Title: A Phase 2, Long-Term Immunogenicity Follow-up Trial of Adult and Elderly Subjects who have Previously Received an Intramuscular Injection of Norovirus GI.1/GII.4 Bivalent Virus-Like Particle Vaccine

NCT Number: NCT03039790

Protocol Approve Date: 05 September 2019

Certain information within this protocol has been redacted (ie, specific content is masked irreversibly from view with a black/blue bar) to protect either personally identifiable information (PPD) or company confidential information (CCI).

This may include, but is not limited to, redaction of the following:

- Named persons or organizations associated with the study.
- Proprietary information, such as scales or coding systems, which are considered confidential information under prior agreements with license holder.
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STATISTICAL ANALYSIS PLAN

TRIAL NUMBER: NOR-213

A Phase 2, Long-Term Immunogenicity Follow-up Trial of Adult and Elderly Subjects who have Previously Received an Intramuscular Injection of Norovirus GI.1/GII.4 Bivalent Virus-Like Particle Vaccine

Long-Term Immunogenicity of the Norovirus GI/GII.4 Bivalent VLP Vaccine in Adults

PHASE 2

Version**:** 1

Date**:** 05 September 2019

Prepared by:

PPD

Based on:

Protocol Version: 3.0 Amendment 2

Protocol Date: 27 March 2018

1.1 Approval Signatures

Study Title: **A Phase 2, Long-Term Immunogenicity Follow-up Trial of Adult and Elderly Subjects who have Previously Received an Intramuscular Injection of Norovirus GI.1/GII.4 Bivalent Virus-Like Particle Vaccine**

Approvals:

	Date
	Date
	Date
	Date

2.0 TABLE OF CONTENTS

LIST OF IN-TEXT TABLES

LIST OF IN-TEXT FIGURES

3.0 LIST OF ABBREVIATIONS

AE	Adverse event
CI	Confidence interval
CCI	[redacted]
eCRF	electronic case report form
ELISA	Enzyme-linked immunosorbent assay
FAS	Full analysis set
GMBT50	50% geometric mean blocking titers
GMT	Geometric mean titers
GSD	Geometric standard deviation
HBGA	Histo-blood group antigen
ICF	Informed consent form
IA	Interim analysis
IM	Intramuscular
MedDRA	Medical Dictionary for Regulatory Activities
MPL	Monophosphoryl lipid A
NoV vaccine	Norovirus GI.1/GII.4 bivalent VLP vaccine
Pan-Ig	Total immunoglobulin
PPS	Per protocol set
PBMC	Peripheral blood mononuclear cell
PT	Preferred term
PVT	Primary vaccinating trial
SAE	Serious adverse event
SAP	Statistical analysis plan
SD	Standard deviation
SOC	System organ class
TLGs	Tables, listings, and graphs
VLP	Vaccine-like particles
WHODrug	World Health Organization Drug Dictionary
WHO-DDE	World Health Organization Drug Dictionary Enhanced

4.0 OBJECTIVES

4.1 Primary Objectives

To evaluate the humoral response after at least 1 dose of NoV vaccine up to 5 years after intramuscular (IM) injection as measured by histo-blood group antigen (HBGA) blocking assay.

4.2 Secondary Objectives

To evaluate the humoral response after at least 1 dose of NoV vaccine up to 5 years after IM injection as measured by total-immunoglobulin (pan-Ig) enzyme-linked immunosorbent assay (ELISA).

CCI [redacted]

4.4 Trial Design

This phase 2, multi-site trial is designed to evaluate descriptively the long-term immunogenicity of at least 1 NoV vaccine administration. Subjects previously enrolled in NOR-107, NOR-210 and NOR-204 will be invited to participate in this long-term follow-up trial corresponding to a duration of up to 5 years post-primary vaccination. The timing of subject entry into NOR-213 with respect to the anniversary of the primary vaccination trial means the duration of subject participation in the present trial will be different. Following inclusion in NOR-213, subjects will have yearly blood draws. Subjects from NOR-107 will enter this trial at the time of their 3rd year post-primary vaccination. For NOR-210 and NOR-204 subjects, entry will correspond to their 2nd year post-primary vaccination.

