STATISTICAL ANALYSIS PLAN

Phase 1: Final Analysis

for

COVIVAC Phase 1/2 Protocol

Version 3.0 dated 27 Sep 2021

Study Title:
A Phase 1/2 Randomized, Placebo-controlled (phase 1) and Active- controlled (phase 2), Observer-blind Trial to Assess the Safety and Immunogenicity of COVIVAC Vaccine Produced by IVAC in Adults 18-59 and ≥ 60 years old in Vietnam

Sponsored by
Institute of Vaccines and Medical Biologicals (IVAC)

Prepared and Distributed by:
Center of Excellence for Biomedical and Public Health Informatics (BIOPHICS), Bangkok, Thailand

Version 1.0
27 May 2022

Protocol Number Code:	COVIVAC Phase 1/2
Development Phase:	Phase 1/2
Products:	**Investigational Vaccine:** Inactivated Newcastle Disease Virus (NDV) chimera expressing a trimeric pre-fusion form of the SARS-CoV-2 Spike (S) protein that contains six proline mutations (HexaPro, HXP); for intramuscular (IM) administration. One formulation of NDV-HXP-S evaluated in this study includes 1.5 mg of the adjuvant CpG 1018 (a 22-mer phosphorothioate-linked oligodeoxynucleotide). **Placebo:** Phosphase-buffered saline (PBS); for IM administration
Form/Route:	Intramuscular
Sponsor:	Institute of Vaccines and Medical Biologicals (IVAC) No. 9, Pasteur Street, Nha Trang City, Khanh Hoa Province, Vietnam
Date of the Analysis Plan:	27 May 2022
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This study was performed in compliance with Good Clinical Practice.

COVIVAC Phase 1/2 STATISTICAL ANALYSIS PLAN- Phase 1

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PROTOCOL TITLE:

A Phase 1/2 Randomized, Placebo-controlled, Observer-blind Trial to Assess the Safety and Immunogenicity of NDV-HXP-S Vaccine produced by IVAC in Adults Aged 18-75 Years in Vietnam

PROTOCOL NUMBER: COVIVAC Phase 1/2

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LIST OF ABBREVIATIONS

Ab	Antibody
ACE2	Angiotensin-converting enzyme 2
ADCC	Antibody-dependent cellular cytotoxicity
ADE	Antibody-dependent enhancement
ADR	Adverse drug reaction
AE	Adverse event
AESI	Adverse event of special interest
ALT	Alanine transaminase
ANCA	Anti-neutrophil cytoplasmic antibody
ARDS	Acute respiratory distress syndrome
AST	Aspartate transaminase
ATC	Anatomical Therapeutic Chemical
BAU	Binding Antibody Units
BIOPHICS	Center of Excellence for Biomedical and Public Health Informatics
BMI	Body Mass Index
BPL	Beta-propiolactone
C	Celsius
CAPA	Corrective action and preventive action
CBER	Center for Biologics Evaluation and Research
CDC	Centers for Disease Control and Prevention
CI	Confidence interval
Cm	Centimeter
CMI	Cell-mediated immunity
COVID-19	Coronavirus disease 2019 (disease caused by SARS-CoV-2)
CREST	Calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia
CRF	Case Report Form
CRO	Contract Research Organization
CSR	Clinical Study Report
D	day(s)
DSMB	Data and Safety Monitoring Board
EC	Ethics Committee
EDC	Electronic Data Capture
ELISA	Enzyme-linked Immunosorbent Assay
ELISpot	Enzyme-linked Immunospot
ELU	ELISA Units
EOS	End of study
ER	Emergency Room
EUA	Emergency Use Authorization
F	Fahrenheit
FDA	US Food and Drug Administration
FIPV	Feline infectious peritonitis virus
G	Group
GCP	Good Clinical Practice
GLP	Good Laboratory Practice

LIST OF ABBREVIATIONS (CONTINUE)

GMC	Geometric mean concentration
GMFR	Geometric mean fold rise
GMP	Good Manufacturing Practice
GMT	Geometric mean titer
HBsAg	Hepatitis B surface antigen
hCG	Serum human gonadotrophic hormone
HCV Ab	Hepatitis C virus antibody
Hgb	Gemoglobin
HIV 1/2 Ab	Human immunodeficiency virus 1 and 2 antibody
HN	Hemagglutinin-neuraminidase
HXP	HexaPro
IATA	International Air Transport Association
IB	Investigator's Brochure
ICF	Informed consent form
ICH	International Conference on Harmonisation
ID	Identification
IIV	Inactivated influenza virus vaccine
IgG	Immunoglobulin G
IL	Interleukin
IM	Intramuscular
IME	Important medical event
IN	Intranasal
INF	Interferon
IP	Investigational product
IRB	Institutional Review Board
ISMMS	Icahn School of Medicine at Mount Sinai
ISO	Internaitonal Organization for Standardization
IP	Investigational product
ISMMS	Icahn School of Medicine at Mount Sinai
IV	Intravenous
IVAC	Institute of Vaccines and Medical Biologicals
LLN	Lower limit of normal range
LLOQ	Lower limit of quantification
LMIC	Low- and middle-income country
LSLV	Last subject last visit
MAAE	Medically-attended adverse event
MedDRA	Medical Dictionary for Regulatory Activities
MERS-CoV	Middle East respiratory syndrome coronavirus
MIS-C	Multisystem inflammatory syndrome in children
mm	Millimeter
ml	Milliliter
MoH	Ministry of Health
N	Nucleocapsid
NAb	Neutralizing antibody
NDV	Newcastle disease virus
NICVB	National Institute for Control of Vaccines and Biological
NIHE	National Institute of Hygiene and Epidemiology
NT_{50}	50% neutralizing antibody titer
NT_{80}	80% neutralizing antibody titer

LIST OF ABBREVIATIONS (CONTINUE)

NTF	Note to file
PBMC	Peripheral blood mononuclear cell
PBS	Phosphate-buffered saline
PE	Physical examination
PI	Principal investigator (the term is used throughout to indicate PI or designee)
PIMMC	Potential immune-mediated medical conditions
Plt	Platelet
PNA	Pseudovirus Neutralization Assay
PPE	Personal protective equipment
PP IMM	Per protocol immunogenicity population
PSRT	Protocol Safety Review Team
PT	Preferred Term
qPCR	Quantitative polymerase chain reaction
R	Recovery
R_0	Reproduction number
RLU	Relative luminescence units
RNA	Ribonucleic acid
RSV	Respiratory syncytial virus
RT-PCR	Reverse transcription polymerase chain reaction
S	Spike
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SARS-CoV	Severe acute respiratory syndrome coronavirus
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SC	Subcutaneous
SOC	System Organ Class
SOP	Standard Operating Procedure
SSP	Study-specific procedure
SUSAR	Suspected unexpected serious adverse reaction
TEAE	Treatment-emergent adverse event
TEN	Toxic epidermal necrolysis
Th	T-helper cell
TLR-9	Toll-like receptor 9
TMF	Trial Master File
ULN	Upper limit of normal range
ULOQ	Upper limit of quantification
US	United States
USP	United States Pharmacopeia
V	Visit number (e.g. V1 = first study visit)
WBC	White blood cell
WHO	World Health Organization
WMA	World Medical Association
WOCBP	Women of childbearing potential
WT	Wild-type

1. PREFACE

This Statistical Analysis Plan (SAP) for "A Phase 1/2 Randomized, Placebo-controlled (phase 1) and Active- controlled (phase 2), Observer-blind Trial to Assess the Safety and Immunogenicity of COVIVAC Vaccine Produced by IVAC in Adults 18-59 and ≥ 60 years old in Vietnam" (Protocol: COVIVAC Phase 1/2) describes and expands upon the statistical information presented in the protocol.

This document describes all planned analyses which will be performed for Phase 1 data of the study and provides reasons and justifications for these analyses. It also includes sample tables, figures, and listings planned for the final analyses (see Appendix 1, Appendix 2, and Appendix 3). 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 provide sufficient detail to meet the requirements identified by the US Food and Drug Administration (FDA) and ICH.

This document contains a review of the study design, general statistical considerations, comprehensive statistical analysis methods for efficacy and safety outcomes, and a list of proposed tables and figures. Any deviation from this SAP will be described and justified in protocol amendments and/or in the Clinical Study Report (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

On 7 January 2020, a novel coronavirus was identified as the cause of a cluster of pneumonia cases first detected in December 2019 in Wuhan, the capital of China's Hubei province,[1] marking the third documented zoonotic transmission event of a coronavirus within the last two decades. Two other highly pathogenic coronaviruses,[1] both of the genus *Betacoronavirus*, also crossed the species barrier during this period: severe acute respiratory syndrome virus (SARS-CoV), which emerged in Guangdong province, China in November 2002, and ultimately led to 8,096 reported cases and 774 deaths in 27 countries before the last infection was detected in July 2003; and the Middle East respiratory syndrome coronavirus (MERS-CoV), which was first detected in Saudi Arabia in June 2012 (where it still circulates in camels) and has led to 2494 laboratory-confirmed cases and 858 deaths.[2] Phylogenic analysis from full-genome sequencing of the novel coronavirus (which became publicly available on 12 January 2020 [GenBank accession no. MN908947.2] indicated that it was also a Betacoronavirus, and that it belonged to the same subgenus (subgenus *Sarbecovirus* [subgroup B]) as SARS-CoV, with which it shares 79% nucleotide identity.[3] Given its taxonomic relationship to SARS-CoV, the novel coronavirus was designated severe acute respiratory syndrome virus 2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses. By 30 January 2020, the international outbreak of SARS-CoV-2 was declared a Public Health Emergency of International Concern by the World Health Organization

(WHO), which on 11 February 2020 named the disease caused by the virus COVID-19 (coronavirus disease 2019). By March 11, 2020, WHO officially declared the outbreak of COVID-19 a global pandemic.

2.1. Burden of Disease

As of 06 January 2021, the confirmed global case count of COVID-19 has risen to over 87 million, and deaths directly due to SARS-CoV-2 infection have surpassed 1.85 million.[4] The large majority of deaths have occurred among the elderly in the United States, Brazil, India and Mexico, which may be largely attributable to poorly implemented control measures (such as surveillance, border closure, quarantine and social distancing) in those countries.[5] While there have been significantly fewer cases to date in most low- and middle-income countries (LMICs), there is great concern about the potential impact of easing of containment efforts, particularly in countries where robust and functioning public health infrastructure is lacking.[6] In addition to the potentially devastating direct disease burden of SARS-CoV-2 in LMICs, the disruptions to routine health services and economic systems due to the pandemic may result in an indirect disease burden of equal or even greater magnitude – a burden that would be borne by all demographic groups. One study has estimated that disruptions to health systems and access to food in LMICs as a result of the COVID-19 pandemic would result in a minimum of 253,500 children under 5 child deaths and 12.200 maternal deaths over a 6-month period. In the worse scenario, there would be 1,157,000 additional under-five child deaths and 56,700 maternal deaths over a 6-month period.[7] In Vietnam, as of 06 January 2021 there have been 1,504 confirmed cases and 35 deaths.

2.2. Pathogen and Clinical Disease

Like all viruses in the *Coronaviridae* family, SARS-CoV-2 is an enveloped, positive-sense, single-stranded RNA virus, with a genome that (in addition to a replicase and accessory proteins) encodes four major structural proteins: the spike surface glycoprotein (S), small envelope protein, matrix protein, and nucleocapsid (N) protein. The diagnosis of COVID-19 is made by detection of SARS-CoV-2 RNA by reverse transcription polymerase chain reaction (RT-PCR), with a common gene target being one of the structural proteins. The coronavirus S protein plays the essential role of mediating cell entry by binding to the host-cell receptor, and thus is the primary determinant of viral tropism.[8] The S proteins of SARS-CoV and SARS-CoV-2 bind to the same primary host receptor, the angiotensin-converting enzyme 2 (ACE2) receptor, whereas MERS-CoV (which belongs to a different coronavirus lineage) uses dipeptidyl peptidase 4.

As is the case for both SARS-CoV and MERS-CoV, the median incubation period of SARS-CoV-2 is approximately four to five days after exposure.[9] Similar to SARS-CoV, pneumonia is the most frequent serious manifestation of SARS-CoV-2 infection, with dry cough, fever, myalgia, headache, dyspnea and sore throat being the most common presenting clinical features.[10] Diarrhea, nausea/vomiting, abdominal pain,[11] smell and taste disorders (i.e., anosmia and dysgeusia),[12] and rhinorrhea are also associated with COVID-19, though less commonly. While the spectrum of symptomatic SARS-CoV-2 infection ranges from mild to critical, most cases of COVID-19 are mild (approximately 80%).[13] In addition, multiple

studies now suggest that asymptomatic infection may be very common – as high as 88% by one report.[14] This is in contrast to SARS-CoV, which uncommonly caused mild or asymptomatic disease.[15]

In patients with severe to critical disease (approximately 15% and 5% of total cases, respectively),[13] dyspnea, hypoxia, cytokine release syndrome, acute respiratory distress syndrome, shock, thromboembolic complications, sudden cardiac death and multiorgan failure have been reported.[16] Most patients who die from COVID-19 are older persons (~80% of deaths occur in those > 65 years old)[17] and/or persons with underlying medical comorbidities (obesity, cardiovascular disease, diabetes, chronic lung disease, cancer, chronic kidney disease, hypertension),[18] although severe illness can occur in otherwise healthy persons of any age. In rare cases children can be severely affected, manifesting clinically as a hyperinflammatory syndrome similar to Kawasaki disease (a rare acute pediatric vasculitis)[19] or toxic shock syndrome;[20] this syndrome has been termed multisystem inflammatory syndrome.[21] In multiple cohort studies, male gender is strongly associated with death from COVID-19.[22],[23]

2.3. Transmission and Infectivity

Like SARS-CoV, there is considerable evidence that SARS-CoV-2 originated in bats, and was transmitted to humans after amplification in an intermediate host such as the pangolin.[24] Human-to-human transmission is thought to occur as a result of direct contact of virus with the mucous membranes of the infected person, primarily via infected respiratory droplets and aerosols. The risk of transmission from an individual with SARS-CoV-2 infection varies by the type and duration of exposure, factors such as the amount of virus in respiratory secretions, and the use of preventive measures. The interval during which an individual with COVID-19 is infectious appears to be highly variable, with duration of viral shedding dependent upon the severity of the illness.[25] However, it is known that SARS-CoV-2 can be transmitted prior to, or in the absence of the development of symptoms, and throughout the course of illness, with highest levels of virus in the upper respiratory tract – and thus perhaps highest infectivity – soon after symptom onset.[26] It is not known to what extent asymptomatic infection has contributed to the pandemic spread of the virus.[27]

2.4. Vaccine Development

Based on a basic reproduction number (R_0) of ~2-3,[28] 60% to 70% of the population would need to develop immunity to SARS-CoV-2 for pandemic spread to be contained in the absence of significant control measures. Recent seroprevalence surveys indicate that population immunity remains well below this threshold in countries with the highest burden of COVID-19.[29] These results make clear that herd immunity cannot be achieved through natural infection without incurring very significant additional costs to society in terms of mortality, morbidity, and ongoing economic and social disruption, and that the only acceptable route to achieving herd immunity is widespread – and ideally rapid – deployment of an effective vaccine.

Studies conducted previously in support of SARS-CoV and MERS-CoV vaccine development were instrumental in accelerating development of SARS-CoV-2 candidates. The fact that many COVID-19 vaccine programs have moved quickly with selection of the S protein as target antigen was due to prior preclinical and human immunology studies on SARS-CoV demonstrating that the S protein of SARS-CoV elicits neutralizing antibodies that are protective against SARS-CoV challenge (by blocking virus attachment and fusion, as well as possibly by triggering FcR-mediated cytolysis or phagocytosis), and that these antibodies persist in convalescent serum of patients who have recovered from SARS.[30] Not long after the onset of the COVID-19 pandemic it was similarly demonstrated that the S protein of SARS-CoV-2 induces anti-S IgG antibodies in infected humans that neutralize the virus in animal models,[31] and that these antibodies persist for many months in convalescent sera.[32] While it is likely that induction of CD8+ T-cells against S as well as other viral proteins [33] plays a complementary role in protection after natural infection, the importance of a robust anti-S IgG neutralizing antibody response in protection against disease after natural infection[34] or experimental vaccination[35] is now incontrovertible.

A large number of vaccine candidates employing a large diversity of vaccine platforms (mRNA, DNA, subunit, viral vectors, nanoparticle) are in development, many candidates that are currently in late stage Phase 3 development.[36] Two of these vaccines, Pfizer/BioNTech's and Moderna's mRNA-based vaccines that encode the full-length S protein with two stabilizing proline mutations (S-2P) have been shown to have an efficacy against COVID-19 of greater than 90% after a two-dose regimen. These results, along with supportive early-phase study results from multiple other S-protein-based candidate vaccines that have elicited high-titer neutralizing antibodies further validate the selection of the S protein as target antigen.[37]

2.5. Risk of Immune Enhancement

In addition to facilitating target antigen selection, preclinical studies of SARS-CoV and MERS-CoV vaccines have also highlighted the potential risk of a SARS-CoV-2 vaccine exacerbating disease caused by subsequent SARS-CoV-2 infection. An inactivated SARS-CoV vaccine was shown to induce disease enhancement in rhesus monkeys subsequently challenged with SARS-CoV, as a result of non-neutralizing antibodies generated by the vaccine against the SARS-CoV S protein.[38] Such antibody-dependent enhancement (ADE) also occurred in cats infected with the Alphacoronavirus feline infectious peritonitis virus (FIPV), after being vaccinated with an inactivated FIPV vaccine.[39] Vaccine-induced non-functional antibodies cause ADE by facilitating viral entry into host cells, by increasing binding efficiency of virus-antibody complexes to host cells via Fc receptors on those cells.[40]

A second mechanism by which immune enhancement of disease may occur is via vaccine-induced inflammation.[41] Apart from activating Fc-receptor mediated endocytosis, vaccine-induced antibodies may elicit Fc-mediated responses, such as complement activation and antibody-dependent cellular cytotoxicity (ADCC), that may contribute to immunopathology. This phenomenon was observed in ferrets and Cynomolgus monkeys challenged with SARS-CoV following vaccination with an inactivated whole SARS-CoV vaccine; [42] the animals developed lung immunopathology characterized by eosinophilic recruitment, increased

mucus production and airway hyperresponsiveness. The same immunopathology was observed in 1966 in children given formalin-inactivated respiratory syncytial virus (RSV) vaccine who subsequently were infected by RSV. [43] Enhancement of RSV disease in that study led to frequent hospitalizations and, in the youngest cohort, two deaths.[44] The prominence of eosinophils with such lung immunopathology has often been interpreted as signifying that this immune enhancement was the result of Th2-biased immune responses.

To date, there has been no evidence of antibody-dependent disease enhancement or immunopathology in animal studies and human trials of SARS-CoV-2 candidate vaccines. This is likely due to the fact that these candidates, including an inactivated SARS-CoV-2 vaccine,[45] have been shown to elicit high-titer anti-S neutralizing antibody responses. SARS-CoV-1 vaccines that elicit neutralizing antibodies against the SARS-CoV S protein were similarly able to protect animals from SARS-CoV challenge without evidence of acute lung injury and immunopathology.[46] In addition, many SARS-CoV-2 vaccine candidates include Th1-polarizing adjuvants to minimize the risk of disease enhancement. Nevertheless, disease enhancement remains a theoretical risk, particularly after waning of antibody responses, and therefore needs to be closely monitored in human clinical trials of SARS-CoV-2 vaccines.

2.6. Introduction to NDV-HXP-S Vaccine

Given the global scope of the COVID-19 pandemic, there is an urgent need for a safe and effective vaccine against COVID-19 that will be affordable and able to be manufactured at a sufficient scale to supply Vietnam and other low- and-middle-income countries. To achieve this aim, IVAC and two other consortium manufacturers – the Government Pharmaceutical Organization (GPO), Thailand and Instituto Butantan, Brazil – are independently developing an inactivated whole chimeric virion vaccine based on a Newcastle Disease Virus (NDV) that has been modified to also express the SARS-CoV-2 S protein on its surface. This technology was invented at the Icahn School of Medicine at Mount Sinai (ISMMS) (New York, New York, USA). Since NDV grows well in embryonated chicken eggs, the NDV chimeric vaccine can be manufactured using the same inexpensive egg-based process employed for inactivated influenza virus vaccine (IIV).[47] In addition to taking advantage of the cost-effectiveness of the manufacturing process, an inactivated chimeric NDV vaccine propagated in eggs (prior to being inactivated by beta-propiolactone [BPL]) is also expected to be as safe as egg-based IIV, which has an excellent safety profile, including in infants, pregnant women, and elderly adults.

As in the case of many COVID-19 vaccines currently in development, the inactivated chimeric NDV vaccine expresses the ectodomain of the SARS-CoV-2 S protein – which is fused to the F protein transmembrane domain of NDV, resulting in abundant expression of membrane-bound S antigen. While many candidate COVID-19 vaccines are targeting the S protein as antigen, the S protein expressed on the surface of the chimeric NDV virion is a much more stable construct than that utilized in other COVID-19 vaccines as it contains six stabilizing proline substitutions – four more than are introduced in the S protein antigen (S-2P) used in a number of COVID-19 candidate vaccines, including the Pfizer/BioNTech and Moderna vaccines. The resulting protein, called “HexaPro” (HXP) and developed by the University of Texas (Austin, TX, USA),[48] is more immunogenic (>10-fold higher) than S-

2P in mice (data unpublished), and also provides higher yields than S-2P when expressed recombinantly. As a result of these properties it is expected that significant dose-sparing will be possible with the NDV-HXP-S vaccine candidate relative to other vaccine candidates expressing the earlier-developed S-2P antigen. Dose-sparing translates to higher production volumes and lower cost of vaccine. Finally it is important to note that HexaPro has also been shown to be more thermostable than S-2P.[48] The fact that NDV-HXP-S is expected to be thermally stable at 2-8 °C is a major advantage of the vaccine over other COVID-19 candidates in development that will require storage at -20°C or even lower temperature.

While it is likely that the whole virion NDV-HXP-S vaccine alone will prove to be highly immunogenic in healthy adults due to endogenous adjuvanticity of the NDV virion, use of exogenous adjuvant may further increase the functional immune response to the vaccine – which may be important to ensure adequate protection in older adults, or possibly provide additional opportunity for dose-sparing. For this reason, the first part of this combined Phase 1/2 study is a first-in-human, Phase 1 evaluation of a 2-dose regimen of both unadjuvanted NDV-HXP-S (at 1 µg, 3 µg, and 10 µg dose levels) and NDV-HXP-S adjuvanted with CpG 1018 (at the 1 µg dose level) in healthy adults. CpG 1018, the adjuvant in the US-licensed HEPLISAV-B® vaccine (Dynavax Technologies Corporation, Emeryville, CA, USA), is a synthetic 22-mer oligodeoxynucleotide that exerts its action by targeting toll-like receptor 9 (TLR-9) expressed on a few key immune-cell types. When used as a vaccine adjuvant, CpG 1018 increases antibody concentrations to co-administered antigen, stimulates helper (CD4+) and cytotoxic (CD8+) T cell populations and generates robust T and B cell memory responses. Additionally, CpG 1018 strongly favors development of the Th1 subset of helper T cells, the type of helper T cell that is essential for protection from infections with viruses and intracellular bacteria. HEPLISAV-B was well-tolerated and shown to have an adequate safety profile in clinical trials in adults.[49] Interim analyses of an ongoing post-marketing study of over 30,000 HEPLISAV-B recipients and more than 35,000 active comparator recipients have raised no safety concerns.

2.7. Purpose of the Analyses

The main purpose of this study is to evaluate the safety, tolerability (primary objective) and immunogenicity (secondary objective) of NDV-HXP-S vaccine across a range of S-antigen dose levels – one with CpG 1018 as adjuvant – with the aim of expeditiously selecting a single candidate to advance to Phase 3 studies. The proposed dosing regimen for the tested vaccines is to administer two doses with 28-day interval. The period of 28 days between prime and boost was selected because it is the acceptable dosing interval for many licensed vaccines and other COVID-19 vaccines which are being developed. The analysis of data from Phase 1 will provide justification for advancement to the Phase 2 segment based on safety evaluations during an initial sentinel dose-escalation stage, and later an interim analysis of safety and immunogenicity (the latter primarily based on pseudovirus neutralization) through 28 and 14 days after the second dose, respectively.

An independent Data and Safety Monitoring Board (DSMB) will review unblinded safety data through Day 57, and on the basis of this review provide a recommendation for advancing

to Phase 2 (the DSMB will also be convened at any time during conduct of the study in the event that a study pause rule is triggered). In addition to this process for assessing adequate safety for advancing to Phase 2, a threshold immune response at Day 43 will be required for a vaccine formulation to be considered for advancement to Phase 2: namely, the observed seroresponse rate (defined as the percentage of subjects in a treatment group with at least a 4-fold rise from baseline in NT_{80} titers) will need to be at least 52% at the lower limit (LL) of the 95% confidence interval (CI) . Based on this criterion, there is less than 10% chance of incorrectly rejecting a vaccine candidate with a true seroresponse rate of 85% or higher, which is estimated to be the minimum response rate that would be consistent with further investment in an additional second-wave COVID-19 vaccine.

If warranted based on safety and immunogenicity, the two optimal NDV-HXP-S formulations will be selected for ongoing evaluation in Part 2 of the study based on results of the Phase 1 interim analysis. The Phase 2 segment of the study will include a sufficient number of older adults aged 60-75 (including those with stable chronic co-morbidities) to determine whether safety and immunogenicity of the vaccine may differ in this older population. It is critical that evaluation of NDV-HXP-S in older adults informs the selection of the NDV-HXP-S candidate to advance to Phase 3 studies (based on safety and immunogenicity through 14 days post-second vaccination in Phase 2), given the higher risk of severe COVID-19 in this age group, and the potential need for a higher dose level of antigen and/or use of adjuvant to achieve a comparable functional immune response as younger adults. Phase 2 immunogenicity and safety data through Day 43 and Day 57, respectively, will determine the vaccine composition to advance to Phase 3, registration, and commercialization. Cell-mediated immunity will also be evaluated in a subset of subjects in the Phase 2 segment as an exploratory objective to assess the S protein-specific T cell response including Th polarization. An exploratory evaluation of the IgG immune response against the NDV HN protein will also be conducted in all Phase 2 subjects to generate hypotheses about the utility of administering a booster dose of NDV-HXP-S vaccine.

In addition to standard safety monitoring throughout the study, subjects will be evaluated for specific adverse event of special interest (AESI); these include potential immune-mediated medical conditions, which may be associated with vaccination. In addition subjects will be closely monitored for adverse events associated with COVID-19 to identify, and treat if indicated, potential cases of COVID-19 during the trial, and to assess for possible vaccine-induced immune enhancement of disease. In addition to mandatory use of masks and other exposure control measures by staff and subjects during clinic visits, study subjects will be instructed to contact the Principal Investigator (PI) if they meet criteria for COVID-19 testing based on specified signs and symptoms; these criteria will be provided to subjects in the form of a fact sheet.

The ultimate aim of developing NDV-HXP-S vaccine for the prevention of COVID-19 is to obtain local registration of the vaccine in Vietnam, followed by prequalification by the WHO, with the goal of providing affordable access to a life-saving COVID-19 vaccine for Vietnam and other LMICs.

This SAP describes the statistical methodology and summaries required to assess the safety

tolerability and immunogenicity of NDV-HXP-S vaccine across a range of S-antigen dose levels to facilitate the selection of two candidates to advance to Phase 2.

3. STUDY OBJECTIVES AND ENDPOINTS – PHASE 1

The Phase 1 study objectives are listed here as in the protocol.

3.1. Study Hypotheses

The study will test the hypotheses that the NDV-HXP-S vaccine (NDV-HXP-S) have an acceptable safety profile and be well-tolerated at all dose levels when administered as a two-dose regimen either without adjuvant (at 1 µg, 3 µg, and 10 µg of S protein per 0.5 ml dose), or with the adjuvant CpG 1018 (at 1 µg of S protein per 0.5 ml dose) and to test that NDV-HXP-S elicit a measurable and dose-dependent neutralizing antibody response.

3.1.1. Primary Objective

Safety and Tolerability

- To assess the safety and tolerability of each of four formulations of NDV-HXP-S (at 1, 3 and 10 µg without adjuvant; and at 1 µg with CpG 1018) after the first and second dose of a two-dose regimen administered at a 28-day interval to adults aged 18-59 years

3.1.2. Secondary Objectives

Immunogenicity

- To assess the functional (neutralizing) humoral immune response elicited by each formulation of NDV-HXP-S, as measured by a SARS CoV-2 pseudovirus-based neutralization assay (PNA), at baseline, 28 days after the first vaccination, and 14 days after the second vaccination (to inform the selection of two formulations for evaluation in Phase 2), and 6 months after the second vaccination
- To assess the Immunoglobulin G (IgG) immune response elicited by each formulation of COVIVAC against the S protein of SARS-CoV-2, as measured by enzyme-linked immunosorbent assay (ELISA), at baseline, 28 days after the first vaccination, and 14 days and 6 months after the second vaccination

3.1.3. Exploratory Objective

- To assess the Immunoglobulin G (IgG) immune response against NDV HN as measured by enzyme-linked immunosorbent assay (ELISA), at baseline, 28 days after the first vaccination, and 14 days, 6 months after the second vaccination *(note: NDV HN ELISA is under development)*
- To assess the NT_{80} immune response elicited by each COVIVAC formulation as measured by PNA at baseline, 28 days after the first vaccination, and 14 days and 6 months after the second vaccination

3.2. Study Endpoints

3.2.1. Primary Endpoints

Safety and Tolerability

- Number and severity of solicited local and systemic AEs during the first 7 days after each vaccination
- Number, severity, and relatedness of clinically significant hematological and biochemical measurements at 7 days post each vaccination
- Number, severity and relatedness of all unsolicited AEs during the first 28 days after each vaccination
- Number, severity and relatedness of SAEs throughout the entire study period
- Number, severity and relatedness of MAAEs throughout the entire study period
- Number, severity and relatedness of AESI throughout the entire study period, including AESI relevant to COVID-19, and potential immune-mediated medical conditions (PIMMC)

3.2.2. Secondary Endpoints

Immunogenicity

- 50% neutralizing antibody (NT_{50}) geometric mean titer (GMT) against SARS-CoV-2 pseudovirus at baseline, 28 days after the first vaccination and 14 days and 6 months after the second vaccination in all the subjects. The primary analysis will be conducted separately for those who are anti-S IgG seronegative at baseline (no pre-screening for SARS-CoV-2 will be carried out)
- Geometric mean fold rise (GMFR) (from baseline) in NT_{50} against SARS-CoV-2 pseudovirus at 28 days after the first vaccination, and 14 days and 6 months after the second vaccination
- Percentage of subjects with NT_{50} seroresponses against SARS-CoV-2 pseudovirus as defined by (1) a $\geq$ 4-fold increase from baseline, and (2) a $\geq$ 10-fold increase from baseline at 28 days after the first vaccination and 14 days and 6 months after the second vaccination
- Anti-S IgG GMT at baseline and at 28 days after the first vaccination and 14 days and 6 months after the second vaccination
- GMFR (from baseline) in anti-S IgG GMT at 28 days after the first vaccination and 14 days and 6 months after the second vaccination
- Percentage of subjects with seroresponses in anti-S IgG titer as defined by (1) a $\geq$ 4-fold increase from baseline, and (2) a $\geq$ 10-fold increase from baseline, at

28 days after the first vaccination and 14 days and 6 months after the second vaccination

3.2.3. Exploratory Endpoint:

- Anti-NDV HN IgG GMT at baseline, 28 days after the first vaccination, and 14 days and 6 months after the second vaccination
- 80% neutralization antibody (NT_{80}) GMT, GMFR and percentage of seroresponders (≥ 4-fold increase from baseline)

3.3. Study Definitions and Derived Variables

3.3.1. Adverse Event

An adverse event is any untoward, undesired, or unplanned event in the form of signs, symptoms, disease, or laboratory or psychological/physiologic observations occurring in a subject enrolled in the clinical trial. This includes all subjects from whom consent has been obtained whether or not they have yet been randomized and received a study product. The event does not need to be causally related to trial participation or receipt of a study product. An AE is temporally related to participation in the study and will be documented as to whether or not it is considered to be related to vaccine. An AE includes, but is not limited to, the following:

- An intercurrent illness or injury during the course of the study
- Any clinically significant worsening of a preexisting condition

3.3.2. Solicited Adverse Event

Solicited adverse events are pre-specified injection-site-specific local and systemic AEs that occur relatively more frequently, or are known to be associated with, immunization, and which are monitored actively as potential indicators of vaccine reactogenicity. Investigators will not be required to assess causality of solicited AEs if the onset is during the solicitation period.

