STATISTICAL ANALYSIS PLAN (SAP)

Protocol Title:	**A Phase 1 Monotherapy Study to Evaluate the Safety Tolerability and Immunogenicity of Vaccination with Candidate Chimpanzee Adenovirus-vectored Hepatitis B Virus Vaccine (ChAdOx1-HBV) in Healthy Participants and Participants with Chronic Hepatitis B infection**
Study Code:	**HBV001**
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STATISTICAL ANALYSIS PLAN

VERSION 01-00, 06 JUNE 2022

A Phase 1 Monotherapy Study to Evaluate the Safety Tolerability and Immunogenicity of Vaccination with Candidate Chimpanzee Adenovirus-vectored Hepatitis B Virus Vaccine (ChAdOx1-HBV) in Healthy Participants and Participants with Chronic Hepatitis B infection

Study Code: HBV001

Prepared by: S-cubed Biometrics Ltd

For: Vaccitech Ltd.

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1. STATISTICAL ANALYSIS PLAN APPROVAL FORM

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1. STATISTICAL ANALYSIS PLAN APPROVAL FORM

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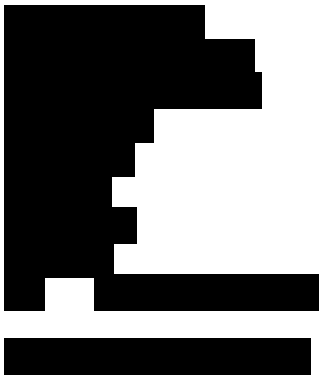

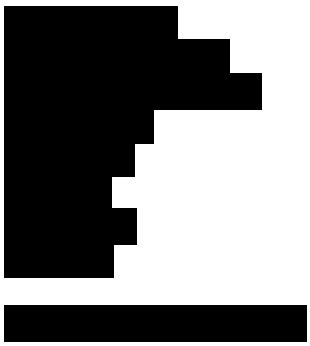

3. LIST OF ABBREVIATIONS

Abbreviation	Definition
AE	Adverse event
ANCOVA	Analysis of covariance
ANOVA	Analysis of variance
ATC	Anatomical Therapeutic Chemical Classification
BLQ	Below the level of quantification
CHB	Chronic hepatitis B virus
CRF	Case Report Form
CSR	Clinical Study Report
DMC	Data Monitoring Committee
FAS	Full Analysis Set
HD	High Dose
ICS	Intracellular Cytokine Staining
ITT	Intention-to-Treat
LD	Low Dose
LFNA	Liver Fine Needle Aspirate
LLN	Lower limit of normal
LOCF	Last observation carried forward
MedDRA	Medical dictionary for regulatory activities
PK	Pharmacokinetics
PP	Per protocol
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SD	Standard deviation
SOC	System Organ Class

TE	Treatment emergent
ULN	Upper limit of normal
WHO	World Health Organisation

4. INTRODUCTION

This statistical analysis plan (SAP) explains in detail the statistical analyses that will be performed for the Vaccitech study HBV001. The analysis is outlined within the study protocol version 9 (24NOV2021, incorporating amendment 8.0), and this SAP contains a more technical and detailed description of those analyses. In particular, information is provided on the definitions of the participant analysis sets, and it also details the list of Tables, Figures and Listings (TFL) that will be produced by S-cubed Biometrics for use and inclusion with the Clinical Study Report (CSR). The SAP has been written and finalised before the database is locked.

The first 3 protocol amendments that were written for this study were written prior to any participants being enrolled into the study. The following amendments have an impact on the analysis:

Amendment 3

- Clarification was given on the HBV disease markers assessed in Healthy Volunteers and the participants with CHB infection on each visit.
- Clarification given that the HDV antibody assessment will be applicable for the participants with CHB infection only

Amendment 2

No changes that impacted the analysis were made in Amendment 2.

Amendment 1

- Transcriptomics were removed at all timepoints as these do not contribute significantly to the study endpoints.
- Clarification of the function of the DMC, which is to review safety and tolerability in HBV001 only (not efficacy and immunogenicity)

The fourth amendment adjusted the inclusion criteria for CHB participants:

Amendment 4

- The inclusion criteria for the acceptable level for HBsAg for the CHB patients was raised from 4000IU/mL to 10000IU/mL.

The later protocol amendments altered the study design as a result of the COVID-19 pandemic and to allow for the investigation of the impact of COVID-19 vaccinations, namely:

Amendment 5

- The exclusion criteria were updated to exclude participants who had received an adenoviral vaccine 3 months prior to screening, or 3 months after vaccination with ChADOx1-HBV.
- The minimum data required to report an SAE was updated to be in line with ICH-GCP guidelines.

Amendment 6

- Addition of 2 cohorts of healthy volunteers.
    - Cohort 5 consisting of 15 healthy volunteers who had received the AZD1222 vaccine and
    - Cohort 6 consisting of 15 health volunteers who had received the Pfizer MRNA vaccine.

Amendment 7

- Amended to allow for the inclusion of participants who had received the Moderna MRNA vaccine in Cohort 6.

Amendment 8

- Amended to allow for participants to have more than two doses of a COVID-19 vaccination.

All exploratory efficacy endpoints will be analysed separately from this SAP and will be an appendix to the Clinical Study Report (CSR).

Any deviations from the protocol- specified analyses, and also deviations from analyses stated within this SAP, will be described within the CSR.

5. STUDY OBJECTIVES

5.1. Primary Objective

Determine the safety and tolerability of different doses of a single vaccination of ChAdOx1 HBV in healthy participants and in participants with chronic hepatitis B virus (CHB) infection and virally suppressed with oral antiviral medication.

5.2. Secondary Objectives

- Determine the immunogenicity of ChAdOx1 HBV in (A) healthy participants and in (B) participants with CHB, virally suppressed with oral antiviral medication.
- Determine the effect of ChAdOx1 HBV on the level of hepatitis B surface antigen (HBsAg) in participants with CHB infection, virally suppressed with oral antiviral medication.
- Cohorts 5 and 6 only: Assess whether the receipt of prior ChAdOx1-SARS-CoV-2 vaccine (AZD1222) results in decreased T cell responses to ChAdOx1-HBV, when administered 10-18 weeks prior to ChAdOx1-HBV.

5.3. Exploratory Objective

Determine the effect of ChAdOx1 HBV on virological and immunological systemic and intrahepatic changes in participants with CHB infection and virally suppressed with oral antiviral medication.

6. STUDY DESIGN

This is a Phase 1, first-in-human study of ChAdOx1-HBV. The study will be conducted in 40 healthy participants and 12 participants with CHB and virally suppressed with oral antiviral medication. This will be an open-label, non-randomised dose escalation study comparing the safety, tolerability and immunogenicity of 2 different doses of ChAdOx1-HBV vaccine. T cell responses in healthy participants who have received a prior two-dose series of AZD1222 will be compared with those who have received at least two doses of the Pfizer mRNA COVID-19 vaccine or the Moderna COVID-19 vaccine. The study design is shown in Figure 1.

Participants will be screened in the period Day -42 to Day -1. Informed consent will be obtained before any study specific procedures are performed. Eligible participants will then attend the clinic to receive study vaccine on Day 0. Participants will be enrolled sequentially.

The study will investigate the study vaccine as shown in Table 1 On Day 0, an electronic diary (eDiary), tape measure and thermometer will be provided to perform self-assessment of local and systemic reactogenicity. All participants will then have a follow-up telephone call on Day 1 and return to the clinic for study assessments on Days 7, 14, 28, 84. Participants in cohorts 1-4 only, will also have follow up visits on Day 56 and Day 168. End of study visit procedures will be performed at the final visit.

Five healthy participants will be administered the low dose first (cohort 1). Dose escalation will only be initiated in the next 5 healthy participants (cohort 2) following Safety Monitoring Committee (SMC) review.

Six CHB participants will be administered the low dose (cohort 3) before the dose escalation is initiated in the remaining 6 CHB participants (cohort 4).

Thirty healthy participants (15 who have received two doses of AZD1222 [cohort 5] and 15 who have received at least two doses of either the Pfizer or Moderna mRNA COVID-19 vaccine [cohort 6]) will be dosed in parallel with the high dose used in cohorts 2 and 4.

The first participant in each of cohorts 1-4 will be assessed for 1 hour in the clinic post-vaccination in case of immediate adverse events (timed after the end of study vaccine administration). All other participants will be assessed for 30 minutes.

Five reviews of the safety, tolerability and available immunogenicity data will be performed by a SMC:

- First review: at least 48 hours after the first healthy participant has received the first low dose of ChAdOx1-HBV vaccine. This review will occur before dosing the remaining participants in cohort 1
- Second review: at least 48 hours after the last healthy participant has received the last low dose of ChAdOx1-HBV vaccine. This review will occur before dosing high dose healthy participants in cohort 2
- Third review: at least 48 hours after the last healthy participant has received the last high dose of ChAdOx1-HBV vaccine. This review will occur before dosing low dose CHB participants in cohort 3
- Fourth review: at least 48 hours after the first CHB participant has received the first low dose of ChAdOx1-HBV vaccine. This review will occur before dosing the remaining low dose CHB participants in cohort 3
- Fifth review: at least 48 hours after the last participant with CHB has received the low dose of ChAdOx1-HBV vaccine cohort 3 before dosing high dose CHB participants in cohort 4

A Data Monitoring Committee (DMC) will be appointed to perform unscheduled reviews of the available safety and tolerability study data and make recommendations concerning the continuation, modification or termination of the study if one of the study stopping or holding rules is met.

