STATISTICAL ANALYSIS PLAN
for
PATH Protocol: ACYWX-001/VAC 046

A Phase 1, Double Blind, Randomized, Controlled Study to Evaluate the Safety and Immunogenicity of a New Meningococcal Conjugate Vaccine Containing Serogroups A, C, Y, W and X in Healthy Adults

Version 2.0

DATE: 23 August 2017

Prepared and distributed by:
The Emmes Corporation
Rockville, Maryland USA

Protocol Number Code:	ACYWX-001/VAC 046
Development Phase:	Phase 1
Products:	Meningococcal (A, C, Y, W, X) Polysaccharide Conjugated Vaccine (freeze-dried), also referred to as MCV-5
Form/Route:	Vaccine/Intramuscular
Indication Studied:	
Sponsor:	PATH 2201 Westlake Avenue, Suite 200, Seattle, WA 98121 USA
Principal Investigator:	Dr. Wilbur H. Chen, MD, MS Chief, Adult Clinical Studies section Center for Vaccine Development University of Maryland School of Medicine 685 W. Baltimore St., Suite 480, Baltimore, MD 21201 Tel: 410-706-1188 Fax: 410-706-6205 Email: wchen@medicine.umaryland.edu
Sponsor Medical Officer	Dr. Abdi Naficy, MD Center for Vaccine Innovation and Access – PATH 455 Massachusetts Ave. NW, Suite 1000, Washington, DC 20001 Email: anaficy@path.org
Vaccine Manufacturer Medical Expert	Dr. Prasad Kulkarni, MD Medical Director, Serum Institute of India Private Ltd. Pune Tel: 91-20-26602384 Fax: 91-20-26993945 Email: drpsk@seruminstitute.com
Medical Monitor:	Robert Lindblad, MD The Emmes Corporation 401 N. Washington St., Suite 700, Rockville, MD 20850
Biostatistician:	Len Dally The Emmes Corporation 401 N. Washington St., Suite 700, Rockville, MD 20850
Clinical Trial Initiation Date:	22 July 2016
Clinical Trial Completion Date:	To be determined
Date of the Analysis Plan:	23 August 2017
Version Number:	2.0

This study was performed in compliance with Good Clinical Practice.

Signature Page

SPONSOR: PATH

STUDY TITLE: A Phase 1, double blind, randomized, controlled study to evaluate the safety and immunogenicity of a new Meningococcal Conjugate Vaccine containing serogroups A,C,Y,W and X in healthy adults.

PROTOCOL NUMBER: PATH ACYWX-001/VAC 046

Principal Investigator: (Dr. Wilbur H. Chen, MD, MS)

Signed: _____ Date: _____

ddMMMyyyy

PATH Medical Officer: (Dr. Abdi Naficy, MD)

Signed: _____ Date: _____

ddMMMyyyy

SIIPL (Serum Institute of India Private Limited): (Dr. Amol Chaudhari, MD)

Signed: _____ Date: _____

ddMMMyyyy

Table of Contents

TABLE OF CONTENTS *(continued)*

TABLE OF CONTENTS *(continued)*

TABLE OF CONTENTS *(continued)*

TABLE OF CONTENTS *(continued)*

TABLE OF CONTENTS *(continued)*

Appendices:

List of Abbreviations

AE	Adverse Event
ALT	Alanine Aminotransferase
Alum	Aluminum phosphate
CDC	Centers for Disease Control
CI	Confidence interval
cm	Centimeter
CMV	conjugated meningococcal vaccines
CPCSEA	Committee for the Purpose of Control and Supervision of Experiments on Animals
CRF	Case report form
CRM	cross reactive material
CSR	Clinical Study Report
CVD	Center for Vaccine Development
EDC	Electronic data capture
ELISA	Enzyme linked immunosorbent assay
FA	Full Analysis
FDA	Food and Drug Administration
FIH	First in human
GMT	Geometric Mean Titer
HBV	Hepatitis B virus
HCG	human chorionic gonadotropin
HCV	Hepatitis C virus
HgB	Hemoglobin
HIV	Human immunodeficiency virus
ICD	Informed consent document
ICH	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
Ig	Immunoglobulin
IM	Intramuscular
IUD	Intrauterine device
MedDRA®	Medical Dictionary for Regulatory Activities
N	Number (typically refers to participants)
PCR	Polymerase chain reaction

List of Abbreviations *(continued)*

PHE	Public Health England
PI	Principal Investigator
PP	Per Protocol
PS	Polysaccharide
PT	Preferred Term
rSBA	rabbit complement serum bactericidal activity
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SBA	serum bactericidal activity
SD	Standard deviation
SDMG	Statistical and Data Management Group
SIIPL	Serum Institute of India Private Limited
SOC	System Organ Class
SRC	Safety Review Committee
TT	Tetanus toxoid
UK	United Kingdom
ULN	Upper limit of normal
USA	United States of America
USP	United States Pharmacopeia
WBC	White blood cells
WHO	World Health Organization

1 PREFACE

The Statistical Analysis Plan (SAP) for “Safety and Immunogenicity of a new Meningococcal Conjugate Vaccine containing serogroups A, C, Y, W and X" (PATH protocol ACYWX-001/VAC-046) describes and expands upon the statistical information presented in the protocol.

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

This document contains four sections: (1) a review of the study design, (2) general statistical considerations, (3) comprehensive statistical analysis methods for efficacy and safety outcomes, and (4) a list of proposed tables and figures. 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

Currently, three polyvalent conjugate vaccines are available to protect against meningococcal disease. All three are tetravalent (serogroups A, C, W, and Y) vaccines; Menactra® (Sanofi Pasteur Inc.), Menveo® (Novartis) and Nimenrix® (GlaxoSmithKline Biologicals).There is vast experience with the use of these vaccines, which are generally well tolerated in all age groups. At this time, there is no licensed vaccine giving protection against meningococcal serogroup X which has caused many outbreaks in Africa and Europe in the recent past.

Following the MenAfriVac® MenA monovalent conjugate vaccine development experience, Serum Institute of India Private Limited (SIIPL) developed a candidate polyvalent conjugate vaccine composed of serogroups A, C, Y, W, and X *Neisseria meningitidis* capsular polysaccharides. The individual polysaccharides are conjugated to protein carriers, cross reactive material (CRM) or tetanus toxoid (TT), and formulated with or without aluminum phosphate (alum) as an adjuvant. The vaccine is intended for the prevention of meningitis and/or septicemia caused by serogroups A, C, Y, W, and X *N. meningitidis* in countries where the disease is endemic and causes large epidemics such as the countries in the African meningitis belt. The target population consists of infants, children and adults covering an age group of 9 months to 55 years.

This first-in-human (FIH) Phase 1 clinical study is designed to evaluate primarily the safety of the study vaccine. The three-group design will allow safety evaluation of the adjuvanted and non-adjuvanted MCV-5 formulations. The quadrivalent (ACYW) Menactra® vaccine has been chosen as a control vaccine

comparator given the large safety database accumulated since the vaccine was introduced in the US in 2005, prequalified by World Health Organization (WHO) and progressively introduced in other countries.

2.1 Purpose of the Analyses

These analyses will assess the safety of the adjuvanted and non-adjuvanted ACYWX with that of a licensed ACYW conjugate vaccine (reference vaccine group).In addition, immunogenicity assessments are planned to evaluate immune responses induced by the adjuvanted and non-adjuvanted study vaccines. The study is not statistically powered to determine significance of any difference. A formal sample size calculation was not performed as this is a Phase 1 trial and the first clinical study with the study vaccine. The study will be performed in 60 adult healthy participants aged 18 to 45 years.

3 STUDY OBJECTIVES AND ENDPOINTS

3.1 Study Objectives

3.1.1 Primary Objective

The primary objective is to evaluate the safety of adjuvanted and non-adjuvanted formulations of MCV-5 vaccine.

3.1.2 Secondary Objective

The secondary objective is to assess the immune response of adjuvanted and non-adjuvanted formulations of MCV-5 vaccine.

3.2 Endpoints

3.2.1 Primary Endpoints

- The occurrence and severity of solicited local and systemic post immunization reactions within seven days following vaccination.
- The occurrence, severity, and relatedness of unsolicited adverse events for 28 days following vaccination, and serious adverse events for 6 months following vaccination.

3.2.2 Secondary Endpoints

- The percentage of participants who show a seroconversion for Meningococcal Polysaccharide (PS) A, C, Y, W and X specific antibodies, i.e., a ≥4-fold increase in post-immunization rabbit complement serum bactericidal activity (rSBA) titer with respect to pre-immunization rSBA titer, at 28 days after a single vaccine dose.
- The percentage of participants who show a post-immunization seroprotection titer for Meningococcal PS A, C, Y, W, and X specific antibodies, defined as rSBA titer of ≥1:8 and ≥1:128 at 28 days after a single vaccine dose.
- Geometric Mean Titers (GMTs) of Meningococcal PS A, C, Y, W and X serogroup-specific antibodies at 28 days after a single vaccine dose, as measured by rSBA assay.

3.3 Study Definitions and Derived Variables

The following definitions and derivations will be used in this study:

- The baseline value will be defined as the last value obtained prior to the vaccination of study product.
- The reference day will be the day of vaccination and will be referred to as Day 1.
- Study days prior to vaccination will be calculated by taking the date minus the vaccination date (reference day).
- Study days occurring on or after the date of vaccination will be calculated by taking the date minus the vaccination date (reference day) and adding 1.
- Age will be calculated from the date of enrollment and will be presented in whole years (truncated integer).
- The calculations for GMTs will be performed by taking the anti-log of the arithmetic mean of the natural log-transformed titers.
- Fold increase will be calculated as the ratio of: $\frac{post-immunizationrSBAtiter}{pre-immunizationrSBAtiter}$
- Seroconversion (4-fold response) will be defined as the following:
    - For participants with a pre-vaccination rSBA titer < 8, a post-vaccination titer ≥ 32;
    - For participants with a pre-vaccination rSBA titer ≥ 8, an increase in rSBA titer of at least 4 times the pre-vaccination titer.
- Seroprotection will be defined as a rSBA titer of ≥ 8 and ≥ 128.
- Prior medications are those medications that started and stopped prior to vaccination.

4 INVESTIGATIONAL PLAN

4.1 Overall Study Design and Plan

This study is a Phase 1, single center, double blinded, randomized, controlled clinical trial to assess the safety and immunogenicity of the adjuvanted and non-adjuvanted formulation of polyvalent conjugate vaccine composed of serogroups A, C, Y, W and X *Neisseria meningitidis* capsular polysaccharides (MCV-5) as compared to the quadrivalent (ACYW) Menactra® vaccine. As this is the first clinical study with the study vaccine, the study will initially be performed in 60 adult healthy participants aged 18 to 45 years old.

The study will have 3 arms with 3 vaccines given in a 1:1:1 ratio; adjuvanted MCV-5, non-adjuvanted MCV-5 and Menactra®. Each participant will receive a single intramuscular (IM) injection of one of the three vaccines and will be followed up to six months after the vaccination. There will be 20 participants per vaccine group.

The vaccinator will be aware of group allocation, although he/she will not be able to influence or decide this allocation nor be part of the safety assessment. This will ensure that the study team, involved in assessment of safety outcomes, as well as participants, are unaware of the identity of the study vaccine

administered to them. This will help rule out bias at the time of assessment. As the reference product and study vaccines are different in appearance and composition, the vaccinator blind cannot be maintained in this study. However, the vaccinator will not be involved in the safety assessment.

In addition, immunogenicity assessments are planned to evaluate any differences in the immune responses induced by the adjuvanted and non-adjuvanted study vaccines and to compare against the reference vaccine. The study, however, is not statistically powered to determine significance of any difference. A formal sample size calculation was not performed as this is a Phase 1 trial and the first clinical study in humans with the study vaccine.

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

Currently, three polyvalent conjugate vaccines are available to protect against meningococcal disease. All three are tetravalent (serogroups A, C, W, and Y) vaccines; Menactra® (Sanofi Pasteur Inc.), Menveo® (Novartis) and Nimenrix® (GlaxoSmithKline Biologicals).There is vast experience with the use of these vaccines, which are generally well tolerated in all age groups. At this time, there is no licensed vaccine giving protection against meningococcal serogroup X which has caused many outbreaks in Africa and Europe in the recent past.

SIIPL has developed a candidate polyvalent conjugate vaccine composed of serogroups A, C, Y, W, and X *Neisseria meningitidis* capsular polysaccharides. The vaccine is intended for the prevention of meningitis and/or septicemia caused by serogroups A, C, Y, W, and X *N. meningitidis* in countries where the disease is endemic and causes large epidemics such as the countries in the African meningitis belt.

The quadrivalent (ACYW) Menactra® vaccine has been chosen as a control vaccine comparator given the large safety database accumulated since the vaccine was introduced in the US in 2005, prequalified by World Health Organization (WHO) and progressively introduced in other countries.

4.3 Selection of Study Population

This will be a single site study conducted at the Center for Vaccine Development (CVD), University of Maryland, Baltimore USA. Approximately 60 healthy adults aged 18-45 years old who meet all eligibility criteria (i.e., meet all inclusion criteria and no exclusion criteria) will be enrolled.

4.3.1 Inclusion Criteria

Male and female participants will be eligible for inclusion if ALL of the following apply at the time of screening:

- Aged 18 to 45 years;
- Written informed consent of participants;
- Healthy as established by medical history, laboratory evaluation and screening evaluations including clinical physical examination.
- Participants must have the following laboratory parameters:
  - Hemoglobin: ≥ 10.5 g/dL for female, ≥ 11.0 g/dL for male
  - White cell count: 3,300 to 12,000 cells/mm^3

- Platelets: 125,000 to 550,000 cells/mm^3
- ALT < 1.25 times the institutional upper limit of normal (ULN)
- Creatinine and total bilirubin ≤ institutional ULN
- Albumin ≥ institutional lower limit of normal.

- Participants are able to understand and comply with planned study procedures and be available for all study visits.
- Female participants must be of non-childbearing potential (defined as surgically sterile or postmenopausal for more than 1 year), or if of childbearing potential must be practicing abstinence or using an effective licensed method of birth control (e.g., history of hysterectomy or tubal ligation; use hormonal or barrier birth control such as implants, injectables, combined oral contraceptives, some intrauterine devices (IUDs), cervical sponges, diaphragms, condoms with spermicidal agents; or must have a vasectomized partner) within one month of vaccination and must agree to continue such precautions for 84 days after vaccination. A woman is eligible if she is monogamous with a vasectomized male.

