STATISTICAL ANALYSIS PLAN

VERSION 01.00, 29OCT2021

A dose finding human experimental infection study in healthy subjects using a GMP-produced SARS-COV-2 wild type strain (SARS-CoV-2 Characterisation Study)

Sponsor Protocol Number: 20IC6437

hVIVO Protocol Number: HVO-vCS-003

Prepared by: S-cubed Biometrics Ltd.

For: hVIVO Services Limited (hVIVO)

Sponsor: Imperial College London

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3. LIST OF ABBREVIATIONS

Abbreviation	Definition
ADCC	Antibody-Dependent Cellular Cytotoxicity
AE	Adverse Event
ALP	Alkaline Phosphatase
ALT	Alanine Aminotransferase
APTT	Activated Partial Thromboplastin Time
AST	Aspartate Aminotransferase
AST	Aspartate Transaminase
AUC	Area Under the Curve
BP	Blood Pressure
BD	Twice Daily
BMI	Body Mass Index
CK	Creatine Kinase
CI	Chief Investigator
CI	Confidence Interval
CMI	Cell Mediated Immunity
CRF	Case Report Form
CRP	C-reactive Protein
COVID-19	Coronavirus Disease 19
DBP	Diastolic blood pressure
DNA	Deoxyribonucleic acid
DP	Decimal Places
DRM	Data review meeting
DSMB	Data Safety Monitoring Board
ECG	Electrocardiogram
ELISA	Enzyme-linked Immunosorbent Assay
EOS	End of Study
FAS	Full Analysis Set
FEV	Forced Expiratory Volume
FEV1	Forced Expiratory Volume in One Second
FI	Febrile Illness
FOT	Forced oscillation technique
FSH	Follicle Stimulating Hormone
FVC	Forced Vital Capacity
GGT	Gamma Glutamyl Transferase
GM	Geometric Mean
GMP	Good Manufacturing Practice
GP	General Practitioner
HAV	Hepatitis A
HbA1c	Haemoglobin A1c
HBV	Hepatitis B

HCV	Hepatitis C
HIV	Human Immunodeficiency Virus
HVC	Human Viral Challenge
HRA	Health Research Authority
ICF	Inform Consent Form
IgA	Immunoglobulin A
IgG	Immunoglobulin G
IgM	Immunoglobulin M
INR	International normalised ratio
LDH	Lactate Dehydrogenase
LLOD	Lower Limit of Detection
LLOQ	Lower Limit of Quantification
LRT	Lower Respiratory Tract
LRTI	Lower Respiratory Tract Illness
LSLV	Last Subject Last visit
MCH	Mean Corpuscular Haemoglobin
MCHC	Mean Corpuscular Haemoglobin Concentration
MCID	Minimal Clinically Important Difference
MCV	Mean Corpuscular Volume
MedDRA	Medical Dictionary for Regulatory Activities
NPS	Nasopharyngeal Swab
PBMC	Peripheral Blood Mononuclear Cell
PCR	Polymerase Chain Reaction
PD	Protocol Deviation
PE	Physical Examination
PEF	Peak Expiratory Flow
PFU	Plaque Forming Unit
PHQ	Patient Health Questionnaire
PI	Principal Investigator
PIS	Patient Information Sheet
PP	Per Protocol
PT	Prothrombin Time
PT	Preferred Term
Q1	Lower Quartile
Q3	Upper Quartile
QDS	Four Times Daily
qRT-PCR	Quantitative Reverse Transcriptase-Polymerase Chain Reaction
RBC	Red Blood Cell
REC	Research Ethics Committee
RNA	Ribonucleic acid
RT-PCR	Reverse Transcriptase-Polymerase Chain Reaction
SARS-COV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SAE	Serious Adverse Event

SAP	Statistical Analysis Plan
SAS	Safety Analysis Set
SBP	Systolic blood pressure
SD	Standard Deviation
SE	Standard Error
SI	Systemic Illness
SoA	Schedule of Activities
SOC	System Organ Class
SOP	Standard Operating Procedure
SpO2	Peripheral arterial oxygen saturation
T	Troponin
TCID50	50% Tissue Culture Infective Dose
TDS	Three Times Daily
TFL	Tables Figures Listings
TSH	Thyroid Stimulating Hormone
TSS	Total Symptoms Score
ULOQ	Upper Limit of Quantification
UPSIT	University of Pennsylvania smell identification test
URT	Upper Respiratory Tract
URTI	Upper Respiratory Tract Illness
VAS	Visual Analogue Scale
VE	Viral Challenge Emergent
VL	Viral Load
WBC	White Blood Cell
WHO	Word Health Organisation

4. INTRODUCTION

This statistical analysis plan (SAP) explains in detail the statistical analyses that will performed for the HVO-vCS-003 Covid Characterisation study. The analysis is outlined within the study protocol (v3.0, dated 08 Feb 2021) and amendments (v4.0, dated 24 Feb 2021, v5.0, dated 11 Mar 2021, v6.0, dated 20 May 2021), and this SAP contains a more technical and detailed description of those analyses. Information is provided on the definitions of the subject 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 databased is locked.

Two analyses will be conducted (after their respective database locks): The Primary (Day 28) Analysis after all subjects have reached the Day 28 follow up, and a Final Analysis at the end of the Day 360 follow-up. This SAP provides a detailed description of the analyses that will be computed at the time of each analysis and has been written and finalised before the database lock for the Primary (Day 28) Analysis. A Data Review Meeting (DRM) will be conducted prior to the Primary (Day 28) Analysis.

The final CSR will be written after the Final analysis, and will contain the final analyses of the study endpoints for both the Primary analysis and the Final analysis. If the data for some of the tertiary endpoints become available at a later stage, (an) additional analysis/analyses may be performed. These analyses may be documented separately to the CSR and may be made available at that time.

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

5. STUDY OBJECTIVES

This study is intended to develop the first human challenge model for wild-type SARS-CoV-2 virus infection in healthy human subjects.

A prospective open label dose escalation study in healthy subjects to establish the safety and identify the infectious dose of SARS CoV-2 challenge virus needed to induce infection and active viral replication in ≥50% of subjects (ideally between 50% to 70%) with minimal or no disease in healthy young adults after intranasal inoculation.

The study will comprehensively describe the attack rate, host immune responses, viral kinetics and clinical disease induced by pre-emptively treated infection in this model.

5.1. Primary Objective

The primary objective is to identify a safe and infectious dose of wild type SARS-CoV-2 in healthy volunteers, suitable for future intervention studies.

5.2. Secondary Objectives

- To further assess SARS-CoV-2 viral infection rates in upper respiratory samples in healthy volunteers, by inoculum dose
- To assess the incidence of symptomatic SARS-CoV-2 infection, in healthy volunteers, by inoculum dose
- To assess the SARS-CoV-2 viral dynamics in upper respiratory samples (AUC, peak, duration, incubation period) in healthy volunteers, by inoculum dose
- To assess the SARS-CoV-2 induced symptoms, in healthy volunteers, by inoculum dose
- To assess the incidence of SARS-CoV-2 illness, in healthy volunteers, by inoculum dose

5.3. Tertiary Objectives

- To explore the safety of wild type SARS-CoV-2 human challenge model in healthy adults
- To explore the SARS-CoV-2 viral infection rates in saliva in healthy volunteers, by inoculum dose
- To explore the SARS-CoV-2 viral dynamics in saliva in healthy volunteers, by inoculum dose
- To explore the host-pathogen relationship in the SARS-CoV-2 human challenge model in healthy adults
- To explore the Minimal Clinically Important Difference (MCID) in instrument change
- To explore environmental contamination in the SARS-CoV-2 human challenge model in healthy adults

6. STUDY DESIGN

6.1. Overall Design

This is a dose optimisation study in which increasing doses of wild-type SARS-CoV-2 ($1x10^1$ $TCID_{50}$, $1x10^2$ $TCID_{50}$ and $1x10^3$ $TCID_{50}$ or higher, as necessary) will be given via nasal administration to different groups of volunteers to achieve a ≥50% attack rate (ideally between 50% and 70%), as determined by positive qPCR detection (viral load ≥LLOQ) in respiratory secretions (mid-turbinate samples and/or throat samples) at two consecutive 12 hourly time points.

For initiation of each new dose level, up to 10 subjects will be included in the first cohort, with a sentinel group of 3 subjects initially assessed for safety and infectivity by the investigators, before proceeding with subsequent inoculations. See Figure 1 below for further details on the dose escalation/de-escalation scheme.

A Data Safety Monitoring Board will review safety and quantitative virology after each cohort and will recommend continuation, dose escalation or de-escalation based on emergent data. A Trial Steering Committee (also known as the Medical Oversight Committee) will provide overall supervision of the project.

Subjects may be given SARS-CoV-2 intervention treatment, depending on the stage of the study.

Initially, subjects, upon evidence of infection, will be treated with a pre-emptive antiviral IV Remdesivir for five days.

Subsequent cohorts, may include one of the following treatment plans:

- Pre-emptive therapy, upon evidence of infection (Remdesivir),
- Early “rescue” therapy, once disease progression criteria are met.
- No pre-emptive or “rescue” therapy

Alternative treatments may be included that have shown compelling evidence of efficacy against SARS-CoV-2, if available, such as the IV REGEN-COV monoclonal antibody cocktail.

Decisions on treatment plans for cohorts of subjects will be made by the CI/PI, and in discussion with the DSMB.

Subjects will remain in quarantine for a minimum of 14 days in a quarantine clinical trials unit (from inoculation), and until these criteria are met:

- For subjects with evidence of infection:
  - Two consecutive swabs with qPCR Ct >33.5 AND negative culture.
  - Lateral flow tests may be used in place of culture, if culture data is not available.
  - A qualitative PCR may be used in place of quantitative PCR, if the latter is not available.
  - At the PI’s discretion if protracted quarantine is deemed to be causing harm to the participant’s mental or physical health and no viable virus is detected by culture or a lateral flow test is negative.
- For non-infected subjects:

- 2 consecutive swabs with undetectable virus by PCR only prior to discharge.

Specific procedures to be performed during the study, as well as their prescribed time points and associated visit windows, are outlined in the protocol Schedule of Assessments (Table 1). Details of each assessment and procedure are provided in Section 5 of the protocol. In summary, subjects will be admitted to the quarantine unit on Day -2, challenged with virus on Day 0 and remain in quarantine until at least Day 14 (which may be extended if the criteria above are not met). Following discharge from quarantine, subjects will return for follow-up visits at Day 28, 90, 180, 270 and 360.

The study will involve dose escalation of SARS-CoV-2 to demonstrate safety and identify an optimum dose in participants with no evidence of previous SARS-CoV-2 infection including no detectable antibodies. Groups of up to 20 individuals will be challenged at a time as shown in Figure 1

