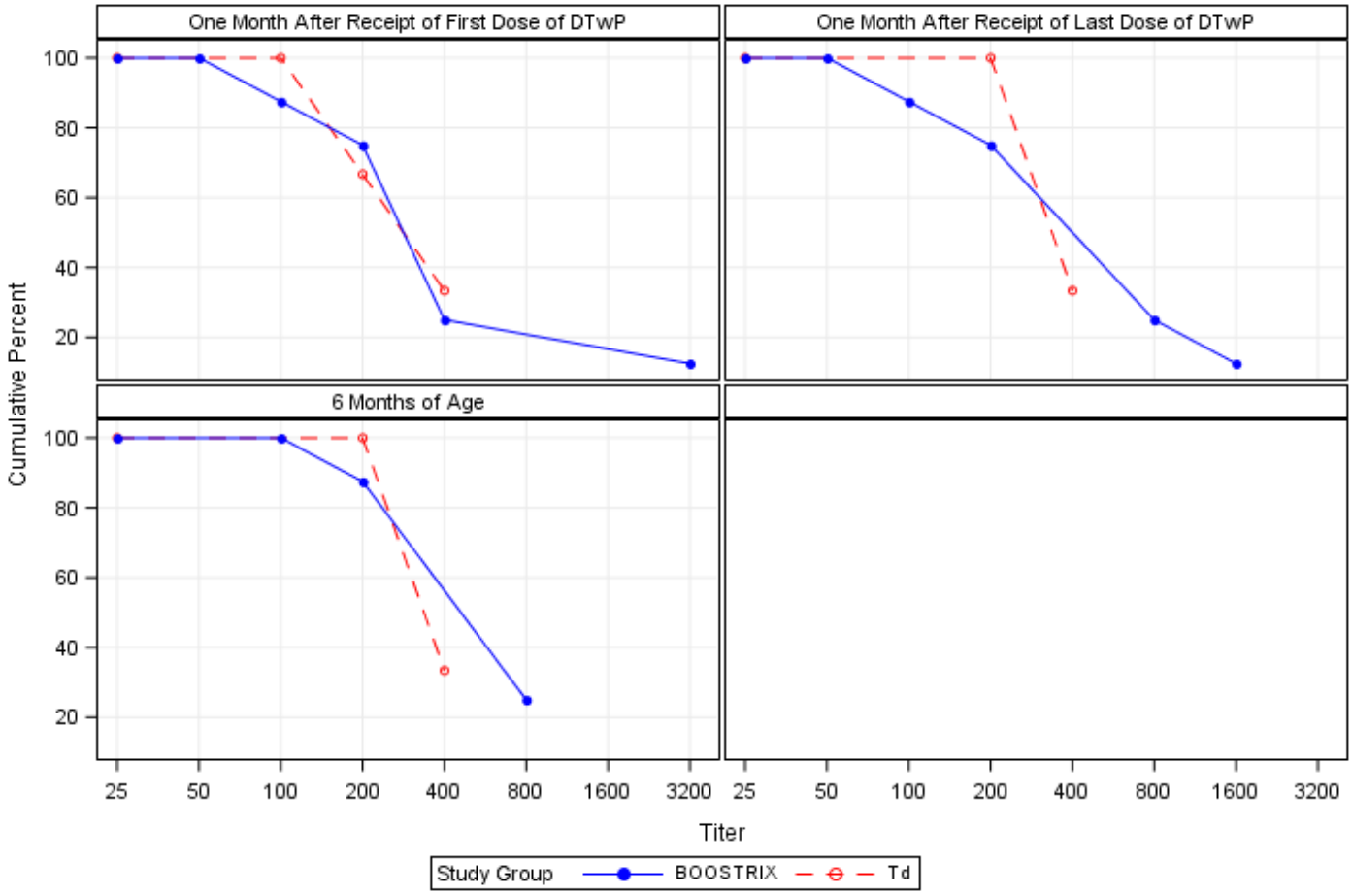


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Figure 14: Reverse Cumulative Distribution of DTwP Antigens to Pertussis Toxin by Time Point and Treatment Group - Infant Per Protocol Population

Figure 15: Reverse Cumulative Distribution of DTwP Antigens to Filamentous Hemagglutinin by Time Point and Treatment Group - Infant Intent-to-Treat Population

Figure 16: Reverse Cumulative Distribution of DTwP Antigens to Filamentous Hemagglutinin by Time Point and Treatment Group - Infant Per Protocol Population

Figure 17: Reverse Cumulative Distribution of DTwP Antigens to Pertactin by Time Point and Treatment Group - Infant Intent-to-Treat Population

Figure 18: Reverse Cumulative Distribution of DTwP Antigens to Pertactin by Time Point and Treatment Group - Infant Per Protocol Population

Figure 19: Reverse Cumulative Distribution of DTwP Antigens to Fimbriae 2 by Time Point and Treatment Group - Infant Intent-to-Treat Population

Figure 20: Reverse Cumulative Distribution of DTwP Antigens to Fimbriae 2 by Time Point and Treatment Group - Infant Per Protocol Population

Figure 21: Reverse Cumulative Distribution of DTwP Antigens to Fimbriae 3 by Time Point and Treatment Group - Infant Intent-to-Treat Population

Figure 22: Reverse Cumulative Distribution of DTwP Antigens to Fimbriae 3 by Time Point and Treatment Group - Infant Per Protocol Population

Figure 23: Reverse Cumulative Distribution of DTwP Antigens to Tetanus by Time Point and Treatment Group - Infant Intent-to-Treat Population

Figure 24: Reverse Cumulative Distribution of DTwP Antigens to Tetanus by Time Point and Treatment Group - Infant Per Protocol Population

Figure 25: Reverse Cumulative Distribution of DTwP Antigens to Diphtheria by Time Point and Treatment Group - Infant Intent-to-Treat Population

Figure 26: Reverse Cumulative Distribution of DTwP Antigens to Diphtheria by Time Point and Treatment Group - Infant Per Protocol Population

Figure 27: Reverse Cumulative Distribution of Serum IgG Antibody Titers to Pertussis Toxin by Time Point and Treatment Group - Maternal Intent-to-Treat Population

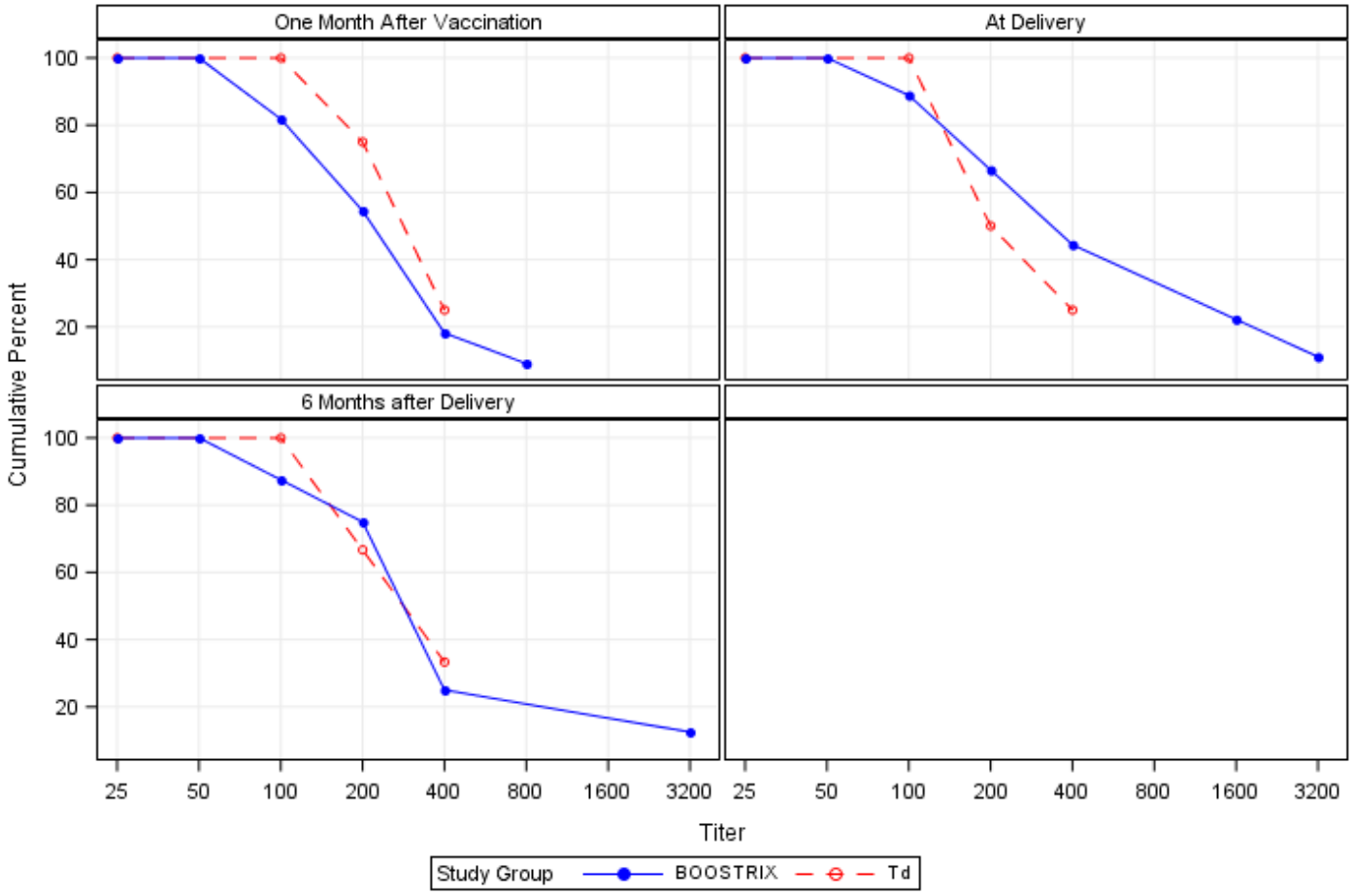

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Figure 28: Reverse Cumulative Distribution of Serum IgG Antibody Titers to Pertussis Toxin by Time Point and Treatment Group - Maternal Per Protocol Population

Figure 29: Reverse Cumulative Distribution of Serum IgG Antibody Titers to Filamentous Hemagglutinin by Time Point and Treatment Group - Maternal Intent-to-Treat Population

Figure 30: Reverse Cumulative Distribution of Serum IgG Antibody Titers to Filamentous Hemagglutinin by Time Point and Treatment Group - Maternal Per Protocol Population

Figure 31: Reverse Cumulative Distribution of Serum IgG Antibody Titers to Pertactin by Time Point and Treatment Group - Maternal Intent-to-Treat Population

Figure 32: Reverse Cumulative Distribution of Serum IgG Antibody Titers to Pertactin by Time Point and Treatment Group - Maternal Per Protocol Population

Figure 33: Reverse Cumulative Distribution of Serum IgG Antibody Titers to Tetanus by Time Point and Treatment Group - Maternal Intent-to-Treat Population

Figure 34: Reverse Cumulative Distribution of Serum IgG Antibody Titers to Tetanus by Time Point and Treatment Group - Maternal Per Protocol Population

Figure 35: Reverse Cumulative Distribution of Serum IgG Antibody Titers to Diphtheria by Time Point and Treatment Group - Maternal Intent-to-Treat Population

Figure 36: Reverse Cumulative Distribution of Serum IgG Antibody Titers to Diphtheria by Time Point and Treatment Group - Maternal Per Protocol Population

Figure 37: Reverse Cumulative Distribution of Breast Milk IgG Antibody Titers to Pertussis Toxin by Time Point and Treatment Group - Maternal Intent-to-Treat Population

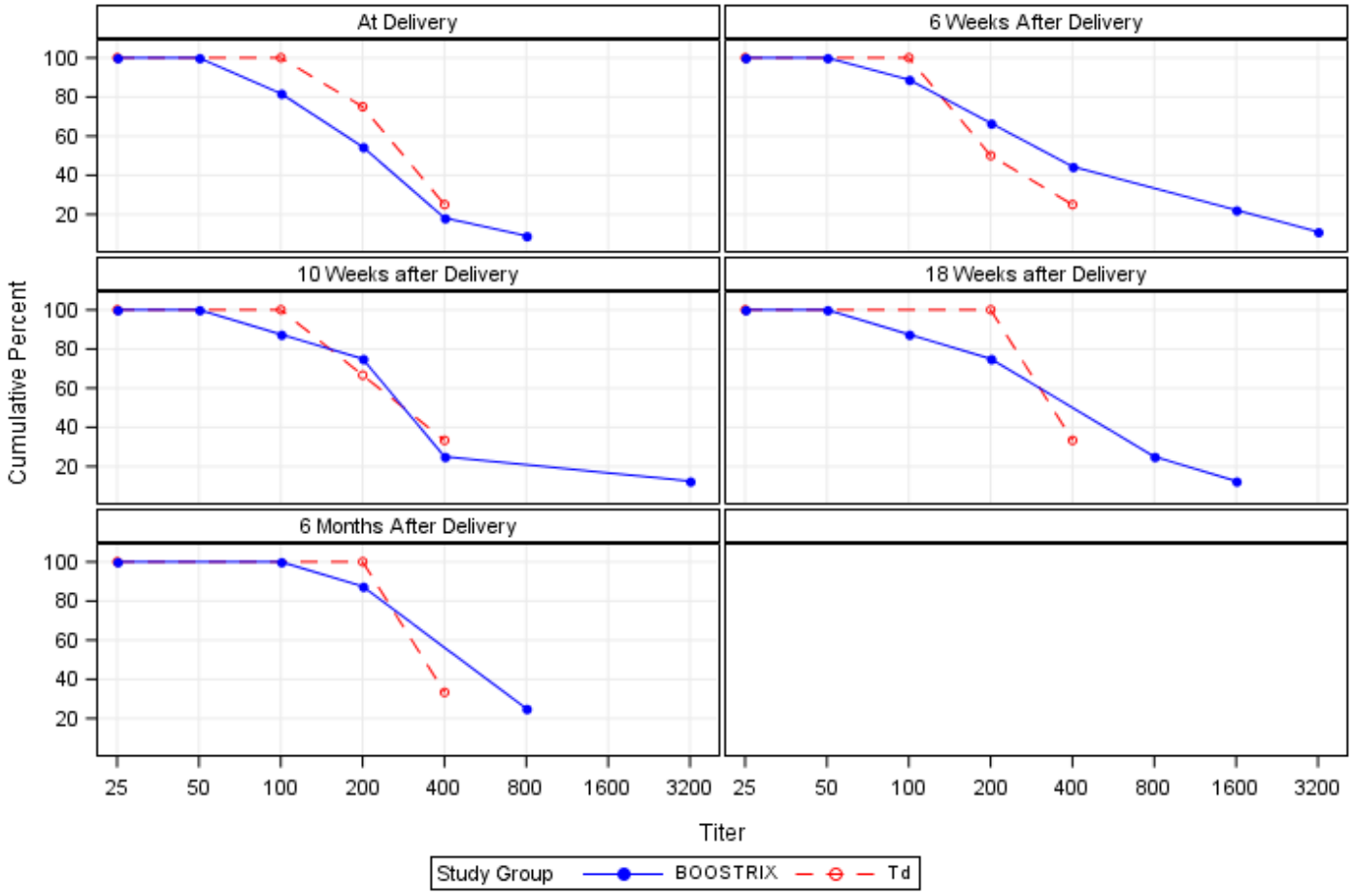

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Figure 38: Reverse Cumulative Distribution of Breast Milk IgG Antibody Titers to Pertussis Toxin by Time Point and Treatment Group - Maternal Per Protocol Population

Figure 39: Reverse Cumulative Distribution of Breast Milk IgG Antibody Titers to Filamentous Hemagglutinin by Time Point and Treatment Group - Maternal Intent-to-Treat Population

Figure 40: Reverse Cumulative Distribution of Breast Milk IgG Antibody Titers to Filamentous Hemagglutinin by Time Point and Treatment Group - Maternal Per Protocol Population

Figure 41: Reverse Cumulative Distribution of Breast Milk IgG Antibody Titers to Pertactin by Time Point and Treatment Group - Maternal Intent-to-Treat Population

Figure 42: Reverse Cumulative Distribution of Breast Milk IgG Antibody Titers to Pertactin by Time Point and Treatment Group - Maternal Per Protocol Population

Figure 43: Reverse Cumulative Distribution of Breast Milk IgG Antibody Titers to Tetanus by Time Point and Treatment Group - Maternal Intent-to-Treat Population

Figure 44: Reverse Cumulative Distribution of Breast Milk IgG Antibody Titers to Tetanus by Time Point and Treatment Group - Maternal Per Protocol Population

Figure 45: Reverse Cumulative Distribution of Breast Milk IgG Antibody Titers to Diphtheria by Time Point and Treatment Group - Maternal Intent-to-Treat Population

Figure 46: Reverse Cumulative Distribution of Breast Milk IgG Antibody Titers to Diphtheria by Time Point and Treatment Group - Maternal Per Protocol Population

Figure 47: Reverse Cumulative Distribution of Breast Milk IgA Antibody Titers to Pertussis Toxin by Time Point and Treatment Group - Maternal Intent-to-Treat Population

Figure 48: Reverse Cumulative Distribution of Breast Milk IgA Antibody Titers to Pertussis Toxin by Time Point and Treatment Group - Maternal Per Protocol Population

Figure 49: Reverse Cumulative Distribution of Breast Milk IgA Antibody Titers to Filamentous Hemagglutinin by Time Point and Treatment Group - Maternal Intent-to-Treat Population

Figure 50: Reverse Cumulative Distribution of Breast Milk IgA Antibody Titers to Filamentous Hemagglutinin by Time Point and Treatment Group - Maternal Per Protocol Population

Figure 51: Reverse Cumulative Distribution of Breast Milk IgA Antibody Titers to Pertactin by Time Point and Treatment Group - Maternal Intent-to-Treat Population

Figure 52: Reverse Cumulative Distribution of Breast Milk IgA Antibody Titers to Pertactin by Time Point and Treatment Group - Maternal Per Protocol Population

Figure 53: Reverse Cumulative Distribution of Breast Milk IgA Antibody Titers to Tetanus by Time Point and Treatment Group - Maternal Intent-to-Treat Population

Figure 54: Reverse Cumulative Distribution of Breast Milk IgA Antibody Titers to Tetanus by Time Point and Treatment Group - Maternal Per Protocol Population

Figure 57: Serum IgG Antibody Titers to Pertussis Toxin Over Time by Treatment Group - Infant Intent-to-Treat Population

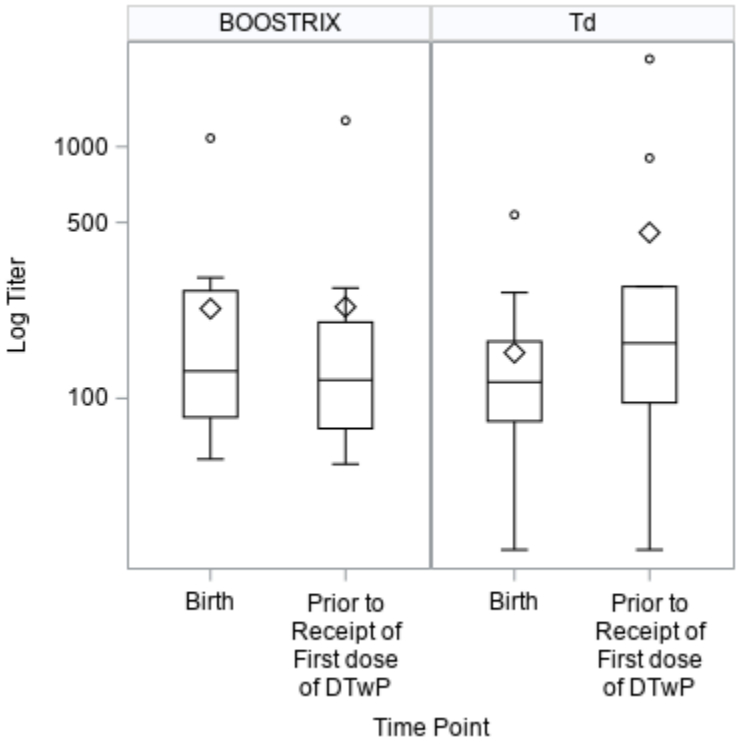

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Figure 58: Serum IgG Antibody Titers to Pertussis Toxin Over Time by Treatment Group - Infant Per Protocol Population

Figure 59: Serum IgG Antibody Titers to Filamentous Hemagglutinin Over Time by Treatment Group - Infant Intent-to-Treat Population

Figure 60: Serum IgG Antibody Titers to Filamentous Hemagglutinin Over Time by Treatment Group - Infant Per Protocol Population

Figure 61: Serum IgG Antibody Titers to Pertactin Over Time by Treatment Group - Infant Intent-to-Treat Population

Figure 62: Serum IgG Antibody Titers to Pertactin Over Time by Treatment Group - Infant Per Protocol Population

Figure 63: Serum IgG Antibody Titers to Tetanus Over Time by Treatment Group - Infant Intent-to-Treat Population

Figure 64: Serum IgG Antibody Titers to Tetanus Over Time by Treatment Group - Infant Per Protocol Population

Figure 65: Serum IgG Antibody Titers to Diphtheria Over Time by Treatment Group - Infant Intent-to-Treat Population

Figure 66: Serum IgG Antibody Titers to Diphtheria Over Time by Treatment Group - Infant Per Protocol Population

Figure 67: DTwP Antibody Titers to Pertussis Toxin Over Time by Treatment Group - Infant Intent-to-Treat Population

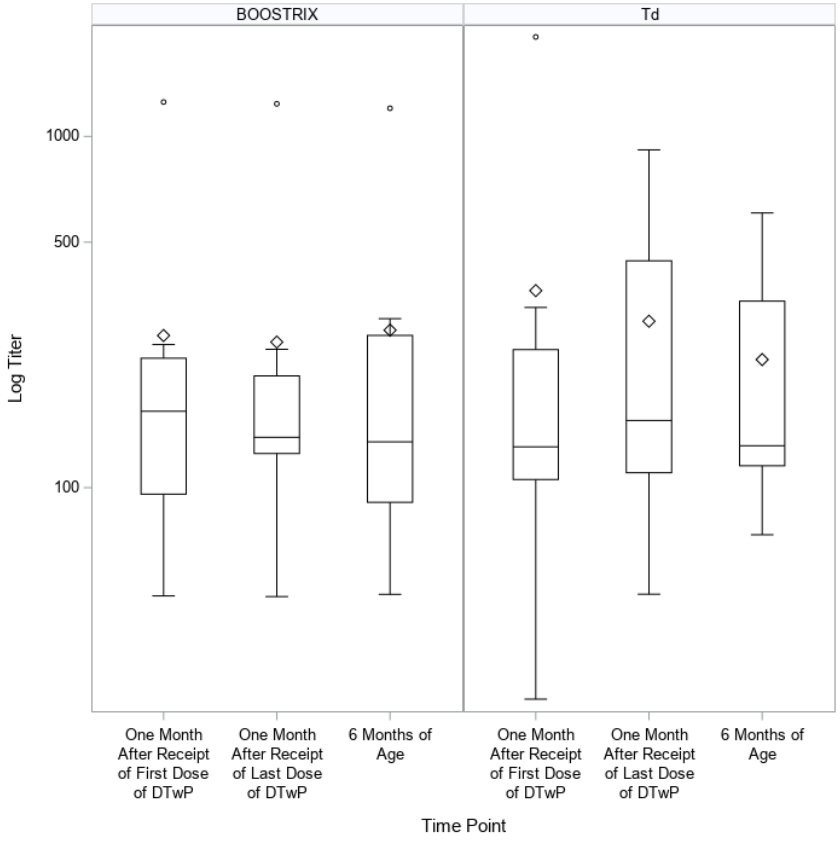

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Figure 68: DTwP Antibody Titers to Pertussis Toxin Over Time by Treatment Group - Infant Per Protocol Population