Trial procedures will include a maximum of 4 visits over 3 years. At each visit, a blood sample, including peripheral blood mononuclear cell (PBMC) isolation (only for the subset of subjects initially included in NOR-107 and NOR-204 trials), CCI [redacted]. At each contact with the subjects, fatal and life threatening serious adverse events (SAEs), NoV vaccine-related SAEs, potential immune-mediated events of medical significance and any procedure-related medical occurrences will be recorded.

It is expected that up to 575 subjects who participated in the selected trials will be available for enrollment. Subject distribution by primary trial number and trial arm is given in Appendix A.The chronology and bridging of relevant trial visits are given in Table 4.a.

Table 4.a Chronology of Visits in the Primary and Current Trials

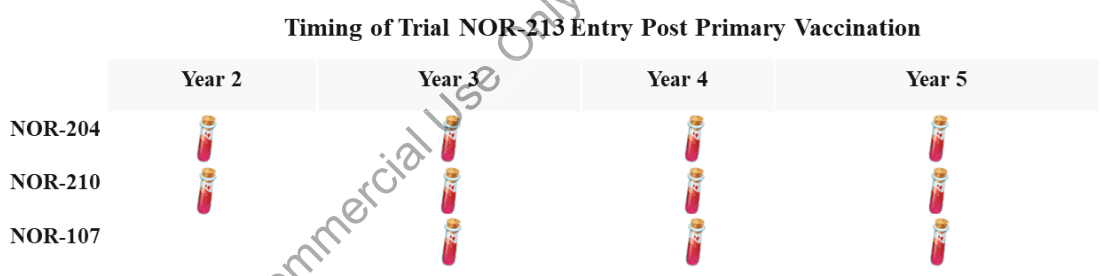
	Visit Day (vaccination trial)									Visit (NOR-213)			
PVT	**1**	**8**	**15**	**28/29**	**35/36**	**56/57**	**183**	**208/211**	**393**	**Y2**	**Y3**	**Y4**	**Y5**
NOR-107	V	–	–	V	–	–	–	–	–	–	–	–	
	B	–	–	B	B	B	–	B	B	–	B	B	B
NOR-210	V	–	–	–	–	–	–	–	–	–	–	–	–
	B	B	B	B	–	–	–	–	–	B	B	B	B
NOR-204	V	–	–	V	–	–	–	–	–	–	–	–	–
	B	B	–	B	B	B	–	B	B	B	B	B	B

PVT=Primary vaccination trial; V=investigational product administration; CCI [redacted]

An interim analysis (IA) is planned when all subjects have provided one blood sample corresponding to at least their first year of participation in NOR-213.

A schematic of the trial design is included as Figure 4.a. A schedule of trial procedures is provided in Appendix B.

Figure 4.a Schematic of Trial Design



Primary Vaccination Trial	Age	Doses	GI.1/GII.4 VLP/MPL (µg)	Blood draws*
NOR-204:	18 to 49 and ≥60 years	1 or 2 doses (Day 1/Day 29)	15/50/0 or 15/50/15	Days 1, 8, 29, 36, 57, 211, 393
NOR-210:	18 to 49 years	1 dose (Day 1)	15/50/0	Days 1, 8, 15, 29
NOR-107:	18 to 64 years	1 (Day 1) or 2 doses (Day 1/Day 28)	11 compositions	Days 1, 28, 35, 56, 208, 393

*Samples taken during the primary vaccination trial may be re-tested in NOR-213

5.0 ANALYSIS ENDPOINTS

5.1 Primary Endpoints (*Immunogenicity*) for this Trial, as Measured by HBGA Blocking Assay

- Geometric mean blocking titers (50%; $GMBT_{50}$) of anti-norovirus GI.1 VLP antibodies.
- $GMBT_{50}$ of anti-norovirus GII.4 VLP antibodies.