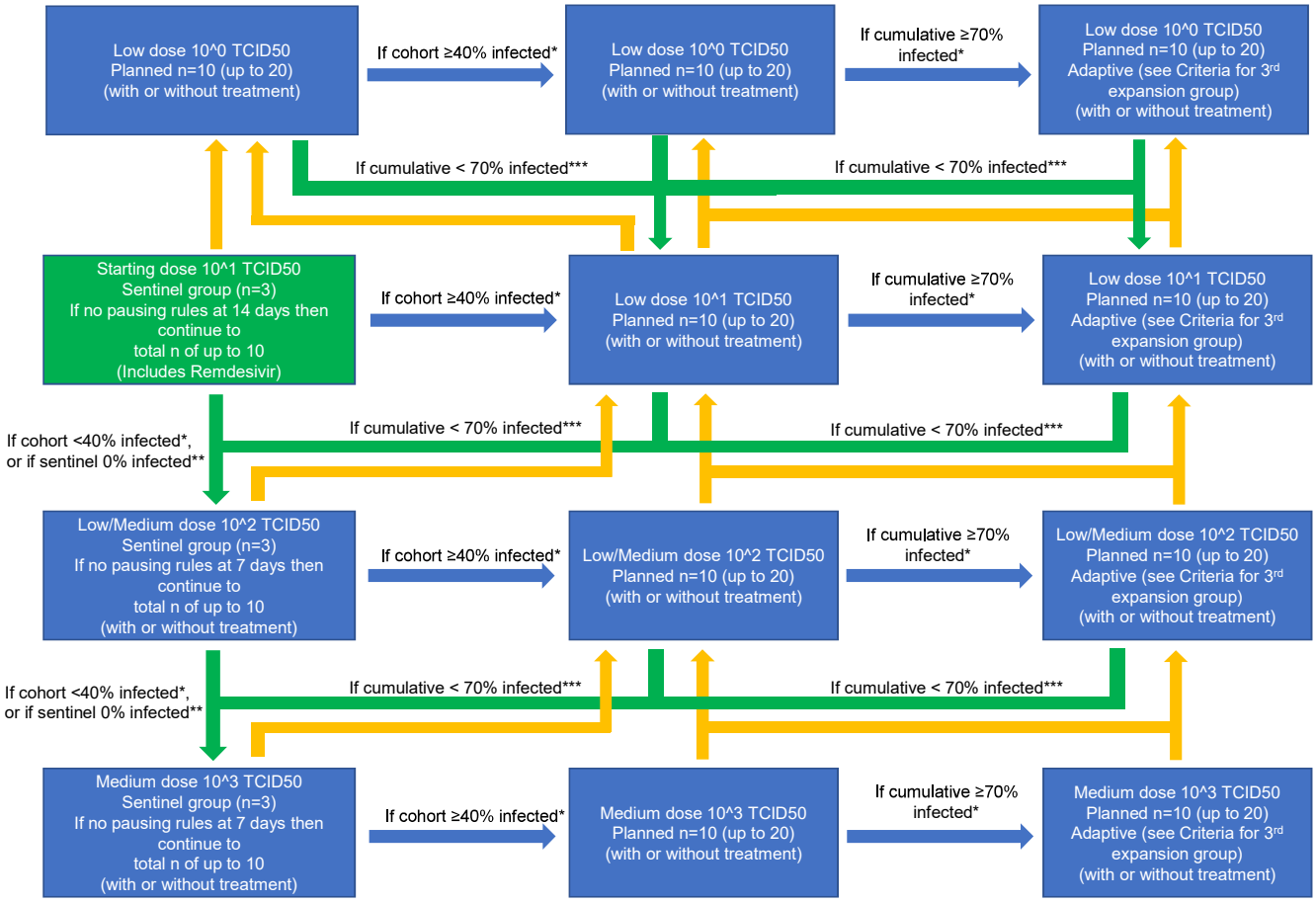

Figure 1: Group and Dose Escalation Scheme

*Next inoculation ~1 week from last participant discharge (minimum 2 weeks of data), if agreed by DSMB, unless symptoms or investigations of concern by CI/PI.
**If no infections in sentinel participants, progress to next dose level (Low dose requires a minimum of 14 days data, higher doses require a minimum of 7 days data).

***If cumulative infection rate of all participants challenged at that dose level is <70%, the CI/PI may choose to progress to the next dose level ~1 week from last participant discharge (minimum 2 weeks of data), if agreed by DSMB, unless symptoms or investigations of concern by CI/PI.

Confirmation (**blue arrow**) of the same dose will occur if the following criteria are met (and in agreement with the DSMB):

- *Safety criteria*:
  - No safety concerns identified at dose level
  - Removal/addition of Remdesivir treatment in expanded cohorts will be decided upon after data review, and in agreement with the DSMB
  - Additional expansion cohorts may be performed.
- *Infectivity/disease criteria*: If the infection criteria **is** met (i.e. ≥40% or ≥70%, as appropriate)*,* **and**
  - <2 infected participants present with any grade 3 symptom of wheeze, shortness of breath, or chest tightness* **and**
  - <2 infected participants have grade 3 physician findings (DPE signs) of abnormal breath sounds (new wheezing, râles, rhonchi, other)

Escalation (**green arrow**) may be performed if **both** of the following criteria are met (and in agreement with the DSMB):

- *Safety criteria:* No safety concerns identified at dose level
- *Infectivity/disease criteria:* If the infection criteria **is not** met (i.e. <40% or <70% as appropriate)*,* **and**
  - <2 infected participants present with any grade 3 symptom of wheeze, shortness of breath, or chest tightness* **and**
  - <2 infected participants have grade 3 physician findings (DPE signs) of abnormal breath sounds (new wheezing, râles, rhonchi, other)

De-escalation (**orange arrow**) may be performed if **either** of the following criteria are met (and in agreement with the DSMB):

- *Safety criteria*:
  - Safety concerns are identified at the dose level, but that do not fulfil study stopping criteria
  - Removal/addition of Remdesivir treatment in expanded cohorts will be decided upon after data review, and in agreement with the DSMB
- *Infectivity/disease criteria*: no infectivity requirement, and
  - ≥2 infected participants present with grade 3 symptoms of wheeze, shortness of breath, or chest tightness * **or**
  - ≥ 2 infected participants have grade 3 physician findings (DPE signs) of abnormal breath sounds (new wheezing, râles, rhonchi, other)

6.2. Randomisation / Treatment Allocation and Blinding

There is no randomisation in this study. There is also no blinding within this study.

6.3. Time and Events Schedule

Table 1: Schedule of Activities

Study Phase	Screening	Inpatient Quarantine																		Extended stay days	Day 15. - 27	Day 28 (+/- 3 days)	Day 90 (+/- 7 days)	Day 180 (+/- 14 days)	Day 270 (+/- 14 days)	Day 360 (+/- 14 days)	Early withdrawal
Study Day	Day -90 to Day -3	D-2	D-1	Day 0 Pre	D0 Challenge	Day 0 Post	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	D14								
Written consent	X*	X																										
Eligibility criteria (+)	X	X[k*]		X																								
Medical & medication history	X																											
Change in medical and medication history		X																				X	X	X	X	X	X
Demographics	X																											
Height & weight, BMI (a)	X	X[k]																										
Patient Health Questionnaire (PHQ-9)	(X)	X[k]																	X		X[W]							
Generalised Anxiety Disorder Questionnaire (GAD-7)	(X)	X[k]																	X		X[W]							
Alcohol breath test	X	X[k]																					X			X	X
Urinalysis	X	X[k]								X			X		X					X			X	X	X	X	X	X

Study Phase		Inpatient Quarantine																								
Study Day	Screening Day -90 to Day -3	D-2	D-1	Day 0 Pre	D0 Challenge	Day 0 Post	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	D14	Extended stay days	Day 15. - 27	Day 28 (+/- 3 days)	Day 90 (+/- 7 days)	Day 180 (+/- 14 days)	Day 270 (+/- 14 days)	Day 360 (+/- 14 days)	Early withdrawal
Urine drugs of abuse & nicotine screen	X	X[k]																					X				X	X
Urine pregnancy test	X			X																X			X				X	X
Complete physical examination	X	X[k]								X			X		X					X	(X)[W]		X	X	X	X	X	X
Directed physical examination (inc nasal)				X		X	X	X	X		X	X		X		X	X	X	X		X							
Vital signs (HR, RR, SBP, DBP, SpO_2 (b) (n)	X	(X)	QDS	QDS			QDS	QDS	QDS	QDS	QDS	QDS	QDS	QDS	QDS	QDS	QDS	QDS	QDS	QDS[x]	QDS[x]		X	X	X	X	X	X
Tympanic temperature (n)	X	(X)	QDS	QDS			QDS	QDS	QDS	QDS	QDS	QDS	QDS	QDS	QDS	QDS	QDS	QDS	QDS	QDS[x]	QDS[x]		X	X	X	X	X	X
Symptom diary cards		(X)	TDS	TDS			TDS	TDS	TDS	TDS	TDS	TDS	TDS	TDS	TDS	TDS	TDS	TDS	TDS	TDS[x]	TDS[x]							
Smell Test (UPSIT)			X[u]				X[u]			X[u]			X[u]			X[u]			X[u]		(X)		X[u]	X[u]	X[u]	X[u]	X[u]	
Cognitive Tests			X[v]	X[v]			X[v]	X[v]	X[v]	X[v]	X[v]	X[v]	X[v]	X[v]	X[v]	X[v]	X[v]	X[v]	X[v]	X[v]			X[v]	X[v]	X[v]	X[v]	X[v]	
Chest X-ray		X[k]																										
Lung CT scan											X[0]	X[0]				X[0]	X[0]											
Echo (p)		X[k]																										
12-lead ECG (n)	X	X[k]		X			X	X	X	X	X	X	X	X	X	X	X	X	X	X	(X)		X	X	X	X	X	X
Spirometry (c)	X	X[k]		X			X	X	X	X	X	X	X	X	X	X	X	X	X	X	(X)		X	X	X	X	X	X

Study Phase		Inpatient Quarantine																							
Study Day	Screening Day -90 to Day -3	D-2	D-1	Day 0 Pre	D0 Challenge	Day 0 Post	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	D14	Extended stay days	Day 15. - 27	Day 28 (+/- 3 days)	Day 90 (+/- 7 days)	Day 180 (+/- 14 days)	Day 270 (+/- 14 days)	Day 360 (+/- 14 days)	Early withdrawal
FOT (c)		X[k]		X			X	X	X	X	X	X	X	X	X	X	X	X	X	X	(X)		X	X	X	X	X	X
Telephone calls(r)																						X						
Product Administration																												
Challenge Virus inoculation					X																							
Administration of SARS-CoV-2 intervention treatment									(X) [y]																			
Collection of blood samples																												
Serum β-HCG pregnancy test (all females) (e)		X[k*]																										
HIV, Hepatitis A, B, & C	X	X[k]																										
Thyroid function test	X	X[k]																										
Coagulation (including d-dimer)	X	X[k]					X	X	X	X	X	X	X	X	X	X	X	X	X	X	(X)		X	X	X	X	X	X
Haematology (f)	X	X[k]		X			X	X	X	X	X	X	X	X	X	X	X	X	X	X	(X)		X	X	X	X	X	X
Biochemistry	X	X[k]					X	X	X	X	X	X	X	X	X	X	X	X	X	X	(X)		X	X	X	X	X	X
Cardiac enzymes (including high sensitivity Troponin)	X	X[k]					X	X	X	X	X	X	X	X	X	X	X	X	X	X	(X)		X	X	X	X	X	X

Study Phase		Inpatient Quarantine																							
Study Day	Screening Day -90 to Day -3	D-2	D-1	Day 0 Pre	D0 Challenge	Day 0 Post	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	D14	Extended stay days	Day 15. - 27	Day 28 (+/- 3 days)	Day 90 (+/- 7 days)	Day 180 (+/- 14 days)	Day 270 (+/- 14 days)	Day 360 (+/- 14 days)	Early withdrawal
Blood - Antibodies SARS-CoV-2	X		X[k]																	X			X	X	X	X	X	X
Blood - plasma markers (h) (g)			X[k]	X			X	X	X	X	X	X	X	X	X	X	X	X	X	X			X	X	X	X	X	
Blood paxgene RNA			X[k]	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X			X	X	X	X	X	
Blood Lithium Heparin – PBMCs, other blood cells, +/- plasma			X[k]						X				X			X				X			X	X	X	X	X	
Collection of respiratory and environmental. Samples																													
Nasopharyngeal swab-Respiratory pathogen screen - e.g. Biofire (i)	(X)	X	(X)[m]																									
Nasopharyngeal swab-tolerance test	X																											
Nasosorption – immunology & virology (q)			BD	X		X	BD	BD	BD	BD	BD	BD	BD	BD	BD	BD	BD	BD	BD	BD[x]	BD[x]		X	X	X	X	X	X
Saliva-virology (j) (g)			X				BD	BD	BD	BD	BD	BD	BD	BD	BD	BD	BD	BD	BD	BD[x]	BD[x]		X					X
Throat FLOQ swab - Virology (j) (g)			X				BD	BD	BD	BD	BD	BD	BD	BD	BD	BD	BD	BD	BD	BD[x]	BD[x]		X	(X)	(X)			X

Study Phase	Screening	Inpatient Quarantine																		Extended stay days	Day 15. - 27	Day 28 (+/- 3 days)	Day 90 (+/- 7 days)	Day 180 (+/- 14 days)	Day 270 (+/- 14 days)	Day 360 (+/- 14 days)	Early withdrawal
Study Day	Day -90 to Day -3	D-2	D-1	Day 0 Pre	D0 Challenge	Day 0 Post	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	D14								
Mid turbinate FLOQ swab - Virology (j) (g) (m)			X				BD	BD	BD	BD	BD	BD	BD	BD	BD	BD	BD	BD	BD	BD[x]	BD[x]		X	(X)	(X)			X
Mid turbinate or nasopharyngeal swab for cells for RNA (g)			X				X		X		X		X			X				X								
Mask wearing sampling (s)			X				X	X	X	X	X	X	X	X	X	X	X	X	X	X	(X)							
Environmental viral sampling (t)			X				X	X	X	X	X	X	X	X	X	X	X	X	X	X	(X)							
Safety Assessments																												
AE recording	X	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	X
SAE recording	X	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	X
Concomitant medications	X	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	X

Table 2: Key notes for SoA

X	Once
BD	Twice Daily. The timing of the baseline assessment will be the guide to establish the windows for subsequent measurements. For scheduling purposes, the baseline assessment will be defined as the first day when BD measurements are performed. Subsequent sampling/measures will be performed at the same time ± 1 hour.