4.3.2 Exclusion Criteria

Participants with any of the following criteria at study entry will not be eligible for participation:

- Previous vaccination against *Neisseria meningitidis*.
- Known exposure to *Neisseria meningitidis* in the past.
- History of meningitis or seizures or any neurological or psychiatric disorder.
- Administration of any other vaccine within 30 days prior or after administration of study vaccines.
- Use of any investigational or non-registered drug or vaccine within 30 days prior to the administration of study vaccines or planned during the study.
- History of allergic disease or known hypersensitivity to any component of the three study vaccines.
- History of Serious Adverse Reactions following administration of TT, Diphtheria Toxoid or CRM containing vaccines.
- History of Guillain-Barré syndrome.
- Confirmed or suspected immunosuppressive or immune-deficient condition.
- A family history of congenital or hereditary immunodeficiency.
- Chronic administration (defined as more than 14 days) of immune-suppressants or other immune-modifying agents within six months prior to administration of study vaccine. (For corticosteroids, this means prednisone, or equivalent, > 0.5 mg/kg/day; topical or inhalable steroids are allowed.)
- Laboratory confirmed infection of either hepatitis B virus (HBVs AG positive on enzyme linked immunosorbent assay (ELISA)) hepatitis C virus (HCV) (anti-HCV positive on ELISA as well as polymerase chain reaction (PCR)) or human immunodeficiency virus (HIV on ELISA).
- Major congenital defects or serious chronic illness.
- Acute or chronic, clinically significant pulmonary, cardiovascular, hepatic, or renal functional abnormality, as determined by medical history, physical examination or laboratory screening tests.
- Known bleeding disorders.
- Administration of immunoglobulins and/or any blood products within the three months preceding the administration of study vaccines or planned administration during the vaccine period.

- History (within the past year) or signs of alcohol or substance abuse.
- Pregnancy or lactation. A negative pregnancy test will be required before vaccination for all women of childbearing potential.
- A Body Mass Index (BMI) above 30.
- Any other condition which, in the opinion of the investigator, might interfere with the study objectives, jeopardize the safety or rights of the participant or make it unlikely the participant could complete the protocol.

4.4 Treatments

4.4.1 Treatments Administered

4.4.1.1 Test Vaccine (MCV-5)

SIIPL's candidate vaccine MCV-5 is a sterile pentavalent polysaccharide-conjugate vaccine composed of serogroups A, C, Y, W and X *Neisseria meningitidis* capsular polysaccharides, conjugated to two different protein carriers, with aluminum phosphate as an adjuvant. Serogroup A & X polysaccharide are separately conjugated to TT while C, Y & W are separately conjugated to recombinant CRM (CRM is a genetic mutant of diphtheria toxin).

The MCV-5 vaccine is provided as a freeze-dried powder in a five-dose vial containing meningococcal A, C, Y, W and X polysaccharides conjugated to TT and CRM protein. The vaccine has to be reconstituted with either adjuvant containing diluents or 0.9% Sodium Chloride Injection, USP as per sections 3.2 and 3.4. No preservative is added either in vaccine or diluents component during manufacture. MCV-5 vaccine must be stored between +2 °C to +8 °C

The adjuvanted diluent containing aluminum phosphate used to prepare the adjuvanted MCV-5 is a sterile white homogeneous suspension provided in a five-dose glass ampoule containing an actual fill volume of 3.1 mL ± 0.1 mL. Each 0.5 mL of adjuvanted diluent contains 125 µg Al_3+ formulated in 0.9% Sodium Chloride. The adjuvanted diluent must be stored between +2 °C to +8 °C and not be frozen.

Adjuvanted MCV-5

The adjuvanted MCV-5 is prepared by reconstituting one vial of MCV-5 with a single ampoule of adjuvant containing diluent. For each participant, 0.5 mL dose will be withdrawn from the reconstituted five-dose adjuvanted MCV-5 vaccine vial using a sterile needle and syringe. For the purpose of this study one vial of reconstituted adjuvanted MCV-5 will be used for only one participant.

Non-Adjuvanted MCV-5

The non-adjuvanted MCV-5 is prepared by reconstituting one vial of MCV-5 with a 3.1 mL of 0.9% Sodium Chloride Injection, USP. For each participant, 0.5 mL dose will be withdrawn from the reconstituted five-dose non-adjuvanted MCV-5 vaccine vial using a sterile needle and syringe.

4.4.1.2 Menactra®

After inspecting and confirming visually for particulate matter and discoloration 0.5 mL dose of vaccine is to be withdrawn from the single-dose vial using a sterile needle and syringe. The single dose 0.5 mL vaccine will be given via intramuscular injection using a needle and syringe in the deltoid muscle.

4.4.2 Method of Assigning Participants to Treatment Groups (Randomization)

The randomization scheme will be generated and maintained by the Statistical and Data Management Group (SDMG) at the Emmes Corporation, Rockville, MD. Enrollment will be performed online using the enrollment module of AdvantageEDC℠, the Emmes Corporation's electronic data capture (EDC) system. Randomization will occur on the day participants are to receive their first study vaccination, after confirmation of eligibility and immediately prior to vaccination.

Eligible participants will be randomized and assigned in a 1:1:1 ratio to the following three treatment groups:

- Adjuvanted Study vaccine (MCV-5),
- Non-adjuvanted Study vaccine (MCV-5),
- Reference vaccine (Menactra®, ACYW).

4.4.3 Blinding

The study and reference vaccines will be prepared and administered by the licensed unblinded pharmacist. All follow-up safety and efficacy evaluations will be performed by blinded clinic staff.

The unblinded pharmacist will refer to the Treatment Key provided for the trial by Emmes to determine the treatment for the participants. The pharmacist will maintain an open label code (provided by Emmes) under locked/secured conditions and will follow the randomization code.

A study-specific emergency unblinding request form has been developed for this study. The Emmes study medical monitor or the unblinded study pharmacist on site responds to requests for emergency unblinding: the release of the treatment codes is made only if necessary to ensure that the participant receives appropriate clinical care.

4.5 Immunogenicity and Safety Variables

The following section describes the collection of immunogenicity and safety variables. For a detailed schedule of activities refer to Appendix I of the protocol. For a list of the primary and secondary immunogenicity and safety variables, refer to section 3.2 of the SAP.

4.5.1 Safety Variables

The safety variables to be assessed are adverse events (AEs), serious adverse events (SAEs), and multiple clinical safety laboratory [including white blood cells (WBC), hemoglobin (HgB), platelets, alanine aminotransferase (ALT), albumin, total bilirubin, and serum creatinine], physical exam, and

vital sign parameters. Solicited systemic and injection site reactions within 7 days of vaccination will be collected. If a solicited sign or symptom has started during the seven days post-vaccination and continues, it will continue to be reported as a reactogenicity symptom. Only when the reactogenicity event is considered an SAE, as defined below, will it be reported on an AE/SAE form in addition to the reactogenicity form. Any symptom starting after seven days post-vaccination will be recorded as an AE. Unsolicited AEs within 28 days of the vaccination will also be collected. SAEs will be collected through Day 180.

4.5.1.1 Reactogenicity Events

Reactogenicity events are adverse events that are common and known to occur following the administration of the study vaccine. These events will be collected in a standard, systematic format using a graded scale based on functional assessment or magnitude of reaction. The reactogenicity adverse events are solicited local injection site reactions and systemic reactions collected on memory aids and assessed by the site at clinic visits. The local symptoms assessed are pain at injection site, erythema at injection site, and swelling at injection site. The systemic symptoms assessed are elevated oral temperature, headache, fatigue/malaise, joint pain/arthralgia, muscle pain/myalgia, diarrhea, anorexia, chills and vomiting.

4.5.1.2 Unsolicited Adverse Events

An adverse event is any untoward medical occurrence in humans, whether or not considered vaccine related, that occurs after the vaccination during the conduct of a clinical trial. Any change from baseline assessment of clinical status, ECGs, routine laboratory tests, X-rays, physical examinations, etc., that is considered clinically significant by the PI is considered an AE.

AEs, including non-solicited injection site and systemic reactions not meeting the criteria for "SAEs" will be captured on the appropriate case report form. All AEs will be followed until resolution or stability or until the participant's participation in the study ends. Resolution of an AE is defined as the return to pretreatment status or stabilization of the condition with the expectation that it will remain chronic. AEs will be graded for severity and relationship to study product. AEs will also be coded by MedDRA® version 19.1 or higher for preferred term and system organ class.

The study site will assign severity grades to indicate the severity of adverse events and reactions. The severity grading criteria are provided in Appendix III of the Protocol and grades AEs from Mild (Grade 1) to Life Threatening (Grade 4).All AEs leading to death are Grade 5 events. AEs are graded with the worst severity grade during the illness/symptom.

When assessing causality of an AE to study product, the PI should consider whether there is a reasonable possibility that the study product caused the event. Reasonable possibility implies there is evidence to suggest that the study product caused the reported event. An affirmative answer designates the event as a suspected adverse reaction, and the AE is considered "related". If the answer is no, then the AE is considered "unrelated". The causality assessment is made on the basis of the available information at the reporting time point. Assessment of causality can change according to follow-up information.

4.5.1.3 Serious Adverse Events

An SAE, including a serious suspected adverse reaction or serious adverse reaction as determined by the PI or the Sponsor, is any event that results in any of the following outcomes:

- Death;
- Life-threatening adverse event (Life-threatening means that the study participant was, in the opinion of the PI or Sponsor, at immediate risk of death from the event as it occurred);
- Inpatient hospitalization or prolongation of existing hospitalization;
- Persistent or significant disability or incapacity or substantial disruption of the ability to conduct normal life function, or;
- Congenital abnormality/birth defect;
- Important medical events that may not result in one of the above outcomes but may jeopardize the health of the study participant or require medical or surgical intervention to prevent one of the outcome listed in the above definition of serious event.

All SAEs will be:

- Recorded on the appropriate SAE report form and sent to the Emmes Coordination Center within 24 hours of the site's knowledge of the event.
- Reported to the Emmes medical monitor who in turn will pass on the information to the Sponsor and SIIPL
- Reported to the site's Independent Safety Monitor
- Reviewed and followed until the event is resolved or determined to be irreversible, chronic, or stable by a study physician

SAEs will be collected on each participant for 180 days after vaccination.

4.5.2 Immunogenicity Variables

Immunogenicity testing for Meningococcal serogroups A, C, Y, W and X specific antibodies using rSBA assay will be performed on sera collected at baseline (Day 1) and 28 days post vaccination (Day 29).The rSBA assay will be conducted at Vaccine Evaluation Unit at Public Health England (PHE) in Manchester UK. Additional immunogenicity assays may be performed by research laboratories to further evaluate post-vaccination immune responses. These exploratory analyses may be done on a sub-sample of participants' sera, if remaining specimen volume is adequate.

5 SAMPLE SIZE CONSIDERATIONS

Since this study is a Phase 1 trial it is designed to provide preliminary safety and immunogenicity data that may support testing the study product in additional larger cohorts in adults and in age-descending studies.

With 20 vaccine recipients per vaccine group, this study's design allows a greater than 90% chance of observing an adverse event (AE) that has an 11% chance of occurrence. Conversely, if no AEs are observed in 20 vaccine recipients, the study will be able to rule out AEs occurring at a rate of approximately 14% based on the upper bounds of the one-sided 95% Confidence Interval (CI).

No formal statistical hypothesis testing is planned for this first time in human Phase 1 study whose objectives are aimed to descriptively evaluate the safety and immunogenicity profile of the study.

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, quartiles, and range (maximum and minimum). The number and percent of participants (based on the population sample size) of observed levels will be reported for all categorical measures. In general, all data will be listed, sorted by treatment and participant, and when appropriate by visit number within participant. All summary tables will be structured with a column for each treatment in the order of adjuvanted MCV-5, non-adjuvanted MCV-5, and Menactra® and will be annotated with the total population size relevant to specific tables/treatment, including any missing observations.

6.2 Timing of Analyses

Analysis of all available safety data up to Day 29 post-vaccination for all 60 participants and all immunogenicity data for the first 30 participants will be performed as soon as the immunogenicity data become available (see Section 6.6). The final analysis will be performed after the completion of the study. Extensive safety monitoring will be ongoing throughout the study.

6.3 Analysis Populations

A tabular listing of all participants, visits, and observations excluded from the full analysis and per protocol populations will be provided in Listing 16.2.3.

6.3.1 Enrolled Population

All screened participants who provide informed consent (IC), regardless of the participant's randomization and treatment status in the trial, will be included in the enrolled population.

6.3.2 Full Analysis Population

All participants in the enrolled population who were randomized and received a study vaccination will be included in the Full Analysis (FA) Population. All safety analyses will be performed using this population. Treatment groups for safety analysis will be assigned according to the actual treatment received at Day 1.

6.3.3 Per Protocol Population

All participants in the FA population who are assigned the study vaccination with no major protocol violations that are determined to potentially interfere with the immunogenicity assessment of the study vaccine and who have at least one immunogenicity assessment will be included in the Per Protocol (PP) population. This population will serve as the primary analysis population for the immunogenicity endpoints.

The criteria for exclusion of participants from the PP population will be established before breaking the blind and will be based on the blinded review of protocol violations.

6.4 Covariates and Subgroups

There is no a priori plan to summarize the immunogenicity or safety endpoints for covariates or subgroups. The protocol does not define any formal subgroup analyses and the study is not adequately powered to perform subgroup analyses.

6.5 Missing Data

In general, all missing data will be treated as missing completely at random and no imputation will be performed except for the safety endpoints as described below. Non-analyzable data (e.g., due to major protocol violations) will be documented in the deviations. For immunogenicity data where the antibody titer is below 1:8 (< 8), an arbitrary value of half the assay's cut-off value, 4, will be used in the analyses for those values.

If some safety data are available for a participant in the FA population, but respective secondary endpoint related data are missing, then the participant will be included in the safety analysis and data will be treated as follows for immediate AEs, unsolicited AEs and serious adverse events (SAEs).

- If Severity is missing for any AE, then it will be considered as an AE of maximum severity (Grade 3) "Severe", unless it is captured as SAE.
- If "Relationship" is missing, then it will be considered as "Related" to the vaccine administered.
- If, for Start date, the day of event/condition is missing due to any adverse event, then it will be imputed as the date of last dose of study vaccine.
- If the Stop date of an adverse event is missing, then it will be treated as ongoing.

For solicited adverse events, the following assumptions will be made:

- If dates are missing, but symptoms are reported, then the day post vaccination will be used to calculate the date of the symptom.
- If a symptom is not reported at any time through Day 7, then no imputation for missing data will be performed. The data will be summarized as not reported on the tables.

6.6 Interim Analyses and Data Monitoring

Extensive safety monitoring will be provided for this protocol. The principal investigator (PI) and/or designated site staff will be responsible for continuous close safety monitoring of all study participants and for alerting the Sponsor if unexpected concerns arise or pause criteria are met.

To facilitate the planning of follow-up trials, analysis of unblinded primary safety data up to Visit 4 (Day 29), by treatment group, will be made available to the Sponsor after all participants have completed this visit and their data have been cleaned and verified. Immunogenicity data for the first 30 recruited participants are expected to be available at the same time and will be part of this analysis. Should recruitment be delayed, this interim analysis will proceed with safety data for available participants up to Day 29 as soon as the immunogenicity data for the first 30 participants becomes available.