Figure 69: DTwP Antibody Titers to Filamentous Hemagglutinin Over Time by Treatment Group - Infant Intent-to-Treat Population

Figure 70: DTwP Antibody Titers to Filamentous Hemagglutinin Over Time by Treatment Group - Infant Per Protocol Population

Figure 71: DTwP Antibody Titers to Pertactin Over Time by Treatment Group - Infant Intent-to-Treat Population

Figure 72: DTwP Antibody Titers to Pertactin Over Time by Treatment Group - Infant Per Protocol Population

Figure 73: DTwP Antibody Titers to Fimbriae 2 Over Time by Treatment Group - Infant Intent-to-Treat Population

Figure 74: DTwP Antibody Titers to Fimbriae 2 Over Time by Treatment Group - Infant Per Protocol Population

Figure 75: DTwP Antibody Titers to Fimbriae 3 Over Time by Treatment Group - Infant Intent-to-Treat Population

Figure 81: Serum IgG Antibody Titers to Pertussis Toxin Over Time by Treatment Group - Maternal Intent-to-Treat Population

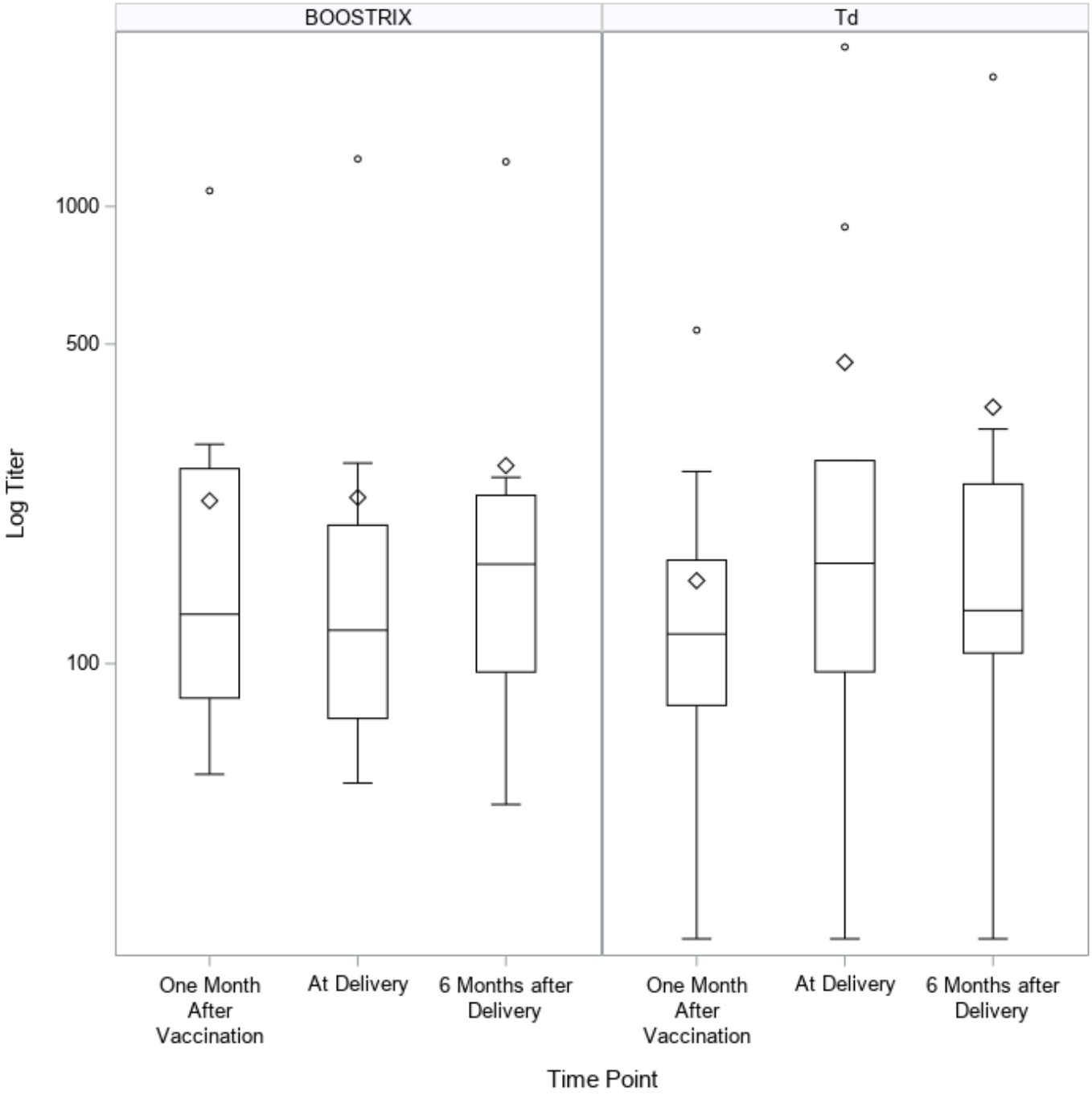

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Figure 82: Serum IgG Antibody Titers to Pertussis Toxin Over Time by Treatment Group - Maternal Per Protocol Population

Figure 83: Serum IgG Antibody Titers to Filamentous Hemagglutinin Over Time by Treatment Group - Maternal Intent-to-Treat Population

Figure 84: Serum IgG Antibody Titers to Filamentous Hemagglutinin Over Time by Treatment Group - Maternal Per Protocol Population

Figure 85: Serum IgG Antibody Titers to Pertactin Over Time by Treatment Group - Maternal Intent-to-Treat Population

Figure 86: Serum IgG Antibody Titers to Pertactin Over Time by Treatment Group - Maternal Per Protocol Population

Figure 87: Serum IgG Antibody Titers to Tetanus Over Time by Treatment Group - Maternal Intent-to-Treat Population

Figure 88: Serum IgG Antibody Titers to Tetanus Over Time by Treatment Group - Maternal Per Protocol Population

Figure 89: Serum IgG Antibody Titers to Diphtheria Over Time by Treatment Group - Maternal Intent-to-Treat Population

Figure 90: Serum IgG Antibody Titers to Diphtheria Over Time by Treatment Group - Maternal Per Protocol Population

Figure 91: Breast Milk IgG Antibody Titers to Pertussis Toxin Over Time by Treatment Group - Maternal Intent-to-Treat Population

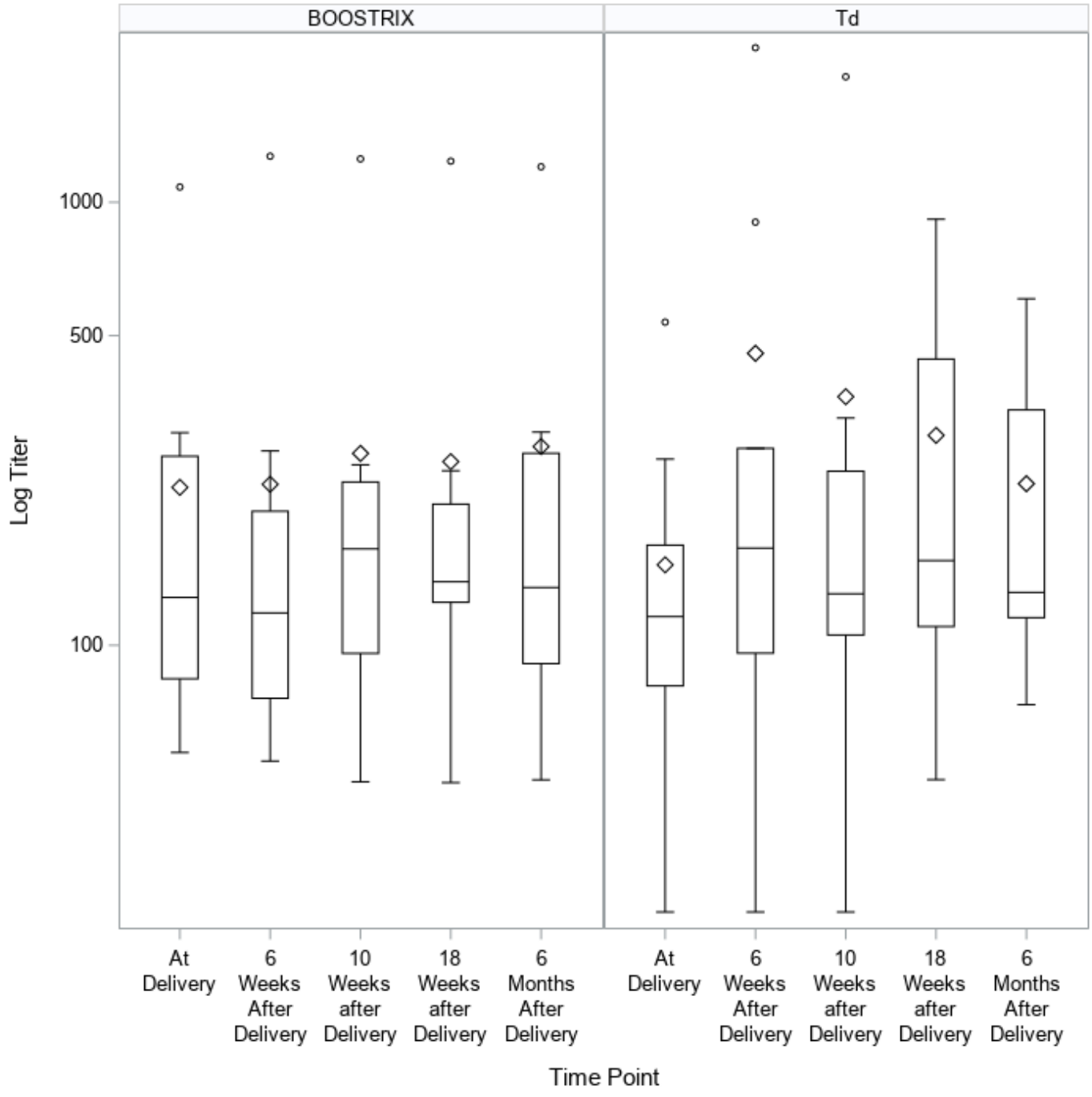

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Figure 111: GMC and 95% Confidence Interval of Serum IgG Antibody Titers to Pertussis Toxin Over Time by Treatment Group - Infant Intent-to-Treat Population

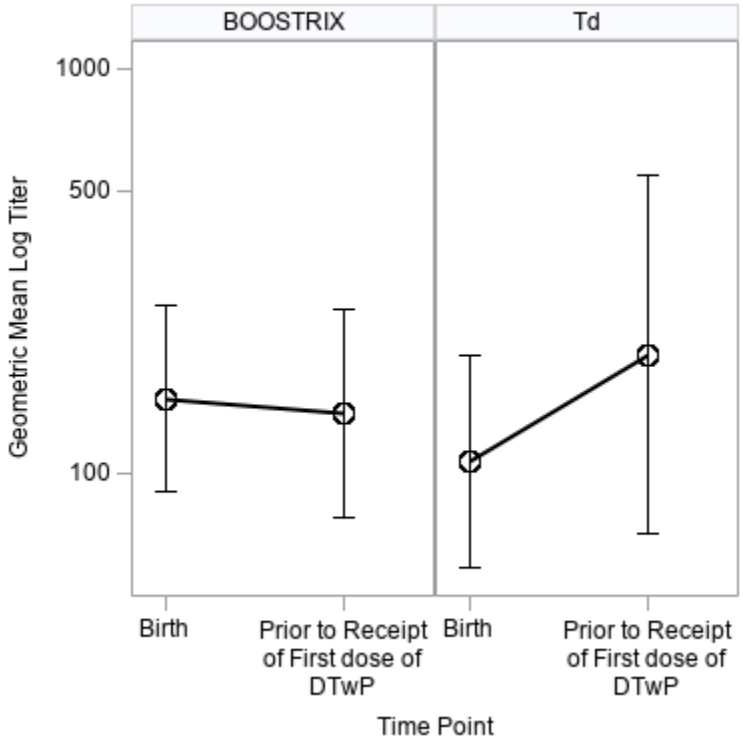

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Figure 112: GMC and 95% Confidence Interval of Serum IgG Antibody Titers to Pertussis Toxin Over Time by Treatment Group - Infant Per Protocol Population

Figure 113: GMC and 95% Confidence Interval of Serum IgG Antibody Titers to Filamentous Hemagglutinin Over Time by Treatment Group – Infant Intent-to-Treat Population

Figure 114: GMC and 95% Confidence Interval of Serum IgG Antibody Titers to Filamentous Hemagglutinin Over Time by Treatment Group - Infant Per Protocol Population

Figure 115: GMC and 95% Confidence Interval of Serum IgG Antibody Titers to Pertactin Over Time by Treatment Group -Infant Intent-to-Treat Population

Figure 116: GMC and 95% Confidence Interval of Serum IgG Antibody Titers to Pertactin Over Time by Treatment Group - Infant Per Protocol Population

Figure 117: GMC and 95% Confidence Interval of Serum IgG Antibody Titers to Tetanus Over Time by Treatment Group - Infant Intent-to-Treat Population

Figure 118: GMC and 95% Confidence Interval of Serum IgG Antibody Titers to Tetanus Over Time by Treatment Group - Infant Per Protocol Population

Figure 119: GMC and 95% Confidence Interval of Serum IgG Antibody Titers to Diphtheria Over Time by Treatment Group - Infant Intent-to-Treat Population

Figure 120: GMC and 95% Confidence Interval of Serum IgG Antibody Titers to Diphtheria Over Time by Treatment Group - Infant Per Protocol Population

Figure 121: GMC and 95% Confidence Interval of DTwP Antibody Titers to Pertussis Toxin Over Time by Treatment Group - Infant Intent-to-Treat Population

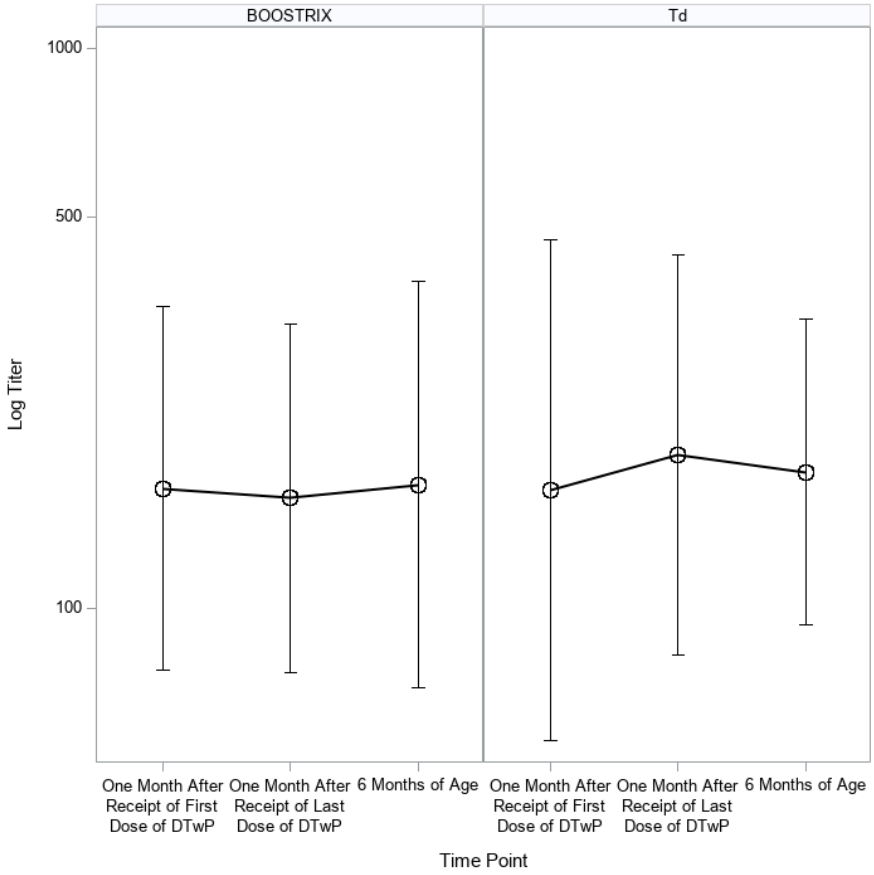

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Figure 122: GMC and 95% Confidence Interval of DTwP Antibody Titers to Pertussis Toxin Over Time by Treatment Group - Infant Per Protocol Population

Figure 123: GMC and 95% Confidence Interval of DTwP Antibody Titers to Filamentous Hemagglutinin Over Time by Treatment Group - Infant Intent-to-Treat Population

Figure 124: GMC and 95% Confidence Interval of DTwP Antibody Titers to Filamentous Hemagglutinin Over Time by Treatment Group - Infant Per Protocol Population

Figure 125: GMC and 95% Confidence Interval of DTwP Antibody Titers to Pertactin Over Time by Treatment Group - Infant Intent-to-Treat Population

Figure 126: GMC and 95% Confidence Interval of DTwP Antibody Titers to Pertactin Over Time by Treatment Group - Infant Per Protocol Population

Figure 127: GMC and 95% Confidence Interval of DTwP Antibody Titers to Fimbriae 2 Over Time by Treatment Group - Infant Intent-to-Treat Population

Figure 128: GMC and 95% Confidence Interval of DTwP Antibody Titers to Fimbriae 2 Over Time by Treatment Group - Infant Per Protocol Population

Figure 129: GMC and 95% Confidence Interval of DTwP Antibody Titers to Fimbriae 3 Over Time by Treatment Group - Infant Intent-to-Treat Population

Figure 130: GMC and 95% Confidence Interval of DTwP Antibody Titers to Fimbriae 3 Over Time by Treatment Group - Infant Per Protocol Population

Figure 131: GMC and 95% Confidence Interval of DTwP Antibody Titers to Tetanus Over Time by Treatment Group - Infant Intent-to-Treat Population

Figure 132: GMC and 95% Confidence Interval of DTwP Antibody Titers to Tetanus Over Time by Treatment Group - Infant Per Protocol Population

Figure 133: GMC and 95% Confidence Interval of DTwP Antibody Titers to Diphtheria Over Time Point Treatment Group - Infant Intent-to-Treat Population

Figure 134: GMC and 95% Confidence Interval of DTwP Antibody Titers to Diphtheria Over Time Point Treatment Group - Infant Per Protocol Population

Figure 135: GMC and 95% Confidence Interval of Serum IgG Antibody Titers to Pertussis Toxin Over Time by Treatment Group - Maternal Intent-to-Treat Population

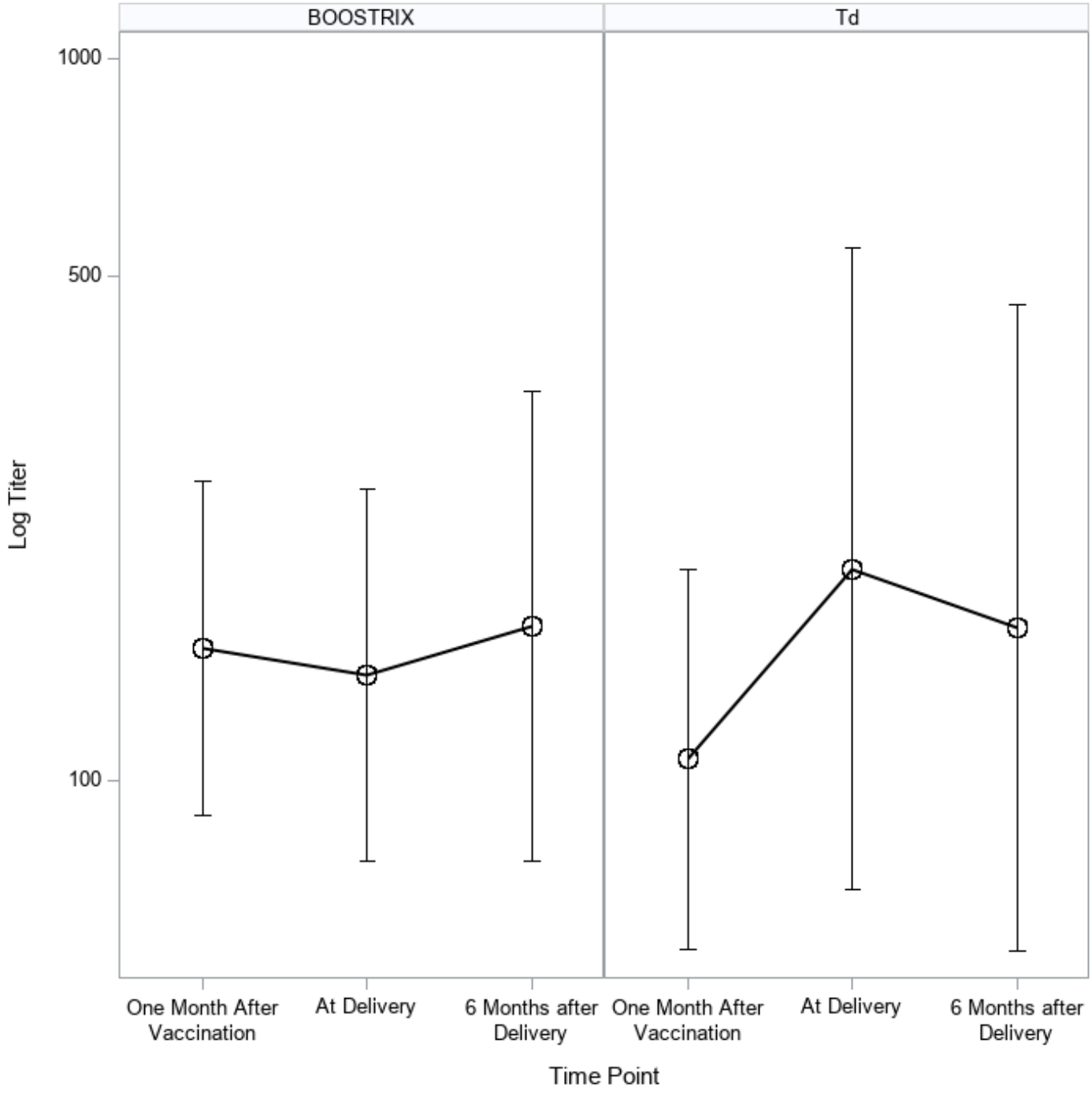

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Figure 136: GMC and 95% Confidence Interval of Serum IgG Antibody Titers to Pertussis Toxin Over Time by Treatment Group - Maternal Per Protocol Population