TDS	Three times daily. The timing of the baseline assessment will be the guide to establish the windows for subsequent measurements. For scheduling purposes, the baseline assessment will be defined as the first day when TDS measurements are performed. Subsequent sampling/measures will be performed at the same time ± 1 hour.
QDS	Four times daily. The timing of the baseline assessment will be the guide to establish the windows for subsequent measurements. For scheduling purposes, the baseline assessment will be defined as the first day when QDS measurements are performed. Subsequent sampling/measures will be performed at the same time ± 1 hour.
T	To determine tolerance of the procedure only (sample will not be tested).
+	Only the applicable Inclusion/Exclusion criteria will be reviewed at each time point.
a	Height will be taken at Screening only.
b	Vital signs will be taken at the same time each day (± 1 hour).
c	Lung function measures will be performed at the same time each day during quarantine (± 1 hour).
d	A serum follicle stimulating hormone (FSH) test will be performed in all post-menopausal women
e	Blood serum pregnancy test (ß-HCG) will be performed in all female subjects
f	Blood will be drawn under non-fasted conditions. Repeat bloods may be drawn under fasted conditions if a lipid profile (triglyceride) or glucose is required (at PI discretion).
g	Samples for related exploratory research
h	Virus serology will be performed to determine eligibility and seroconversion.
i	Nasopharyngeal swab for respiratory virus screen to assess for the presence of other respiratory viruses; if found positive the subject will not be eligible for the current quarantine.
j	Post inoculation Nasal virology samples will be collected and used for RT-qPCR and viral culture assay (as appropriate). Samples may be used for related exploratory research
k + k*	Can be performed on Study Day -2 or Study Day -1. *Special Note:* k* Serum pregnancy test should be performed on either day -2 or -1, prior to Urine Pregnancy Test on Day 0 (pre-inoculation).
l	Study specific consent may occur on admission, providing all required eligibility information has been collected through the HRA approved study specific Screening process
m	If for the study, mid turbinate FLOQ swabs are not available (e.g. national shortage), nasopharyngeal FLOQ swabs may be taken as a viable alternative. The study should endeavor to be consistent in swab type across all the participants.
n	Assessments may additionally be continuously monitored (e.g. core temperature; vital signs (HR, RR, SBP, DBP, SpO_2), activity, sleep, ECG) as per Section 5.
o	CT scan to be performed in all participants on day 5 or 6 and Day 10 or 11 dependent upon scanner availability; CT scan to be performed only in participants with PCR confirmed infection or symptoms consistent with COVID-19.
p	Baseline echo may be obtained at either screening or at entry to quarantine on Day -2/Day-1
q	Two sets of nasosorption will be taken at each time point. Each set consists of 2 nasosorptions, 1 for each nostril (i.e. total of 4 nasosorption devices per time point). Timing between sampling of the sets should be at least 5 minutes apart. Samples may be used for: cytokines/chemokines, sIgA, and virology, as well as stored for future usage
r	Telephone calls with participants every 2 to 3 days
s	Participant will be asked to wear a single-use facemask for up to 60 minutes, 1 – 3 times a day to capture exhaled virus

t	Environmental viral sampling may be performed in rooms up to twice a day
u	The UPSIT is designed to be self-administered after explanation of the test by study staff and will be performed once before virus inoculation and then at least every third day starting from Day 1, though the test can be conducted more frequently at the discretion of the PI/study physician. If at Day 28 anosmia has subsided and smell has returned the UPSIT test can stop. If anosmia is still present UPSIT should continue until resolution or the end of the study.
v	Once daily, at the same time each day (+/- 1 hour) during quarantine and similar timing where possible during follow-up visits
w	Before discharge from quarantine each participant will undergo a complete physical examination (the date of this may vary dependent upon length of stay) and repeat GAD-7 and PHQ-9 questionnaires once.
x	Procedures should be performed at the appropriate scheduled timings, up until the point of discharge.
y	Subjects may be given SARS-CoV-2 intervention treatment, depending on the stage of the study. Treatment plans for subjects include one of the following: • Pre-emptive therapy, upon evidence of infection (Remdesivir, once daily IV for 5 days) • Rescue therapy, once disease progression criteria is met (e.g., REGEN-COV, once IV) • No pre-emptive or rescue therapy
Notes:	Parenthesis indicates the assessment may be optional, or at the PI's discretion. Study specific consent may occur on the day of admission, providing all required eligibility information has been collected and the study fully explained to the participant through earlier screening visits and remote appointments process For all subjects QDS/TDS assessments on Day 0, the first assessment will be pre-virus challenge. The PI may perform additional safety assessments as required. Where any nasal sampling time points occur together, the order of sampling will typically be (1) Nasosorptions followed by (2) mid turbinate swab (3) Nasopharyngeal swab.

6.4. Interim Analysis / Data Monitoring

No interim analyses are planned to be performed, however, there will be two analyses: a primary analysis (up to study Day 28) and a final analysis (up to Day 360). Further detail of this is given in Section 10.1.2.

The safety profile will be assessed on an on-going basis by the study Investigators. The Principal Investigators (PI) and relevant Investigators (as per the trial delegation log) will be reviewing safety issues and SAEs as they arise. The Chef Investigator (CI) will be informed of any safety concerns.

Safety reviews are planned as follows:

- After the first 3 volunteers at each dose level (Sentinels), available safety data will be reviewed by the PI, CI and relevant investigators, before inoculating further subjects

- After each cohort has been challenged, a review will be performed by the chair of Data Safety Monitoring Board (DSMB) (or full DSMB at the discretion of the DSMB chair) before proceeding with challenge of further volunteers.

The DSMB will review safety data accumulated after each cohort and evaluate frequency of events, safety and infection rate / symptom data. The DSMB will make recommendations to the investigators concerning the conduct, continuation or modification of the study.

7. STUDY ENDPOINTS

Any updates made here to the endpoints specified in the protocol are detailed in Section 11.

7.1. Primary Endpoint(s)

The primary focus of the study is to identify a safe and infectious level of wild-type SARS-COV-2 Challenge. Hence, the Primary endpoints are as follows:

- To evaluate the safety of wild type SARS-CoV-2 challenge in healthy subjects by assessing:
    - Occurrence of unsolicited AEs within 30 days post-viral challenge (Day 0) up to Day 28 follow up.
    - Occurrence of SAEs related to the viral challenge from the viral challenge (Day 0) up to Day 28 follow up.
- To identify a SARS-Cov-2 inoculum dose that safely induces laboratory confirmed infection in ≥50% of subjects (ideally between 50% and 70%). Laboratory confirmed infection is defined as:
    - Two quantifiable greater than lower limit of quantification (≥LLOQ) RT-PCR measurements from mid turbinate and/or throat samples, reported on 2 or more consecutive timepoints, starting from Day 2 up to discharge from quarantine.

7.2. Secondary Endpoints

- To assess the incidence of laboratory confirmed infection rates using both mid turbinate and/or throat swabs, as defined by:
    - Variant 2: Occurrence of at least one quantifiable (≥LLOQ) SARS-CoV-2 viral cell culture measurement, starting from Day 2 up to discharge from quarantine.
- To assess the incidence of lab-confirmed symptomatic SARS-CoV-2 infection using mid turbinate and/or throat swabs, defined as:
    - Variant 1:
        - Occurrence of at least two quantifiable (≥LLOQ) RT-PCR measurements, reported on 2 or more consecutive timepoints, starting from Day 2 up to discharge from quarantine, AND
        - Either one or more positive clinical symptoms of any grade from two different categories in the symptom scoring system (Upper Respiratory, Lower Respiratory, Systemic), or one Grade 2 symptom from any category
    - Variant 2:
        - Occurrence of at least one quantifiable (≥LLOQ) SARS-CoV-2 viral cell culture measurement, starting from Day 2 up to discharge from quarantine, AND
        - Either one or more positive clinical symptoms of any grade from two different categories in the symptom scoring system (Upper Respiratory, Lower Respiratory, Systemic), or one Grade 2 symptom from any category
- To assess the viral dynamics, as measured by:
    - Area under the viral load-time curve (VL-AUC) of SARS-CoV-2 as determined by qRT-PCR, starting from Day 2 up to discharge from quarantine.

  - Peak viral load of SARS-CoV-2 as defined by the maximum viral load determined by quantifiable (≥LLOQ) qRT-PCR measurements, from Day 2 up to discharge from quarantine.
  - Duration of SARS-CoV-2 quantifiable (≥LLOQ) qRT-PCR measurements, starting from Day 2 up to discharge from quarantine. Duration is defined as the time (hours) from the first quantifiable of the two viral quantifiable positives used to assess infection until first confirmed undetectable assessment after their peak measure (after which no further virus is detected).
  - Incubation period of SARS-CoV-2 qRT-PCR measurements. Incubation period is defined as the time (hours) from inoculation to the first quantifiable of the two viral quantifiable positives used to assess infection, starting from Day 2 up to discharge from quarantine.

- The above endpoints will also be evaluated using quantitative cell culture.
- To assess the SARS-CoV-2 induced symptoms
  - Sum total symptoms diary card score: sum total clinical symptoms (TSS) as measured by graded symptom scoring system, starting one day post-viral challenge (Day 1) up to Day 14.
  - Area under the curve over time (TSS-AUC) of total clinical symptoms (TSS) as measured by graded symptom scoring system (categorical and visual analogue scales), starting one day post-viral challenge (Day 1) up to Day 14.
  - Peak symptoms diary card score: peak total clinical symptoms (TSS) as measured by graded symptom scoring system (categorical and visual analogue scales, starting one day post-viral challenge (Day 1) up to Day 14.
  - Peak daily symptom score: Individual maximum daily sum of symptom score starting one day post-viral challenge (Day 1) up to Day 14.
- The incidence of:
  - Upper Respiratory Tract illness (URT)
  - Lower Respiratory Tract illness (LRT)
  - Systemic illness (SI)
  - Febrile illness (FI)
  - Proportion of Subjects with Grade 3 symptoms on any occasion at any time from the last assessment on Day 0 to quarantine discharge
  - Proportion of Subjects with Grade 2 or higher symptoms on any occasion at any time from the last assessment on Day 0 to quarantine discharge
  - Proportion of Subjects with Grade 2 or higher Symptoms on two separate occasions at any time from the last assessment on Day 0 to quarantine discharge
  - Proportion of Subjects with any symptom (grade >=1) on any occasion at any time from the last assessment on Day 0 to quarantine discharge
  - Proportion of Subjects with any symptom (grade >=1) on two separate occasions at any time from the last assessment on Day 0 to quarantine discharge

7.3. Tertiary (Exploratory) Endpoints

- To explore safety related measures of wild type SARS-CoV-2 challenge in healthy subjects by assessing:
    - Changes in smell (anosmia/parosmia) and cognition through infection
    - Pulmonary changes due to experimental infection, as measured by:
        - High-resolution CT
        - Spirometry (FEV1, FVC)
        - Forced Oscillatory Technique (FOT)
    - Association of ABO blood group and susceptibility to infection
    - Occurrence of haematological and biochemical laboratory abnormalities during the quarantine period.
    - Use of concomitant medications within 30 days post-viral challenge (Day 0 up to Day 28 follow up).

- To measure the laboratory confirmed infection rates in saliva, as defined by:
    - Occurrence of at least two quantifiable (≥LLOQ) RT-PCR measurements, reported on 2 or more consecutive timepoints, starting from Day 2 up to discharge from quarantine.
    - Occurrence of at least one quantifiable (≥LLOQ) SARS-CoV-2 viral cell culture measurement, starting from Day 2 up to discharge from quarantine.

- To assess viral dynamics in saliva, as defined by:

  - Area under the viral load-time curve (VL-AUC) of SARS-CoV-2 as determined by qRT-PCR measurements in saliva, starting from Day 2 up to discharge from quarantine.
  - Peak viral load of SARS-CoV-2 as defined by the maximum viral load determined by quantifiable qRT-PCR measurements in saliva, starting from Day 2 up to discharge from quarantine.
  - Duration of SARS-CoV-2 quantifiable qRT-PCR measurements in saliva, starting from Day 2 up to discharge from quarantine. Duration is defined as the time (hours) from first the quantifiable of the two viral quantifiable positives used to assess infection until first confirmed undetectable assessment after their peak measure (after which no further virus is detected).
  - Incubation period of SARS-CoV-2 qRT-PCR measurements in saliva. Incubation period is defined as the time (hours) from inoculation to the first quantifiable of the two viral quantifiable positives used to assess infection, starting from Day 2 up to discharge from quarantine.
  - The above endpoints may also be evaluated using quantitative cell culture.