The following specific solicited AEs will be monitored for this study:

Local solicited AEs assessed at the injection site:

- Pain or tenderness
- Swelling or induration
- Erythema

Systemic solicited AEs:

- Fever (defined as oral temperature ≥ 38°C)
- Headache
- Fatigue or malaise
- Myalgia
- Arthralgia

- Nausea or vomiting

3.3.3. Unsolicited Adverse Event

An unsolicited adverse event is any AE reported spontaneously by the subject, observed by the study staff during study visits or those identified during review of medical records or source documents. Solicited AEs with an onset after the seven-day solicitation period will be considered unsolicited AEs. In the absence of a diagnosis, abnormal physical examination findings or abnormal clinical safety laboratory test results that are assessed by the investigator to be clinically significant will be recorded as an AE.

3.3.4. Medically-Attended Adverse Event

A medically-attended adverse event is an unsolicited AE for which the subject received medical attention, such as during an emergency room visit or a visit to or from medical personnel (e.g., medical doctor).

3.3.5. Adverse Event of Special Interest

An adverse event of special interest (AESI) is an AE of scientific and medical concern specific to the Sponsor's product or program, for which ongoing monitoring and rapid communication by the investigator to the Sponsor can be appropriate. Such an event might warrant further investigation in order to characterize and understand it.

The AESI to be monitored in this study include the following:

- Potential immune-mediated medical conditions (PIMMC), given that vaccination has been associated with autoimmunity
- AEs associated with COVID-19, given the importance to subject safety of managing any occurrence of COVID-19, and the possible association of vaccination with enhancement of COVID-19

3.3.6. Protocol-Related Adverse Event

A protocol-related adverse event is an AE that occurs from the time of enrollment until the EOS visit that is not considered to be related to receipt of the study vaccine, but is considered by the PI/designee or the Sponsor to be related to the research conditions, i.e., related to the fact that a subject is participating in the study. For example, a protocol-related AE may be an untoward event occurring during blood sampling or other protocol-specified activity.

3.3.7. Treatment-Emergent Adverse Event

A treatment-emergent AE is defined as an AE that is not present prior to administration of the study product, or, if present prior to the administration of the study medication, increases in intensity after administration of the study medication during the course of the study.

3.3.8. Serious Adverse Event

An SAE is a specific AE that:

- Results in death.

- Is life-threatening.*
- Requires inpatient hospitalization or prolongation of an existing hospitalization.**
- Results in a persistent or significant disability or incapacity.***
- Results in a congenital anomaly or birth defect.

***Life-threatening** refers to immediate risk of death as the event occurred per the reporter. A life-threatening event does not include an event that, had it occurred in a more severe form, might have caused death but, as it actually occurred, did not create an immediate risk of death.

For example, hepatitis that resolved without evidence of hepatic failure would not be considered life-threatening, even though hepatitis of a more severe nature can be fatal. Similarly, an allergic reaction resulting in angioedema of the face would not be life-threatening, even though angioedema of the larynx, allergic bronchospasm, or anaphylaxis can be fatal.

****Hospitalization** is an admission to a health facility in the situation where there is an AE. A period of observation at a clinical trial site is not considered to represent hospitalization for the purposes of SAE reporting. Hospitalization or prolongation of a hospitalization constitutes a criterion for an AE to be serious; however, it is not in itself considered an SAE. In absence of an AE, a hospitalization or prolongation of a hospitalization should not be reported as an SAE by the PI/designee on a SAE form. Such situations include, but are not limited to, the following:

- A hospitalization for a preexisting condition that has not worsened.
- Hospitalization for social reasons.

*****Disability** is defined as a substantial disruption in a person's ability to conduct normal life functions. If there is any doubt about whether the information constitutes an SAE, the information is treated as an SAE.

Medical and scientific judgment should be exercised in deciding whether expedited reporting is appropriate in other situations, such as **important medical events** that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the patient or may require intervention to prevent one of the other outcomes listed in the definition above. These should also usually be considered serious. Examples of such events are intensive treatment in an emergency room or at home for allergic bronchospasm, or blood dyscrasias or convulsions that do not result in hospitalization.

3.3.9. Severity (Intensity) of Adverse Event

The severity of all solicited AEs will be graded from Mild (Grade 1) to Potentially Life Threatening (Grade 4). All AEs leading to death are Grade 5 events. Adverse events are graded based on the worst severity grade during the illness/symptoms. All other unsolicited AEs will be classified as an AE and graded based on the AE severity scale in table of severity grading below. The grading scales for solicited and unsolicited AEs have been derived from the *Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events* (Version 2.1, July 2017), from the US National Institutes of Health.

Table of Severity Grading – Protocol Table 6

Grade	Description
1	Causes no or minimal interference with normal daily activities; intervention not indicated
2	Interferes with but does not prevent normal daily activities; intervention indicated
3	Prevents normal daily activities; intervention or hospitalization indicated
4	Causes inability to perform basic self-care activities; intervention indicated to prevent permanent impairment, persistent disability, or death

3.3.10. Causal Relationship of an Adverse Event

A suspected adverse drug reaction (ADR) means any AE for which there is a reasonable possibility that the study vaccine caused the AE. A reasonable possibility means there is evidence to suggest a causal relationship between the vaccine and the AE. All cases judged by either the PI/designee or the Sponsor as having a reasonable suspected causal relationship to the study vaccine will qualify as ADRs. Medical judgment will be used to determine the relationship, considering all relevant factors, including pattern of reaction, temporal relationship, confounding factors such as concomitant medication, concomitant diseases, and relevant history.

The likelihood of the relationship of the AE to study vaccine is to be recorded as follows:

- Related: There is a reasonable causal relationship between the vaccine administered and the AE.
- Not Related: There is no reasonable causal relationship between the vaccine administered and the AE.

Note: solicited reactogenicity events will not be judged for relatedness.

3.3.11. Assessment of Outcome of Adverse Event

The outcome of the AE will be assessed and recorded as per the following categories:

- Ongoing
- Recovered/resolved
- Recovered/resolved with sequelae
- Fatal
- Unknown

3.3.12. Adverse Event Recording and Reporting

Recording and reporting of all AEs will occur from signing of the ICF (enrollment) through 28 days post-second injection (Visit 6) for each study subject receiving study product. SAEs, MAAEs, and AESI will be recorded throughout the study period. The Study staff must completely and promptly record each AE in the source documentation and on the AE CRF,

regardless of relationship to the vaccine administered/procedure as determined by the PI/designee. The PI/designee will attempt, if possible, to establish a diagnosis based on the signs and symptoms. When a diagnosis for the reported signs or symptoms is known, the PI/designee will report the diagnosis as the AE, not the signs and symptoms. Adverse events will be classified by MedDRA term and by severity/intensity, relatedness, and outcome.

Enrolled subjects who subsequently screen fail (i.e., who never underwent randomization) will have any AEs recorded from enrollment until the time they are determined to be ineligible for randomization or withdraw consent. These AEs will be listed in separate appendices from those subjects randomized and vaccinated. For the purposes of data capture they will be closed at the point the subject is deemed ineligible.

Reporting of AEs will follow the regulatory guidelines of the Ministry of Health and NIHE's Ethics Committee (EC) in regard to requirements, processes and forms.

3.3.13. Serious Adverse Event Reporting

If an AE is classified as serious, an SAE form will be completed and submitted within 24 hours of the PI/designee becoming aware of the SAE, including information on the location, severity, relatedness, and clinical summary of the event to the Sponsor to initiate any PSRT evaluation and any additional reporting requirements. In addition, the SAE submission will follow the regulatory guidelines of the Ministry of Health and NIHE's IRB in regards to requirements, processes and forms. It is the responsibility of the Sponsor to ensure that Dynavax Technologies Corporation (manufacturer of the adjuvant CpG 1018) and the other Consortium manufacturers are notified of SAEs and other notable safety events per agreed procedures and timelines. Any SAE deemed related to study vaccine that is ongoing at the time of last subject last visit (LSLV) will continue to be followed until it is resolved, assessed to be resolved with sequelae, or assessed to be stable/chronic. SAEs deemed not related to study vaccine that are unresolved at the time of LSLV will be classified as ongoing.

3.3.14. Unanticipated Problems

All unanticipated problems will be reported in the continuing review report submitted to the Ministry of Health and NIHE's IRB per reporting requirements of each regulatory body. All serious unanticipated problems involving risk to participants or others will be promptly (within 48 hours) reported by telephone, by email, or by facsimile to the Sponsor. Follow-up reports will be submitted as soon as additional information becomes available.

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

This prospective, single-center, randomized, placebo-controlled, observer-blind Phase 1/2 study includes two separate parts. The treatment groups to be evaluated in each part of the study (and their corresponding sample size) are presented in Table 1.

Table 1: Treatment Groups - Protocol Table 3

Group	Sample Size	Study Product
1	20	Placebo
2	25	NDV-HXP-S 1 µg
3	25	NDV-HXP-S 3 µg
4	25	NDV-HXP-S 10 µg
5	25	NDV-HXP-S 1 µg + CpG1018 1.5 mg

Phase 1 study designed to evaluate the safety, tolerability, and immunogenicity of the NDV-HXP-S vaccine at three different dose levels (1, 3, and 10 µg) without adjuvant, and at one dose level (1 µg) with the adjuvant CpG 1018, in a total of 120 subjects aged 18-59 years. Eligible subjects will be randomly assigned to receive study vaccine or placebo as an IM injection in the deltoid muscle at Visit [V]1 as part of one of four sequential groups of escalating antigen dose level or added adjuvant. Each group will be divided into two sequential subgroups, a sentinel subgroup (n=6) and a larger subgroup (n=24) that includes the remaining subjects to be evaluated at that dose level (or for that formulation in the case of the one adjuvanted treatment group). Initially, a sentinel subgroup of 6 subjects will be randomized to receive NDV-HXP-S 1 µg or placebo in a 5:1 ratio (subjects within a sentinel subgroup will receive the first injection only after immediate reactogenicity assessments of the prior subject in the subgroup are completed). Sentinel subjects will be monitored for reactogenicity and safety through Day 8 (Visit 2), including for the initial 24 hours post-injection in clinic. If the PSRT has no safety concerns based on blinded review of all safety data, including clinical laboratory results, through Visit 2, the second subgroup of 24 subjects will be randomized to receive NDV-HXP-S 1 µg or placebo at the same ratio; on the same day, the sentinel subgroup (n=6) for the second dose level to be evaluated (NDV-HXP-S 3 µg) can be randomized to receive study vaccine or placebo in a 5:1 ratio, and so on for the subsequent dose level and formulation (see Table 2).

Table 2: Phase 1 Dose Escalation Steps – Protocol Table 4

Subgroup	Escalation Steps													
Dose 1µg & Placebo (5+1)	V1	V2												
Dose 1µg & Placebo (20+4)			V1	V2										
Dose 3µg & Placebo (5+1)			V1	V2										
Dose 3µg & Placebo (20+4)					V1	V2								
Dose 10µg & Placebo (5+1)					V1	V2								
Dose 10µg & Placebo (20+4)										V1	V2			
Dose 1µg+CpG & Placebo (5+1)										V1	V2			
Dose 1µg+CpG & Placebo (20+4)													V1	V2
Review			**PSRT**			**PSRT**			**PSRT**			**PSRT**		

V1 = Visit 1 (Day 1)
V2 = Visit 2 (Day 8)
PSRT = Protocol Safety Review Team meeting

The PSRT will review blinded safety, reactogenicity and clinical laboratory data accrued on a weekly basis until D43 of the last subject in each phase of the study, then at least once monthly until the end of the study. Subjects will receive 2 doses of assigned IP on D1 and D29 (V1 and V3), and be assessed in clinic for safety and reactogenicity at 7 days after each vaccination (V2 and V4), for safety at 28 days after the second vaccination (V6), and for safety and immunogenicity assessments at baseline (V1), 28 days after the first vaccination (V3) and 14, 168 and 336 days after the second vaccination (V5, V7, and V8, EOS Visit).

An interim analysis of Phase 1 data conducted after the last subject last visit for V6 (D57) will serve as the basis for decisions about down-selection and advancing to Part 2 of the study (Phase 2). Down selection and advancement to Part 2 (Phase 2) will be based on the following parameters:

- Post-dose 2 immunogenicity results at the aggregate treatment level
  - A threshold immune response at Day 43 will be required: the observed seroresponse rate in a treatment group (defined as the percentage of subjects with at least a 4-fold rise from baseline in 80% neutralizing antibody titers) will need to be ≥52% at the LL of the 95% CI for that treatment (vaccine formulation) to be considered for advancement to Phase 2.
- Post-dose 1 and post-dose 2 safety results including all solicited and unsolicited adverse events, serious adverse events, and clinical laboratory results.

The following process will be followed for the decision about down-selection and advancing Part 2 (Phase 2):

- The DSMB will review the unblinded safety data and provide a recommendation to the Sponsor on whether the safety profile is acceptable for advancing a formulation to Phase 2.
- The Sponsor will review the DSMB recommendation in conjunction with the immunogenicity data and select two formulations to advance to Phase 2.
    - If multiple formulations achieve the threshold immune response (as well as have an adequate safety and tolerability profile per the DSMB), the Sponsor will select two formulations to advance to Phase 2 based on consideration of such factors as the relative functional immunogenicity of these formulations, opportunity for dose sparing, and opportunity to limit cost and possible supply constraints associated with use of the CpG adjuvant.
- The selection and recommendation to advance to Phase 2 along with the interim report will be jointly reviewed by NIHE's IRB and MoH prior to Phase 2 enrollment.

4.2. Selection of Study Population

4.2.1. Description of Study Population

For Phase 1, the study population will consist of eligible, Vietnamese male and female adults aged 18-59 years old, inclusive.

4.2.2. Inclusion Criteria for Enrollment

Participants are eligible for Phase 1 study if they fulfill the inclusion criteria below:

- Adult 18 through 59 years of age inclusive at the time of randomization.
- Healthy, as defined by absence of clinically significant medical condition, either acute or chronic, as determined by medical history, physical examination, screening laboratory test results, and clinical assessment of the investigator.
- Has provided written informed consent prior to performance of any study-specific procedure.
- Has a body mass index (BMI) of 17 to 40 kg/m^2, inclusive, at screening.
- Resides in study site area and is able and willing to adhere to all protocol visits and procedures.
- If a woman is of childbearing potential, must not be breastfeeding or be pregnant (based on a negative urine pregnancy test at screening and during the 24 hours prior to receipt of the first dose of IP), must plan to avoid pregnancy for at least 28 days after the last dose of IP, and be willing to use an adequate method of contraception consistently and have a repeated pregnancy test prior to the second (last) dose of IP.

4.2.3. Exclusion Criteria for Enrollment

Participants will be ineligible for this study for any of the following conditions or reasons:

- Use of any investigational medicinal product within 90 days prior to randomization or planned use of such a product during the period of study participation.
- History of administration of any non-study vaccine within 28 days prior to administration of study vaccine or planned within 3 months after enrolment.

  Note: receipt of any COVID-19 vaccine that is licensed or granted Emergency Use Authorization in Vietnam during the course of study participation is not exclusionary if administered after Visit 5.

- Previous receipt of investigational vaccine for SARS or MERS, or any investigational or licensed vaccine that may have an impact on interpretation of the trial results.
- History of hypersensitivity reaction to any prior vaccination or known hypersensitivity to any component of the study vaccine.
- History of egg or chicken allergy.
- History of angioedema.
- History of anaphylaxis.
- Acute illness (moderate or severe) and/or fever (body temperature measured orally ≥38°C).
- Any abnormal vital sign deemed clinically relevant by the PI.
- Abnormality in screening laboratory test deemed exclusionary by the PI in consultation with the Sponsor.
- A positive serologic test for hepatitis B (HBsAg) or hepatitis C (HCV Ab).
- History of laboratory-confirmed COVID-19 (RT-PCR positive to SARS-CoV-2).
- History of confirmed HIV.
- History of laboratory-confirmed COVID-19.
- History of malignancy, excluding non-melanoma skin and cervical carcinoma in situ.
- Any confirmed or suspected immunosuppressive or immunodeficient state.
- Administration of immunoglobulin or any blood product within 90 days prior to first study injection or planned administration during the study period.
- Administration of any long-acting immune-modifying drugs (e.g., infliximab or rituximab) or the chronic administration (defined as more than 14 days) of immunosuppressants within six months prior to first study injection, or planned administration during the study period (includes systemic corticosteroids at doses equivalent to ≥ 0.5 mg/kg/day of prednisone; the use of topical steroids including inhaled and intranasal steroids is permitted).
- History of known disturbance of coagulation or blood disorder that could cause anemia or excess bleeding (e.g, thalassemia, coagulation factor deficiencies).
- Recent history (within the past year) or signs of alcohol or substance abuse.
- Any medical, psychiatric or behavior condition that in the opinion of the PI may interfere with the study objectives, pose a risk to the subject, or prevent the subject from completing the study follow- up.
- Employee of any person employed by the Sponsor, the contract research organization (CRO), the PI, study site personnel, or site.

Note: specific exclusion criteria (e.g., ≥ Grade 2 acute illness, or abnormal vital sign deemed clinically relevant by the PI/designee) will be reassessed at both vaccination visits. Any subject who cannot be vaccinated due to an acute abnormality assessed at a vaccination visit (Visit 1 or Visit 3) may return once the acute issue has resolved, if deemed appropriate by the PI/designee. A minimum of 48 hours must have passed after a documented fever before a subject can be vaccinated. This safety requirement will not be deemed a protocol deviation should the visit fall outside the vaccination window; however, it will be encouraged to maintain the vaccination window whenever possible in these situations. Clinical laboratory test results and vital signs used to determine subject eligibility will be those obtained at screening. These tests may be repeated once if deemed appropriate by the investigator and determined to be due to a transient condition that has resolved. In addition, a test may also be repeated for test results determined to be spurious by the investigator (e.g., following improper specimen collection). The last measurement will be taken as the baseline for purposes of analysis.

4.3. Study Product

4.3.1. Product Descriptions

NDV-HXP-S is an inactivated NDV chimera expressing a trimeric pre-fusion form of the SARS-CoV-2 S protein that contains six proline mutations (HexaPro). The vaccine is a clear and slightly opalescent liquid.

All study vaccine products to be administered on a given day (based on the study stage) will be formulated separately by the assigned site staff under aseptic conditions at the start of the clinic day. A detailed mixing procedure will be provided in the Pharmacy Manual or SOP for study product preparation. Each vaccine product will be formulated by filling a 4 ml (4R) [with the height of 46 mm and diameter of 16/1 mm] USP Type I glass vial with bulk drug substance, bulk adjuvant (if indicated based on formulation) and phosphate-buffered saline (PBS) to allow for five 0.5 ml doses per vial, as well as sufficient residual volume for possible dose verification. Each vial label will include the following information: name of the medicinal product, composition, fill volume, route of administration, lot number, manufacturing date, storage condition, and a cautionary statement (“For Clinical Trial Use Only”).

The placebo control is PBS (pH 7.2), manufactured by IVAC and tested by National Institute for Control of Vaccines and Biological (NICBV).

4.3.2. Identity of Investigational Product

Investigational Vaccine:

Inactivated Newcastle Disease Virus (NDV) chimera expressing a trimeric pre-fusion form of the SARS-CoV-2 Spike (S) protein that contains six proline mutations (HexaPro, HXP); for intramuscular (IM) administration. One formulation of NDV-HXP-S evaluated in this study includes 1.5 mg of the adjuvant CpG 1018 (a 22-mer phosphorothioate-linked oligodeoxynucleotide).

Placebo:

Phosephate-buffered saline (PBS); for IM administration

4.4. Method of Assigning Participants to Treatment Groups (Randomization)

The randomization scheme was generated and maintained by Center of Excellence for Biomedical and Public Health Informatics (BIOPHICS).

Randomization for Part 1 (Phase 1) will be conducted after accumulation of 120 eligible subjects. Randomization will be stratified by gender and age (less than 40 years old and 40 to 59 years old, with approximately 50% of subjects in each age stratum). This is to ensure the groups are as similar (homogenous) as possible to ensure the down-selection of formulations is not biased by differences in demographic characteristics of the groups (such as age and gender). Randomization details will be outlined in a Randomization Plan prior to study initiation.

Each group will be divided into two subgroups, a sentinel subgroup (n=6) and a larger subgroup (n=24) that includes the remaining subjects to be evaluated at that dose level (or for that formulation in the case of the one adjuvanted treatment group). Initially, a sentinel subgroup of 6 subjects will be randomized to receive NDV-HXP-S 1 µg or placebo in a 5:1 ratio. Sentinel subjects will be monitored for reactogenicity and safety through Day 8 (Visit 2), including for the initial 24 hours post-injection in clinic. If the PSRT has no safety concerns based on blinded review of all safety data, including clinical laboratory results, through Visit 2, the second subgroup of 24 subjects will be randomized to receive NDV-HXP-S 1 µg or placebo at the same ratio; on the same day, the sentinel subgroup (n=6) for the second dose level to be evaluated (NDV-HXP-S 3 µg) can be randomized to receive study vaccine or placebo in a 5:1 ratio, and so on for the subsequent dose level and formulation (see Table 2). The same procedure will be used for the NDV-HXP-S 10 µg and NDV-HXP-S 1 µg + CpG arms for a total of n=25 in each active group and n=20 in the placebo group. Randomization will be stratified by age (less than 40 years old and 40 to 59 years old) and gender with approximately 25% of subjects in each age & gender stratum.

4.5. Blinding

A limited number of appropriately trained, unblinded study staff, including the site pharmacist, will be responsible for preparing study products (in accordance with the randomly determined assignment), administering the study vaccine, and handling all drug accountability procedures. These personnel will not participate in the other aspects of the clinical trial, to help ensure the integrity of the blind at the site. The unblinded staff will not reveal subjects' randomization assignments to subjects, or staff associated with the Sponsor, CRO, or site.

Randomization data are kept strictly confidential, and should be accessible only to authorized persons, until the time of unblinding.

4.5.1. Unblinding Procedure

In the event of a medical emergency, the PI/designee may require that the blind be broken

for the subject experiencing the emergency when knowledge of the subject's treatment assignment may influence the subject's clinical care. Every effort will be made not to unblind the subject unless it is considered absolutely necessary for the welfare of the subject. Prior to unblinding, the investigator is encouraged (to the extent possible, without jeopardizing the subject's health) to contact the Sponsor (or designee) to discuss the decision to break the blind.

Unblinding will occur according to the emergency unblinding SOP, to which there will be 24-hour access. Documentation of the unblinding event will be captured by the unblinded staff. The PI/designee will be expected to provide a rationale for the necessity of unblinding, based on the expectation that knowledge of the subject's treatment assignment will have a meaningful impact on the subject's medical care in the short term. If a subject's treatment assignment is unblinded, the subject will remain in the study and continue with protocol-defined study visits and procedures, unless there is another reason for subject discontinuation. The decision to unblind will be communicated to all regulatory bodies as required. At the end of the study, documentation of all unblinded subjects (and the rationale for unblinding) will be incorporated into the TMF.

4.6. Prior and Concomitant Therapy

All concomitant medications will be recorded in source documents from Visit 1 (Day 1) through Visit 6 (Day 57). After Visit 6, only those concomitant medications associated with AESI, MAAEs, and SAEs will be recorded. Details on concomitant medications to be recorded include the generic and/or trade name, indication, dosage, regimen, route of administration, and start and end dates of the medication.

The following concomitant medications are prohibited during the study; however, they must not be withheld by the treating physician if clinically indicated to treat a subject:

- Any investigational medicinal product other than the study product
- Administration of immunoglobulins or any blood products
- Administration of any long-acting immune-modifying drugs (e.g., infliximab or rituximab) or the chronic administration (defined as more than 14 days) of immunosuppressive medications (includes systemic corticosteroids at doses equivalent to ≥ 0.5 mg/kg/day of prednisone; the use of topical steroids including inhaled and intranasal steroids is permitted).

Use of any prohibited medication must be recorded in the CRF. Whether a subject who uses a prohibited medication will be included in the Per Protocol Population will be evaluated on a case by case basis.

4.7. Treatment Compliance

Eligible subjects will be randomly assigned to receive 2 doses of study vaccine or placebo as IM injections in the deltoid muscle on D1 (V1) and D29 (V3), and be assessed in clinic for safety and reactogenicity at 7 days after each vaccination (V2 and V4), for safety at 28 days after the second vaccination (V6), and for safety and immunogenicity assessments at baseline (V1), 28 days after the first vaccination (V3) and 14, 168 and 336 days after the second

vaccination (V5, V7, and V8, end-of-study [EOS] Visit).

4.8. Protocol Deviation

A protocol deviation is any noncompliance with the clinical trial protocol, GCP, site SOP requirements, or departure from applicable regulatory requirements. The noncompliance may be either on the part of the subject or the site team/PI.

Major protocol deviations are a subset of protocol deviations that may significantly impact the completeness, accuracy, and/or reliability of the study data or that may significantly affect a subject's rights, safety, or well-being. Examples of major protocol deviations may include: failure to obtain informed consent, failure to report SAEs, enrolling subjects in violation of key eligibility criteria designed to ensure a specific subject population, or failing to collect data necessary to interpret primary endpoints, as this may compromise the scientific value of the trial.

When appropriate, corrective actions and preventive actions (CAPAs) will be developed by the site to address deviations, and will be implemented promptly. These practices will be consistent with ICH E6 Guidelines.

4.9. Safety and Immunogenicity Variables

The following section describes the collection of safety and immunogenicity variables.

4.9.1. Safety Variables

4.9.1.1. Reactogenicity Events

Refer to Section 3.3.2

4.9.1.2. Unsolicited Adverse Event

Refer to Section 3.3.3

4.9.1.3. Serious Adverse Event (SAE)

Refer to Section 3.3.8 for the definition of SAE.

4.9.1.4. Severity of Adverse Event

Refer to Section 3.3.9 for the details describing severity.

4.9.1.5. Causality of Adverse Event

Refer to Section 3.3.10 for details on determining causality.

4.9.2. Immunogenicity Variables

- The functional (neutralizing) humoral immune response elicited by each formulation of NDV-HXP-S, as measured by a SARS-CoV-2 pseudovirus-based neutralization assay (PNA)
- The Immunoglobulin G (IgG) immune response elicited by each formulation of

NDV-HXP-S against the S protein of SARS-CoV-2, as measured by enzyme-linked immunosorbent assay (ELISA)

5. SAMPLE SIZE CONSIDERATIONS

This Phase 1/2 study has a two-part selection design with group elimination after the first part (i.e. Phase 1). A total of 25 (n_1) subjects per group will be randomized across 4 candidates and one placebo group (n_1=20) in the first phase. Assay titers will be analyzed on the log scale. The sample size and power calculations assume an interim analysis will be conducted after D43 of the first phase to eliminate two candidate groups by selecting the two groups with the largest means. Additionally, the observed seroresponse rate (defined as the percentage of subjects in a treatment group with at least a 4-fold rise from baseline in 80% neutralizing antibody titers) will need to be at least 52% at the lower limit of the 95% exact confidence interval. Based on this criterion, there is less than 10% chance of incorrectly failing to consider advancing a vaccine candidate with a true seroresponse rate of 85% or higher, which is estimated to be the minimum response rate that would be consistent with further investment in an additional second-wave COVID-19 vaccine. The Sponsor may consider other factors in selecting the two most suitable candidates to advance to second phase. In the second phase, 125 and 50 (n_2) additional subjects will be randomized to the two candidate groups and the placebo group, respectively. The final analysis will be conducted on the full samples from the first and second phase ($n_1 + n_2$).

Safety: Assuming 25 evaluable subjects per group in the first phase (and for elderly subjects enrolled in the second phase) and 150 total subjects ($n_1 + n_2$) in the two candidate groups included in the second phase, the probability of observing at least one serious or severe adverse event by the underlying rate is shown in Table 7 in the protocol. If no events are observed, the upper bound of the exact 95% confidence interval would be 13.7% for the three eliminated groups and 2.4% in the two selected groups.

Immunogenicity: Groups with seroresponse below 52% at the lower limit of the 95% exact confidence interval will not be considered for selection for the second phase. This provides 90% power to correctly advance candidates with a true seroresponse rate ≥85%.

This is a two-stage selection design for selecting the group with the largest mean. Power for selecting the candidate with the largest true mean is driven both by the variability and the smallest difference between the highest mean and the means in the other three candidate groups.

Table 8 in the protocol shows the power to correctly select the candidate with the largest true mean in the first phase (to advance to the second phase) and the overall power for the Phase 1/2 by minimum fold-difference (on the titer scale) between the highest mean and the other means, assuming log10 variability of 0.5. These calculations assume in the first phase there are n_1=22 evaluable subjects in the four candidate groups, two groups are eliminated after the first phase, there are n_2=112 additional evaluable subjects in the remaining two candidate groups at D43 of second phase ($n_1 + n_2$=134), and $\mu_4 > \mu_1 = \mu_2 = \mu_3$.

6. GENERAL STATISTICAL CONSIDERATIONS

6.1. General Principles

All analyses will be tabulated by vaccination received, including a column for the total across all subjects. Baseline demographics and characteristics, including age, height, weight, sex, race ethnicity, and BMI will be summarized for both the exposed and per protocol populations by treatment group using descriptive statistics (mean, standard deviation, median, 1st and 3rd quartiles, minimum and maximum for continuous and frequencies, percentage, proportions, and exact Clopper-Pearson 95% confidence intervals (CIs) for categorical). All percentages will be presented to one decimal place.

Medical history will be listed and summarized by category. Using the WHO Drug Dictionary, concomitant medications will be tabulated by anatomical therapeutic chemical (ATC) classification, preferred drug name and treatment group. Medical history will be tabulated by MedDRA System Organ Class (SOC), Preferred Term (PT) and treatment group.

Summaries of subject disposition will be prepared for all subjects, including the number and percent of subjects screened, enrolled, study population of full analysis and per protocol, completed and not completed study within each study population, as well as a CONSORT diagram. The reasons for screen failures, abnormal with clinically significant of laboratory results, and COVID-19 associated symptoms will be summarized and listed.

A summary and listing of visit attendance will be prepared, in addition to a summary and listing of study product administration and sample collection/availability for each sample.

6.2. Timing of Analyses

Interim analyses will be performed after the last subject in the first phase has completed Visit 6 (Day 57) assessments and all the results are available. A final analysis on all safety and immunogenicity data will be performed after the study ends, when all additional safety and

immunogenicity data have been collected following the last subject's last study visit (Visit 7, Day 197), and the database is cleaned and locked.

6.3. Analysis Populations

6.3.1. Enrolled Population

All subjects who provide written informed consent, regardless of the subject's screening, randomization, and treatment status in the study.

6.3.2. Exposed Population

All subjects in the enrolled population who were randomized and received at least one vaccination dose (i.e., were accrued).

6.3.3. Safety Analysis Population

All subjects in the exposed population for whom any safety data is available. All safety analyses will be performed using this population. The denominators for different safety endpoints may vary according to the number of subjects with available data for the specific endpoint. For instance, the solicited local and systemic adverse event endpoint will be based only on those who have the corresponding CRF data regardless of other safety data. Treatment groups for safety analysis will be assigned according to the actual treatment received.

6.3.4. Full Analysis Population

All subjects in the exposed population for whom any post-study product administration immunogenicity results are available. An immunogenicity analysis will also be performed using this population.

6.3.5. Per Protocol Population

All subjects in the exposed population who have no major protocol deviations that are determined to potentially interfere with the immunogenicity assessment of the study product.