Figure 137: GMC and 95% Confidence Interval of Serum IgG Antibody Titers to Filamentous Hemagglutinin Over Time by Treatment Group - Maternal Intent-to-Treat Population

Figure 138: GMC and 95% Confidence Interval of Serum IgG Antibody Titers to Filamentous Hemagglutinin Over Time by Treatment Group - Maternal Per Protocol Population

Figure 139: GMC and 95% Confidence Interval of Serum IgG Antibody Titers to Pertactin Over Time by Treatment Group - Maternal Intent-to-Treat Population

Figure 140: GMC and 95% Confidence Interval of Serum IgG Antibody Titers to Pertactin Over Time by Treatment Group - Maternal Per Protocol Population

Figure 141: GMC and 95% Confidence Interval of Serum IgG Antibody Titers to Tetanus Over Time by Treatment Group - Maternal Intent-to-Treat Population

Figure 142: GMC and 95% Confidence Interval of Serum IgG Antibody Titers to Tetanus Over Time by Treatment Group - Maternal Per Protocol Population

Figure 143: GMC and 95% Confidence Interval of Serum IgG Antibody Titers to Diphtheria Over Time by Treatment Group - Maternal Intent-to-Treat Population

Figure 144: GMC and 95% Confidence Interval of Serum IgG Antibody Titers to Diphtheria Over Time by Treatment Group - Maternal Per Protocol Population

Figure 145: GMC and 95% Confidence Interval of Breast Milk IgG Antibody Titers to Pertussis Toxin Over Time by Treatment Group - Maternal Intent-to-Treat Population

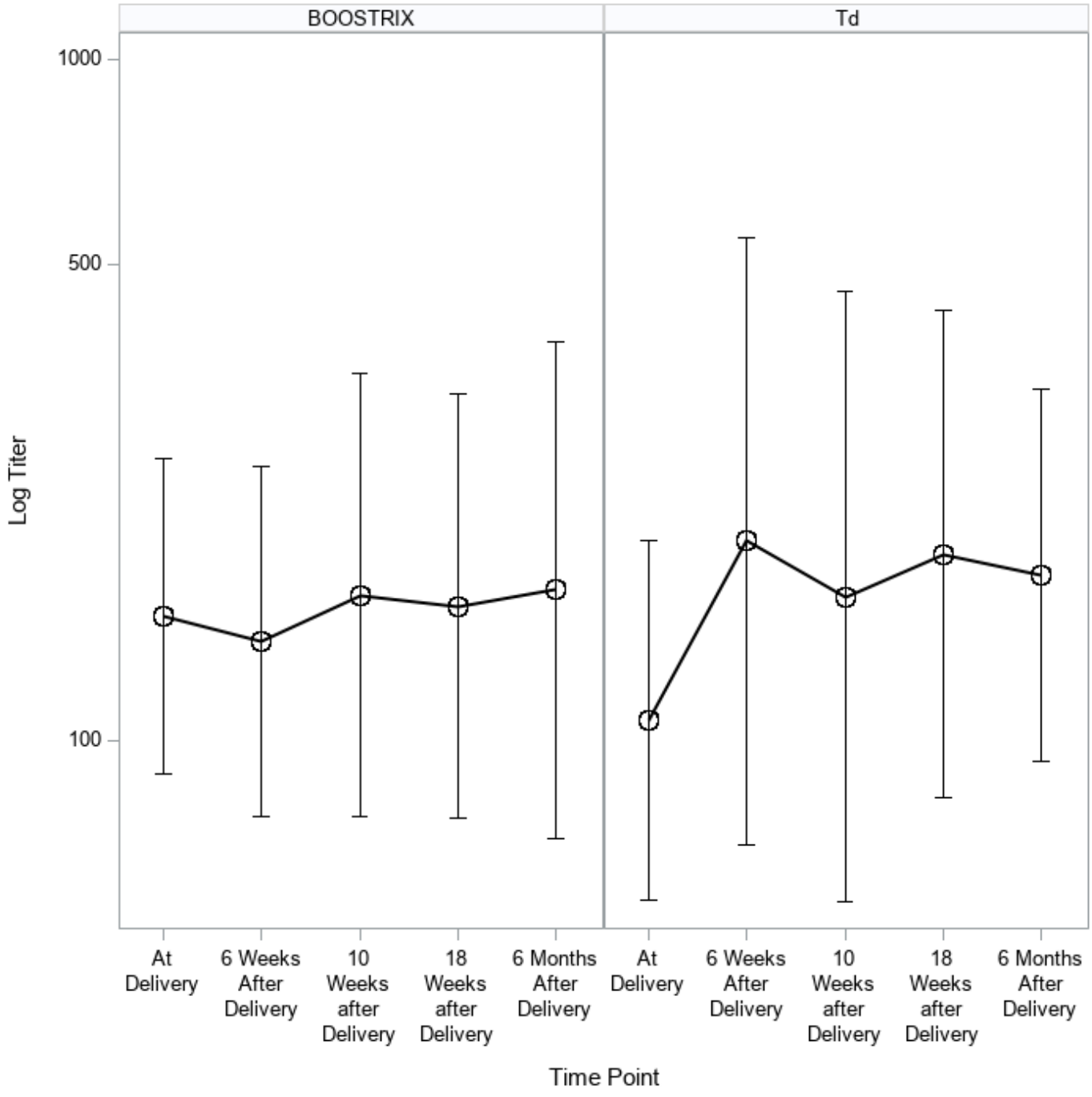

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Figure 146: GMC and 95% Confidence Interval of Breast Milk IgG Antibody Titers to Pertussis Toxin Over Time by Treatment Group - Maternal Per Protocol Population

Figure 147: GMC and 95% Confidence Interval of Breast Milk IgG Antibody Titers to Filamentous Hemagglutinin Over Time by Treatment Group - Maternal Intent-to-Treat Population

Figure 148: GMC and 95% Confidence Interval of Breast Milk IgG Antibody Titers to Filamentous Hemagglutinin Over Time by Treatment Group - Maternal Per Protocol Population

Figure 149: GMC and 95% Confidence Interval of Breast Milk IgG Antibody Titers to Pertactin Over Time by Treatment Group - Maternal Intent-to-Treat Population

Figure 150: GMC and 95% Confidence Interval of Breast Milk IgG Antibody Titers to Pertactin Over Time by Treatment Group - Maternal Per Protocol Population

Figure 151: GMC and 95% Confidence Interval of Breast Milk IgG Antibody Titers to Tetanus Over Time by Treatment Group - Maternal Intent-to-Treat Population

Figure 152: GMC and 95% Confidence Interval of Breast Milk IgG Antibody Titers to Tetanus Over Time by Treatment Group - Maternal Per Protocol Population

Figure 153: GMC and 95% Confidence Interval of Breast Milk IgG Antibody Titers to Diphtheria Over Time by Treatment Group - Maternal Intent-to-Treat Population

Figure 154: GMC and 95% Confidence Interval of Breast Milk IgG Antibody Titers to Diphtheria Over Time by Treatment Group - Maternal Per Protocol Population

Figure 155: GMC and 95% Confidence Interval of Breast Milk IgA Antibody Titers to Pertussis Toxin Over Time by Treatment Group - Maternal Intent-to-Treat Population

Figure 156: GMC and 95% Confidence Interval of Breast Milk IgA Antibody Titers to Pertussis Toxin Over Time by Treatment Group - Maternal Per Protocol Population

Figure 157: GMC and 95% Confidence Interval of Breast Milk IgA Antibody Titers to Filamentous Hemagglutinin Over Time by Treatment Group - Maternal Intent-to-Treat Population

Figure 158: GMC and 95% Confidence Interval of Breast Milk IgA Antibody Titers to Filamentous Hemagglutinin Over Time by Treatment Group - Maternal Per Protocol Population

Figure 159: GMC and 95% Confidence Interval of Breast Milk IgA Antibody Titers to Pertactin Over Time by Treatment Group - Maternal Intent-to-Treat Population

Figure 160: GMC and 95% Confidence Interval of Breast Milk IgA Antibody Titers to Pertactin Over Time by Treatment Group - Maternal Per Protocol Population

Figure 161: GMC and 95% Confidence Interval of Breast Milk IgA Antibody Titers to Tetanus Over Time by Treatment Group - Maternal Intent-to-Treat Population

Figure 165: Infant Cytokines Over Time by Treatment Group – IFN-γ, IL-10, IL-12p70, and IL-12/IL-23p40 – Infant Intent-to-Treat Population

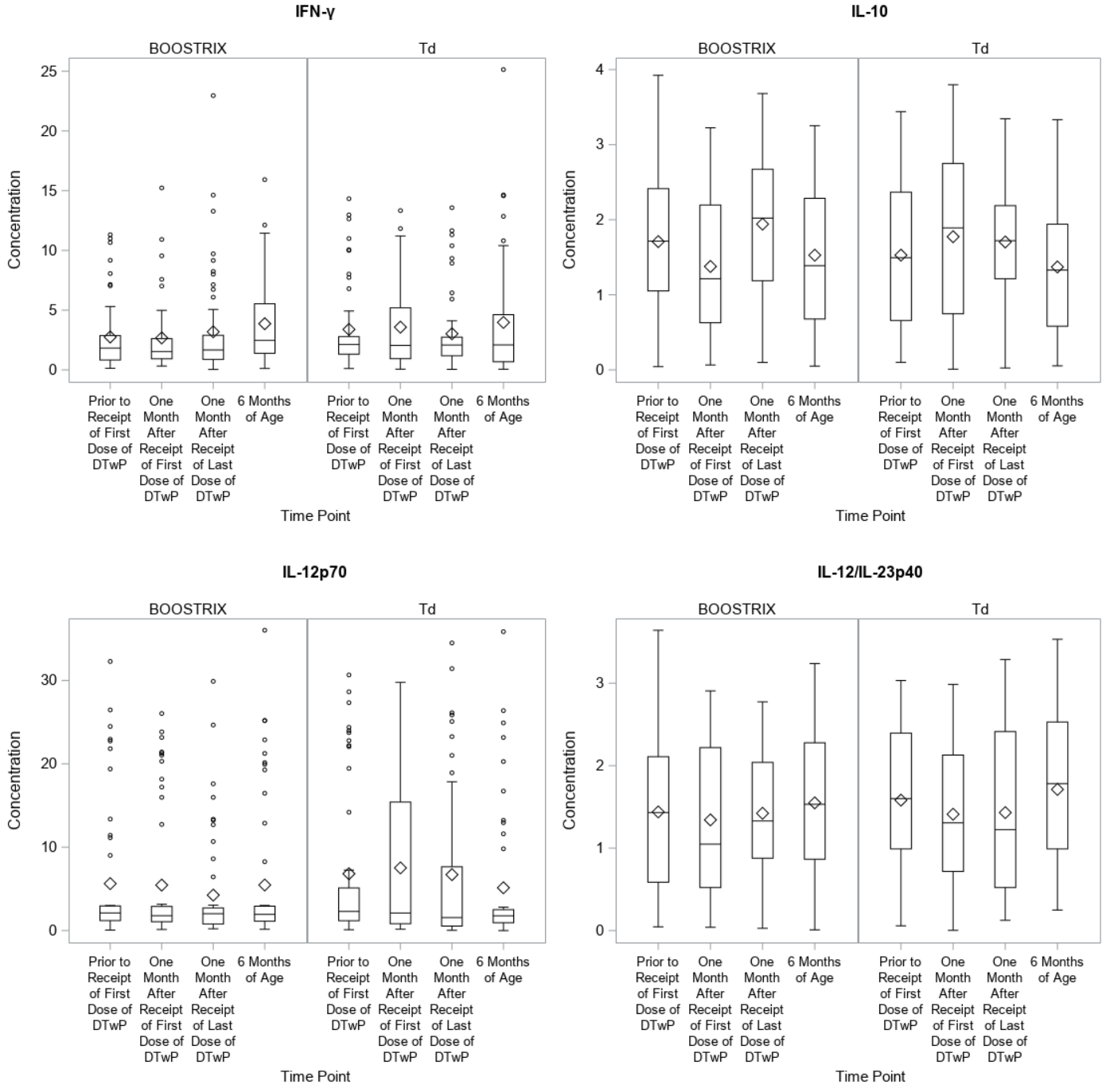

Figure 166: Infant Cytokines Over Time by Treatment Group – IL-13, IL-15, IL-16, and IL-17A -- Infant Intent-to-Treat Population

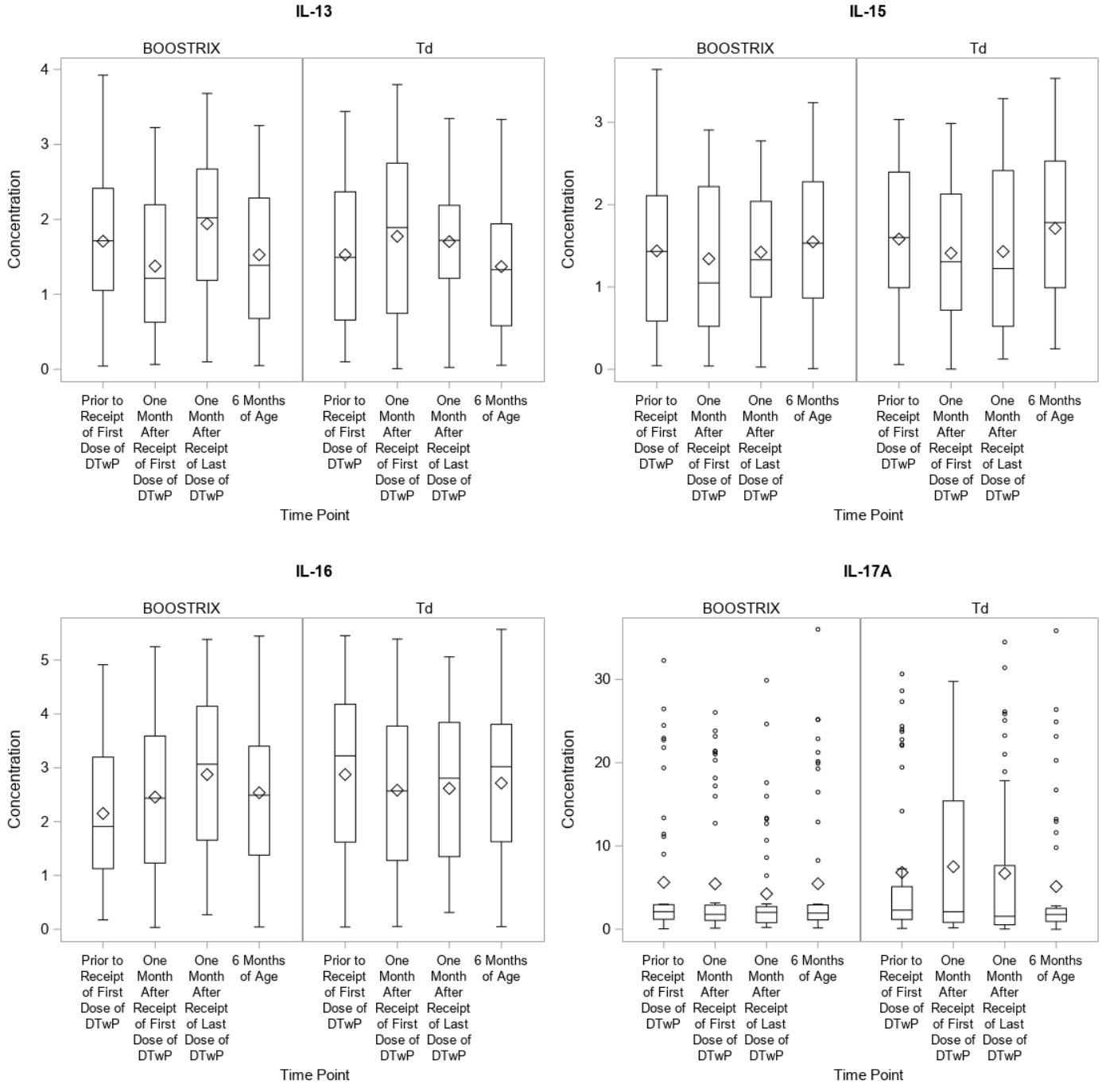

Figure 167: Infant Cytokines Over Time by Treatment Group -- IL-1α, IL-1β, IL-2, and IL-4 -- Infant Intent-to-Treat Population

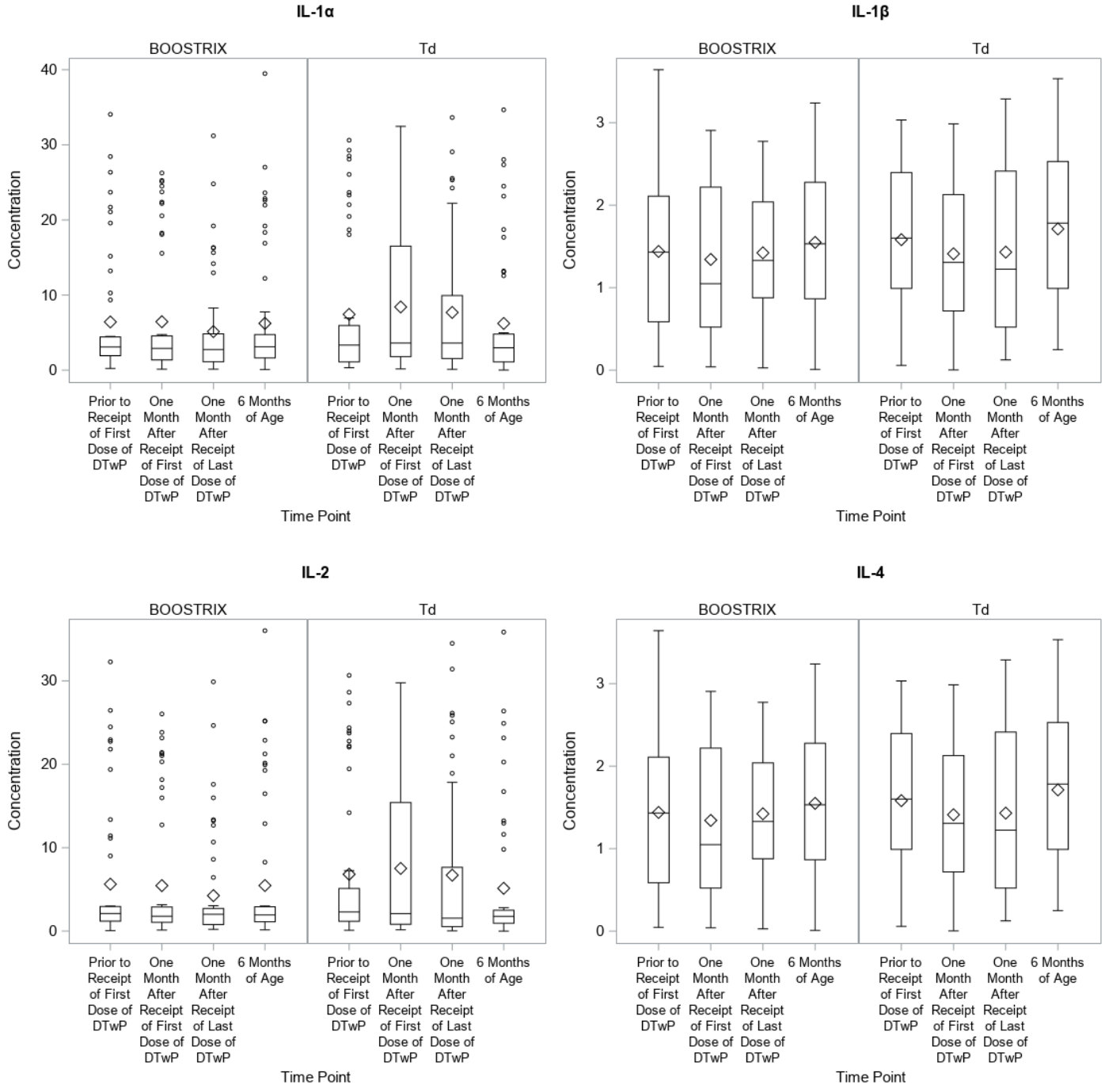

Figure 168: Infant Cytokines Over Time by Treatment Group – IL-5, IL-6, IL-7, and IL-8 – Infant Intent-to-Treat Population

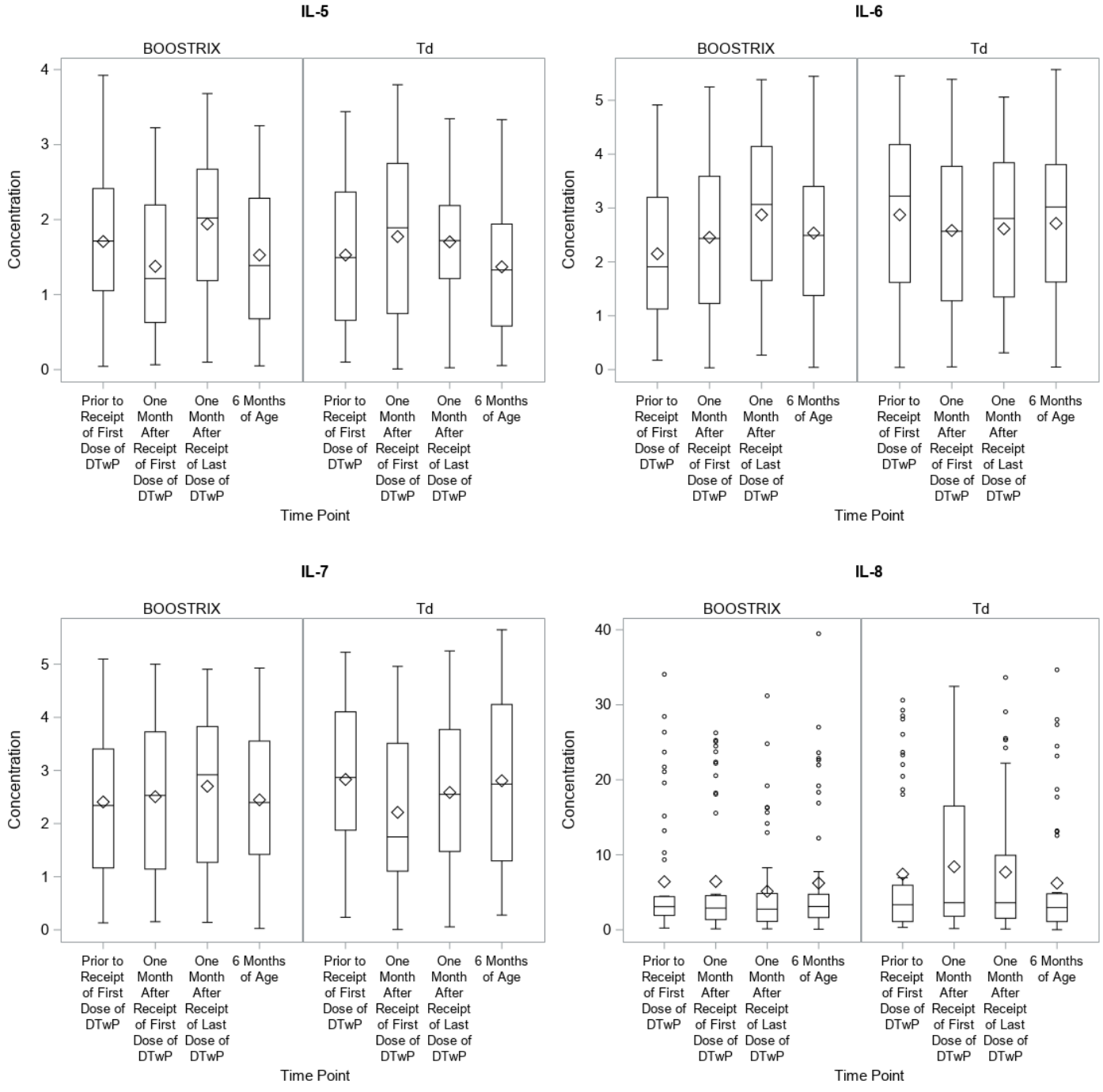

Figure 169: Infant Cytokines Over Time by Treatment Group – TNF- α, and TNF- β -- Infant Intent-to-Treat Population