6.1. Study Procedures Flow Chart

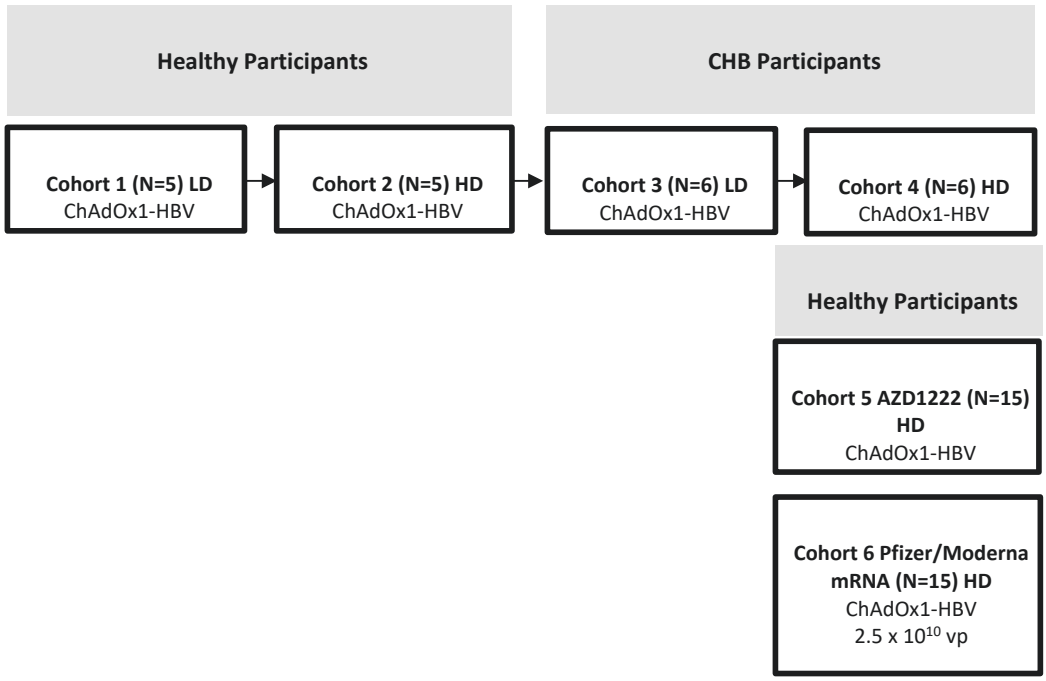

Figure 1: Overall Study Design

Abbreviations: ChAdOx1-HBV=chimpanzee adenovirus-vectored hepatitis B virus vaccine; CHB=chronic hepatitis B virus; HD=high dose; LD=low dose; N=number of participants; vp=viral particles.

6.2. Treatment Allocation

Table 1: Study Vaccine Treatment Groups in HBV001

Treatment Cohort	Vaccine Single Dose	N
Cohort 1 LD Healthy Participants	ChAdOx1-HBV 2.5×10^9 vp	5
Cohort 2 HD Healthy Participants	ChAdOx1-HBV 2.5×10^{10} vp	5
Cohort 3 LD Participants with CHB	ChAdOx1-HBV 2.5×10^9 vp	6
Cohort 4 HD Participants with CHB	ChAdOx1-HBV 2.5×10^{10} vp	6
Cohort 5 HD Healthy Participants who have been vaccinated with AZD1222 COVID-19 vaccine	ChAdOx1-HBV 2.5×10^{10} vp	15
Cohort 6 HD Healthy Participants who have been vaccinated with Pfizer or Moderna mRNA COVID-19 vaccines	ChAdOx1-HBV 2.5×10^{10} vp	15

Abbreviations: ChAdOx1-HBV=chimpanzee adenovirus-vectored hepatitis B virus vaccine; CHB=chronic hepatitis B virus; HD=high dose; LD=low dose; vp=viral particles

This will be an open-label, non-randomised dose escalation study. All participants will be assigned to a dose in a sequential manner. Participants will receive study vaccine on Day 0 only.

6.3. Time and Events Schedule

Visit/Call	Screen	Vaccination			Follow-up						End of Study
Timepoint	Day-42 to -1	Day 0			Day 1	Day 7±1	Day 14±1	Day 28±2	Day 56±3 (cohorts 1-4)	Day 84±7[a]	Day 168±7 (cohorts 1-4)
		Pre-	0	Post-							
Informed consent	X										
Baseline/eligibility variables											
Demographics	X										
Inclusion and exclusion criteria	X	X									
Height and Weight	X										
Medical and disease history	X	X									
HIV Ab, HCV Ab, HBsAg, HDV Ab[b]	X										
Urinalysis	X										
Urine pregnancy test (β-hCG) [c]	X	X						X	X	X	X
Laboratory eligibility and safety tests											
Haematology [d]	X	X				X	X	X	X	X	X
Biochemistry[d]	X	X				X	X	X	X	X	X
Liver function tests[e]	X	X				X	X	X	X	X	X
Study vaccination											
Vaccination			X								
Post-vaccination observation[f]				X							
Other Safety assessments											
Full physical examination	X	X									
Directed physical examination if required						X	X	X	X	X	X
Vital signs[g]	X	X		X		X	X	X	X	X	X
Local/systemic reactogenicity [h]		X		X	X						
Unsolicited adverse events [i]	X	X	X	X	X	X	X	X			

Visit/Call	Screen	Vaccination			Follow-up						End of Study
Timepoint	Day-42 to -1	Day 0			Day 1	Day 7±1	Day 14±1	Day 28±2	Day 56±3 (cohorts 1-4)	Day 84±7[a]	Day 168±7 (cohorts 1-4)
		Pre-	0	Post-							
Serious adverse events and adverse events of special interest	X	X	X	X	X	X	X	X	X	X	X
Prior and concomitant medications	X	X	X	X	X	X	X	X	X	X	X
Blood for HBV disease markers											
Healthy participants (HBsAb, HBcAb)		X									X[j]
CHB (HBV DNA, HBsAg quantitative)	X	X						X	X	X	X
CHB (HBeAg, anti-HBe, anti-HBs, pgRNA, HBcAg, anti-HBc)		X						X	X	X	X
Immunogenicity assessments											
Blood for cellular immunogenicity [k]		X					X	X	X	X	X
Blood for neutralising antibodies (cohorts 5 and 6 only)			X							X	
Liver fine needle aspirates[l]†	X									X	

Visit/Call	Screen	Vaccination			Follow-up						End of Study
Timepoint	Day-42 to -1	Day 0			Day 1	Day 7±1	Day 14±1	Day 28±2	Day 56±3 (cohorts 1-4)	Day 84±7[a]	Day 168±7 (cohorts 1-4)
		Pre-	0	Post-							

Abbreviations: ALP=alkaline phosphatase; ALT=alanine transaminase; aPTT=activated partial thromboplastin time; AST=aspartate transaminase; CHB=chronic hepatitis B virus; DNA=desoxyribonucleic acid; GGT=gamma-glutamyl transpeptidase; HBcAb=hepatitis B core antibody; HBsAb=hepatitis B surface antibody; β-hCG=beta human chorionic gonadotrophin; HBcAg=hepatitis B core-related antigen; HBV=hepatitis B virus; HBeAg=hepatitis B e antigen; HBsAg=hepatitis B surface antigen; HCV=Hepatitis C virus; HDV=Hepatitis D virus; HIV=human immunodeficiency virus; ICS=intracellular cytokine staining; INR= international normalised ratio; LFNA=liver fine needle aspirate; pgRNA=pre-genomic RNA; PBMCs=peripheral blood mononuclear cells; PT=prothrombin time

†Optional assessments

[a] End of Study Visit for cohorts 5 and 6

[b] HDV Ab serology and HBsAg quantitative test will be done in CHB participants only; HBsAg qualitative test will be done in healthy participants; all participants will be tested for HIV and HCV serology

[c] Female participants only

[d] Full haematology (including PT/INR and aPTT) and biochemistry panel

[e] Measurement of ALP, GGT, ALT, AST and total bilirubin

[f] The first participant in each cohort will be assessed for 1 hour in case of immediate adverse events (timed after the end of study vaccine administration). All other participants will be assessed for 30 minutes

[g] Pulse, blood pressure and temperature

[h] Captured during clinic visits and then via eDiary for 3 days post-vaccination

[i] Recorded in the eCRF from the date the informed consent is signed, at all clinic visits to cover the period since the previous visit and during the visit and up to 28 days post-vaccination

[j] If negative at baseline, at discretion of the investigator

[k] To be processed into PBMCs for analysis by ICS

[l] Only in CHB participants who consent to LFNAs after confirming eligibility. Coagulation profile must be assessed prior to repeat LFNA on Day 84. For those consenting to LFNAs, blood for PT/INR and aPTT testing must be collected

6.4. Interim Analysis / Data Monitoring

A Data Monitoring Committee (DMC) will be appointed to perform unscheduled reviews of the available safety and tolerability study data and make recommendations concerning the continuation, modification or termination of the study if one of the study stopping or holding rules is met.

7. STUDY ENDPOINTS

7.1. Primary Safety Endpoint(s)

Incidence of safety and reactogenicity events:

- Adverse events and/or adverse events leading to study discontinuation
- Serious adverse events
- Grade ≥3 local and systemic reactions

7.2. Secondary Endpoints

- A multi-parameter index made of CD4+ magnitude, CD4+ avidity, and CD8+ magnitude
- Mean reduction in HBsAg titre at Week 12 (Day 84) and Week 24 (Day 168) post-vaccination (last visit)
- Proportion of CHB participants with hepatitis B e-antigen (HBeAg) and HBsAg loss
- Proportion of CHB participants with HBeAg and HBsAg seroconversion
- Reduction of hepatitis B deoxyribonucleic acid (DNA) levels
- Total T cell response to the antigens encoded by ChAdOx1-HBV as measured in a peptide-stimulated ELISpot assay

7.3. Exploratory Endpoints

- Effect on serum hepatitis B core-related antigen (HBcAg)
- Effect on serum hepatitis B circulating pre-genomic ribonucleic acid (pgRNA)
- Liver fine needle aspirate (LFNA) assays will be used to quantify and characterise intrahepatic immune and parenchymal cells and/or hepatitis B virus (HBV) DNA and ribonucleic acid (RNA) transcripts
- Effect of prior AZD1222 on the CD4+ and CD8+ T cell magnitude and phenotype as measured by multiparameter flow cytometry

8. SAMPLE SIZE

The number of participants is based on feasibility considerations rather than formal sample size calculations. A total of 10 healthy participants and 12 participants with CHB infection is considered sufficient to confirm the safety, tolerability and immunogenicity of ChAdOx1-HBV and to answer the objectives of the study before progressing to larger studies.

The sample size for cohorts 5 and 6 is based on the ELISpot results of ChAdOx1-HBV administered to healthy adults at a dose of 2.5×10^{10} which resulted in a mean of 1,000 +/-500 spot forming units in three adults who had samples examined by same day analysis at Oxford University. Assuming the same response in 15 volunteers in each cohort, the sample size is powered to detect a 45% decrease in the T cell response in the participants receiving prior AZD1222 compared to the Pfizer/Moderna mRNA COVID-19 vaccine.

9. STUDY ANALYSIS SETS

Analysis sets defined below (and where any participant or specific data from a participant will be excluded) will be reviewed (and updated if required) against the study database at the data review meeting (DRM). The database at this time will be nearly final (i.e. meeting may result in further data queries/changes post meeting), so participant inclusion/exclusion from analysis sets defined at this meeting, will be further checked (post meeting) against a locked database, and will then be finalised.