This population will serve as the primary analysis population for the immunogenicity endpoints. The population will be adapted by time point to include all eligible subjects' data up to the time of disqualifying protocol deviation. The criteria (e.g., intake of prohibited medication expected to influence the immune response) for exclusion of subjects from the per protocol population, and determination of any exclusions based on a blinded review of the data, will be established before database freeze and lock for both interim and final analyses, respectively.

6.4. Covariates and Subgroups

No covariates will be used in the analyses. No subgroup analyses will be performed in Phase 1.

6.5. Missing Data and Outliers

Missing immunogenicity data will not be imputed and will be analyzed as if they were randomly missing. Over the study period, the frequency and percentage of subjects who discontinue from the study will be provided by treatment group. All subjects who discontinue post-randomization will be further described regarding their time to and their reasons for discontinuation. For subjects who discontinue from the study, their data collected before discontinuation will be analyzed under the analysis populations as applicable.

6.6. Interim Analyses and Data Monitoring

6.6.1. Interim Analysis

Interim analyses will be performed after the last subject in the first phase has completed Visit 6 (Day 57) assessments and all the results are available. At the time of the interim analysis, safety results (unblinded to the DSMB only) and immunogenicity results (unblinded at group level only) will aid in the selection of formulations to evaluate in the second phase of the study. The interim report will include Tables 4-5, 8-11, 17, 29, 31, 34, 36, 39-42, 60, 64 and 90-119 as well as Listings 7-9.

6.6.2. Data Monitoring

The PI/designee will be responsible for continuous monitoring of all study subjects' safety. In case of urgent need, subjects will have the means to get in contact with study staff at any time (24 hours per day). The PI/designee will also be available by cell phone 24-hours per day for medical emergencies.

Safety will be monitored routinely throughout the study by the PSRT, which includes the PI/designee and other site investigators, the IVAC Clinical Lead, and the Medical Monitor. The PSRT will be continuously involved in safety monitoring and be available to address any urgent medical queries or safety concerns related to any subject's participation in the study. Data management personnel will ensure that the PSRT receives immediate notification of all reported SAEs and any other predefined AEs (e.g., Grade 3 AEs). The PSRT will convene to review blinded safety data on a weekly basis until D43 of the last subject in each phase, then at least once monthly until the end of the study.

During meetings the PSRT will review blinded safety reports and review any outstanding medical or safety queries from the previous review. The blinded safety reports will contain at a minimum, subject disposition and discontinuations, all new Grade 3 and persistent (beyond 6 days post-IP administration) solicited AEs, and all new unsolicited AEs. Cumulative safety data reports will also be made available continuously for review by PSRT members. In addition, the PSRT will review all major protocol deviations in an expedited manner and all other protocol deviations at least on a monthly basis to assess for any potential safety implications, and will provide guidance in the preparation of corrective action plans. The PSRT may also discuss any other study conduct issues that impact study integrity and subject safety, including but not limited to data quality and critical monitoring findings. The PSRT may refer any safety concerns to the DSMB.

A DSMB, composed of at least three independent members with expertise in vaccine clinical trials, will be convened to provide additional safety oversight. In Phase 1, the DSMB will meet to review unblinded safety data through Day 57 (V6), and on the basis of this review provide a recommendation for advancing to Phase 2 (i.e. the DSMB will indicate whether advancement to Phase 2 is warranted based on the reviewed safety data, and whether specific NDV-HXP-S formulations should not be considered for advancement due to safety concerns).

The DSMB will also meet if a study pause rule is met, or the PSRT elects to implement a study pause. If this occurs, no further enrollment will occur, and no study product will be administered until the DSMB approves lifting the pause based on unblinded review of all safety data accrued during the trial. If the study is permanently terminated, subjects who have already received study product will continue with all scheduled protocol visits and assessments; however, they will not receive any further study product.

DSMB reviews will indicate whether or not safety concerns were identified, and whether the trial should continue without change, be modified, or be terminated. The Sponsor will carefully consider the DSMB recommendations. If the Sponsor does not agree with these recommendations, a meeting will be held between the Sponsor, PI, and DSMB to reach consensus on the appropriate action(s) to take in regard to the trial. However, if attempts to reach consensus fail, the Sponsor's opinion will prevail. In such situations, the Sponsor will inform the MoH and NIHE's EC of the Sponsor's perspective, and any changes to the trial. The PSRT, PI or IVAC Clinical Lead may also seek additional guidance from the DSMB as dictated by the occurrence of certain events that do not warrant a study pause.

6.7. Multicenter Studies

Not applicable, Phase 1 is a single center study.

6.8. Multiple Comparisons/Multiplicity

As the two-stage selection design relies on ranking of GMTs, not testing of differences between candidate groups, no adjustment for multiplicity will be performed.

7. STUDY PARTICIPANTS

7.1. Disposition of Participants

Summaries of subject disposition will be prepared for all subjects, including the number and percent enrolled, screened, randomized, and administered study product (Table 5), as well as a CONSORT diagram (Figure 1) describing study participation and discontinuation. The reasons for screen failures and discontinuations will be summarized and listed (Table 6, Listing 1).

7.2. Protocol Deviations

A summary of subject-specific protocol deviations will be presented by study group in the exposed population. The reasons for the deviation will be also included (Table 4, Listing 2). Protocol deviation may lead to exclusion from the PP population. The summary of analysis population will be presented by study group and visit (Table 7).

8. SAFETY EVALUATION

8.1. Demographic and Other Baseline Characteristics

Baseline demographics and characteristics, including age, height, weight, sex, race, ethnicity, and BMI will be summarized for both the exposed and per protocol populations by treatment group using descriptive statistics (mean, standard deviation, median, 25th and 75th quartiles, minimum and maximum for continuous and rates for categorical). Summary tables will be seperated by type of data as continuous and catergorical (See Table 8 through Table 11). A listing of individual demographics will be provided (Listing 3).

8.1.1. Medical History

Medical history will be tabulated by MedDRA System Organ Class (SOC), Preferred Term (PT) and treatment group (Table 12 through Table 15, Listing 4).

8.1.2. Concomitant Medications

Using the WHO Drug Dictionary, concomitant medications will be tabulated by anatomical therapeutic chemical (ATC) classification, preferred drug name and treatment group (Table 120). The vaccination history within the past one year will be summarized (Table 16). Individual subject listing will be prepared for all concomitant medications (Listing 6).

8.2. Measurements of Visit Compliance and Research Sample Collection

A summary of the number of subjects completing each scheduled visit and the number providing research sample results at each visit will be prepared (Table 17).

8.3. Adverse Events

All safety assessment will take place in the safety analysis population, according to the treatment received. All subject-level percentages (solicited/unsolicited AEs, clinical safety laboratory abnormalities, etc.) will be supplemented with two-sided 95% CIs computed via the Clopper-Pearson method. Individual summaries (denominators for percentages) will be limited to the number of subjects with the appropriate analysis population with the data available for analysis for the given endpoint. Summaries will be provided overall by group and by stage (Table 39, Table 41, Table 42, Table 60, Table 64).

The non-serious adverse events from combined solicited and unsolicited (excluding serious adverse event) that being reported during the first 28 days after each vaccination will be summarized with the number of subject by vaccination groups. This combined data will be summarized by System Organ Class (SOC) and Preferred Term (PT) also (Table 39 and Table 40).

8.3.1. Solicited Events and Symptoms

Solicited local and systemic adverse events: Percentages of subjects experiencing each solicited AE within 30 minutes observation period and during the first 7 days after each dose vaccination

will be presented for each symptom (Table 29, Table 31 ,Table 34, Table 36). All solicited AEs will also be summarized according to defined severity grading scales (Table 30, Table 32, Table 35, Table 37). Comparison of solicited AE of different dose levels will be done for overall dose, first dose and second dose of each symptom. Data listings of all solicited AEs will be provided by subject (Listing 7).

Clinically significant hematological and biochemical measurements: For clinical safety laboratory data collected at screening and 7 days post-first administration of study product (Visit 2, Day 8) and post-second administration of study product (Visit 4, Day 36), individual Hgb, WBC count, Plt, AST, ALT, total bilirubin, and creatinine values will be presented as number of subjects out of range (above and below normal range as appropriate) and tabulated by toxicity grading, relatedness, and study group (Table 60 through Table 68). In addition, mean percentage changes from baseline (95% CI)) will be presented. Plot of laboratory results evaluated both pre, post-first and second vaccination will be presented (Appendix 2.B.- Figure 2 through Figure 8).

8.3.2. Unsolicited Adverse Events

Overall number of subject experiencing unsolicited AEs, including SAEs, onset during the first 28 days after each dose vaccination will be summarized by vaccine groups and relatedness (Table 41). Number of subject experiencing SAEs throughout the entired study period will also be presented (Table 42). All unsolicited AEs with onset during the first 28 days following each dose administration will be assessed for severity and as either related or not related to study product by the investigator (Table 43 and Table 44).

AESI, MAAEs, and SAEs: All AESI, MAAEs, and SAEs through Visit 7 (Day 197) will be recorded and the number, severity, and relatedness to study product will be summarized (Table 45 through Table 49). Subject-wise data listing for all unsolicited AEs will be provided (Listing 7).

When an AE occurs more than once for a subject, the subject will be counted only once for the corresponding PT according to the maximum severity of the events.

Medically-attended adverse events (MAAEs) are unsolicited AEs for which the subject received medical attention, such as during an emergency room visit or a visit to or from medical personnel (e.g., medical doctor).

Adverse events of special interest (AESIs) for this study include:

- Potential immune-mediated medical condition (PIMMC), given that vaccination has been associated with autoimmunity
- AEs associated with COVID-19, given the importance of subject safety of managing any occurrence of COVID-19, and the possible association of vaccination with enhancement of COVID-19

8.4. Deaths, Serious Adverse Events and Other Significant Adverse Events

A listing of all data related to deaths, SAEs and other significant AEs will be presented (See

Appendix 1.D., Listing 8).

8.5. Pregnancies

All WOCBP will be monitored for pregnancy during the study and for the use of adequate contraception until completion of Visit 6 (Day 57). If a female subject becomes pregnant after Visit 1 (Day 1) but prior to Visit 3 (Day 29), no further study product will be administered. The subject will be encouraged to complete all remaining study visits for safety assessments alone, and if possible and agreed to by the subject, continue to be followed through the pregnancy outcome. The pregnancy and its outcome will be documented, even if birth occurs after the scheduled end of the study for the subject.

8.6. Clinical Laboratory Evaluations

Screening viral serology assessments for Hepatitis B (HBsAg) and Hepatitis C (HCV Ab) will be described as categorical variables on a demographics table (Table 28).

Clinical safety laboratory values (serum hematology and chemistry) are collected at screening and 7 days post-vaccination for each dose. They will be summarized for the safety analysis population. Hematology and chemistry results evaluated at screening will be summarized as continuous variables by vaccine groups (Table 24 through Table 27).

Screening and post-vaccination (Day 8 and Day 36) serum hematology and chemistry will be graded by severity. Grade 2 or higher were automatically considered as clinically significant and reported as AE, while Grade 1 abnormalities were subject to investigator opinion.

Continuous summaries of laboratory parameters (Hgb, WBC count, Plt, AST, ALT, total bilirubin, and creatinine) and the change from baseline will be computed by time point (including unscheduled visits, in chronological order) and treatment group, including mean, standard deviation, median, 1st and 3rd quartiles (IQR) and range, for all observations regardless of abnormality status (see Table 60 through Table 68). Summaries will also be produced presenting the proportion of each severity grading using the number of subjects that provided a sample as denominator, as well as those considered clinically significant, using the maximum severity for a given subject, where relevant. A summary of safety laboratory abnormalities will be prepared by parameter, severity (by grade and any abnormality), and time point. Fisher's exact 2-tailed test will be used to test the differences in abnormality rates across all groups, by time point for scheduled visits, and overall.

Figures will be prepared for each laboratory parameter using boxplots to describe the distribution of values and changes from baseline across visits, by group, incorporating unique points and/or colors for abnormalities (Figure 2 through Figure 8).

A listing of all lab results will be prepared, in addition to a listing only for abnormalities, and each will include the parameter, study day (Visit), value, units, change from baseline, LLN/ULN, and abnormality grade (Listing 9A, Listing 9B, Appendix 3).

8.7. Vital Signs and Physical Evaluations

Vital sign measurements including systolic and diastolic blood pressure (mmHg), temperature (°C), pulse (beats/min) and respiratory rate (breaths/minute) will be assessed at each visit, including change from pre-first vaccination and pre-second vaccination (Table 69 through Table 80). Vital signs will be tabulated by visit and vaccination group, including mean, standard deviation, median and range. A full listing will be prepared (Listing 10, Appendix 3) and will include study visit, value, units and change from baseline.

Physical exam results, including number and proportion of participants with abnormalities, will be summarized for the safety analysis population and presented in Appendix 1.H. (Table 81 through Table 89), by vaccination group. A full listing will be prepared (Listing 12, Appendix 3).

9. IMMUNOGENICITY

The analysis of immunogenicity will be performed on the per protocol population as the primary analysis and the full analysis population as a secondary analysis. Analyses described below will be summarized in the interim analyses for all subjects included in the first phase of the study. Relative endpoints derived from Geometric Mean Fold Rise (GMFR) will include all subjects from the per protocol population. Absolute endpoints such as those derived from the Geometric Mean Titer (GMT) will exclude baseline seropositive subjects (i.e., subjects with anti-S IgG antibody titer ≥ LLOQ of the assay at baseline).

Immunogenicity data will be descriptively summarized including the mean, SD, median, range (min and max), GMT, and 95% CI for the GMT with one-half the lower limit of quantification (LLOQ) and with the upper limit of quantification (ULOQ) used as the observed value, whenever these limits are met. For estimation of the GMT, GMT ratio, and corresponding confidence limits, analyses will incorporate censoring where appropriate and log-scale coefficients will be back-transformed in order to compute the estimate and corresponding confidence limits for the relevant quantity. GMFRs will be computed using estimates of the log difference of the paired samples, with corresponding CIs computed via the *t*-distribution, utilizing the antilog transformation to present the ratio. Analyses of binary variables will include 95% CIs computed via the Clopper-Pearson method. Additionally, the distribution of the titers will be summarized using reverse cumulative distribution curves. (Figure 27 through Figure 32).

The immunogenicity ananlysis part will be summarized in term of GMT ratio comparing between dose levels and dose with and without adjuvant. The comparing doses of GMT ratio (95% CI) will be performed for the following pairwise: (1) NDV-HXP-S 1 μg vs. 3 μg, (2) 1 μg vs. 10 μg, (3) 3 μg vs. 10 μg, (4) 1 μg vs. 1 μg+CPG, (5) 3 μg vs. 1 μg+CPG, (6) 10 μg vs. 1 μg+CPG.

9.1. NT_{50} and NT_{80} against SARS-CoV-2 Pseudovirus

The pseudovirus neutralization assay (PNA) will be used to quantify the functional humoral immune response against SARS-CoV-2 by measuring the 50% and 80% neutralizing titer (NT_{50} and NT_{80}) against a SARS-CoV-2 pseudovirus.

The results generated from the central laboratory (NEXELIS, Canada) for SARS-CoV-2 PNA will be reported with titer units "NT_{50}" and "NT_{80}". A correlation factor of 1/1.872 will be applied to convert the reported results from NT_{50} titer to IU/mL which is the assigned unit for WHO International Standard.

The following formula shall be used for converting NT_{50} titer to IU/mL:

Result (IU/mL) = Result (NT_{50} titer)/ 1.872

The NT_{50} and NT_{80} GMT against SARS-CoV-2 pseudovirus will be described along with its 95% CI at baseline (D1), 28 days after the first vaccination (D29), and 14 days (D43) and 6 months (D197) after the second vaccination in subjects who are anti-S IgG seronegative (i.e., anti-S IgG value less than LLOQ of the assay) at baseline (Table 90, Table 91, Table 94, Table 95, Appendix 1). The NT_{50} will also be described via the geometric mean concentration (GMC) in IU/mL along with the its 95% CI at D1, D29, D43 and D197.

The GMT ratio with 95% CI for pairwise comparison of NT_{50} and NT_{80} GMT values between dose levels and dose with and without adjuvant will be presented at 28 days after the first vaccination, and 14 days, 6 months and 12 months after the second vaccination for each pair (Table 92, Table 93, Table 96, Table 97).

The GMFR from baseline in NT_{50} and NT_{80} against SARS-CoV-2 pseudovirus at 28 days after the first vaccination, and 14 days, 6 months and 12 months after the second vaccination will be calculated along with its 95% CI for each study group (Table 98 through Table 101, Appendix 1).

Number and percentage (with 95% CI) of subjects with NT_{50} and NT_{80} seroresponses against SARS-CoV-2 pseudovirus as defined by (1) a $\geq$ 4-fold increase from baseline, and (2) a $\geq$ 10-fold increase from baseline at 28 days after the first vaccination, and 14 days, 6 months and 12 months after the second vaccination will be summarized at each time point for each study group (Table 102 through Table 109, Appendix 1).

9.2. Anti-S IgG Assessed by ELISA

Anti-S IgG antibody titers will be measured by ELISA assay which detects IgG antibodies to the full-length pre-fusion Spike protein of SARS-CoV-2.

Serum antibody concentration will be reported from the central laboratory (NEXELIS, Canada) in ELISA Units (ELU)/mL. A correlation factor of 1/7.9815 will be applied to convert the reported results from ELU/mL to Binding Antibody Units (BAU)/mL which is the assigned unit for WHO International Standard.

The following formula shall be used for converting concentration units from ELU/mL to BAU/mL:

Result (BAU/mL) = Result (ELU/mL)/ 7.9815

Anti-S IgG antibody results will be summarized at baseline, 28 days after the first vaccination, and 14 days, 6 months and 12 months after the second study injection. The summarization of the anti-S IgG antibody titers will be performed for the overall and by study group at each time point.

The summarization will include GMTs with 95% CIs, including baseline (Table 110, Table 111, Appendix 1), GMT ratio with 95% CI for pairwise comparison between vaccine groups (Table 112, Table 118, Appendix 1), GMFR from baseline with 95% CI (Table 114, Table 115, Appendix 1), and percent of subjects with ≥ 4-fold and ≥ 10-fold increase in the anti-S IgG antibody titers compared with baseline (Table 116 through Table 119, Appendix 1).

10. REPORTING CONVENTIONS

P-values will be reported to 3 decimal places; p-values less than 0.001 will be reported as "<0.001" and p-values greater than 0.999 will be reported as ">0.999". Means and medians will be presented to one decimal place more than the raw value, standard deviations and confidence intervals will be presented to 2 extra decimals. Percentages will be reported to one decimal and corresponding 95% CIs will be to two decimals. Percentages less than 0.1% (or <0.01%) will be reported as "<0.1" (or "<0.01"), percentages >99.9% (or >99.99%) will be reported as ">99.9" (">99.99") and 100% will be reported as "100".

11. TECHNICAL DETAILS

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

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

For SARS-CoV-2 PNA, NT_{50} and NT_{80} will be determined based on the dilution of serum required to achieve 50% and 80% reduction in relative luminescence units (RLU) value compared to pseudoparticle control. The results generated from the central laboratory will be reported with titer units "NT_{50}" and "NT_{80}". In order to covert the reported values from the laboratory to be according to the WHO International Standard, a correlation factor of 1/1.872 will be applied to convert the reported results from NT_{50} titer to GMC in IU/mL which is the assigned unit for WHO International Standard. Hence, data analyses for PNA NT_{50} results will be expressed in IU/mL.

Anti-S IgG antibody titers will be measured by ELISA assay which detects IgG antibodies to the full-length pre-fusion Spike protein of SARS-CoV-2. According to the study endpoints, serum antibody concentration will be reported from the central laboratory in ELISA Units (ELU)/mL. A correlation factor of 1/7.9815 will be applied to convert the reported results from ELU/mL to Binding Antibody Units (BAU)/mL which is the assigned unit for WHO International Standard. Hence, data analyses for anti-S IgG results will be expressed in BAU/mL.

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APPENDIX 1. TABLES

LIST OF TABLES

Appendix 1.A. Characteristics at Screening

Tables copied from the protocol:

Table 1: Treatment Groups - Protocol Table 3 (see Table 1 in Section 4.1.)

Table 2: Phase 1 Dose Escalation Step – Protocol Table 4 (see Table 2 in Section 4.1.)

Table 3: Schedule of Study Visits and Procedures – Protocol Table 5

VISIT	Screen	V1	V2	V3	V4	V5	V6	V7
Study Day (allowed window in days)	**-42 to 1**	**1**	**8 (+3)**	**29 (+3)**	**36 (+3)**	**43 (+3)**	**57 (+7)**	**197 (+14)**
Informed consent	✓							
Demographics	✓							
Medical History	✓							
Concomitant medications[A]	✓	✓	✓	✓	✓	✓	✓	✓
Eligibility check	✓			~				
Vital signs	✓	✓^✓	✓	✓^✓	✓	✓	✓	✓
Complete physical exam	✓							
Targeted physical exam[B]		✓	✓	✓	✓	✓	✓	✓
Clinical chemistry[C]	✓		✓		✓			
Hematology[D]	✓		✓		✓			
Viral serology tests[E]	✓							
Urine pregnancy test[F]	✓	✓ ✓		✓				
Unsolicited AEs[G]	✓	✓	✓	✓	✓	✓	✓	✓
Concomitant medications[H]	✓		✓	✓	✓	✓	✓	✓
Randomization		✓		~				
Blood for humoral immunity		✓		✓		✓		✓
Blood for CMI[I]		✓				✓		✓
Administer study product		✓		✓				
Observation/solicited AEs		✓		✓				
Provide Diary Card		✓		✓				
Review Diary Card			✓		✓			
Exit study								
Blood volumes (mL):								
Safety laboratory tests (Phase 1 only)	4		4		4			
HBV and HCV screening	2		0		0			
Humoral immunity		10		10		10		10
Cell-mediated immunity		16				16		16

~ Confirmation
^ Evaluations will be conducted twice – before and after vaccination
[A] After Visit 6, only medications associated with an AESI, MAAE or SAE will be recorded.
[B] Targeted PE will be conducted only in the event of new symptom, sign or, until Visit 6, any new AE; or, after Visit 6, any new AESI, MAAE or SAE.
[C] Serum creatinine, ALT, AST, total bilirubin; only in Phase 1.
[D] WBC count, hemoglobin, platelets; only in Phase 1.
[E] HBsAg, HCV Ab
[F] Women of childbearing potential (WOCBP) only
[G] After Visit 6, only AESI, MAAEs, and SAEs will be recorded.
[H] After Visit 6, only concomitant medications associated with a newly reported AESI, MAAE or SAE will be recorded
[I] Only in subset of subjects in Phase 2
Remark: 1 month = 28 days (4 weeks)

Table 4: Distribution of Protocol Deviations by Category, Type and Study Group

Category	Deviation Type	All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Eligibility/enrollment	Any type	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Did not meet inclusion/exclusion criteria but enrolled						
	Informed consent not taken						
	Incorrect informed consent process						
	Other						
Vaccination procedure	Any type						
	Randomized to wrong treatment arm: Dosed with wrong treatment arm at V1						
	Wrong treatment arm administered at 2nd dose						
	Dosed when withdrawal/discontinuation criteria were met						
	Incorrect vaccination procedure						
	Damaged/ expired IP/ quarantined kit used without prior approval						
	Other						
Missed procedures	Any type						
	Pre-vaccination blood sample missed to be collected from eligible subject but subject continued in the study						
	Post-vaccination blood sample missed to be collected from eligible subject						
	Assessmens at scheduled visits were not performed						
	Post-vaccination assessment missed						
	DC/thermometer and/or ruler not provided to subject after vaccination						
	Other						

Table 4: Distribution of Protocol Deviations by Category, Type and Study Group (continued)

Category	Deviation Type	All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Visit window	Any type						
	Out of window visit						
	Missed visit/ visit not conducted						
	Missed vaccine administration						
	Delayed vaccine administration						
	Other						
etc.	etc.						

Note: Number of subjects in the safety analysis population

Table 5: Subject Disposition by Study Group

Status	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Screened	xxx	NA	NA	NA	NA	NA
Not eligible	xxx					
Eligible	xxx					
Not randomized	xxx					
[Reason 1]	xxx					
[Reason 2]	xxx					
[etc.]	xxx					
Randomized	xxx					
Received 1st dose vaccination	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Received 2nd dose vaccination	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
[Reason 1]						
[etc.]						
Completed Day 29 visit						
Completed Day 57 visit						
Completed the study						
Not completing the study						
Reason for not completing the study						
- Serious adverse event						
- Non-serious adverse event						
- Protocol deviation						
- Consent withdrawal						

Table 5: Subject Disposition by Study Group (continued)

Status	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
- Migrated / Moved from the study area						
- Lost to follow-up						
- Other reason						
Safety analysis population						
Full analysis population						
Per protocol population						

Note: + CpG1018 1.5 mg (Adjuvant)
"xx" represent the value number.
"xx.x %" is the percentage calculated from total number of 1st dose vaccinated subjects (N).

Table 6: Summary of Screen Failures

Inclusion/Exclusion Category	Inclusion/Exclusion Criterion	n[a]	%[b]
Inclusion and Exclusion	Number of subjects failing any eligibility criterion	xx	xx.xx
Inclusion	Any inclusion criteria		
	[inclusion criteria 1]		
	[inclusion criteria 2]		
	[inclusion criteria 3]		
	…..		
Exclusion	Any exclusion criteria		
	[exclusion criteria 1]		
	[exclusion criteria 2]		
	[exclusion criteria 3]		
	……		

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

Note: Include all inclusion and exclusion criteria listed in the protocol.

Table 7: Analysis Populations by Study Group and Visit

Visit	Reason subjects excluded	All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 20)	3 µg (N = 20)	10 µg (N = 20)	1 µg + CpG (N = 20)	
Total vaccinated	Number vaccinated Number not vaccinated [Reason 1] [Reason 2] [etc.]						
Per protocol population[2]							
Baseline (D1)	Included Excluded [Reason excluded] [etc.]						
28 days after the first vaccination (D29)	Included Excluded [Reason excluded] [etc.]						
14 days after the second vaccination (D43)	Included Excluded [Reason excluded] [etc.]						
6 months after the second vaccination (D197)	Included Excluded [Reason excluded] [etc.]						
12 months after the second vaccination (D365)	Included Excluded [Reason excluded] [etc.]						
etc.							

N = Number of participant in Enrolled population.

[1] Denominator for percentage is N. [2] Denominator for percentage is number vaccinated. Reasons for exclusion do not missing data, which is specific to each parameter.

Table 8: Summary of Categorical General Characteristics at Screening, Exposed Population

Characteristics	All (N=120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Sex, n (%)						
Male	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Female	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Race, n (%)						
Asian	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ethnicity, n (%)						
Kinh	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Note: + CpG1018 1.5 mg (Adjuvant)
"xx" represent the value number.

Table 9: Summary of Categorical General Characteristics at Screening, Per Protocol Population

Characteristics	All (N=120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Sex, n (%)						
Male	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Female	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Race, n (%)						
Asian	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ethnicity, n (%)						
Kinh	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Note: + CpG1018 1.5 mg (Adjuvant)
"xx" represent the value number.

Table 10: Summary of Continuous General Characteristics at Screening, Exposed Population

	All (N=120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Age (years)						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
Weight (kg)						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
Height (cm)						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
BMI (kg/m^2)						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx

Note: + CpG1018 1.5 mg (Adjuvant)
"xx" represent the value number.

Table 11: Summary of Continuous General Characteristics at Screening, Per Protocol Population

	All (N=120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Age (years)						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
Weight (kg)						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
Height (cm)						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
BMI (kg/m^2)						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx

Note: + CpG1018 1.5 mg (Adjuvant)
"xx" represent the value number.

Table 12: Overall Events of Medical History by System Organ Class (SOC) and Preferred Term (PT)

System Organ Class (SOC)	Preferred Term (PT)	All (NE = xx)	COVIVAC				Placebo (NE = xx)
			1 µg (NE = xx)	3 µg (NE = xx)	10 µg (NE = xx)	1 µg + CpG (NE = xx)	
All SOC	All PT	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
SOC 1	All						
	PT 1						
	PT 2						
	…..						
SOC 2	All						
	PT 1						
	PT 2						
	……						

Note: + CpG1018 1.5 mg (Adjuvant)
"xx" represent the value number.
"NE" represent the number of medical history events

Table 13: Overall Number of Subjects at Least One Medical History by System Organ Class (SOC) and Preferred Term (PT)

System Organ Class (SOC)	Preferred Term (PT)	All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
All SOC	All PT	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
SOC 1	All						
	PT 1						
	PT 2						
	…..						
SOC 2	All						
	PT 1						
	PT 2						
	……						

Note: + CpG1018 1.5 mg (Adjuvant)
"xx" represent the value number.
"N" represent the number of subject who has at least one medical history.

Table 14: Number of Subjects at Least One Past Medical History by System Organ Class (SOC) and Preferred Term (PT)

System Organ Class (SOC)	Preferred Term (PT)	All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
All SOC	All PT	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
SOC 1	All						
	PT 1						
	PT 2						
	…..						
SOC 2	All						
	PT 1						
	PT 2						
	……						

Note: + CpG1018 1.5 mg (Adjuvant)
"xx" represent the value number.
"N" represent the number of subject who has at least one medical history.

Table 15: Number of Subjects at Least One Current Medical History by System Organ Class (SOC) and Preferred Term (PT)

System Organ Class (SOC)	Preferred Term (PT)	All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
All SOC	All PT	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
SOC 1	All						
	PT 1						
	PT 2						
	…..						
SOC 2	All						
	PT 1						
	PT 2						
	……						

Note: + CpG1018 1.5 mg (Adjuvant)
"xx" represent the value number.
"N" represent the number of subject who has at least one medical history.

Table 16: Number of Subjects Receiving at Least One Vaccination in the Past 1 Year

Vaccine	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
…….	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
…….						
…….						

Note: + CpG1018 1.5 mg (Adjuvant)
"xx" represent the value number.
"N" represent the number of subject who has at least one medical history.

Table 17: Summary of Visit Attendance and Sample Collection[1], Exposed Population

Day	Study Visit							
	Screening	**1[2]**	**8**	**29[2]**	**36**	**43**	**57**	**197**
Completed visits								
1 µg (N = 25)	x (%)	x (%)	x (%)	x (%)	x (%)	x (%)	x (%)	x (%)
3 µg (N = 25)	x (%)	x (%)	x (%)	x (%)	x (%)	x (%)	x (%)	x (%)
10 µg (N = 25)	x (%)	x (%)	x (%)	x (%)	x (%)	x (%)	x (%)	x (%)
1 µg + CpG (N = 25)	x (%)	x (%)	x (%)	x (%)	x (%)	x (%)	x (%)	x (%)
Placebo (N = 20)	x (%)	x (%)	x (%)	x (%)	x (%)	x (%)	x (%)	x (%)
All (N= 120)	x (%)	x (%)	x (%)	x (%)	x (%)	x (%)	x (%)	x (%)
Functional humoral immune response by PNA								
1 µg (N = 25)		x (%)				x (%)		x (%)
3 µg (N = 25)		x (%)				x (%)		x (%)
10 µg (N = 25)		x (%)				x (%)		x (%)
1 µg + CpG (N = 25)		x (%)				x (%)		x (%)
Placebo (N = 20)		x (%)				x (%)		x (%)
All (N= 120)		x (%)				x (%)		x (%)
Anti-S IgG response by ELISA								
1 µg (N = 25)		x (%)				x (%)		x (%)
3 µg (N = 25)		x (%)				x (%)		x (%)
10 µg (N = 25)		x (%)				x (%)		x (%)
1 µg + CpG (N = 25)		x (%)				x (%)		x (%)
Placebo (N = 20)		x (%)				x (%)		x (%)
All (N= 120)		x (%)				x (%)		x (%)

Note: N = number of participants in the safety analysis population.

[1] Samples collected and assay results available.

[2] Vaccination day

Data are only expected at visits indicated by x (%).