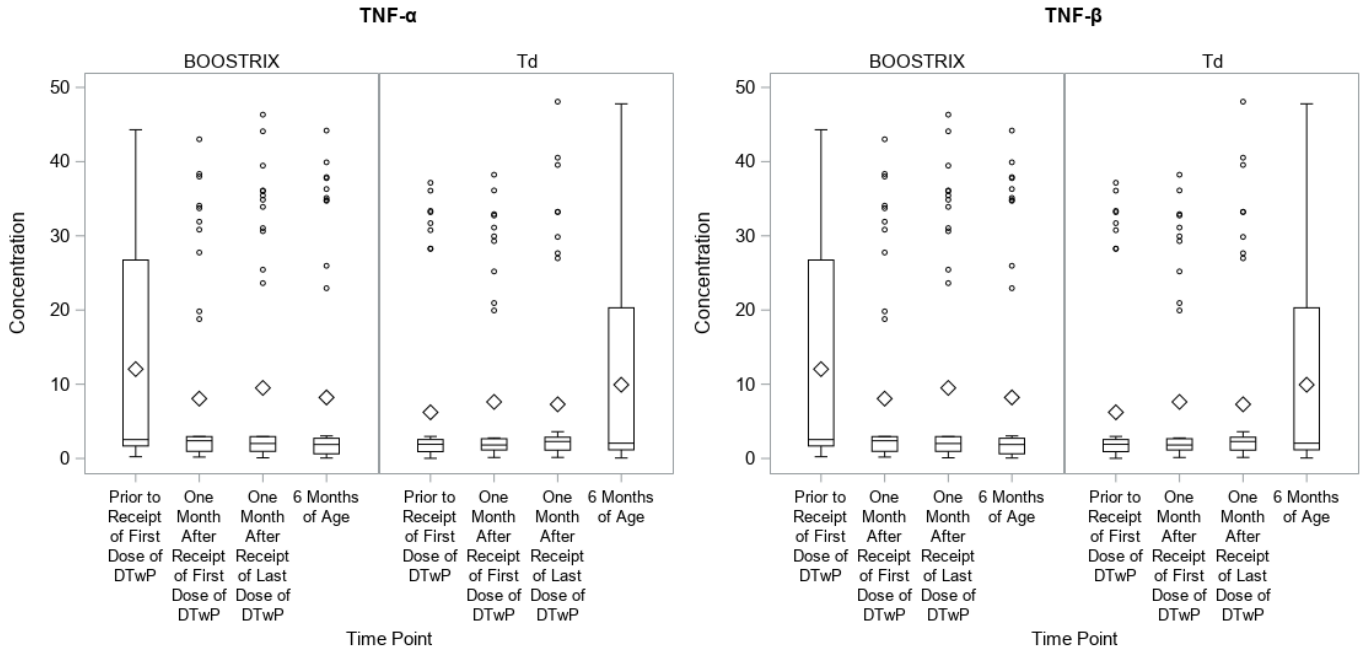

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Figure 170: Infant Cytokines Over Time by Treatment Group – IFN-γ, IL-10, IL-12p70, and IL-12/IL-23p40 – Infant Per Protocol Population

Figure 171: Infant Cytokines Over Time by Treatment Group – IL-13, IL-15, IL-16, and IL-17A -- Infant Per Protocol Population

Figure 172: Infant Cytokines Over Time by Treatment Group -- IL-1α, IL-1β, IL-2, and IL-4 --Infant Per Protocol Population

Figure 173: Infant Cytokines Over Time by Treatment Group – IL-5, IL-6, IL-7, and IL-8 – Infant Per Protocol Population

Figure 174: Infant Cytokines Over Time by Treatment Group – TNF- α, and TNF- β -- Infant Per Protocol Population

Figure 175: Maternal Cytokines Over Time by Treatment Group – IFN-γ, IL-10, IL-12p70, and IL-12/IL-23p40 – Maternal Intent-to-Treat Population

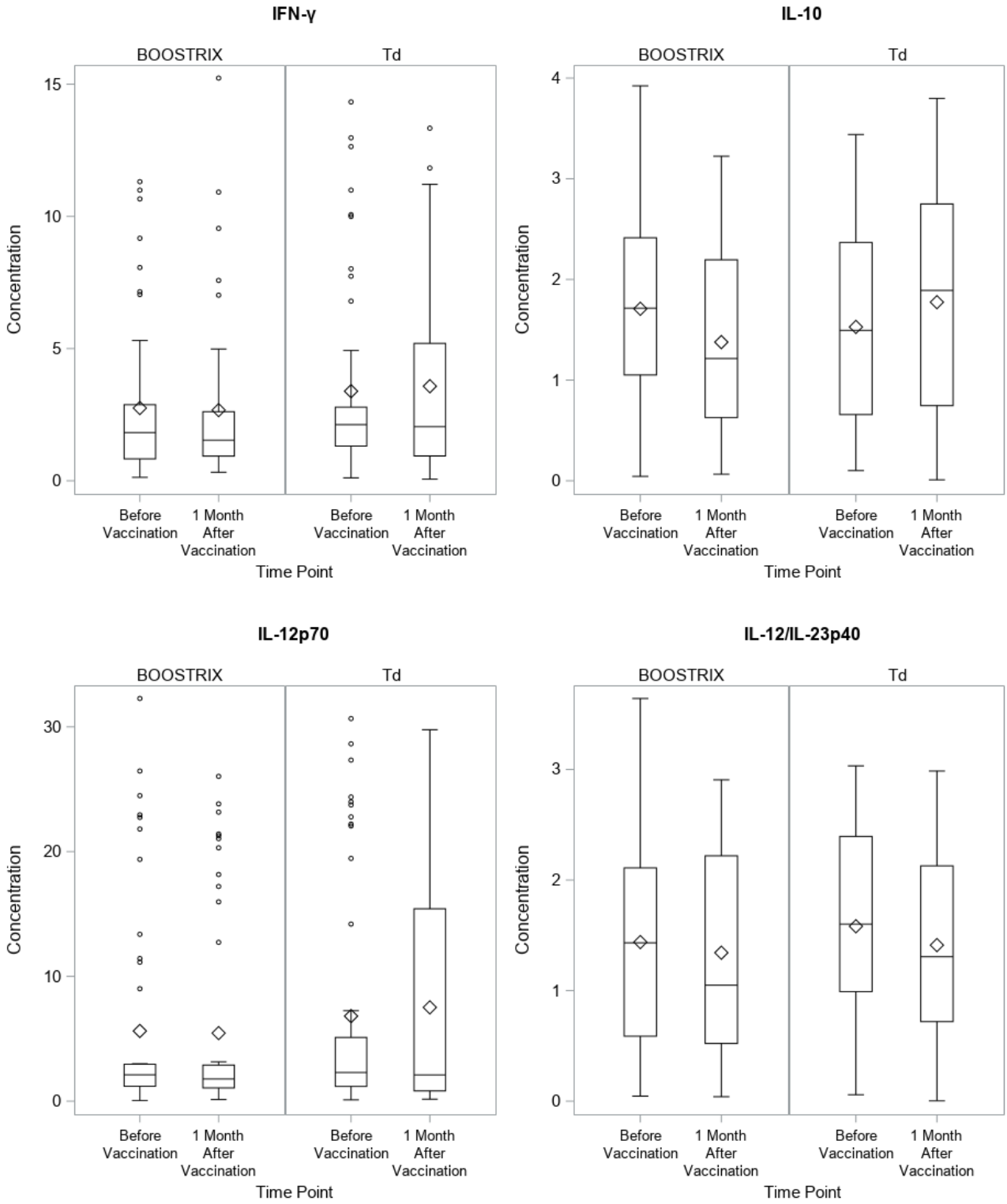


Figure 176: Maternal Cytokines Over Time by Treatment Group – IL-13, IL-15, IL-16, and IL-17A – Maternal Intent-to-Treat Population

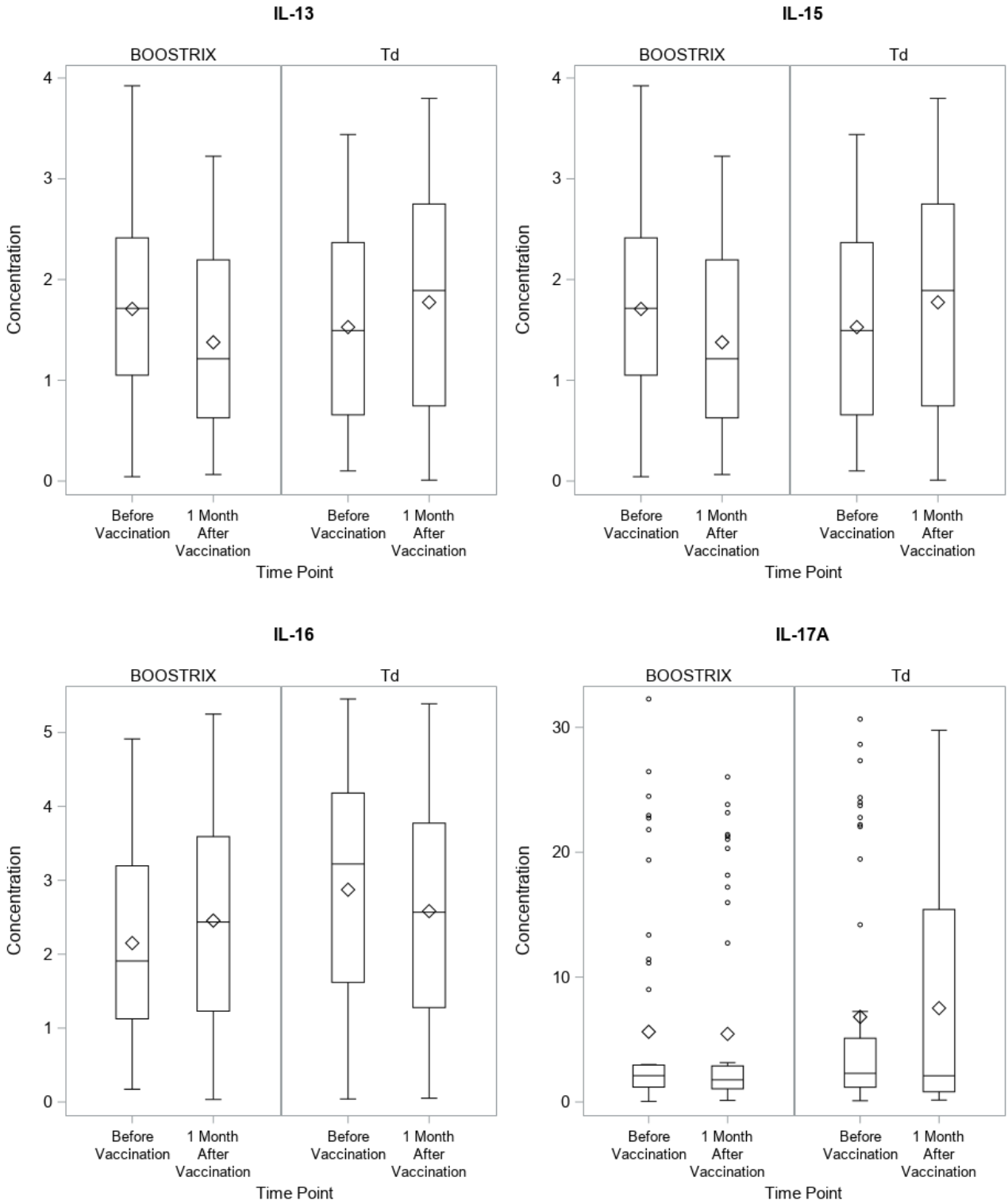


Figure 177: Maternal Cytokines Over Time by Treatment Group – IL-1α, IL-1β, IL-2, and IL-4 – Maternal Intent-to-Treat Population

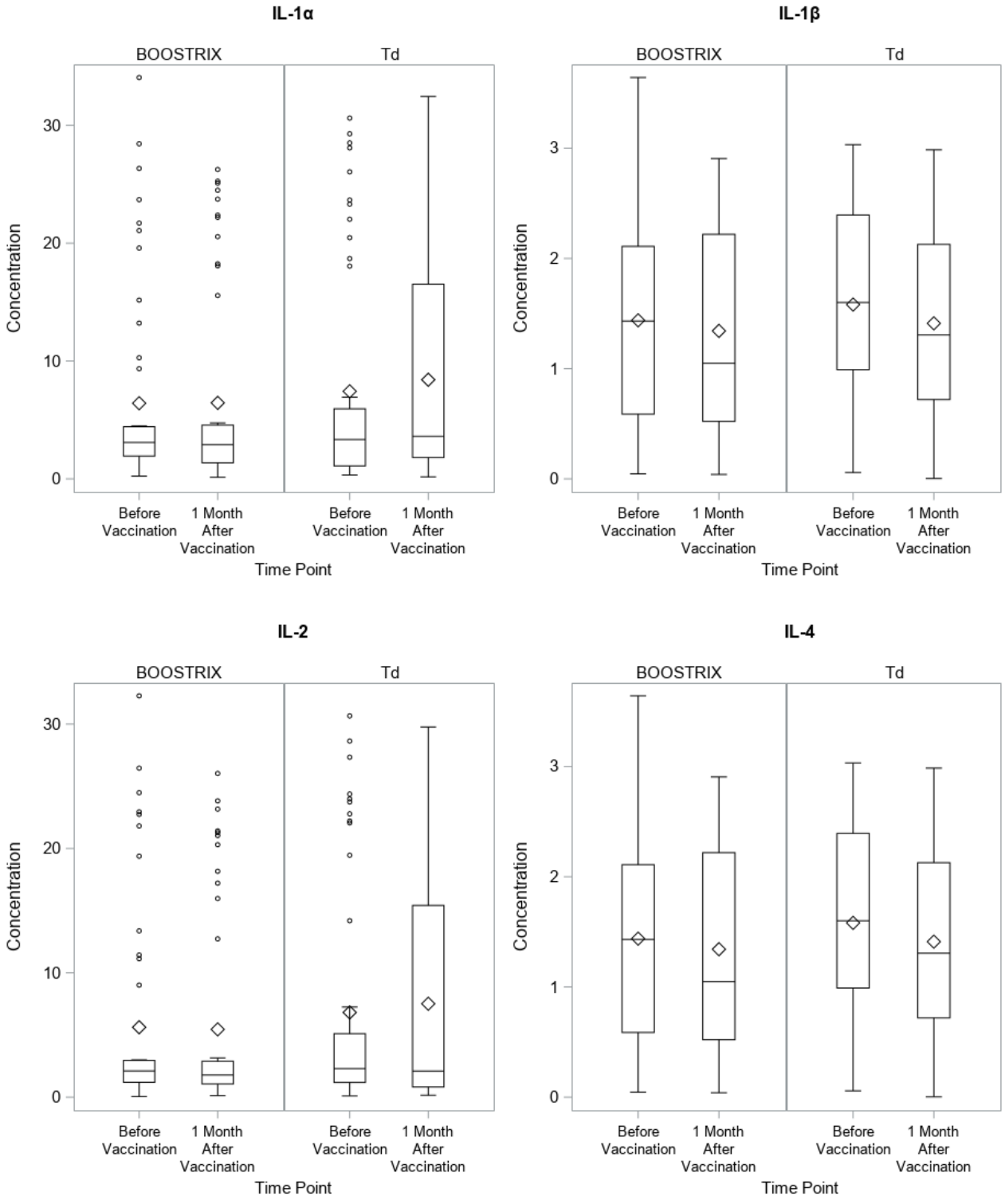


Figure 178: Maternal Cytokines Over Time by Treatment Group – IL-5, IL-6, IL-7, and IL-8 – Maternal Intent-to-Treat Population

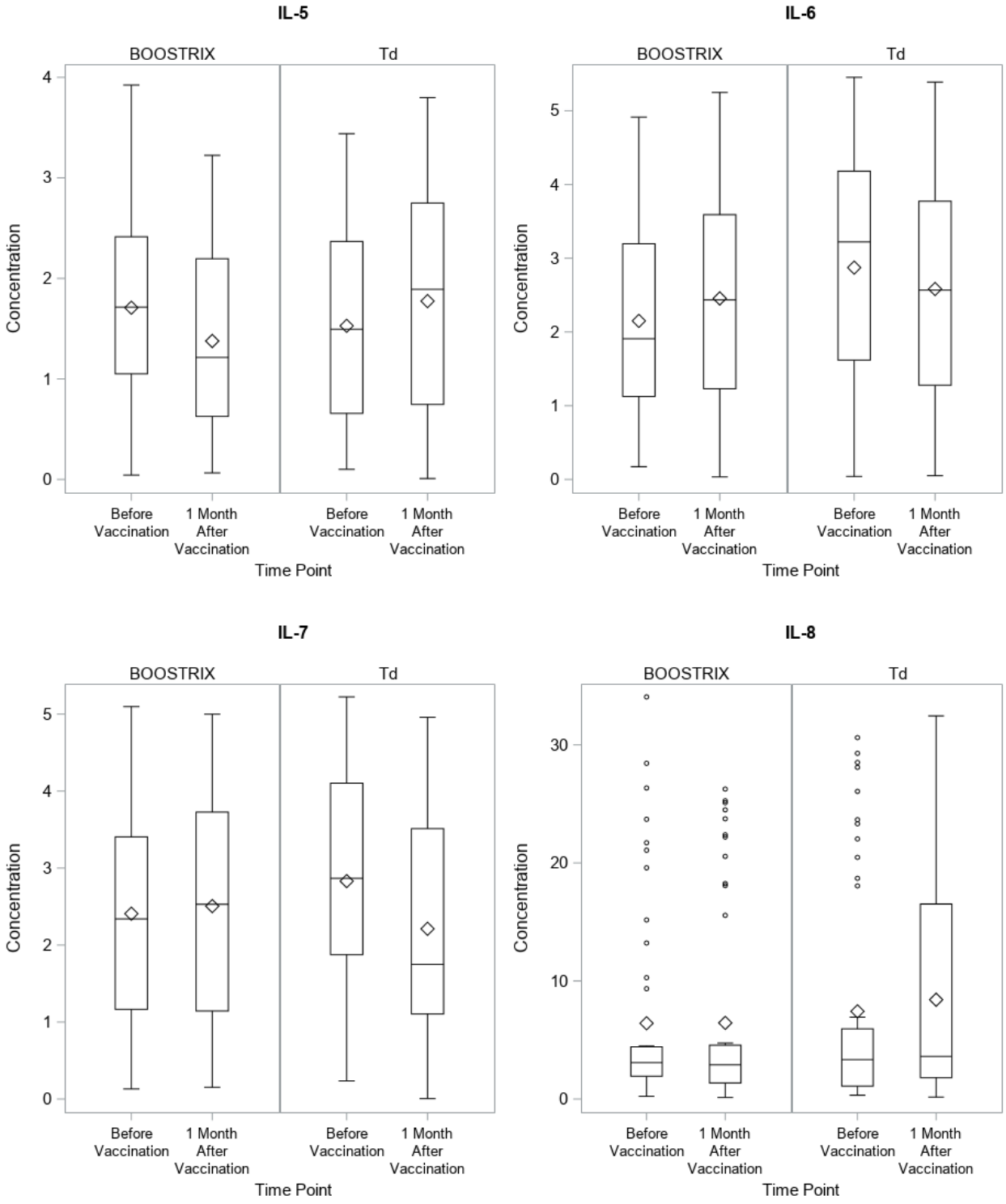
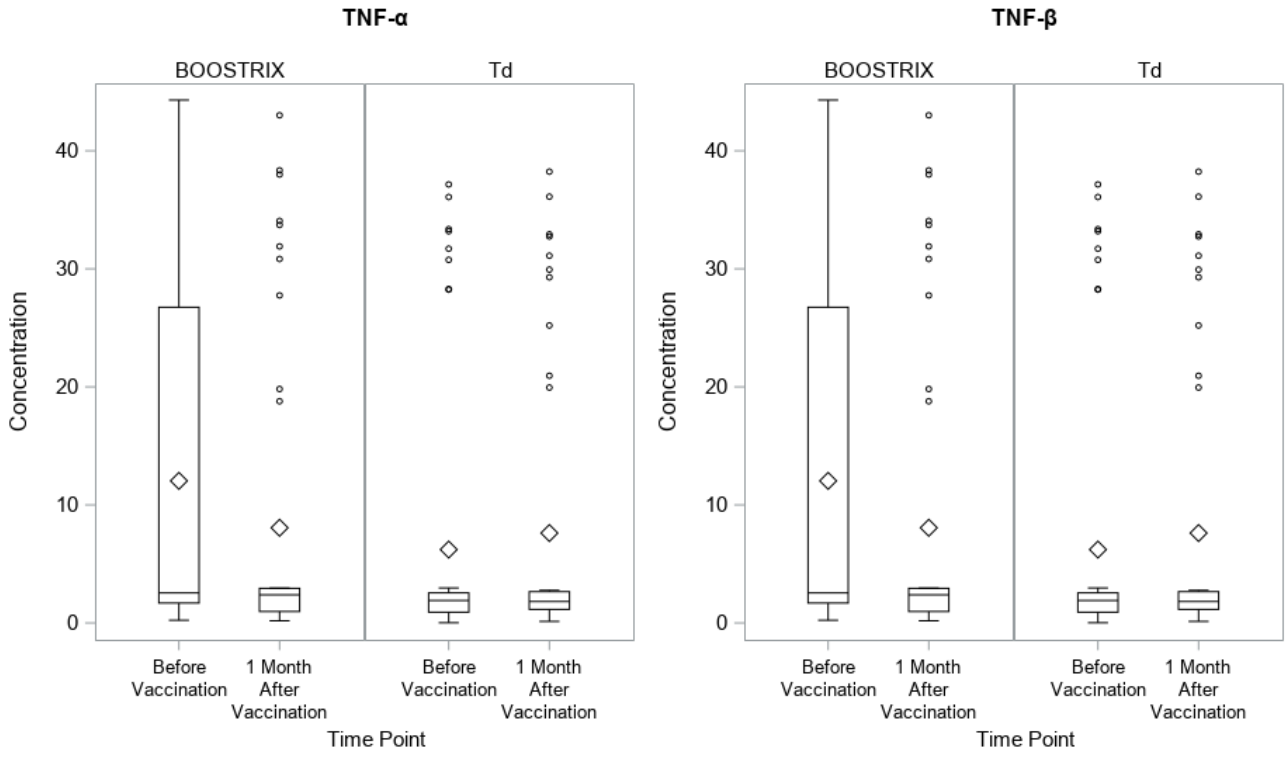