5.2 Secondary Endpoints (*Immunogenicity*) for this Trial, as Measured by pan-Ig ELISA

- Geometric mean titers (GMT) of anti-norovirus GI.1 VLP antibodies.
- GMT of GII.4 VLP antibodies.

CCI

[redacted]

6.0 DETERMINATION OF SAMPLE SIZE

This trial is descriptive and will only enroll subjects who previously received at least 1 dose of NoV vaccine, have baseline and post-vaccination data, and completed the primary vaccination trial according to protocol. Sample size was not based on formal statistical power calculations.

7.0 METHODS OF ANALYSIS AND PRESENTATION

7.1 General Principles

Considering all participants in this trial were exposed to at least 1 dose of NoV vaccine in a prior trial (the PVT, see section 4.4), baseline values will be the same as the ones previously identified and used in the PVT, and in general are the last observed value prior to the first dose of investigational product (either NoV vaccine or placebo).

All statistical analyses will be conducted using SAS® Version 9.4 or higher.

Statistical hypothesis testing is not planned for the trial. CCI [redacted]

With the possible exception of derived variable, means and medians will be presented to 1 more decimal place than the recorded data. The standard deviations (SDs) will be presented to 2 more decimal places than the recorded data. Parameter estimate will be presented using the same number of decimal places as the parameter estimate. Percentages will be presented to 1 decimal place (e.g., 80.3%). Where appropriate and otherwise specified, variables will be summarized descriptively by trial visit. For categorical variables, the count and percent of each possible value will be tabulated. Unless specified otherwise, the denominator for the percent will be based on the number of subjects who provided non-missing responses to the categorical variable at the visit being summarized. For continuous variables descriptive statistics may include the number of subjects (with non-missing values), mean (arithmetic or geometric), median, SD (or geometric standard deviation [GSD]), minimum, and maximum values.

Data analysis will be performed and presented based on a number of different subject groupings, such as:

- By primary vaccination trial and trial arm;
- Vaccine Composition (XXµg of GI.1/ XXµg of GII.4/XXXµg of $Al(OH)_3$ with or without XXµg of MPL) and dose regimen, pooled across trials; namely
    - 15/50/500/0 single dose: trials NOR-107, NOR-210, NOR-204
    - 15/50/500/15 single dose: trials NOR-107, NOR-204
    - 15/50/500/0 dual dose: trials NOR-107, NOR-204

The above will be repeated where applicable, for subjects aged 18 to 59 years, inclusive, and ≥60 years to provide descriptive data based on age.

All data collected during the trial, unless otherwise specified, will be presented in subject data listings; including screen failure subjects with screen failure reasons.

7.1.1 Definition of Trial Days

Day 1 is defined as the date on which a subject was first administered investigational product (either vaccine or placebo) in the PVT. Other trial days are defined relative to Day 1; with Day -1 being the day prior to Trial Day 1, Day 1 being Trial Day 1, and Day 365 being Year 1 follow-up visit, etc.

7.1.2 Definition of Trial Visit Windows

The presentation of the trial CCI results will include results from the PVT along with the long term follow up from this trial. The data from the visits from the PVT will use the visit windows defined for each of the individual PVTs. For results where subjects are pooled across trials the following visits will be presented together Days: 28/29; 35/36; 56/57; and 208/211. The NOR-213 visits (Year 2 etc.) will be indexed by the electronic case report form (eCRF) pages rather than actual dates with windows.

The trial protocol provides a window of +/- 2 month for subjects to complete their annual visits. In the analyses, a windowing convention of +/- 62 days will be used to determine the analysis value for a given trial visit for observed data analyses. Under certain circumstances, subjects may encounter clinical circumstances that warrant a delay in blood sampling. In the event of multiple values, the value that has a collection date nearest the visit data will be used. In the event that two results are equidistant from the expected visit date, the later result will be used.