6.6.1 Safety Review Committee

A Safety Review Committee (SRC), comprised of the PI, a medical expert with experience in vaccine pharmacovigilance not involved with the study, the Emmes medical monitor, SIIPL and PATH medical officer will monitor safety throughout the duration of the study. The Emmes study statistician with assistance of the data management staff will prepare safety reports as needed for SRC discussions. During the vaccination period, the SRC will review weekly safety data. At any time during the study, the Emmes Coordinating Center will notify the SRC of ad hoc review if pause criteria may have been met. The SRC reviews will be summarized with consensus recommendations to the study Sponsor as to whether there are safety concerns and whether the study should continue without change, be modified, or be stopped. The SRC may request review of unblinded safety data by the pharmacovigilance expert in its deliberation. SRC consensus recommendations regarding modifying or stopping further enrolment may involve Sponsor consultation with the local regulatory authority.

6.6.2 Study Pause Rule

The following study pause rules will automatically pause or halt further vaccinations. However participants already enrolled will continue to be followed for safety during the pause. These pause rules refer to suspected adverse reactions and will be triggered automatically if any of the events described below are met during the conduct of the study:

- One or more participants experience a serious adverse reaction.
- One or more participants experience a Grade 4 injection site reaction.
- Two or more participants experience the same Grade 3 injection site reaction.
- Two or more participants experience the same severe (Grade 3) systemic reactogenicity signs or symptoms, within seven days following vaccination.
- Two or more participants experience the same vaccine-related Grade 3 or higher clinical (including fever) or laboratory abnormality.

6.7 Multicenter Studies

This is a single site study.

6.8 Multiple Comparisons/Multiplicity

This is a FIH study so the primary purpose of statistical comparisons is to screen out potential solicited reactogenicity events that need further clinical evaluation. Therefore, the statistical analyses are not considered formal statistical hypothesis tests and it is acknowledged that there will be inflated Type I errors (i.e., inflated false statistical significances) from performing multiple unadjusted comparisons.

7 STUDY PARTICIPANTS

7.1 Participant Disposition

Screened participants who were ineligible for enrollment in the study will be summarized by inclusion and exclusion criteria and other reasons for ineligibility (Table 14.1.1). The composition of analysis populations, including reasons for participant exclusion, by treatment group, is presented in Table 14.1.2.

The disposition of participants in the study will be tabulated by treatment group and overall (Table 14.1.3). This table will show the number of participants screened, enrolled, received vaccination, completed Visit 4 (Day 29), completed follow-up, and in PP population.

A flowchart presenting the disposition of study participants, adapted from the CONSORT statement [32] will be included (Figure 14.1.1). The flowchart includes the number of participants eligible, enrolled and randomized, lost to follow-up, and analyzed, by treatment group.

A listing of participants who discontinued or terminated early from the study and who were excluded from the FA population and the PP population will be included in Listings 16.2.1 and 16.2.3, respectively.

7.2 Protocol Deviations

A summary of protocol deviations will be presented by the deviation category, reason, and treatment group in Table 10.2.1. This table will provide both the number of participants and the number of deviations for each category and treatment group.

All participant-specific protocol deviations and non-participant-specific protocol deviations will be included as data listings (Listings 16.2.2.1 and 16.2.2.2, respectively).

TABLE 10.2.1:
Distribution of Protocol Deviations by Category, Reason, and Treatment Group

Category	Deviation Reason	Adjuvanted MCV-5 (N=X)		Non-adjuvanted MCV-5 (N=X)		Menactra® (N=X)		All Participants (N=X)	
		# of Parti.	# of Dev.	# of Parti.	# of Dev.	# of Parti.	# of Dev.	# of Parti.	# of Dev.
Eligibility/enrollment	Any type	x	x	x	x	x	x	x	x
	Participant illness	x	x	x	x	x	x	x	x
	Unable to comply	x	x	x	x	x	x	x	x
	Participant refusal	x	x	x	x	x	x	x	x
	Clinic error	x	x	x	x	x	x	x	x
	Pharmacy error	x	x	x	x	x	x	x	x
	Laboratory error	x	x	x	x	x	x	x	x
	Investigator/study decision	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x
Product administration schedule	Any type	x	x	x	x	x	x	x	x
	Participant illness	x	x	x	x	x	x	x	x
	Unable to comply	x	x	x	x	x	x	x	x
	Participant refusal	x	x	x	x	x	x	x	x
	Clinic error	x	x	x	x	x	x	x	x
	Pharmacy error	x	x	x	x	x	x	x	x
	Laboratory error	x	x	x	x	x	x	x	x
	Investigator/study decision	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x
Follow-up visit schedule	Any type	x	x	x	x	x	x	x	x
	Participant illness	x	x	x	x	x	x	x	x
	Unable to comply	x	x	x	x	x	x	x	x
	Participant refusal	x	x	x	x	x	x	x	x
	Clinic error	x	x	x	x	x	x	x	x
	Pharmacy error	x	x	x	x	x	x	x	x
	Laboratory error	x	x	x	x	x	x	x	x
	Investigator/study decision	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x

TABLE 10.2.1:
Distribution of Protocol Deviations by Category, Reason, and Treatment Group (*continued*)

Category	Deviation Reason	Adjuvanted MCV-5 (N=X)		Non-adjuvanted MCV-5 (N=X)		Menactra® (N=X)		All Participants (N=X)	
		# of Parti.	# of Dev.	# of Parti.	# of Dev.	# of Parti.	# of Dev.	# of Parti.	# of Dev.
Protocol procedure / assessment	Any type	x	x	x	x	x	x	x	x
	Participant illness	x	x	x	x	x	x	x	x
	Unable to comply	x	x	x	x	x	x	x	x
	Participant refusal	x	x	x	x	x	x	x	x
	Clinic error	x	x	x	x	x	x	x	x
	Pharmacy error	x	x	x	x	x	x	x	x
	Laboratory error	x	x	x	x	x	x	x	x
	Investigator/study decision	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x
Product administration	Any type	x	x	x	x	x	x	x	x
	Participant illness	x	x	x	x	x	x	x	x
	Unable to comply	x	x	x	x	x	x	x	x
	Participant refusal	x	x	x	x	x	x	x	x
	Clinic error	x	x	x	x	x	x	x	x
	Pharmacy error	x	x	x	x	x	x	x	x
	Laboratory error	x	x	x	x	x	x	x	x
	Investigator/study decision	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x
Blinding policy / procedure	Any type	x	x	x	x	x	x	x	x
	Participant illness	x	x	x	x	x	x	x	x
	Unable to comply	x	x	x	x	x	x	x	x
	Participant refusal	x	x	x	x	x	x	x	x
	Clinic error	x	x	x	x	x	x	x	x
	Pharmacy error	x	x	x	x	x	x	x	x
	Laboratory error	x	x	x	x	x	x	x	x
	Investigator/study decision	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x

[Implementation: Only include the Deviation categories and reasons reported in the study.]

8 IMMUNOGENICITY EVALUATION

The secondary and exploratory immunogenicity outcomes for the study are based on the rSBA titer for Meningococcal serogroup A, C, Y, W and X specific antibodies. For each participant, the rSBA titer will be measured at Day 1 prior to vaccination and at Day 29 (28 days post vaccination).All immunogenicity analyses will be conducted using the PP population and FA population. Individual participant data listings of immunogenicity will be presented in Listing 16.2.6.

Due to the hypothesis generating nature of multiple statistical comparisons for immunogenicity associated with multiple endpoints for this early phase FIH study, all estimations will be carried out using a two-sided 5% Type I error rate without an adjustment for multiple comparisons.

8.1 Secondary Endpoint - a 4-fold response in rSBA titer

The percentage of participants with a 4-fold response in rSBA titer against serogroups A, C, W, Y and X will be defined as follows:

- For participants with a pre-vaccination rSBA < 8, a post-vaccination titer >=32.
- For participants with a pre-vaccination rSBA titer ≥ 8, a post-vaccination rSBA titer of at least 4 times the pre-vaccination titer.

The number and percentage of participants with a 4-fold response in rSBA titer will be summarized at Day 29, along with two-sided 95% exact confidence intervals (CIs) for each of the proportions. Two-sided exact 95% CIs for the three pair-wise proportion differences between the three treatment groups will be computed using the unconditional exact method proposed by Chan and Zhang (1999).(Note: In SAS, this is the RISKDIFF(METHOD=FMSCORE) option in PROC FREQ).

Table 14.2.1.1 will summarize the number and percentage of participants with a 4-fold response in rSBA titer for each of the five serogroups and 95% CIs for each treatment group and treatment group comparison. CIs will be visualized graphically in Forest plots as depicted in Figure 14.2.1.2.

8.2 Secondary Endpoint - percentages of participants with rSBA titer ≥ cut-off

The number and percentages of participants with rSBA titer ≥8 and ≥128 for each of the five serogroups will be summarized at Day 1 and Day 29, along with two-sided 95% exact confidence intervals (CIs) for each of the proportions. Two-sided exact 95% CIs for the three pair-wise proportion differences between the three treatment groups will be computed using the unconditional exact method proposed by Chan and Zhang (1999).(Note: In SAS, this is the RISKDIFF(METHOD=FMSCORE) option in PROC FREQ).

Table 14.2.2.1 will summarize the number and percentages of participants with rSBA titer ≥8 and ≥128 for each of the five serogroups and 95% CIs for each treatment group and treatment group comparison at Day 1 and Day 29. CIs will be visualized graphically in Forest plots as depicted in Figure 14.2.2.2.

8.3 Secondary Endpoint - Geometric Mean Titers

The number of observations, geometric mean titer (GMT) and geometric 95% confidence interval will be reported. For rSBA titers below the assay detection of 8, an arbitrary value of half of the assay's cut-off (or 4) will be used. The GMT for each of the 5 serogroups will be calculated as the exponentiation of the mean of the natural logarithms of the rSBA titer. The two-sided 95% confidence intervals of GMTs for serogroups A, C, W, Y, and X will be calculated by exponentiating the lower and upper limits of the 95% CIs of the natural logarithms of the rSBA titer. The computation of the 95% CIs of the natural logarithms of the rSBA titer will be based on the t-distribution. Two-sided 95% CIs for the ratios of GMTs between treatment groups will be constructed using the log normal distribution. The log values will be used to construct a CI using the t-distribution for the mean difference between three pair-wise treatment groups. The mean difference and the corresponding CI limits will then be exponentiated to obtain the GMT ratio and the corresponding CI. If the values deviate from the log normal distribution, a non-parametric method may be used for the analysis of the GMT.

Table 14.2.3.1 will summarize the GMTs and 95% CIs per serogroup for each treatment group and treatment group comparison at Day 1 and Day 29. CIs will be visualized graphically in Forest plots as depicted in Figure 14.2.3.2.

9 SAFETY EVALUATION

9.1 Demographic and Other Baseline Characteristics

Summaries of sex, ethnicity, and race will be presented by treatment group and overall in Table 14.1.4.1 for all participants in the FA population. Ethnicity will be categorized as Hispanic or Latino, or not Hispanic and not Latino. In accordance with NIH reporting policy, participants may self-designate as belonging to more than one race or may refuse to identify a race, the latter reflected in the CRF as “No” to each racial option. Participants belonging to more than one race will be categorized as multi-racial and participants refusing to identify with a race will be classified as unknown on the table. Age will be summarized in years by treatment group and overall in Table 14.1.4.2.

Individual participant listings will be presented for all demographic characteristics (Listing 16.2.4.1).

9.2 Concurrent Illnesses and Medical Conditions

All current illnesses and past pre-existing medical conditions will be coded using MedDRA® dictionary version 19.1 or higher. Summaries of participant's pre-existing medical conditions will be presented by MedDRA® system organ class (SOC) and preferred term (PT) and treatment group (Table 14.1.5) for all participants in the FA population.

Individual data listings will be presented for all pre-existing medical conditions (Listing 16.2.4.2).

9.3 Measurements of Treatment Compliance

All participants were to receive a single dose of study product administered in the clinic. Any participants who were enrolled but not vaccinated will be presented by treatment group and by site as part of the

participant disposition table (Table 14.1.3).A summary of the dates of vaccination will be presented by treatment group in Table 14.1.6.

9.4 Adverse Events

All safety analyses will be presented using the FA population.

Any medical condition that is present at the time that the participant is screened will be considered baseline and not reported as an AE, unless it worsens in severity or increases in frequency during the study. A treatment-emergent adverse event is one that is observed after baseline or worsens in severity or increases in frequency during the study. Solicited and unsolicited adverse events (AEs) will be analyzed separately. When calculating the incidence of AEs (i.e., on a per participant basis), each participant will be counted once and any repetitions within a participant will be ignored; the denominator will be the total population size. For tables summarizing severity, the severity will be summarized as the maximum severity experienced by that participant for a particular AE or symptom. All adverse events reported will be included in the summaries and analyses.

9.4.1 Primary Summary of Adverse Events

The primary safety objective is to evaluate the safety of adjuvanted and non-adjuvanted formulations of MCV-5 vaccine in healthy adults. To accomplish this objective, an overall summary of adverse events will be presented in Table 14.3.1.1. The table will summarize the number and percentage of participants in each treatment group experiencing the following:

- immediate solicited AEs within 60 minutes post-vaccination;
- solicited local or systemic post vaccination reactogenicity reactions within seven days following vaccination (Days one through seven);
- any SAE;
- any unsolicited AE;
- any Grade 2 or greater solicited local or systemic post vaccination reactions within seven days following vaccination;
- any Grade 2 or greater unsolicited AE;
- any unsolicited AE judged to be related to study product; and
- any Grade 2 or greater unsolicited AE following vaccination judged to be related to study product.

Note: summaries of unsolicited AEs will include SAEs.

9.4.2 Solicited Events and Symptoms

Systemic and local solicited adverse events were collected 60 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: elevated oral temperature, headache, fatigue/malaise, joint pain/arthralgia,

muscle pain/myalgia, diarrhea, anorexia, chills and vomiting. Local events include: pain at injection site, erythema at injection site, and swelling at injection site.

The proportion of participants, within each treatment arm, 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 option) will be presented (Table 14.3.1.2).

For each systemic and local event, any systemic event, any local event, and any solicited event, the maximum severity over 7 days after each vaccination will be summarized for the FA population. The number and percentage of participants reporting each event will be summarized by the maximum severity for each treatment group. For each event the denominator is the number of participants with non-missing data for the specific event (Table 14.3.1.3).

The number and percentage of participants reporting any solicited adverse event, any local symptom, any systemic symptom and for each individual symptom will be summarized for each day post vaccination by Treatment group (Table 14.3.1.4).The percent of participants reporting any systemic solicited event and any local solicited event will be displayed graphically in a bar chart in Figures 14.3.1.5.1 and 14.3.1.5.2, respectively.

Fisher's exact test will be used to compare the proportion of participants with solicited local and systemic reactogenicity events between each of the MCV-5 groups and the Menactra® group. The results will be summarized in Table 14.3.1.6.

The primary purpose of the statistical comparisons is to screen out potential solicited reactogenicity events that need further clinical evaluation. Therefore, they are not considered formal statistical hypothesis tests and it is acknowledged that there will be inflated Type I errors (i.e., inflated false statistical significances) from performing multiple unadjusted comparisons.