Figure 179: Maternal Cytokines Over Time by Treatment Group – TNF- α, and TNF- β – Maternal Intent-to-Treat Population



Figures with similar format:

Figure 180: Maternal Cytokines Over Time by Treatment Group – IFN-γ, IL-10, IL-12p70, and IL-12/IL-23p40 – Maternal Per Protocol Population

Figure 181: Maternal Cytokines Over Time by Treatment Group – IL-13, IL-15, IL-16, and IL-17A -- Maternal Per Protocol Population

Figure 182: Maternal Cytokines Over Time by Treatment Group -- IL-1α, IL-1β, IL-2, and IL-4 -- Maternal Per Protocol Population

Figure 183: Maternal Cytokines Over Time by Treatment Group – IL-5, IL-6, IL-7, and IL-8 – Maternal Per Protocol Population

Figure 184: Maternal Cytokines Over Time by Treatment Group – TNF- α, and TNF- β – Maternal Per Protocol Population

Figures with similar format:

Figure 185: GMC and 95% CI of Infant Cytokines Over Time by Treatment Group – IFN-γ, IL-10, IL-12p70, and IL-12/IL-23p40 – Infant Intent-to-Treat Population

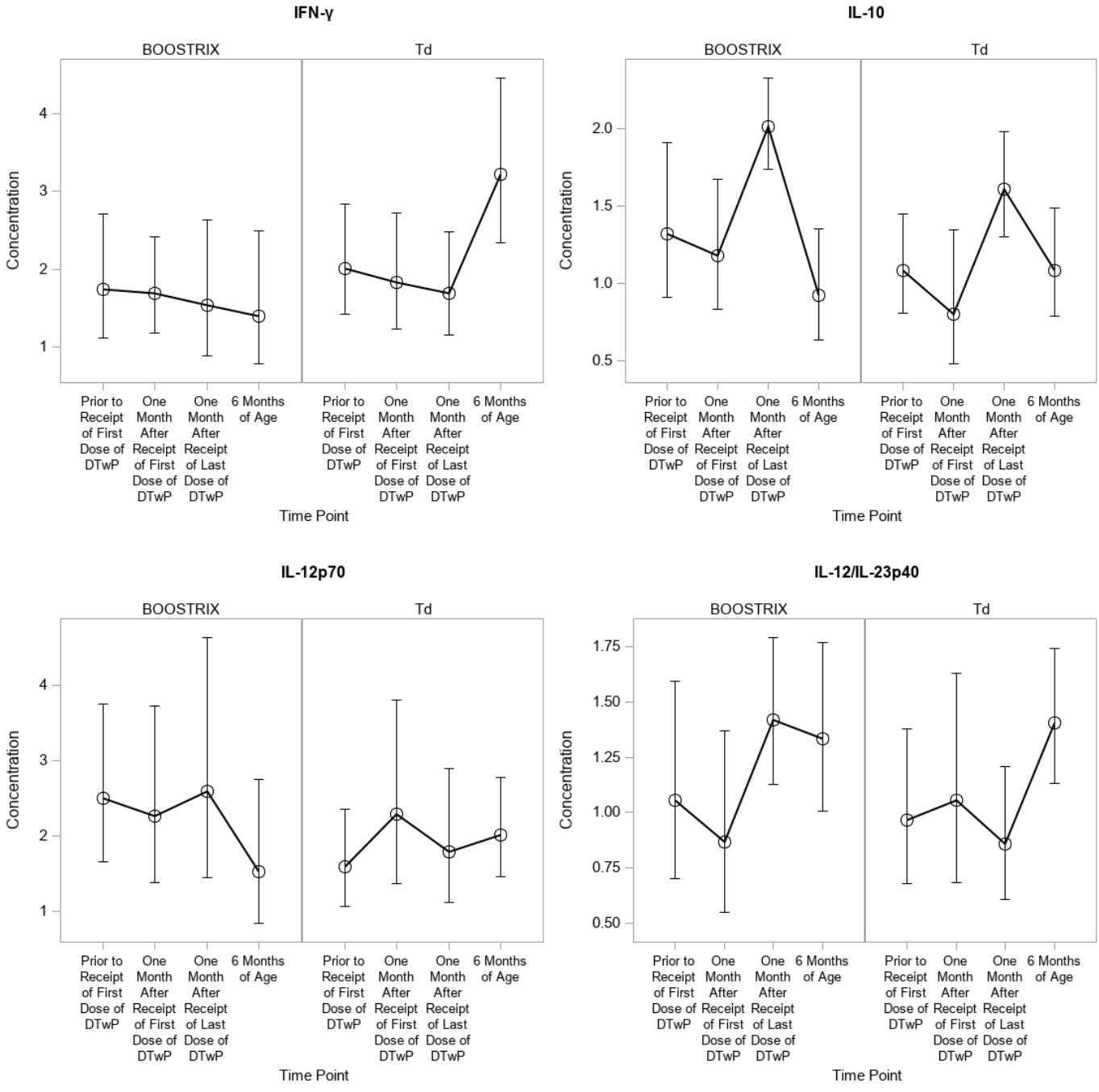


Figure 186: GMC and 95% CI of Infant Cytokines Over Time by Treatment Group – IL-13, IL-15, IL-16, and IL-17A -- Infant Intent-to-Treat Population

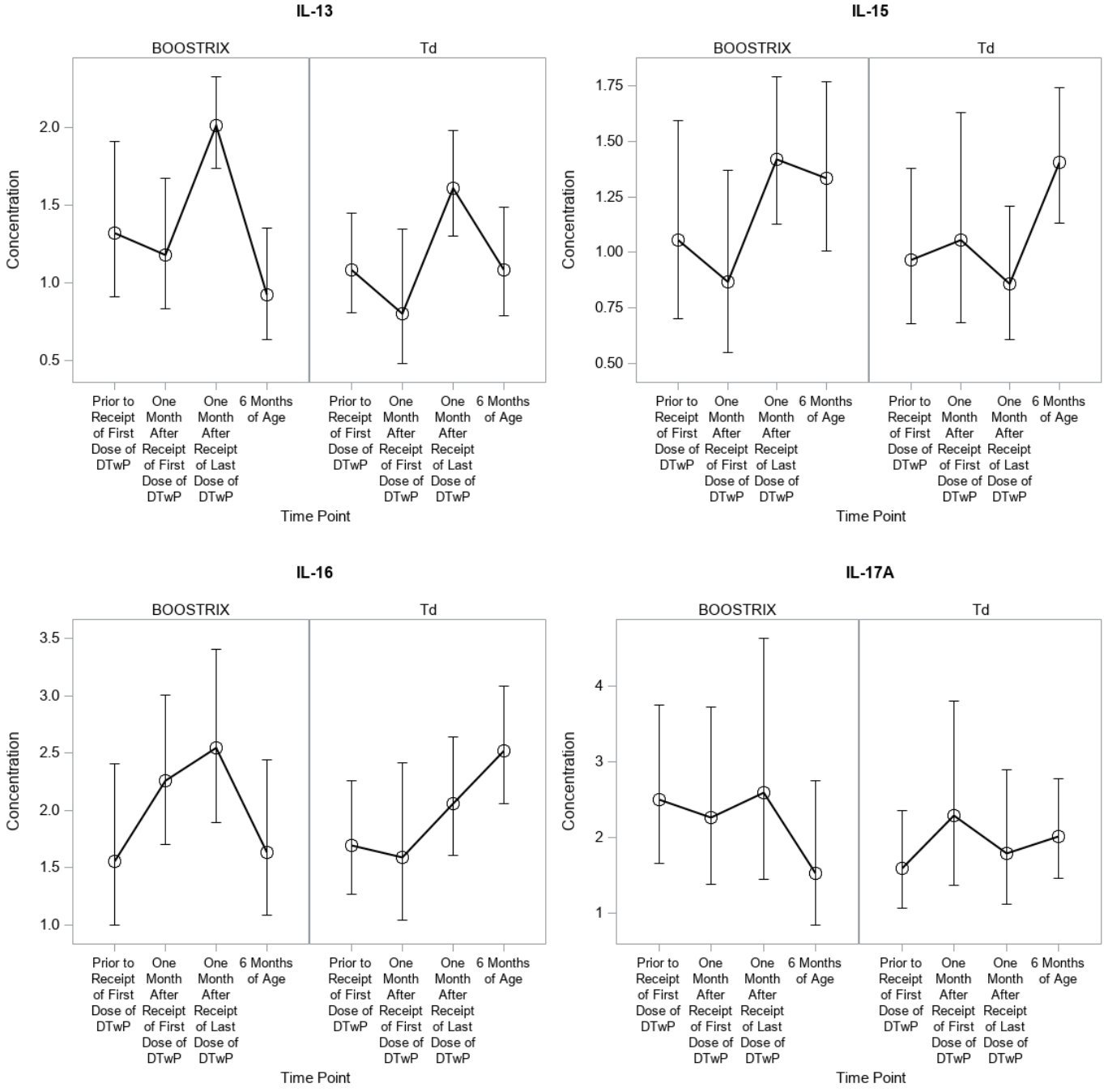


Figure 187: GMC and 95% CI of Infant Cytokines Over Time by Treatment Group -- IL-1α, IL-1β, IL-2, and IL-4 --Infant Intent-to-Treat Population

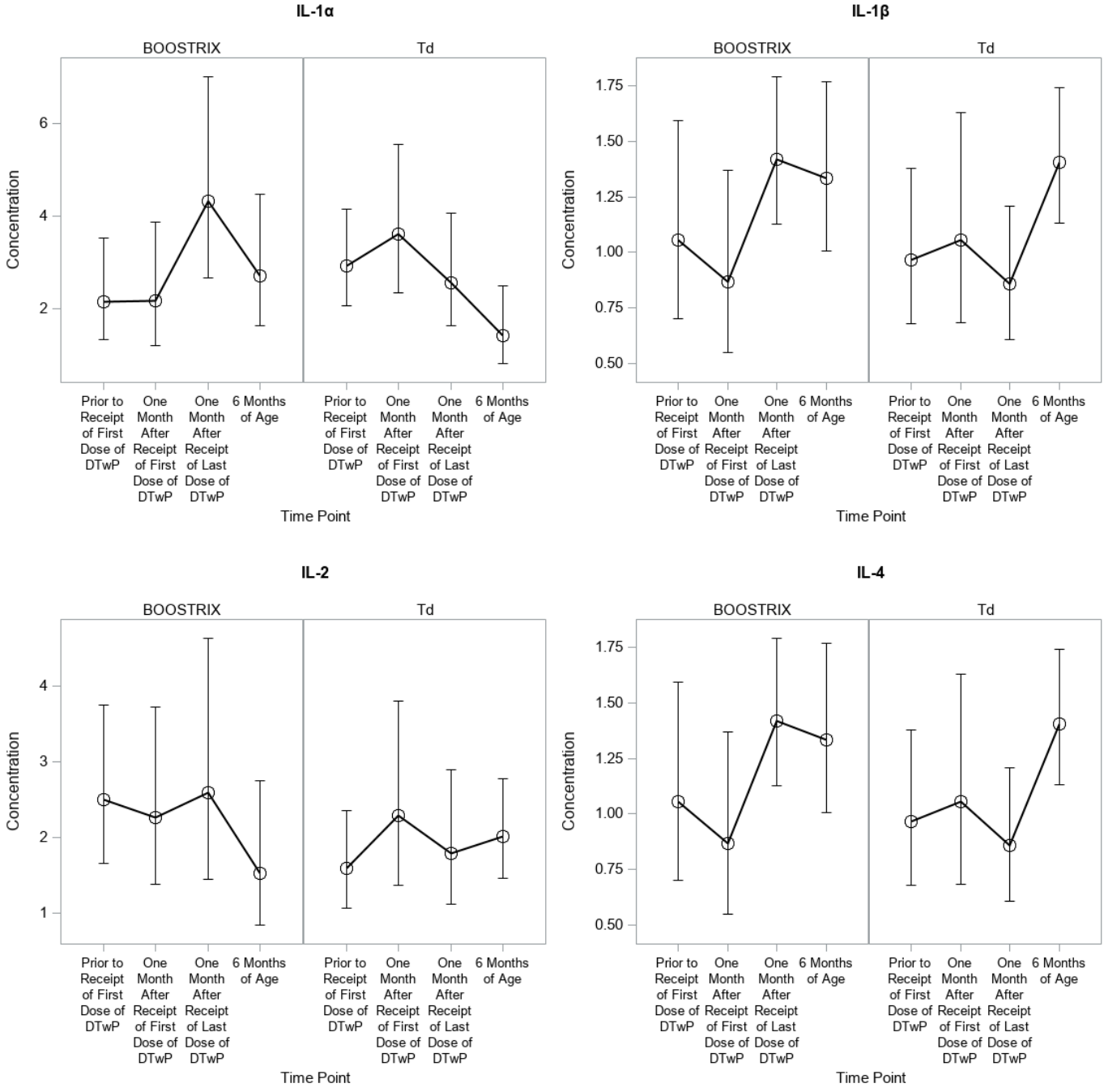


Figure 188: GMC and 95% CI of Infant Cytokines Over Time by Treatment Group – IL-5, IL-6, IL-7, and IL-8 – Infant Intent-to-Treat Population

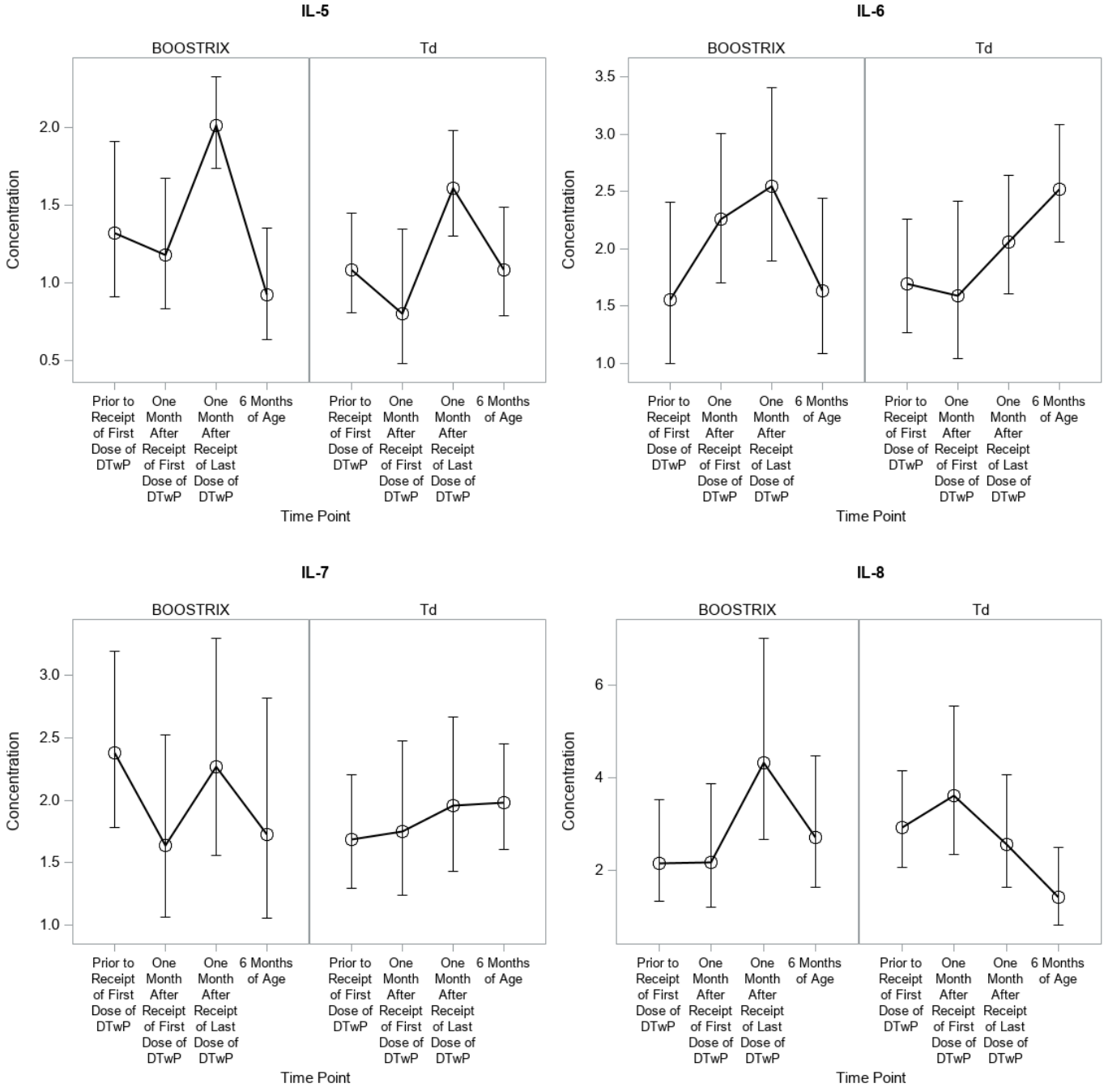
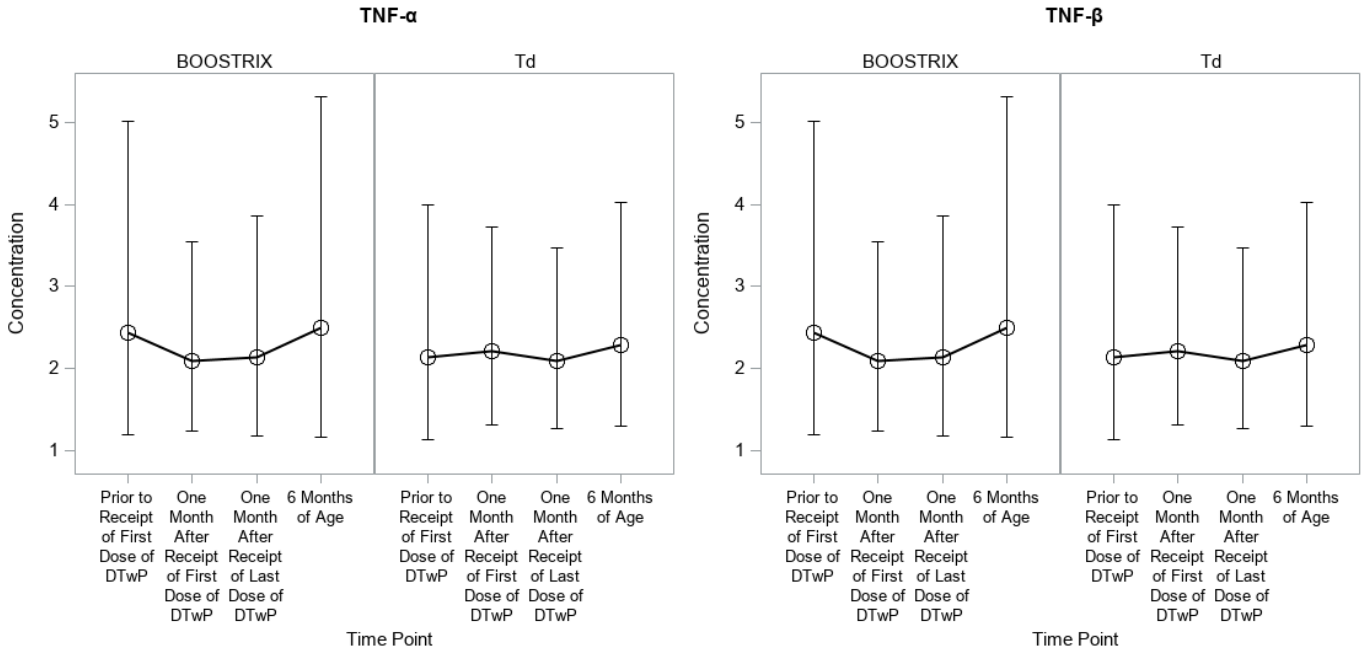


Figure 189: GMC and 95% CI of Infant Cytokines Over Time by Treatment Group –TNF- α, and TNF- β – Infant Intent-to-Treat Population



Figures with similar format:

Figure 190: GMC and 95% CI of Infant Cytokines Over Time by Treatment Group – IFN-γ, IL-10, IL-12p70, and IL-12/IL-23p40 – Infant Per Protocol Population

Figure 191: GMC and 95% CI of Infant Cytokines Over Time by Treatment Group – IL-13, IL-15, IL-16, and IL-17A -- Infant Per Protocol Population

Figure 192: GMC and 95% CI of Infant Cytokines Over Time by Treatment Group -- IL-1α, IL-1β, IL-2, and IL-4 --Infant Per Protocol Population

Figure 193: GMC and 95% CI of Infant Cytokines Over Time by Treatment Group – IL-5, IL-6, IL-7, and IL-8 – Infant Per Protocol Population

Figure 194: GMC and 95% CI of Infant Cytokines Over Time by Treatment Group – TNF- α, and TNF- β – Infant Per Protocol Population

Figure 195: GMC and 95% CI of Maternal Cytokines Over Time by Treatment Group – IFN-γ, IL-10, IL-12p70, and IL-12/IL-23p40 – Maternal Intent-to-Treat Population