7.1.3 Handling of Missing Values

Titers Measured Below (or Above) the LLoQ (or ULoQ)

A titer value measured below LLoQ will be imputed to a value that is half of the LLoQ in summaries and analyses, but will be listed as reported in the raw serology data. For example, a serologic assay with LLoQ = 30 generally reports values below LLoQ as "<30". The data listings will present the values as "<30", while values of 15 (30/2) are to be used in the summaries and analyses. Titer values measured as above ULoQ will be imputed at the ULoQ value.

Missing or Partial Dates

Partial dates will be presented as recorded in the listings. Missing and partial AE start dates will be imputed only to determine the relationship between the start date of the event and the first dose date.

Subjects who participated in trials NOR-107, NOR-210 and NOR-204 will have already reached 1 year or more post-primary vaccination with NoV vaccine at the time of trial NOR-213 start. Therefore, dose date will not be considered for the imputation of missing or partial dates of AE start dates.

- AE start date month/year available and day missing: first day of the month will be used.
- AE start date year available and month/day missing: set the start date as January 1.
- AE start date completely missing: set the date as NOR-213 ICF date.

7.2 Analysis Sets

The following analysis sets are defined for this trial:

Full Analysis Set (FAS): All subjects with data from at least 1 follow-up time point.

The FAS will be the primary analysis set used for safety analyses.

Per Protocol Set (PPS): All subjects in the FAS who do not have major protocol violations that potentially confound the primary endpoint. Note for NOR-204 and NOR-107, only PPS from PVT will be included in PPS of NOR-213. Since no PPS was defined in NOR-210, all safety subjects will be considered. Prior to the IA a review of subject data will be performed and criteria for the PPS will be finalized and documented.

The PPS will be the primary analysis set used for immunogenicity analyses.

7.3 Disposition of Subjects

General trial information, for NOR-213, will be presented in a table. The following data fields are included: date of first signed informed consent form (ICF), date of last subject's last visit/contact, date of last procedure for collection of data for primary endpoint, Medical Dictionary for Drug Regulatory Activities (MedDRA) version, World Health Organization Drug Dictionary (WHODrug) version, and SAS version. For the above, the proper interpretation of last subject is the subject with the earliest date for the visit of interest, and not necessarily the last subject to enter the trial.

Subjects who sign a NOR-213 ICF and are not identified as a screen failure will be considered enrolled into NOR-213 and will be counted in the FAS. The following tabulations will be created for these subjects: (1) number of subjects by PVT, site and trial arm; (2) subject disposition, number completing the trial and number not completing the trial, as well as reasons for early dropout by PVT and trial arm; (3) tabulation of significant protocol deviations by PVT and trial arm.

For each of the primary vaccination trials a complete accounting of all vaccinated subjects (any subject that received one or more doses of investigational product) will be attempted. Subjects will be identified into one of the following mutually exclusive groups: (1) enrolled into NOR-213 (counted FAS), (2) eligible but not enrolled into NOR-213, (3) non-eligible for NOR-213, or Screen failure. Hypothetically, if a subject wasn't eligible for NOR-213 participation but was enrolled nevertheless, they will be counted in #1, above.

In addition analysis populations (FAS, PPS) and CCI (from PVT NOR-204 and NOR-107) will also be presented.

Subjects identified as NOR-213 screen failures will be included in the following tabulations: (1) Reasons for Failure, and (2) demographics descriptive statistics.

7.4 Demographic and Other Baseline Characteristics

Demographic data will be extracted from the PVTs; therefore, for example, the subject age is from the time vaccination with investigational product and not from the time of entry into trial

NOR-213. The variables to be included in the demographic summary include: age (yrs), sex, ethnicity, and race. This will be summarized for each PVT and trial arm for the FAS, PPS and CCI

7.5 Medical History and Concurrent Medical Conditions

Medical history and concurrent medical conditions will be coded using the MedDRA coding system using the current MedDRA version and will be documented in all relevant tables, listings, and graphs (TLGs). Medical history includes any significant conditions or diseases that have disappeared or resolved at or prior to signing of the NOR-213 ICF; while a concurrent medical condition is any significant condition/disease that is ongoing at the time of signing the ICF. Medical history and concurrent medical conditions reported in the PVTs will not be included in the above.