Solicited adverse events by participant will be presented in Listing 16.2.7.1.1 for systemic events and Listing 16.2.7.1.2 for local events.

9.4.3 Unsolicited Adverse Events

The proportion of participants reporting at least one unsolicited adverse event will be summarized by MedDRA® system organ class and preferred term for each treatment group and overall. Denominators for percentages are the number of participants in the FA population. A 95% CI calculated using Clopper-Pearson methodology from a binomial distribution (SAS PROC FREQ with a binomial option) will be presented for each MedDRA® system organ class and preferred term (Table 14.3.1.7)

Unsolicited adverse events by participant will be presented in Listing 16.2.7.2.

The following summaries for unsolicited adverse events will be presented by treatment group:

- Participant level summary of maximum severity and relationship to study product by MedDRA® SOC and PT (Table 14.3.1.8.1);
- Participant level summary of related unsolicited events by maximum severity, MedDRA® SOC and PT (Table 14.3.1.8.2);

- Participant incidence of unsolicited adverse events over time by MedDRA® SOC and PT (Days 1-8, Days > 8) (Table 14.3.1.9.1);
- Participant incidence of related unsolicited adverse events over time by MedDRA® SOC and PT (Days 1-8, Days > 8) (Table 14.3.1.9.2);
- Total frequency of adverse events over time by MedDRA® SOC and PT (Days 1-8, Days > 8) (Table 14.3.1.10);
- Participant listing of non-serious adverse events of moderate or greater severity (Table 14.3.2.2);
- Bar chart of the frequency of events for non-serious adverse events by maximum severity and MedDRA® SOC (Figure 14.3.1.11);

9.5 Deaths, Serious Adverse Events and other Significant Adverse Events

A listing of deaths and SAEs (Table 14.3.2.1) will be presented including Participant ID, Adverse Event Description, number of days post dose and number of days post dose it became serious, Reason Reported as an SAE, Relationship to Treatment, Alternate Etiology if not Related, Outcome, Duration of Event (days), and whether participant discontinued due to the AE.

9.6 Pregnancies

For any participants in the FA population who became pregnant during the study, every attempt was made to follow these participants to completion of pregnancy to document the outcome, including information regarding any complications with pregnancy and/or delivery. If more than 5 pregnancies are reported, a table summarizing the total pregnancies, number of live births, and number of spontaneous abortions, elective abortions or still births by treatment will be presented. In addition, a listing of all pregnancies and outcomes will be presented (Listing 16.2.11).

9.7 Clinical Laboratory Evaluations

Safety clinical laboratory evaluations will be performed at Screening and at Day 8 at the site's designated laboratory and will include: hemoglobin (HgB), white blood cells (WBC), platelet counts, alanine transaminase (ALT), albumin, total bilirubin, and creatinine. In addition, screening laboratory tests will include serum HCG pregnancy tests, for females of childbearing potential only, and screening for HIV, HCV and HBV.

The distribution of laboratory results by severity, scheduled study day and treatment group will be presented in Table 14.3.4.1 for any laboratory parameter and each individual laboratory parameter. The observed and change from screening measurements will be summarized using descriptive statistics including mean, standard deviation, median, 25th and 75th percentiles, minimum and maximum values by scheduled study day, for each laboratory parameter in Table 14.3.4.2. Graphical presentation of changes in laboratory values will be presented using box plots as depicted in Figure 14.3.4.3 for each laboratory parameter. Unscheduled or repeated follow-up tests for medical or safety reasons will be listed and included in the maximum post-baseline row on the summary tables, but will otherwise be excluded from tabular and graphical summaries.

Participant visits with abnormal laboratory results, Grade 1 severity or higher, will be presented in Table 14.3.4.4.

Listings of all individual clinical laboratory results will be provided by hematology, biochemistry and serology (Listings 16.2.8.1-16.2.8.3, respectively).Results meeting the protocol defined toxicity of Grade 1 or higher will have their grade provided in parentheses after the result.

9.8 Vital Signs and Physical Evaluations

Vital sign measurements included systolic blood pressure, diastolic blood pressure, heart rate and oral temperature, along with height and weight at Screening. Vital signs were assessed at Screening, Day 1, Day 8, Day 29 and Day 85. Systolic Abnormalities in systolic and diastolic blood pressure will be tabulated by grade, visit and treatment group (Table 14.3.5.1). Diastolic and systolic blood pressure and heart rate will be summarized over time graphically using box plots for participants in the FA population (Figure 14.3.5.2).Listings of all individual vital sign measurements will be provided in Listing 16.2.9.1.

Physical Examinations were performed at Screening, Day 1, Day 8, Day 29, and Day 85. Any abnormal or change in physical examination data from Day 1 will be listed for each participant by visit and treatment group. The following body systems will be assessed: HEENT, Skin, Back, Neck, Chest, Abdomen, Neurological, and Musculoskeletal (Listing 16.2.9.2).

9.9 Concomitant Medications

Concomitant medications are those medications taken at the same time or after vaccination. Prior medications are those medications that were started and stopped prior to vaccination. Both prior and concomitant medications will be classified according to a standardized drug code. The use of prior and concomitant medications taken during the study will be summarized by medication name and treatment group (Table 14.3.6).

Individual participant listings will be presented for all prior and concurrent medications (Listing 16.2.10).

10 REPORTING CONVENTIONS

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

11 TECHNICAL DETAILS

SAS version 9.3 or above will be used to generate all tables, figures and listings.

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

13 REFERENCES

14 TABLES, FIGURES, AND LISTINGS

GENERAL ASSUMPTIONS:

Implementation Notes:

- All figures presented are sample figures and do not include real study data.
- The number of participants presented are not real study data, but generic examples of how to present the data for the different treatment groups. The number of participants will be dependent upon the data observed in the study.
- The total number of participants for each treatment group are not actual numbers, but generic examples of how to present the data for the different treatment groups. The total number of participants will be dependent upon the data observed in the study.

14.1 Demographics

FIGURE 14.1.1:
Consort Flow Diagram

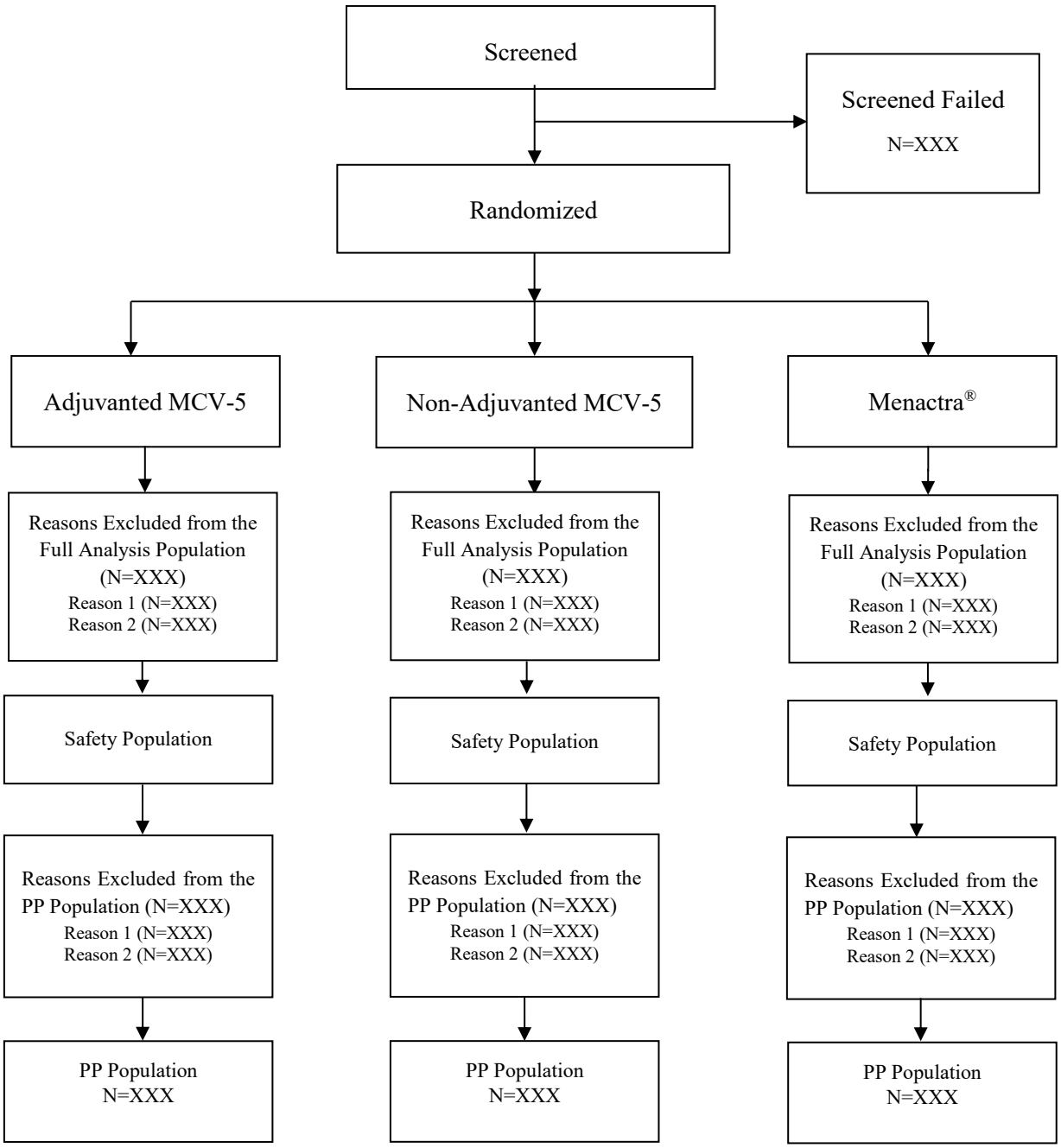


TABLE 14.1.1:
Ineligibility Summary of Screen Failures

Inclusion/ Exclusion Category	Inclusion/Exclusion Criterion	Number of Times Item Marked Ineligible
Any	Any inclusion/exclusion criterion	X
Inclusion	Any inclusion criterion	X
	1. Aged 18 to 45 years	X
	2. Read, signed, and dated informed consent form	X
	3. Healthy as established at screening	X
	4. Lab results fall within the protocol parameters	X
	5. Ability to understand and comply with study procedures	X
	6. Agrees to adequate contraception, if applicable	X
	7. Negative pregnancy test, if applicable	X
Exclusion	Any exclusion criterion	X
	1. Previous vaccination against *Neisseria meningitidis*	X
	2. Known exposure to *Neisseria meningitidis* in the past.	X
	3. History of meningitis or seizures or any neurological or psychiatric disorder	X
	4. Receipt of other vaccine within 30 days prior or after vaccination	X
	5. Use of other experimental agents within 30 days prior or after vaccination	X
	6. History of allergic disease or known hypersensitivity	X
	7. History of SAE following Tetanus Toxoid, Diphtheria Toxoid or CRM	X
	8. History of Guillain-Barré syndrome	X
	9. Confirmed or suspected immunosuppressive or immune-deficient condition	X
	10. Family History of congenital or hereditary immunodeficiency	X
	11. Chronic administration of immune-suppressants 6 months before vaccination	X
	12. Laboratory confirmed Hepatitis B, Hepatitis C, or HIV	X
	13. Major congenital defects or serious chronic illness	X
	14. Acute or chronic, clinically significant pulmonary, cardiovascular, hepatic or renal functional abnormality	X
	15. Known bleeding disorders	X
	16. Receipt of blood products or immunoglobulin 3 months before vaccination	X
	17. History or signs of alcohol or substance abuse	X
	18. Pregnant or breastfeeding	X
	19. Body Mass Index equal to or above 30	X
	20. Other conditions	X
Other	Other Reasons	X
	Time commitment	X
	Concern of potential risks	X
	Number of procedures/blood draws	X
	Unable to contact participant	X
	Other	X

Note: SAE = serious adverse event; HIV = human immunodeficiency virus.

TABLE 14.1.2:
Analysis Populations by Treatment Group

Analysis Populations	Reason Participants Excluded	Adjuvanted MCV-5 (N=X)		Non-adjuvanted MCV-5 (N=X)		Menactra® (N=X)		All Participants (N=X)	
		n	%	n	%	n	%	%	n
Full Analysis Population	Any Reason	x	x.x	x	x.x	x	x.x	x	x.x
	Not Randomized	x	x.x	x	x.x	x	x.x	x	x.x
	Randomized but not vaccinated	x	x.x	x	x.x	x	x.x	x	x.x
Per Protocol Population	Any Reason	x	x.x	x	x.x	x	x.x	x	x.x
	No Valid Immunogenicity Assessment	x	x.x	x	x.x	x	x.x	x	x.x
	Major Protocol Violation	x	x.x	x	x.x	x	x.x	x	x.x

N=Number of participants enrolled in the study.

TABLE 14.1.3:
Participant Disposition by Treatment Group

Participant Disposition	Adjuvanted MCV-5 (N=XX)		Non-adjuvanted MCV-5 (N=XX)		Menactra® (N=XX)		All Participants (N=XX)	
	n	%	n	n	n	%	n	%
Screened							xx	--
Enrolled/Randomized	xx	100.0	xx	100.0	xx	100.0	xx	100.0
Received Vaccination	xx	xx.x	xx	xx.x	xx	xx.x	xx	xx.x
Completed Visit 3 (Day 8)	xx	xx.x	xx	xx.x	xx	xx.x	xx	xx.x
Completed Visit 4 (Day 29)	xx	xx.x	xx	xx.x	xx	xx.x	xx	xx.x
Completed Visit 5 (Day 85)	xx	xx.x	xx	xx.x	xx	xx.x	xx	xx.x
Completed Follow-up at 6 Months Post-Vacc [a]	xx	xx.x	xx	xx.x	xx	xx.x	xx	xx.x
Per Protocol population [b]	xx	xx.x	xx	xx.x	xx	xx.x	xx	xx.x
Early Termination / Reason								
Any reason	xx	xx.x	xx	xx.x	xx	xx.x	xx	xx.x
SAE (other than death)								
AE (other than SAE)								
Lost to follow-up								
Non-compliance / protocol deviation								
Voluntary withdrawal								
Withdrawn by investigator								
Termination of site or study by sponsor								
Death								
Enrolled but not vaccinated								
Other								

N=Number of participants enrolled in the study.

[a] Refer to Listing 16.2.1 for reasons participants discontinued or terminated early.

[b] Refer to Listing 16.2.3 for reasons participants are excluded from the immunogenicity analysis.