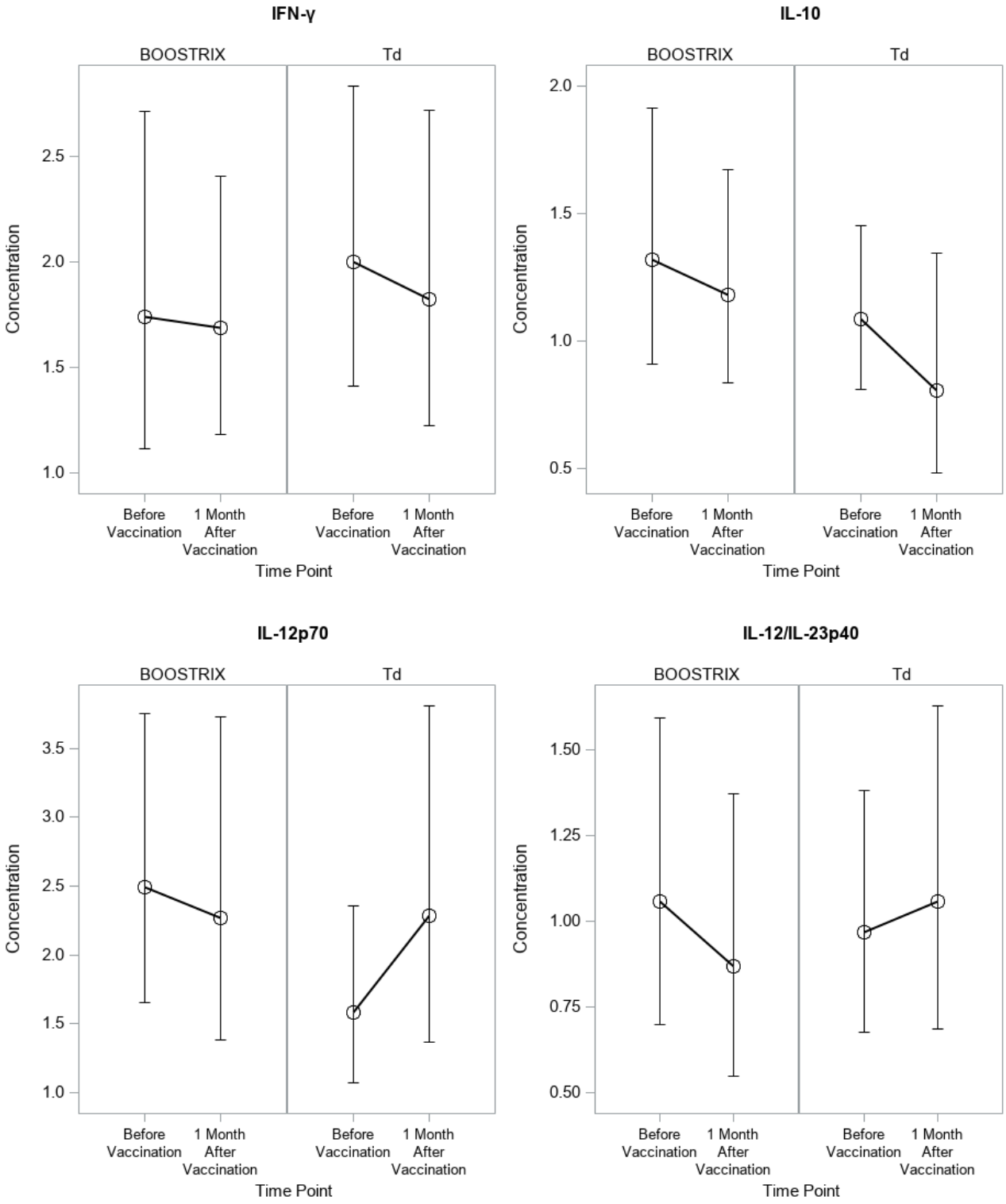


Figure 196: GMC and 95% CI of Maternal Cytokines Over Time by Treatment Group – IL-13, IL-15, IL-16, and IL-17A -- Maternal Intent-to-Treat Population

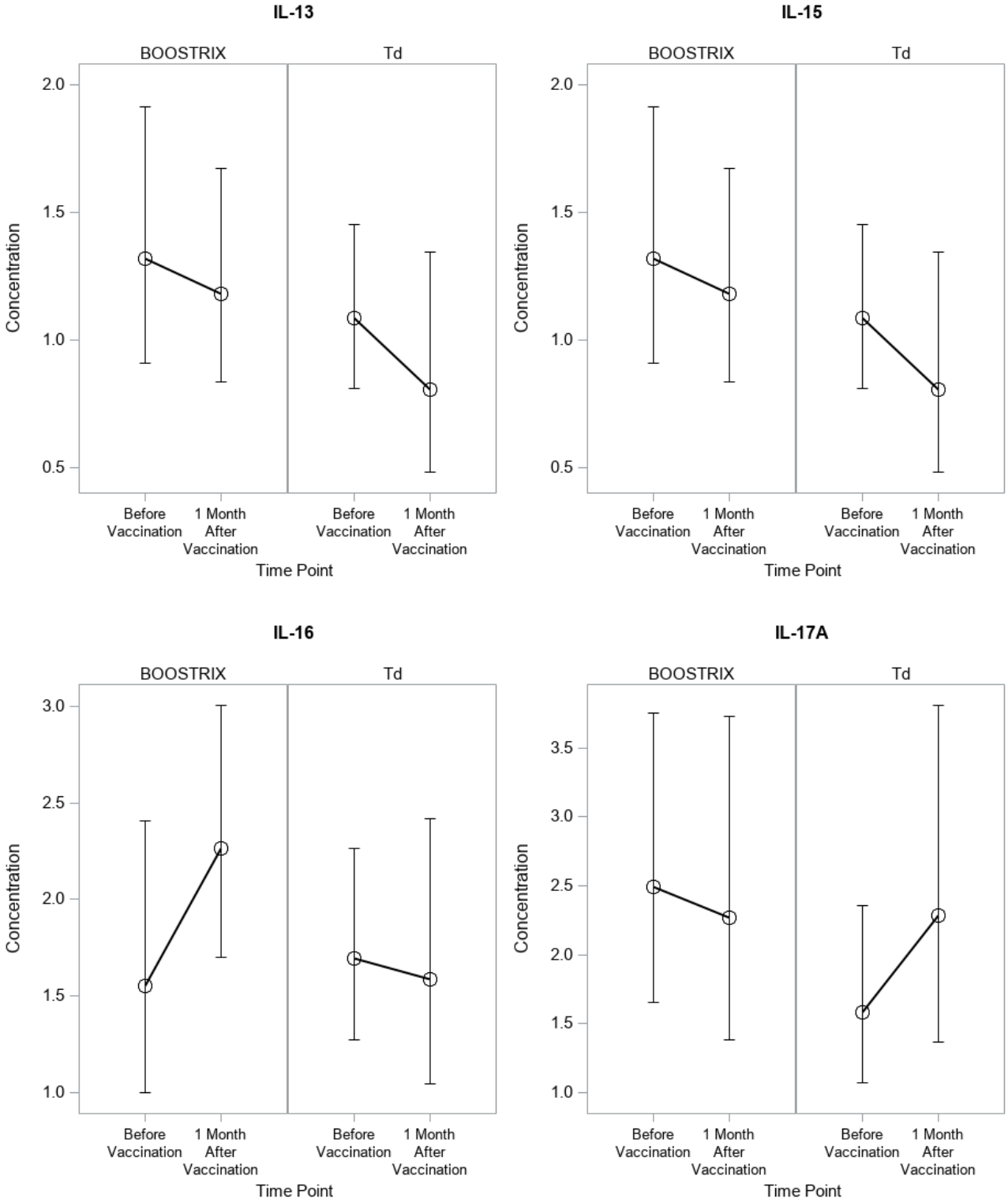


Figure 197: GMC and 95% CI of Maternal Cytokines Over Time by Treatment Group - IL-1α, IL-1β, IL-2, and IL-4 -- Maternal Intent-to-Treat Population

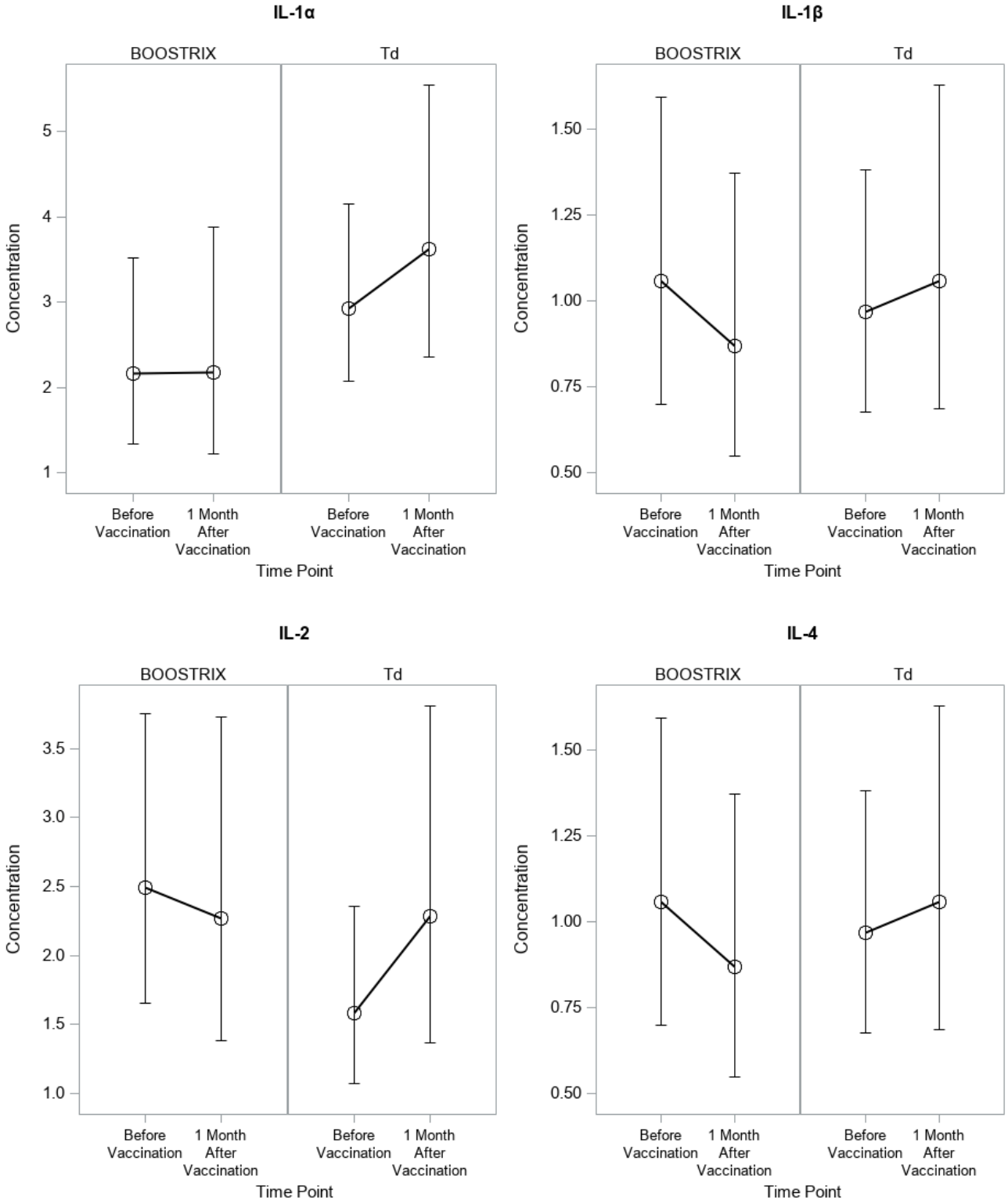


Figure 198: GMC and 95% CI of Maternal Cytokines Over Time by Treatment Group –IL-5, IL-6, IL-7, and IL-8 – Maternal Intent-to-Treat Population

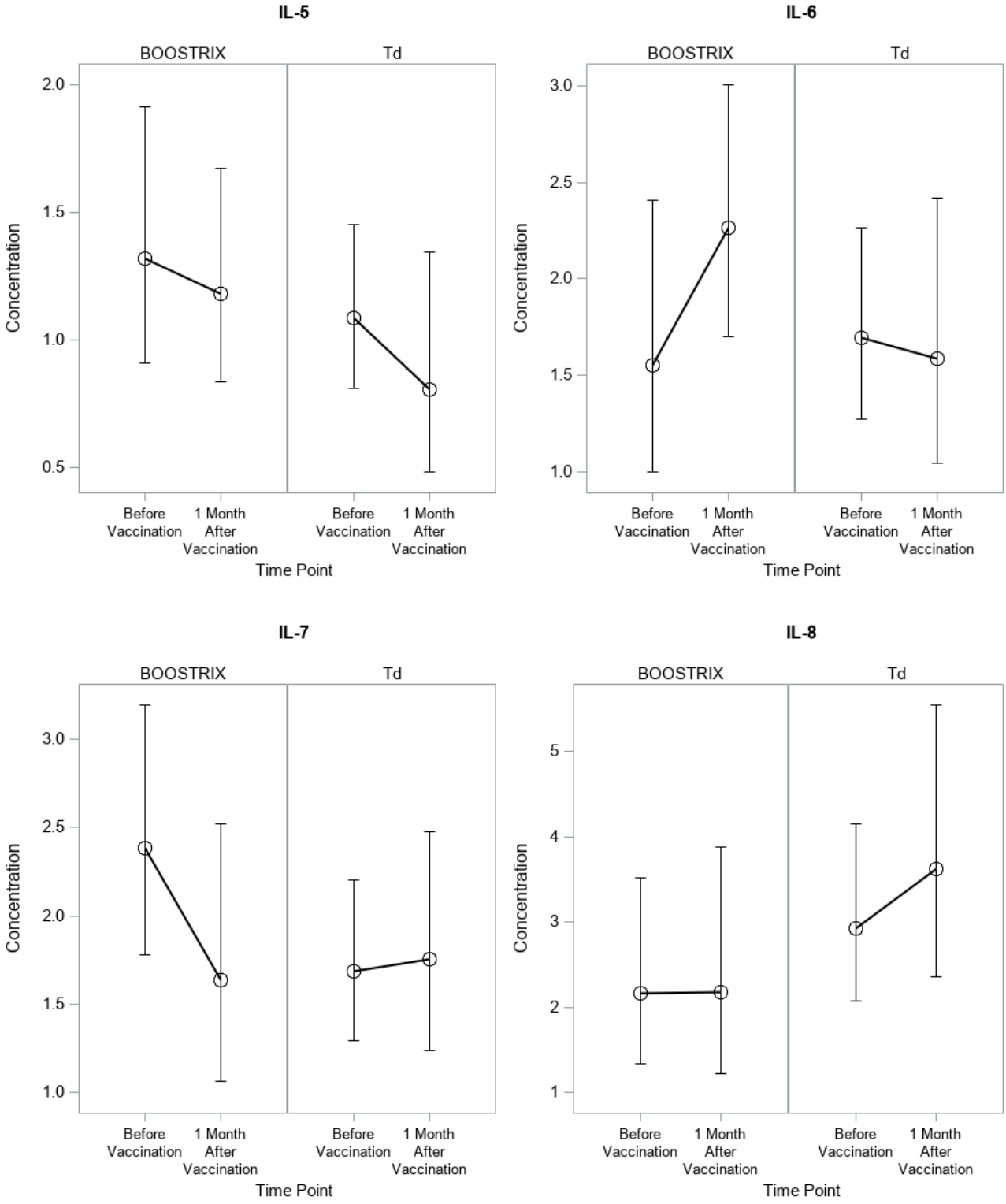
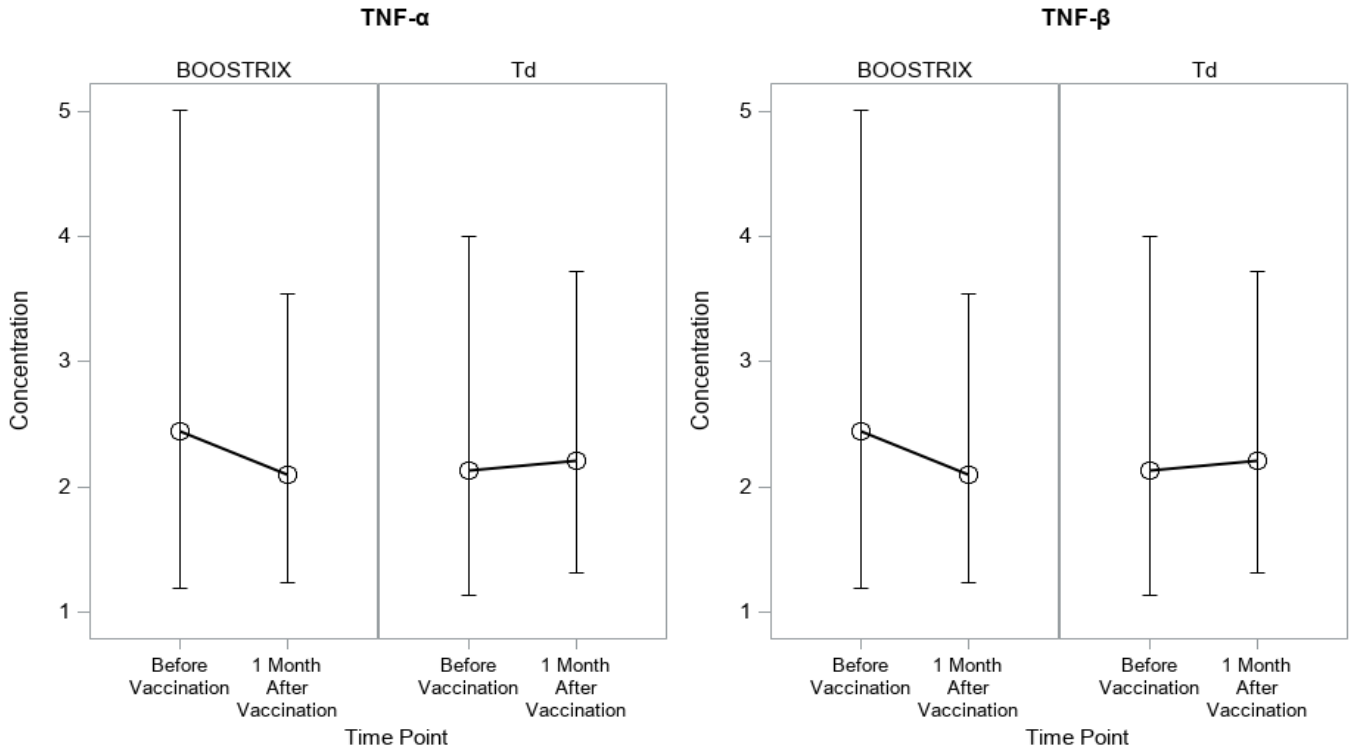


Figure 199: GMC and 95% CI of Maternal Cytokines Over Time by Treatment Group –TNF- α, and TNF- β – Maternal Intent-to-Treat Population



Figures with similar format:

Figure 200: GMC and 95% CI of Maternal Cytokines Over Time by Treatment Group – IFN-γ, IL-10, IL-12p70, and IL-12/IL-23p40 – Maternal Per Protocol Population

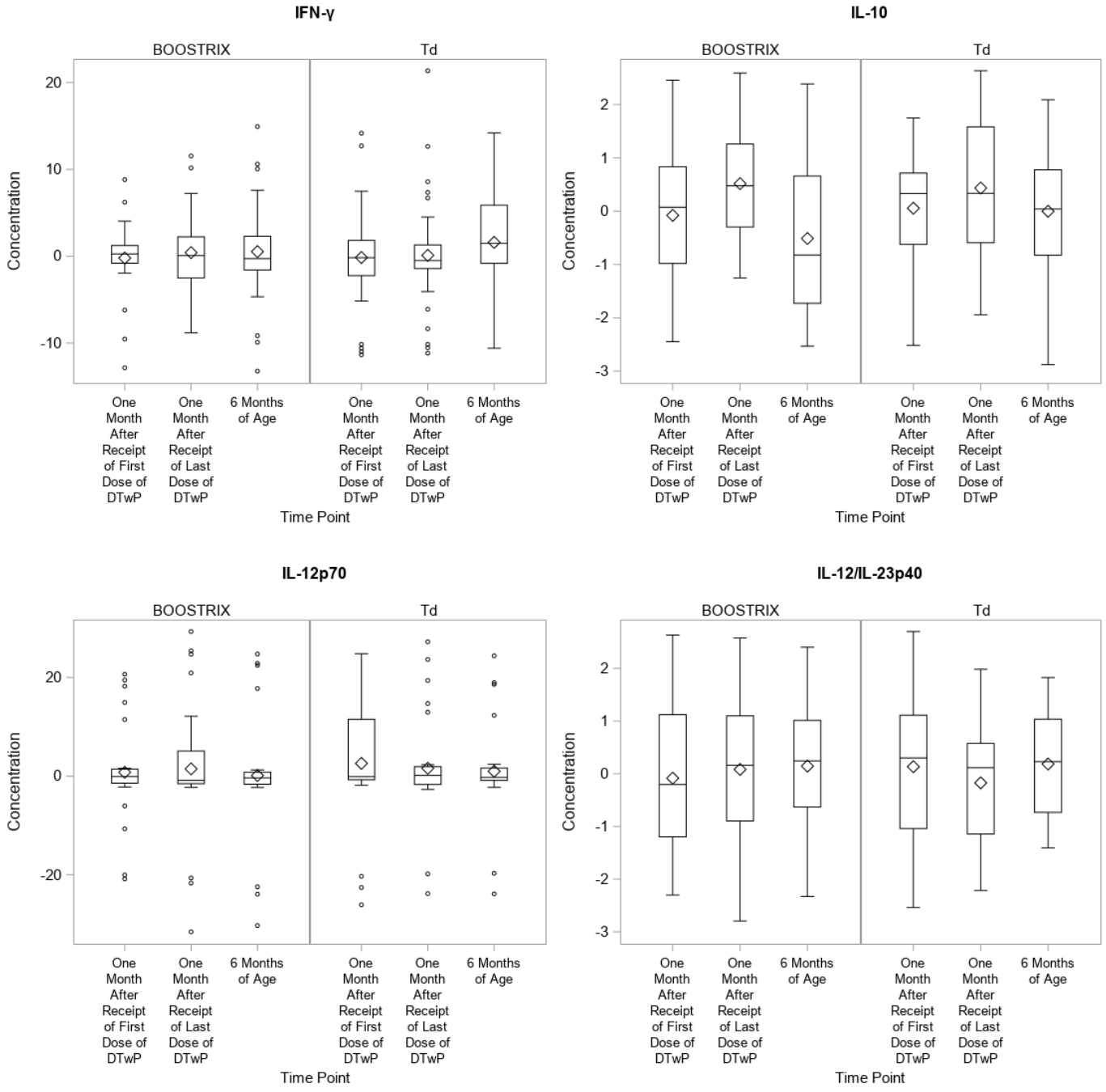
Figure 201: GMC and 95% CI of Maternal Cytokines Over Time by Treatment Group – IL-13, IL-15, IL-16, and IL-17A -- Maternal Per Protocol Population

Figure 202: GMC and 95% CI of Maternal Cytokines Over Time by Treatment Group - IL-1α, IL-1β, IL-2, and IL-4 -- Maternal Per Protocol Population

Figure 203: GMC and 95% CI of Maternal Cytokines Over Time by Treatment Group –IL-5, IL-6, IL-7, and IL-8 – Maternal Per Protocol Population

Figure 204: GMC and 95% CI of Maternal Cytokines Over Time by Treatment Group –TNF- α, and TNF- β – Maternal Per Protocol Population

Figure 205: Change from Baseline by Cytokine, Time Point, and Treatment Group — IFN-γ, IL-10, IL-12p70, and IL-12/IL-23p40 – Infant Intent-to-Treat Population



Figures with similar format:

Figure 206: Change from Baseline by Cytokine, Time Point, and Treatment Group – IL-13, IL-15, IL-16, and IL-17A -- Infant Intent-to-Treat Population

Figure 207: Change from Baseline by Cytokine, Time Point, and Treatment Group -- IL-1α, IL-1β, IL-2, and IL-4 -- Infant Intent-to-Treat Population

Figure 208: Change from Baseline by Cytokine, Time Point, and Treatment Group –IL-5, IL-6, IL-7, and IL-8 – Infant Intent-to-Treat Population

Figure 209: Change from Baseline by Cytokine, Time Point, and Treatment Group –TNF- α, and TNF- β – Infant Intent-to-Treat Population