Table 18: Solicited Injection Site and Systemic Reactions Toxicity Grading Table- Protocol Appendix 1

Reaction to Injectable Product	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life Threatening (Grade 4)
Pain/ Tenderness	Does not interfere with activity	Some interference with activity OR Repeated use of non-narcotic pain reliever > 24 hours	Significant; prevents daily activity OR Any use of narcotic pain reliever	Emergency room (ER) visit or hospitalization
Erythema[a]	2.5 – 5 cm	5.1 – 10 cm	> 10 cm and/or ulceration OR secondary infection OR phlebitis OR sterile abscess OR drainage	Necrosis or exfoliative dermatitis
Swelling/ Induration[a]	2.5 – 5 cm and does not interfere with activity	5.1 – 10 cm OR Interferes with activity	> 10 cm OR prevents daily activity and/or ulceration OR secondary infection OR phlebitis OR sterile abscess OR drainage	Necrosis
Temperature (oral)	38.0 – 38.4°C 100.4 – 101.1°F	38.5 – 38.9°C 101.2 – 102.0°F	39.0 – 40°C 102.1 – 104°F	> 40°C > 104°F
Headache	No interference with activity	Some interference with activity OR Repeated use of nonnarcotic pain reliever >24 hours	Significant; prevents daily activity OR Any use of narcotic pain reliever	ER visit or hospitalization
Fatigue/ Malaise	No interference with activity	Some interference with activity	Significant; prevents daily activity	ER visit or hospitalization
Myalgia	No interference with activity	Some interference with activity	Significant; prevents daily activity	ER visit or hospitalization
Arthralgia	No interference with activity	Some interference with activity	Significant; prevents daily activity	ER visit or hospitalization
Nausea/ Vomiting	No interference with activity	Some interference with activity	Prevents daily activity OR Requires outpatient IV hydration	ER visit or hospitalization for hypotensive shock

[a] For erythema and swelling/induration, longest diameter should be noted in centimeters. Swelling/induration should be evaluated and graded using the functional scale as well as the actual measurement.

The grading scales for local and systemic AEs have been derived from *Guidance for Industry, Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials*, U.S. Department of Health and Human Services, FDA, CBER, September 2007 (https://www.fda.gov/media/73679/download) and the *Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events* (Version 2.1, July 2017) from the US NIH (https://rsc.niaid.nih.gov/sites/default/files/daidsgradingcorrectedv21.pdf).

Table 19: Vital Signs Toxicity Grading – Protocol Appendix 2

Vital Signs[a]	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life Threatening (Grade 4)
Tachycardia – beats per minute	101 – 115	116 – 130	> 130	Hospitalization for arrhythmia
Bradycardia – beats per minute[b]	50 – 54	45 – 49	< 45	ER visit or hospitalization for arrhythmia
Hypertension (systolic) – mm Hg	141 – 150	151 – 165	> 165	ER visit or hospitalization for malignant hypertension
Hypertension (diastolic) – mm Hg	91 – 99	100 – 105	> 105	ER visit or hospitalization for malignant hypertension
Hypotension (systolic) – mm Hg	85 – 89	80 – 84	< 80	ER visit or hospitalization for hypotensive shock
Respiratory Rate – breaths per minute	21 – 23	24 – 27	> 27	Intubation

[a] Subject should be at rest for all vital sign measurements.

[b] Grade 1 bradycardia or grade 1 tachypnea will not be considered an abnormality for this study, unless judged to be clinically significant by the PI in consultation with the Sponsor.

The grading scales for abnormal vital signs have been derived from *Guidance for Industry, Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials*, U.S. Department of Health and Human Services, FDA, CBER, September 2007.

Table 20: Serum Toxicity Grading – Protocol Appendix 3

Serum	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life Threatening (Grade 4)
Creatinine (mg/dL)	1.1 – 1.3 x ULN	> 1.3 – 1.8 x ULN OR increase of > 0.3 above baseline	> 1.8 – < 3.5 x ULN OR increase of 1.5 – < 2.0 x above baseline	≥ 3 .5 x ULN OR increase of > 2.0 x above baseline
Liver function tests – AST, ALT increased	1.25 – < 2.5 x ULN	2.5 – <5.0 x ULN	5.0 – < 10.0 x ULN	≥ 10.0 x ULN
Total bilirubin	1.1 – < 1.6 x ULN	1.6 – < 2.6 x ULN	2.6 – < 5.0 x ULN	≥ 5.0 x ULN

Abbreviation: ULN = upper limit of normal range

Note: the laboratory values provided in this table serve as guidelines and are dependent upon institutional normal parameters.

The grading scales for laboratory abnormalities have been derived from *Guidance for Industry, Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials*, U.S. Department of Health and Human Services, FDA, CBER, September 2007, and the *Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events* (Version 2.1, July 2017) from the US NIH.

Table 21: Hematology Toxicity Grading – Protocol Appendix 3

Hematology	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life Threatening (Grade 4)
Hemoglobin [Female] (g/dL)	11.0 – 12.0	9.5 – 10.9	8.0 – 9.4	< 8.0
Hemoglobin [Male] (g/dL)	12.5 – 13.5	10.5 – 12.4	8.5 – 10.4	< 8.5
OR Hemoglobin, change from baseline value (g/dL)	1.0 – 1.5	1.6 – 2.0	2.1 – 5.0	> 5.0
WBC, increased (cell/mm^3)	10,800 – 15,000	15,001 – 20,000	20,001 – 25,000	> 25,000
WBC, decreased (cell/mm^3)	2,500 – 3,400	1,500 – 2,499	1,000 – 1,499	< 1,000
Platelets, decreased (cell/mm^3)	100,000 – <125,000	50,000 – < 100,000	25,000 – < 50,000	< 25,000

Abbreviation: ULN = upper limit of normal range

Note: the laboratory values provided in this table serve as guidelines and are dependent upon institutional normal parameters.

The grading scales for laboratory abnormalities have been derived from *Guidance for Industry, Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials*, U.S. Department of Health and Human Services, FDA, CBER, September 2007, and the *Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events* (Version 2.1, July 2017) from the US NIH.

Table 22: Vital Sign at Screening

	All	COVIVAC				Placebo
	(N =120)	1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	(N = 20)
Systolic blood pressure (mmHg)						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
Diastolic blood pressure (mmHg)						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
Pulse rate (beats /min.)						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
Respiratory rate (breaths/min.)						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx

Table 22: Vital Sign at Screening (continued)

	All	COVIVAC				Placebo
	(N =120)	1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	(N = 20)
Temperature (°C)						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
Route						
Oral	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
…	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Note: + CpG1018 1.5 mg (Adjuvant)
"xx" represent the value number.

Table 23: Physical Examination at Screening

	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
General Appearance, n (%)						
Normal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Abnormal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Clinically sig**	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Not done	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
HEENT, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Cardiovascular, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Respiratory, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Abdomen, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						

Table 23: Physical Examination at Screening (continued)

	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Musculoskeletal, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Extremity/Skin, n (%)						
Normal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Abnormal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Clinically sig**						
Not done	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Neurological, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Lymph Nodes, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Other, n (%)						
….						

Note: + CpG1018 1.5 mg (Adjuvant)
"xx" represent the value number.
** Abnormal result clinically significant

Table 24: Hematology Test at Screening

	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Hemoglobin (g/dL)						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
White Blood Cell (WBC) (x 10^3/µL)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
Platelets (x 10^3/µL)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						

Note: + CpG1018 1.5 mg (Adjuvant)
"xx" represent the value number.

Table 25: Abnormality of Hematology Test with Clinically Significant Result at Screening

	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Hemoglobin (g/dL)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
White Blood Cell (WBC) ($x\ 10^3/\mu L$)						
Platelets ($x\ 10^3/\mu L$)						

Note: + CpG1018 1.5 mg (Adjuvant)
"xx" represent the value number.
Only subjects with abnormality of hematology result will be considered in this table.

Table 26: Chemistry Test at Screening

	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Creatinine (mg/dL)						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
ALT (U/L)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
AST (U/L)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
Total bilirubin (mg/dL)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						

Note: + CpG1018 1.5 mg (Adjuvant)
"xx" represent the value number.

Table 27: Abnormality of Chemistry Test with Clinically Significant Result at Screening

	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Creatinine (mg/dL)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ALT (U/L)						
AST (U/L)						
Total bilirubin (mg/dL)						

Note: + CpG1018 1.5 mg (Adjuvant)
"xx" represent the value number.
Only subjects with abnormality of chemistry result will be considered in this table.

Table 28: Viral Serology Result at Screening

	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
HBsAg						
Positive						
Negative						
Not done						
N/A						
HCV Ab						
Positive						
Negative						
Not done						
N/A						

Note: + CpG1018 1.5 mg (Adjuvant)
"xx" represent the value number.

Appendix 1.B. Reactogenicity - Local Reactions

Table 29: Local Reaction at 30 minutes after Vaccination in Safety Analysis Population

Reaction		All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
		n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Pain OR Tenderness	1st Dose	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)
	p-value=	x.xxxx					
	2nd Dose	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)
	p-value=	x.xxxx					
Swelling OR Induration	1st Dose	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)
	p-value=	x.xxxx					
	2nd Dose	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)
	p-value=	x.xxxx					
Erythema	1st Dose	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)
	p-value=	x.xxxx					
	2nd Dose	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)
	p-value=	x.xxxx					

Note: *Two-sided 95% CIs computed via the Clopper-Pearson method
Comparing overall dose levels; P-value based on Chi-square test

Table 30: Local Reaction by Severity within 30 minutes after Vaccination in Safety Analysis Population

	All (N = 120)	COVIVAC				Placebo
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Pain OR Tenderness						
1st Dose						
None	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)
Mild	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)
Moderate	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)
Severe	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)
Potentially life-threatening	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)
p-value = x.xxxx						
2nd Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						

Table 30: Local Reaction by Severity within 30 minutes after Vaccination in Safety Analysis Population (continued)

Reaction	All (N = 120)	COVIVAC				Placebo
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Swelling OR Induration						
1st Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						
2nd Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						

Table 30: Local Reaction by Severity within 30 minutes after Vaccination in Safety Analysis Population (continued)

Reaction	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Erythema						
1st Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						
2nd Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						

Note: *Two-sided 95% CIs computed via the Clopper-Pearson method
Comparing overall dose levels; P-value based on Chi-square test;

Table 31: Local Reaction Started During Day 1 - Day 7 after Vaccination in Safety Analysis Population

Reaction		All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
		n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Pain OR Tenderness	1st Dose	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)
	p-value=	x.xxxx					
	2nd Dose						
	p-value=						
Swelling OR Induration	1st Dose						
	p-value=						
	2nd Dose						
	p-value=						
Erythema	1st Dose						
	p-value=						
	2nd Dose						
	p-value=						

Note: *Two-sided 95% CIs computed via the Clopper-Pearson method
Comparing overall dose levels; P-value based on Chi-square test

Table 32: Local Reaction by Severity Started during Day 1 - Day 7 after Vaccination in Safety Analysis Population

	All (N = 120)	COVIVAC				Placebo
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Pain OR Tenderness						
1st Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						
2nd Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						

Table 32: Local Reaction by Severity Started during Day 1 - Day 7 after Vaccination in Safety Analysis Population (continue)

Reaction	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Swelling OR Induration						
1st Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						
2nd Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						

Table 32: Local Reaction by Severity Started during Day 1 - Day 7 after Vaccination in Safety Analysis Population (continued)

Reaction	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Erythema						
1st Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						
2nd Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						

Note: *Two-sided 95% CIs computed via the Clopper-Pearson method
Comparing overall dose levels; P-value based on Fisher's exact test

Table 33: Incidence of New Onset and Ongoing Local Reaction Reported on each Day During Day 1- Day 7 after Vaccination in Safety Analysis Population

Reaction		All (N = 120)	COVIVAC			1 µg + CpG (N = 25)	Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)		
		n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Pain OR Tenderness	**1st Dose**						
	Day 1						
	Day 2						
	Day 3						
	……..						
	Day 7						
	2nd Dose						
	Day 1						
	Day 2						
	Day 3						
	……..						
	Day 7						
Swelling OR Induration	**1st Dose**						
	Day 1						
	Day 2						
	Day 3						
	……..						
	Day 7						
	2nd Dose						
	Day 1						
	Day 2						
	Day 3						
	……..						
	Day 7						

Table 33: Incidence of New Onset and Ongoing Local Reaction Reported on each Day During Day 1- Day 7 after Vaccination in Safety Analysis Population (continued)

Reaction		All (N = 120)	COVIVAC			1 µg + CpG (N = 25)	Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)		
		n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Erythema	**1st Dose**						
	Day 1						
	Day 2						
	Day 3						
	……..						
	Day 7						
	2nd Dose						
	Day 1						
	Day 2						
	Day 3						
	……..						
	Day 7						

Note: Comparing overall dose levels; P-value based on Chi-square test.

Appendix 1.C. Reactogenicity - Systemic Reactions

Table 34: Systemic Reaction within 30 minutes after Vaccination in Safety Analysis Population

Reaction		All (N = 120)	COVIVAC			1 µg + CpG (N = 25)	Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)		
		n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Fever (≥ 38 °C)	1st Dose	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)
	p-value=	x.xxxx					
	2nd Dose	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)
	p-value=	x.xxxx					
Headache	1st Dose						
	p-value=						
	2nd Dose						
	p-value=						
Fatigue OR Malaise	1st Dose						
	p-value=						
	2nd Dose						
	p-value=						
Myalgia	1st Dose						
	p-value=						
	2nd Dose						
	p-value=						
Arthralgia	1st Dose						
	p-value=						

Table 34: Systemic Reaction within 30 minutes after Vaccination in Safety Analysis Population (continued)

Reaction		All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
		n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Arthralgia	2nd Dose	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)
	p-value=	x.xxxx					
Nausea OR Vomiting	1st Dose						
	p-value=						
	2nd Dose						
	p-value=						

Note: *Two-sided 95% CIs computed via the Clopper-Pearson method
Comparing overall dose levels; P-value based on Chi-square test.

Table 35: Systemic Reaction by Severity within 30 minutes after Vaccination in Safety Analysis Population

Reaction	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Fever (≥ 38 °C)						
1st Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						
2nd Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						

Table 35: Systemic Reaction by Severity within 30 minutes after Vaccination in Safety Analysis Population (continued)

Reaction	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Headache						
1st Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						
2nd Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						

Table 35: Systemic Reaction by Severity within 30 minutes after Vaccination in Safety Analysis Population (continued)

Reaction	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Fatigue OR Malaise						
1st Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						
2nd Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						

Table 35: Systemic Reaction by Severity within 30 minutes after Vaccination in Safety Analysis Population (continued)

Reaction	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Myalgia						
1st Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						
2nd Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						

Table 35: Systemic Reaction by Severity within 30 minutes after Vaccination in Safety Analysis Population (continued)

Reaction	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Arthralgia						
1st Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						
2nd Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						

Table 35: Systemic Reaction by Severity within 30 minutes after Vaccination in Safety Analysis Population (continued)

Reaction	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Nausea OR Vomiting						
1st Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						
2nd Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						

Note: *Two-sided 95% CIs computed via the Clopper-Pearson method
Comparing overall dose levels; P-value based on Fisher's exact test.

Table 36: Systemic Reaction Started During Day 1 - Day 7 after Vaccination in Safety Analysis Population

Reaction		All (N = 120)	COVIVAC			1 µg + CpG (N = 25)	Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)		
		n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Fever (≥ 38 °C)	1st Dose	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)
	p-value=	x.xxxx					
	2nd Dose	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)
	p-value=	x.xxxx					
Headache	1st Dose						
	p-value=						
	2nd Dose						
	p-value=						
Fatigue OR Malaise	1st Dose						
	p-value=						
	2nd Dose						
	p-value=						
Myalgia	1st Dose						
	p-value=						
	2nd Dose						
	p-value=						
Arthralgia	1st Dose						
	p-value=						

Table 36: Systemic Reaction Started during Day 1 - Day 7 after Vaccination in Safety Analysis Population (continue)

Reaction		All (N = 120)	COVIVAC 1 µg (N = 25)	COVIVAC 3 µg (N = 25)	COVIVAC 10 µg (N = 25)	COVIVAC 1 µg + CpG (N = 25)	Placebo (N = 20)
		n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Arthralgia	2nd Dose	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)
	p-value=	x.xxxx					
Nausea OR Vomiting	1st Dose						
	p-value=						
	2nd Dose						
	p-value=						

Note: *Two-sided 95% CIs computed via the Clopper-Pearson method
Comparing overall dose levels; P-value based on Chi-square test.

Table 37: Systemic Reaction by Severity Started during Day 1 - Day 7 after Vaccination in Safety Analysis Population

Reaction	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Fever (≥ 38 °C)						
1st Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						
2nd Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						

Table 37: Systemic Reaction by Severity Started during Day 1 - Day 7 after Vaccination in Safety Analysis Population (continued)

Reaction	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Headache						
1st Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						
2nd Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						

Table 37: Systemic Reaction by Severity Started during Day 1 - Day 7 after Vaccination in Safety Analysis Population (continued)

Reaction	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Fatigue OR Malaise						
1st Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						
2nd Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						

Table 37: Systemic Reaction by Severity Started during Day 1 - Day 7 after Vaccination in Safety Analysis Population (continued)

Reaction	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Myalgia						
1st Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						
2nd Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						

Table 37: Systemic Reaction by Severity Started during Day 1 - Day 7 after Vaccination in Safety Analysis Population (continued)

Reaction	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Arthralgia						
1st Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						
2nd Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						

Table 37: Systemic Reaction by Severity Started during Day 1 - Day 7 after Vaccination in Safety Analysis Population (continued)

Reaction	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Nausea OR Vomiting						
1st Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						
2nd Dose						
None						
Mild						
Moderate						
Severe						
Potentially life-threatening						
p-value =						

Note: *Two-sided 95% CIs computed via the Clopper-Pearson method
Comparing overall dose levels; P-value based on Fisher's exact test.;

Table 38: Incidence of New Onset and Ongoing Local Reaction Reported on each Day During Day 1 - Day 7 after Vaccination in Safety Analysis Population

Reaction		All (N = 120)	COVIVAC			1 µg + CpG (N = 25)	Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)		
		n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Fever (≥ 38 °C)	**1st Dose**						
	Day 1						
	Day 2						
	Day 3						
	……..						
	Day 7						
	2nd Dose						
	Day 1						
	Day 2						
	Day 3						
	……..						
	Day 7						
Headache	**1st Dose**						
	Day 1						
	Day 2						
	Day 3						
	……..						
	Day 7						
	2nd Dose						
	Day 1						
	Day 2						
	Day 3						
	……..						
	Day 7						

Table 38: Incidence of New Onset and Ongoing Local Reaction Reported on each Day During Day 1 - Day 7 after Vaccination in Safety Analysis Population (continued)

Reaction		All (N = 120)	COVIVAC			1 µg + CpG (N = 25)	Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)		
		n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Fatigue OR Malaise	**1st Dose**						
	Day 1						
	Day 2						
	Day 3						
	……..						
	Day 7						
	2nd Dose						
	Day 1						
	Day 2						
	Day 3						
	……..						
	Day 7						
Myalgia	**1st Dose**						
	Day 1						
	Day 2						
	Day 3						
	……..						
	Day 7						
	2nd Dose						
	Day 1						
	Day 2						
	Day 3						
	……..						
	Day 7						

Table 38: Incidence of New Onset and Ongoing Local Reaction Reported on each Day During Day 1 - Day 7 after Vaccination in Safety Analysis Population (continued)

Reaction		All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
		n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Arthralgia	**1st Dose**						
	Day 1						
	Day 2						
	Day 3						
	……..						
	Day 7						
	2nd Dose						
	Day 1						
	Day 2						
	Day 3						
	……..						
	Day 7						
Nausea or Vomiting	**1st Dose**						
	Day 1						
	Day 2						
	Day 3						
	……..						
	2nd Dose						
	Day 1						
	Day 2						
	Day 3						
	……..						
	Day 7						

Note: *Two-sided 95% CIs computed via the Clopper-Pearson method

Appendix 1.D. Adverse Events

Table 39: Overall Number of Subjects with Non-Serious Adverse Events from Combined Solicited and Unsolicited Adverse Events Onset during the First 28 days after each Vaccination in Safety Analysis Population

	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Overall, n (%)						
with one or more adverse events	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)
with no adverse event						
with vaccine-related adverse events						
After 1st Dose Vaccination						
with one or more adverse events						
with no adverse event						
with vaccine-related adverse events						
After 2nd Dose Vaccination						
with one or more adverse events						
with no adverse event						
with vaccine-related adverse events						

Note: *Two-sided 95% CIs computed via the Clopper-Pearson method

Table 40: Summary of Non-Serious Adverse Events from Combined Solicited and Unsolicited Adverse Events Onset during the First 28 days after each Vaccination by MedDRA term in Safety Analysis Population

System Organ Class (SOC)	Preferred Term (PT)	All (N = 120)		COVIVAC								Placebo (N = 20)	
				1 µg (N = 25)		3 µg (N = 25)		10 µg (N = 25)		1 µg + CpG (N = 25)			
		NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)
Overall All SOC	All PT	$_{x}^{x}$	xx (xx.x %)	xx	xx (xx.x %)	xx	xx (xx.x %)	xx	xx (xx.x %)	xx	xx (xx.x %)	xx	xx (xx.x %)
SOC 1	All PT 1 PT 2												
SOC 2	All PT 1 PT 2												
1st Dose All SOC	All PT												
SOC 1	All PT 1 PT 2												
SOC 2	All PT 1 PT 2												
2nd Dose All SOC	All PT												
SOC 1	All PT 1 PT 2												
SOC 2	All PT 1 PT 2												

Note: "N" is the total number of subject in each group and "xx" represent the value number.
"NE" is number of events.
"n" is number of subject who has at least one adverse event.

Table 41: Overall Number of Subjects with Adverse Events Onset during the First 28 days after each Vaccination in Safety Analysis Population

	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Overall Adverse event, n (%)						
with one or more adverse events	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)
with no adverse event						
with vaccine-related adverse events						
withdrawn due to an adverse event						
Adverse event, n (%)						
1st Dose Vaccination						
with one or more adverse events						
with no adverse event						
with vaccine-related adverse events						
withdrawn due to an adverse event						
2nd Dose Vaccination						
with one or more adverse events						
with no adverse event						
with vaccine-related adverse events						
withdrawn due to an adverse event						
Serious adverse event, n (%)						
1st Dose Vaccination						
with one or more serious adverse events						
with no serious adverse event						
with vaccine-related serious adverse events						
withdrawn due to a serious adverse event						
SAEs leading to death						

Table 41: Overall Number of Subjects with Adverse Events Onset during the First 28 days after each Vaccination in Safety Analysis Population (continue)

	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
Serious adverse event, n (%)						
2nd Dose Vaccination						
with one or more serious adverse events	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)
with no serious adverse event						
with vaccine-related serious adverse events						
withdrawn due to a serious adverse event						
SAEs leading to death						
Medically-attended AEs, n (%)						
1st Dose Vaccination						
with one or more MAAEs						
with no MAAE						
with vaccine-related MAAEs						
withdrawn due to an MAAE						
2nd Dose Vaccination						
with one or more MAAEs						
with no MAAE						
with vaccine-related MAAEs						
withdrawn due to an MAAE						

Table 41: Overall Number of Subjects with Adverse Events Onset during the First 28 days after each Vaccination in Safety Analysis Population (continue)

	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
AEs of special interest, n (%)						
1st Dose Vaccination						
with one or more AESIs	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)
Potential immune-mediated medical conditions (PIMMC) Associated with COVID-19						
with no AESI						
with vaccine-related AESIs						
withdrawn due to an AESI						
2nd Dose Vaccination						
with one or more AESIs						
Potential immune-mediated medical conditions (PIMMC) Associated with COVID-19						
with no AESI						
with vaccine-related AESIs						
withdrawn due to an AESI						

Note: "N" is the total number of subject in each group and "xx" represent the value number.

Table 42: Overall Number of Subjects with Serious Adverse Events throughout the Entire Study Period in Safety Analysis Population

	All (N = 120)	**COVIVAC**				**Placebo (N = 20)**
		1 µg (N = 25)	**3 µg (N = 25)**	**10 µg (N = 25)**	**1 µg + CpG (N = 25)**	
	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)	n (%) (95% CI*)
with one or more serious adverse events	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)	xx (xx.x%) (xx.x-xx.x)
with no serious adverse event						
with vaccine-related serious adverse events						
with medically-attended serious AE (MAAEs)						
with serious adverse events of special interest (AESI)						
Potential immune-mediated medical conditions (PIMMC)						
Associated with COVID-19						
withdrawn due to a serious adverse event						
SAEs leading to death						

Note: "N" is the total number of subject in each group and "xx" represent the value number.

Table 43: Number of Subjects with Serious Adverse Events Onset during the First 28 days after each Vaccination by Severity

	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
1st Dose Vaccination						
with one or more serious adverse events by severity*	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade1 (Mild)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade2 (Moderate)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx(xx.xx%)	xx (xx.x%)
Grade3 (Severe)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade4 (Potentially life-threatening)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with no serious adverse event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with vaccine-related serious adverse events by severity*	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade1 (Mild)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade2 (Moderate)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade3 (Severe)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade4 (Potentially life-threatening)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with specific adverse events						
System Organ Class Term **Preferred Term**						
…… ……	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 43: Number of Subjects with Serious Adverse Events Onset during the First 28 days after each Vaccination by Severity (continue)

	All (N = 120)	COVIVAC 1 µg (N = 25)	COVIVAC 3 µg (N = 25)	COVIVAC 10 µg (N = 25)	COVIVAC 1 µg + CpG (N = 25)	Placebo (N = 20)
2nd Dose Vaccination						
with one or more serious adverse events by severity*	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade1 (Mild)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade2 (Moderate)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade3 (Severe)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade4 (Potentially life-threatening)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with no serious adverse event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with vaccine-related serious adverse events by severity*	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade1 (Mild)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade2 (Moderate)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade3 (Severe)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade4 (Potentially life-threatening)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with specific adverse events						
System Organ Class Term **Preferred Term**						
…… ……	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Note: "N" is the total number of subject in each group and "xx" represent the value number.

***** Maximum severity grade will be considered.

Table 44: Number of Subjects with Serious Adverse Events by Severity throughout the Study Period

	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
with one or more serious adverse events by severity*	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade1 (Mild)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade2 (Moderate)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade3 (Severe)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade4 (Potentially life-threatening)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with no serious adverse event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with vaccine-related serious adverse events by severity*	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade1 (Mild)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade2 (Moderate)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade3 (Severe)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade4 (Potentially life-threatening)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with specific adverse events						
System Organ Class Term **Preferred Term**						
…… ……	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Note: "N" is the total number of subject in each group and "xx" represent the value number.

***** Maximum severity grade will be considered.

Table 45: Number of Subjects with Medically-Attended AEs (MAAEs) by Severity throughout the Study Period

		All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
with one or more MAAEs by severity*		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade1 (Mild)		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade2 (Moderate)		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade3 (Severe)		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade4 (Potentially life-threatening)		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with no MAAE		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with vaccine-related MAAEs by severity*		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade1 (Mild)		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade2 (Moderate)		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade3 (Severe)		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade4 (Potentially life-threatening)		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with specific adverse events							
System Organ Class Term	**Preferred Term**						
……	……	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Note: "N" is the total number of subject in each group and "xx" represent the value number.

***** Maximum severity grade will be considered.

Table 46: Number of Subjects with Adverse Events of Special Interest (AESI) by Severity throughout the Study Period

	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
with one or more AESI by severity*	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade1 (Mild)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade2 (Moderate)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade3 (Severe)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade4 (Potentially life-threatening)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with no AESI	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with vaccine-related AESI by severity*	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade1 (Mild)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade2 (Moderate)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade3 (Severe)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade4 (Potentially life-threatening)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with specific adverse events						
System Organ Class Term **Preferred Term**						
…… ……	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Note: "N" is the total number of subject in each group and "xx" represent the value number.

***** Maximum severity grade will be considered.

Table 47: Number of Subjects with Adverse Events of Special Interest (AESI) Relevant to COVID-19 by Severity throughout the Study Period

	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
with one or more AESIs relevant to COVID-19 by severity*	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade1 (Mild)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade2 (Moderate)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade3 (Severe)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade4 (Potentially life-threatening)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with no AESI relevant to COVID-19	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with vaccine-related AESI by severity*	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade1 (Mild)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade2 (Moderate)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade3 (Severe)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade4 (Potentially life-threatening)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with specific adverse events						
System Organ Class Term **Preferred Term**						
…… ……	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Note: "N" is the total number of subject in each group and "xx" represent the value number

***** Maximum severity grade will be considered.

Table 48: Number of Subjects with Adverse Events of Potential Immune-Mediated Medical Conditions (PIMMC) by Severity throughout the Study Period

	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
with one or more AEs of PIMMC by severity*	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade1 (Mild)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade2 (Moderate)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade3 (Severe)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade4 (Potentially life-threatening)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with no AE of PIMMC	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with vaccine-related AEs of PIMMC by severity*	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade1 (Mild)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade2 (Moderate)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade3 (Severe)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade4 (Potentially life-threatening)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with specific adverse events						
System Organ Class Term **Preferred Term**						
…… ……	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx xx.xx%)

Note: "N" is the total number of subject in each group and "xx" represent the value number.

***** Maximum severity grade will be considered.

Table 49: Duration Days of Adverse Event During First 28 Days Post Vaccination by Severity Grade

	Severity	All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
AE During the first 28 days post –first vaccination	All, Mean of days (SD)						
	Mild						
	Moderate						
	Severe						
	Potentially life-threatening						
	Related, Mean of days (SD)						
	Mild						
	Moderate						
	Severe						
	Potentially life-threatening						
AE During the first 28 days post – second vaccination	All, Mean of days (SD)						
	Mild						
	Moderate						
	Severe						
	Potentially life-threatening						
	Related, Mean of days (SD)						
	Mild						
	Moderate						
	Severe						
	Potentially life-threatening						

Table 49: Duration Days of Adverse Event During First 28 Days Post Vaccination by Severity Grade (continued)

	Severity	All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
SAE During the first 28 days post – first vaccination	All, Mean of days (SD)						
	Mild						
	Moderate						
	Severe						
	Potentially life-threatening						
	Related, Mean of days (SD)						
	Mild						
	Moderate						
	Severe						
	Potentially life-threatening						
SAE During the first 28 days post – second vaccination	All, Mean of days (SD)						
	Mild						
	Moderate						
	Severe						
	Potentially life-threatening						
	Related, Mean of days (SD)						
	Mild						
	Moderate						
	Severe						
	Potentially life-threatening						

Table 49: Duration Days of Adverse Event During First 28 Days Post Vaccination by Severity Grade (continued)

	Severity	All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
MAAE During the first 28 days post – first injection	All, Mean of days (SD)						
	Mild						
	Moderate						
	Severe						
	Potentially life-threatening						
	Related, Mean of days (SD)						
	Mild						
	Moderate						
	Severe						
	Potentially life-threatening						
MAAE During the first 28 days post – second injection	All, Mean of days (SD)						
	Mild						
	Moderate						
	Severe						
	Potentially life-threatening						
	Related, Mean of days (SD)						
	Mild						
	Moderate						
	Severe						
	Potentially life-threatening						

Table 49: Duration Days of Adverse Event During First 28 Days Post Vaccination by Severity Grade (continued)

	Severity	All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
AESI During the first 28 days post – first injection	All, Mean of days (SD)						
	Mild						
	Moderate						
	Severe						
	Potentially life-threatening						
	Related, Mean of days (SD)						
	Mild						
	Moderate						
	Severe						
	Potentially life-threatening						
AESI During the first 28 days post – second injection (Visit 6 (Day 57))	All, Mean of days (SD)						
	Mild						
	Moderate						
	Severe						
	Potentially life-threatening						
	Related, Mean of days (SD)						
	Mild						
	Moderate						
	Severe						
	Potentially life-threatening						

Table 50: Summary of Adverse Events during the First 28 days after each Vaccination by MedDRA term

System Organ Class (SOC)	Preferred Term (PT)	All (N = xx)		COVIVAC								Placebo (N = 20)	
				1 µg (N = 25)		3 µg (N = 25)		10 µg (N = 25)		1 µg + CpG (N = 25)			
		NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)
Overall													
All SOC	All PT												
SOC 1	All												
	PT 1												
	PT 2												
SOC 2	All												
	PT 1												
	PT 2												
1st dose													
All SOC	All PT												
SOC 1	All												
	PT 1												
	PT 2												
SOC 2	All												
	PT 1												
	PT 2												
2nd dose													
All SOC	All PT												
SOC 1	All												
	PT 1												
	PT 2												
SOC 2	All												
	PT 1												
	PT 2												

Note: “N” is the total number of patient in each group and “xx” represent the value number.
“NE” is number of events.
“n” is number of subject who has at least one adverse event.