TABLE 14.1.4.1:
Summary of Demographic and Baseline Characteristics by Treatment Group
- Full Analysis Population

Statistic	Adjuvanted MCV-5 (N=X)	Non-adjuvanted MCV-5 (N=X)	Menactra® (N=X)	All Participants (N=X)
Sex, n (%)				
Male	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Female	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Ethnicity, n (%)				
Not Hispanic or Latino	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Hispanic or Latino	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Not Reported	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Unknown	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Race, n (%)				
American Indian or Alaskan Native	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Asian	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Native Hawaiian or Other Pacific Islander	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Black or African American	x (x.x)	x (x.x)	x (x.x)	x (x.x)
White	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Age (years)				
Mean (SD)	x.x	x.x	x.x	x.x
Median	x.xx	x.xx	x.xx	x.xx
IQR	x	x	x	x
Range	x.x	x.x	x.x	x.x
Height (cm)				
Mean (SD)	x.x	x.x	x.x	x.x
Median	x.xx	x.xx	x.xx	x.xx
IQR	x	x	x	x
Range	x.x	x.x	x.x	x.x
Weight (kg)				
Mean (SD)	x.x	x.x	x.x	x.x
Median	x.xx	x.xx	x.xx	x.xx
IQR	x	x	x	x
Range	x.x	x.x	x.x	x.x

N = Number of participants in the Full Analysis population. n = Number of participants reporting the response.

TABLE 14.1.4.2:
Summary of Demographic and Baseline Characteristics by Treatment Group
- Per-Protocol Population

Statistic	Adjuvanted MCV-5 (N=X)	Non-adjuvanted MCV-5 (N=X)	Menactra® (N=X)	All Participants (N=X)
Sex, n (%)				
Male	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Female	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Ethnicity, n (%)				
Not Hispanic or Latino	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Hispanic or Latino	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Not Reported	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Unknown	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Race, n (%)				
American Indian or Alaskan Native	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Asian	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Native Hawaiian or Other Pacific Islander	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Black or African American	x (x.x)	x (x.x)	x (x.x)	x (x.x)
White	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Age (years)				
Mean (SD)	x.x	x.x	x.x	x.x
Median	x.xx	x.xx	x.xx	x.xx
IQR	x	x	x	x
Range	x.x	x.x	x.x	x.x
Height (cm)				
Mean (SD)	x.x	x.x	x.x	x.x
Median	x.xx	x.xx	x.xx	x.xx
IQR	x	x	x	x
Range	x.x	x.x	x.x	x.x
Weight (kg)				
Mean (SD)	x.x	x.x	x.x	x.x
Median	x.xx	x.xx	x.xx	x.xx
IQR	x	x	x	x
Range	x.x	x.x	x.x	x.x

N = Number of participants in the Full Analysis population. n = Number of participants with a response.

TABLE 14.1.5.1:
Summary of Pre-Existing Medical Conditions by Treatment Group - Full Analysis Population

	Adjuvanted MCV-5 (N=X)		Non-adjuvanted MCV-5 (N=X)		Menactra® (N=X)		All Participants (N=X)	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Medical Problem	xx	xx.x	xx	xx.x	xx	xx.x	xx	xx.x
Head	xx	xx.x	xx	xx.x	xx	xx.x	xx	xx.x
Eyes	xx	xx.x	xx	xx.x	xx	xx.x	xx	xx.x
Ears	xx	xx.x	xx	xx.x	xx	xx.x	xx	xx.x
Nose								
Throat/Mouth								
Cardiovascular								
Heart/Veins or Arteries								
Respiratory								
Gastrointestinal								
Stomach								
Intestines								
Etc.								

N= Number of participants in the Full Analysis population; n = Number of participants reporting medical history within the specified SOC. A participant is only counted once per SOC.

TABLE 14.1.5.2:
Summary of Pre-Existing Medical Conditions by Treatment Group - Per-Protocol Population

As above

14.2 Immunogenicity Analysis

TABLE 14.2.1.1(a):
Secondary Analysis of Percentages of Participants with a ≥4-fold Increase in rSBA Titer on Day 29, by Serogroup - Per Protocol Population

	Meningococcal Polysaccharide									
Treatment Group (Number of Participants)	**A**		**C**		**Y**		**W**		**X**	
	n (%)	**95% CI[a]**	**n (%)**	**95% CI[a]**	**n (%)**	**95% CI[a]**	**n (%)**	**95% CI[a]**	**n (%)**	**95% CI[a]**
≥ 4-Fold Increase										
Adjuvanted MCV-5 (N=XX)	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x
Non-adjuvanted MCV-5 (N=XX)	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x
Menactra® (N=XX)	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x
Treatment Group Difference	**%**	**95% CI[a]**	**%**	**95% CI[a]**	**%**	**95% CI[a]**	**%**	**95% CI[a]**	**%**	**95% CI[a]**
Adjuvanted MCV-5 - Non-Adjuvanted MCV-5	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x
Adjuvanted MCV-5 - Menactra®	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x
Non-Adjuvanted MCV-5 - Menactra®	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x

[a] Unconditional exact 95% CIs method proposed by Chan and Zhang (1999).

TABLE 14.2.1.1(b):
Secondary Analysis of Percentages of Participants with a ≥4-fold increase in rSBA Titer, by Serogroup - Full Analysis Population

As above

FIGURE 14.2.1.2.1:
Reverse Cumulative Distribution Curves of rSBA Titers by Serogroup, Treatment Group and Day - Per-Protocol Population

Examples

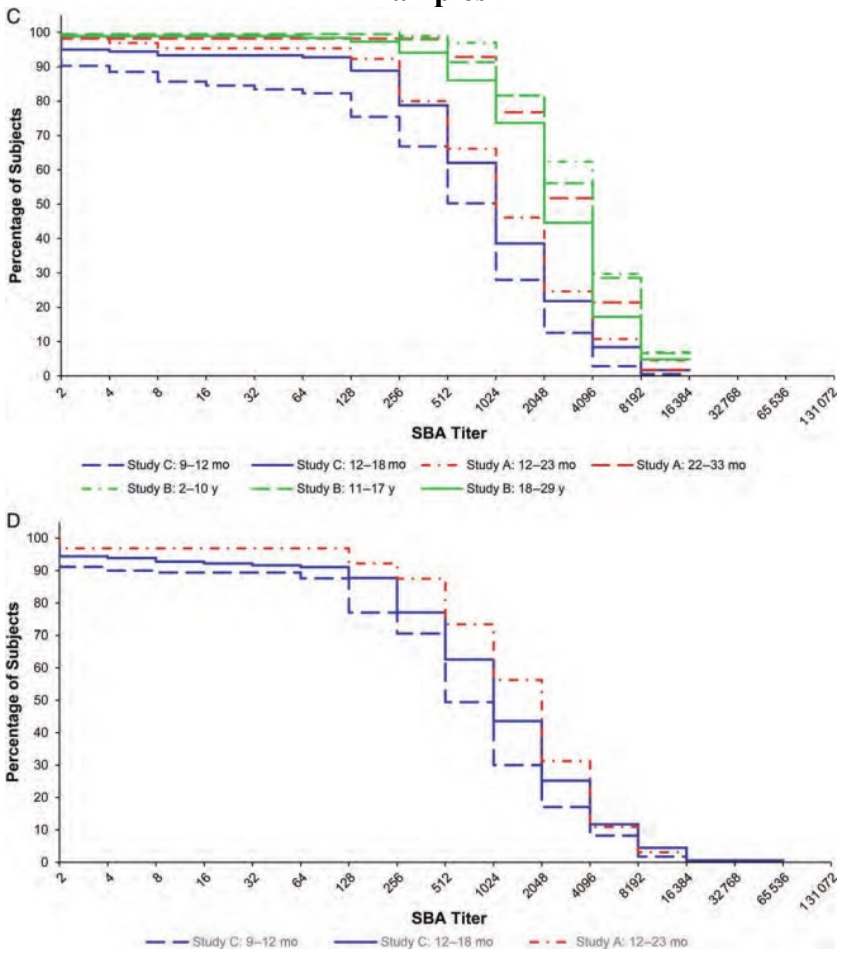


FIGURE 14.2.1.2.2:
Reverse Cumulative Distribution Curves of rSBA Titers by Serogroup, Treatment Group and Day - Full Analysis Population

As above

TABLE 14.2.2.1(a):
Secondary Analysis of Percentages of Participants with rSBA Titers ≥8, by serogroup - Per Protocol Population

Treatment Group (Number of Participants)	Meningococcal Polysaccharide									
	A		C		Y		W		X	
	n (%)	95% CI[a]	n (%)	95% CI[a]	n (%)	95% CI[a]	n (%)	95% CI[a]	n (%)	95% CI[a]
Baseline										
Adjuvanted MCV-5 (N=XX)	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x
Non-adjuvanted MCV-5 (N=XX)	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x
Menactra® (N=XX)	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x
Treatment Group Difference	**%**	**95% CI[a]**	**%**	**95% CI[a]**	**%**	**95% CI[a]**	**%**	**95% CI[a]**	**%**	**95% CI[a]**
Adjuvanted MCV-5 - Non-Adjuvanted MCV-5	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x
Adjuvanted MCV-5 - Menactra®	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x
Non-Adjuvanted MCV-5 - Menactra®	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x
Day 29										
Adjuvanted MCV-5 (N=XX)	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x
Non-adjuvanted MCV-5 (N=XX)	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x
Menactra® (N=XX)	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x	x (x.x)	xx.x - xx.x
Treatment Group Difference	**%**	**95% CI[a]**	**%**	**95% CI[a]**	**%**	**95% CI[a]**	**%**	**95% CI[a]**	**%**	**95% CI[a]**
Adjuvanted MCV-5 - Non-Adjuvanted MCV-5	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x
Adjuvanted MCV-5 - Menactra®	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x
Non-Adjuvanted MCV-5 - Menactra®	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x	xx.x	xx.x-xx.x

[a] Unconditional exact 95% CIs method proposed by Chan and Zhang (1999).

TABLE 14.2.2.1(b):
Secondary Analysis of Percentages of Participants with rSBA Titers ≥8, by serogroup - Full Analysis Population

TABLE 14.2.2.1(c):
Secondary Analysis of Percentages of Participants with rSBA Titers ≥128, by serogroup – Per-Protocol Population

TABLE 14.2.2.1(d):
Secondary Analysis of Percentages of Participants with rSBA Titers ≥128, by serogroup – Full Analysis Population

As above.

TABLE 14.2.3.1(a):
Secondary Analysis of rSBA Geometric Mean Titers per Serogroup - Per Protocol Population

Treatment Group (Number of Participants)	Meningococcal Polysaccharide									
	A		C		Y		W		X	
	GMT	95% CI	GMT	95% CI	GMT	95% CI	GMT	95% CI	GMT	95% CI
Day 1 (Baseline)										
Adjuvanted MCV-5 (N=XX)										
Non-adjuvanted MCV-5 (N=XX)										
Menactra® (N=XX)										
Treatment Group Comparisons	**Ratio**	**95% CI**	**Ratio**	**95% CI**	**Ratio**	**95% CI**	**Ratio**	**95% CI**	**Ratio**	**95% CI**
Adjuvanted MCV-5 vs Non-Adjuvanted MCV-5										
Adjuvanted MCV-5 vs Menactra®										
Non-Adjuvanted MCV-5 vs Menactra®										
Day 29										
Adjuvanted MCV-5 (N=XX)										
Non-adjuvanted MCV-5 (N=XX)										
Menactra® (N=XX)										
Treatment Group Comparisons	**Ratio**	**95% CI**	**Ratio**	**95% CI**	**Ratio**	**95% CI**	**Ratio**	**95% CI**	**Ratio**	**95% CI**
Adjuvanted MCV-5 vs Non-Adjuvanted MCV-5										
Adjuvanted MCV-5 vs Menactra®										
Non-Adjuvanted MCV-5 vs Menactra®										
Fold-Rise From Baseline	**GMFR**	**95% CI**	**GMFR**	**95% CI**	**GMFR**	**95% CI**	**GMFR**	**95% CI**	**GMFR**	**95% CI**
Adjuvanted MCV-5										
Non-adjuvanted MCV-5										
Menactra®										

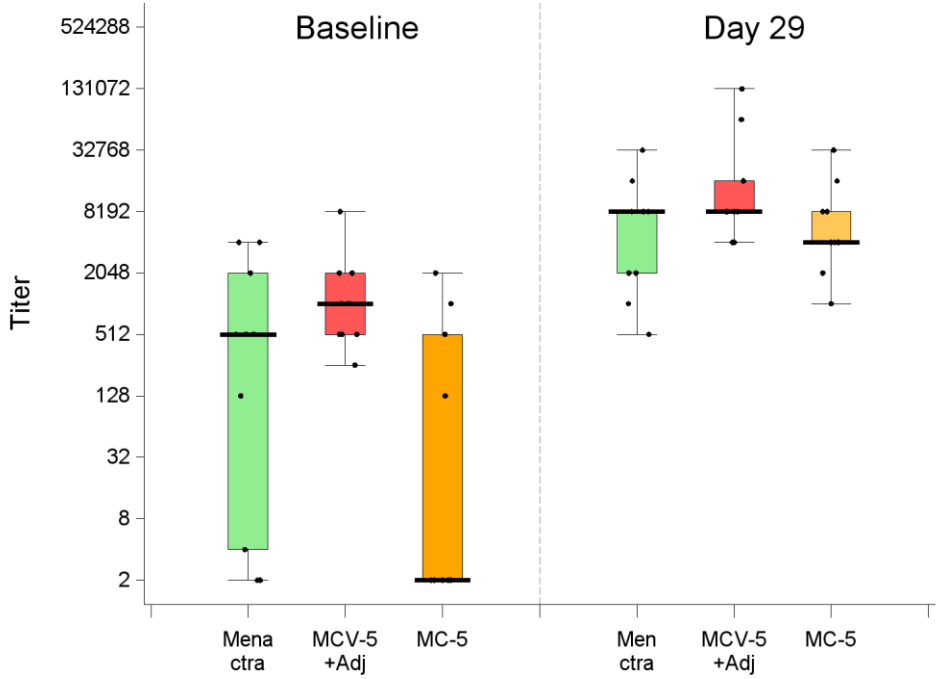
GMT = Geometric Mean Titer; CI = Confidence Interval; GMFR = Geometric Mean Fold Rise; Ratio = Ratio of GMT.

TABLE 14.2.3.1(b):
Secondary Analysis of rSBA Geometric Mean Titers per Serogroup - Full Analysis Population

Treatment Group (Number of Participants)	Meningococcal Polysaccharide									
	A		C		Y		W		X	
	GMT	95% CI	GMT	95% CI	GMT	95% CI	GMT	95% CI	GMT	95% CI
Day 1 (Baseline)										
Adjuvanted MCV-5 (N=XX)										
Non-adjuvanted MCV-5 (N=XX)										
Menactra® (N=XX)										
Treatment Group Comparisons	**Ratio**	**95% CI**	**Ratio**	**95% CI**	**Ratio**	**95% CI**	**Ratio**	**95% CI**	**Ratio**	**95% CI**
Adjuvanted MCV-5 vs Non-Adjuvanted MCV-5										
Adjuvanted MCV-5 vs Menactra®										
Non-Adjuvanted MCV-5 vs Menactra®										
Day 29										
Adjuvanted MCV-5 (N=XX)										
Non-adjuvanted MCV-5 (N=XX)										
Menactra® (N=XX)										
Treatment Group Comparisons	**Ratio**	**95% CI**	**Ratio**	**95% CI**	**Ratio**	**95% CI**	**Ratio**	**95% CI**	**Ratio**	**95% CI**
Adjuvanted MCV-5 vs Non-Adjuvanted MCV-5										
Adjuvanted MCV-5 vs Menactra®										
Non-Adjuvanted MCV-5 vs Menactra®										
Fold-Rise From Baseline	**GMFR**	**95% CI**	**GMFR**	**95% CI**	**GMFR**	**95% CI**	**GMFR**	**95% CI**	**GMFR**	**95% CI**
Adjuvanted MCV-5										
Non-adjuvanted MCV-5										
Menactra®										

GMT = Geometric Mean Titer; CI = Confidence Interval; GMFR = Geometric Mean Fold Rise; Diff = Difference in GMFR.