- The primary, secondary, and tertiary endpoints may be explored in relation to immunological levels at baseline and after SARS-CoV-2 challenge. Assays performed on serum and mucosal samples may include, but are not limited to:
  - Humoral immunity / systems serology SARS-CoV-2 (for example: SARS-CoV-2 neutralizing titres, ELISAs to IgG, IgM, IgA, sIgA, ADCC)
  - Proteomic levels and changes (for example, cytokine and chemokines)
  - Cellular cell quantification and quality of immunity (for example T and B cell frequencies, phenotypes and functionality assays, ELISPOTs, ICS, cytokine/chemokine responses)
  - Transcriptome levels and changes (for example, RNAseq, single cell RNAseq, microarray, PCR)
  - Human genomics in relation to SARS-CoV-2 susceptibility, infection (e.g., HLA typing, SNPs, GWAS)
  - Viral genomics to assess the possible emergence of mutations in SARS-CoV-2 over the duration of the study.
  - Viral genomics in relation to SARS-CoV-2 population changes through infection.
  - Microbiome analysis in relation to viral infection, disease and susceptibility (e.g., PCR, NGS, 16s rRNA).
- To explore the average amount of instrument-assessed change for all subjects who rate themselves as "a little better" or "somewhat better". Instruments include but are not limited to:
  - Symptom diary card (Categorical Scale)
  - Symptom diary card (Visual Analogue Scale)
- To explore the environmental contamination of SARS-CoV-2 as a result of infection in subjects, as measured by:
  - Air sampling for virus detection and quantification

- Exhaled breath sampling with the use of a face mask for virus detection and quantification
- Surface swabbing for virus detection and quantification

8. SAMPLE SIZE

The primary objective of the study is to identify a safe and infectious dose of wild type SARS-CoV-2 in healthy volunteers, suitable for future intervention studies. No formal sample size calculation has been performed for this early stage dose finding study. However, a sample size of up to an expected 30 subjects for a dose level and treatment regimen (made up of 3 cohorts of up to an expected 10 subjects, including the dose expansion cohort), with a total of up to 90 subjects overall, is felt sufficient to meet the primary objective of escalating/expanding the dose in a safe manner whilst providing information on the attack rate.

The initial dose level administered will include a sentinel group of 3 subjects. As described in Section 4 of the protocol, if none of the 3 subjects in this initial dose level sentinel group become infected then the dose will be escalated, i.e. based on a target attack rate of 70%, the probability of seeing at least 1 subject in the 3 sentinel subjects being infected is 97.3%. Hence, if no subjects are infected then dose escalation will occur.

See below for further statistical rationale for the dose escalation/expansion scheme.

8.1. Cohort and Dose Escalation

An overview of the cohort and dose escalation scheme is presented in Figure 4. The following describes the statistical aspects to support the cohort and dose escalation scheme in relation to the first, second and third groups each of an expected 10 subjects (i.e. the first, second and third cohorts, respectively) at each dose level.

To support future studies, a target attack rate of 70% has been deemed desirable and should not be below 50%. A two-sided 95% confidence interval (CI) approach will be used for assessing the precision of the point estimate for the attack rate. This approach is consistent with previous human infection dose escalation studies[43].This approach is consistent with previous human infection dose escalation studies. Given that sample sizes are relatively small, an exact (Clopper-Pearson) confidence interval will be used. The assessment of the early (first and second) cohorts of the dose escalation scheme will be based primarily on safety together with clinically relevant fixed attack rate criteria. Subject numbers will then be expanded with a third cohort at the selected dose level and a 95% CI calculated to obtain a level of precision for the observed attack rate.

First Cohort:

For the first cohort, criteria for escalation, de-escalation and expansion, require no further statistical justification, i.e. dose expansion, escalation and de-escalation are based on a combination of safety and a clinically relevant fixed attack rate criterion.

Second Cohort:

For the second cohort, criteria for escalation, de-escalation and expansion are based on combination of safety and clinically relevant fixed attack rate criterion. A group size made up of subjects from the first and second cohorts will be used to show early indications of the attack rate. However, this is not based on statistical considerations.

Third Cohort (expansion group):

The dose expansion cohort should only take place when it is believed that an appropriate dose has been identified after the completion of the second cohort. Using "≥70% infected" as the criterion to expand to the third cohort, is a reasonable criterion to use based on targeting a 70% target attack rate, but also reducing the risk of seeing an attack rate of less than 50%, after an expected 30 subjects. This is similar to previous human infection dose escalation studies. If however an observed ≥70% attack rate after the first 2 cohorts at any dose level has not been achieved (even after reaching the highest dose) then expansion could be undertaken at the "most promising" dose (providing the attack rate after the second cohort is high enough. So, if a 70% attack rate is never reached after the first 2 cohorts at any dose level then the "≥70% infected" criterion becomes a "guide".

For the level of precision, once say 30 subjects are recruited, and an observed 21 out of 30 (70%) subjects are infected then this provides a 95% CI of (51%, 85%), and therefore this provides the necessary CI width to have the lower bound above the required 50%. In addition to this, by recruiting the third cohort (e.g. 30 subjects in total), this allows for inspection of any variation in the attack rate between the 3 cohorts at a particular dose level, and also increases the chance of potentially seeing any less frequent adverse events

9. STUDY ANALYSIS SETS

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

The following analysis sets are defined for this study:

9.1. Safety Analysis Set

The Safety Analysis Set (SAS) will consist of all subjects who were inoculated with wild-type SARS-COV-2 Challenge virus.

9.2. Full Analysis Set

The Full Analysis Set (FAS) will consist of all subjects who were inoculated with wild-type SARS-COV-2 Challenge virus. The FAS will be the primary analysis set for all primary, secondary and exploratory endpoints. The FAS will be identical to the SAS for this study.

9.3. Per Protocol Analysis Set

The Per Protocol (PP) Analysis Set will consist of all FAS subjects that are sero-suitable, have no major protocol deviations and who completed the quarantine period up to the final day of quarantine. The PP Analysis Set will be the secondary analysis set for pre-specified primary, secondary and exploratory endpoints.

10. PLANNED STATISTICAL METHODS

10.1. Statistical Considerations

10.1.1. General definitions

In all applicable summary presentations of safety endpoints, Baseline is defined as the last non-missing assessment value for a subject, for that particular parameter, that is prior to viral challenge, unless over-ruled after review of data at the DRM or otherwise stated in the appropriate endpoint sections below.

For non-safety endpoints, the baseline definition (if required) is as per the appropriate endpoint sections below, and the first assessment to be used should be the assessment that was taken at the time of administration of the viral challenge.

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

If any subjects remain in quarantine beyond day 14 any viral load data collected up to the point of discharge will be used for endpoint derivations. Any symptoms data collected beyond day 14 will not be used in endpoint derivations for the primary analysis but will be listed.

A subject is defined as completing the study when they have completed all visits up to, and including, the final follow-up visit at Day 360 (+/- 14 days).

10.1.2. Sequence of Analysis

Two separate sets of analyses will be conducted: the primary analysis after all subjects have reached the Day 28 follow up, and a final analysis following the completion of the study (LSLV), up to Day 360.

- The Primary (Day 28) Analysis will be performed when data, up to and including the study Day 28 visit, are clean and available for all subjects.
- The Final Analysis will be performed when all endpoint data up to study follow-up end (Day 360) are available and locked.

The Infection, Viral load and symptoms scores endpoints will be summarised at the Day 28 analysis only (as data is only collected for these up to Day 14, or quarantine discharge), with all other endpoints being summarised in both the Primary and Final analyses.

This SAP provides a detailed description of the analyses that will be computed at the time of each analysis. Section 10 of this SAP describes the analyses that apply to either or both analysis timepoints, whereas Section 13 states which of these analyses will be produced for each of the analysis timepoints. Note: in cases where specific assessment time points differ between the Primary (Day 28) Analysis and Final Analysis timepoints, these will be made clear in the analysis descriptions in Section 10 or in the table shells in Section 14.

The final CSR will be written after the Final analysis, and will contain the final analyses of the study endpoints for both the Primary analysis and the Final analysis. If the data for some tertiary endpoints become available at a later stage, (an) additional analysis/analyses may be performed. These analyses may be documented separately to the CSR and may be made available to the Sponsor and Investigators at that time.

10.1.3. Data Presentation

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

Summary tables will be presented for all subjects for demographic, baseline and safety data. For efficacy data the tables and figures will use combinations of the following labels when summarising the data (See Section 10.1.7 for more details of the subgroups):

- 10^1 $TCID_{50}$
- Infected
- Not infected
- Remdesivir
- No Remdesivir
- All subjects

The scheduled protocol visits will be labelled in (applicable) report presentations as follows:

- Screening
- Admission (D-2/-1)
- Day -2
- Day -1
- Day 0 Pre-Challenge
- Day 0 Challenge
- Day 0 Post-Challenge
- Day 1, ….. Day 14, Day 15, Day 16, Day 17, Day 18, Day 19, Day 20 (to include all days while subjects are still in quarantine).
- Day 28
- Day 90
- Day 180
- Day 270
- Day 360
- Early Withdrawal

Depending on the endpoint, baseline may be defined as either Screening, Admission D-2/-1, Day -2, Day -1 or Day 0 Pre-Challenge.

Where duplicate information is collected on both the database and on the vendor data transfer(s) (e.g., sampling date and time) this information will be reconciled by data management and then the information from the vendor data transfer(s) will be included in subject Listings.

All variables will be listed to the same number of decimal places as reported. Descriptive statistics for all endpoints that are continuous data will have the following summary statistics presented in the following order: n, mean (and/or geometric mean, where applicable) (rounded to one more decimal place than recorded), standard deviation (rounded to two more decimal places than recorded), standard error (rounded to two more decimal places than recorded), median (rounded to one more decimal place than recorded), lower quartile (rounded to one more decimal place than recorded), upper quartile (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 subject analysis set or the number of non-missing observations. The specific approach is detailed within each relevant table template (Section 14). A 95% confidence interval (CI) may be presented for certain pre-specified endpoints.

The geometric mean (GM) cannot be derived if there are zeros present in the data so before deriving any GM the zeros should be replaced by a small number. The number used should reflect the data and should be specified within the relevant endpoint sections, if no replacement is specified 1 should be used. The GM should then be derived as below:

$$GM = \text{anti-log}\left(\text{mean}\left(\log_{10}\left(\text{endpoint values} + 1 \right) \right) \right) - 1$$

Any data that is recorded as below the lower limit of quantification (<LLOQ) or below to lower of detection (<LLOD) will be presented as <LLOQ or <LLOD, respectively, in listings, but will be replaced for all summaries. The number to use as a replacement is given in Appendix 1 (Section 15.1), unless otherwise stated in the relevant endpoint sections. Any data that is recorded as above the upper limit of quantification will be presented as >ULOQ in listings but will be replaced as stated in Appendix 1 (Section 15.1).

All collected data will be included within subject listings.

10.1.4. Statistical Testing and Estimation

No formal statistical comparison is planned. Primary, secondary and exploratory endpoints will be analysed descriptively.

A 95% CI will be calculated and displayed for a number of pre-specified endpoints (specified within the relevant endpoints sections and tables in Section 14). For proportions this will be the Clopper-Pearson Exact CI, while for continuous endpoints this will be based on the Student's t-distribution.

10.1.5. Handling of Dropouts or Missing Data

Given the majority of the study takes place within quarantine it is very rare for missing data to occur. On the rare occasion that missing data does occur it will not be imputed. Only observed data at each scheduled visit will be reported. However, for some endpoints, mechanisms will be put in place with

the aim of reducing the impact of missing data. These will be outlined within the relevant endpoint sections.

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

10.1.6. Multiple Comparison/Multiplicity

As no statistical analysis is planned there are no multiplicity issues in this study.

10.1.7. Examination of Subgroups

Infected (lab-confirmed)

The Infected subgroup is defined as those subjects that fulfil the following criteria:

- Two quantifiable (≥LLOQ) RT-PCR measurements from mid turbinate or throat samples, reported on 2 or more consecutive timepoints, starting from Day 2 up to Quarantine discharge.

Uninfected

All subjects that do not meet the criteria for the Infected subgroup are considered Uninfected.

Remdesivir

Subjects may be split by whether they received Remdesivir as part of their participation in the study or not.