9.1. Safety Analysis Set

The safety analysis set will consist of all participants who received at least one vaccination. Data will be summarised according to the dose of vaccination actually received. All safety analyses will be performed on the safety analysis set. Participants who receive a different dose to the one they were assigned at enrolment, will be presented according to the treatment they actually received.

9.2. Per-Protocol Analysis Set

The per-protocol analysis set will consist of all participants in the safety analysis set who received the correct study vaccine and who had no major protocol deviations that might impact or bias analytic results. All major protocol deviations will be documented on the protocol deviation tracker. Those participants with major protocol deviations leading to exclusion from the Per-Protocol analysis set will be discussed at the DRM.

Major protocol deviations leading to exclusion from the Per-Protocol Analysis Set may include, but are not limited to:

- failing inclusion/exclusion criteria
- not receiving the correct dose of vaccine.

The per-protocol analysis set definition will be used for the immunogenicity analysis set (in Section 9.3), but no data will be presented for the per-protocol analysis set itself.

9.3. Immunogenicity Analysis Set

The immunogenicity analysis set will consist of all participants in the per-protocol set who have available immunogenicity data to evaluate the immunogenicity endpoints and did not have any major protocol deviations that would impact the results of the immunological analysis.

10. PLANNED STATISTICAL METHODS

10.1. Statistical Considerations

10.1.1. General definitions

Definition of baseline

Baseline is defined as the last non-missing value for a participant, for the particular parameter, that is prior to the administration of study vaccine.

Study completion definition

A participant completes the study by engaging in study activities up to and including the End of Study Visit at Day 168 (+/- 7 days), for cohorts 1 to 4, and Day 84 (+/- 7 days) for cohorts 5 and 6.

Treatment Group

There are six treatment groups in this study; the Healthy Participants and CHB participants are split into high and low doses of vaccination. Healthy participants in the high dose group are further split into those with no previous exposure to ChAdOx1 vectored vaccines, those with recent previous exposure to Covid-19 ChAdOx1 vectored vaccine (cohort 5) and those with previous exposure to Covid-19 mRNA based vaccines (cohort 6).

Results below limit of detection and quantification

Immunogenicity results that are below the limit of quantification or detection (i.e. reported as <X or BLQ) will be replaced by 0 for any summaries but will be listed as reported.

Geometric Mean and Standard Deviation

The geometric mean (GM) and geometric standard deviation (GSD) are obtained by calculating the mean and SD of the log-transformed data and back-transforming these. If there are any zero values in the data a small number should be added to all values before log-transformation and then subtracted from the resulting GM. This small number will be 1 unless stated otherwise.

GM = antilog (mean (log(value + S))) – S, where S is a small number, relative to the non-zero results.

GSD = antilog(standard deviation(log(value + S)))

10.1.2. Data Presentation

The specific format and content of each data presentation is shown in Section 14.

Summary tables will be presented by treatment group and also for safety summaries, demographic and baseline data, for all participants.

Within all Tables and Figures values for treatment group will be labelled as follows:

- “Healthy Participants – Low Dose”
- “Healthy Participants – High Dose”

- “Healthy Participants: Covid-19 vaccinated – ChAdOx1”
- “Healthy Participants: Covid-19 vaccinated – mRNA”
- “CHB Participants – Low Dose”
- “CHB Participants – High Dose”
- “Total”

For disposition summaries the participants that were screened but not vaccinated with ChAdOx1-HBV may be presented as:

- “Screen Failure”

Within Listings treatment groups will be identified as follows:

- “HP – LD”
- “HP – HD”
- “HP – HD – ChAdOx1”
- “HP – HD – mRNA”
- “CHB – LD”
- “CHB – HD”
- “SF”

And the ordering of treatment groups shown here represent the order they will appear in Tables.

The scheduled protocol visits will be labelled in the report presentations as follows:

- “Screening”
- “Day 0 – pre dose”
- “Day 0 – post dose”
- “Day 1”
- “Day 7”
- “Day 14”
- “Day 28”
- “Day 56”
- “Day 84”
- “Day 168”

Within summary presentations it is envisaged that only scheduled protocol visit values will be used for post-baseline time points. Within the clinical database, a number of data points may be labelled as unscheduled. These data points will be included within participant Listings only. However, at the DRM the occurrence of such non-scheduled data will be reviewed for each participant to decide if (and how) any such data point(s) should be included within summary presentations. Any such decisions will be documented in the DRM minutes.

Where duplicate information is collected (and reconciled) on both the CRF and on the non-CRF vendor data transfer(s) (e.g. sampling date) then only the CRF recorded information will be included in participant listings.

All variables will be listed to the same number of decimal places as reported. Descriptive statistics for all endpoints that are continuous will have the following summary statistics presented in the following order: n, mean (rounded to one more decimal place than recorded), standard deviation (rounded to two more decimal places than recorded), median (rounded to one more decimal place than recorded), minimum (as recorded), and maximum (as recorded).

Categorical variables will be summarised using proportions (counts and percentages). All percentages in summary tables will be calculated using as the denominator, either the participant analysis set or the number of non-missing observations. The specific approach is detailed within each (relevant) table template (Section 14).

All collected data will be included within participant listings.

10.1.3. Statistical Testing and Estimation

No formal statistical analysis is planned.

10.1.4. Handling of Dropouts or Missing Data

No imputation methods will be used to manage the occurrence of missing data. Only observed data at each scheduled visit will be reported.

For adverse events and concomitant medications, the approach to handle missing dates has been described in Section 10.8.1 and Section 10.5 respectively. For any other data which has partial dates, these dates will be completed using a suitably conservative approach.

10.1.5. Interim Analysis and Data Monitoring

No interim analyses are planned.

10.1.6. Multicentre Studies

Due to the small number of participants enrolled in this study, no by centre presentations will be produced.

10.1.7. Multiple Comparison/Multiplicity

No statistical analysis is planned and therefore there are no multiplicity issues in this study.

10.1.8. Examination of Subgroups

Due to the small number of participants enrolled in this study, no subgroup analysis will be performed.

10.1.9. Software

Data will be reported using SAS (version 9.4 or later).

10.2. Participant Disposition

The number of participants who were screen failures, who received the vaccine, the number withdrawing from the study (also split by reason for withdrawal) and completing the study, and the numbers in each analysis population will be summarised for all participants and by treatment group.

Participants who fail any inclusion/exclusion criteria will be listed.

10.3. Protocol Deviations

Protocol deviations will be listed using information collected on the spreadsheet provided by the project manager.

Participant data will be reviewed for major protocol deviations by a qualified clinical reviewer prior to database lock at the data review meeting. Participants with any major protocol deviations will be documented within the Protocol Deviations tracker.

10.4. Demographic and other baseline characteristics

Unless otherwise described, the Safety analysis set will be used in summaries of demographic and baseline data. No statistical testing will be used to compare treatment groups for different baseline characteristics.

10.4.1. Demographics

Demographic variables at Screening including sex, age, race, height (cm), weight (kg) and body mass index will be summarised by treatment group and across all participants. The denominator will be the number of participants in the analysis set.

Age at screening (in years) will be calculated as:

Largest Integer ≤ [(date of screening visit – date of birth + 1)/365.25].

Body mass index at screening (BMI, expressed in kg/m^2) will be calculated as:

BMI (kg/m^2) = Weight (kg) / [height (m)]^2.

10.4.2. Substance Use

All social habits data will be listed only.

10.4.3. Allergies

All allergy data will be listed only.

10.4.4. Medical History

Medical history data will be listed.

10.5. Prior and Concomitant medications

Concomitant therapies will be coded to their generic name and ATC class using the WHODrug dictionary, Global version (September 2019).

A medication will be assigned as being prior to study treatment or concomitant with study treatment, based on the start and stop dates of the medication and the date of vaccination. If the medication stop date is before the date of the vaccination, the medication will be assigned as being prior to study treatment. In all other situations, the medication will be assigned as being concomitant with study treatment.

Concomitant medications will be separately summarised by treatment group (and for all participants), ATC Class and generic name for the Safety analysis set. Prior medications will be identified in a participant listing. If a participant has separate periods of taking specific medications, then that medication is only counted once within the specific period of observation (i.e. prior or concomitant) where it is taken.

10.6. Study treatment exposure

This study involves a single vaccination on Day 0. The number of participants vaccinated is presented in the participant disposition table (Section 10.2). The vaccination must be taken for inclusion in all analysis sets.

The detail of the vaccination including whether the vaccine was administered, date, time the vaccine was removed from the freezer, time of administration, location of administration, dose given, and whether the participant was observed for the appropriate time will be listed.

10.7. Immunogenicity Analysis

All immunogenicity (efficacy) analyses will be performed on the Immunogenicity Set. The Immunogenicity analysis set is considered the primary analysis population for the immunogenicity (efficacy) analyses.

10.7.1. Primary Endpoint Analysis

The primary objective of this study is to determine the safety and tolerability of different doses of a single vaccination of ChAdOx1-HBV in healthy participants and in participants with CHB infection and virally suppressed with oral antiviral medication. See Section 10.8 for details of the Primary Safety analysis.

There are no primary efficacy analyses.

10.7.2. Secondary Endpoint Analyses

For all immunogenicity data, any results that are <X will be replaced by 0 for summaries.

A multi-parameter index made of CD4+ magnitude, CD4+ avidity, and CD8+ magnitude

The multi-parameter index is made of CD4+ magnitude, CD4+ avidity, and CD8+ magnitude at each scheduled follow-up (Day 28, Day 56, Day 84 and Day 168) using intracellular cytokine staining (ICS) data from a flow cytometer. All ICS data will be background-subtracted and presented in listings. Negative, background-subtracted responses will be set to 0.

Any additional analyses that may be conducted on ICS data will be performed outside of this SAP and described *a priori* within a separate document prepared by Vaccitech.

Mean reduction in HBsAg titre at Day 84 and Day 168 post-vaccination (last visit)

For the CHB participants only (expected number of participants is 12), the reduction in HBsAg titre is derived by subtracting the follow-up log_{10}-transformed HBsAg from the baseline log_{10}-transformed HBsAg at each scheduled follow-up (Day 28, Day 56, Day 84 and Day 168). The HBsAg titre and the reduction in the HBsAg titre will be summarised by visit. The summary of HBsAg titres will include the GM and GSD, derived as in Section 10.1.1.

This secondary endpoint specifically references Day 84 (+/- 7 days) and Day 168 (+/- 7 days); other follow-up visits are provided as supportive analyses.

Proportion of CHB participants with HBeAg and HBsAg loss

For the CHB participants only (expected number of participants is 12), loss of HBeAg and HBsAg will be a binary outcome (loss / no loss) and will be provided directly by the Immunology laboratory. Loss will be assessed at each follow-up visit (Day 28, Day 56, Day 84 and Day 168). HBeAg and HBsAg loss will be listed.