Table 51: Summary of Serious Adverse Events throughout the Entire Study Period by MedDRA term

System Organ Class (SOC)	Preferred Term (PT)	All (N = xx)		COVIVAC								Placebo (N = 20)	
				1 µg (N = 25)		3 µg (N = 25)		10 µg (N = 25)		1 µg + CpG (N = 25)			
		NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)
All SOC	All PT												
SOC 1	All												
	PT 1												
	PT 2												
SOC 2	All												
	PT 1												
	PT 2												

Note: "N" is the total number of patient in each group and "xx" represent the value number.
"NE" is number of events.
"n" is number of subject who has at least one adverse event.

Table 52: Summary of Serious Adverse Event during the First 28 days after each Vaccination by Criteria

Criteria	All (N = 120)		COVIVAC								Placebo (N = 20)	
			1 µg (N = 25)		3 µg (N = 25)		10 µg (N = 25)		1 µg + CpG (N = 25)			
	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)
Overall												
All												
Results in death												
Is life-threatening												
Requires inpatient hospitalization or prolongation of an existing hospitalization												
Results in persistent or significant disability or incapacity												
Results in a congenital anomaly or birth defect												
Is medically significant												
1st dose												
All												
Results in death												
Is life-threatening												
Requires inpatient hospitalization or prolongation of an existing hospitalization												
Results in persistent or significant disability or incapacity												
Results in a congenital anomaly or birth defect												
Is medically significant												
2nd dose												
All												
Results in death												
Is life-threatening												

Criteria	All (N = 120)		COVIVAC 1 µg (N = 25)		COVIVAC 3 µg (N = 25)		COVIVAC 10 µg (N = 25)		COVIVAC 1 µg + CpG (N = 25)		Placebo (N = 20)	
	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)
Requires inpatient hospitalization or prolongation of an existing hospitalization												
Results in persistent or significant disability or incapacity												
Results in a congenital anomaly or birth defect												
Is medically significant												

Note: NE – Number of events
n (%) – Number of subject and percentage

Table 53: Summary of Serious Adverse Event throughout the Study Period by Criteria

Criteria	All (N = 120)		COVIVAC 1 µg (N = 25)		COVIVAC 3 µg (N = 25)		COVIVAC 10 µg (N = 25)		COVIVAC 1 µg + CpG (N = 25)		Placebo (N = 20)	
	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)
All												
Results in death												
Is life-threatening												
Requires inpatient hospitalization or prolongation of an existing hospitalization												
Results in persistent or significant disability or incapacity												
Results in a congenital anomaly or birth defect												
Is medically significant												

Note: NE – Number of events
n (%) – Number of subject and percentage

Table 54: Summary of Adverse Event by Outcome during the First 28 Days after each Vaccination

Outcome	All (N = xx)		COVIVAC								Placebo (N = 20)	
			1 µg (N = 25)		3 µg (N = 25)		10 µg (N = 25)		1 µg + CpG (N = 25)			
	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)
Overall												
All												
Ongoing												
Recovered/Resolved												
Recovered/Resolved with sequelae												
Fatal												
Unknown												
1st Dose												
All												
Ongoing												
Recovered/Resolved												
Recovered/Resolved with sequelae												
Fatal												
Unknown												
2nd Dose												
All												
Ongoing												
Recovered/Resolved												
Recovered/Resolved with sequelae												
Fatal												
Unknown												

Table 55: Summary of Serious Adverse Event by Outcome throughout the Study Period

Outcome	All (N = xx)		COVIVAC								Placebo (N = 20)	
			1 µg (N = 25)		3 µg (N = 25)		10 µg (N = 25)		1 µg + CpG (N = 25)			
	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)
All												
Ongoing												
Recovered/Resolved												
Recovered/Resolved with sequelae												
Fatal												
Unknown												

Table 56: Summary of Adverse Event during the First 28 Days after each Vaccination by Relationship to Study Vaccine

Relationship to Study Vaccine	All (N = xx)		COVIVAC								Placebo (N = 20)	
			1 µg (N = 25)		3 µg (N = 25)		10 µg (N = 25)		1 µg + CpG (N = 25)			
	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)
Overall												
All												
Related												
Not related												
1st Dose												
All												
Related												
Not related												
2nd Dose												
All												
Related												
Not related												

Table 57: Summary of Serious Adverse Event throughout the Study Period by Relationship to Study Vaccine

Relationship to Study Vaccine	All (N = xx)		COVIVAC								Placebo (N = 20)	
			1 µg (N = 25)		3 µg (N = 25)		10 µg (N = 25)		1 µg + CpG (N = 25)			
	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)
All												
Related												
Not related												

Table 58: Summary of Adverse event by Action Taken to the Study Vaccine during the First 28 Days after each Vaccination

Action Taken to the Study Vaccine	All (N = xx)		COVIVAC								Placebo (N = 20)	
			1 µg (N = 25)		3 µg (N = 25)		10 µg (N = 25)		1 µg + CpG (N = 25)			
	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)
Overall												
All												
Withdrawn												
Delayed												
Continued												
Not applicable												
1st Dose												
All												
Withdrawn												
Delayed												
Continued												
Not applicable												
2nd Dose												
All												
Withdrawn												
Delayed												
Continued												
Not applicable												

Table 59: Summary of Serious Adverse Event by Action Taken to the Study Vaccine throughout the Study Period

Action Taken to the Study Vaccine	All (N = xx)		COVIVAC								Placebo (N = 20)	
			1 µg (N = 25)		3 µg (N = 25)		10 µg (N = 25)		1 µg + CpG (N = 25)			
	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)	NE	n (%)
All												
Withdrawn												
Delayed												
Continued												
Not applicable												

Note: NE: Number of events
n: Number of subject with at least one AE / %: (n/N)*100

Appendix 1.E. Hematology Results

Table 60: Overall Number of Subjects with Any Abnormal Hematology Results in Safety Analysis Population

	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Overall, n (%)						
with hemoglobin abnormal result	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with WBC abnormal result	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with platelet abnormal result	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with one or more abnormal result	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with no abnormal result	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Visit 2 (Day 8)						
with hemoglobin abnormal result						
with WBC abnormal result						
with platelet abnormal result						
with one or more abnormal result						
with no abnormal result						
Visit 4 (Day 36)						
with hemoglobin abnormal result						
with WBC abnormal result						
with platelet abnormal result						
with one or more abnormal result						
with no abnormal result						

Table 61: Hemoglobin Value at each Follow-up Visit Compared to Baseline

Hemoglobin (g/dL)	All (N = 120)	COVIVAC			1 µg + CpG (N = 25)	Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)		
Baseline						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild						
Moderate						
Severe						
Potentially life threatening						
Visit 2 (Day 8)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value=						

Table 61: Hemoglobin Value at each Follow-up Visit Compared to Baseline (continued)

Hemoglobin (g/dL)	All (N = 120)	COVIVAC			1 µg + CpG (N = 25)	Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)		
Change between Day 8 and Baseline						
Mean of % Difference (95% CI)						
Visit 4 (Day 36)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value=						
Change between Day 36 and Baseline						
Mean of % Difference (95% CI)						

Note: + CpG1018 1.5 mg (Adjuvant)

* P-value based on paired t test/ Wilcoxon signed-rank test

** P-value based on Mc Nemar chi-square test, Normality of results (Normal/Abnormal) will be tested significant difference.

A significance test comparing a baseline (pre-vaccination) with a follow up measurement separately in vaccination group.

Severity grading

Hemoglobin (g/dL)	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life Threatening (Grade 4)
Female	11.0 – 12.0	9.5 – 10.9	8.0 – 9.4	< 8.0
Male	12.5 – 13.5	10.5 – 12.4	8.5 – 10.4	< 8.5
Change from baseline value (g/dL)	1.0 – 1.5	1.6 – 2.0	2.1 – 5.0	> 5.0

Table 62: White Blood Cell Count Value at each Follow-up Visit Compared to Baseline

WBC (x 10^3/µL)	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Baseline						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild						
Moderate						
Severe						
Potentially life threatening						
Visit 2 (Day 8)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value=						

Table 62: White Blood Cell Count Value at each Follow-up Visit Compared to Baseline (continued)

WBC (x 10^3/µL)	All (N = 120)	COVIVAC			1 µg + CpG (N = 25)	Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)		
Change between Day 8 and Baseline						
Mean of % Difference (95% CI)						
Visit 4 (Day 36)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value=						
Change between Day 36 and Baseline						
Mean of % Difference (95% CI)						

Note: + CpG1018 1.5 mg (Adjuvant)

* P-value based on paired t test/ Wilcoxon signed-rank test

** P-value based on Mc Nemar chi-square test, Normality of results (Normal/Abnormal) will be tested significant difference.

A significance test comparing a baseline (pre-vaccination) with a follow up measurement separately in vaccination group.

Severity grading

WBC (cell/mm^3)	**Mild (Grade 1)**	**Moderate (Grade 2)**	**Severe (Grade 3)**	**Potentially Life Threatening (Grade 4)**
Increased (cell/mm^3)	10,800 – 15,000	15,001 – 20,000	20,001 – 25,000	> 25,000
Decreased (cell/mm^3)	2,500 – 3,400	1,500 – 2,499	1,000 – 1,499	< 1,000

Table 63: Platelets Count Value at each Follow-up Visit Compared to Baseline

Platelets (x 10^3/µL)	All (N = 120)	COVIVAC			1 µg + CpG (N = 25)	Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)		
Baseline						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild						
Moderate						
Severe						
Potentially life threatening						
Visit 2 (Day 8)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value=						

Table 63: Platelets Count Value at each Follow-up Visit Compared to Baseline (continued)

Platelets (x 10^3/µL)	All (N = 120)	COVIVAC 1 µg (N = 25)	COVIVAC 3 µg (N = 25)	COVIVAC 10 µg (N = 25)	1 µg + CpG (N = 25)	Placebo (N = 20)
Change between Day 8 and Baseline						
Mean of % Difference (95% CI)						
Visit 4 (Day 36)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value=						
Change between Day 36 and Baseline						
Mean of % Difference (95% CI)						

Note: + CpG1018 1.5 mg (Adjuvant)

* P-value based on paired t test/ Wilcoxon signed-rank test

** P-value based on Mc Nemar chi-square test, Normality of results (Normal/Abnormal) will be tested significant difference.

A significance test comparing a baseline (pre-vaccination) with a follow up measurement separately in vaccination group.

Severity grading

Platelets (cell/mm^3)	**Mild (Grade 1)**	**Moderate (Grade 2)**	**Severe (Grade 3)**	**Potentially Life Threatening (Grade 4)**
Decreased	100,000 – <125,000	50,000 – < 100,000	25,000 – < 50,000	< 25,000

Appendix 1.F. Chemistry Results

Table 64: Overall Number of Subjects with Any Abnormal Chemistry Results in Safety Analysis Population

	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Overall, n (%)						
with Creatinine abnormal result	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with ALT abnormal result	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with AST abnormal result	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with total bilirubin abnormal result	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with one or more abnormal result	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with no abnormal result	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Visit 2 (Day 8)						
with Creatinine abnormal result						
with ALT abnormal result						
with AST abnormal result						
with total bilirubin abnormal result						
with one or more abnormal result						
with no abnormal result						
Visit 4 (Day 36)						
with Creatinine abnormal result						
with ALT abnormal result						
with AST abnormal result						
with total bilirubin abnormal result						
with one or more abnormal result						
with no abnormal result						

Table 65: Creatinine Value at each Follow-up Visit Compared to Baseline in Safety Analysis Population

Creatinine (µmol/L)	All (N = 120)	COVIVAC			1 µg + CpG (N = 25)	Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)		
Baseline						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
Visit 2 (Day 8)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						

Table 65: Creatinine Value at each Follow-up Visit Compared to Baseline in Safety Analysis Population (continue)

Creatinine (µmol/L)	All (N = 120)	COVIVAC			1 µg + CpG (N = 25)	Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)		
Change between Day 8 and Baseline						
Mean of % Difference (95% CI)						
Visit 4 (Day 36)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
Change between Day 8 and Baseline						
Mean of % Difference (95% CI)						

Note: + CpG1018 1.5 mg (Adjuvant)

* P-value based on Kruskal Wallis Test

Severity grading

	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life Threatening (Grade 4)
Creatinine (mg/dL)	1.1 – 1.3 x ULN	> 1.3 – 1.8 x ULN OR increase of > 0.3 above baseline	> 1.8 – < 3.5 x ULN OR increase of 1.5 – < 2.0 x above baseline	≥ 3.5 x ULN OR increase of > 2.0 x above baseline

ULN = upper limit of normal range

Table 66: ALT Value at each Follow-up Visit Compared to Baseline in Safety Analysis Population

ALT (U/L)	All (N = 120)	COVIVAC			1 µg + CpG (N = 25)	Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)		
Baseline						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
Visit 2 (Day 8)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						

Table 66: ALT Value at each Follow-up Visit Compared to Baseline in Safety Analysis Population (continue)

ALT (U/L)	All (N = 120)	COVIVAC 1 µg (N = 25)	COVIVAC 3 µg (N = 25)	COVIVAC 10 µg (N = 25)	1 µg + CpG (N = 25)	Placebo (N = 20)
Change between Day 8 and Baseline						
Mean of % Difference (95% CI)						
Visit 4 (Day 36)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
Change between Day 8 and Baseline						
Mean of % Difference (95% CI)						

Note: + CpG1018 1.5 mg (Adjuvant)
* P-value based on Kruskal Wallis Test
Severity grading

ALT (U/L)	**Mild (Grade 1)**	**Moderate (Grade 2)**	**Severe (Grade 3)**	**Potentially Life Threatening (Grade 4)**
ALT increased	1.25 – < 2.5 x ULN	2.5 – <5.0 x ULN	5.0 – < 10.0 x ULN	≥ 10.0 x ULN

ULN = upper limit of normal range

Table 67: AST Value at each Follow-up Visit Compared to Baseline in Safety Analysis Population

AST (U/L)	All (N = 120)	COVIVAC			1 µg + CpG (N = 25)	Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)		
Baseline						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
Visit 2 (Day 8)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						

Table 67: AST Value at each Follow-up Visit Compared to Baseline in Safety Analysis Population (continue)

AST (U/L)	All (N = 120)	COVIVAC 1 µg (N = 25)	COVIVAC 3 µg (N = 25)	COVIVAC 10 µg (N = 25)	1 µg + CpG (N = 25)	Placebo (N = 20)
Change between Day 8 and Baseline						
Mean of % Difference (95% CI)						
Visit 4 (Day 36)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
Change between Day 8 and Baseline						
Mean of % Difference (95% CI)						

Note: + CpG1018 1.5 mg (Adjuvant)
* P-value based on Kruskal Wallis Test
Severity grading

AST (U/L)	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life Threatening (Grade 4)
1.25 – < 2.5 x ULN	2.5 – <5.0 x ULN	5.0 – < 10.0 x ULN	≥ 10.0 x ULN	1.25 – < 2.5 x ULN

ULN = upper limit of normal range

Table 68: Total Bilirubin Value at each Follow-up Visit Compared to Baseline in Safety Analysis Population

Total bilirubin (µmol/L)	All (N = 120)	COVIVAC			1 µg + CpG (N = 25)	Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)		
Baseline						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
Visit 2 (Day 8)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						

Table 68: Total Bilirubin Value at each Follow-up Visit Compared to Baseline in Safety Analysis Population (continued)

Total bilirubin (µmol/L)	All (N = 120)	COVIVAC 1 µg (N = 25)	COVIVAC 3 µg (N = 25)	COVIVAC 10 µg (N = 25)	1 µg + CpG (N = 25)	Placebo (N = 20)
Change between Day 8 and Baseline						
Mean of % Difference (95% CI)						
Visit 4 (Day 36)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
Change between Day 8 and Baseline						
Mean of % Difference (95% CI)						

Note: + CpG1018 1.5 mg (Adjuvant)
* P-value based on Kruskal Wallis Test
Severity grading

Bilirubin (mg/dL)	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life Threatening (Grade 4)
Bilirubin	1.1 – < 1.6 x ULN	1.6 – < 2.6 x ULN	2.6 – < 5.0 x ULN	≥ 5.0 x ULN

ULN = upper limit of normal range

Appendix 1.G. Vital Signs

Table 69: Overall Number of Subject with Abnormal of Vital Sign result at Post -First Vaccination

	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Overall, n (%)						
Systolic Blood Pressure (mmHg)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Diastolic Blood Pressure (mmHg)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pulse (Beats/min)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Respiratory Rate (Breaths/min)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Temperature (°C)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with one or more abnormal result	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with no abnormal result	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Post-first vaccination						
Systolic Blood Pressure (mmHg)						
Diastolic Blood Pressure (mmHg)						
Pulse (Beats/min)						
Respiratory Rate (Breaths/min)						
Temperature (°C)						
with one or more abnormal result						
with no abnormal result						
Visit 2 (Day 8)						
Systolic Blood Pressure (mmHg)						
Diastolic Blood Pressure (mmHg)						
Pulse (Beats/min)						
Respiratory Rate (Breaths/min)						
Temperature (°C)						
with one or more abnormal result						
with no abnormal result						

Table 70: Overall Number of Subject with Abnormal of Vital Sign at Post- Second Vaccination

	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Overall, n (%)						
Systolic Blood Pressure (mmHg)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Diastolic Blood Pressure (mmHg)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pulse (Beats/min)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Respiratory Rate (Breaths/min)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Temperature (°C)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with one or more abnormal result	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with no abnormal result	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Post-second vaccination						
Systolic Blood Pressure (mmHg)						
Diastolic Blood Pressure (mmHg)						
Pulse (Beats/min)						
Respiratory Rate (Breaths/min)						
Temperature (°C)						
with one or more abnormal result						
with no abnormal result						
Visit 4 (Day 36)						
Systolic Blood Pressure (mmHg)						
Diastolic Blood Pressure (mmHg)						
Pulse (Beats/min)						
Respiratory Rate (Breaths/min)						
Temperature (°C)						
with one or more abnormal result						
with no abnormal result						
Visit 5 (Day 43)						
Systolic Blood Pressure (mmHg)						
Diastolic Blood Pressure (mmHg)						
Pulse (Beats/min)						
Respiratory Rate (Breaths/min)						
Temperature (°C)						

Table 70: Overall Number of Subject with Abnormal of Vital Sign at Post- Second Vaccination (continued)

	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Temperature (°C)						
with one or more abnormal result						
with no abnormal result						
Visit 6 (Day 57)						
Systolic Blood Pressure (mmHg)						
Diastolic Blood Pressure (mmHg)						
Pulse (Beats/min)						
Respiratory Rate (Breaths/min)						
Temperature (°C)						
with one or more abnormal result						
with no abnormal result						
Visit 7 (Day 197)						
Systolic Blood Pressure (mmHg)						
Diastolic Blood Pressure (mmHg)						
Pulse (Beats/min)						
Respiratory Rate (Breaths/min)						
Temperature (°C)						
with one or more abnormal result						
with no abnormal result						

Table 71: Systolic Blood Pressure (mmHg) Post-first Vaccination Compared to Pre-first Vaccination

	All	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Pre-first vaccination						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
Post-first vaccination						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
*p-value =		x.xxx	x.xxx	x.xxx	x.xxx	
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						
Change between pre and 30 minutes post vaccination						
Mean of % Difference (95% CI)						

Table 71: Systolic Blood Pressure (mmHg) Post-first Vaccination Compared to Pre-first Vaccination (continued)

	All	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Visit 2 (Day 8)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						
Change between pre and Day 8 post vaccination						
Mean of % Difference (95% CI)						

Note: + CpG1018 1.5 mg (Adjuvant)
* P-value based on paired t test/ Wilcoxon signed-rank test
** P-value based on Mc Nemar chi-square test, Normality of results (Normal/Abnormal) will be tested significant difference.
A significance test comparing a baseline (pre-vaccination) with a follow up measurement separately in vaccination group.
"xx" represent the value number.

Vital Signs Toxicity Grading	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life Threatening (Grade 4)
Hypertension (systolic) – mm Hg	141 – 150	151 – 165	> 165	ER visit or hospitalization for malignant hypertension
Hypotension (systolic) – mm Hg	85 – 89	80 – 84	< 80	ER visit or hospitalization for hypotensive shock

Table 72: Systolic Blood Pressure (mmHg) Post–second Vaccination Compared to Pre–second Vaccination

	All	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Pre-second vaccination						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
Post-second vaccination						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
*p-value =		x.xxx	x.xxx	x.xxx	x.xxx	
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
*p-value =						
Change between pre and 30 minutes post vaccination						
Mean of % Difference (95% CI)						

Table 72: Systolic Blood Pressure (mmHg) Post–second Vaccination Compared to Pre–second Vaccination (continued)

	All	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Visit 4 (Day 36)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
*p-value =						
Change between pre and Day 36 post vaccination						
Mean of % Difference (95% CI)						
Visit 5 (Day 43)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						

Table 72: Systolic Blood Pressure (mmHg) Post–second Vaccination Compared to Pre–second Vaccination (continued)

	All	COVIVAC			1 µg + CpG (N = 25)	Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)		
Change between pre and Day 43 post vaccination						
Mean of % Difference (95% CI)						
Visit 6 (Day 57)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
*p-value =						
Change between pre and Day 57 post vaccination						
Mean of % Difference (95% CI)						
Visit 7 (Day 197)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						

Table 72: Systolic Blood Pressure (mmHg) Post–second Vaccination Compared to Pre–second Vaccination (continued)

	All	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Severe						
Potentially life threatening						
**p-value =						
Change between pre and Day 197 post vaccination						
Mean of % Difference (95% CI)						

Note: + CpG1018 1.5 mg (Adjuvant)
* P-value based on paired t test/ Wilcoxon signed-rank test
** P-value based on Mc Nemar chi-square test, Normality of results (Normal/Abnormal) will be tested significant difference.
A significance test comparing a baseline (pre-vaccination) with a follow up measurement separately in vaccination group.
"xx" represent the value number.

Vital Signs Toxicity Grading	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life Threatening (Grade 4)
Hypertension (systolic) – mm Hg	141 – 150	151 – 165	> 165	ER visit or hospitalization for malignant hypertension
Hypotension (systolic) – mm Hg	85 – 89	80 – 84	< 80	ER visit or hospitalization for hypotensive shock

Table 73: Diastolic Blood Pressure (mmHg) Post-first Vaccination Compared to Pre-first Vaccination

	All	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Pre-first vaccination						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
Post-first vaccination						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
*p-value =		x.xxx	x.xxx	x.xxx	x.xxx	
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						
Change between pre and 30 minutes post vaccination						
Mean of % Difference (95% CI)						
Visit 2 (Day 8)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						

Table 73: Diastolic Blood Pressure (mmHg) Post-first Vaccination Compared to Pre-first Vaccination (continued)

	All	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						
Change between pre and Day 8 post vaccination						
Mean of % Difference (95% CI)						

Note: + CpG1018 1.5 mg (Adjuvant)
* P-value based on paired t test/ Wilcoxon signed-rank test
** P-value based on Mc Nemar chi-square test, Normality of results (Normal/Abnormal) will be tested significant difference.
A significance test comparing a baseline (pre-vaccination) with a follow up measurement separately in vaccination group.
"xx" represent the value number.

Vital Signs Toxicity Grading	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life Threatening (Grade 4)
Hypertension (diastolic) – mm Hg	91 – 99	100 – 105	> 105	ER visit or hospitalization for malignant hypertension

Table 74: Diastolic Blood Pressure (mmHg) Post–second Vaccination Compared to Pre–second Vaccination

	All	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Pre-second vaccination						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
Post-second vaccination						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
*p-value =		x.xxx	x.xxx	x.xxx	x.xxx	
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						
Change between pre and 30 minutes post vaccination						
Mean of % Difference (95% CI)						
Visit 4 (Day 36)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						

Table 74: Diastolic Blood Pressure (mmHg) Post–second Vaccination Compared to Pre–second Vaccination (continued)

	All	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						
Change between pre and Day 36 post vaccination						
Mean of % Difference (95% CI)						
Visit 5 (Day 43)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						
Change between pre and Day 43 post vaccination						
Mean of % Difference (95% CI)						
Visit 6 (Day 57)						
n						

Table 74: Diastolic Blood Pressure (mmHg) Post–second Vaccination Compared to Pre–second Vaccination (continued)

	All	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						
Change between pre and Day 57 post vaccination						
Mean of % Difference (95% CI)						
Visit 7 (Day 197)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						

Table 74: Diastolic Blood Pressure (mmHg) Post–second Vaccination Compared to Pre–second Vaccination (continued)

All	COVIVAC				Placebo (N = 20)
	1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Change between pre and Day 197 post vaccination					
Mean of % Difference (95% CI)					

Note: + CpG1018 1.5 mg (Adjuvant)

* P-value based on paired t test/ Wilcoxon signed-rank test

** P-value based on Mc Nemar chi-square test, Normality of results (Normal/Abnormal) will be tested significant difference.

A significance test comparing a baseline (pre-vaccination) with a follow up measurement separately in vaccination group.

"xx" represent the value number.

Vital Signs Toxicity Grading	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life Threatening (Grade 4)
Hypertension (diastolic) – mm Hg	91 – 99	100 – 105	> 105	ER visit or hospitalization for malignant hypertension

Table 75: Pulse (Beats/min) Post-first Vaccination Compared to Pre-first Vaccination

	All	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Pre-first vaccination						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
Post-first vaccination						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
*p-value =		x.xxx	x.xxx	x.xxx	x.xxx	
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						
Change between pre and 30 minutes post vaccination						
Mean of % Difference (95% CI)						
Visit 2 (Day 8)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						

	All	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						
Change between pre and Day 8 post vaccination						
Mean of % Difference (95% CI)						

Note: + CpG1018 1.5 mg (Adjuvant)

* P-value based on paired t test/ Wilcoxon signed-rank test

** P-value based on Mc Nemar chi-square test, Normality of results (Normal/Abnormal) will be tested significant difference.

A significance test comparing a baseline (pre-vaccination) with a follow up measurement separately in vaccination group.

Vital Signs Toxicity Grading	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life Threatening (Grade 4)
Tachycardia – beats per minute	101 – 115	116 – 130	> 130	Hospitalization for arrhythmia
Bradycardia – beats per minute [b]	50 – 54	45 – 49	< 45	ER visit or hospitalization for arrhythmia

[b] Grade 1 bradycardia or grade 1 tachypnea will not be considered an abnormality for this study, unless judged to be clinically significant by the PI.

Table 76: Pulse (Beats/min) Post–second Vaccination Compared to Pre–second Vaccination

	All	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Pre-second vaccination						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
Post- second vaccination						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
*p-value =		x.xxx	x.xxx	x.xxx	x.xxx	
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						
Change between pre and 30 minutes post vaccination						
Mean of % Difference (95% CI)						
Visit 4 (Day 36)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						

Table 76: Pulse (Beats/min) Post–second Vaccination Compared to Pre–second Vaccination (continued)

	All	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						
Change between pre and Day 36 post vaccination						
Mean of % Difference (95% CI)						
Visit 5 (Day 43)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						
Change between pre and Day 43 post vaccination						
Mean of % Difference (95% CI)						
Visit 6 (Day 57)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						

Table 76: Pulse (Beats/min) Post–second Vaccination Compared to Pre–second Vaccination (continued)

	All	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						
Change between pre and Day 57 post vaccination						
Mean of % Difference (95% CI)						
Visit 7 (Day 197)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						
Change between pre and Day 197 post vaccination						
Mean of % Difference (95% CI)						

Table 76: Pulse (Beats/min) Post–second Vaccination Compared to Pre–second Vaccination (continued)

Note: + CpG1018 1.5 mg (Adjuvant)
* P-value based on paired t test/ Wilcoxon signed-rank test
** P-value based on Mc Nemar chi-square test, Normality of results (Normal/Abnormal) will be tested significant difference.
A significance test comparing a baseline (pre-vaccination) with a follow up measurement separately in vaccination group.

Vital Signs Toxicity Grading	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life Threatening (Grade 4)
Tachycardia – beats per minute	101 – 115	116 – 130	> 130	Hospitalization for arrhythmia
Bradycardia – beats per minute [a]	50 – 54	45 – 49	< 45	ER visit or hospitalization for arrhythmia

[a] Grade 1 bradycardia or grade 1 tachypnea will not be considered an abnormality for this study, unless judged to be clinically significant by the PI.

Table 77: Respiratory Rate (Breaths/min) Post-first Vaccination Compared to Pre-first Vaccination

	All	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Pre-first vaccination						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
Post-first vaccination						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
*p-value =		x.xxx	x.xxx	x.xxx	x.xxx	
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						
Change between pre and 30 minutes post vaccination						
Mean of % Difference (95% CI)						
Visit 2 (Day 8)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						

	All	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						
Change between pre and Day 8 post vaccination						
Mean of % Difference (95% CI)						

Note: + CpG1018 1.5 mg (Adjuvant)

* P-value based on paired t test/ Wilcoxon signed-rank test

** P-value based on Mc Nemar chi-square test, Normality of results (Normal/Abnormal) will be tested significant difference.

A significance test comparing a baseline (pre-vaccination) with a follow up measurement separately in vaccination group.

Vital Signs Toxicity Grading	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life Threatening (Grade 4)
Respiratory Rate – breaths per minute	21 – 23	24 – 27	> 27	Intubation

Table 78: Respiratory Rate (Breaths/min) Post–second Vaccination Compared to Pre–second Vaccination

	All	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Pre-second vaccination						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
Post-second vaccination						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
*p-value =		x.xxx	x.xxx	x.xxx	x.xxx	
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						
Change between pre and 30 minutes post vaccination						
Mean of % Difference (95% CI)						
Visit 4 (Day 36)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						

Table 78: Respiratory Rate (Breaths/min) Post–second Vaccination Compared to Pre–second Vaccination (continued)

	All	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						
Change between pre and Day 36 post vaccination						
Mean of % Difference (95% CI)						
Visit 5 (Day 43)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						
Change between pre and Day 43 post vaccination						
Mean of % Difference (95% CI)						
Visit 6 (Day 57)						
n						

Table 78: Respiratory Rate (Breaths/min) Post–second Vaccination Compared to Pre–second Vaccination (continued)

	All	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						
Change between pre and Day 57 post vaccination						
Mean of % Difference (95% CI)						
Visit 7 (Day 197)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						

Table 78: Respiratory Rate (Breaths/min) Post–second Vaccination Compared to Pre–second Vaccination (continued)

All	COVIVAC				Placebo (N = 20)
	1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Change between pre and Day 197 post vaccination					
Mean of % Difference (95% CI)					

Note: + CpG1018 1.5 mg (Adjuvant)

* P-value based on paired t test/ Wilcoxon signed-rank test

** P-value based on Mc Nemar chi-square test, Normality of results (Normal/Abnormal) will be tested significant difference.

A significance test comparing a baseline (pre-vaccination) with a follow up measurement separately in vaccination group.

Vital Signs Toxicity Grading	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life Threatening (Grade 4)
Respiratory Rate – breaths per minute	21 – 23	24 – 27	> 27	Intubation

Table 79: Temperature (°C) Post-first Vaccination Compared to Pre-first Vaccination

	All	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Pre-first vaccination						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
Post-first vaccination						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
*p-value =		x.xxx	x.xxx	x.xxx	x.xxx	
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
*p-value =						
Change between pre and 30 minutes post vaccination						
Mean of % Difference (95% CI)						
Visit 2 (Day 8)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						

	All	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
*p-value =						
Change between pre and Day 8 post vaccination						
Mean of % Difference (95% CI)						

Note: + CpG1018 1.5 mg (Adjuvant)

* P-value based on paired t test/ Wilcoxon signed-rank test

** P-value based on Mc Nemar chi-square test, Normality of results (Normal/Abnormal) will be tested significant difference.