Frequencies and percentages of subjects by medical history and concurrent medical conditions will be tabulated by MedDRA system organ class (SOC) and preferred term (PT) for each PVT and trial arm for the FAS, and will not be repeated across PVT groupings (eg. all subjects pooled) unless necessary. Multiple entries for an individual patient under the same SOC/PT will only be counted once.

7.6 Medication History and Concomitant Medications

Medication history and concomitant medications will be coded using the World Health Organization Drug Dictionary Enhanced (WHO-DDE) coding system using the current version and will be documented on all relevant TLGs. Medication history includes all prior prescription medications and vaccines that was taken but ended before signing the NOR-213 ICF, while concomitant medications include medications taken between the time of signing the ICF through the end of trial and will not repeated for the across PVT groupings unless data suggests a need. Medication history and concomitant medications reported in the PVTs will not be included in the above.

Frequencies and percentages of subjects by medication history and concomitant medications will be tabulated by preferred medication name for each PVT and trial arm for the FAS. Subjects with multiple uses of a medication or concomitant medication will be counted once for a given preferred medication name.

7.7 Trial Vaccine Exposure and Compliance

Measurements of investigational product (i.e. trial vaccine) exposure or compliance are not applicable for this trial.

7.8 Efficacy Analysis

Vaccine efficacy will not be evaluated in this trial.

7.9 Pharmacokinetic/Pharmacodynamic Analysis

Not applicable.

7.10 Other Outcomes

The co-primary endpoints (immunogenicity) for this trial, as measured by HBGA blocking assay are:

- Geometric mean blocking titers ($GMBT_{50}$) of anti-norovirus GI.1 VLP antibodies.
- $GMBT_{50}$ of anti-norovirus GII.4 VLP antibodies.

Geometric mean titers (GMT or $GMBT_{50}$) will be calculated, for each relevant time point as antilogarithm of Σ(log transformed titer/n), where n is the number of subjects with a titer value in the summation; the GSD will be calculated as the antilogarithm transformation of the standard deviation of the log-transformed titers; their 95% CIs will be calculated as the anti-log transformation of upper and lower limits for a two-sided CI of the mean of the log-transformed titers. Pre-vaccination is the baseline value found in the PVT. The same statistics will be calculated for the secondary endpoints, pan-Ig ELISA GI.1 and pan-Ig ELISA GII.4.

For all endpoints, descriptive summary statistics and their 95% confidence intervals (CI) will be computed for each time point by the groups given in Section 7.1. Sensitivity analysis based on FAS will be provided for primary endpoint and selected analyses.

Individual titers value will be presented using boxplots on the Log scale; boxplots for each of the subject sets identified in Section 7.1.

Seroresponse rate for this trial is defined as the percentage of subjects with a 4-fold rise or greater from the baseline titers in the PVT, in serum anti-NoV antibody titers for GI.1 VLP or GII.4 VLP separately, as measured by Pan-Ig ELISA or HBGA. The seroresponse rates and 95% CIs will be summarized, and the 95% CI will be calculated using the exact (Clopper-Pearson) method. These summaries will be provided for the subjects in the PPS and FAS.

CCI

[redacted]

7.11 Safety Analysis

7.11.1 Serious Adverse Events and Adverse Events of Special Interest

The FAS will be used for all safety analyses. Tabulations will be made for serious adverse events and potential immune-mediated events as defined in the trial protocol. Important to note that the AE collection criteria in the PVT and this trial (safety follow up in NOR-213 has been restricted to few safety parameters) differ significantly, hence the pulling of AEs from both trials is not practical. Therefore, the start up for observing SAE is unique to each PVT; namely, NOR-107 from Year 3 visit to Year 5, NOR-210 from Year 2 to Year 5, and NOR-204 from Year 2 to Year 5.

Fatal and life threatening SAEs, NoV vaccine-related SAEs and important medical events (potential immune–mediated events) and any procedure-related medical occurrences will be reported in this trial and coded using the MedDRA.