Proportion of CHB participants with HBeAg and HBsAg seroconversion

For the CHB participants only (expected number of participants 12), seroconversion of HBeAg and HBsAg is defined as loss of response to the antigen (defined as a value below the limit of detection (i.e. Not detected)) and development of antibody to either HBeAg or surface antigen (HBsAg) (defined as a measurable value above the limit of detection (i.e. Detected)).

The number and percentage of CHB participants meeting the criteria for seroconversion will be summarised. The denominator will be the number of CHB participants in the analysis set with non-missing data.

Reduction of hepatitis B DNA levels

For CHB participants only (expected number of participants is 12), the reduction of hepatitis B DNA levels is assessed by subtracting the DNA levels at each follow-up visit (Day 28, Day 56, Day 84 and Day 168) from the DNA levels pre vaccination (Day 0). In addition, the maximum reduction (at any timepoint) will be calculated. The hepatitis B DNA levels will be log transformed (base 10) prior to any calculations, and summaries will be presented on the log-scale.

Total T cell response to the antigens encoded by ChAdOx1-HBV as measured in a peptide-stimulated ELISpot assay

Assessment of immune response by ELISpot assay will be based on the number of IFN-γ spot-forming units (SFU) per 10^6 PBMC in response to stimulation with each antigenic peptide pool. Responses are background (DMSO)-subtracted and will be summarized by the following combinations of stimulation conditions: Core, Pol1-Pol4, Pre S1/S2/S, and Sli.

Background-subtracted results that do not exceed a positivity threshold of 25 will be set to 0. Background-subtraction resulting in negative values will be set to 0.

Background-subtracted ELISpot responses at each immunology timepoint and their changes from baseline will be summarized by treatment group and combination of stimulation antigens. ELISpot results will also be listed.

Role of recent previous exposure to a different ChAdOx1 vectored vaccine (cohorts 5 and 6)

For participants in cohorts 5 and 6 the anti-vector immunity is assessed by a multi-parameter index made of CD4+ magnitude and CD8+ magnitude (see above) and by the titre of anti-vector neutralising antibodies.

T cell responses will be background-subtracted and presented in listings. Negative, background-subtracted responses will be set to 0.

10.7.3. Exploratory Efficacy Analysis

The following exploratory efficacy endpoints will be analysed separately from this SAP and will be an appendix to the Clinical Study Report. Any data collected within the study database will be listed:

- Effect on serum hepatitis B core related antigen (HBcAg)
- Effect on serum hepatitis B circulating pre genomic ribonucleic acid (pgRNA)
- Liver fine needle aspirate (LFNA) assays will be used to quantify and characterise intrahepatic immune and parenchymal cells and/or HBV DNA and RNA transcripts.
- Effect of prior AZD1222 on the CD4+ and CD8+ T cell magnitude and phenotype as measured by multiparameter flow cytometry

10.8. Safety Analysis

All analyses of safety endpoints will be descriptive. The safety analysis set will be used for all safety presentations. No statistical analysis of safety data will be performed.

10.8.1. Adverse Events and Serious Adverse Events

All adverse events will be coded using MedDRA, Version 22.1.

An adverse event is treatment emergent if the onset date is on or after the date of vaccination. Should any onset date for an adverse event be missing or only a partial date recorded (such that it cannot be determined if the event onset was prior to start of study treatment or not) then it will be assumed that the event is treatment emergent, unless the adverse event stop date indicates otherwise. Any adverse event with an onset date earlier than the date of vaccination will be classified as a pre-treatment adverse event. Time is not collected and will not be used in the identification of treatment emergent AEs.

If a participant experiences more than one AE with the same preferred term, that preferred term will be counted only once. It will be assigned the greatest observed severity and the strongest relationship to study treatment among those events for the tables in which those characteristics are summarised.

Treatment-emergent AEs will be summarised by:

- Treatment group, system organ class, and preferred term;
- Treatment group, system organ class, preferred term and severity;
- Treatment group, system organ class, preferred term and severity for only those events that are judged to be related to study treatment;

Treatment-emergent vaccine-related (i.e. where "related" = Yes) AEs will be summarised by:

- Treatment group, system organ class, preferred term;

Treatment-emergent adverse events of special interest, where events of special interest will be noted in the database, will be reported by:

- Treatment group, system organ class, and preferred term;

A summary table of adverse event incidence will also be presented by treatment group and overall to include the number and percentage of participants with at least one: TEAE, TEAE severity (Grade 1 to 5 separately, and additionally those subjects with a Grade 3, 4 or 5), vaccine related TEAE, vaccine related severity (Grade 1 to 5 separately, and additionally those subjects with a Grade 3, 4 or 5), SAE, vaccine related SAE, TEAE leading to withdrawal from the study.

Note: 'Adverse Event Leading to Discontinuation from the Study' will be those Participants that withdrew from the study due to an adverse event.

Serious adverse events and adverse events directly resulting in withdrawal from study will be listed by treatment group.

In all AE summary tables results will be displayed ordered in terms of decreasing frequency of SOC occurrence (based on total across treatment groups), and within each SOC also ordered in terms of decreasing frequency of preferred term occurrence (also based on total across treatment groups). In all AE summary tables, in addition to presenting the information by treatment group, a total column (treatment groups combined) will also be presented.

10.8.2. Local and Systemic Reactions

Local and systemic reactions are collected by the investigator pre and post vaccination on Day 0. In addition, local and systemic reactions are captured in the participant diary card on Days 1, 2 and 3. The worst incidence of each local and systemic reaction post vaccination for each participant will be summarised.

The size of swelling (induration) and redness (erythema) is measured in mm. The largest injection site swelling post vaccination and the largest area of redness post vaccination will be summarised.

Pain and warmth at the site are collected on a five-point scale including, none (grade 0), no interference with daily activities (grade 1), some interference with daily activities (grade 2), significant interference preventing daily activities (grade 3), and ER visit or hospitalisation visit (grade 4). The worst degree of pain and separately worst degree of warmth post vaccination will be summarised.

The severity of redness and swelling will be derived for each participant as:

- <2.5cm – Grade 0,
- 2.5 to 5cm – Grade 1,
- 5.1 to 10cm – Grade 2,

- >10cm – Grade 3.

The number and percentage of participants with each degree of worst pain, worst warmth, worst redness and worst swelling will be summarised; the denominator will be the number of participants in the safety analysis set.

Systemic reactions include muscle ache (myalgia), fatigue, headache, nausea, feverishness, chills, joint ache (arthralgia) and malaise. Each of these items are collected on a five-point scale including, none (grade 0), no interference with daily activities (grade 1), some interference with daily activities (grade 2), significant interference preventing daily activities (grade 3), and ER visit or hospitalisation visit (grade 4). The worst reaction will be summarised for each systemic reaction as the number and percent of participants, the denominator will be the number of participants in the analysis set.

The temperature will be graded as:

- <38.0 – Grade 0,
- 38.0 to 38.4 – Grade 1,
- 38.5 to 38.9 – Grade 2
- 39.0 to 40.0 – Grade 3
- >40.0 – Grade 4

Worst temperature will then be summarised, along with the worst temperature severity. Only the temperature recorded as part of the local and systemic reactions (i.e. on the corresponding CRF page or subject diary) will be summarised in this table.

Additionally, a table will summarise the number of participants who experienced any of the symptoms.

Missing data will not be imputed and diary card data will be summarised as collected.

All Diary Card and Investigator reported local and systemic reactions will be listed.

10.8.3. Laboratory Variables

The following haematology and chemistry (including Liver Function) parameters will be included within data presentations (and presented in the units as shown):

- Haematology: Haemoglobin (g/L), White Cell Count (10**9/L), Platelets (10**9/L), Haematocrit (L/L), Red Cell Count (10**12/L), Mean Cell Volume (fl), Mean Cell Hgb (pg), Mean Cell Hgb Concentration (g/L), Neutrophils (10**9/L), Lymphocytes (10**9/L), Monocytes (10**9/L), Eosinophils (10**9/L), Basophils (10**9/L), APTT (secs), Fibrinogen (g/L), PT (secs), INR.
- Chemistry (including Liver Function): Sodium (mmol/L), Potassium (mmol/L), Urea (umol/L), Creatinine (umol/L), Total Bilirubin (umol/L), ALT (IU/L), AST (IU/L), Gamma GT (IU/L), Alkaline Phosphatase (IU/L) and Albumin (g/L).

Any other laboratory parameters collected as part of the study (including urinalysis) will only be included in listings. Laboratory data collected in different units to that shown will be converted to the above specified units (if possible) and both will be shown in the listings.

Toxicity grades will be calculated for relevant laboratory parameters, as per Appendix 1 of the study protocol (Section 15.1**Error! Reference source not found.**). Shift tables will be presented showing

changes in each toxicity grade from the baseline grade to the maximum post-baseline grade for each treatment group.

10.8.4. Vital Signs

Vital signs parameters (temperature (C), pulse rate (bpm), systolic blood pressure (mmHg) and diastolic blood pressure (mmHg)) will be listed.

Toxicity grades will be calculated for relevant vital sign parameters, as per Appendix 1 of the study protocol (Section **Error! Reference source not found.**). Shift tables will be presented showing changes in each toxicity grade from the baseline grade to the maximum post-baseline grade for each treatment group.

10.8.5. Physical Examination

Physical examination results will be listed.

11. CHANGES TO THE PROTOCOL SPECIFIED ANALYSIS DETAILED IN THE STATISTICAL ANALYSIS PLAN

The following changes have been made in the SAP compared to the protocol specified analysis:

- Data Presentations for laboratory parameters, vital signs and physical examination data have been modified to take account of the low number of participants in this study, i.e. fewer types of summary presentations will be produced, and data listings can be referred to for further detail.
- The per-protocol analysis set definition was updated to clarify that only those with major protocol deviations that are judged to impact or bias the analytic results of the study would be excluded.

12. REFERENCES

13. TABLES, FIGURES AND LISTINGS

13.1. Specific Presentation Details

Tables, listings and figures will be provided in a WORD document. All summary tables and figures will have source data footnotes that refer to the relevant listings. Dates will appear as ddmmmyyyy; times as hh:mm, on the 24-hour clock. All listings will be ordered by treatment group, centre, participant number and scheduled visit. For the presentation of summary data, values will be aligned based on the unit column, and not left/right justified. For example:

Parameter	n	xx	xx
	Mean	xx.x	xx.x
	SD	xx.xx	xx.xx
	Median	xx.x	xx.x
	Min, Max	xx, xx	xx, xx

All tables, listings and figures will have the SAS program name, output filename and date of production in the footnote.