A significance test comparing a baseline (pre-vaccination) with a follow up measurement separately in vaccination group.

"xx" represent the value number.

Vital Signs Toxicity Grading	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life Threatening (Grade 4)
Temperature (oral)	38.0 – 38.4°C 100.4 – 101.1°F	38.5 – 38.9°C 101.2 – 102.0°F	39.0 – 40°C 102.1 – 104°F	> 40°C > 104°F

Table 80: Temperature (°C) Post–second Vaccination Compared to Pre–second Vaccination

	All	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Pre-second vaccination						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
Post-second vaccination						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median (q1-q3)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)	xx (xx-xx)
Min-Max	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx	xx-xx
*p-value =		x.xxx	x.xxx	x.xxx	x.xxx	
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						
Change between pre and 30 minutes post vaccination						
Mean of % Difference (95% CI)						
Visit 4 (Day 36)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						

Table 80: Temperature (°C) Post–second Vaccination Compared to Pre–second Vaccination (continued)

	All	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						
Change between pre and Day 36 post vaccination						
Mean of % Difference (95% CI)						
Visit 5 (Day 43)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						
Change between pre and Day 43 post vaccination						
Mean of % Difference (95% CI)						
Visit 6 (Day 57)						
n						

Table 80: Temperature (°C) Post–second Vaccination Compared to Pre–second Vaccination (continued)

	All	COVIVAC			1 µg + CpG (N = 25)	Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)		
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						
Change between pre and Day 57 post vaccination						
Mean of % Difference (95% CI)						
Visit 7 (Day 197)						
n						
Mean (SD)						
Median (q1-q3)						
Min-Max						
*p-value =						
Normal						
Abnormal						
Mild						
Moderate						
Severe						
Potentially life threatening						
**p-value =						
Change between pre and Day 197 post vaccination						

Table 80: Temperature (°C) Post–second Vaccination Compared to Pre–second Vaccination (continued)

	All	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Mean of % Difference (95% CI)						

Note: + CpG1018 1.5 mg (Adjuvant)

* P-value based on paired t test/ Wilcoxon signed-rank test

** P-value based on Mc Nemar chi-square test, Normality of results (Normal/Abnormal) will be tested significant difference.

A significance test comparing a baseline (pre-vaccination) with a follow up measurement separately in vaccination group.

"xx" represent the value number.

Vital Signs Toxicity Grading	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life Threatening (Grade 4)
Temperature (oral)	38.0 – 38.4°C 100.4 – 101.1°F	38.5 – 38.9°C 101.2 – 102.0°F	39.0 – 40°C 102.1 – 104°F	> 40°C > 104°F

Appendix 1.H. Physical Examinations

Table 81: Overall Number of Subject with Abnormal of Any Physical Examination Result Post -First Vaccination

	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Visit 2 (Day 8)						
General Appearance						
HEENT						
Cardiovascular						
Respiratory						
Abdomen						
Musculoskeletal						
Extremity/Skin						
Neurological						
Lymph Nodes						
with one or more abnormal result						
with no abnormal result						

Table 82: Overall Number of Subject with Abnormal of Any Physical Examination Result Post-Second Vaccination

	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Overall, n (%)						
General Appearance	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
HEENT	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Cardiovascular	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Respiratory	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abdomen	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Musculoskeletal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Extremity/Skin	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Neurological	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lymph Nodes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with one or more abnormal result	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
with no abnormal result	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Visit 4 (Day 36)						
General Appearance						
HEENT						
Cardiovascular						
Abdomen						
Musculoskeletal						
Extremity/Skin						
Neurological						
Lymph Nodes						
with one or more abnormal result						
with no abnormal result						
Visit 5 (Day 43)						
General Appearance						
HEENT						
Cardiovascular						
Respiratory						
Abdomen						
Musculoskeletal						

Table 82: Overall Number of Subject with Abnormal of Any Physical Examination Result Post -Second Vaccination (continued)

	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Extremity/Skin						
Neurological						
Lymph Nodes						
with one or more abnormal result						
with no abnormal result						
Visit 6 (Day 57)						
General Appearance						
HEENT						
Cardiovascular						
Respiratory						
Abdomen						
Musculoskeletal						
Extremity/Skin						
Neurological						
Lymph Nodes						
with one or more abnormal result						
with no abnormal result						
Visit 7 (Day 197)						
General Appearance						
HEENT						
Cardiovascular						
Respiratory						
Abdomen						
Musculoskeletal						
Extremity/Skin						
Neurological						
Lymph Nodes						
with one or more abnormal result						
with no abnormal result						

Table 83: Physical Examination at Visit 1 Pre-first Vaccination (Day 1)

	All	COVIVAC				Placebo
	(N = 120)	1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	(N = 20)
General Appearance, n (%)						
Normal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Abnormal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Clinically sig**	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Not done	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
HEENT, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Cardiovascular, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Respiratory, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Abdomen, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						

Table 83: Physical Examination at Visit 1 Pre-first Vaccination (Day 1) (continued)

	All	COVIVAC				Placebo
	(N = 120)	1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	(N = 20)
Musculoskeletal, n (%)						
Normal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Abnormal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Clinically sig**	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Not done	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Extremity/Skin, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Neurological, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Lymph Nodes, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Other, n (%)						
…….						

Note: + CpG1018 1.5 mg (Adjuvant)
** abnormal result with clinically significant.
"xx" represent the value number.

Table 84: Physical Examination at Visit 2 (Day 8)

	All	COVIVAC				Placebo
	(N = 120)	1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	(N = 20)
General Appearance, n (%)						
Normal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Abnormal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Clinically sig**	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Not done	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
HEENT, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Cardiovascular, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Respiratory rate, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Abdomen, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						

Table 84: Physical Examination at Visit 2 (Day 8) (continued)

	All	COVIVAC				
		1 µg	3 µg	10 µg	1 µg + CpG	Placebo
	(N = 120)	(N = 25)	(N = 25)	(N = 25)	(N = 25)	(N = 20)
Musculoskeletal, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Extremity/Skin, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Neurological, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Lymph Nodes, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Other, n (%)						
….						

Note: + CpG1018 1.5 mg (Adjuvant)
** abnormal result with clinically significant.
"xx" represent the value number.

Table 85: Physical Examination at Visit 3 Pre-second Vaccination (Day 29)

	All	COVIVAC				Placebo
	(N = 120)	1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	(N = 20)
General Appearance, n (%)						
Normal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Abnormal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Clinically sig**	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Not done	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
HEENT, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Cardiovascular, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Respiratory rate, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Abdomen, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						

Table 85: Physical Examination at Visit 3 Pre-second Vaccination (Day 29) (continued)

	All	COVIVAC				Placebo
	(N = 120)	1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	(N = 20)
Musculoskeletal, n (%)						
Normal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Abnormal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Clinically sig**	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Not done	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Extremity/Skin, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Neurological, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Lymph Nodes, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Other, n (%)						
….						

Note: + CpG1018 1.5 mg (Adjuvant)
** abnormal result with clinically significant.
"xx" represent the value number.

Table 86: Physical Examination at Visit 4 (Day 36)

	All	COVIVAC				Placebo
	(N = 120)	1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	(N = 20)
General Appearance, n (%)						
Normal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Abnormal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Clinically sig**	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Not done	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
HEENT, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Cardiovascular, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Respiratory rate, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Abdomen, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						

Table 86: Physical Examination at Visit 4 (Day 36) (continued)

	All	COVIVAC				Placebo
	(N = 120)	1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	(N = 20)
Musculoskeletal, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Extremity/Skin, n (%)						
Normal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Abnormal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Clinically sig**	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Not done	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Neurological, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Lymph Nodes, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Other, n (%)						
…….						

Note: + CpG1018 1.5 mg (Adjuvant)
** abnormal result with clinically significant.
"xx" represent the value number.

Table 87: Physical Examination at Visit 5 (Day 43)

	All	COVIVAC				Placebo
	(N = 120)	1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	(N = 20)
General Appearance, n (%)						
Normal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Abnormal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Clinically sig**	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Not done	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
HEENT, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Cardiovascular, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Respiratory rate, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Abdomen, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						

Table 87: Physical Examination at Visit 5 (Day 43) (continued)

	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Musculoskeletal, n (%)						
Normal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Abnormal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Clinically sig**	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Not done	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Extremity/Skin, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Neurological, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Lymph Nodes, n (%)						
Normal Normal						
Abnormal						
Clinically sig**						
Not done						
Other, n (%)						
……						

Table 88: Physical Examination at Visit 6 (Day 57)

	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
General Appearance, n (%)						
Normal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Abnormal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Clinically sig**	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Not done	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
HEENT, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Cardiovascular, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Respiratory rate, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Abdomen, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						

Table 88: Physical Examination at Visit 6 (Day 57) (continued)

	All	COVIVAC				Placebo
	(N = 120)	1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	(N = 20)
Musculoskeletal, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Extremity/Skin, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Neurological, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Lymph Nodes, n (%)						
Normal Normal						
Abnormal						
Clinically sig**						
Not done						
Other, n (%)						
……						

Note: + CpG1018 1.5 mg (Adjuvant)
** abnormal result with clinically significant.
"xx" represent the value number.

Table 89: Physical Examination at Visit 7 (Day 197)

	All (N = 120)	COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
General Appearance, n (%)						
Normal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Abnormal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Clinically sig**	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Not done	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
HEENT, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Cardiovascular, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Respiratory rate, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Abdomen, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						

Table 89: Physical Examination at Visit 7 (Day 197) (continued)

	All	COVIVAC				Placebo
	(N = 120)	1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	(N = 20)
Musculoskeletal, n (%)						
Normal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Abnormal	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Clinically sig**	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Not done	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Extremity/Skin, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Neurological, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Lymph Nodes, n (%)						
Normal						
Abnormal						
Clinically sig**						
Not done						
Other, n (%)						
……						

Note: + CpG1018 1.5 mg (Adjuvant)
** abnormal result with clinically significant.
"xx" represent the value number.

Appendix 1.I. Immunogenicity Analysis - 50% and 80% Neutralizing Antibody (NT_{50} and NT_{80})

Table 90A: Summary of Geometric Mean Titer (GMT) of NT_{50} against SARS-CoV-2 Pseudovirus in Full Analysis Population

NT_{50} Measure		All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Baseline (D1)	GMT (95% CI)	n = xx xx.xx (xx.xx-xx.xx)	n = xx xx.xx (xx.xx-xx.xx)	n = xx xx.xx (xx.xx-xx.xx)	n = xx xx.xx (xx.xx-xx.xx)	n = xx xx.xx (xx.xx-xx.xx)	n = xx xx.xx (xx.xx-xx.xx)
28 days after the first vaccination (D29)	GMT (95% CI)						
14 days after the second vaccination (D43)	GMT (95% CI)						
6 months after the second vaccination (D197)	GMT (95% CI)						

Note: GMTs calculation, titers of <10 were assigned as titer of 5.

NT_{50} GMTs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 90A-1: Summary of Geometric Mean Titer (GMT) of NT_{50} against SARS-CoV-2 Pseudovirus in Full Analysis Population by Age Group

NT_{50} Measure			All (N = 120)	COVIVAC				Placebo (N = 20)
				1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Baseline (D1)	18-39 yr.	GMT (95% CI)						
	40-59 yr.	GMT (95% CI)						
28 days after the first vaccination (D29)	18-39 yr.	GMT (95% CI)						
	40-59 yr.	GMT (95% CI)						
14 days after the second vaccination (D43)	18-39 yr.	GMT (95% CI)						
	40-59 yr.	GMT (95% CI)						
6 months after the second vaccination (D197)	18-39 yr.	GMT (95% CI)						
	40-59 yr.	GMT (95% CI)						

Note: GMTs calculation, titers of <10 were assigned as titer of 5.

NT_{50} GMTs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 90A-2: Summary of Geometric Mean Titer (GMT) of NT_{50} against SARS-CoV-2 Pseudovirus in Full Analysis Population by Gender

NT_{50} Measure			All (N = 120)	COVIVAC				Placebo (N = 20)
				1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Baseline (D1)	Male	GMT (95% CI)						
	Female	GMT (95% CI)						
28 days after the first vaccination (D29)	Male	GMT (95% CI)						
	Female	GMT (95% CI)						
14 days after the second vaccination (D43)	Male	GMT (95% CI)						
	Female	GMT (95% CI)						
6 months after the second vaccination (D197)	Male	GMT (95% CI)						
	Female	GMT (95% CI)						

Note: GMTs calculation, titers of <10 were assigned as titer of 5.
NT_{50} GMTs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 90B: Summary of Geometric Mean Concentration (GMC) in IU/mL of NT_{50} against SARS-CoV-2 Pseudovirus in Full Analysis Population

NT_{50} Measure		All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Baseline (D1)	GMC (95% CI)						
28 days after the first vaccination (D29)	GMC (95% CI)						
14 days after the second vaccination (D43)	GMC (95% CI)						
6 months after the second vaccination (D197)	GMC (95% CI)						

Note: NT_{50} GMCs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 90B-1: Summary of Geometric Mean Concentration (GMC) in IU/mL of NT_{50} against SARS-CoV-2 Pseudovirus in Full Analysis Population by Age Group

NT_{50} Measure			All (N = 120)	COVIVAC				Placebo (N = 20)
				1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Baseline (D1)	18-39 yr.	GMC (95% CI)						
	40-59 yr.	GMC (95% CI)						
28 days after the first vaccination (D29)	18-39 yr.	GMC (95% CI)						
	40-59 yr.	GMC (95% CI)						
14 days after the second vaccination (D43)	18-39 yr.	GMC (95% CI)						
	40-59 yr.	GMC (95% CI)						
6 months after the second vaccination (D197)	18-39 yr.	GMC (95% CI)						
	40-59 yr.	GMC (95% CI)						

Note:NT_{50} GMCs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 90B-2: Summary of Geometric Mean Concentration (GMC) in IU/mL of NT_{50} against SARS-CoV-2 Pseudovirus in Full Analysis Population by Gender

NT_{50} Measure			All (N = 120)	COVIVAC				Placebo (N = 20)
				1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Baseline (D1)	Male	GMC (95% CI)						
	Female	GMC (95% CI)						
28 days after the first vaccination (D29)	Male	GMC (95% CI)						
	Female	GMC (95% CI)						
14 days after the second vaccination (D43)	Male	GMC (95% CI)						
	Female	GMC (95% CI)						
6 months after the second vaccination (D197)	Male	GMC (95% CI)						
	Female	GMC (95% CI)						

Note: NT_{50} GMCs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 91A: Summary of Geometric Mean Titer (GMT) of NT_{50} against SARS-CoV-2 Pseudovirus in Per Protocol Population

NT_{50} Measure		All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Baseline (D1)	GMT (95% CI)						
28 days after the first vaccination (D29)	GMT (95% CI)						
14 days after the second vaccination (D43)	GMT (95% CI)						
6 months after the second vaccination (D197)	GMT (95% CI)						

Note: NT_{50} GMTs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 91A-1: Summary of Geometric Mean Titer (GMT) of NT_{50} against SARS-CoV-2 Pseudovirus in Per Protocol Population by Age Group

NT_{50} Measure			All (N = 120)	COVIVAC				Placebo (N = 20)
				1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Baseline (D1)	18-39 yr.	GMT (95% CI)						
	40-59 yr.	GMT (95% CI)						
28 days after the first vaccination (D29)	18-39 yr.	GMT (95% CI)						
	40-59 yr.	GMT (95% CI)						
14 days after the second vaccination (D43)	18-39 yr.	GMT (95% CI)						
	40-59 yr.	GMT (95% CI)						
6 months after the second vaccination (D197)	18-39 yr.	GMT (95% CI)						
	40-59 yr.	GMT (95% CI)						

Note: NT_{50} GMTs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 91A-2: Summary of Geometric Mean Titer (GMT) of NT_{50} against SARS-CoV-2 Pseudovirus in Per Protocol Population by Gender

NT_{50} Measure			All (N = 120)	COVIVAC				Placebo (N = 20)
				1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Baseline (D1)	Male	GMT (95% CI)						
	Female	GMT (95% CI)						
28 days after the first vaccination (D29)	Male	GMT (95% CI)						
	Female	GMT (95% CI)						
14 days after the second vaccination (D43)	Male	GMT (95% CI)						
	Female	GMT (95% CI)						
6 months after the second vaccination (D197)	Male	GMT (95% CI)						
	Female	GMT (95% CI)						

Note: NT_{50} GMTs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 91B: Summary of Geometric Mean Concentration (GMC) in IU/mL of NT_{50} against SARS-CoV-2 Pseudovirus in Per Protocol Population

NT50 Measure		All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Baseline (D1)	GMC (95% CI)						
28 days after the first vaccination (D29)	GMC (95% CI)						
14 days after the second vaccination (D43)	GMC (95% CI)						
6 months after the second vaccination (D197)	GMC (95% CI)						

Note: NT_{50} GMCs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 91B-1: Summary of Geometric Mean Concentration (GMC) in IU/mL of NT_{50} against SARS-CoV-2 Pseudovirus in Per Protocol Population by Age Group

NT_{50} Measure			All (N = 120)	COVIVAC				Placebo (N = 20)
				1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Baseline (D1)	18-39 yr.	GMC (95% CI)						
	40-59 yr.	GMC (95% CI)						
28 days after the first vaccination (D29)	18-39 yr.	GMC (95% CI)						
	40-59 yr.	GMC (95% CI)						
14 days after the second vaccination (D43)	18-39 yr.	GMC (95% CI)						
	40-59 yr.	GMC (95% CI)						
6 months after the second vaccination (D197)	18-39 yr.	GMC (95% CI)						
	40-59 yr.	GMC (95% CI)						

Note: NT_{50} GMCs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 91B-2: Summary of Geometric Mean Concentration (GMC) in IU/mL of NT_{50} against SARS-CoV-2 Pseudovirus in Per Protocol Population by Gender

NT_{50} Measure			All (N = 120)	COVIVAC				Placebo (N = 20)
				1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Baseline (D1)	Male	GMC (95% CI)						
	Female	GMC (95% CI)						
28 days after the first vaccination (D29)	Male	GMC (95% CI)						
	Female	GMC (95% CI)						
14 days after the second vaccination (D43)	Male	GMC (95% CI)						
	Female	GMC (95% CI)						
6 months after the second vaccination (D197)	Male	GMC (95% CI)						
	Female	GMC (95% CI)						

Note: NT_{50} GMCs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 92A: Summary of Geometric Mean Titer Ratio (GMT Ratio) of NT_{50} against SARS-CoV-2 Pseudovirus in Full Analysis Population

NT_{50} Measure GMT ratio (95% CI)	COVIVAC					
	1 µg vs 3 µg	1 µg vs 10 µg	3 µg vs 10 µg	1 µg vs 1 µg + CpG	3 µg vs 1 µg + CpG	10 µg vs 1 µg + CpG
Baseline (D1)						
28 days after the first vaccination (D29)						
14 days after the second vaccination (D43)						
6 months after the second vaccination (D197)						

Note: NT_{50} GMTs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 92A-1: Summary of Geometric Mean Titer Ratio (GMT Ratio) of NT_{50} against SARS-CoV-2 Pseudovirus in Full Analysis Population by Age Group

NT_{50} Measure GMT ratio (95% CI)		COVIVAC					
		1 µg vs 3 µg	1 µg vs 10 µg	3 µg vs 10 µg	1 µg vs 1 µg + CpG	3 µg vs 1 µg + CpG	10 µg vs 1 µg + CpG
Baseline (D1)	18-39 yr.						
	40-59 yr.						
28 days after the first vaccination (D29)	18-39 yr.						
	40-59 yr.						
14 days after the second vaccination (D43)	18-39 yr.						
	40-59 yr.						
6 months after the second vaccination (D197)	18-39 yr.						
	40-59 yr.						

Note: NT_{50} GMTs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 92A-2: Summary of Geometric Mean Titer Ratio (GMT Ratio) of NT_{50} against SARS-CoV-2 Pseudovirus in Full Analysis Population by Gender

NT_{50} Measure GMT ratio (95% CI)		COVIVAC					
		1 µg vs 3 µg	1 µg vs 10 µg	3 µg vs 10 µg	1 µg vs 1 µg + CpG	3 µg vs 1 µg + CpG	10 µg vs 1 µg + CpG
Baseline (D1)	Male						
	Female						
28 days after the first vaccination (D29)	Male						
	Female						
14 days after the second vaccination (D43)	Male						
	Female						
6 months after the second vaccination (D197)	Male						
	Female						

Note: NT_{50} GMTs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 93A: Summary of Geometric Mean Titer Ratio (GMT Ratio) of NT_{50} against SARS-CoV-2 Pseudovirus in Per Protocol Population

NT_{50} Measure GMT ratio (95% CI)	COVIVAC					
	1 µg vs 3 µg	1 µg vs 10 µg	3 µg vs 10 µg	1 µg vs 1 µg + CpG	3 µg vs 1 µg + CpG	10 µg vs 1 µg + CpG
Baseline (D1)						
28 days after the first vaccination (D29)						
14 days after the second vaccination (D43)						
6 months after the second vaccination (D197)						

Note: NT_{50} GMTs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 93A-1: Summary of Geometric Mean Titer Ratio (GMT Ratio) of NT_{50} against SARS-CoV-2 Pseudovirus in Per Protocol Population by Age Group

NT_{50} Measure GMT ratio (95% CI)		COVIVAC					
		1 µg vs 3 µg	1 µg vs 10 µg	3 µg vs 10 µg	1 µg vs 1 µg + CpG	3 µg vs 1 µg + CpG	10 µg vs 1 µg + CpG
Baseline (D1)	18-39 yr.						
	40-59 yr.						
28 days after the first vaccination (D29)	18-39 yr.						
	40-59 yr.						
14 days after the second vaccination (D43)	18-39 yr.						
	40-59 yr.						
6 months after the second vaccination (D197)	18-39 yr.						
	40-59 yr.						

Note: NT_{50} GMTs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 93A-2: Summary of Geometric Mean Titer Ratio (GMT Ratio) of NT_{50} against SARS-CoV-2 Pseudovirus in Per Protocol Population by Gender

NT_{50} Measure GMT ratio (95% CI)		**COVIVAC**					
		1 µg vs 3 µg	**1 µg vs 10 µg**	**3 µg vs 10 µg**	**1 µg vs 1 µg + CpG**	**3 µg vs 1 µg + CpG**	**10 µg vs 1 µg + CpG**
Baseline (D1)	Male						
	Female						
28 days after the first vaccination (D29)	Male						
	Female						
14 days after the second vaccination (D43)	Male						
	Female						
6 months after the second vaccination (D197)	Male						
	Female						

Note: NT_{50} GMTs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 94: Summary of Geometric Mean Titer (GMT) of NT_{80} against SARS-CoV-2 Pseudovirus in Full Analysis Population

NT_{80} Measure		All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Baseline (D1)	GMT (95% CI)						
28 days after the first vaccination (D29)	GMT (95% CI)						
14 days after the second vaccination (D43)	GMT (95% CI)						
6 months after the second vaccination (D197)	GMT (95% CI)						

Note: NT_{80} GMTs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 94-1: Summary of Geometric Mean Titer (GMT) of NT_{80} against SARS-CoV-2 Pseudovirus in Full Analysis Population by Age Group

NT_{80} Measure			All (N = 120)	COVIVAC				Placebo (N = 20)
				1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Baseline (D1)	18-39 yr.	GMT (95% CI)						
	40-59 yr.	GMT (95% CI)						
28 days after the first vaccination (D29)	18-39 yr.	GMT (95% CI)						
	40-59 yr.	GMT (95% CI)						
14 days after the second vaccination (D43)	18-39 yr.	GMT (95% CI)						
	40-59 yr.	GMT (95% CI)						
6 months after the second vaccination (D197)	18-39 yr.	GMT (95% CI)						
	40-59 yr.	GMT (95% CI)						

Note: NT_{80} GMTs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 94-2: Summary of Geometric Mean Titer (GMT) of NT_{80} against SARS-CoV-2 Pseudovirus in Full Analysis Population by Gender

	NT_{80} Measure		All (N = 120)	COVIVAC				Placebo (N = 20)
				1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Baseline (D1)	Male	GMT (95% CI)						
	Female	GMT (95% CI)						
28 days after the first vaccination (D29)	Male	GMT (95% CI)						
	Female	GMT (95% CI)						
14 days after the second vaccination (D43)	Male	GMT (95% CI)						
	Female	GMT (95% CI)						
6 months after the second vaccination (D197)	Male	GMT (95% CI)						
	Female	GMT (95% CI)						

Note: NT_{80} GMTs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 95: Summary of Geometric Mean Titer (GMT) of NT_{80} against SARS-CoV-2 Pseudovirus in Per Protocol Population

NT_{80} Measure		**All (N = 120)**	**COVIVAC**				**Placebo (N = 20)**
			1 µg (N = 25)	**3 µg (N = 25)**	**10 µg (N = 25)**	**1 µg + CpG (N = 25)**	
Baseline (D1)	GMT (95% CI)						
28 days after the first vaccination (D29)	GMT (95% CI)						
14 days after the second vaccination (D43)	GMT (95% CI)						
6 months after the second vaccination (D197)	GMT (95% CI)						

Note: NT_{80} GMTs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 95-1: Summary of Geometric Mean Titer (GMT) of NT_{80} against SARS-CoV-2 Pseudovirus in Per Protocol Population by Age Group

NT_{80} Measure			All (N = 120)	COVIVAC				Placebo (N = 20)
				1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Baseline (D1)	18-39 yr.	GMT (95% CI)						
	40-59 yr.	GMT (95% CI)						
28 days after the first vaccination (D29)	18-39 yr.	GMT (95% CI)						
	40-59 yr.	GMT (95% CI)						
14 days after the second vaccination (D43)	18-39 yr.	GMT (95% CI)						
	40-59 yr.	GMT (95% CI)						
6 months after the second vaccination (D197)	18-39 yr.	GMT (95% CI)						
	40-59 yr.	GMT (95% CI)						

Note: NT_{80} GMTs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 95-2: Summary of Geometric Mean Titer (GMT) of NT_{80} against SARS-CoV-2 Pseudovirus in Per Protocol Population by Gender

	NT_{80} Measure		All (N = 120)	COVIVAC				Placebo (N = 20)
				1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Baseline (D1)	Male	GMT (95% CI)						
	Female	GMT (95% CI)						
28 days after the first vaccination (D29)	Male	GMT (95% CI)						
	Female	GMT (95% CI)						
14 days after the second vaccination (D43)	Male	GMT (95% CI)						
	Female	GMT (95% CI)						
6 months after the second vaccination (D197)	Male	GMT (95% CI)						
	Female	GMT (95% CI)						

Note: NT_{80} GMTs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 96: Summary of Geometric Mean Titer Ratio (GMT Ratio) of NT_{80} against SARS-CoV-2 Pseudovirus in Full Analysis Population

NT_{80} Measure GMT ratio (95% CI)	**COVIVAC**					
	1 µg vs 3 µg	**1 µg vs 10 µg**	**3 µg vs 10 µg**	**1 µg vs 1 µg + CpG**	**3 µg vs 1 µg + CpG**	**10 µg vs 1 µg + CpG**
Baseline (D1)						
28 days after the first vaccination (D29)						
14 days after the second vaccination (D43)						
6 months after the second vaccination (D197)						

Note: NT_{80} GMTs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 96-1: Summary of Geometric Mean Titer Ratio (GMT Ratio) of NT_{80} against SARS-CoV-2 Pseudovirus in Full Analysis Population by Age Group

NT_{80} Measure GMT ratio (95% CI)		COVIVAC					
		1 µg vs 3 µg	1 µg vs 10 µg	3 µg vs 10 µg	1 µg vs 1 µg + CpG	3 µg vs 1 µg + CpG	10 µg vs 1 µg + CpG
Baseline (D1)	18-39 yr.						
	40-59 yr.						
28 days after the first vaccination (D29)	18-39 yr.						
	40-59 yr.						
14 days after the second vaccination (D43)	18-39 yr.						
	40-59 yr.						
6 months after the second vaccination (D197)	18-39 yr.						
	40-59 yr.						

Note: NT_{80} GMTs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 96-2: Summary of Geometric Mean Titer Ratio (GMT Ratio) of NT_{80} against SARS-CoV-2 Pseudovirus in Full Analysis Population by Gender

NT_{80} Measure GMT ratio (95% CI)		COVIVAC					
		1 µg vs 3 µg	1 µg vs 10 µg	3 µg vs 10 µg	1 µg vs 1 µg + CpG	3 µg vs 1 µg + CpG	10 µg vs 1 µg + CpG
Baseline (D1)	Male						
	Female						
28 days after the first vaccination (D29)	Male						
	Female						
14 days after the second vaccination (D43)	Male						
	Female						
6 months after the second vaccination (D197)	Male						
	Female						

Note: NT_{80} GMTs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 97: Summary of Geometric Mean Titer Ratio (GMT Ratio) of NT_{80} against SARS-CoV-2 Pseudovirus in Per Protocol Population

NT_{80} Measure GMT ratio (95% CI)	COVIVAC					
	1 µg vs 3 µg	1 µg vs 10 µg	3 µg vs 10 µg	1 µg vs 1 µg + CpG	3 µg vs 1 µg + CpG	10 µg vs 1 µg + CpG
Baseline (D1)						
28 days after the first vaccination (D29)						
14 days after the second vaccination (D43)						
6 months after the second vaccination (D197)						

Note: NT_{80} GMTs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 97-1: Summary of Geometric Mean Titer Ratio (GMT Ratio) of NT_{80} against SARS-CoV-2 Pseudovirus in Per Protocol Population by Age Group

NT_{80} Measure GMT ratio (95% CI)		COVIVAC					
		1 µg vs 3 µg	1 µg vs 10 µg	3 µg vs 10 µg	1 µg vs 1 µg + CpG	3 µg vs 1 µg + CpG	10 µg vs 1 µg + CpG
Baseline (D1)	18-39 yr.						
	40-59 yr.						
28 days after the first vaccination (D29)	18-39 yr.						
	40-59 yr.						
14 days after the second vaccination (D43)	18-39 yr.						
	40-59 yr.						
6 months after the second vaccination (D197)	18-39 yr.						
	40-59 yr.						

Note: NT_{80} GMTs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 97-2: Summary of Geometric Mean Titer Ratio (GMT Ratio) of NT_{80} against SARS-CoV-2 Pseudovirus in Per Protocol Population by Gender

NT_{80} Measure GMT ratio (95% CI)		COVIVAC					
		1 µg vs 3 µg	1 µg vs 10 µg	3 µg vs 10 µg	1 µg vs 1 µg + CpG	3 µg vs 1 µg + CpG	10 µg vs 1 µg + CpG
Baseline (D1)	Male						
	Female						
28 days after the first vaccination (D29)	Male						
	Female						
14 days after the second vaccination (D43)	Male						
	Female						
6 months after the second vaccination (D197)	Male						
	Female						

Note: NT_{80} GMTs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 98A: Summary of Geometric Mean Fold Rise (GMFR) from Baseline of NT_{50} Titers against SARS-CoV-2 Pseudovirus in Full Analysis Population

NT_{50} Measure		COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	GMFR from baseline (95% CI)					
14 days after the second vaccination (D43)	GMFR from baseline (95% CI)					
6 months after the second vaccination (D197)	GMFR from baseline (95% CI)					

Note: Geometric Mean Fold Rise (GMFR) is the geometric mean of the ratios of post-vaccination to the pre-first vaccination at D1 (baseline).

Table 98A-1: Summary of Geometric Mean Fold Rise (GMFR) from Baseline of NT_{50} Titers against SARS-CoV-2 Pseudovirus in Full Analysis Population by Age Group

	NT_{50} Measure		COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	18-39 yr.	GMFR from baseline (95% CI)					
	40-59 yr.	GMFR from baseline (95% CI)					
14 days after the second vaccination (D43)	18-39 yr.	GMFR from baseline (95% CI)					
	40-59 yr.	GMFR from baseline (95% CI)					
6 months after the second vaccination (D197)	18-39 yr.	GMFR from baseline (95% CI)					
	40-59 yr.	GMFR from baseline (95% CI)					

Note: Geometric Mean Fold Rise (GMFR) is the geometric mean of the ratios of post-vaccination to the pre-first vaccination at D1 (baseline).