SAEs will be summarized by each PVT and trial arm, as well as a summary for all pooled subjects, by SOC and PT. Summaries for SAEs will include total number of events and number of subjects reporting the event. The rate of events per 100 patient years may be summarized if necessary. Summaries will be provided for the duration of the whole trial and may be by yearly interval. Subjects will be included in the yearly interval if they complete the follow-up visit for the previous year and if subject disposition doesn't disqualify their exclusion; specifically, when the discontinuation date falls in-between Year A and Year B, then the subject will be evaluable for Years A, B and not C, where A<B<C.

Counting SAEs and determining patient-years of follow-up for yearly intervals is detailed as follows:

- SAEs will be counted from yearly visit to yearly visit. Therefore, if an event happens on the same day as a yearly visit then the event will be assumed to happen after the visit, i.e. the intervals are left sided closed and right sided open. Hypothetically if a subject has 350 days between visits Year 1 and Year 2, and simultaneously has an SAE on the same day as the Year 2 visit, then that event will be counted in the Year 2 summary; the event would never be double counted.
- Patient years is determined by summing the total number of follow-up days, for each subject, and then dividing by 365.25.
- A patient's days of follow-up will be counted from yearly visit to yearly visit. Hypothetically if a subject has 350 days between their Year 1 visit and their Year 2 visit then that subject will contribute 350 days to the calculation of the patient years.

A high-level summary will be presented that provides total number of events and total number of subjects, for any SAE, death, or event resulting in subject withdrawal. All SAE will also be presented in data listing.

A separate table for potential immune–mediated events of medical significance will be provided. In addition, all AEs, including threatening SAEs, NoV vaccine-related SAEs, potential immune–mediated events of medical significance and any procedure-related medical occurrences will be presented in a table.

7.11.2 Clinical Laboratory Evaluations

Not applicable.

7.11.3 Vital Signs

Not applicable.

7.11.4 12-Lead ECGs

Not applicable.

7.11.5 Other Observations Related to Safety

Not applicable.

7.12 Interim Analysis

An IA will be performed after all subjects have provided one blood sample corresponding to at least the first year of participation in NOR-213 and the data for that trial segment have been sufficiently reviewed for accuracy and correctness. An interim report will be developed based on this analysis.

7.13 Changes in the Statistical Analysis Plan

Not applicable.

8.0 REFERENCES

1. Protocol – NOR-213. A Phase 2, Long-Term Immunogenicity Follow-up Trial of Adult and Elderly Subjects who have Previously Received an Intramuscular Injection of Norovirus GI.1/GII.4 Bivalent Virus-Like Particle Vaccine, dated 27 March, 2018, version 3.0.
2. Clinical Study Report – NOR-107 Day 208. A Phase II, Randomized, Controlled, Double-Blind, Dosage and Adjuvant Justification, Safety and Immunogenicity Trial of Intramuscular Norovirus GI.1/GII.4 Bivalent Virus-Like Particle Vaccine Adjuvanted with Aluminum Hydroxide and with or without Monophosphoryl Lipid A in Adults, dated 02 December 2016, version 2.0.
3. Clinical Study Report – NOR 107 Day 393, A Phase II, Randomized, Controlled, Dosage and Adjuvant Justification, Safety and Immunogenicity Study of Intramuscular Norovirus GI.1/GII.4 Bivalent Virus-Like Particle (VLP) Vaccine combined with Aluminum Hydroxide [$Al(OH)_3$], with and without Monophosphoryl Lipid A (MPL) Adjuvant in Adults, dated 02 December 2016, version 1.0.
4. Clinical Study Report – NOR 204, A Phase II, Randomized, Double-blind, Safety and Immunogenicity Trial of Norovirus GI.1/GII.4 Bivalent Virus-Like Particle (VLP) Vaccine In Healthy Elderly Adults, dated 13 September 2018, version 1.0.
5. Clinical Study Report – NOR 210, Phase II, Single Arm, Open Label Trial for Serologic Assay Validation, Proficiency Testing, Safety and Immunogenicity of the Intramuscular Norovirus GI.1/GII.4 Bivalent Virus-Like Particle Vaccine, dated 26 August 2016, version 1.0.