All tables, listings and figures will include the following study header and footer:

Page x of y

Vaccitech HBV001

Table x.x
Title
analysis set

Source Data: Listing 16.2.x {Source data footnote only appears for tables, where x references relevant listing number}

Program: xxxxxxxxx Output: xxxxxxx Date: xxxxxxxxx

13.2. List of Tables

14.3.6	Shift Summary of Vital Signs Results by Maximum Toxicity Grade– Safety Analysis Set

13.3. List of Listings

Listing Number	Listing Title
16.2.1.1	Participant Disposition
16.2.1.2	Failed Inclusion and Exclusion Criteria
16.2.2	Protocol Deviations
16.2.3	Participant Analysis Sets
16.2.4.1	Demographic Data
16.2.4.2	Reproductive Status and Contraception
16.2.4.3.1	Substance Use: Smoking
16.2.4.3.2	Substance Use: Alcohol
16.2.4.3.3	Substance Use: Recreational Drugs
16.2.4.4	Allergies
16.2.4.5	Medical History
16.2.4.6	Prior and Concomitant Medications
16.2.5	Vaccination Administration
16.2.6.1.1	Local and Systemic Reactions
16.2.6.1.2	Diary Card: Medications Taken
16.2.6.2	HBV Disease Markers
16.2.6.3	ELISpot
16.2.6.4	ICS
16.2.6.5	Neutralising Antibody Sample Collection
16.2.7	Adverse Events
16.2.8.1	Haematology
16.2.8.2	Chemistry (including Liver Function Tests)
16.2.8.3	Urinalysis
16.2.8.4	HIV, HCV and HDV Serology
16.2.8.5	Urine Pregnancy

16.2.9	Vital Signs
16.2.10	Physical Examination
16.2.11	Visit Dates
16.2.12	Covid-19 Vaccination

14.TABLE AND LISTING SHELLS

Table 14.1.1
Disposition
All Participants

	Healthy Participants				CHB Participants				Healthy Participants Covid-19 Vaccinated							
	Low Dose (N=xx)		High Dose (N=xx)		Low Dose (N=xx)		High Dose (N=xx)		ChAdOx1 (N=xx)		mRNA (N=xx)		Total (N=xx)	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Screen Failure [1]	XX		XX		XX		XX		XX		XX		XX	
Vaccinated	XX		XX		XX		XX		XX		XX		XX	
Safety Analysis Set [2]	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
PP Analysis Set [3]	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Immunogenicity Analysis Set [4]	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Completed Study [5]	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Did not Complete Study	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Reason for Withdrawal:														
Reason 1	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)	XX	(XX.X)	XX	(XX.X)

[1] Participants who were screened but not vaccinated with ChAdOx1-HBV.
[2] Safety Analysis Set consists of all participants who received at least one vaccination. Data will be summarised according to the dose of vaccination actually received.
[3] Per Protocol (PP) Analysis Set consists of all participants in the safety analysis set who received the correct study vaccine and who had no major protocol deviations
[4] Immunogenicity Analysis Set consists of all participants in the per-protocol set who have available immunogenicity data to evaluate the immunogenicity endpoints and did not have any major protocol deviations that would impact on the results of the immunological analysis
[5] A participant completes the study by engaging in study activities up to and including the End of Study Visit at Day 168 (+/- 7 days).
Percentages are based on the number of vaccinated participants.

All COVID-19 vaccinated participants were given the high dose of ChAdOx1-HBV vaccine.

Table 14.1.2
Demography
Safety Analysis Set

		Healthy Participants		CHB Participants		Healthy Participants Covid-19 Vaccinated		
		Low Dose (N=xx)	High Dose (N=xx)	Low Dose (N=xx)	High Dose (N=xx)	ChAdOx1 (N=xx)	mRNA (N=xx)	Total (N=xx)
Sex								
Male	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Female	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Age at Screening (years)	N	XX	XX	XX	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Race								
Asian	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Black	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
White or Caucasian	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Other	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Height (cm)	n	XX	XX	XX	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Weight at screening (kg)	n	XX	XX	XX	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
BMI at screening (kg/m^2)	n	XX	XX	XX	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX

Percentages are based on the number of participants in the analysis set.
All COVID-19 vaccinated participants were given the high dose of ChAdOx1-HBV vaccine.

Table 14.1.3
Concomitant Medications
Safety Analysis Set

	Healthy Participants		CHB Participants		Healthy Participants Covid-19 Vaccinated		
Drug Class (L2)/ WHO Drug Name	Low Dose (N=xx)	High Dose (N=xx)	Low Dose (N=xx)	High Dose (N=xx)	ChAdOx1 (N=xx)	mRNA (N=xx)	Total (N=xx)
Number of Participants with any Concomitant Medication	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Drug Class 1	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
WHO Drug Name 1	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
WHO Drug Name 2	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Drug Class 2	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
WHO Drug Name 1	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
WHO Drug Name 2	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)

All medications are coded using the WHO Drug Dictionary, Global Version (September 2019).
Concomitant medications correspond to medications where the stop date is not before the vaccination date.
The table shows distinct number of participants with each WHO Drug name/Drug Class.
Percentages are based on the safety analysis set.
All COVID-19 vaccinated participants were given the high dose of ChAdOx1-HBV vaccine.

Table 14.2.1
Reduction in HBsAg titre post-vaccination in CHB participants
Immunogenicity Analysis Set

		CHB Participants					
		Low Dose (N=xx)		High Dose (N=xx)		Total (N=xx)	
HBsAg (IU/mL)		Absolute	Change	Absolute	Change	Absolute	Change
Baseline	n	XX		XX		XX	
	GM	XX.X		XX.X		XX.X	
	GSD	XX.XX		XX.XX		XX.XX	
	Median	XX.X		XX.X		XX.X	
	Min, Max	XX, XX		XX, XX		XX, XX	
Day 28	n	XX	XX	XX	XX	XX	XX
	GM	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	GSD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Day 56	n	XX	XX	XX	XX	XX	XX
	GM	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	GSD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Day 84 [1]	n	XX	XX	XX	XX	XX	XX
	GM	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	GSD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Day 168 [1]	n	XX	XX	XX	XX	XX	XX
	GM	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	GSD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX

GM = antilog(mean(log(HbsAg))), GSD = antilog(sd(log(HbsAg)))
A summary of the change is obtained by summarising the difference in the log-transformed results (log(HbsAg at baseline) – log(HbsAg at follow-up)) and back-transforming. The mean change is then the GM ratio, where a GM ratio > 1 is equivalent to a reduction in HbsAg.
[1] Visits at Day 84 and Day 168 are the protocol defined secondary endpoints of the study.

Table 14.2.2
Proportion of CHB participants with HBeAg and HBsAg Seroconversion
Immunogenicity Analysis Set

		CHB Participants		
		Low Dose (N=xx)	High Dose (N=xx)	Total (N=xx)
HBeAg and HBsAg Seroconversion				
Yes	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)
No	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)

Seroconversion is defined as the loss of response to the antigen HbeAg and HbsAg and the development of antibody to HbeAg and HbsAg (i.e. [HbeAg and HbsAg < LLOD] and [anti-HBs and anti-Hbe >= LLOD]).
The denominator is the number of participants with non-missing data at baseline and follow-up.

Table 14.2.3
Reduction in Hepatitis B DNA levels in CHB participants
Immunogenicity Analysis Set

		CHB Participants					
		Low Dose (N=xx)		High Dose (N=xx)		Total (N=xx)	
Hepatitis B DNA ()log10 copies/mL)		Absolute	Change	Absolute	Change	Absolute	Change
Baseline	n	XX		XX		XX	
	Mean	XX.X		XX.X		XX.X	
	SD	XX.XX		XX.XX		XX.XX	
	Median	XX.X		XX.X		XX.X	
	Min, Max	XX, XX		XX, XX		XX, XX	
Day 28	n	XX	XX	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Day 56	n	XX	XX	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Day 84	n	XX	XX	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Day 168	n	XX	XX	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Maximum Change	n		XX		XX		XX
	Mean		XX.X		XX.X		XX.X
	SD		XX.XX		XX.XX		XX.XX
	Median		XX.X		XX.X		XX.X
	Min, Max		XX, XX		XX, XX		XX, XX

Change in hepatitis B DNA levels is defined by subtracting the DNA levels at each follow-up visit (Day 28, Day 56, Day 84 and Day 168) from the DNA levels pre vaccination (Day 0). A positive change is equivalent to a reduction in DNA levels.
The denominator is the number of participants in the analysis set.

Programming Note: The data may be provided as copies/ml - this should be transformed to log10 copies/ml before summarising

Table 14.2.4
Background-subtracted T-Cell response (ELISpot)
Immunogenicity Analysis Set

		Healthy Participants				Healthy Participants Covid-19 Vaccinated					
		Low Dose (N=xx)		High Dose (N=xx)		ChAdOx1 (N=xx)		mRNA (N=xx)		Total (N=xx)	
Stimulation Antigen Visit		Absolute	Change	Absolute	Change	Absolute	Change	Absolute	Change	Absolute	Change
Core											
Baseline	n	XX		XX		XX		XX		XX	
	Mean	XX.X		XX.X		XX.X		XX.X		XX.X	
	SD	XX.XX		XX.XX		XX.XX		XX.XX		XX.XX	
	Median	XX.X		XX.X		XX.X		XX.X		XX.X	
	Min, Max	XX, XX		XX, XX		XX, XX		XX, XX		XX, XX	
Day XXX	n	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX

[Repeat for each visit]
[Repeat for each stimulation antigen]

All COVID-19 vaccinated participants were given the high dose of ChAdOx1-HBV vaccine.

Background-subtracted results that were less than 0 were replaced with 0 prior to summarising.

Programming Note: This table should also include the CHD participants, both high and low dose, which will be shown on the next page.