Figure 210: Change from Baseline by Cytokine, Time Point, and Treatment Group — IFN-γ, IL-10, IL-12p70, and IL-12/IL-23p40 – Infant Per Protocol Population

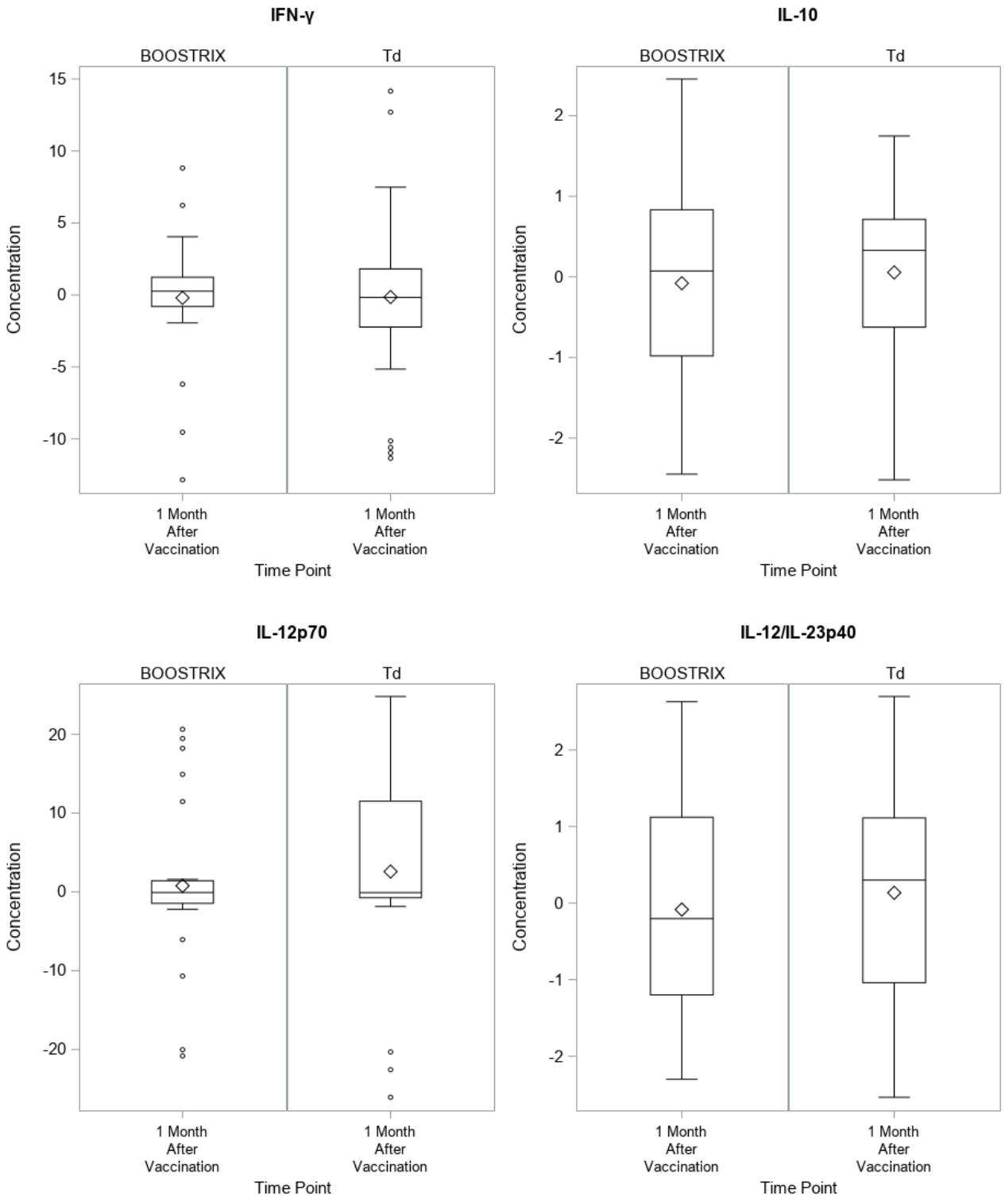
Figure 211: Change from Baseline by Cytokine, Time Point, and Treatment Group – IL-13, IL-15, IL-16, and IL-17A -- Infant Per Protocol Population

Figure 212: Change from Baseline by Cytokine, Time Point, and Treatment Group -- IL-1α, IL-1β, IL-2, and IL-4 -- Infant Per Protocol Population

Figure 213: Change from Baseline by Cytokine, Time Point, and Treatment Group –IL-5, IL-6, IL-7, and IL-8 – Infant Per Protocol Population

Figure 214: Change from Baseline by Cytokine, Time Point, and Treatment Group –TNF- α, and TNF- β – Infant Per Protocol Population

Figure 215: Change from Baseline by Cytokine, Time Point, and Treatment Group — IFN-γ, IL-10, IL-12p70, and IL-12/IL-23p40 – Maternal Intent-to-Treat Population



Figures with similar format:

Figure 216: Change from Baseline by Cytokine, Time Point, and Treatment Group – IL-13, IL-15, IL-16, and IL-17A -- Maternal Intent-to-Treat Population

Figure 217: Change from Baseline by Cytokine, Time Point, and Treatment Group -- IL-1α, IL-1β, IL-2, and IL-4 -- Maternal Intent-to-Treat Population

Figure 218: Change from Baseline by Cytokine, Time Point, and Treatment Group –IL-5, IL-6, IL-7, and IL-8 – Maternal Intent-to-Treat Population

Figure 219: Change from Baseline by Cytokine, Time Point, and Treatment Group –TNF- α, and TNF- β – Maternal Intent-to-Treat Population

Figure 220: Change from Baseline by Cytokine, Time Point, and Treatment Group — IFN-γ, IL-10, IL-12p70, and IL-12/IL-23p40 – Maternal Per Protocol Population

Figure 221: Change from Baseline by Cytokine, Time Point, and Treatment Group – IL-13, IL-15, IL-16, and IL-17A -- Maternal Per Protocol Population

Figure 222: Change from Baseline by Cytokine, Time Point, and Treatment Group -- IL-1α, IL-1β, IL-2, and IL-4 -- Maternal Per Protocol Population

Figure 223: Change from Baseline by Cytokine, Time Point, and Treatment Group –IL-5, IL-6, IL-7, and IL-8 – Maternal Per Protocol Population

Figure 224: Change from Baseline by Cytokine, Time Point, and Treatment Group –TNF- α, and TNF- β – Maternal Per Protocol Population

14.3.1.1 Solicited Adverse Events

Figure 225: Maximum Severity of Solicited Systemic Symptoms per Subject by Day Post Treatment

[Implementation Note: A sample Figure is shown below. For the CSR the Figure will include Pre-dose, post-dose and days 1, 2, 3, 4, 5, 6, 7and 8 post dose. There will be a panel for BOOSTRIX, Td and All Subjects.]

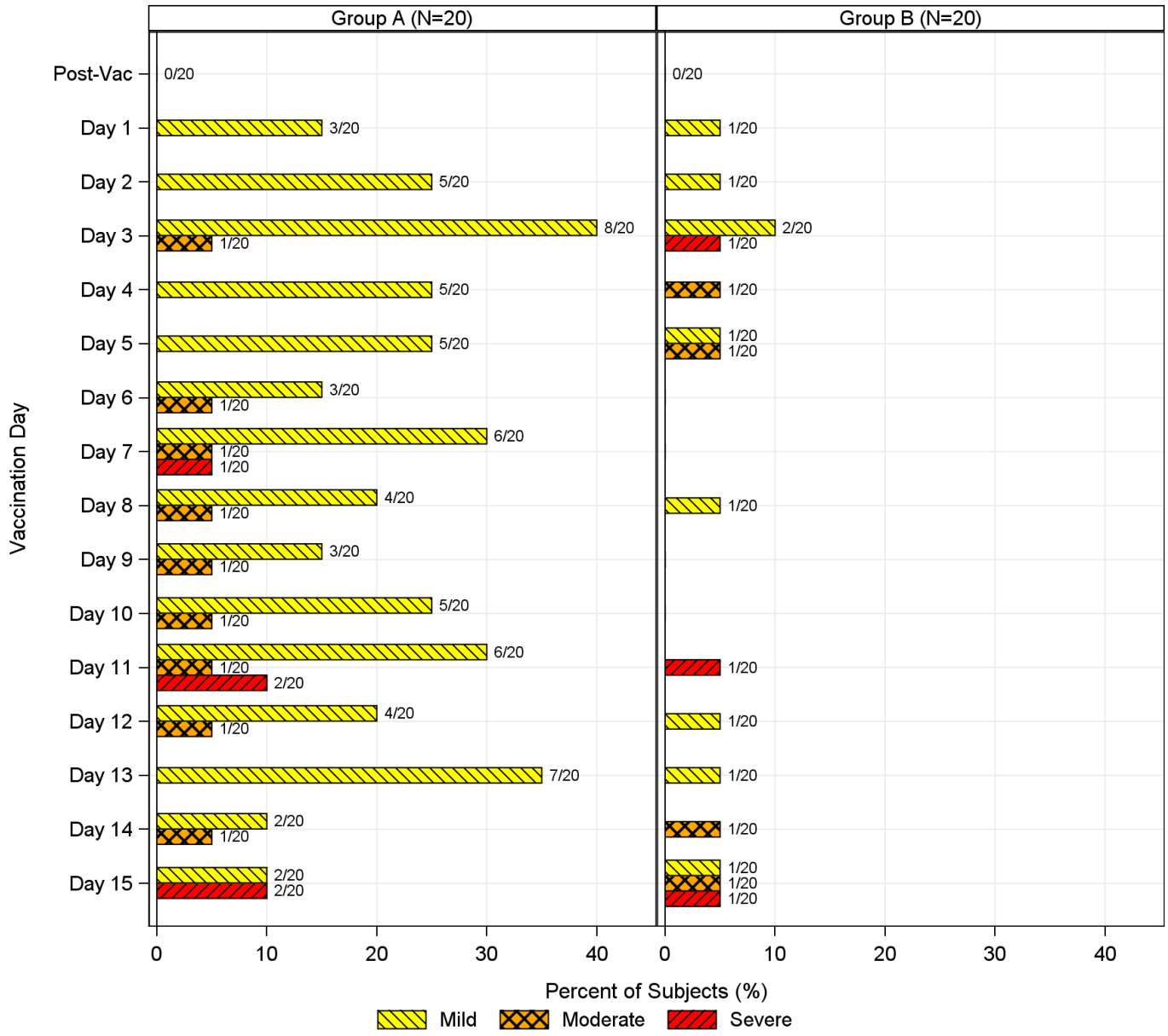
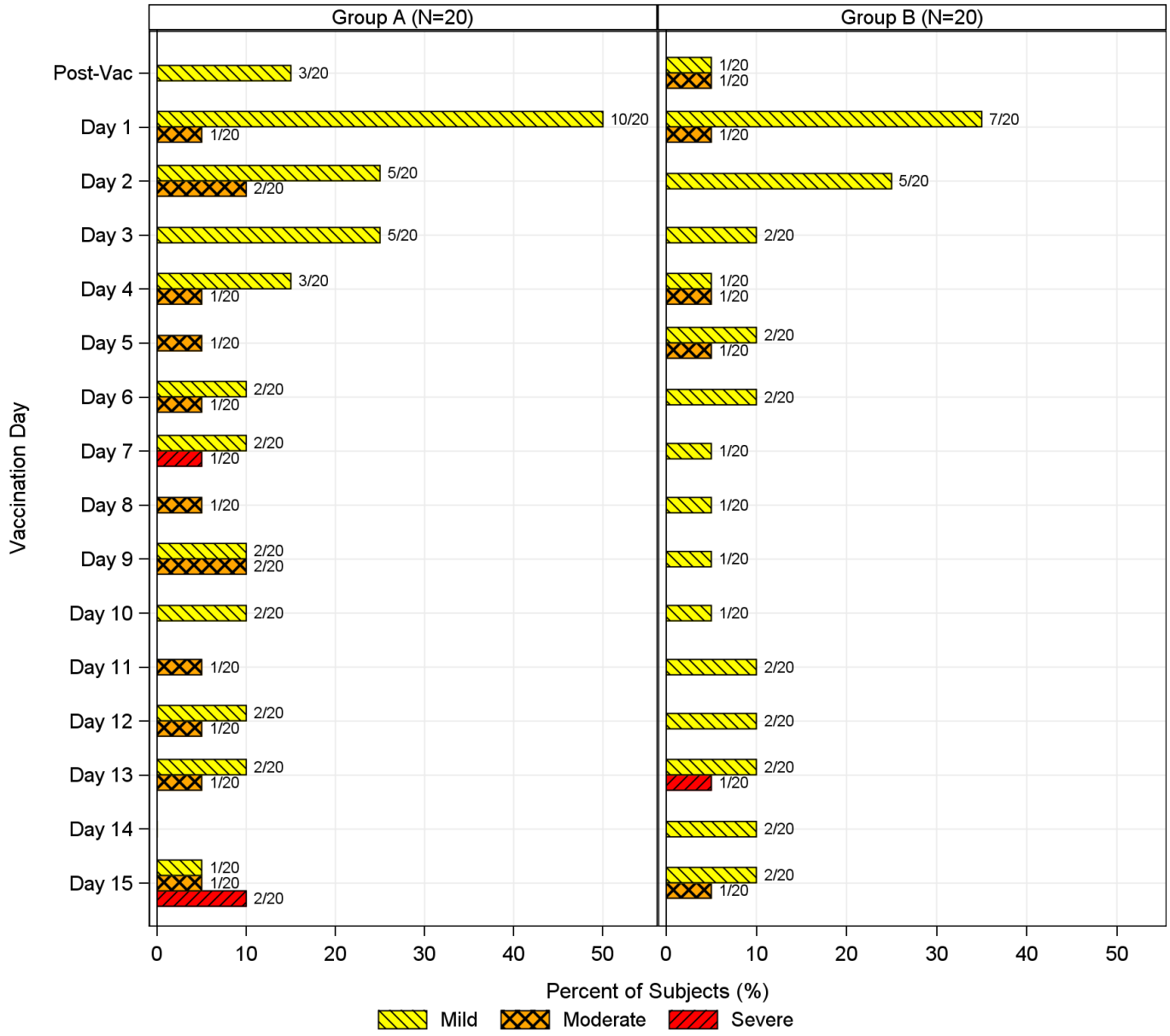


Figure 226: Maximum Severity of Solicited Local Symptoms per Subject by Day Post Treatment

[Implementation Note: A sample Figure is shown below. For the CSR the Figure will include Pre-dose, post-dose and days 1, 2, 3, 4, 5, 6, 7 and 8 post dose. There will be a panel for BOOSTRIX, Td and All Subjects.]



14.3.1.2 Unsolicited Adverse Events

Figure 227: Frequency of Related Adverse Events by MedDRA System Organ Class and Severity

[Implementation Note: A sample Figure is shown below. There will be a panel for BOOSTRIX, Td and All Subjects.]

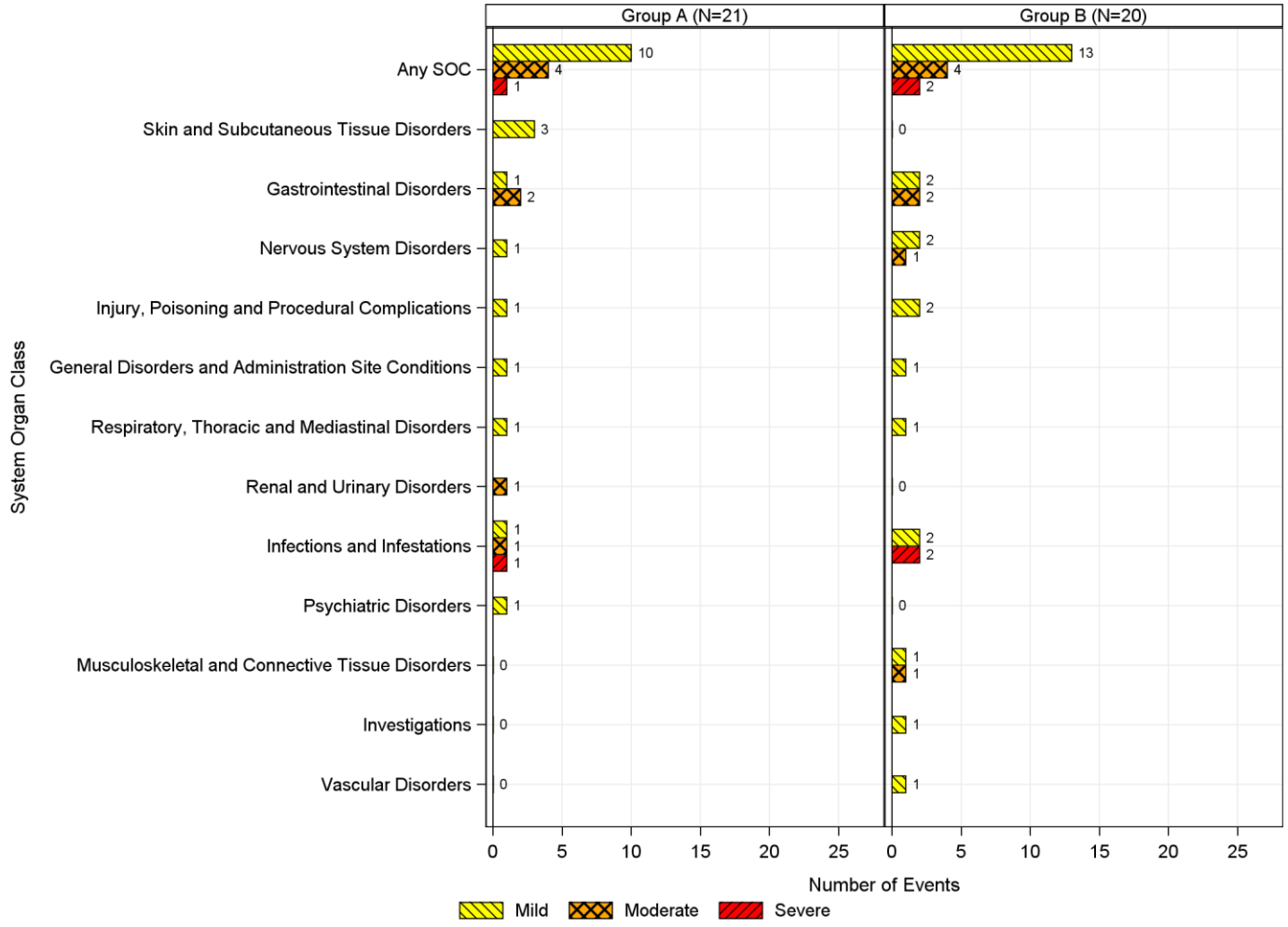


Figure 228: Incidence of Related Adverse Events by MedDRA® System Organ Class and Maximum Severity

[Implementation Note: A sample Figure is shown below. There will be a panel for BOOSTRIX, Td and All Subjects.]

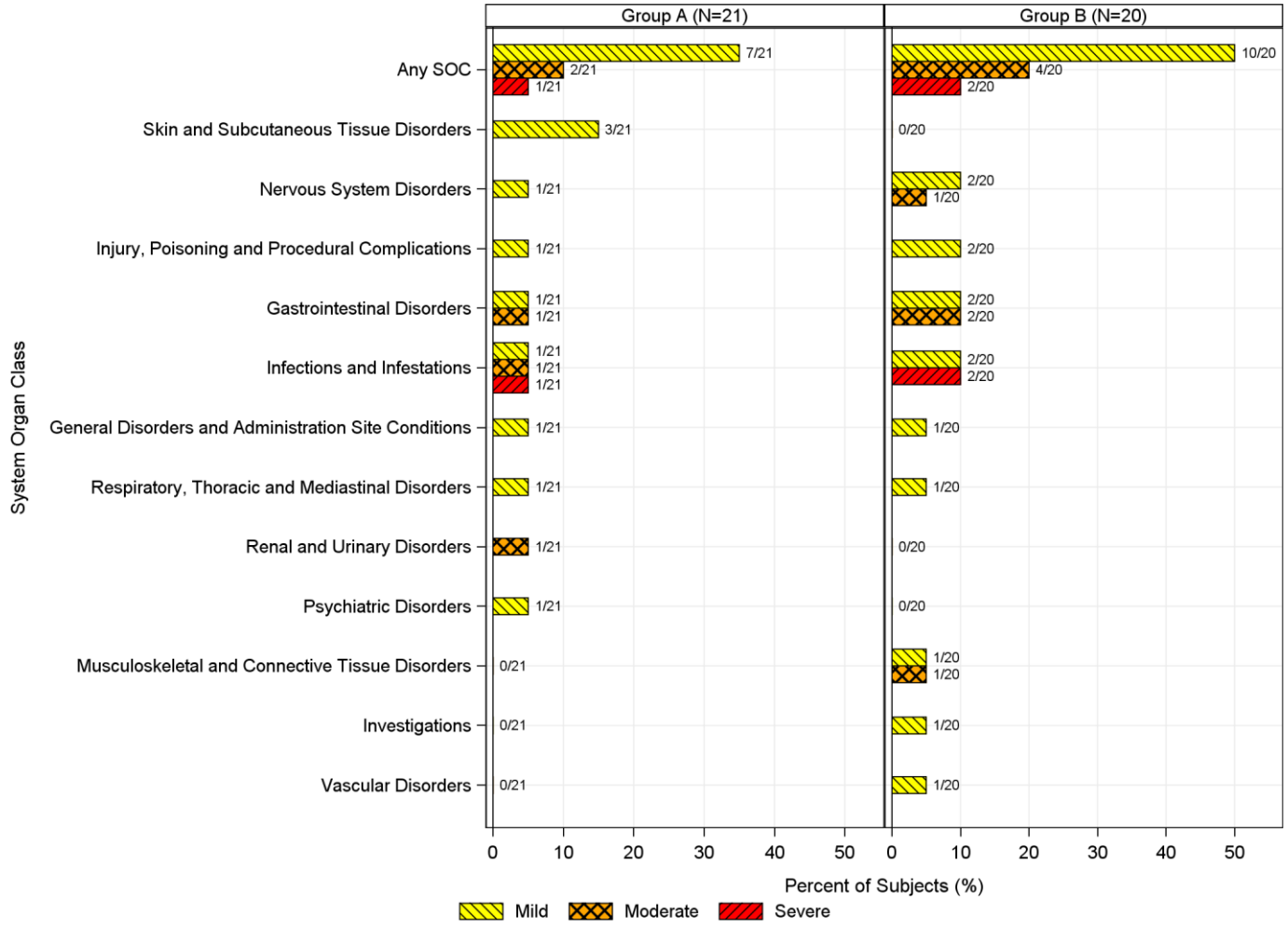


Figure 229: Frequency of Pregnancy-Related Adverse Events by MedDRA System Organ Class and Severity – Maternal Subjects

[Implementation Note: A sample Figure is shown below. There will be a panel for BOOSTRIX, Td and All Subjects. This Figure will summarize pregnancy-related symptoms.]