10.1.8. Model checking and sensitivity analyses

As no formal statistical analysis will be undertaken no model checking will be carried out.

A number of endpoints are typically log-normally distributed, such as total symptoms scores, for these endpoints the geometric mean (GM) will also be displayed in summaries (Specified within the tables in Section 14) and if CIs are displayed for these endpoints they will be the 95% CI for the GM.

10.1.9. Data Conversion (CDISC)

For the reporting of this study both CDISC SDTM (SDTM version 1.4 and SDTM Implementation Guide version 3.2) and ADaM (ADaM version 2.1 and ADaM Implementation Guide version 1.1) standards will be applied.

10.1.10. Software

Data will be reported using SAS version 9.4.

10.2. Subject Disposition

The number of subjects receiving Challenge Virus, receiving at least one dose of Remdesivir, not receiving Remdesivir, withdrawing from the study (also split by reason for withdrawal), completing

the study Day 28 visit, completing the study (Day 360 visit), and the numbers in each analysis set, will be summarised across all subjects.

10.3. Protocol Deviations

Subject data will be reviewed for major protocol deviations prior to database lock at a planned Data Review Meeting (DRM), and decisions will be documented within the meeting minutes. At this meeting, subjects will be reviewed for their inclusion/exclusion from the PP analysis set. Protocol deviations will be listed.

10.4. Demographic and other baseline characteristics

The SAS analysis set will be used in summaries of demographic and baseline data.

10.4.1. Demographics

Demographic variables at Screening; sex, age, race, ethnicity, height (cm), weight (kg) and body mass index (BMI) will be summarised across all subjects.

Age at screening and BMI are recorded in the database and as such do not need to be calculated.

10.4.2. Substance Use History

History of smoking, alcohol and drugs will be summarised.

10.4.3. Medical History

Medical history data will be coded using MedDRA version 24.0 (March 2021). Medical history will be listed.

10.5. Prior and Concomitant medications

Concomitant medication terms will be coded using the World Health Organisation (WHO) Drug Dictionary Enhanced (WHO Drug Global, version 2021 (March 1, 2021)). Medications will be assigned as being prior to or concomitant with viral challenge, based on the start and stop dates of the medication and the date of viral challenge.

If the medication stop date is before the date of viral challenge, the medication will be assigned as being prior to viral challenge. In all other situations, the medication will be assigned as being concomitant with viral challenge.

Note: Start and Stop times will not be used for determining if a medication is concomitant or not.

All concomitant medications from viral challenge will be summarised, using the Safety Analysis Set by Drug Class (L2) and preferred base name (01001), separately for the period from viral challenge up to Day 28 and from Day 28 to Day 360. Prior medications will be identified in a subject listing. If a subject has separate periods of taking specific medications, then that medication is only counted once within the period of observation (i.e., prior to viral challenge or concomitant) where it is taken.

10.6. Exposure

The number of subjects inoculated will be summarised within the subject disposition table (Section 10.2).

The exposure to Remdesivir will be summarised as total dose received and length of exposure.

These will be defined as follows:

Length of exposure (days) = Date of last dose – Date of first dose +1.

Total dose received (mg) = 200 + [(length of exposure – 1)*100]

10.7. Endpoint Analysis

Note: Some safety endpoints are defined as primary and secondary endpoints in the protocol, however their details are described in the safety endpoints section (10.8).

All analyses will be performed on the FAS analysis set. The FAS analysis set will be considered the primary analysis population. The sensitivity of the analysis of the primary endpoint and selected pre-specified secondary and tertiary endpoints will be evaluated using the PP analysis set. Analysis using the PP analysis set will only be done if the population differs from that of the full analysis set. Similarity / difference in conclusion from these two analyses will be discussed in the CSR.

10.7.1. Primary Endpoint Analysis

The primary (non-safety) endpoint is RT-PCR confirmed infection (Variant 1), defined as:

> Two quantifiable (≥LLOQ) RT-PCR measurements from mid turbinate and/or throat samples, reported on 2 or more consecutive timepoints, from the first (morning) assessment on Day 2 to discharge from quarantine.

A subject will be defined as having met the criteria if they have quantifiable measurements at 2 consecutive timepoints using any combination of the mid-turbinate and throat samples (i.e., they could have; a positive throat sample followed by a positive mid-turbinate sample at the next assessment, 2 consecutive positive throat samples or 2 consecutive positive mid-turbinate samples). The number and percentage of subjects who meet this criterion will be summarised for all subjects, along with the 95% Clopper-Pearson CI.

Subjects with no recorded data meeting the definition of this endpoint will be treated as not having met the endpoint, i.e., they will be treated as uninfected.

10.7.2. Secondary Endpoint Analysis

Secondary endpoint analyses will be performed on the following endpoints, based on the FAS, as well as a sensitivity analysis using the PP analysis set:

10.7.2.1 Viral culture confirmed Infection

Viral culture confirmed infection (Variant 2), defined as:

- Variant 2: Occurrence of at least one quantifiable (≥LLOQ) SARS-CoV-2 viral culture measurement, from the first (morning) assessment on Day 2 to discharge from quarantine.

A subject will be defined as having met the criteria if they have quantifiable measurements at 2 consecutive timepoints using any combination of the mid-turbinate and throat samples.

Subjects with no recorded data meeting the infection definition will be treated as not having met the endpoint, i.e., they will be treated as uninfected.

10.7.2.2 Lab-confirmed Symptomatic Infection

Subjects are defined as having lab-confirmed symptomatic infection when they experience symptoms (as outlined below) AND meet the definition of lab-confirmed infection.

The two definitions of lab-confirmed symptomatic infection are:

Variant 1:

- Occurrence of at least two quantifiable (≥LLOQ) RT-PCR measurements, reported on 2 or more consecutive timepoints, from the first (morning) assessment on Day 2 to discharge from quarantine, AND
- Either one or more positive clinical symptoms of any grade (≥ grade 1) from two different categories in the symptom scoring system (Upper Respiratory, Lower Respiratory, Systemic), or one Grade 2 symptom from any category, from the first (morning) assessment on Day 1 to (discharge from quarantine.

Variant 2:

- Occurrence of at least one quantifiable (≥LLOQ) SARS-CoV-2 viral culture measurement, from the first (morning) assessment on Day +2 to discharge from quarantine, AND
- Either one or more positive clinical symptoms of any grade (≥ grade 1) from two different categories in the symptom scoring system (Upper Respiratory, Lower Respiratory, Systemic), or one Grade 2 symptom from any category, from the first (morning) assessment on Day 1 to discharge from quarantine.

The symptomatic element of the criteria above will be derived from the symptom diary cards.

Subjects fill in symptom diary cards from admission on Day -2 until discharge from quarantine. The subject will fill the symptom card in once on Day -2, three times each day until the day before discharge and up to 3 times on the day of discharge dependent on the time of discharge.

There are 19 symptoms for each subject to grade at each assessment:

- Upper Respiratory Tract (URT): runny nose, stuffy nose, sore throat, sneezing, earache, hoarse voice, eye soreness.
- Lower Respiratory Tract (LRT): cough, shortness of breath, chest tightness, wheeze.
- Systemic: headache, malaise/tiredness, muscle and/or joint ache, chilliness/feverishness, dizziness, rashes, blisters, diarrhoea.

Subjects will grade each of the symptoms on a scale of 0 to 3 (0-4 for shortness of breath and wheeze):

- grade 0: No symptoms,

- grade 1: just noticeable,
- grade 2: clearly bothersome from time to time but does not interfere with me doing my normal daily activities,
- grade 3: Quite bothersome most or all of the time, and it stops me participating in activities,
- grade 4: Symptoms at rest. (Shortness of Breath and Wheeze only).

The lab-confirmed infected element of the criteria will be derived based on the results of the throat and the mid-turbinate samples.

Subjects with no recorded data meeting the infection definition will be treated as not having met the endpoint, i.e., they will be treated as uninfected.

The number and percentage of subjects who meet the two different criteria of lab-confirmed symptomatic infection will be summarised, along with the 95% Clopper-Pearson CI.

10.7.2.3 Viral Dynamics

Viral dynamics will all be evaluated separately using the results from qRT-PCR and SARS-CoV-2 viral culture.

10.7.2.3.1 Area under the Viral Load Time Curve (qRT-PCR)

The area under the curve (AUC) of SARS-COV-2 viral load, as determined by qRT-PCR, will be calculated separately using:

(1) the results of mid-turbinate samples only,

(2) the results of throat samples only,

The AUC will be derived based on samples taken twice a day from the first (morning) assessment on Day 2 to discharge from quarantine. The viral data will be provided as log10 copies /ml and will be used to calculate the AUC using the trapezoid rule [1], using hours as the unit of time.

As samples are scheduled to be taken twice daily for the duration of quarantine , in order to calculate the AUC, the actual time that the assessment was collected will be used within the AUC calculation. The AUC will then be derived for each subject from Day 2 up the last day in quarantine. In order to derive the AUC the subject must have a non-missing result for the start of the period (i.e. the morning of Day 2), and have at least one non-missing result available for every day up to, and including, their final day in quarantine. Any missing qRT-PCR data will be reviewed at the DRM, for its potential impact on this endpoint, and any decisions to include subjects that fail these criteria above will be documented in the DRM minutes.

Note: For the reporting of AUC, where appropriate, qRT-PCR values that are 'Not Detected' (i.e., <LLOD) or are at or below the limit of quantification (i.e., <LLOQ) will be re-assigned using the substitution values shown in the table in Appendix1 (Section 15.1).

The AUC analyses will be summarised for all subjects as well as for those infected and not infected, those who took Remdesivir and those who did not, along with the 95% CI.

A sensitivity analysis will be presented where the viral load AUC is calculated up until planned day of discharge from quarantine (Day 14). This will also be summarised for all subjects as well as for those infected and not infected and those who took Remdesivir and those who did not, along with the 95% CI.

In addition, the mean qRT-PCR values (+/- 1 Standard Error (SE)) will be displayed graphically by day and assessment, and infection subgroup. Another figure displaying the mean qRT-PCR values (+/- 1 SE) over each day and assessment will be presented for those subjects who took Remdesivir vs those that did not.

[Line graph: y-axis = mean of qRT-PCR (log10 copies/mL), x-axis = day, one line for each of infected and uninfected on same plot].

Note: For multiple assessments taken within each day, all 1st /2nd assessments will have mean values separately calculated and plotted as two separate means within each day. These two means will be shown equally spaced along the x-axis within the graph.

10.7.2.3.2 Peak Viral Load of SARS-CoV-2 (qRT-PCR)

Peak viral load of SARS-CoV-2 viral load as determined by qRT-PCR is defined as the maximum viral load from the quantifiable (>= LLOQ) qRT-PCR measurements, starting on Day 2 up to quarantine discharge. This will be summarised separately for mid-turbinate and throat samples.

Where a subject does not have a quantifiable viral load throughout the duration of their stay in quarantine (i.e., remaining below LLOQ as either detectable ('Detected' result) or undetectable ('Not Detected' result) they will be given a peak equivalent to a detected or undetected value, respectively. See Appendix1 (Section 15.1) for the values to use.

The peak viral load will be summarised for all subjects as well as for those infected and not infected, those who took Remdesivir and those who did not.

10.7.2.3.3 Duration of SARS-CoV-2 (qRT-PCR)

The duration of SARS-CoV-2 viral load as determined by qRT-PCR is defined as the duration (in hours) from the first quantifiable result (of the 2 quantifiable results that indicate lab-confirmed infection) until the first confirmed unquantifiable assessment after the peak measure (after which no further virus is detected), starting from Day 2 up to quarantine discharge, separately for mid-turbinate and throat sample results.

Subjects who did not have a confirmed unquantifiable (i.e., <LLOQ, detected or not detected) assessment after their peak will be censored at their last quantifiable assessment. Subjects who do not meet the criteria for lab-confirmed infection (have 2 quantifiable results reported on 2 or more consecutive timepoints) will be excluded from the analysis.

Kaplan-Meier plots [2] will be displayed showing the duration of SARS-CoV-2 (with the time axis as days since first quantifiable result). A table will accompany the plot and will display the Kaplan-Meier estimates of the cumulative proportion of subjects' event free at specific time points.

The duration of SARS-CoV-2 will be summarised for all subjects as well as for those who took Remdesivir and those who did not, using the FAS.

10.7.2.3.4 Incubation Period of SARS-CoV-2 (qRT-PCR)

The incubation period of SARS-CoV-2 viral load as determined by qRT-PCR is defined as the time (hours) from inoculation to the first quantifiable result (of the 2 quantifiable results that indicate lab-confirmed infection), starting from Day 2 up to quarantine discharge. This will be summarised separately for mid-turbinate and throat samples.