FIGURE 14.2.3.2.1:
Geometric Mean Titers for rSBA Titer per Serogroup by Treatment Group - Per-Protocol Population



Boxes extend from the 25th to 75th percentiles.

Black horizontal lines indicate the median.

FIGURE 14.2.3.2.2:
Geometric Mean Titers for rSBA Titer per Serogroup by Treatment Group - Full Analysis Population

14.3 Adverse Events

14.3.1 AE Tables

TABLE 14.3.1.1:
Summary of Overall Adverse Events - Safety Population

	Adjuvanted MCV-5 (N=X)		Non-adjuvanted MCV-5 (N=X)		Menactra® (N=X)	
	n	%	n	%	n	%
Solicited Adverse Events						
Any Solicited Adverse Event within 60 minutes post-vaccination	xx	xx.x	xx	xx.x	xx	xx.x
Any Solicited Adverse Event 1-7 days post- vaccination[1]	xx	xx.x	xx	xx.x	xx	xx.x
Any Local Solicited Event 1-7 days post-vaccination [1]	xx	xx.x	xx	xx.x	xx	xx.x
Any Systemic Solicited Event 1-7 days post-vaccination [1]	xx	xx.x	xx	xx.x	xx	xx.x
Any Grade 2 or greater Solicited Local or Systemic Event 1-7 days post-vaccination[1]	xx	xx.x	xx	xx.x	xx	xx.x
Unsolicited Adverse Events						
Any Serious Adverse Event[2]	xx	xx.x	xx	xx.x	xx	xx.x
At Least 1 Unsolicited Adverse Event[3]	xx	xx.x	xx	xx.x	xx	xx.x
Any Grade 2 or greater Unsolicited Adverse Event[3]	xx	xx.x	xx	xx.x	xx	xx.x
Any Related Unsolicited Adverse Event[3]	xx	xx.x	xx	xx.x	xx	xx.x
Any Grade 2 or greater Related Unsolicited Adverse Event[3]	xx	xx.x	xx	xx.x	xx	xx.x

N = Number of participants in the Full Analysis population; n = Number of participants reporting at least one of the specified conditions.
A participant is only counted once per row.
Unsolicited adverse events (AEs) include both serious and non-serious AEs.
[1] Excludes events within 60 minutes of vaccination
[2] Serious adverse events (SAEs) were to be collected for 6 months following vaccination.
[3] Unsolicited AEs were to be reported for 28 days following vaccination.

TABLE 14.3.1.2:
Number and Percentage of Participants Experiencing Solicited Events, by Symptom and Treatment Group - Full Analysis Population

Symptom	Adjuvanted MCV-5 (N=X)		Non-adjuvanted MCV-5 (N=X)		Menactra® (N=X)		MCV-5 + Adj versus Menactra p-value[1]	MCV-5 versus Menactra p-value[1]
	n (%)	(95% CI)	n (%)	(95% CI)	n (%)	(95% CI)		
Local Reactions								
Pain at injection site								
Erythema at injection site								
Swelling at injection site								
Any Local Symptom								
Systemic Symptoms								
Fever								
Headache								
Fatigue/malaise								
Joint pain/arthralgia								
Muscle pain/myalgia								
Diarrhea								
Anorexia								
Chills								
Vomiting								
Any Systemic Symptom								
Any Systemic or Local Symptom								

N = number of participants in the Full Analysis population.

[1] Fisher's exact 2-tailed test of the proportion of participants with an event.

TABLE 14.3.1.3:
Number and Percentage of Participants Experiencing Solicited Events by Symptom, Maximum Severity and Treatment Group - Safety Population

Symptom	Severity	Adjuvanted MCV-5 (N=X)		Non-adjuvanted MCV-5 (N=X)		Menactra® (N=X)	
		n	%	n	%	n	%
Any Symptom	None						
	Mild						
	Moderate						
	Severe						
	Life-Threatening						
Any Local Symptom	None						
	Mild						
	Moderate						
	Severe						
	Life-Threatening						
Pain at Injection Site	None						
	Mild						
	Moderate						
	Severe						
	Life-Threatening						
Erythema at Injection Site	None						
	Mild						
	Moderate						
	Severe						
Swelling at injection site	None						
	Mild						
	Moderate						
	Severe						
	Life-Threatening						

N = Number of participants in the Full Analysis population; Severity is based off of the maximum severity reported post vaccination.

TABLE 14.3.1.3:
Number and Percentage of Participants Experiencing Solicited Events by Symptom, Maximum Severity and Treatment Group - Safety Population

Symptom	Severity	Adjuvanted MCV-5 (N=X)		Non-adjuvanted MCV-5 (N=X)		Menactra® (N=X)	
		n	%	n	%	n	%
Any Systemic Symptom	None						
	Mild						
	Moderate						
	Severe						
	Life-Threatening						
Elevated Oral Temperature	None						
	Mild						
	Moderate						
	Severe						
	Life-Threatening						
Headache	None						
	Mild						
	Moderate						
	Severe						
	Life-Threatening						
Fatigue/malaise	None						
	Mild						
	Moderate						
	Severe						
	Life-Threatening						
Joint pain/arthralgia	None						
	Mild						
	Moderate						
	Severe						
	Life-Threatening						
Muscle pain/myalgia	None						
	Mild						
	Moderate						
	Severe						
	Life-Threatening						
Diarrhea	None						
	Mild						
	Moderate						
	Severe						
	Life-Threatening						
Anorexia	None						
	Mild						
	Moderate						

TABLE 14.3.1.3:
Number and Percentage of Participants Experiencing Solicited Events by Symptom, Maximum Severity and Treatment Group - Safety Population

Symptom	Severity	Adjuvanted MCV-5 (N=X)		Non-adjuvanted MCV-5 (N=X)		Menactra® (N=X)	
		n	%	n	%	n	%
	Severe						
	Life-Threatening						
Chills	None						
	Mild						
	Moderate						
	Severe						
	Life-Threatening						
Vomiting	None						
	Mild						
	Moderate						
	Severe						
	Life-Threatening						

N = Number of participants in the Full Analysis population; Severity is based off of the maximum severity reported post vaccination.

TABLE 14.3.1.4:
Number and Percentage of Participants Experiencing Solicited Events by Severity, at 60 minutes and at Day 1 through Day 8 Post Vaccination by Treatment Group - Full Analysis Population

TABLE 14.3.1.4(a) Any Local or Systemic Symptom

	60 mins (N=X)	Day 1 (N=X)	Day 2 (N=X)	Day 3 (N=X)	Day 4 (N=X)	Day 5 (N=X)	Day 6 (N=X)	Day 7 (N=X)	Day 8 (N=X)
Adjuvanted MCV-5									
N									
None – n (%)									
Mild – n (%)									
Moderate – n (%)									
Severe – n (%)									
Life-Threatening – n (%)									
Not Reported – n (%)									
MCV-5									
N									
None – n (%)									
Mild – n (%)									
Moderate – n (%)									
Severe – n (%)									
Life-Threatening – n (%)									
Not Reported – n (%)									
Menactra®									
N									
None – n (%)									
Mild – n (%)									
Moderate – n (%)									
Severe – n (%)									
Life-Threatening – n (%)									
Not Reported – n (%)									

N = Number of participants in the Full Analysis Population. Severity is the maximum severity reported for each participant for each day.

TABLE 14.3.1.4:
Number and Percentage of Participants Experiencing Solicited Events by Severity, Day Post Vaccination and Treatment Group - Full Analysis Population

Continue for each symptom

TABLE 14.3.1.4(b) Any Local Reaction

TABLE 14.3.1.4(c) Pain at injection site

TABLE 14.3.1.4(d) Erythema at injection site

TABLE 14.3.1.4(e) Swelling at injection site

TABLE 14.3.1.4(f) Any Systemic Symptom

TABLE 14.3.1.4(g) Fever

TABLE 14.3.1.4(h) Headache

TABLE 14.3.1.4(i) Fatigue/malaise

TABLE 14.3.1.4(j) Joint pain/arthralgia

TABLE 14.3.1.4(k) Muscle pain/myalgia

TABLE 14.3.1.4(l) Diarrhea

TABLE 14.3.1.4(m) Anorexia

TABLE 14.3.1.4(n) Chills

TABLE 14.3.1.4(o) Vomiting

FIGURE 14.3.1.5.1(a):
Maximum Severity of Solicited Systemic Symptoms per Participant by Days Post Vaccination and Treatment Group - Full Analysis Population -Adjuvanted MCV-5

(N=XX)

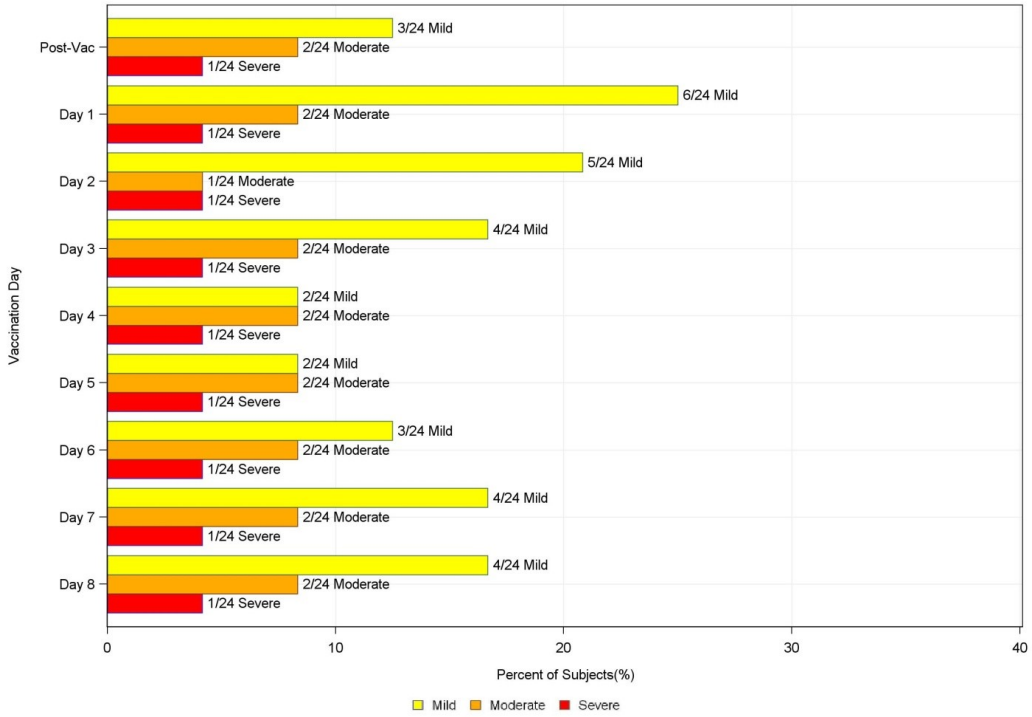


FIGURE 14.3.1.5.1(b):
Maximum Severity of Solicited Systemic Symptoms per Participant by Days Post Vaccination and Treatment Group - Full Analysis Population - Non-adjuvanted MCV-5

FIGURE 14.3.1.5.1(c):
Maximum Severity of Solicited Systemic Symptoms per Participant by Days Post Vaccination and Treatment Group - Full Analysis Population - Menactra®

FIGURE 14.3.1.5.2(a):
Maximum Severity of Solicited Local Reactions per Participant by Days Post Vaccination and Treatment Group - Full Analysis Population - Adjuvanted MCV-5

(N=XX)

FIGURE 14.3.1.5.2(b):
Maximum Severity of Solicited Local Reactions per Participant by Days Post Vaccination and Treatment Group - Full Analysis Population - Non-adjuvanted MCV-5

FIGURE 14.3.1.5.2(c):
Maximum Severity of Solicited Local Reactions per Participant by Days Post Vaccination and Treatment Group - Full Analysis Population - Menactra®

Same format as Figure 14.3.1.5.1.

TABLE 14.3.1.6:
Number and Percentage of Participants Experiencing Unsolicited Adverse Events with 95% Confidence Intervals by MedDRA® System Organ Class and Preferred Term, and Treatment Group - Full Analysis Population

MedDRA® Preferred Term	Adjuvanted MCV-5 (N=X)		Non-adjuvanted MCV-5 (N=X)		MCV-5 combined N=		Menactra® (N=X)	
	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
Any SOC								
Any PT								
[SOC 1]								
Any PT								
[PT 1]								
[PT 2]								
[SOC 2]								
Any PT								
[PT 1]								
[PT 2]								

N= Number of participants in the Full Analysis Population. A participant is only counted once per preferred term and system organ class.

TABLE 14.3.1.7:
Number and Percentage of Participants Experiencing Unsolicited Adverse Events
by MedDRA® System Organ Class and Preferred Term, Maximum Severity, and Treatment Group - Full Analysis Population

		Adjuvanted MCV-5 (N=X)		Non-adjuvanted MCV-5 (N=X)		MCV-5 combined N=		Menactra® (N=X)	
		n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
At least one AE									
Any AE	Any Severity								
Gastrointestinal disorders									
Any PT	Mild								
	Moderate								
	Severe								
	Life threatening								
	Death								
Axillary pain	Mild								
	Moderate								
	Severe								
	Life threatening								
	Death								
Etc., for all others	Mild								
	Moderate								
	Severe								
	Life threatening								
	Death								

Participants can contribute only one observation per PT/vaccination, based on maximum severity.
Percentages are based on number of participants per arm who received study vaccination.
Includes unsolicited AEs reported as serious (if any).
No participants reported the same event twice.
The following AEs were ongoing on day 28: Mild Injection site discoloration on day 1, resolved on day 84. Mild Blood pressure increased on day 28, resolved on day 84.