Table 98A-2: Summary of Geometric Mean Fold Rise (GMFR) from Baseline of NT_{50} Titers against SARS-CoV-2 Pseudovirus in Full Analysis Population by Gender

NT_{50} Measure			COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	Male	GMFR from baseline (95% CI)					
	Female	GMFR from baseline (95% CI)					
14 days after the second vaccination (D43)	Male	GMFR from baseline (95% CI)					
	Female	GMFR from baseline (95% CI)					
6 months after the second vaccination (D197)	Male	GMFR from baseline (95% CI)					
	Female	GMFR from baseline (95% CI)					

Note: Geometric Mean Fold Rise (GMFR) is the geometric mean of the ratios of post-vaccination to the pre-first vaccination at D1 (baseline).

Table 99A: Summary of Geometric Mean Fold Rise (GMFR) from Baseline of NT_{50} Titers against SARS-CoV-2 Pseudovirus in Per Protocol Population

NT_{50} Measure		COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	GMFR from baseline (95% CI)					
14 days after the second vaccination (D43)	GMFR from baseline (95% CI)					
6 months after the second vaccination (D197)	GMFR from baseline (95% CI)					

Note: Geometric Mean Fold Rise (GMFR) is the geometric mean of the ratios of post-vaccination to the pre-first vaccination at D1 (baseline).

Table 99A-1: Summary of Geometric Mean Fold Rise (GMFR) from Baseline of NT_{50} Titers against SARS-CoV-2 Pseudovirus in Per Protocol Population by Age Group

	NT_{50} Measure		COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	18-39 yr.	GMFR from baseline (95% CI)					
	40-59 yr.	GMFR from baseline (95% CI)					
14 days after the second vaccination (D43)	18-39 yr.	GMFR from baseline (95% CI)					
	40-59 yr.	GMFR from baseline (95% CI)					
6 months after the second vaccination (D197)	18-39 yr.	GMFR from baseline (95% CI)					
	40-59 yr.	GMFR from baseline (95% CI)					

Note: Geometric Mean Fold Rise (GMFR) is the geometric mean of the ratios of post-vaccination to the pre-first vaccination at D1 (baseline).

Table 99A-2: Summary of Geometric Mean Fold Rise (GMFR) from Baseline of NT_{50} Titers against SARS-CoV-2 Pseudovirus in Per Protocol Population by Gender

NT_{50} Measure			COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	Male	GMFR from baseline (95% CI)					
	Female	GMFR from baseline (95% CI)					
14 days after the second vaccination (D43)	Male	GMFR from baseline (95% CI)					
	Female	GMFR from baseline (95% CI)					
6 months after the second vaccination (D197)	Male	GMFR from baseline (95% CI)					
	Female	GMFR from baseline (95% CI)					

Note: Geometric Mean Fold Rise (GMFR) is the geometric mean of the ratios of post-vaccination to the pre-first vaccination at D1 (baseline).

Table 100: Summary of Geometric Mean Fold Rise (GMFR) from Baseline of NT_{80} Titers against SARS-CoV-2 Pseudovirus in Full Analysis Population

NT_{80} Measure		COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	GMFR from baseline (95% CI)					
14 days after the second vaccination (D43)	GMFR from baseline (95% CI)					
6 months after the second vaccination (D197)	GMFR from baseline (95% CI)					

Note: Geometric Mean Fold Rise (GMFR) is the geometric mean of the ratios of post-vaccination to the pre-first vaccination at D1 (baseline).

Table 100-1: Summary of Geometric Mean Fold Rise (GMFR) from Baseline of NT_{80} Titers against SARS-CoV-2 Pseudovirus in Full Analysis Population by Age Group

	NT_{80} Measure		COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	18-39 yr.	GMFR from baseline (95% CI)					
	40-59 yr.	GMFR from baseline (95% CI)					
14 days after the second vaccination (D43)	18-39 yr.	GMFR from baseline (95% CI)					
	40-59 yr.	GMFR from baseline (95% CI)					
6 months after the second vaccination (D197)	18-39 yr.	GMFR from baseline (95% CI)					
	40-59 yr.	GMFR from baseline (95% CI)					

Note: Geometric Mean Fold Rise (GMFR) is the geometric mean of the ratios of post-vaccination to the pre-first vaccination at D1 (baseline).

Table 100-2: Summary of Geometric Mean Fold Rise (GMFR) from Baseline of NT_{80} Titers against SARS-CoV-2 Pseudovirus in Full Analysis Population by Gender

NT_{80} Measure			COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	Male	GMFR from baseline (95% CI)					
	Female	GMFR from baseline (95% CI)					
14 days after the second vaccination (D43)	Male	GMFR from baseline (95% CI)					
	Female	GMFR from baseline (95% CI)					
6 months after the second vaccination (D197)	Male	GMFR from baseline (95% CI)					
	Female	GMFR from baseline (95% CI)					

Note: Geometric Mean Fold Rise (GMFR) is the geometric mean of the ratios of post-vaccination to the pre-first vaccination at D1 (baseline).

Table 101: Summary of Geometric Mean Fold Rise (GMFR) from Baseline of NT_{80} Titers against SARS-CoV-2 Pseudovirus in Per Protocol Population

NT_{80} Measure		COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	GMFR from baseline (95% CI)					
14 days after the second vaccination (D43)	GMFR from baseline (95% CI)					
6 months after the second vaccination (D197)	GMFR from baseline (95% CI)					

Note: Geometric Mean Fold Rise (GMFR) is the geometric mean of the ratios of post-vaccination to the pre-first vaccination at D1 (baseline).

Table 101-1: Summary of Geometric Mean Fold Rise (GMFR) from Baseline of NT_{80} Titers against SARS-CoV-2 Pseudovirus in Per Protocol Population by Age Group

	NT_{80} Measure		**COVIVAC**				**Placebo (N = 20)**
			1 µg (N = 25)	**3 µg (N = 25)**	**10 µg (N = 25)**	**1 µg + CpG (N = 25)**	
28 days after the first vaccination (D29)	18-39 yr.	GMFR from baseline (95% CI)					
	40-59 yr.	GMFR from baseline (95% CI)					
14 days after the second vaccination (D43)	18-39 yr.	GMFR from baseline (95% CI)					
	40-59 yr.	GMFR from baseline (95% CI)					
6 months after the second vaccination (D197)	18-39 yr.	GMFR from baseline (95% CI)					
	40-59 yr.	GMFR from baseline (95% CI)					

Note: Geometric Mean Fold Rise (GMFR) is the geometric mean of the ratios of post-vaccination to the pre-first vaccination at D1 (baseline).

Table 101-2: Summary of Geometric Mean Fold Rise (GMFR) from Baseline of NT_{80} Titers against SARS-CoV-2 Pseudovirus in Per Protocol Population by Gender

NT_{80} Measure			COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	Male	GMFR from baseline (95% CI)					
	Female	GMFR from baseline (95% CI)					
14 days after the second vaccination (D43)	Male	GMFR from baseline (95% CI)					
	Female	GMFR from baseline (95% CI)					
6 months after the second vaccination (D197)	Male	GMFR from baseline (95% CI)					
	Female	GMFR from baseline (95% CI)					

Note: Geometric Mean Fold Rise (GMFR) is the geometric mean of the ratios of post-vaccination to the pre-first vaccination at D1 (baseline).

Table 102A: Percentage of Subjects with NT_{50} Titer Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 4-fold Increase from Baseline in Full Analysis Population

NT_{50} Measure ≥ 4-fold (Titer)		**All (N = 120)**	**COVIVAC**				**Placebo (N = 20)**
			1 µg (N = 25)	**3 µg (N = 25)**	**10 µg (N = 25)**	**1 µg + CpG (N = 25)**	
28 days after the first vaccination (D29)	n (%) (95% CI)						
14 days after the second vaccination (D43)	n (%) (95% CI)						
6 months after the second vaccination (D197)	n (%) (95% CI)						

Note: The 95% CIs are computed via the Clopper-Pearson method.

Table 102A-1: Percentage of Subjects with NT_{50} Titer Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 4-fold Increase from Baseline in Full Analysis Population by Age Group

	NT_{50} Measure ≥ 4-fold (Titer)		**All (N = 120)**	**COVIVAC**				**Placebo (N = 20)**
				1 µg (N = 25)	**3 µg (N = 25)**	**10 µg (N = 25)**	**1 µg + CpG (N = 25)**	
28 days after the first vaccination (D29)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						
14 days after the second vaccination (D43)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						
6 months after the second vaccination (D197)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						

Note: The 95% CIs are computed via the Clopper-Pearson method.

Table 102A-2: Percentage of Subjects with NT_{50} Titer Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 4-fold Increase from Baseline in Full Analysis Population by Gender

	NT_{50} Measure ≥ 4-fold (Titer)		**All (N = 120)**	**COVIVAC**				**Placebo (N = 20)**
				1 µg (N = 25)	**3 µg (N = 25)**	**10 µg (N = 25)**	**1 µg + CpG (N = 25)**	
28 days after the first vaccination (D29)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						
14 days after the second vaccination (D43)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						
6 months after the second vaccination (D197)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						

Note: The 95% CIs are computed via the Clopper-Pearson method.

Table 103A: Percentage of Subjects with NT_{50} Titer Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 4-fold Increase from Baseline in Per Protocol Population

NT_{50} Measure ≥ 4-fold (Titer)		**All (N = 120)**	**COVIVAC**				**Placebo (N = 20)**
			1 µg (N = 25)	**3 µg (N = 25)**	**10 µg (N = 25)**	**1 µg + CpG (N = 25)**	
28 days after the first vaccination (D29)	n (%) (95% CI)						
14 days after the second vaccination (D43)	n (%) (95% CI)						
6 months after the second vaccination (D197)	n (%) (95% CI)						

Note: The 95% CIs are computed via the Clopper-Pearson method.

Table 103A-1: Percentage of Subjects with NT_{50} Titer Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 4-fold Increase from Baseline in Per Protocol Population by Age Group

	NT_{50} Measure ≥ 4-fold (Titer)		**All (N = 120)**	**COVIVAC**				**Placebo (N = 20)**
				1 µg (N = 25)	**3 µg (N = 25)**	**10 µg (N = 25)**	**1 µg + CpG (N = 25)**	
28 days after the first vaccination (D29)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						
14 days after the second vaccination (D43)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						
6 months after the second vaccination (D197)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						

Note: The 95% CIs are computed via the Clopper-Pearson method.

Table 103A-2: Percentage of Subjects with NT_{50} Titer Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 4-fold Increase from Baseline in Per Protocol Population by Gender

	NT_{50} Measure ≥ 4-fold (Titer)		**All (N = 120)**	**COVIVAC**				**Placebo (N = 20)**
				1 µg (N = 25)	**3 µg (N = 25)**	**10 µg (N = 25)**	**1 µg + CpG (N = 25)**	
28 days after the first vaccination (D29)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						
14 days after the second vaccination (D43)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						
6 months after the second vaccination (D197)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						

Note: The 95% CIs are computed via the Clopper-Pearson method.

Table 104: Percentage of Subjects with NT_{80} Titer Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 4-fold Increase from Baseline in Full Analysis Population

NT_{80} Measure ≥ 4-fold (Titer)		**All (N = 120)**	**COVIVAC**				**Placebo (N = 20)**
			1 µg (N = 25)	**3 µg (N = 25)**	**10 µg (N = 25)**	**1 µg + CpG (N = 25)**	
28 days after the first vaccination (D29)	n (%) (95% CI)						
14 days after the second vaccination (D43)	n (%) (95% CI)						
6 months after the second vaccination (D197)	n (%) (95% CI)						

Note: The 95% CIs were computed via the Clopper-Pearson method.

Table 104-1: Percentage of Subjects with NT_{80} Titer Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 4-fold Increase from Baseline in Full Analysis Population by Age Group

	NT_{80} Measure ≥ 4-fold (Titer)		**All (N = 120)**	**COVIVAC**				**Placebo (N = 20)**
				1 µg (N = 25)	**3 µg (N = 25)**	**10 µg (N = 25)**	**1 µg + CpG (N = 25)**	
28 days after the first vaccination (D29)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						
14 days after the second vaccination (D43)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						
6 months after the second vaccination (D197)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						

Note: The 95% CIs are computed via the Clopper-Pearson method.

Table 104-2: Percentage of Subjects with NT_{80} Titer Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 4-fold Increase from Baseline in Full Analysis Population by Gender

	NT_{80} Measure ≥ 4-fold (Titer)		**All (N = 120)**	**COVIVAC**				**Placebo (N = 20)**
				1 µg (N = 25)	**3 µg (N = 25)**	**10 µg (N = 25)**	**1 µg + CpG (N = 25)**	
28 days after the first vaccination (D29)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						
14 days after the second vaccination (D43)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						
6 months after the second vaccination (D197)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						

Note: The 95% CIs are computed via the Clopper-Pearson method.

Table 105: Percentage of Subjects with NT_{80} Titer Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 4-fold Increase from Baseline in Per Protocol Population

NT_{80} Measure ≥ 4-fold (Titer)		**All (N = 120)**	**COVIVAC**				**Placebo (N = 20)**
			1 µg (N = 25)	**3 µg (N = 25)**	**10 µg (N = 25)**	**1 µg + CpG (N = 25)**	
28 days after the first vaccination (D29)	n (%) (95% CI)						
14 days after the second vaccination (D43)	n (%) (95% CI)						
6 months after the second vaccination (D197)	n (%) (95% CI)						

Note: The 95% CIs were computed via the Clopper-Pearson method.

Table 105-1: Percentage of Subjects with NT_{80} Titer Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 4-fold Increase from Baseline in Per Protocol Population by Age Group

	NT_{80} Measure ≥ 4-fold (Titer)		**All (N = 120)**	**COVIVAC**				**Placebo (N = 20)**
				1 µg (N = 25)	**3 µg (N = 25)**	**10 µg (N = 25)**	**1 µg + CpG (N = 25)**	
28 days after the first vaccination (D29)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						
14 days after the second vaccination (D43)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						
6 months after the second vaccination (D197)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						

Note: The 95% CIs are computed via the Clopper-Pearson method.

Table 105-2: Percentage of Subjects with NT_{80} Titer Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 4-fold Increase from Baseline in Per Protocol Population by Gender

	NT_{80} Measure ≥ 4-fold (Titer)		**All (N = 120)**	**COVIVAC**				**Placebo (N = 20)**
				1 µg (N = 25)	**3 µg (N = 25)**	**10 µg (N = 25)**	**1 µg + CpG (N = 25)**	
28 days after the first vaccination (D29)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						
14 days after the second vaccination (D43)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						
6 months after the second vaccination (D197)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						

Note: The 95% CIs are computed via the Clopper-Pearson method.

Table 106A: Percentage of Subjects with NT_{50} Titer Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 10-fold Increase from Baseline in Full Analysis Population

NT50 Measure ≥ 10-fold (Titer)		All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	n (%) (95% CI)						
14 days after the second vaccination (D43)	n (%) (95% CI)						
6 months after the second vaccination (D197)	n (%) (95% CI)						

Note: The 95% CIs were computed via the Clopper-Pearson method.

Table 106A-1: Percentage of Subjects with NT_{50} Titer Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 10-fold Increase from Baseline in Full Analysis Population by Age Group

	NT_{50} Measure ≥ 10-fold (Titer)		All (N = 120)	COVIVAC				Placebo (N = 20)
				1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						
14 days after the second vaccination (D43)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						
6 months after the second vaccination (D197)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						

Note: The 95% CIs are computed via the Clopper-Pearson method.

Table 106A-2: Percentage of Subjects with NT_{50} Titer Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 10-fold Increase from Baseline in Full Analysis Population by Gender

	NT_{50} Measure ≥ 10-fold (Titer)		**All (N = 120)**	**COVIVAC**				**Placebo (N = 20)**
				1 µg (N = 25)	**3 µg (N = 25)**	**10 µg (N = 25)**	**1 µg + CpG (N = 25)**	
28 days after the first vaccination (D29)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						
14 days after the second vaccination (D43)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						
6 months after the second vaccination (D197)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						

Note: The 95% CIs are computed via the Clopper-Pearson method.

Table 107A: Percentage of Subjects with NT_{50} Titer Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 10-fold Increase from Baseline in Per Protocol Population

NT50 Measure ≥ 10-fold (Titer)		All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	n (%) (95% CI)						
14 days after the second vaccination (D43)	n (%) (95% CI)						
6 months after the second vaccination (D197)	n (%) (95% CI)						

Note: The 95% CIs were computed via the Clopper-Pearson method.

Table 107A-1: Percentage of Subjects with NT_{50} Titer Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 10-fold Increase from Baseline in Per Protocol Population by Age Group

	NT_{50} Measure ≥ 10-fold (Titer)		**All (N = 120)**	**COVIVAC**				**Placebo (N = 20)**
				1 µg (N = 25)	**3 µg (N = 25)**	**10 µg (N = 25)**	**1 µg + CpG (N = 25)**	
28 days after the first vaccination (D29)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						
14 days after the second vaccination (D43)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						
6 months after the second vaccination (D197)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						

Note: The 95% CIs are computed via the Clopper-Pearson method.

Table 107A-2: Percentage of Subjects with NT_{50} Titer Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 10-fold Increase from Baseline in Per Protocol Population by Gender

	NT_{50} Measure ≥ 10-fold (Titer)		All (N = 120)	COVIVAC				Placebo (N = 20)
				1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						
14 days after the second vaccination (D43)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						
6 months after the second vaccination (D197)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						

Note: The 95% CIs are computed via the Clopper-Pearson method.

Table 108: Percentage of Subjects with NT_{80} Titer Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 10-fold Increase from Baseline in Full Analysis Population

NT_{80} Measure ≥ 10-fold (Titer)		**All (N = 120)**	**COVIVAC**				**Placebo (N = 20)**
			1 µg (N = 25)	**3 µg (N = 25)**	**10 µg (N = 25)**	**1 µg + CpG (N = 25)**	
28 days after the first vaccination (D29)	n (%) (95% CI)						
14 days after the second vaccination (D43)	n (%) (95% CI)						
6 months after the second vaccination (D197)	n (%) (95% CI)						

Note: The 95% CIs were computed via the Clopper-Pearson method.

Table 108-1: Percentage of Subjects with NT_{80} Titer Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 10-fold Increase from Baseline in Full Analysis Population by Age Group

	NT_{80} Measure ≥ 10-fold (Titer)		All (N = 120)	COVIVAC				Placebo (N = 20)
				1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						
14 days after the second vaccination (D43)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						
6 months after the second vaccination (D197)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						

Note: The 95% CIs are computed via the Clopper-Pearson method.

Table 108-2: Percentage of Subjects with NT_{80} Titer Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 10-fold Increase from Baseline in Full Analysis Population by Gender

	NT_{80} Measure ≥ 10-fold (IU/mL)		**All (N = 120)**	**COVIVAC**				**Placebo (N = 20)**
				1 µg (N = 25)	**3 µg (N = 25)**	**10 µg (N = 25)**	**1 µg + CpG (N = 25)**	
28 days after the first vaccination (D29)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						
14 days after the second vaccination (D43)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						
6 months after the second vaccination (D197)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						

Note: The 95% CIs are computed via the Clopper-Pearson method.

Table 109: Percentage of Subjects with NT_{80} Titer Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 10-fold Increase from Baseline in Per Protocol Population

NT_{80} Measure ≥ 10-fold (Titer)		All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	n (%) (95% CI)						
14 days after the second vaccination (D43)	n (%) (95% CI)						
6 months after the second vaccination (D197)	n (%) (95% CI)						

Note: The 95% CIs were computed via the Clopper-Pearson method.

Table 109-1: Percentage of Subjects with NT_{80} Titer Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 10-fold Increase from Baseline in Per Protocol Population by Age Group

	NT_{80} Measure ≥ 10-fold (Titer)		All (N = 120)	COVIVAC				Placebo (N = 20)
				1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						
14 days after the second vaccination (D43)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						
6 months after the second vaccination (D197)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						

Note: The 95% CIs are computed via the Clopper-Pearson method.

Table 109-2: Percentage of Subjects with NT_{80} Titer Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 10-fold Increase from Baseline in Per Protocol Population by Gender

	NT_{80} Measure ≥ 10-fold (IU/mL)		**All (N = 120)**	**COVIVAC**				**Placebo (N = 20)**
				1 µg (N = 25)	**3 µg (N = 25)**	**10 µg (N = 25)**	**1 µg + CpG (N = 25)**	
28 days after the first vaccination (D29)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						
14 days after the second vaccination (D43)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						
6 months after the second vaccination (D197)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						

Note: The 95% CIs are computed via the Clopper-Pearson method.

Appendix 1.J. Immunogenicity Analysis – Anti-S IgG Assessed by ELISA

Table 110: Summary of Geometric Mean Concentration (GMC) in BAU/mL of Anti-S IgG assessed by ELISA in Full Analysis Population

Anti-S IgG Measure (BAU/mL)		All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Baseline (D1)	GMC (95% CI)						
28 days after the first vaccination (D29)	GMC (95% CI)						
14 days after the second vaccination (D43)	GMC (95% CI)						
6 months after the second vaccination (D197)	GMC (95% CI)						

Note: GMCs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 110-1: Summary of Geometric Mean Concentration (GMC) in BAU/mL of Anti-S IgG assessed by ELISA in Full Analysis Population by Age Group

Anti-S IgG Measure (BAU/mL)			All (N = 120)	COVIVAC				Placebo (N = 20)
				1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Baseline (D1)	18-39 yr.	GMC (95% CI)						
	40-59 yr.	GMC (95% CI)						
28 days after the first vaccination (D29)	18-39 yr.	GMC (95% CI)						
	40-59 yr.	GMC (95% CI)						
14 days after the second vaccination (D43)	18-39 yr.	GMC (95% CI)						
	40-59 yr.	GMC (95% CI)						
6 months after the second vaccination (D197)	18-39 yr.	GMC (95% CI)						
	40-59 yr.	GMC (95% CI)						

Note: GMCs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 110-2: Summary of Geometric Mean Concentration (GMC) in BAU/mL of Anti-S IgG assessed by ELISA in Full Analysis Population by Gender

Anti-S IgG Measure (BAU/mL)			All (N = 120)	COVIVAC				Placebo (N = 20)
				1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Baseline (D1)	Male	GMC (95% CI)						
	Female	GMC (95% CI)						
28 days after the first vaccination (D29)	Male	GMC (95% CI)						
	Female	GMC (95% CI)						
14 days after the second vaccination (D43)	Male	GMC (95% CI)						
	Female	GMC (95% CI)						
6 months after the second vaccination (D197)	Male	GMC (95% CI)						
	Female	GMC (95% CI)						

Note: GMCs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 111: Summary of Geometric Mean Concentration (GMC) in BAU/mL of Anti-S IgG assessed by ELISA in Per Protocol Population

Anti-S IgG Measure (BAU/mL)		All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Baseline (D1)	GMC (95% CI)						
28 days after the first vaccination (D29)	GMC (95% CI)						
14 days after the second vaccination (D43)	GMC (95% CI)						
6 months after the second vaccination (D197)	GMC (95% CI)						

Note: GMCs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 111-1: Summary of Geometric Mean Concentration (GMC) in BAU/mL of Anti-S IgG assessed by ELISA in Per Protocol Population by Age Group

Anti-S IgG Measure (BAU/mL)			All (N = 120)	COVIVAC				Placebo (N = 20)
				1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Baseline (D1)	18-39 yr.	GMC (95% CI)						
	40-59 yr.	GMC (95% CI)						
28 days after the first vaccination (D29)	18-39 yr.	GMC (95% CI)						
	40-59 yr.	GMC (95% CI)						
14 days after the second vaccination (D43)	18-39 yr.	GMC (95% CI)						
	40-59 yr.	GMC (95% CI)						
6 months after the second vaccination (D197)	18-39 yr.	GMC (95% CI)						
	40-59 yr.	GMC (95% CI)						

Note: GMCs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 111-2: Summary of Geometric Mean Concentration (GMC) in BAU/mL of Anti-S IgG assessed by ELISA in Per Protocol Population by Gender

Anti-S IgG Measure (BAU/mL)			All (N = 120)	COVIVAC				Placebo (N = 20)
				1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
Baseline (D1)	Male	GMC (95% CI)						
	Female	GMC (95% CI)						
28 days after the first vaccination (D29)	Male	GMC (95% CI)						
	Female	GMC (95% CI)						
14 days after the second vaccination (D43)	Male	GMC (95% CI)						
	Female	GMC (95% CI)						
6 months after the second vaccination (D197)	Male	GMC (95% CI)						
	Female	GMC (95% CI)						

Note: GMCs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 112: Summary of Geometric Mean Concentration Ratio (GMC Ratio) of Anti-S IgG assessed by ELISA in Full Analysis Population

Anti-S IgG GMC ratio (95% CI)	COVIVAC					
	1 µg vs 3 µg	1 µg vs 10 µg	3 µg vs 10 µg	1 µg vs 1 µg + CpG	3 µg vs 1 µg + CpG	10 µg vs 1 µg + CpG
Baseline (D1)						
28 days after the first vaccination (D29)						
14 days after the second vaccination (D43)						
6 months after the second vaccination (D197)						

Note: Anti-S IgG GMCs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 112-1: Summary of Geometric Mean Concentration Ratio (GMC Ratio) of Anti-S IgG assessed by ELISA in Full Analysis Population by Age Group

Anti-S IgG GMC ratio (95% CI)		COVIVAC					
		1 µg vs 3 µg	1 µg vs 10 µg	3 µg vs 10 µg	1 µg vs 1 µg + CpG	3 µg vs 1 µg + CpG	10 µg vs 1 µg + CpG
Baseline (D1)	18-39 yr.						
	40-59 yr.						
28 days after the first vaccination (D29)	18-39 yr.						
	40-59 yr.						
14 days after the second vaccination (D43)	18-39 yr.						
	40-59 yr.						
6 months after the second vaccination (D197)	18-39 yr.						
	40-59 yr.						

Note: Anti-S IgG GMCs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 112-2: Summary of Geometric Mean Concentration Ratio (GMC Ratio) of Anti-S IgG assessed by ELISA in Full Analysis Population by Gender

Anti-S IgG GMC ratio (95% CI)		COVIVAC					
		1 µg vs 3 µg	1 µg vs 10 µg	3 µg vs 10 µg	1 µg vs 1 µg + CpG	3 µg vs 1 µg + CpG	10 µg vs 1 µg + CpG
Baseline (D1)	Male						
	Female						
28 days after the first vaccination (D29)	Male						
	Female						
14 days after the second vaccination (D43)	Male						
	Female						
6 months after the second vaccination (D197)	Male						
	Female						

Note: Anti-S IgG GMCs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 113: Summary of Geometric Mean Concentration Ratio (GMC Ratio) of Anti-S IgG assessed by ELISA in Per Protocol Population

Anti-S IgG GMC ratio (95% CI)	COVIVAC					
	1 µg vs 3 µg	1 µg vs 10 µg	3 µg vs 10 µg	1 µg vs 1 µg + CpG	3 µg vs 1 µg + CpG	10 µg vs 1 µg + CpG
Baseline (D1)						
28 days after the first vaccination (D29)						
14 days after the second vaccination (D43)						
6 months after the second vaccination (D197)						

Note: Anti-S IgG GMCs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 113-1: Summary of Geometric Mean Concentration Ratio (GMC Ratio) of Anti-S IgG assessed by ELISA in Per Protocol Population by Age Group

Anti-S IgG GMC ratio (95% CI)		COVIVAC					
		1 µg vs 3 µg	1 µg vs 10 µg	3 µg vs 10 µg	1 µg vs 1 µg + CpG	3 µg vs 1 µg + CpG	10 µg vs 1 µg + CpG
Baseline (D1)	18-39 yr.						
	40-59 yr.						
28 days after the first vaccination (D29)	18-39 yr.						
	40-59 yr.						
14 days after the second vaccination (D43)	18-39 yr.						
	40-59 yr.						
6 months after the second vaccination (D197)	18-39 yr.						
	40-59 yr.						

Note: Anti-S IgG GMCs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 113-2: Summary of Geometric Mean Concentration Ratio (GMC Ratio) of Anti-S IgG assessed by ELISA in Per Protocol Population by Gender

Anti-S IgG GMC ratio (95% CI)		COVIVAC					
		1 µg vs 3 µg	1 µg vs 10 µg	3 µg vs 10 µg	1 µg vs 1 µg + CpG	3 µg vs 1 µg + CpG	10 µg vs 1 µg + CpG
Baseline (D1)	Male						
	Female						
28 days after the first vaccination (D29)	Male						
	Female						
14 days after the second vaccination (D43)	Male						
	Female						
6 months after the second vaccination (D197)	Male						
	Female						

Note: Anti-S IgG GMCs are analyzed from subjects with seronegative anti-S IgG at baseline.

Table 114: Summary of Geometric Mean Fold Rise (GMFR) from Baseline of Anti-S IgG Concentration assessed by ELISA in Full Analysis Population

Anti-S IgG Measure		COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	GMFR from baseline (95% CI)					
14 days after the second vaccination (D43)	GMFR from baseline (95% CI)					
6 months after the second vaccination (D197)	GMFR from baseline (95% CI)					

Note: Geometric Mean Fold Rise (GMFR) is the geometric mean of the ratios of post-vaccination to the pre-first vaccination at D1 (baseline).

Table 114-1: Summary of Geometric Mean Fold Rise (GMFR) from Baseline of Anti-S IgG Concentration assessed by ELISA in Full Analysis Population by Age Group

Anti-S IgG Measure			COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	18-39 yr.	GMFR from baseline (95% CI)					
	40-59 yr.	GMFR from baseline (95% CI)					
14 days after the second vaccination (D43)	18-39 yr.	GMFR from baseline (95% CI)					
	40-59 yr.	GMFR from baseline (95% CI)					
6 months after the second vaccination (D197)	18-39 yr.	GMFR from baseline (95% CI)					
	40-59 yr.	GMFR from baseline (95% CI)					

Note: Geometric Mean Fold Rise (GMFR) is the geometric mean of the ratios of post-vaccination to the pre-first vaccination at D1 (baseline).

Table 114-2: Summary of Geometric Mean Fold Rise (GMFR) from Baseline of Anti-S IgG Concentration assessed by ELISA in Full Analysis Population by Gender

Anti-S IgG Measure			COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	Male	GMFR from baseline (95% CI)					
	Female	GMFR from baseline (95% CI)					
14 days after the second vaccination (D43)	Male	GMFR from baseline (95% CI)					
	Female	GMFR from baseline (95% CI)					
6 months after the second vaccination (D197)	Male	GMFR from baseline (95% CI)					
	Female	GMFR from baseline (95% CI)					

Note: Geometric Mean Fold Rise (GMFR) is the geometric mean of the ratios of post-vaccination to the pre-first vaccination at D1 (baseline).

Table 115: Summary of Geometric Mean Fold Rise (GMFR) from Baseline of Anti-S IgG Concentration assessed by ELISA in Per Protocol Population

Anti-S IgG Measure		COVIVAC				Placebo (N = 20)
		1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	GMFR from baseline (95% CI)					
14 days after the second vaccination (D43)	GMFR from baseline (95% CI)					
6 months after the second vaccination (D197)	GMFR from baseline (95% CI)					

Note: Geometric Mean Fold Rise (GMFR) is the geometric mean of the ratios of post-vaccination to the pre-first vaccination at D1 (baseline).

Table 115-1: Summary of Geometric Mean Fold Rise (GMFR) from Baseline of Anti-S IgG Concentration assessed by ELISA in Per Protocol Population by Age Group

Anti-S IgG Measure			COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	18-39 yr.	GMFR from baseline (95% CI)					
	40-59 yr.	GMFR from baseline (95% CI)					
14 days after the second vaccination (D43)	18-39 yr.	GMFR from baseline (95% CI)					
	40-59 yr.	GMFR from baseline (95% CI)					
6 months after the second vaccination (D197)	18-39 yr.	GMFR from baseline (95% CI)					
	40-59 yr.	GMFR from baseline (95% CI)					

Note: Geometric Mean Fold Rise (GMFR) is the geometric mean of the ratios of post-vaccination to the pre-first vaccination at D1 (baseline).