Subjects who do not meet the criteria for lab-confirmed infection (have 2 quantifiable results reported on 2 or more consecutive timepoints) will be excluded from the analysis.

The incubation period of SARS-CoV-2 will be summarised for all subjects using the FAS.

10.7.2.3.5 Area under the Viral Load Time Curve (Viral Culture)

The AUC of SARS-COV-2 viral load as determined by viral culture will be determined in a similar way as for the AUC of SARS-COV-2 based on qRT-PCR (Section 10.7.2.3.1).

Note: Viral culture is only performed where the qRT-PCR result is positive and, as such, it is assumed that when the qRT-PCR result is negative the viral culture is also negative and when the qRT-PCR result is invalid or missing the culture result is also assumed to be missing. Additionally, for the reporting of AUC, where appropriate, values that are 'Not Detected' or are at or below the limit of quantification will be re-assigned using the substitution values shown in the table in Appendix 15.1.

The AUC analyses will be summarised for all subjects as well as for those infected and not infected, those who took Remdesivir and those who did not, along with the 95% CI. The mean SARS-CoV-2 viral culture values (+/- 1 Standard Error (SE)) will be displayed graphically by day, assessment, and infection subgroup.

[Line graph: y-axis = mean of SARS-CoV-2 viral culture, x-axis = day, one line for each of infected and uninfected on same plot].

Note: For multiple assessments taken within each day, all 1st /2nd assessments will have mean values separately calculated and plotted as two separate means within each day. These two means will be shown equally spaced along the x-axis within the graph.

10.7.2.3.6 Peak Viral Load of SARS-CoV-2 (SARS-CoV-2 viral culture)

Peak viral load of SARS-CoV-2 viral load as determined by viral culture is defined as the maximum viral load determined by the quantifiable SARS-CoV-2 viral culture measurements in samples starting on Day 2 up quarantine discharge. This will be derived and summarised in the same way as for qRT-PCR above (Section 10.7.2.3.2).

10.7.2.3.7 Duration of SARS-CoV-2 (SARS-CoV-2 viral culture)

The duration of SARS-CoV-2 viral load as determined by viral culture will be derived and summarised in the same way as for qRT-PCR viral load above (Section 10.7.2.3.3).

10.7.2.3.8 Incubation Period of SARS-CoV-2 (SARS-CoV-2 viral culture)

The incubation period of SARS-CoV-2 viral load as determined by viral culture will be derived and summarised in the same way as for qRT-PCR viral load above (Section 10.7.2.3.4).

10.7.2.4 Self-reported Symptoms

10.7.2.4.1 Sum Total Symptom Scores (TSS)

The sum total symptom scores is based on the symptom diary cards that are filled out 3 times per day from the first (morning) assessment on Day 1 until the first (morning) assessment on Day 14 (planned day of quarantine discharge). Each assessment consists of the grades given by the subjects to a list of 19 symptoms on the symptom diary card (further detail on the symptoms and grades is given in Section 10.7.2.2).

Individual total symptom scores are derived for each assessment as the total of all of the grades given on the individual diary card. This can range from 0 (if all symptoms graded as 0) to 59 (if all symptoms graded as 3 and shortness of breath and wheeze are graded as 4).

The three individual total symptom scores on each day are then summed to give a daily total symptom score for that day. The sum total symptoms scores is then the sum of the daily TSS given from day 1 to day 14, which will be the sum of the 40 individual scores for the time period.

If, for an individual assessment, any of the 19 symptoms scores are missing, on an otherwise completed symptom card, the missing scores are assumed to be 0 (i.e., did not have the symptom) and the individual total symptom score derived as usual. If all of the 19 symptom scores are missing for a particular symptom card then the individual total symptom score for that assessment will be missing.

If any of the individual total symptom scores are missing then the sum total clinical symptoms score cannot be derived for that subject and will be set to missing.

The sum total clinical symptoms scores will be summarised for all subjects as well as for those infected and not infected, those who took Remdesivir and those who did not, including the GM and the 95% CI for the GM.

The mean individual total symptoms scores (+/- 1 SE) will be plotted by infection subgroup.

[Line graph: y-axis = mean of individual total symptoms score, x-axis = day, one line for each of infected and uninfected on same plot].

Note: For multiple assessments taken within each day, all 1^{st} /2^{nd} /3^{rd} assessments will have mean values separately calculated and plotted as three separate means within each day. These three means will be shown equally spaced along the x-axis within the graph.

10.7.2.4.2 Area Under the Curve of the Total Clinical Symptom Scores (AUC-TSS)

The Area under the curve of the total clinical symptoms scores (AUC-TSS) will be derived using the individual total symptoms scores from the first (morning) assessment on Day 1 until the first (morning) assessment on Day 14 (planned day of quarantine discharge) for each subject using the trapezium rule [1].

The AUC calculation will use the time of completion of each assessment. The AUC will only be derived if the individual total symptoms score is non-missing for both the first (morning) assessment on Day 1 and the first (morning) assessment on Day 14 and that at most one score is missing for each day (i.e., that at least 2 of the 3 individual total symptoms scores are non-missing).

The AUC will be derived as for AUC for viral load (Section 10.7.2.3.1) and summarised for all subjects as well as for those infected and not infected, those who took Remdesivir and those who did not, including the GM and the 95% CI for the GM.

10.7.2.4.3 Peak Total Clinical Symptoms Scores

The peak total clinical symptom score for each subject is the maximum of all of the individual total symptom score given by a subject from the first (morning) assessment on Day 1 until the first (morning) assessment on Day 14 (planned day of quarantine discharge).

If a subject has no available individual total symptoms scores (i.e. there are no non-missing symptom cards available for a subject) the peak score will be missing.

The peak total clinical symptom score will be summarised for all subjects as well as for those infected and not infected, those who took Remdesivir and those who did not, including the GM and the 95% CI for the GM.

10.7.2.4.4 Peak Daily Total Clinical Symptom Scores

The peak daily total clinical symptom score will be the maximum of the daily total symptom scores from Day 2 to Day 13 (the days for which 3 symptom diary cards are available).

The peak daily total clinical symptom score will be summarised for all subjects as well as for those infected and not infected, those who took Remdesivir and those who did not, including the GM.

10.7.2.5 SARS-CoV-2 Illness Incidence

The results of the physical examinations and the symptom diary cards will be used to determine the presence of a number of illness endpoints. The incidence of each of these illnesses will be summarised in terms of counts, and percentages, by dose group.

10.7.2.5.1 Upper Respiratory Tract Illness (URTI)

A subject will be considered to have upper respiratory tract illness (URTI) if he/she has any one of either a URT (diary card) self-reported symptom or a URT (physical examination (PE)) sign, as specified below, on two consecutive scheduled assessments (from the last assessment on Day 0 to the first (morning) assessment on Day 14 (quarantine discharge)), where at least one of which must attain Grade 2 severity, or if any of the following attain Grade 3 severity once. Note: URT (diary card) symptoms and URT (PE) signs should not be combined in this algorithm and should be assessed and used separately. The individual URT (physicians PE) signs are:

- Otitis
- Pharyngitis
- Nasal discharge
- Sinus tenderness

The individual URT (diary card) self-reported symptoms are:

- Rhinorrhoea (runny nose), where “runny nose” is taken from the relevant symptom diary card “runny nose” symptom.
- Nasal congestion (stuffy nose), where “stuffy nose” is taken from the relevant symptom diary card “stuffy nose” symptom.
- Sneezing
- Sore throat
- Earache
- Hoarse Voice
- Eye Soreness

Subjects with no recorded data meeting the definition of this endpoint will be treated as not having met the endpoint.

The number and proportion of subjects with upper respiratory tract illness will be summarised for all subjects as well as for those infected and not infected, those who took Remdesivir and those who did not..

10.7.2.5.2 Lower Respiratory Tract Illness (LRTI)

A subject will be considered to have lower respiratory tract illness (LRTI) if he/she has any one of either a LRT (diary card) self-reported symptom or a LRT (PE) sign, as specified below, on two consecutive scheduled assessments (from the last assessment on Day 0 to the first (morning) assessment on Day 14 (quarantine discharge)), where at least one of which must attain Grade 2 severity, or if any of the following attain Grade 3 severity once. Note: LRT (diary card) symptoms and LRT (PE) signs should not be combined in this algorithm and should be assessed separately.

The individual LRT (physicians PE) signs are:

- New wheezes, rhonchi, stridor, crepitations

The individual LRT (diary card) self-reported symptoms are:

- Cough
- Shortness of breath
- Chest tightness
- Wheeze

Subjects with no recorded data meeting the definition of this endpoint will be treated as not having met the endpoint.

The number and proportion of subjects with lower respiratory tract illness will be summarised for all subjects as well as for those infected and not infected, those who took Remdesivir and those who did not.

10.7.2.5.3 Systemic Illness (SI)

A subject will be considered to have SI if he/she:

- Fulfils the criteria for febrile illness (see Section 10.7.2.5.4) or fulfils the definition of upper respiratory tract illness (see Section 10.7.2.5.1) and/or lower respiratory tract illness (see Section 10.7.2.5.2)

and

- has any one of Systemic (diary card) self-reported symptoms on two consecutive scheduled assessments (from the last assessment on Day 0 to the first (morning) assessment on Day 14 (quarantine discharge)), where at least one of which must attain Grade 2 severity, or if any of the following attain Grade 3 severity once.

  The individual Systemic (diary card) symptoms are:

  - Headache
  - Malaise/tiredness
  - Muscle and/or joint ache
  - Chilliness/feverishness
  - Dizziness

- Rashes
- Blisters
- Diarrhoea

Subjects with no recorded data meeting the definition of this endpoint will be treated as not having met the endpoint.

The number and proportion of subjects with Systemic illness will be summarised for all subjects as well as for those infected and not infected, those who took Remdesivir and those who did not.

10.7.2.5.4 Febrile Illness (FI)

Febrile illness is defined as any occurrence of temperature ≥ 37.9°C (using all assessments from the last assessment on Day 0 to the first (morning) assessment on Day 14 (quarantine discharge)).

Subjects with no recorded data meeting the definition of this endpoint will be treated as not having met the endpoint.

The number and proportion of subjects with febrile illness will be summarised for all subjects as well as for those infected and not infected, those who took Remdesivir and those who did not.

10.7.2.5.5 Symptom Grades

These endpoints are defined as the number and proportion of subjects who meet specific criteria related to the symptoms recorded in their diary cards.

- Grade 3 symptoms on any occasion at any time from the last assessment on Day 0 to first (morning) assessment on Day 14 (quarantine discharge).
- Grade 2 or higher symptoms on any occasion at any time from the last assessment on Day 0 to first (morning) assessment on Day 14 (quarantine discharge).
- Grade 2 or higher Symptoms on two separate occasions at any time from the last assessment on Day 0 to first (morning) assessment on Day 14 (quarantine discharge).
- Any symptom (grade >=1) on any occasion at any time from the last assessment on Day 0 to first (morning) assessment on Day 14 (quarantine discharge).
- Any symptom (grade >=1) on two separate occasions at any time from the last assessment on Day 0 to first (morning) assessment on Day 14 (quarantine discharge).

For each criterion, any subjects with incomplete data or no recorded symptoms meeting the definition for the endpoint will be treated as not having met the endpoint (i.e., did not experience symptoms as outlined in the specific criteria).

The number and percentage of subjects who meet each criterion will be summarised for all subjects as well as for those infected and not infected, those who took Remdesivir and those who did not.

10.7.3. Tertiary Analysis

Some of the tertiary endpoints are covered within the safety section (high-resolution CT, Spirometry, forced oscillatory technique (FOT), haematology and biochemistry abnormalities and concomitant medications). Other tertiary endpoints will not be considered within this SAP and the analysis of these will be described elsewhere.

10.7.3.1 Smell

The University of Pennsylvania Smell Identification Test (UPSIT) will be used to evaluate change in smell. The test score (out of 40) will be summarised for all subjects as well as for those infected and not infected, those who took Remdesivir and those who did not at each visit. No imputation will be done for this, only observed values will be summarised.

The index of absolute dysfunction will be generated from this test score as shown in Table 3. A shift table of the change from baseline in index of absolute dysfunction will be presented for all subjects as well as for those infected and not infected, those who took Remdesivir and those who did not.

Table 3: Olfactory index of absolute dysfunction based on UPSIT scores

Index	Female	Male
Anosmia	Score < 19	Score < 19
Severe Microsmia	19 <= Score < 26	19 <= Score < 26
Microsmia	26 <= Score < 31	26 <= Score < 30
Mild Microsmia	31 <= Score < 35	30 <= Score < 34
Normosmia	Score >= 35	Score >= 34

10.7.3.2 Cognition

Effects on cognition will not be summarised within the SAP and will be investigated separately.