TABLE 14.3.1.8:
Number and Percentage of Participants Experiencing Unsolicited Adverse Events Related to Study Product, by MedDRA® System Organ Class and Preferred Term, Maximum Severity, and Treatment Group - Full Analysis Population

Same format as Table 14.3.1.7

TABLE 14.3.1.9.1:
Number and Percentage of Participants Experiencing Unsolicited Adverse Events
by MedDRA® System Organ Class and Preferred Term, Days Post Vaccination and Treatment Group - Full Analysis Population

MedDRA® System Organ Class	MedDRA® Preferred Term	Adjuvanted MCV-5				Non-adjuvanted MCV-5				Combined MCV-5				Menactra®			
		Days 1-8 (N=X)		Days 8+ (N=X)		Days 1-8 (N=X)		Days 8+ (N=X)		Days 1-8 (N=X)		Days 8+ (N=X)		Days 1-8 (N=X)		Days 8+ (N=X)	
		n	%	N	%	n	%	n	%	n	%	n	%	n	%	n	%
Any SOC	Any PT																
[SOC 1]	Any PT																
	[PT 1]																
	[PT 2]																
[SOC 2]	Any PT																
	[PT 1]																
	[PT 2]																

Note: N=Number of participants in the Full Analysis population. For each time period, a participant is only counted once per preferred term and system organ class.

TABLE 14.3.1.9.2:
Number and Percentage of Participants Experiencing Related Unsolicited Adverse Events by MedDRA® System Organ Class and Preferred Term, Days Post Vaccination and Treatment Group - Full Analysis Population

MedDRA® System Organ Class	MedDRA® Preferred Term	Adjuvanted MCV-5				Non-adjuvanted MCV-5				Combined MCV-5				Menactra®			
		Days 1-8 (N=X)		Days 8+ (N=X)		Days 1-8 (N=X)		Days 8+ (N=X)		Days 1-8 (N=X)		Days 8+ (N=X)		Days 1-8 (N=X)		Days 8+ (N=X)	
		n	%	N	%	n	%	n	%	n	%	n	%	n	%	n	%
Any SOC	Any PT																
[SOC 1]	Any PT																
	[PT 1]																
	[PT 2]																
[SOC 2]	Any PT																
	[PT 1]																
	[PT 2]																

Note: N=Number of participants in the Full Analysis population. For each time period, a participant is only counted once per preferred term and system organ class.

TABLE 14.3.1.10:
Number of Unsolicited Adverse Events
by MedDRA® System Organ Class and Preferred Term, Days Post Vaccination and Treatment Group - Full Analysis Population

MedDRA® System Organ Class	MedDRA® Preferred Term	Adjuvanted MCV-5		Non-adjuvanted MCV-5		Combined MCV-5		Menactra®	
		Days 1-8 (N=X)	Days 8+ (N=X)	Days 1-8 (N=X)	Days 8+ (N=X)	Days 1-8 (N=X)	Days 8+ (N=X)	Days 1-8 (N=X)	Days 8+ (N=X)
		# of Events	# of Events	# of Events	# of Events	# of Events	# of Events	# of Events	# of Events
Any SOC	Any PT								
[SOC 1]	Any PT								
	[PT 1]								
	[PT 2]								
[SOC 2]	Any PT								
	[PT 1]								
	[PT 2]								

Note: N=Number of participants in the Full Analysis population. For each time period, a participant is only counted once per preferred term and system organ class.

FIGURE 14.3.1.11.1:
Proportion of Participants with Unsolicited, Non-Serious Adverse Events, by MedDRA® System Organ Class and Maximum Severity per Participant - Full Analysis Population - Adjuvanted MCV-5

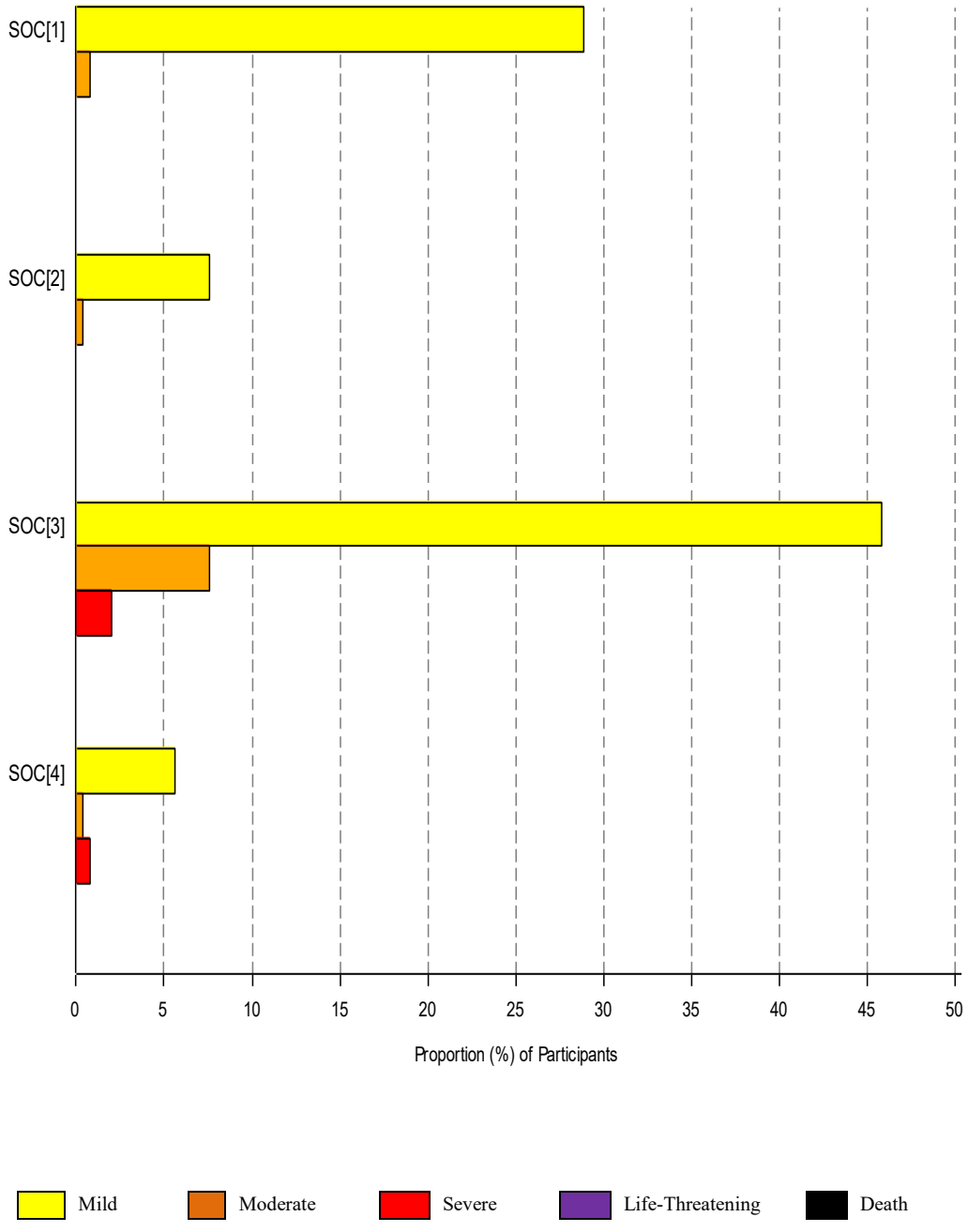


FIGURE 14.3.1.11.2:
Proportion of Participants with Unsolicited, Non-Serious Adverse Events, by MedDRA® System Organ Class and Maximum Severity per Participant - Full Analysis Population - Non-Adjuvanted MCV-5

FIGURE 14.3.1.11.3:
Proportion of Participants with Unsolicited, Non-Serious Adverse Events, by MedDRA® System Organ Class and Maximum Severity per Participant - Full Analysis Population - Menactra®

14.3.2 AE and SAE Listings

TABLE 14.3.2.1:
Listing of Deaths, Serious Adverse Events and Other Significant Events

Participant ID	Treatment Group	Adverse Event description	AE Start Date	# of Days Post Dose	Severity	Outcome	Resolution Date / Ongoing	Duration (Days)	Reasonable possibility that the study product caused the event?

(continued)

Participant ID	Adverse Event description	MedDRA® System Organ Class	MedDRA® Preferred Term	SAE / If Yes, Reason Reported as an SAE	Event Evaluated for Halting Criteria?	Comments

TABLE 14.3.2.2:
Listing of Non-Serious, Unsolicited, Moderate or Severe Adverse Events

Participant ID	Treatment Group	Adverse Event	Start Date	# of Days Post Dose	Severity	Outcome	Resolution Date / Ongoing	Duration (Days)	Reasonable possibility that the study product caused the event?

(continued)

Participant ID	Adverse Event description	MedDRA® System Organ Class	MedDRA® Preferred Term	SAE / If Yes, Reason Reported as an SAE	Event Evaluated for Halting Criteria?	Comments

14.3.3 Narratives of Deaths, Other Serious and Significant Adverse Events

[This is a place holder for this section in the CSR.]

TABLE 14.3.4.1:
Laboratory Results by Parameter, Maximum Severity, Study Day, and Treatment Group - Full Analysis Population

Treatment Group	N	None	Mild / Grade 1	Moderate / Grade 2	Severe / Grade 3	Life-Threatening / Grade 4	Missing
		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Baseline							
Adjuvanted MCV-5	x	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
Non-Adjuvanted MCV-5	x						
Menactra®	x						
Day 8							
Adjuvanted MCV-5	x						
Non-Adjuvanted MCV-5	x						
Menactra®	x						
Maximum Severity Post-Baseline[1]							
Adjuvanted MCV-5	x						
Non-Adjuvanted MCV-5	x						
Menactra®	x						

[1] Includes values collected at unscheduled visits.

Table 14.3.4.1: Laboratory Results by Parameter, Maximum Severity, Study Day and Treatment Group - Full Analysis Population (Continued)

Hemoglobin (g/dL)

Time Point	Treatment Group	N	None		Mild/ Grade 1 (Low)		Moderate/ Grade 2 (Low)		Severe/ Grade 3 (Low)		Life-Threatening/ Grade 4 (Low)		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%
Baseline	Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Non-Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Menactra®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Day 8	Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Non-Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Menactra®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Max Severity Post Baseline[1]	Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Non-Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Menactra®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

[1] Includes values collected at unscheduled visits.

Table 14.3.4.1: Laboratory Results by Parameter, Maximum Severity, Study Day and Treatment Group - Full Analysis Population (Continued)

Platelet Counts (cells/mm^3)

Time Point	Treatment Group	N	None		Mild/ Grade 1 (Low)		Moderate/ Grade 2 (Low)		Severe/ Grade 3 (Low)		Life-Threatening/ Grade 4 (Low)		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%
Baseline	Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Non-Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Menactra®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Day 8	Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Non-Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Menactra®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Max Severity Post Baseline[1]	Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Non-Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Menactra®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

[1] Includes values collected at unscheduled visits.

Table 14.3.4.1: Laboratory Results by Parameter, Maximum Severity, Study Day and Treatment Group - Full Analysis Population (Continued)

White Blood Cells (cells/mm^3)

Time Point	Treatment Group	N	None		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Life-Threatening/ Grade 4		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%
Baseline	Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Non-Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Menactra®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Day 8	Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Non-Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Menactra®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Max Severity Post Baseline[1]	Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Non-Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Menactra®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

[1] Includes values collected at unscheduled visits.

Table 14.3.4.1: Laboratory Results by Parameter, Maximum Severity, Study Day and Treatment Group - Full Analysis Population (Continued)

Alanine Aminotransferase (ALT) (U/L)

Time Point	Treatment Group	N	None		Mild/ Grade 1 (High)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (High)		Life Threatening/ Grade 4 (High)		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%
Baseline	Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Non-Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Menactra®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Day 8	Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Non-Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Menactra®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Max Severity Post Baseline[1]	Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Non-Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Menactra®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

[1] Includes values collected at unscheduled visits.

Table 14.3.4.1: Laboratory Results by Parameter, Maximum Severity, Study Day and Treatment Group - Full Analysis Population (Continued)

Creatinine (mg/dL)

Time Point	Treatment Group	N	None		Mild/ Grade 1 (High)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (High)		Life Threatening/ Grade 4 (High)		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%
Baseline	Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Non-Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Menactra®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Day 8	Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Non-Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Menactra®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Max Severity Post Baseline[1]	Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Non-Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Menactra®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

[1] Includes values collected at unscheduled visits.

Table 14.3.4.1: Laboratory Results by Parameter, Maximum Severity, Study Day and Treatment Group - Full Analysis Population (Continued)

Total Bilirubin (mg/dL)

Time Point	Treatment Group	N	None		Mild/ Grade 1 (High)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (High)		Severe/ Grade 4 (High)		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%
Baseline	Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Non-Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Menactra®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Day 8	Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Non-Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Menactra®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Max Severity Post Baseline[1]	Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Non-Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Menactra®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

[1] Includes values collected at unscheduled visits.

Table 14.3.4.1: Laboratory Results by Parameter, Maximum Severity, Study Day and Treatment Group - Full Analysis Population (Continued)

Albumin (g/dL)

Time Point	Treatment Group	N	None		Mild/ Grade 1 (Low)		Moderate/ Grade 2 (Low)		Severe/ Grade 3 (Low)		Missing	
			n	%	n	%	n	%	n	%	n	%
Baseline	Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Non-Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Menactra®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Day 8	Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Non-Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Menactra®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Max Severity Post Baseline[1]	Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Non-Adjuvanted MCV-5	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Menactra®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

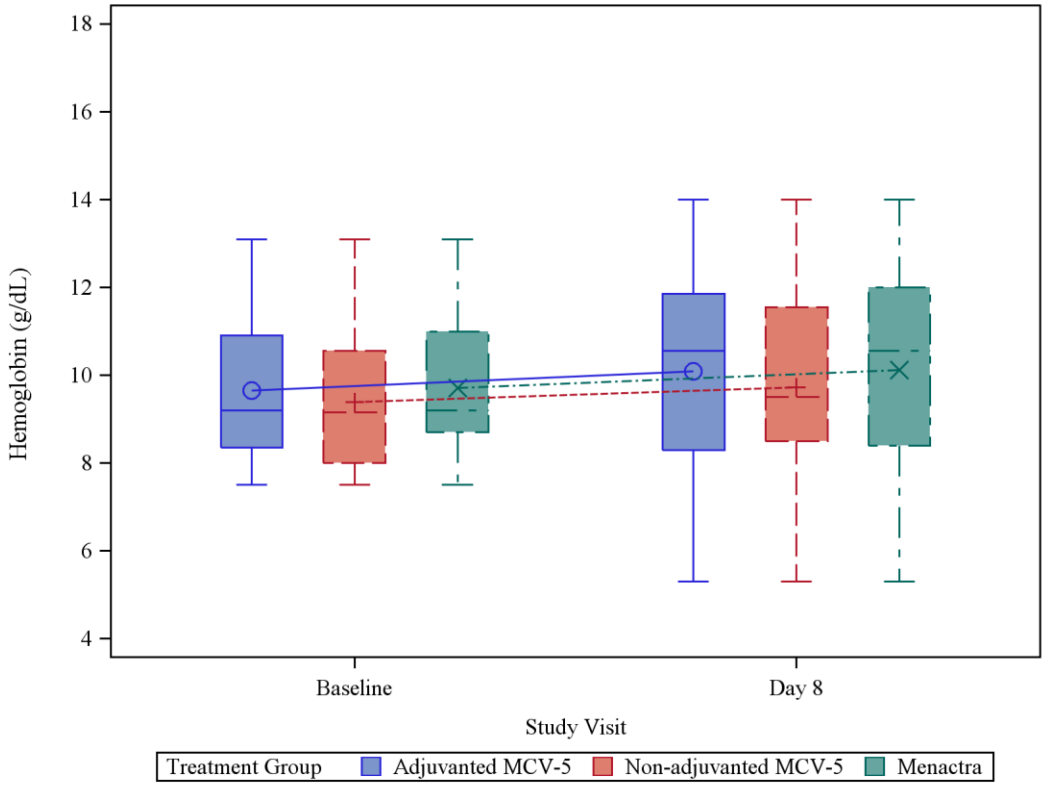
[1] Includes values collected at unscheduled visits.