Table 115-2: Summary of Geometric Mean Fold Rise (GMFR) from Baseline of Anti-S IgG Concentration assessed by ELISA in Per Protocol Population by Gender

Anti-S IgG Measure			COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	Male	GMFR from baseline (95% CI)					
	Female	GMFR from baseline (95% CI)					
14 days after the second vaccination (D43)	Male	GMFR from baseline (95% CI)					
	Female	GMFR from baseline (95% CI)					
6 months after the second vaccination (D197)	Male	GMFR from baseline (95% CI)					
	Female	GMFR from baseline (95% CI)					

Note: Geometric Mean Fold Rise (GMFR) is the geometric mean of the ratios of post-vaccination to the pre-first vaccination at D1 (baseline).

Table 116: Percentage of Subjects with Seroresponses in Anti-S IgG Concentration in BAU/mL assessed by ELISA as defined by a ≥ 4-fold Increase from Baseline in Full Analysis Population

Anti-S IgG Measure ≥ 4-fold		All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	n (%) (95% CI)						
14 days after the second vaccination (D43)	n (%) (95% CI)						
6 months after the second vaccination (D197)	n (%) (95% CI)						

Note: The 95% CIs were computed via the Clopper-Pearson method.

Table 116-1: Percentage of Subjects with Seroresponses in Anti-S IgG Concentration in BAU/mL assessed by ELISA as defined by a ≥ 4-fold Increase from Baseline in Full Analysis Population by Age Group

	Anti-S IgG Measure ≥ 4-fold		**All (N = 120)**	**COVIVAC**				**Placebo (N = 20)**
				1 µg (N = 25)	**3 µg (N = 25)**	**10 µg (N = 25)**	**1 µg + CpG (N = 25)**	
28 days after the first vaccination (D29)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						
14 days after the second vaccination (D43)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						
6 months after the second vaccination (D197)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						

Note: The 95% CIs were computed via the Clopper-Pearson method.

Table 116-2: Percentage of Subjects with Seroresponses in Anti-S IgG Concentration in BAU/mL assessed by ELISA as defined by a ≥ 4-fold Increase from Baseline in Full Analysis Population by Gender

	Anti-S IgG Measure ≥ 4-fold		All (N = 120)	COVIVAC				Placebo (N = 20)
				1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						
14 days after the second vaccination (D43)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						
6 months after the second vaccination (D197)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						

Note: The 95% CIs were computed via the Clopper-Pearson method.

Table 117: Percentage of Subjects with Seroresponses in Anti-S IgG Concentration in BAU/mL assessed by ELISA as defined by a ≥ 4-fold Increase from Baseline in Per Protocol Population

Anti-S IgG Measure ≥ 4-fold		All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	n (%) (95% CI)						
14 days after the second vaccination (D43)	n (%) (95% CI)						
6 months after the second vaccination (D197)	n (%) (95% CI)						

Note: The 95% CIs were computed via the Clopper-Pearson method.

Table 117-1: Percentage of Subjects with Seroresponses in Anti-S IgG Concentration in BAU/mL assessed by ELISA as defined by a ≥ 4-fold Increase from Baseline in Per Protocol Population by Age Group

	Anti-S IgG Measure ≥ 4-fold		All (N = 120)	COVIVAC				Placebo (N = 20)
				1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						
14 days after the second vaccination (D43)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						
6 months after the second vaccination (D197)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						

Note: The 95% CIs were computed via the Clopper-Pearson method.

Table 117-2: Percentage of Subjects with Seroresponses in Anti-S IgG Concentration in BAU/mL assessed by ELISA as defined by a ≥ 4-fold Increase from Baseline in Per Protocol Population by Gender

	Anti-S IgG Measure ≥ 4-fold		All (N = 120)	COVIVAC				Placebo (N = 20)
				1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						
14 days after the second vaccination (D43)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						
6 months after the second vaccination (D197)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						

Note: The 95% CIs were computed via the Clopper-Pearson method.

Table 118: Percentage of Subjects with Seroresponses in Anti-S IgG Concentration in BAU/mL assessed by ELISA as defined by a ≥ 10-fold Increase from Baseline in Full Analysis Population

Anti-S IgG Measure ≥ 10-fold		All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	n (%) (95% CI)						
14 days after the second vaccination (D43)	n (%) (95% CI)						
6 months after the second vaccination (D197)	n (%) (95% CI)						

Note: The 95% CIs were computed via the Clopper-Pearson method.

Table 118-1: Percentage of Subjects with Seroresponses in Anti-S IgG Concentration in BAU/mL assessed by ELISA as defined by a ≥ 10-fold Increase from Baseline in Full Analysis Population by Age Group

	Anti-S IgG Measure ≥ 10-fold		**All (N = 120)**	**COVIVAC**				**Placebo (N = 20)**
				1 µg (N = 25)	**3 µg (N = 25)**	**10 µg (N = 25)**	**1 µg + CpG (N = 25)**	
28 days after the first vaccination (D29)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						
14 days after the second vaccination (D43)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						
6 months after the second vaccination (D197)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						

Note: The 95% CIs were computed via the Clopper-Pearson method.

Table 118-2: Percentage of Subjects with Seroresponses in Anti-S IgG Concentration in BAU/mL assessed by ELISA as defined by a ≥ 10-fold Increase from Baseline in Full Analysis Population by Gender

	Anti-S IgG Measure ≥ 10-fold		All (N = 120)	COVIVAC				Placebo (N = 20)
				1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						
14 days after the second vaccination (D43)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						
6 months after the second vaccination (D197)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						

Note: The 95% CIs were computed via the Clopper-Pearson method.

Table 119: Percentage of Subjects with Seroresponses in Anti-S IgG Concentration in BAU/mL assessed by ELISA as defined by a ≥ 10-fold Increase from Baseline in Per Protocol Population

Anti-S IgG Measure ≥ 10-fold		All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	n (%) (95% CI)						
14 days after the second vaccination (D43)	n (%) (95% CI)						
6 months after the second vaccination (D197)	n (%) (95% CI)						

Note: The 95% CIs were computed via the Clopper-Pearson method.

Table 119-1: Percentage of Subjects with Seroresponses in Anti-S IgG Concentration in BAU/mL assessed by ELISA as defined by a ≥ 10-fold Increase from Baseline in Per Protocol Population by Age Group

	Anti-S IgG Measure ≥ 10-fold		**All (N = 120)**	**COVIVAC**				**Placebo (N = 20)**
				1 µg (N = 25)	**3 µg (N = 25)**	**10 µg (N = 25)**	**1 µg + CpG (N = 25)**	
28 days after the first vaccination (D29)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						
14 days after the second vaccination (D43)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						
6 months after the second vaccination (D197)	18-39 yr.	n (%) (95% CI)						
	40-59 yr.	n (%) (95% CI)						

Note: The 95% CIs were computed via the Clopper-Pearson method.

Table 119-2: Percentage of Subjects with Seroresponses in Anti-S IgG Concentration in BAU/mL assessed by ELISA as defined by a ≥ 10-fold Increase from Baseline in Per Protocol Population by Gender

	Anti-S IgG Measure ≥ 10-fold		All (N = 120)	COVIVAC				Placebo (N = 20)
				1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
28 days after the first vaccination (D29)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						
14 days after the second vaccination (D43)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						
6 months after the second vaccination (D197)	Male	n (%) (95% CI)						
	Female	n (%) (95% CI)						

Note: The 95% CIs were computed via the Clopper-Pearson method.

Appendix 1.L. Concomitant Medication

Table 120: Concomitant Medication by Pharmacological Class According to WHO DD

Anatomical Main Group	Therapeutic Subgroup	All (N = 120)	COVIVAC				Placebo (N = 20)
			1 µg (N = 25)	3 µg (N = 25)	10 µg (N = 25)	1 µg + CpG (N = 25)	
All		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ATC 1		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ATC 2		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ATC 3		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

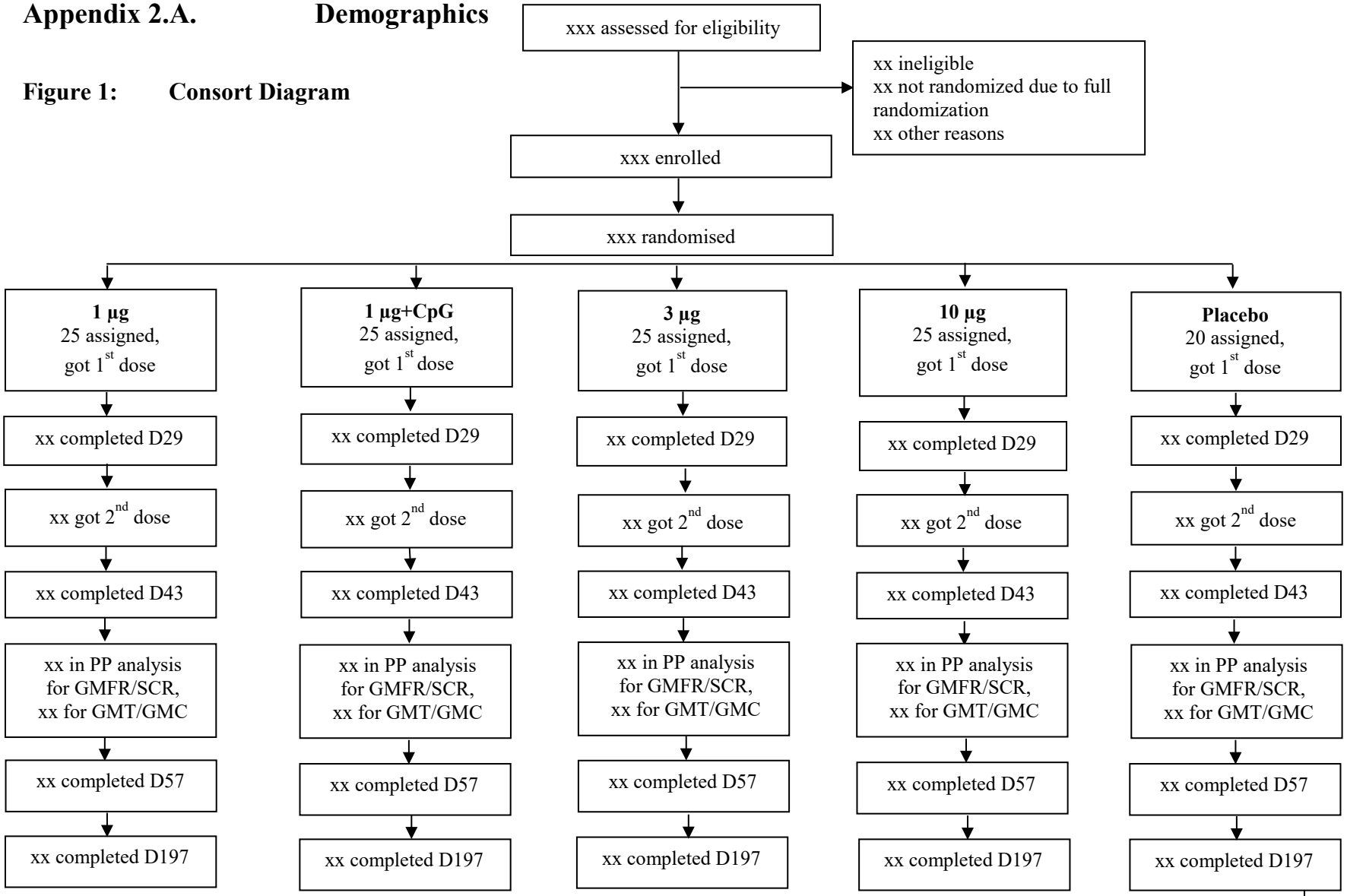
Note: Number of subject with at least one concomitant medication in a given pharmacological class

APPENDIX 2. FIGURES

LIST OF FIGURES

Appendix 2.A. Demographics

Figure 1: Consort Diagram



Appendix 2.B. Laboratory Values

Figure 2: Hemoglobin (g/dL) from Baseline Across Visit by Vaccination Groups

Mock data was used to prepare the dummy plot.

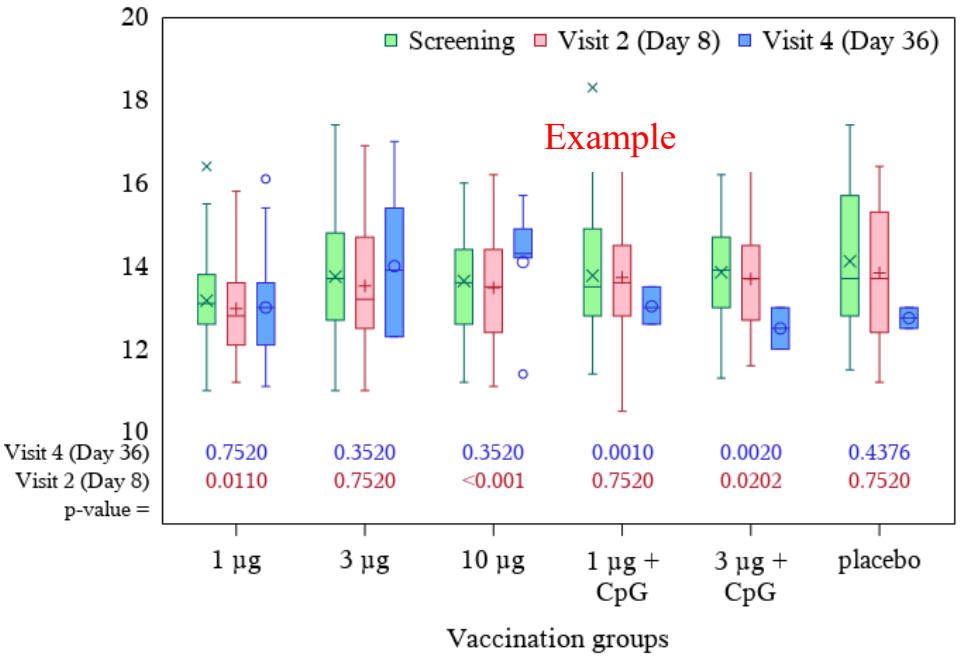


Figure 3: White Blood Cell (WBC) (x 10^3/µL) from Baseline Across Visit by Vaccination Groups

Figure 4: Platelets (x 10^3/µL) from Baseline Across Visit by Vaccination Groups

Figure 5: Creatinine (mg/dL) from Baseline Across Visit by Vaccination Groups

Figure 6: ALT (U/L) from Baseline Across Visit by Vaccination Groups

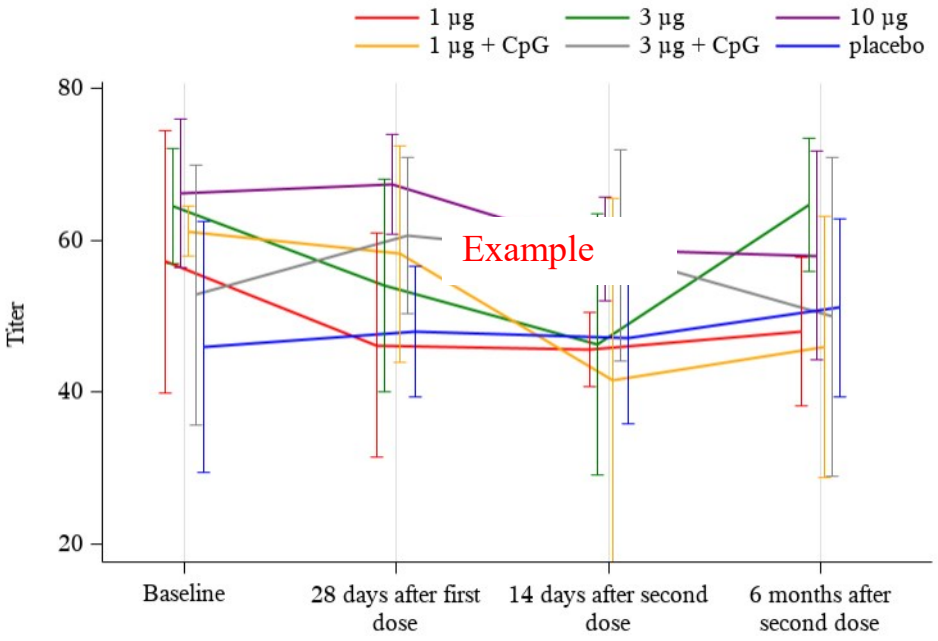
Figure 7: AST (U/L) from Baseline Across Visit by Vaccination Groups

Figure 8: Total Bilirubin (mg/dL) from Baseline Across Visit by Vaccination Groups

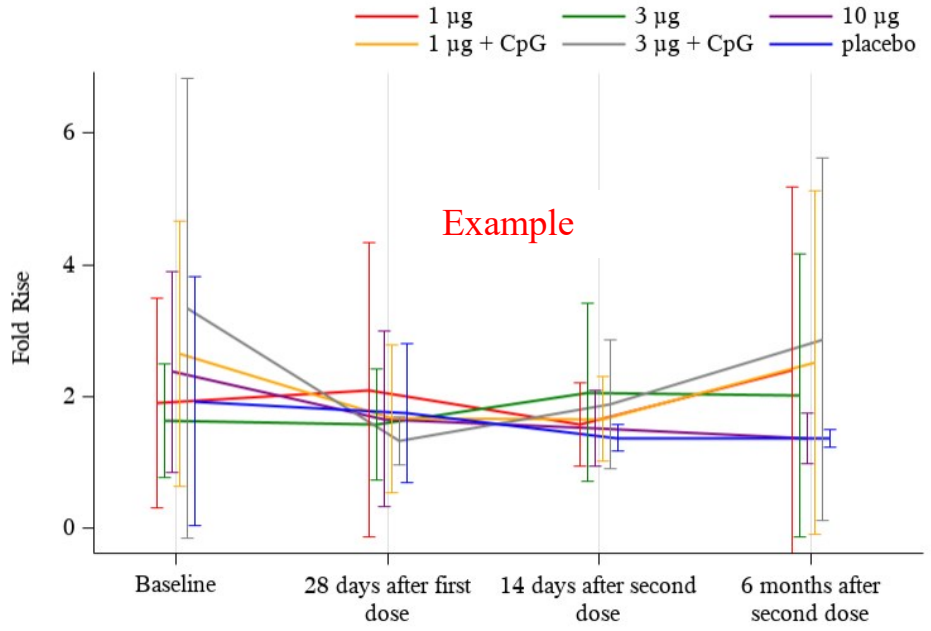
Box and whisker plot will be presented for all laboratory results.

Appendix 2.C. Immunogenicity - Geometric Mean Titer (GMT), Geometric Mean Fold Rise (GMFR)

Figure 9: Geometric Mean Titer (GMT), Geometric Mean Fold Rise (GMFR) of NT_{50} against SARS-CoV-2 Pseudovirus in Full Analysis Population



Bars represent geometric mean titer and 95% CI



Bars represent geometric mean fold-rise (GMFR) and 95% CI

Figure 10: Geometric Mean Titer (GMT), Geometric Mean Fold Rise (GMFR) of NT_{50} against SARS-CoV-2 Pseudovirus in Per Protocol Analysis Population

Figure 11: Geometric Mean Titer (GMT), Geometric Mean Fold Rise (GMFR) of NT_{80} against SARS-CoV-2 Pseudovirus in Full Analysis Population

Figure 12: Geometric Mean Titer (GMT), Geometric Mean Fold Rise (GMFR) of NT_{80} against SARS-CoV-2 Pseudovirus in Per Protocol Analysis Population

Figure 13: Geometric Mean Concentration (GMC), Geometric Mean Fold Rise (GMFR) of Anti-S IgG assessed by ELISA in Full Analysis Population

Figure 14: Geometric Mean Concentration (GMC), Geometric Mean Fold Rise (GMFR) of Anti-S IgG assessed by ELISA in Per Protocol Analysis Population

Appendix 2.D. Immunogenicity - Seroresponses

Figure 15: NT_{50} Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 4-fold Increase from Baseline in Full Analysis Population

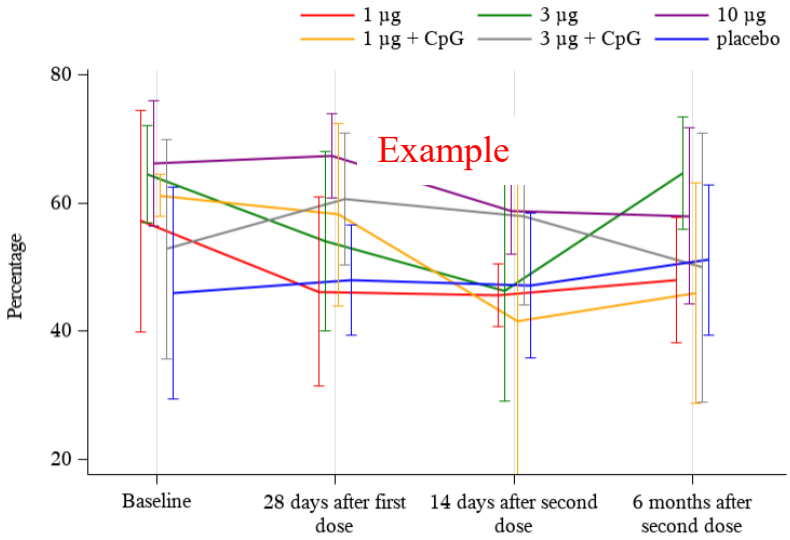


Figure 16: Percentage of Subjects with NT_{50} Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 4-fold Increase from Baseline in Per Protocol Analysis Population

Figure 17: Percentage of Subjects with NT_{80} Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 4-fold Increase from Baseline in Full Analysis Population

Figure 18: Percentage of Subjects with NT_{80} Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 4-fold Increase from Baseline in Per Protocol Analysis Population

Figure 19: Percentage of Subjects with NT_{50} Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 10-fold Increase from Baseline in Full Analysis Population

Figure 20: Percentage of Subjects with NT_{50} Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 10-fold Increase from Baseline in Per Protocol Analysis Population

Figure 21: Percentage of Subjects with NT_{80} Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 10-fold Increase from Baseline in Full Analysis Population

Figure 22: Percentage of Subjects with NT_{80} Seroresponses against SARS-CoV-2 Pseudovirus as defined by a ≥ 10-fold Increase from Baseline in Full Analysis Population

Figure 23: Percentage of Subjects with Seroresponses in Anti-S IgG Concentration (BAU/mL) assessed by ELISA as defined by a ≥ 4-fold Increase from Baseline in Full Analysis Population

Figure 24: Percentage of Subjects with Seroresponses in Anti-S IgG Concentration (BAU/mL) assessed by ELISA as defined by a ≥ 4-fold Increase from Baseline in Per Protocol Analysis Population

Figure 25: Percentage of Subjects with Seroresponses in Anti-S IgG Concentration (BAU/mL) assessed by ELISA as defined by a ≥ 10-fold Increase from Baseline in Full Analysis Population

Figure 26: Percentage of Subjects with Seroresponses in Anti-S IgG Concentration (BAU/mL) assessed by ELISA as defined by a ≥ 10-fold Increase from Baseline in Per Protocol Analysis Population

Appendix 2.E. Immunogenicity – Reverse Cumulative

Figure 27: NT_{50} Titer Seroresponses against SARS-CoV-2 Pseudovirus Reverse Cumulative Distribution Curves in Full Analysis Population

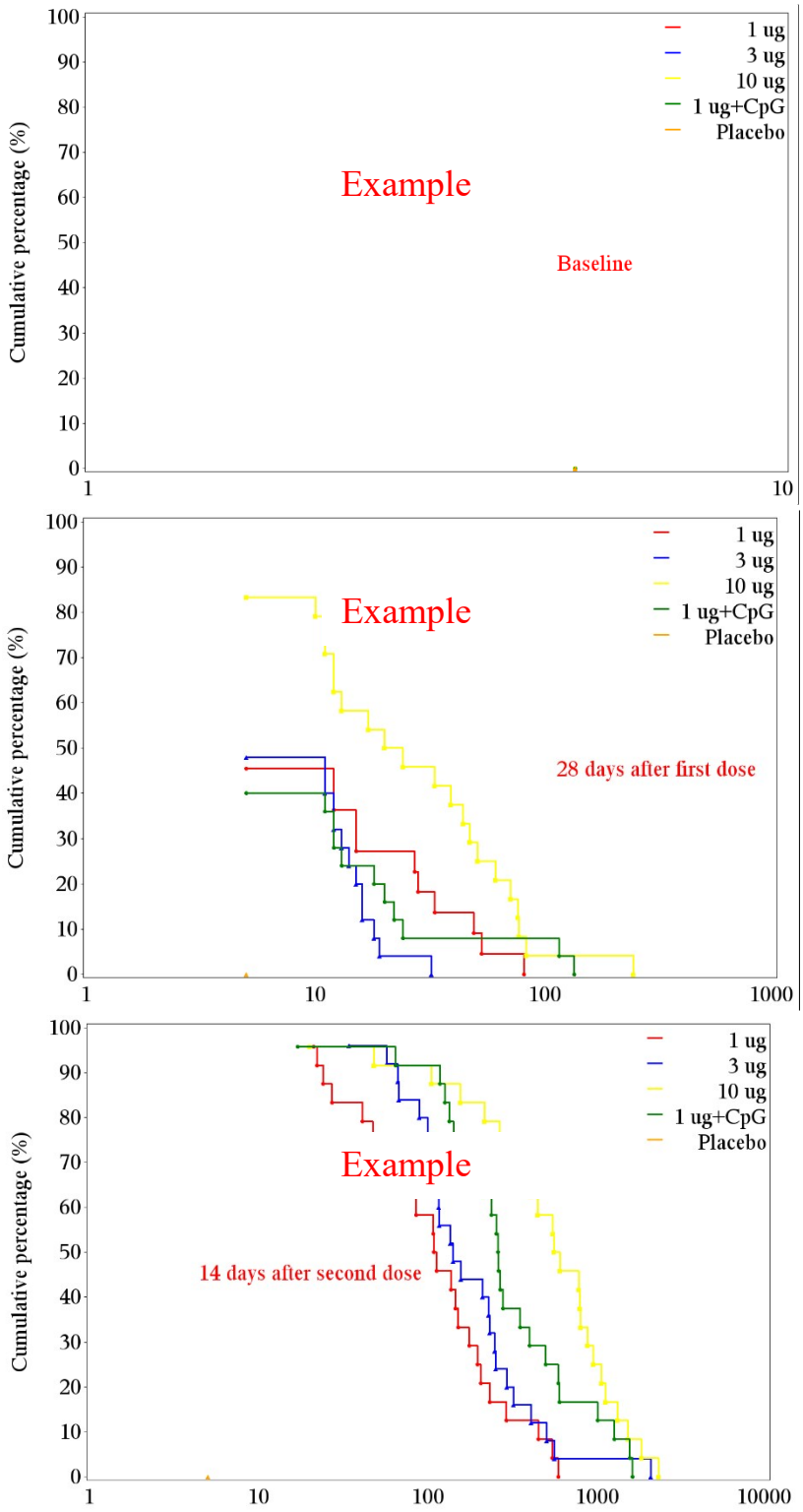


Figure 28: NT_{50} Titer Seroresponses against SARS-CoV-2 Pseudovirus Reverse Cumulative Distribution Curves in Per Protocol Analysis Population

Figure 29: NT_{80} Titer Seroresponses against SARS-CoV-2 Pseudovirus Reverse Cumulative Distribution Curves in Full Analysis Population

Figure 30: NT_{80} Titer Seroresponses against SARS-CoV-2 Pseudovirus Reverse Cumulative Distribution Curves in Per Protocol Analysis Population

Figure 31: Anti-S IgG Concentration (BAU/mL) Assessed by ELISA Reverse Cumulative Distribution Curves in Full Analysis Population

Figure 32: Anti-S IgG Concentration (BAU/mL) Assessed by ELISA Reverse Cumulative Distribution Curves in Per Protocol Analysis Population

APPENDIX 3. LISTINGS

Listing 1: Reasons of Incomplete Study

Subject ID	Reason	Vaccination Group

Listing 2: Subject Specific Protocol Deviation

Subject ID	Reason for Deviation	Vaccination Group

Listing 3: Demographics

Subject ID	Vaccination Group	Sex	Age (years)	Height (cm)	Weight (kg)	BMI	Race

Listing 4: Medical History

Subject ID	Vaccination Group	Diagnosis	Past/Current	System Organ Class (SOC)	Preferred Term (PT)

Listing 5: Concomitant Medications

Subject ID	Vaccination Group	Medication	Medication Start Date	Medication End Date/ Ongoing	Indication (MH, PIR, AE)	Anatomical Main Group	Therapeutic Subgroup

Listing 6: Solicited Local and Systemic Reactions with Severity Grade

Subject ID	Vaccination Group	After Dose (1st/2nd)	Reaction	Follow-up Time Point*	Severity Grade

* Follow-up time point: 30 minutes or 7 days after vaccination

Listing 7: Unsolicited Adverse Events

Subject ID	Vaccination Group	Vaccination Date	AE#	Verbatim Term	System Organ Class (SOC)	Preferred Term (PT)	Start Date	End Date/ Ongoing	Serious? (Y/N)	MAAE?	AESI?	Severity	Outcome	Relationship to study vaccine	Action taken to study vaccine

Listing 8: Serious Adverse Events

Subject ID	Vaccination Group	Vaccination Date	AE#	Verbatim Term	System Organ Class (SOC)	Preferred Term (PT)	Start Date	End Date/ Ongoing	MAAE?	AESI?	Severity	Outcome	Relationship to study vaccine	Action taken to study vaccine

Listing 9A: All Clinical Laboratory Values

Subject ID	Vaccination Group	Parameter	Units	Reference Range	Visit	Value	% Change from Baseline	Severity
		Hemoglobin	g/dL		Baseline			
					Visit 2 (Day 8)			
					Visit 4 (Day 36)			
		White Blood Cell	$x10^3/\mu L$		Baseline			
					Visit 2 (Day 8)			
					Visit 4 (Day 36)			
		Platelets	$x10^3/\mu L$		Baseline			
					Visit 2 (Day 8)			
					Visit 4 (Day 36)			
		Creatinine	mg/dL		Baseline			
					Visit 2 (Day 8)			
					Visit 4 (Day 36)			
		AST (SGPT)	U/L		Baseline			
					Visit 2 (Day 8)			
					Visit 4 (Day 36)			
		ALT (SGOT)	U/L		Baseline			
					Visit 2 (Day 8)			
					Visit 4 (Day 36)			
		Total Bilirubin	mg/dL		Baseline			
					Visit 2 (Day 8)			
					Visit 4 (Day 36)			

Listing 9B: Abnormal Clinical Laboratory Values

Subject ID	Vaccination Group	Parameter	Units	Reference Range	Visit	Value	% Change from Baseline	Severity
		Hemoglobin	g/dL		Baseline			
					Visit 2 (Day 8)			
					Visit 4 (Day 36)			
		White Blood Cell	$x10^3/\mu L$		Baseline			
					Visit 2 (Day 8)			
					Visit 4 (Day 36)			
		Platelets	$x10^3/\mu L$		Baseline			
					Visit 2 (Day 8)			
					Visit 4 (Day 36)			
		Creatinine	mg/dL		Baseline			
					Visit 2 (Day 8)			
					Visit 4 (Day 36)			
		AST (SGPT)	U/L		Baseline			
					Visit 2 (Day 8)			
					Visit 4 (Day 36)			
		ALT (SGOT)	U/L		Baseline			
					Visit 2 (Day 8)			
					Visit 4 (Day 36)			
		Total Bilirubin	mg/dL		Baseline			
					Visit 2 (Day 8)			
					Visit 4 (Day 36)			

Listing 10: Vital Sign Results

Subject ID	Vaccination Group	Parameter	Visit	Value	Change from Baseline

Listing 11: Physical Examination Results

Subject ID	Vaccination Group	Parameter	Visit	Normality (Normal/ Abnormal/ Not done)	If abnormal, clinically significant (Yes/No)

Listing 12: NT50 and NT80 against SARS-CoV-2 Pseudovirus

Subject ID	Vaccination Group	Visit	NT50 (IU/mL)	NT80 (IU/mL)

Listing 13: Anti-S IgG Titers assessed by ELISA

Subject ID	Vaccination Group	Visit	Anti-S IgG titer (BAU/mL)