Table 14.3.1.1
Overall Summary of Treatment-Emergent Adverse Events
Safety Analysis Set

	Healthy Participants		CHB Participants		Healthy Participants Covid-19 Vaccinated		
	Low Dose (N=xx)	High Dose (N=xx)	Low Dose (N=xx)	High Dose (N=xx)	ChAdOx1 (N=xx)	mRNA (N=xx)	Total (N=xx)
Number of Events	XX	XX	XX	XX	XX	XX	XX
Number of Participants with any Adverse Event	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Grade 1	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Grade 2	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Grade 3	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Grade 4	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Grade 5	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Grade 3, 4 or 5	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Number of Participants with any Adverse Event of Special Interest	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Number of Participants with any Related Adverse Event	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Number of Participants with any Related Adverse Event	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Grade 1	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Grade 2	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Grade 3	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Grade 4	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Grade 5	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Grade 3, 4 or 5	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Number of Participants with any Serious Adverse Event	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Number of Participants with any Related Serious Adverse Event	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Number of Participants with any Adverse Event Leading to Withdrawal from the Study	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)

Treatment-emergent events are those events with an onset on or after vaccination.
If a participant experiences more than one event, then the event with the worst severity is included in the severity level summarisation.
Event Severity: Grade 1 = Mild, Grade 2 = Moderate, Grade 3 = Severe, Grade 4 = Life Threatening and Grade 5 = Death.
Percentages are based on the number of participants in the safety analysis set.
All COVID-19 vaccinated participants were given the high dose of ChAdOx1-HBV vaccine.

Programming Note(s):
To detect a Participant with an Adverse Event Leading to Withdrawal from the Study, use the study completion page where the Participant(s) withdrew from the study due to an adverse event.

Table 14.3.1.2
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Analysis Set

	Healthy Participants		CHB Participants		Healthy Participants Covid-19 Vaccinated		
System Organ Class/ Preferred Term [1]	Low Dose (N=xx)	High Dose (N=xx)	Low Dose (N=xx)	High Dose (N=xx)	ChAdOx1 (N=xx)	mRNA (N=xx)	Total (N=xx)
Number of Events	XX	XX	XX	XX	XX	XX	XX
Number of Participants with any adverse event	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
System Organ Class 1	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 1	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 2	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
System Organ Class 2	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 1	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 2	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)

Treatment-emergent events are those events with an onset on or after vaccination.
Table shows distinct number of participants with events for each system organ class/preferred term.
Percentages are based on the number of participants in the safety analysis set.
All COVID-19 vaccinated participants were given the high dose of ChAdOx1-HBV vaccine.
[1] MedDRA Version 22.1.

Programming Note(s):
Repeat table for treatment-emergent adverse events of special interest (table 14.3.1.3).
AESIs are flagged (as AESIs) on the study database.
Repeat table for Vaccine-related treatment-emergent adverse events (table 14.3.1.5).

Table 14.3.1.4
Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Severity
Safety Analysis Set

System Organ Class/ Preferred Term [1]/	Healthy Participants		CHB Participants		Healthy Participants Covid-19 Vaccinated		
Severity	Low Dose (N=xx)	High Dose (N=xx)	Low Dose (N=xx)	High Dose (N=xx)	ChAdOx1 (N=xx)	mRNA (N=xx)	Total (N=xx)
System Organ Class 1	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Grade 1	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Grade 2	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Grade 3	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Grade 4	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Grade 5	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Preferred Term 1	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Grade 1	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Grade 2	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Grade 3	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Grade 4	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Grade 5	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)

Treatment-emergent events are those events with an onset on or after vaccination.
This table shows distinct number of participants with events for each system organ class/preferred term/severity.
If a participant experienced a specific event more than once, then the event with the worst severity is summarised.
Event Severity: Grade 1 = Mild, Grade 2 = Moderate, Grade 3 = Severe, Grade 4 = Life Threatening and Grade 5 = Death.
Percentages are based on the number of participants in the safety analysis set.
All COVID-19 vaccinated participants were given the high dose of ChAdOx1-HBV vaccine.
[1] MedDRA Version 22.1.

Table 14.3.2.1
Listing of Participants with Serious Adverse Events
Safety Analysis Set

Cohort/ Participant	Adverse Event (verbatim) / Preferred Term / MedDRA SOC [1]	Start Date (study day) / Stop Date (Study day)	Severity [2]	TE [3] / Serious	Special Interest / Related to Study Drug	Outcome	Treatments Provided
xxxxxxx / xxxx	xxxxxxxxx/ xxxxxx/ xxxxxx	ddmmmyyyy (xx) / ddmmmyyyy (xx)	Grade 1/ Grade 2/ Grade 3/ Grade 4	Yes/No Yes/No	Yes/No Yes/No	xxxxxxx	xxxxxxxxxx

[1] MedDRA Version 22.1.
[2] TE = Treatment-emergent. An adverse event is Treatment-emergent if the start date is on or after the vaccination.

Table 14.3.2.2
Listing of Participants with Adverse Events Directly Resulting in Study Withdrawal
Safety Analysis Set

Cohort/ Participant	Adverse Event (verbatim) / Preferred Term / MedDRA SOC [1]	Start Date (study day) / Stop Date (Study day)	Severity [2]	TE [3] / Serious	Special Interest / Related to Study Drug	Outcome	Treatments Provided
xxxxxxx / xxxx	xxxxxxxxx/ xxxxxx/ xxxxxx	ddmmmyyyy (xx) / ddmmmyyyy (xx)	Grade 1/ Grade 2/ Grade 3/ Grade 4	Yes/No Yes/No	Yes/No Yes/No	xxxxxxx	xxxxxxxxxx

[1] MedDRA Version 22.1.
[2] TE = Treatment-Emergent. An adverse event is treatment-emergent if the start date is on or after vaccination.

Table 14.3.3.1
Local Reactions
Safety Analysis Set

		Healthy Participants		CHB Participants		Healthy Participants Covid-19 Vaccinated		
		Low Dose (N=xx)	High Dose (N=xx)	Low Dose (N=xx)	High Dose (N=xx)	ChAdOx1 (N=xx)	mRNA (N=xx)	Total (N=xx)
Size of Swelling (mm)	N	XX	XX	XX	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Q1, Q3	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Size of Redness (mm)	N	XX	XX	XX	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX, XX
	Q1, Q3	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	
Swelling								
0	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
1	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
2	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
3	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
4	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Redness								
0	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
1	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
2	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
3	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
4	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Pain								
0	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
1	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
2	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
3	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
4	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Warmth								
0	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
1	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
2	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
3	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
4	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)

The distinct number of participants with each local reaction between Day 0 and Day 3 is presented. The reactions on Day 0 are recorded by the investigator, whereas the reactions on Day 1 – Day 3 are recorded by the participant in a diary card.
For each participant, the worst incidence of each local reaction is reported (i.e. the largest swelling/ redness, the most severe pain or warmth). Percentages are based on the number of non-missing observations.
Severity: 0 = None, 1 = No interference with daily activities, 2 = Some interference with daily activities, 3 = Significant interference with daily activities, 4 = ER visit or hospitalization.
All COVID-19 vaccinated participants were given the high dose of ChAdOx1-HBV vaccine.

Table 14.3.3.2
Systemic Reactions
Safety Analysis Set

		Healthy Participants		CHB Participants		Healthy Participants Covid-19 Vaccinated		
		Low Dose (N=xx)	High Dose (N=xx)	Low Dose (N=xx)	High Dose (N=xx)	ChAdOx1 (N=xx)	mRNA (N=xx)	Total (N=xx)
Temperature (C)	N	XX	XX	XX	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Q1, Q3	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Temperature								
0	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
1	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
2	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
3	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
4	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Muscle Ache								
0	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
1	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
2	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
3	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
4	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Fatigue								
0	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
1	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
2	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
3	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
4	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Headache								
0	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
1	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
2	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
3	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
4	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Nausea								
0	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
1	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
2	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
3	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
4	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Feverishness								
0	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
1	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
2	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
3	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
4	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)

Chills								
0	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
1	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
2	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
3	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
4	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Joint ache								
0	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
1	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
2	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
3	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
4	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Malaise								
0	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
1	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
2	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
3	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
4	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)

The distinct number of participants with each local reaction between Day 0 and Day 3 is presented. The reactions on Day 0 are recorded by the investigator, whereas the reactions on Day 1 – Day 3 are recorded by the participant in a diary card.
For each participant, the worst incidence of each systemic reaction is reported (i.e. the highest temperature, the most severe muscle ache, fatigue, headache, nausea or feverishness).
Percentages are based on the number of non-missing observations.
Severity: 0 = None, 1 = No interference with daily activities, 2 = Some interference with daily activities, 3 = Significant interference with daily activities, 4 = ER visit or hospitalization.
All COVID-19 vaccinated participants were given the high dose of ChAdOx1-HBV vaccine.

Table 14.3.3.3
Any Reaction
Safety Analysis Set

		Healthy Participants		CHB Participants		Healthy Participants Covid-19 Vaccinated		
		Low Dose (N=xx)	High Dose (N=xx)	Low Dose (N=xx)	High Dose (N=xx)	ChAdOx1 (N=xx)	mRNA (N=xx)	Total (N=xx)
Any Reaction	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Any Local Reaction	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Swelling	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Redness	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Pain	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Warmth								
Any Systemic Reaction	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Temperature	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Muscle Ache	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Fatigue	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Headache	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Nausea	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Feverishness	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Chills	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Joint Ache	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Malaise	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)

The distinct number of participants who experienced reactions of Grade 1 or higher between Day 0 and Day 3 is presented. The reactions on Day 0 are recorded by the investigator, whereas the reactions on Day 1 – Day 3 are recorded by the participant in a diary card.
Percentages are based on the number of non-missing observations.
All COVID-19 vaccinated participants were given the high dose of ChAdOx1-HBV vaccine.

Table 14.3.4
Shift Summary of Haematology Results by Maximum Toxicity Grade
Safety Analysis Set

	Healthy Participants Low Dose (N=XXX)						
	Maximum Post-baseline Grade						
Lab Parameter Baseline Grade [n (%)]	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total	Missing
Lab parameter 1							
Grade 0	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx	xx
Grade 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx	xx
Grade 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx	xx
Grade 3	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx	xx
Grade 4	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx	xx
Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx	xx
Missing	xx	xx	xx	xx	xx	xx	xx
Lab parameter 2							
Grade 0	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx	xx
Grade 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx	xx
Grade 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx	xx
Grade 3	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx	xx
Grade 4	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx	xx
Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx	xx
Missing	xx	xx	xx	xx	xx	xx	xx
...							

Note: Total is the number of subjects with at least 1 post-baseline result, and percentages are based on the row total.
Note: Baseline is defined as the nearest assessment completed prior to vaccination.

Programming note(s):
(1) The table will have separate pages for each cohort, i.e. Healthy Participants low dose, Healthy Participants high dose, CHB Participants low dose, CHB Participants high dose, Healthy Participants - Covid-19 Vaccinated: ChAdOx1, Healthy Participants - Covid-19 Vaccinated: mRNA.
(2) The "Lab Parameter" is each of the haematology toxicity criteria in Section **Error! Reference source not found.** Note, some laboratory parameters have 2 toxicity criteria (e.g. hyper and hypo)

Table 14.3.5
Shift Summary of Chemistry Results by Maximum Toxicity Grade
Safety Analysis Set

Use the same table shell as for Table 14.3.4, but apply chemistry toxicity criteria instead

Table 14.3.6
Shift Summary of Vital Signs Results by Maximum Toxicity Grade
Safety Analysis Set

Use the same table shell as for Table 14.3.4, but apply vital signs toxicity criteria instead
For temperature only use the temperature recorded as part of the vital signs assessments.