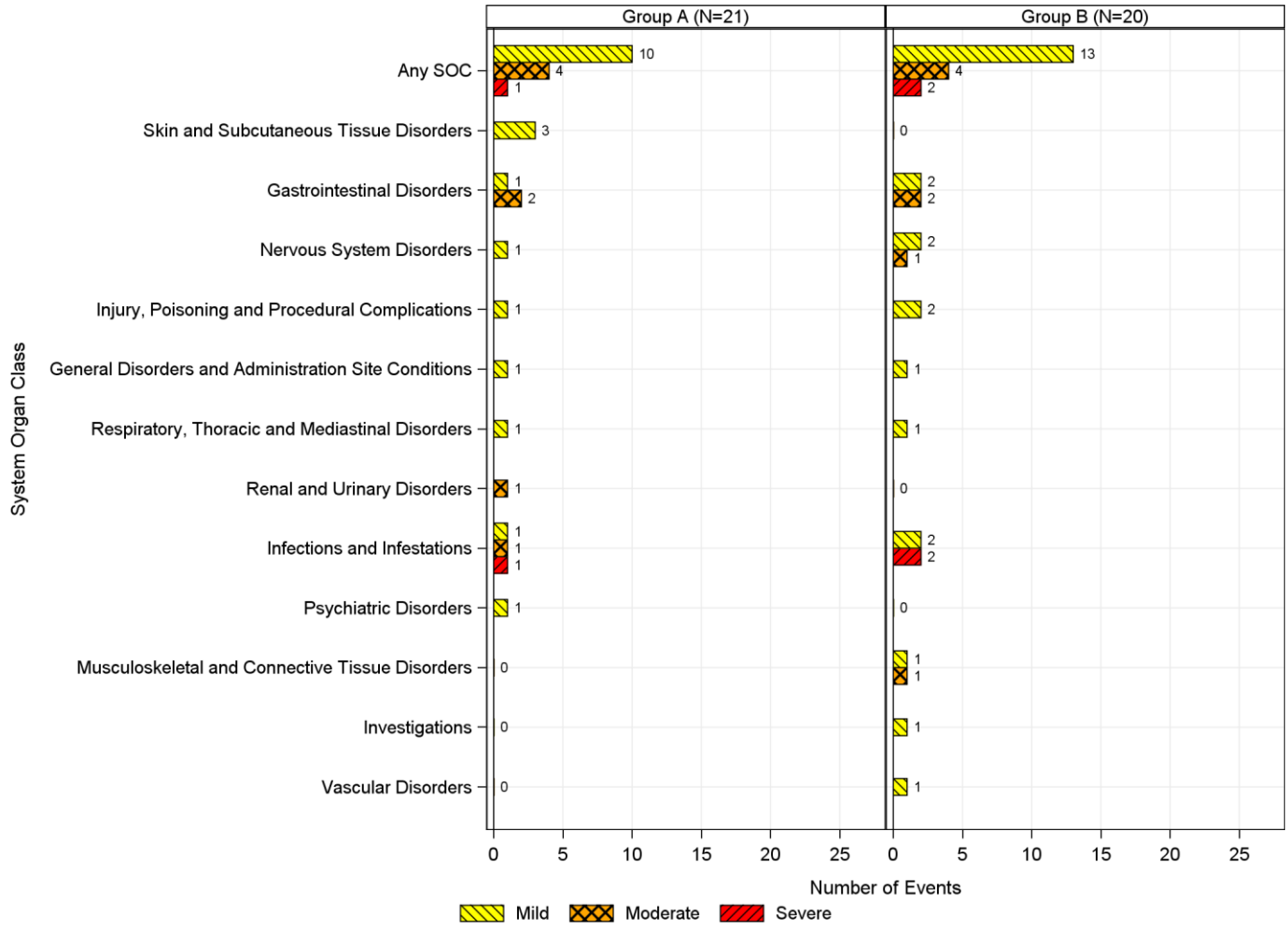


Figure 230: Incidence of Pregnancy-Related Adverse Events by MedDRA System Organ Class and Maximum Severity – Maternal Subjects

[Implementation Note: A sample Figure is shown below. There will be a panel for BOOSTRIX, Td and All Subjects. This Figure will summarize pregnancy-related symptoms.]

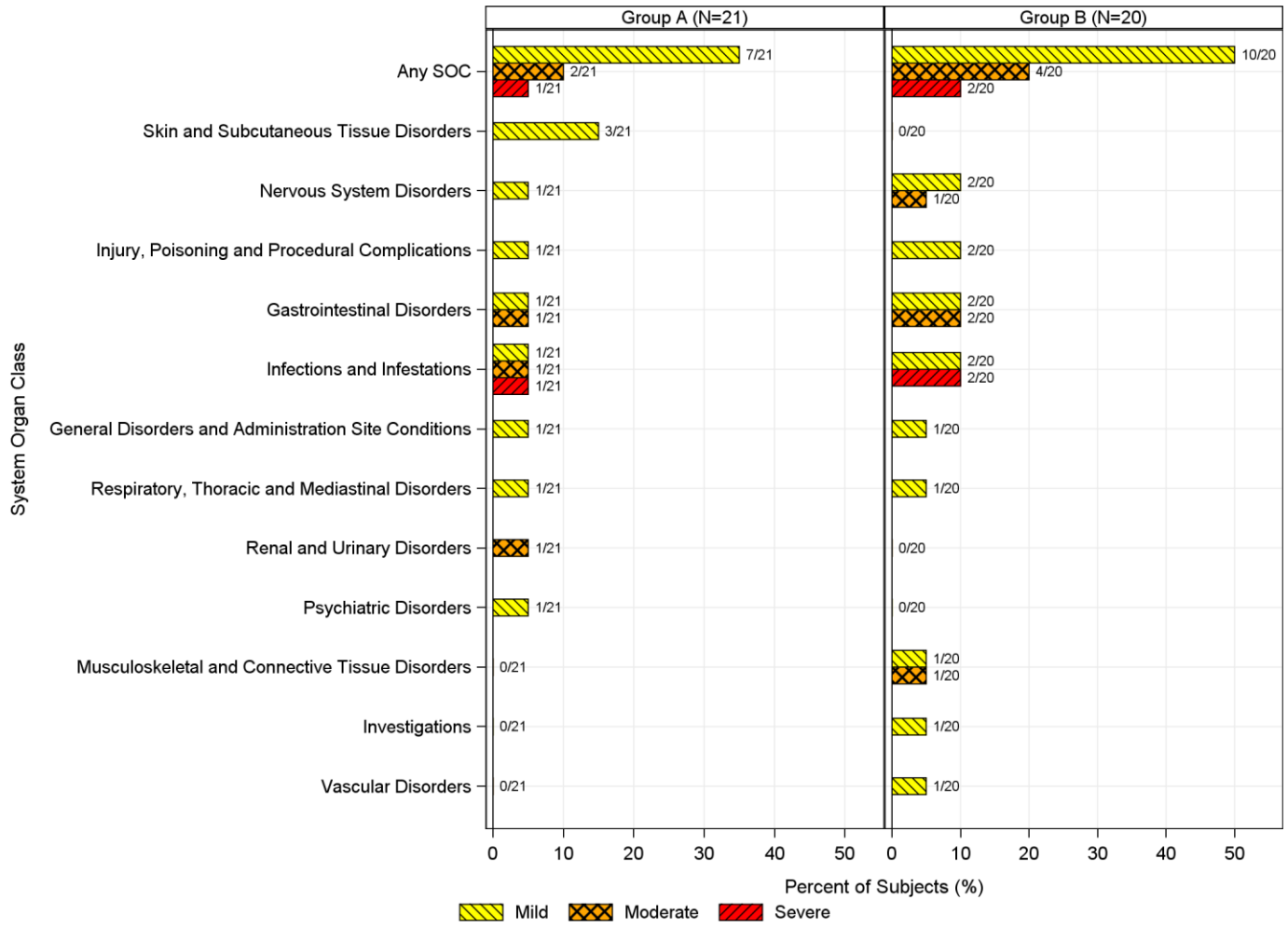


Figure 231: Frequency of Infancy-Related Adverse Events by MedDRA System Organ Class and Severity – Infant Subjects

[Implementation Note: A sample Figure is shown below. There will be a panel for BOOSTRIX, Td and All Subjects. The Figure will summarize infancy-related symptoms.]

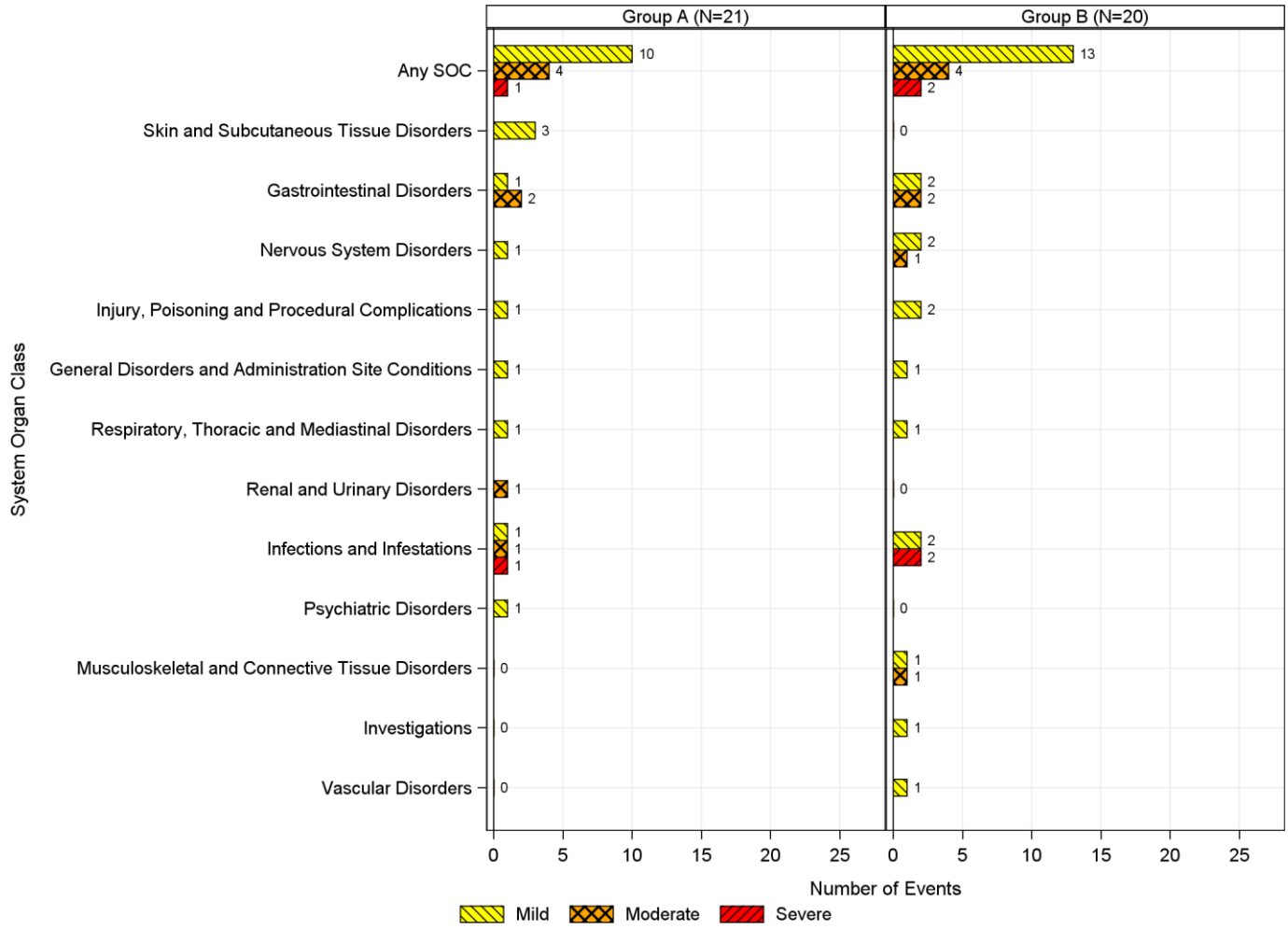
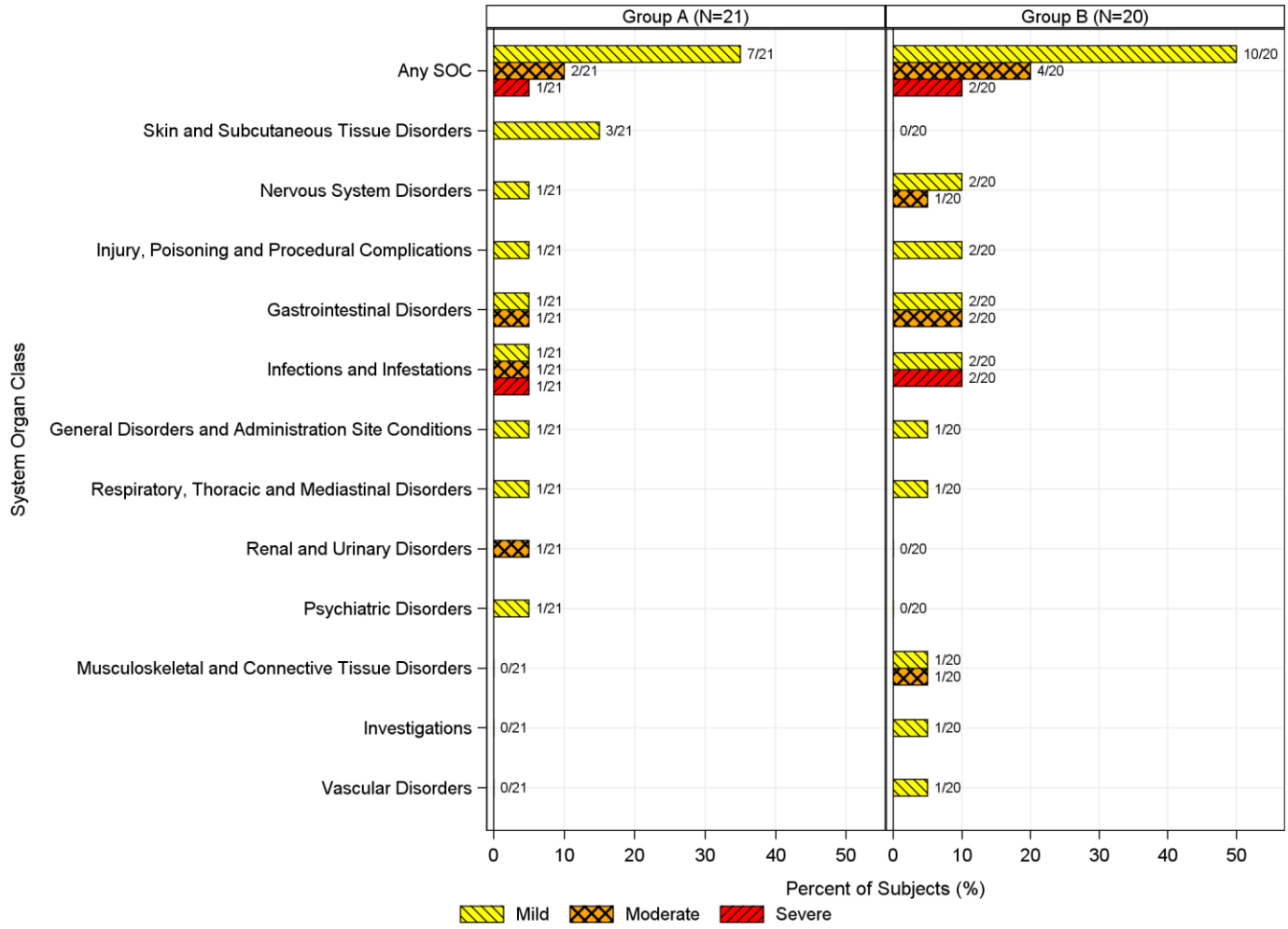


Figure 232: Incidence of Infancy-Related Adverse Events by MedDRA System Organ Class and Maximum Severity – Infant Subjects

[Implementation Note: A sample figure is shown below. There will be a panel for BOOSTRIX, Td and All Subjects. The figure will summarize infancy-related symptoms.]

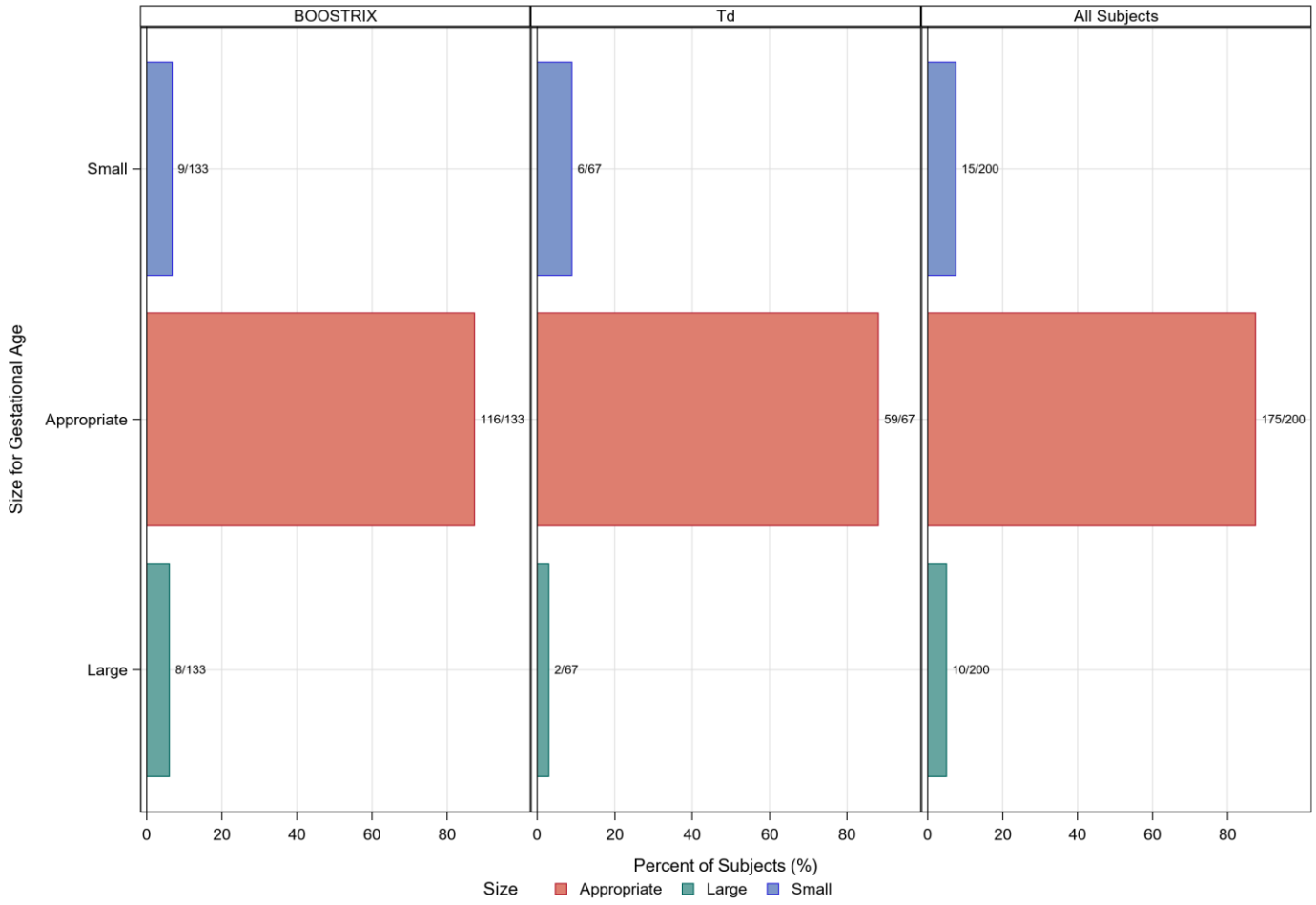


14.3.5 Displays of Laboratory Results

Not Applicable.

14.4 Pregnancy Reports

Figure 233: Infant Size for Gestational Age at Birth by Treatment Group



APPENDIX 3. LISTINGS MOCK-UPS

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	Maternal/Infant	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	Maternal/ Infant	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 the Efficacy Analysis

Listing 4: 16.2.3: Subjects Excluded from Analysis Populations

Treatment Group	Maternal/Infant	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: Maternal Demographic Data

Treatment Group	Subject ID	Age at Enrollment (years)	Ethnicity	Race	Other Ethnic Group	Gestational Age at Vaccination (weeks)

Listing 6: 16.2.4.2: Infant Demographic Data

Treatment Group	Subject ID	Sex	Gestation Age (weeks)	Ethnicity	Race	Other Ethnic Group	Delivery	Apgar Score (1, 5, 10 Minutes)	Birth Weight (kg)	Length at Birth (cm)	Head Circumference at Birth (cm)

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

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

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

Not Applicable.

16.2.6 Individual Immunogenicity Response Data

Listing 8: 16.2.6: Individual Immunogenicity Response Data (Antibody)

Treatment Group	Subject ID	Maternal/Infant	Planned Time Point	Actual Study Day	Tdap/DTwP	Serum IgG/Serum IgA/Breast Milk	Antibody Tested	Titer

Listing 9: 16.2.6: Individual Immunogenicity Response Data (Cytokine)

Treatment Group	Subject ID	Maternal/Infant	Planned Time Point	Actual Study Day	Cytokine Tested	Result

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	NOCMC?	In Not Related, Alternative Etiology	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: 61.										

Listing 13: 16.2.7.3: Pregnancy or Infancy Related Adverse Events

Adverse Event	Severity	SAE?	Relationship to Study Treatment	If Not Related, Alternative Etiology	Subject Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Treatment Group: , Subject ID:, Maternal/Infant, AE Number:								
Comments:								
Treatment Group: , Subject ID: Maternal/Infant, AE Number:								
Comments:								
Note: For additional details about SAEs, see Table: 61.								

16.2.8 Individual Laboratory Measurements

Not Applicable.

16.2.9 Vital Signs and Physical Exam Findings

Listing 14: 16.2.9.1: Maternal Subject Vital Signs

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

Listing 15: 16.2.9.1: Infant Subject Vital Signs

Treatment Group	Subject ID	Planned Time Point	Actual Study Day	Axillary Temperature (°C)	Respiratory Rate (breaths/min)	Heart Rate (beats/min)

Listing 16: 16.2.9.2: Physical Exam Findings

Treatment Group	Subject ID	Maternal/Infant	Planned Time Point	Actual Study Day	Body System	Abnormal Finding	Reported as an AE? (AE Description; Number)

16.2.10 Concomitant Medications

Listing 17: 16.2.10: Concomitant Medications

Treatment Group	Subject ID	Maternal/Infant	CM Number	Medication	Medication Start Day	Medication End Day	Indication	Taken for an AE? (AE Description; Number)	Taken for a condition on Medical History? (MH Description; Number)	ATC Level 1 (ATC Level 2)

16.2.11 Pregnancy Reports

Listing 18: 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 19: 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	Congenital Anomalies?	Illnesses/ Hospitalizations within 1 Month of Birth?
Note: Congenital Anomalies are included in the Adverse Event listing.											

Listing 20: 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 21: 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