TABLE 14.3.4.2:
Summary Statistics of Laboratory Results by Parameter, Study Visit and Treatment Group - Full Analysis Population

Laboratory Parameter	Time Point	Treatment Group	N	Mean	Standard Deviation	Median	25th-75th Percentile	Min, Max
Hemoglobin (g/dL)	Baseline	Adjuvanted MCV-5	x	xx.x	xx.x	xx.x	xx.x - xx.x	xx.x, xx.x
		Non-Adjuvanted MCV-5	x	xx.x	xx.x	xx.x	xx.x - xx.x	xx.x, xx.x
		Menactra®	x	xx.x	xx.x	xx.x	xx.x - xx.x	xx.x, xx.x
	Day 8	Adjuvanted MCV-5	x	xx.x	xx.x	xx.x	xx.x - xx.x	xx.x, xx.x
		Non-Adjuvanted MCV-5	x	xx.x	xx.x	xx.x	xx.x - xx.x	xx.x, xx.x
		Menactra®	x	xx.x	xx.x	xx.x	xx.x - xx.x	xx.x, xx.x
	Day 8, Change from Baseline	Adjuvanted MCV-5	x	xx.x	xx.x	xx.x	xx.x - xx.x	xx.x, xx.x
		Non-Adjuvanted MCV-5	x	xx.x	xx.x	xx.x	xx.x - xx.x	xx.x, xx.x
		Menactra®	x	xx.x	xx.x	xx.x	xx.x - xx.x	xx.x, xx.x
Platelet Count (cells/mm^3)	Baseline	Adjuvanted MCV-5	x	xx.x	xx.x	xx.x	xx.x - xx.x	xx.x, xx.x
		Non-Adjuvanted MCV-5	x	xx.x	xx.x	xx.x	xx.x - xx.x	xx.x, xx.x
		Menactra®	x	xx.x	xx.x	xx.x	xx.x - xx.x	xx.x, xx.x
	Day 8	Adjuvanted MCV-5	x	xx.x	xx.x	xx.x	xx.x - xx.x	xx.x, xx.x
		Non-Adjuvanted MCV-5	x	xx.x	xx.x	xx.x	xx.x - xx.x	xx.x, xx.x
		Menactra®	x	xx.x	xx.x	xx.x	xx.x - xx.x	xx.x, xx.x
	Day 8, Change from Baseline	Adjuvanted MCV-5	x	xx.x	xx.x	xx.x	xx.x - xx.x	xx.x, xx.x
		Non-Adjuvanted MCV-5	x	xx.x	xx.x	xx.x	xx.x - xx.x	xx.x, xx.x
		Menactra®	x	xx.x	xx.x	xx.x	xx.x - xx.x	xx.x, xx.x

Note: Continue for all laboratory tests: White Blood Cells (cells/mm^3), ALT (U/L), Creatinine (mg/dL), Total Bilirubin (mg/dL), Albumin (g/dL).

FIGURE 14.3.4.3:
Laboratory Results by Scheduled Visits: Mean Value at Baseline and Day 8 by Laboratory Parameter and Treatment Group - Full Analysis Population



Note: Continue for all laboratory tests: Platelet Counts (cells/mm^3), White Blood Cells (cells/mm^3), Alanine Aminotransferase (ALT) (U/L), Creatinine (mg/dL), Total Bilirubin (mg/dL), Albumin (g/dL).

TABLE 14.3.4.4:
Listing of Abnormal Laboratory Results

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

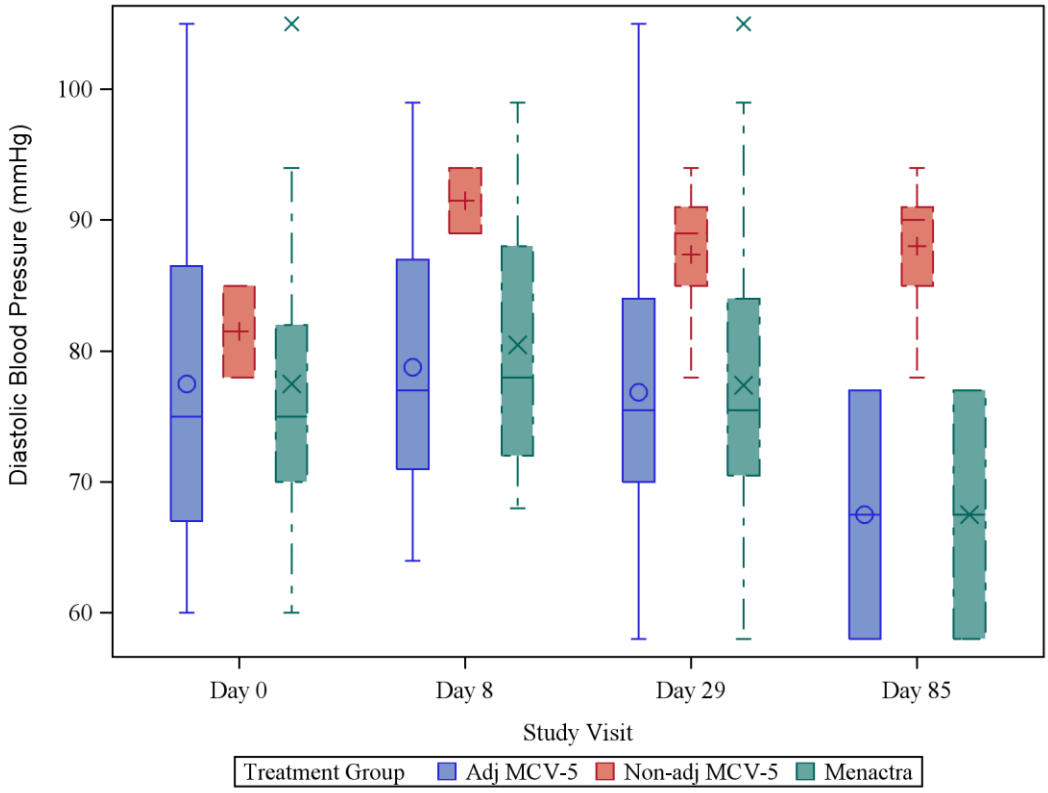
[Implementation Note: This listing only includes abnormal laboratory results. A complete listing of all laboratory results is included in the listings document. In the Laboratory Parameter column, indicate the units after the parameter, e.g., Hemoglobin (g/dL).The grade will be included in parentheses after the result, e.g., 16.2 (Grade 1).]

TABLE 14.3.5.1:
Distribution of Vital Signs by Grade, Study Visit, and Treatment Group - Full Analysis Population

Adjuvanted MCV-5 (N=XX)									
		Pre-Vaccination (N=X)		Visit 3 (Day 8) (N=X)		Visit 4 (Day 29) (N=X)		Visit 5 (Day 85) (N=X)	
Vital Sign Assessment	**Grade**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Diastolic Blood Pressure (mm Hg)	Normal	x	xx.x	x	xx.x	x	xx.x	x	xx.x
	Hypertension Grade 1	x	xx.x	x	xx.x	x	xx.x	x	xx.x
	Hypertension Grade 2	x	xx.x	x	xx.x	x	xx.x	x	xx.x
	Hypertension Grade 3	x	xx.x	x	xx.x	x	xx.x	x	xx.x
Systolic Blood Pressure (mm Hg)	Normal	x	xx.x	x	xx.x	x	xx.x	x	xx.x
	Hypertension Grade 1	x	xx.x	x	xx.x	x	xx.x	x	xx.x
	Hypertension Grade 2	x	xx.x	x	xx.x	x	xx.x	x	xx.x
	Hypertension Grade 3	x	xx.x	x	xx.x	x	xx.x	x	xx.x

Repeat for all treatment groups: Non-adjuvanted MCV-5 and Menactra®

FIGURE 14.3.5.2:
Vital Sign Measurements by Scheduled Visits: Mean Values from Baseline to Day 85 by Vital Sign and Treatment Group - Full Analysis Population



Note: Continue for all vital signs: Systolic Blood Pressure (mmHg), Heart Rate (beats/min)

TABLE 14.3.6:
Concomitant Medications Summary by Treatment Group - Full Analysis Population

		Study Group		
		Adjuvanted MCV-5	Non-adjuvanted MCV-5	Menactra®
ATC1	**Drug name (preferred)**	**n**	**n**	**n**
[e.g., ANTIINFECTIVES FOR SYSTEMIC USE]	[e.g., TRUVADA]			
Total				

14.4 Listings

LISTING 16.2.1:
Early Terminations or Discontinued Participants

Participant ID	Treatment Group	Category	Reason for Early Termination	Study Day

LISTING 16.2.2.1:
Participant-Specific Protocol Deviations

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

LISTING 16.2.2.2:
Non-Participant-Specific Protocol Deviations

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

LISTING 16.2.3:
Participants Excluded from the Immunogenicity Analysis

Participant ID	Treatment Group	Analyses in which Participant is Included	Analyses from which Participant is Excluded	Results Available?	Reason Participant Excluded
		[e.g., Safety, ITT, PP]	[e.g., Safety, ITT, PP, Day x]		

LISTING 16.2.4.1:
Demographic Data

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

LISTING 16.2.4.2:
Pre-Existing Medical Conditions

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

[Implementation Note: "Condition Start Day" and "Condition End Day" are relative to enrollment (which is Day 1, day before enrollment is Day -1).Rather than use exact study days, categorize as follows:

- > 5 years prior to enrollment
- 1-5 years prior to enrollment
- 1-12 months prior to enrollment
- Within 1 month of enrollment
- During study
- If ongoing, display "Ongoing" in the "Condition End Day" column]

LISTING 16.2.5:
Compliance and/or Drug Concentration Data

Not Applicable

LISTING 16.2.6:
Individual Immunogenicity Response Data

Participant ID	Treatment Group	Assay	Planned Time Point	Actual Study Day	Titer

LISTING 16.2.7.1.1:
Solicited Local Events

Participant ID	Treatment Group	Vaccination	Post Dose Day	Assessment*	Pain at Injection Site	Erythema (cm)	Erythema Severity	Swelling (cm)	Swelling Severity
				MA	None/Mild/ Moderate/Severe	XX	None/Mild/ Moderate/Severe	XX	None/Mild/ Moderate/Severe
				Clinic					

* MA = Data reported by participant on the Memory Aid and reviewed by clinic staff and reported in Solicited Events eCRF.

Clinic = Data collected by clinic staff during physical exam or symptom assessment (treatment administration record, in-clinic assessment, etc.)

LISTING 16.2.7.1.2:
Solicited Systemic Events

Participant ID	Treatment Group	Post Dose Day	Assessment*	Oral Temperature	Headache	Fatigue/Malaise	Joint Pain/Arthralgia	Muscle Pain/Myalgia
			MA	xx (Mild)	None/Mild/ Moderate/Severe	None/Mild/ Moderate/Severe	None/Mild/ Moderate/Severe	None/Mild/ Moderate/Severe
			Clinic					

(continued)

Participant ID	Treatment Group	Post Dose Day	Assessment*	Diarrhea	Anorexia	Chills	Vomiting
			MA	None/Mild/ Moderate/Severe	None/Mild/ Moderate/Severe	None/Mild/ Moderate/Severe	None/Mild/ Moderate/Severe
			Clinic				

* MA = Data reported by participant on the Memory Aid and reviewed by clinic staff and reported in Solicited Events eCRF.

Clinic = Data collected by clinic staff during physical exam or symptom assessment (treatment administration record, in-clinic assessment, etc.)

[Implementation Note: To indicate severity for quantitative symptoms (e.g., temperature, measurements), include the grade in parentheses after the number, e.g., 100.7 (Mild).]

LISTING 16.2.7.2:
Unsolicited Adverse Events

Participant ID	Treatment Group	Adverse Event Description	AE start date	# of Days Post Dose	Severity	Outcome	Duration (Days)	End date	Reasonable possibility that study product caused event?	SAE / If Yes, reason reported as an SAE?	MedDRA® System Organ Class	MedDRA® Preferred Term	Comments

Note: For additional details about SAEs, see Table: 14.3.2.1.

LISTING 16.2.8.1:
Individual Clinical Laboratory Results – Hematology

Participant ID	Treatment Group	Sex	Age (years)	Planned Study Day	Actual Study Day	Hemoglobin (g/dL)	Platelets (cells/mm^3)	White Blood Cells (cells/mm^3)

[Implementation Note: This listing includes all laboratory results, scheduled and unscheduled. The severity should be included in parentheses after the result of the abnormal results; e.g., 16.2 (Mild).]

LISTING 16.2.8.2:
Individual Clinical Laboratory Results – Biochemistry

Participant ID	Treatment Group	Sex	Age	Planned Study Day	Actual Study Day	ALT (IU/L)	Albumin (g/dL)	Total Bilirubin (mg/dL)	Serum Creatinine (mg/dL)

[Implementation Note: This listing includes all laboratory results, scheduled and unscheduled. The severity should be included in parentheses after the result of the abnormal results; e.g., 16.2 (Mild).]

LISTING 16.2.8.3:
Individual Clinical Laboratory Results – Serology

Participant ID	Treatment Group	Sex	Age (years)	Planned Study Day	Actual Study Day	HBsAg	Anti-HCV	HIV Elisa

[Implementation Note: This listing includes all laboratory results, scheduled and unscheduled. If the Anti-HCV is positive, then the Anti-HCV PCR Result will be placed in parenthesis after the initial Anti-HCV result.]

LISTING 16.2.9.1:
Vital Signs

Participant ID	Treatment Group	Planned Study Day	Actual Study Day	Height (cm)	Weight (kg)	Temperature (°Celsius)	Systolic BP (mmHg)	Diastolic BP (mmHg)	Heart Rate (Beats/Min)

[Implementation Note: This listing includes all vital sign assessments, scheduled and unscheduled.]

LISTING 16.2.9.2:
Physical Exam Findings

Participant ID	Treatment Group	Planned Time Point	Actual Study Day	Body System	Abnormal Finding	Reported as AE? (AE Number)

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

LISTING 16.2.10:
Concomitant Medications

Participant ID	Treatment Group	CM Number	Medication Name	Medication Start Day	Medication End Day	Indication	Drug Name	ATC1

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

- *<1 year prior to enrollment*
- *1-5 years prior to enrollment*
- *1-12 months prior to enrollment*

If ongoing, display "Ongoing" in the "Medication End Day" column.]