Listing 16.2.1.1
Participant Disposition

Cohort	Participant	Protocol Version Date	Informed Consent Date	CHB Diagnosis Date	Agreed to LFNA	Vaccination Date	Completed Study	Completion / Withdrawal Date (Study Day)	Reason for Withdrawal
xxxxxxx	xxxxxx	ddmmmyyyy	ddmmmyyyy	ddmmmyyyy	Yes/No	ddmmmyyyy	Yes/No	ddmmmyyyy	xxxxxxxxxxxx

CHB = Chronic Hepatitis B Virus Participant, HP = Healthy Participant, LFNA = Liver Fine Needle Aspirate.

Listing 16.2.1.2
Failed Inclusion and Exclusion Criteria

Cohort	Participant	Inclusion/Exclusion Criteria not met
xxxxxxx	xxxxxx	xxxxxxxxxxxxxxxxxxx

Programming note(s):
This listing is not required if no participants fail the criteria.

Listing 16.2.2
Protocol Deviations

Cohort	Participant	Deviations Reported	Date Reported	Start Date (Study Day)	End Date (Study Day)	Deviation Category [a]	Other, Specify	Deviation Details/Comments	Major/Minor
xxxxxxx	xxxxxx	Yes/No	ddmmyyyy	ddmmyyyy (xx)	ddmmyyyy (xx)	xx	xxxx	xxxxxxxxxx	Major/Minor

[1] Deviation categories: 1 = Informed consent procedure. 2 = Inclusion/exclusion criteria. 3 = Visit window. 4 = Study procedure / assessment window. 5 = Concomitant Study procedure / assessment performance. 6 = Missing assessment / sample. 7 = Subject error. 8 = Investigational product, 9 = Concomitant medication / therapy. 8 = SAE reporting. 9 = Randomisation. 10 = Other.

Listing 16.2.3
Analysis Sets

Cohort	Participant	Safety Analysis Set [1]	Per Protocol Analysis Set [2]	Immunogenicity Analysis Set [3]
xxxxxxx	xxxxxx	Yes / No	Yes / No	Yes / No

[1] Safety Analysis Set = all participants who received a vaccination.
[2] Per Protocol (PP) Analysis Set = all participants in the safety analysis set who received the correct study vaccine and who had no major protocol deviations.
[3] The immunogenicity analysis set = all participants in the per-protocol set who have available immunogenicity data to evaluate the immunogenicity endpoints and did not have any major protocol deviations that would impact on the results of the immunological analysis.

Listing 16.2.4.1
Demographics

Cohort	Participant	Age at screening (years)	Sex	Race	Height (cm)	Weight (kg)	BMI (kg/m^2)
xxxxxxx	xxxxxx	xx	Male / Female	xxxxxxxxxx	xxx	xx.xx	xx.xx

Age = Largest Integer ≤ [(date of screening visit – date of birth + 1)/365.25].
BMI (kg/m2) = Weight (kg) / [height (m)]^2.

Listing 16.2.4.2
Reproductive Status and Contraception

Cohort	Participant	Child bearing potential	Methods of Contraception
xxxxxxx	xxxxxx	Yes / No – post menopausal / No – surgically sterile	xxxxxxxxxxxxxx

Programming note(s):
List all methods of contraception indicated.

Listing 16.2.4.3.1
Substance Use: Smoking

Cohort	Participant	Status	End Date	Number per Day [1]	Number of years	Tobacco / Water pipes per week	unit	Number of years
xxxxxxx	xxxxxx	xxxxxxxxxx	ddmmyyyy	xx	xx	xx	oz / g	xx

[1] Number of cigarettes, cigars, spliffs, cigarillos or pipes.

Listing 16.2.4.3.2
Substance Use: Alcohol

Cohort	Participant	Status	Last alcohol drunk date	Units per week
xxxxxxx	xxxxxx	xxxxxx	ddmmmyyyy	xx

Listing 16.2.4.3.3
Substance Use: Recreational Drugs

Cohort	Participant	Status	Last drugs used date	Details
xxxxxxx	xxxxxx	xxxxxx	ddmmmyyyy	xxxxxxxxxxxxxxx

Listing 16.2.4.4
Allergies

Cohort	Participant	Any Allergy	Type	Present	Detail
xxxxxxx	xxxxxx	Yes/No	Drug	Yes/No	xxxxxx
			Food	Yes/No	xxxxxx
			Insect	Yes/No	xxxxxx
			Latex	Yes/No	xxxxxx
			Mould	Yes/No	xxxxxx
			Pet	Yes/No	xxxxxx
			Pollen	Yes/No	xxxxxx
			Other	Yes/No	xxxxxx

Listing 16.2.4.5
Medical History

Cohort	Participant	Medical Condition / Preferred Term [1] / MedDRA SOC	Start Date (Study Day)	End Date (Study Day)	Ongoing	Concomitant medication Taken for this condition?
xxxxxxx	xxxxxx	Xxxxxxxxxx	ddmmyyyy	ddmmyyyy	Yes / No	Yes / No

[1] MedDRA Version 22.1.

Listing 16.2.4.6
Prior and Concomitant Medications

Cohort	Participant	Medication (Verbatim)/ WHO Drug Name [1] / Preferred Name / Drug Class (L2)	Start Date / Time (Study Day)	End Date / Time (Study Day)	Ongoing	Indication	Dose / Dose Units	Freq [2] / Route [3]	P/c [4]
xxxxxxx	xxxxxx	xxxxxxxxx	ddmmyyyy / hh:mm (xx)	ddmmyyyy / hh:mm (xx)	Yes / No	xxxxxx	xxx	xxx / xxx	P / C

[1] WHO Drug Global Version 2019:3, September 1, 2019. L2: The second level of Anatomical Therapeutic Chemical (ATC) classification.
[2] QD = Once a day, BD = Twice a day, PRN = As needed, TDS = Three times a day, QDS = Four times a day.
[3] PO = oral, TOP = topical, PRN = Take as needed.
[4] P=Prior to vaccine, C=Concomitant with vaccine.

If the medication stop date is before the vaccination date, the medication will be assigned as being prior to vaccine. In all other cases, the medication is assigned as being concomitant with vaccine treatment.

* = Estimated date/time

Programming Notes: concatenate * to end of start and/or stop date if they are estimated.
update footnotes 2 and 3 to reflect codes used in actual data

Listing 16.2.5
Vaccination Administration

Cohort	Participant	Vaccine administered?	Date/time administered	If no, Reason not done	Time removed from freezer	Vial number / Batch number / Expiry Date	Dose given	Location	First Participant	Observed for required time [1]
xxxxxxx	xxxxxx	Yes/No	ddmmmyyyy hh:mm	xxxxxxx	hh:mm	xxxxx/ xxxxx / ddmmmyyyy	xxxx	xxxxxxx	Yes/No	Yes/No

[1] The required time is 60 minutes for the first participant of each cohort and 30 minutes for all others.

Listing 16.2.6.1.1
Local and Systemic Reactions

Cohort	Participant	Vaccination Date / Time (Study Day)	Reaction	Day 0 Pre	Day 0 Post	Day 1	Day 2	Day 3
xxxxxxx	xxxxxx	ddmmyyyy / hh:mm (xx)	Date	ddmmmyyyy	ddmmmyyyy	ddmmmyyyy	ddmmmyyyy	ddmmmyyyy
			Time	hh:mm	hh:mm	hh:mm	hh:mm	hh:mm
			Temperature (C)	xx.x	xx.x	xx.x	xx.x	xx.x
			Injection site swelling	yes/no	yes/no	yes/no	yes/no	yes/no
			Size of swelling (mm)	xx.x	xx.x	xx.x	xx.x	xx.x
			Injection site redness	yes/no	yes/no	yes/no	yes/no	yes/no
			Size of redness (mm)	xx.x	xx.x	xx.x	xx.x	xx.x
			Pain (at injection site)	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4
			Warmth (at injection site)	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4
			Muscle ache	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4
			Tiredness	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4
			Headache	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4
			Nausea	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4
			Feverishness	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4
			Chills	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4
			Joint ache	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4
			Generally feeling unwell	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4	0/1/2/3/4
			Medication Taken	yes/no	yes/no	yes/no	yes/no	yes/no
			Visit to A&E	yes/no	yes/no	yes/no	yes/no	yes/no

* = indicates worst post-baseline incidence/highest value
All local and systemic reactions recorded on Day 0 (pre and post) are as recorded by the investigator. The reactions recorded Day 1 to day 3 are recorded by the participant in a diary card.
Severity: 0 = None, 1 = No interference with daily activities, 2 = Some interference with daily activities, 3 = Significant interference with daily activities, 4 = ER visit or hospitalization.
Medication Taken and Visit to A&E are yes if these were recorded as such for any symptom at the specific timepoint.

Programming note: place a "*" against the worst post-baseline incidence/highest value for each reaction for each participant, in the event of a tie the first one should be flagged. If all 0 then none should be flagged
Programming note: The numeric grade should be displayed in the listing.

Listing 16.2.6.1.2
Diary Card: Medications Taken

Cohort	Participant	Study Day	Date/time	Symptom(s)	Medication Taken	Medication Name	Dose taken (units)	Number of times taken	Additional symptoms this medication refers to
xxxxxxx	xxxxxx	0/1/2/3	ddmmmyyyy hh:mm	xxxxxx	xxxxx	xxxxxxx	xxxxx	xx	xxxxx

Programming Note: Only display details for the days on which medication was taken. If no medication taken throughout then this listing will be empty
Programming Note: Symptoms should list all of the symptoms that this medication was listed against on the specific day it was taken.

Listing 16.2.6.2
HBV Disease Markers

Cohort	Participant	Visit	Date/time	Parameter	Result	Comments
xxxxxxx	xxxxxx	Day x	ddmmyyyy / hh:mm	HBV DNA		
				HBV pgRNA		
				Hepatitis B surface Antibody		
				Hepatitis B surface Antigen		
				Hepatitis B core Antibody		
				Hepatitis B core Antigen		
				Hepatitis B e Antibody		
				Hepatitis B e Antigen		
				Multi-parameter index		
				HBeAg loss		
				HBsAg loss		
				HbeAg and HBsAg seroconversion		

Programming Note: The parameters will not be available for all participants at all visits. For healthy participants we should only expect hepatitis B surface antigen, hepatitis B surface antibody and hepatitis B core antibody.