10.7.3.3 Association of ABO Blood Group and Susceptibility to Infection

No analysis on blood group will be carried out within the analysis defined in the SAP.

10.7.3.4 Saliva Samples

Saliva sample results will not be analysed as part of the analysis described within the SAP.

10.7.3.5 Immunogenicity at Baseline

This data will not be analysed within the SAP.

10.7.3.6 Instrument Assessed Change

Instrument assessed change will not be included within the SAP defined analysis.

10.7.3.7 Environmental Contamination Sampling

The analysis of the environmental contamination sampling data will not be described in the SAP and will be presented elsewhere.

10.8. Safety Analysis

The primary objective of the study is to find a safe and infectious level of SARS-CoV-2 challenge safety endpoints. Hence, a number of primary and secondary endpoints are safety endpoints.

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

All adverse events will be coded using MedDRA, Version 24.0 (March 2021).

An adverse event is defined as viral challenge emergent if the onset date is on or after the date of inoculation. 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 the date of inoculation) then it will be assumed that the event is viral challenge emergent, unless the adverse event stop date indicates otherwise. Any adverse event with an onset date earlier than the date of inoculation will be classified as a pre- viral challenge adverse event.

If a subject 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 viral challenge among those events for the tables in which those characteristics are summarised.

Viral challenge-emergent AEs will be summarised within 28 days of viral challenge (up to Day 28), from Day 28 to the end of follow-up (Day 360) and over the entire study period (up to Day 360) by:

- Overall summary showing number of events, number of subjects with events (also split by severity; mild, moderate, severe, life-threatening, death), number of subjects with SAEs, number of subjects with related events (probably related, possibly related, definitely related), number of subjects with events leading to discontinuation from the study.
- System organ class, and preferred term;
- System organ class, preferred term and severity;
- System organ class, preferred term viral challenge related AEs;

  'Related' will correspond to AEs where relationship to viral challenge is recorded on the AE CRF as being 'Possibly', 'Probably', 'Definitely', or a relationship is not given.

Viral challenge-emergent SAEs that are related to viral challenge within 28 days of viral challenge (up to Day 28), from Day 28 to the end of follow-up (Day 360) and over the entire study period (up to Day 360) will be summarised by

- System organ class, and preferred term.

AEs and SAEs will be displayed for the infected, uninfected (where infection status is as defined in Section 10.1.7) and all subjects. Additionally, adverse events will also be summarised according to whether subjects received Remdesivir or not.

Serious adverse events and adverse events directly resulting in withdrawal from study will be listed. Pre viral challenge AEs will also be listed.

In all AE summary tables results will be displayed ordered in terms of decreasing frequency of SOC occurrence , and within each SOC also ordered in terms of decreasing frequency of preferred term occurrence.

10.8.2. Laboratory Variables

The following haematology, biochemistry, cardiac enzymes, coagulation and thyroid function tests will be included within summary presentations (and presented in the units as shown):

- Haematology: platelet count (x10^9/L), white blood cell (WBC) count (absolute) (x10^9/L), neutrophils (% and absolute (x10^9/L)), lymphocytes (% and absolute (x10^9/L)), haemoglobin (g/L).
- Coagulation: D-dimer (ng/mL).
- Biochemistry: C-reactive protein (CRP) (mg/L), alanine transaminase (ALT) (IU/L).
- Cardiac Enzymes: Troponin (T) (ng/L), High sensitivity Troponin (T) (ng/L).

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

Laboratory values outside the reference range will be identified in the subject listings as above or below the reference range. Laboratory values that are below the level of quantification (BLQ) will be set to zero in computations for summary presentations but will be noted as below the detection limit in subject listings. Laboratory values that are missing will remain missing but will be noted as such in listings.

Observed parameter values and changes from baseline will be summarised for the above highlighted haematology, chemistry, coagulation, cardiac enzymes and thyroid function parameters. Baseline will be the latest results obtained prior to viral challenge. For Haematology this will likely be those results obtained on Day 0 Pre-Challenge, for other safety lab parameters (chemistry, cardiac enzymes thyroid and coagulation) this will likely be the labs performed at admission. The urinalysis parameters will be listed.

In addition the toxicity grade will be summarised for each lab parameter for which toxicity grade criteria are available (See Appendix 2 Section 15.2 for the details of the toxicity grades for these parameters). These toxicity grades will be summarised and presented using stacked bar charts.

For any lab parameters where toxicity criteria is not available stacked bar charts will be produced for the normal range (i.e. low, normal and high).

Unscheduled visit assessments will be included within subject listings only.

10.8.3. Vital Signs

Vital signs parameters (Heart Rate (beats per minute), systolic blood pressure (mmHg), diastolic blood pressure (mmHg), respiratory rate (breaths per minute), peripheral arterial oxygen saturation (%), tympanic temperature (^{O}C)) will be summarised for all scheduled protocol visits and assessments.

10.8.4. Physical Examination

Physical examination (both complete and directed) results will be listed.

10.8.5. Electrocardiogram

The absolute and change from baseline in each of the ECG parameters (Heart Rate (bpm), PR interval (sec), QRS duration (sec), QT interval (sec), QTc interval (sec), QTcB interval (sec), QTcF interval (sec) and RR interval (sec)) will be listed for all subjects. Baseline will be the results on Day 0 Pre-Challenge.

10.8.6. Spirometry

Spirometry, both absolute and change from baseline, will be summarised and will include FEV_1(absolute), FEV_1(% predicted), Forced vital capacity (FVC) (absolute), FVC (% predicted), FEV_1/FVC ratio (absolute) and FEV_1/FVC ratio (% predicted).

10.8.7. FOT

Forced Oscillation Technique data will be listed.

10.8.8. Chest X-ray

A chest x-ray will be done at admission. The results will be listed only.

10.8.9. Lung CT Scan

CT scans will be performed on subjects that have lab-confirmed infection, and/or symptoms consistent with Covid-19. The results will be listed only.

10.8.10. Echocardiogram

An echocardiogram will be carried out at admission. The results of which will be listed.

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

Some endpoints have been updated slightly from the definitions within the protocol, or their definitions have been clarified. Below is a summary of these updates.

The infection and symptomatic infection endpoints that are based on detectable sample results have been removed.

It is evident that there is no real difference between the infection rate based on mid-turbinate and throat samples and so the infection definitions will be based on all of the sample results and we will not display the mid-turbinate and throat samples separately.

The timeframe for the viral load endpoints has been updated to be from Day 2, rather than 24 hours after challenge so as to ensure that the inoculated virus is no longer present. The timeframe has also been clarified for all viral load endpoints to be up to the day of discharge from quarantine, with a sensitivity analysis included to examine the impact of only using data up to the planned day of discharge (Day 14).

The number of participants with Grade 2 or higher symptoms was duplicated within the protocol and so one of these has been removed from the SAP analysis.

12. REFERENCES

[1] Matthews JNS, Altman DG, Campbell MJ, Royston P. Analysis of serial measurements in medical research. *Br Med J* (1990); 300: 230-5.

[2] Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. Journal of American Statistical Association. 1958; 53:457-481.

13. TABLES, FIGURES AND LISTINGS

13.1. Specific Presentation Details

Tables, Listings and Figures will be provided in pdf and WORD format. All summary Tables and Figures will have source data footnotes that refer to the relevant Listings. Dates will appear as ddmmmyyyy and times as hh:mm (24-hour clock times). All Listings will be ordered subject number and scheduled visit. Any unscheduled visit information will also be included within the Listings, identified as unscheduled.

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 (SD)	xx.x (xx.xx)	xx.x (xx.xx)
	%CV	xx.x	xx.x
	SE	xx.xx	xx.xx
	Median	xx.x	xx.x
	Q1, Q3	xx.x, xx.x	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:

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HVO-vCS-003

Table x.x
Title ("Primary (Day 28) Analysis" or "Final Analysis")
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

Note: Tables will not be produced for the Per Protocol (PP) Analysis Set if the PP Analysis Set is identical to the original (Full Analysis Set) Table.

The Analysis column of the table illustrates which of the tables will be produced for the Primary (Day 28) Analysis (P), the Final (Day 360) Analysis (F) and both Primary and Final (P, F) Analyses.

Table Number	Table Title	Analysis
14.1.1	Subject Disposition – All Subjects	P, F
14.1.2	Demography – Safety Analysis Set	P
14.1.3	Substance Use History – Safety Analysis Set	P
14.1.4.1	Concomitant Medications from Viral Challenge to Day 28 – Safety Analysis Set	P
14.1.4.2	Concomitant medications from Day 28 to Day 360 – Safety Analysis Set	F
14.2.1.1	qRT-PCR-confirmed (>=LLOQ) SARS-Cov-2 Infection (Variant 1, Day 2 to Discharge) by Mid-Turbinate and Throat Samples - Full Analysis Set	P
14.2.1.2	qRT-PCR-confirmed (>=LLOQ) SARS-Cov-2 Infection (Variant 1, Day 2 to Discharge) by Mid-Turbinate and Throat Samples – Per Protocol Analysis Set	P
14.2.2.1	Viral culture-confirmed (>=LLOQ) SARS-Cov-2 Infection (Variant 2, Day 2 to Discharge) by Mid-Turbinate and Throat Samples - Full Analysis Set	P
14.2.2.2	Viral culture-confirmed (>=LLOQ) SARS-Cov-2 Infection (Variant 2, Day 2 to Discharge) by Mid-Turbinate and Throat Samples – Per Protocol Analysis Set	P
14.2.3.1.1	qRT-PCR-confirmed (>=LLOQ) symptomatic SARS-Cov-2 Infection (Variant 1, Day 2 to Discharge) by Mid-Turbinate and Throat Samples - Full Analysis Set	P
14.2.3.1.2	qRT-PCR-confirmed (>=LLOQ) symptomatic SARS-Cov-2 Infection (Variant 1, Day 2 to Discharge) by Mid-Turbinate and Throat Samples – Per Protocol Analysis Set	P
14.2.3.2.1	Viral culture-confirmed (>=LLOQ) symptomatic SARS-Cov-2 Infection (Variant 2, Day 2 to Discharge) by Mid-Turbinate and Throat Samples - Full Analysis Set	P

14.2.3.2.2	Viral culture-confirmed (>=LLOQ) symptomatic SARS-Cov-2 Infection (Variant 2, Day 2 to Discharge) by Mid-Turbinate and Throat Samples – Per Protocol Analysis Set	P
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13.3. List of Figures

Note: Figures will not be produced for the Per Protocol (PP) Analysis Set if the PP Analysis Set is identical to the original (Full Analysis Set).

The Analysis column of the table illustrates which of the figures will be produced for the Primary (Day 28) Analysis (P), the Final (Day 360) Analysis (F) and both Primary and Final (P, F) Analyses.

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13.4. List of Listings

The Analysis column of the table illustrates which of the tables will be produced for the Primary (Day 28) Analysis (P), the Final (Day 360) Analysis (F) and both Primary and Final (P, F) Analyses.

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16.2.3	Subject Analysis Sets	P
16.2.4.1	Demographics	P
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16.2.4.7	Screening Questionnaires	P
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16.2.4.9	Prior and Concomitant Medications	P, F
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16.2.14	Chest X-ray	P

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16.2.18	Visit Dates	P, F

14.TABLE AND LISTING SHELLS

Table 14.1.1
Subject Disposition
All Subjects

	All Subjects (N=xx)	
	n	(%)
Enrolled	XX	
Safety Analysis Set [1]	XX	(XX.X)
Full Analysis Set [2]	XX	(XX.X)
PP Analysis Set [3]	XX	(XX.X)
Received at least one dose of Remdesivir	XX	(XX.X)
Did not receive Remdesivir	XX	(XX.X)
Completed Day 28 Visit [4]	XX	(XX.X)
Completed Study [5]	XX	(XX.X)
Early Withdrawal [6]	XX	(XX.X)
Reason for Withdrawal		
Withdrawal by Subject	XX	(XX.X)
Investigator's decision	XX	(XX.X)
Non-compliance with study requirements	XX	(XX.X)
Termination of study by sponsor	XX	(XX.X)
Adverse Event or Serious Adverse Event	XX	(XX.X)
Death	XX	(XX.X)
Pregnancy	XX	(XX.X)
Lost to follow-up	XX	(XX.X)
Other	XX	(XX.X)

[1] Safety Analysis Set = all subjects who were inoculated with wild-type SARS-COV-2 Challenge virus.
[2] Full Analysis Set = all subjects who were inoculated with wild-type SARS-COV-2 Challenge virus.
[3] Per Protocol (PP) Analysis Set = all subjects who were inoculated, had no major protocol deviations and completed the quarantine period (up to Day 14).
[4] Completed Day 28 Visit = Completed up to and including study visit Day 28.
[5] Completed Study = Completed up to and including study visit Day 360.
[6] Early Withdrawal = Withdrew from the study prior to Day 360 visit.
Note: Percentages are based on the number of enrolled subjects.