9.0 APPENDICES

9.1 Appendix A: Subject Distribution by Primary Vaccination Trial

			Subject Counts			CCI
Study	**Arm-Composition**	**Dosing schedule**	**Dosed**	**Completed**	**Per Protocol Set**	
NOR-107	1A: 15/15/500/50	Day 1	30	30	30	
	2A: 15/50/500/50	Day 1	30	30	29	
	3A: 50/50/500/50	Day 1	30	30	28	
	4A: 15/15/500/15	Day 1	31	31	29	
	5A: 15/50/500/15	Day 1	30	30	30	
	6A: 50/50/500/15	Day 1	31	31	31	
	7A: 15/15/500/0	Day 1	30	30	30	
	8A: 15/50/500/0	Day 1	32	32	32	
	9A: 50/50/500/0	Day 1	29	29	28	
	10A: 50/150/500/0	Day 1	30	30	30	
	11A: 15/50/167/0	Day 1	29	27	24	
	8B: 15/50/500/0	Days 1, 28	28	28	28	
	10B: 50/150/500/0	Days 1, 28	29	29	29	
	11B: 15/50/167/0	Days 1, 28	31	31	30	
NOR-210	8A: 15/50/500/0	Day 1	50	48	NA	
NOR-204	8A: 15/50/500/0	Day 1	76	73	72	
	8B: 15/50/500/0	Day 1, 29	74	69	67	
	5A: 15/50/500/15	Day 1	72	68	66	
	5B: 15/50/500/15	Day 1, 29	72	66	66	
	8A: 15/50/500/0	Day 1	25	24	24	

CCI

Note: Vaccine composition is given as XXµg of GI.1/ XXµg of GII.4c/XXXµg of aluminum hydroxide [$Al(OH)_3$]/XXµg of monophosphoryl lipid A (MPL);

9.2 Appendix B: Schedule of Trial Procedures

Primary Vaccination Trial	NOR-107	NOR-210	NOR-204	NOR-213 Time After First Vaccination				
Vaccination 1 (day)	1	1	1					
Vaccination 2 (day)	28	-	29					
Blood draw(s) (days)	**1, 28, 35, 56, 208, 393**	**1, 8, 15, 29**	**1, 8, 29, 36, 57, 211, 393**	**Year 2**		**Year 3**	**Year 4**	**Year 5**
NOR-213				**Screening[a]**	**Trial Entry**	**Year 1**	**Year 2**	**Year 3/ Trial End/ ET**
NOR-107						**X[a, c]**		
NOR-210					**X[a, c]**			
NOR-204					**X[a, c]**			
Procedure								
Visit					X	X	X	X
Visit window					±2 m	±2 m	±2 m	±2 m
Signed informed consent				X				
Eligibility criteria checked				X				
Demographics				X				
Medical history/prior medication				X				
Concomitant medication[b]					X	X	X	X
Enrollment[c]				X				
AE recording[d]					X	X	X	X
Procedure-related medical occurrences					X	X	X	X

CCI [redacted]

Notes: ET=Early Termination.

(a) Screening procedures to be performed prior to any trial procedures being performed. This should coincide with a scheduled visit.

(b) Concomitant medication related to adverse events (AEs) and serious adverse events (SAEs).

(c) After eligibility has been confirmed during the screening visit, subjects will be enrolled into the trial. Screening may coincide with the trial entrance visit.

(d) Recording of AEs in the subject's electronic case report form (eCRF) is limited to fatal and life threatening SAEs, NoV vaccine-related SAEs, potential immune–mediated events of medical significance and any procedure-related medical occurrences and must be recorded in the subject's source documents.

CCI [redacted]

CCI

[redacted]

Signature Page for NOR-213 Statistical Analysis Plan, Version 1.0, 05 September
Title:

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Approval	PPD Statistics 12-Sep-2019 15:34:05 GMT+0000
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