Listing 16.2.6.3
ELISpot

Cohort	Participant	Visit	Date	Lab Test	Sample	IFNg SFC/10^6 PBMC Raw Data	IFNg SFC/10^6 PBMC Background Corrected
xxxxxxx	xxxxxx	Day x	ddmmyyyy	Genotype C/ Control	xxx	xx	xx

Listing 16.2.6.4
ICS

Cohort	Participant	Visit	Date	Lab Test	Stimulating Condition	Sample	Result
xxxxxxx	xxxxxx	Day x	ddmmyyyy	Genotype C/ Genotype D	xxxxx	%CD4_CD154 %CD4_IFNg %CD4_IFNg+IL2 %CD4_IFNg+TNFa %CD4_IFNg+TNFa+ IL2 %CD4_IL2 %CD4_IL2+TNFa %CD4_TNFa %CD8_CD107a %CD8_IFNg %CD8_IFNg+IL2 %CD8_IFNg+TNFa %CD8_IFNg+TNFa+ IL2 %CD8_IL2 %CD8_IL2+TNFa %CD8_TNFa CD4_CD107a MFI CD4_IFNg MFI CD4_IL2 MFI CD4_TNFa MFI CD8_CD107a MFI CD8_IFNg MFI CD8_IL2 MFI CD8_TNFa MFI	xxx

Listing 16.2.6.5
Neutralising Antibody Sample Collection

Cohort	Participant	Visit	Date	Time
xxxxxxx	xxxxxx	Day x	ddmmyyyy	

Listing 16.2.7
Adverse Events

Cohort/ Participant	Adverse Event (verbatim) / Preferred Term / MedDRA SOC [1]	Start Date (Study day) / Stop Date (Study day)	Severity [2]	TE [3] / Serious	Special Interest / Related to Study Drug	Outcome	Treatments Provided
xxxxxxx / xxxx	xxxxxxxxx/ xxxxxx/ xxxxxx	ddmmmyyyy (xx) / ddmmmyyyy (xx)	Grade 1/ Grade 2/ Grade 3/ Grade 4	Yes/No Yes/No	Yes/No Yes/No	xxxxxxx	xxxxxxxxxx

[1] MedDRA Version 22.1.
[2] Event Severity: Grade 1 = Mild, Grade 2 = Moderate, Grade 3 = Severe, Grade 4 = Life Threatening and Grade 5 = Death.
[3] TE = Treatment Emergent. An event is considered vaccine-emergent if the start date of the adverse event is on or after vaccination.

Programming note(s):
Only participants with AEs will be shown in this listing.

Listing 16.2.8.1
Haematology

Parameter	Cohort	Participant	Study Day	Date	Standard Result	Unit	Range Low	Range High	Clin Sig.	Flag	Toxicity Criteria	Toxicity Grade
xxxx	xxxxxxx	xxxxxx	xxxx	ddmmyyyy	xx.x	xx	xx.x	xx.x	Yes/No	H/L	xxxxx	x

= Baseline grade.
* = Maximum post-baseline grade.

Programming Note(s):
List by parameter first, then subject and then day/date.
If more than one Toxicity criteria apply to a laboratory parameter (e.g. hyper and hypo) then list them all.
Include all data collected, including any unscheduled data.
If there is a tie for the maximum post-baseline result then all should be flagged.

Repeat for the following listing:
16.2.8.2 Chemistry (including Liver Function Tests).

Listing 16.2.8.3
Urinalysis

Parameter	Cohort	Participant	Study Day	Date	Original Result	Unit	Standard Result	Unit	Toxicity Criteria	Toxicity Grade
xxxxxxx		xxxxxx	xxxx	ddmmyyyy						

Listing 16.2.8.4
HIV, HCV and HDV Serology

Cohort	Participant	Visit	Date/time	HCV Antibody	HIV Antibody	HDV Antibody
xxxxxxx	xxxxxx	xxxx	ddmmyyyy hh:mm	Detected/Not Detected	Detected/Not Detected	Detected/Not Detected

Listing 16.2.8.5
Urine Pregnancy Test

Cohort	Participant	Visit	Date	Result	Comments
xxxxxxx	xxxxxx	xxxx	ddmmyyyy	Positive / Negative	xxxxxxxxxxxxxxxxx

Listing 16.2.9
Vital Signs

Parameter	Cohort	Participant	Visit	Date	Time Started Sitting	Collection Time	Result	Unit	Toxicity Criteria	Toxicity Grade
Temperature	xxxxxxx	xxxxxx	xxxx	ddmmyyyy	hh:mm	hh:mm	xx.xx	xx	xxx	x

= Baseline grade.
* = Maximum post-baseline grade.

Programming Note(s):
List by parameter first, then subject and then day/date.
If more than one Toxicity criteria apply to a laboratory parameter (e.g. hyper and hypo) then list them all.
Include all data collected, including any unscheduled data.
If there is a tie for the maximum post-baseline result then all should be flagged.

Listing 16.2.10
Physical Examination

Cohort	Participant	Visit	Date	Body System	Finding	Comments
xxxxxxx	xxxxxx	xxxx	ddmmmyyyy	Skin Respiratory Cardiovascular Abdominal Lymphatic	Normal / Abnormal Not Clinically Significant / Abnormal Clinically Significant / Not Done	xxxxxxx

A complete physical examination was performed at screening and Day 0 (prior to vaccination). Directed physical examinations were performed as required at each follow-up visits

Programming note(s):
Include complete and directed physical examinations.
Only body systems reported are included for directed physical examinations.

Listing 16.2.11
Visit Dates

Cohort	Participant	Visit	Date	Source of Unscheduled Visit	Reason for unscheduled visit	Comments
xxxxxxx	xxxxxx	xxxx	ddmmyyyy	xxxxxxxxxx		xxxxxxxxxxxx

Listing 16.2.12
Covid-19 Vaccination

Cohort	Participant	Vaccination Type(1 and 2)	Date of Vaccination 1	Date of Vaccination 2	Vaccination Type (3)	Date of Vaccination 3
xxxxxxx	xxxxxx	xxxx	ddmmyyyy	ddmmyyyy	xxxx	ddmmyyyy

15.APPENDICES

15.1. Appendix 1: Toxicity Grade Criteria for Lab Parameters

Table 2: Toxicity Grade Criteria for Values Below Normal Range (Chemistry)

	LOW			
Analyte	**1**	**2**	**3**	**4**
Sodium (Hyponatremia)	132-134	130-131	125-129	<125
Potassium (Hypokalemia)	3.5-3.6	3.3-3.4	3.1-3.2	<3.1
Albumin (Hypoalbuminemia)	2.8-3.1	2.5-2.7	<2.5	N/A
Glucose (Hypoglycemia)	65-69	55-64	45-54	<45

Table 3:Toxicity Grade Criteria for Values Above Normal Range (Chemistry)

	HIGH			
Analyte	**1**	**2**	**3**	**4**
Sodium (Hypernatremia)	144-145	146-147	148-150	>150
Potassium (Hyperkalemia)	5.1-5.2	5.3-5.4	5.5-5.6	>5.6
BUN	23-26	27-31	>31	
Creatinine	1.5-1.7	1.8-2.0	2.1-2.5	>2.5
Total Bilirubin if normal ASL-AST	1.1-1.5*ULN	1.6-2.0*ULN	2.0-3.0*ULN	>3.0*ULN
Total Bilirubin if AST/ ALT elevated	1.1-1.25*ULN	1.26-1.5*ULN	1.51-1.75*ULN	>1.75*ULN
ALP	1.1-2.0*ULN	2.1-3.0*ULN	3.1-10*ULN	>10*ULN
AST	1.1-2.5*ULN	2.6-5.0*ULN	5.1-10*ULN	>10*ULN
ALT	1.1-2.5*ULN	2.6-5.0*ULN	5.1-10*ULN	>10*ULN

Table 4: Toxicity Grade Criteria for Values Below Normal Range (Haematology)

	LOW			
Analyte	**1**	**2**	**3**	**4**
Haemoglobin (Female)	11.0-12.0	9.5-10.9	8.0-9.4	<8.0
Haemoglobin (Male)	12.5-13.5	10.5-12.4	8.5-10.4	<8.5
Platelets	125-140	100-124	25-99	<25
WBC	2.5-3.5	1.5-2.49	1.0-1.49	<1.0
Neutrophils	1.5-2.0	1.0-1.49	0.5-0.99	<0.5
Lymphocytes	0.75-1.0	0.74-0.5	0.25-0.49	<0.25

Table 5: Toxicity Grade Criteria for Values Above Normal Range (Haematology)

	HIGH			
Analyte	**1**	**2**	**3**	**4**
WBC	10.8-15.0	15.1-20.0	20.1-25.0	>25.0
Eosinophils	0.6-1.5	1.51-5.0	>5.0	N/A

Table 6: Toxicity Grade Criteria for Values Outside Normal Range (Coagulation)

	LOW			
Analyte	**1**	**2**	**3**	**4**
Prothrombin time	1.0-1.10*ULN	1.11-1.20*ULN	1.21-1.25*ULN	>1.25*ULN
PTT	1.0-1.2*ULN	1.21-1.4*ULN	1.41-1.5*ULN	>1.5*ULN
Fibrinogen (above normal)	150-200	125-149	100-124	<100
Fibrinogen (below normal)	400-500	501-600	>600	N/A

Table 7: Toxicity Grade Criteria for Values Outside Normal Range (Urinalysis)

	LOW			
Analyte	**1**	**2**	**3**	**4**
Protein	Trace	1+	2+	Hospitalisation or dialysis
Glucose	Trace	1+	2+	Hospitalisation or hyperglycaemia

15.2. Appendix 2: Toxicity Grade Criteria For Vital Signs

Table 8: Toxicity Grade Criteria for Vital Signs

Vital Signs	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life-threatening (Grade 4)
Fever (°C) (°F)	38.0 – 38.4 100.4 – 101.1	38.5 – 38.9 101.2 – 102.0	39.0 – 40 102.1 – 104	> 40 > 104
Tachycardia – beats per minute	101 – 115	116 – 130	> 130	ER visit or hospitalization for arrhythmia
Bradycardia – beats per minute	50 – 54	45 – 49	< 45	ER visit or hospitalization for arrhythmia
Hypertension (systolic) – mm Hg	141 – 150	151 – 155	> 155	ER visit or hospitalization for malignant hypertension
Hypertension (diastolic) – mm Hg	91 – 95	96 – 100	> 100	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	17 – 20	21 – 25	> 25	Intubation