Table 14.1.2
Demography
Safety Analysis Set

		All Subjects (N=xx)
Sex		
Male	n (%)	XX (XX.X)
Female	n (%)	XX (XX.X)
Age at Screening (years)	n	XX
	Mean (SD)	XX.X (XX.XX)
	SE	XX.XX
	Median	XX.X
	Q1, Q3	XX.X, XX.X
	Min, Max	XX, XX
BMI at Screening	n	XX
	Mean (SD)	XX.X (XX.XX)
	SE	XX.XX
	Median	XX.X
	Q1, Q3	XX.X, XX.X
	Min, Max	XX, XX
[Repeat for Height and Weight at screening]		
Race		
Asian	n (%)	XX (XX.X)
Black or African American	n (%)	XX (XX.X)
White	n (%)	XX (XX.X)
Hawaiian or Pacific Islander	n (%)	XX (XX.X)
Native Indian or Alaskan	n (%)	XX (XX.X)
Other	n (%)	XX (XX.X)
Ethnicity		
Hispanic or Latino	n (%)	XX (XX.X)
Not Hispanic or Latino	n (%)	XX (XX.X)

Note: Percentages are based on the number of non-missing observations.
BMI=Body Mass Index.

Programming Note: If there are any subjects for whom sex and/or race and/or ethnicity is missing then include a missing row along with the n and %.

Table 14.1.3
Substance Use History
Safety Analysis Set

		All Subjects (N=xx)
Smoking History		
Never Smoked	n (%)	XX (XX.X)
Current Smoker	n (%)	XX (XX.X)
Previous Smoker	n (%)	XX (XX.X)
Alcohol History		
Never	n (%)	XX (XX.X)
Current User	n (%)	XX (XX.X)
Previous User	n (%)	XX (XX.X)

Note: Percentages are based on the Safety Analysis Set.

Programming note: If any categorical parameters have missing values for certain subjects, then include a missing value category.

Table 14.1.4.1
Concomitant Medications up from Viral Challenge to Day 28
Safety Analysis Set

Drug Class (L2)/ WHO Drug Preferred Base Name [1]	All Subjects (N=xx) n	%
Number of Subjects with any Medication	XX	(XX.X)
Drug Class 1	XX	(XX.X)
WHO Drug Name 1	XX	(XX.X)
WHO Drug Name 2	XX	(XX.X)
Drug Class 2	XX	(XX.X)
WHO Drug Name 1	XX	(XX.X)
WHO Drug Name 2	XX	(XX.X)

[1] All medications will be coded using the WHO Drug Dictionary Global version 2021 (March 1, 2021).

Concomitant medications correspond to medications where the medication start date will not be later than Day 28 post-viral challenge and the medication stop date is not before the date of viral challenge.
Table shows distinct number of subjects with each WHO Drug name/Drug Class.
Percentages are based on the Safety Analysis Set.

Table template should also be used for Table 14.1.4.2.

Table 14.2.1.1
qRT-PCR-confirmed (>=LLOQ) SARS-Cov-2 Infection (Variant 1, Day 2 to Discharge) by Mid-Turbinate and Throat Samples
Full Analysis Set

Sample Type	All Subjects (N=xx)	
	n (%)	95% CI
Mid-Turbinate and/or Throat	XX (XX.X)	(X.XX, X.XX)

Note: LLOQ=Lower Limit of Quantification.
Note: Clopper-Pearson 95% CI

This table template should be used for Table 14.2.1.2, 14.2.2.1, 14.2.2.2, 14.2.3.1.1, 14.2.3.1.2, 14.2.3.2.1, 14.2.3.2.2

Table 14.2.4.1.1.1
Viral Load AUC (Day 2 to Discharge) by Mid-Turbinate or Throat Samples qRT-PCR
Full Analysis Set

	Remdesivir (N=xx)			No Remdesivir (N=xx)			
Viral Load AUC (hours*Log10 copies/mL)	Infected (N=xx)	Uninfected (N=xx)	All (N=xx)	Infected (N=xx)	Uninfected (N=xx)	All (N=xx)	All Subjects (N=xx)
Mid-Turbinate							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
%CV	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SE	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
95% CI	(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)
Throat							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
%CV	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SE	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
95% CI	(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)

Note %CV is derived for the AUC, based on the log10 copies/mL

This table layout will also be used for tables 14.2.4.1.1.2, 14.2.4.1.2.1, 14.2.5.1.1.1, 14.2.5.1.1.2,

Table 14.2.4.2.1
Peak Viral Load (Day 2 to Discharge) by Mid-Turbinate and Throat Samples qRT-PCR
Full Analysis Set

	Remdesivir (N=xx)			No Remdesivir (N=xx)			
Peak Viral Load (log 10 copies / mL)	Infected (N=xx)	Uninfected (N=xx)	All (N=xx)	Infected (N=xx)	Uninfected (N=xx)	All (N=xx)	All Subjects (N=xx)
Mid-Turbinate							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
%CV	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SE	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
Throat							
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
%CV	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SE	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

This table template will be used for Table 14.2.4.2.2, 14.2.5.2.1, 14.2.5.2.2

Table 14.2.4.3.1.1
Duration of SARS-CoV-2 (Day 2 to Discharge) by Mid-Turbinate and Throat Samples qRT-PCR, Kaplan-Meier Analysis
Full Analysis Set

		Remdesivir (N=xx)			No Remdesivir (N=xx)			All Subjects (N=xx)		
Sample Type	Time (days)	n	N#	Kaplan-Meier Estimate	n	N#	Kaplan-Meier Estimate	n	N#	Kaplan-Meier Estimate
Mid-Turbinate	Xx	xx	xx	0.xxx	xx	xx	0.xxx	xx	xx	0.xxx
	Xx	xx	xx	0.xxx	xx	xx	0.xxx	xx	xx	0.xxx
	Xx	xx	xx	0.xxx	xx	xx	0.xxx	xx	xx	0.xxx
	Xx	xx	xx	0.xxx	xx	xx	0.xxx	xx	xx	0.xxx
	Xx	xx	xx	0.xxx	xx	xx	0.xxx	xx	xx	0.xxx
	Xx	xx	xx	0.xxx	xx	xx	0.xxx	xx	xx	0.xxx
	Xx	xx	xx	0.xxx	xx	xx	0.xxx	xx	xx	0.xxx
	Xx	xx	xx	0.xxx	xx	xx	0.xxx	xx	xx	0.xxx
	Xx	xx	xx	0.xxx	xx	xx	0.xxx	xx	xx	0.xxx
	Q1 (days)		xx.x			xx.x			xx.x	
	Median (days)		xx.x			xx.x			xx.x	
	Q3 (days)		xx.x			xx.x			xx.x	
Throat	Xx	xx	xx	0.xxx	xx	xx	0.xxx	xx	xx	0.xxx
	Xx	xx	xx	0.xxx	xx	xx	0.xxx	xx	xx	0.xxx
	Xx	xx	xx	0.xxx	xx	xx	0.xxx	xx	xx	0.xxx
	Xx	xx	xx	0.xxx	xx	xx	0.xxx	xx	xx	0.xxx
	Xx	xx	xx	0.xxx	xx	xx	0.xxx	xx	xx	0.xxx
	Xx	xx	xx	0.xxx	xx	xx	0.xxx	xx	xx	0.xxx
	Xx	xx	xx	0.xxx	xx	xx	0.xxx	xx	xx	0.xxx
	Xx	xx	xx	0.xxx	xx	xx	0.xxx	xx	xx	0.xxx
	Xx	xx	xx	0.xxx	xx	xx	0.xxx	xx	xx	0.xxx
	Q1 (days)	xx.x	xx.x	xx.x						
	Median (days)	xx.x	xx.x	xx.x						
	Q3 (days)	xx.x	xx.x	xx.x						

Note: N is the number of subjects in the Full Analysis Set. n is the number of subjects with a confirmed undetectable assessment after their peak measure, by the end of the period. N# is the number of subjects at risk.
Note: Day 1 is the first day of detectable viral load, not study Day 1.

This table layout will also be used for tables 14.2.4.3.1.2, 14.2.5.3.1.1, 14.2.5.3.1.2

Programming note: Q1, the median and Q3 are derived from the Kaplan-Meier analysis.

Table 14.2.4.4.1
Incubation of SARS-CoV-2 (Day 2 to Discharge) by Mid-Turbinate and Throat Samples qRT-PCR
Full Analysis Set

Incubation (Days)	All Subjects (N=xx)
Mid-Turbinate	
n	XX
Mean (SD)	XX.X (XX.XX)
%CV	XX.X
SE	XX.XX
Median	XX.X
Q1, Q3	XX.X, XX.X
Min, Max	XX, XX
Throat	
n	XX
Mean (SD)	XX.X (XX.XX)
%CV	XX.X
SE	XX.XX
Median	XX.X
Q1, Q3	XX.X, XX.X
Min, Max	XX, XX

Note: Incubation is defined as the time from viral challenge to the first quantifiable sample.

This table template will be used for Table 14.2.4.4.2, 14.2.5.4.1, 14.2.5.4.2

Table 14.2.6.1.1
Sum Total Symptom Score (Day 1 to Day 14)
Full Analysis Set

	Remdesivir (N=xx)			No Remdesivir (N=xx)			
Sum Total Symptom Score	Infected (N=xx)	Uninfected (N=xx)	All (N=xx)	Infected (N=xx)	Uninfected (N=xx)	All (N=xx)	All Subjects (N=xx)
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
GM	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
%CV	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SE	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
95% CI [1]	(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)

Note %CV is derived for the TSS based on the unlogged data.
[1] 95% CI is derived by back-transforming the 95% CI obtained based on the logged data.

This table layout will also be used for tables 14.2.6.1.2, 14.2.6.2.1, 14.2.6.2.2

Programming note: Add an appropriate footnote to show the geometric mean calculation used.

Table 14.2.6.3.1
Peak Total Symptom Score (Day 1 to Day 14)
Full Analysis Set

	Remdesivir (N=xx)			No Remdesivir (N=xx)			
Peak Total Symptom Score	Infected (N=xx)	Uninfected (N=xx)	All (N=xx)	Infected (N=xx)	Uninfected (N=xx)	All (N=xx)	All Subjects (N=xx)
n	XX	XX	XX	XX	XX	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
GM	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
%CV	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SE	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

Note %CV is derived for the TSS based on the unlogged data.

This table layout will also be used for tables 14.2.6.3.2, 14.2.6.4.1, 14.2.6.4.2

Programming note: Add an appropriate footnote to show the geometric mean calculation used.

Table 14.2.7.1.1
Proportion of Subjects for each Symptom Definition (Day 0 to Day 14)
Full Analysis Set

	Remdesivir (N=xx)			No Remdesivir (N=xx)			
Endpoint Definition	Infected (N=xx) n (%)	Uninfected (N=xx) n (%)	All (N=xx) n (%)	Infected (N=xx) n (%)	Uninfected (N=xx) n (%)	All (N=xx) n (%)	All Subjects (N=xx) n (%)
Grade 1 or Higher on Any Occasion	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Grade 2 or Higher on Any Occasion	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Grade 3 or Higher on Any Occasion	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Grade 1 or Higher on Two Separate Occasions	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Grade 2 or Higher on Two Separate Occasions	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)

This table template should be used for table 14.2.7.1.2

Table 14.2.7.2.1
Incidence of Virus Illness Outcomes
Full Analysis Set

	Remdesivir (N=xx)			No Remdesivir (N=xx)			
Number of subjects with illness	Infected (N=xx)	Uninfected (N=xx)	All (N=xx)	Infected (N=xx)	Uninfected (N=xx)	All (N=xx)	All Subjects (N=xx)
URTI Incidence (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
LRTI Incidence (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
SI Incidence (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
FI Incidence (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)

Note: Percentages are based on the Full Analysis Set.
URTI = Upper Respiratory Tract Illness, LRTI = Lower Respiratory Tract Illness, SI = Systemic Illness, FI = Febrile Illness

This table template should be used for table 14.2.7.2.2

Table 14.2.8.1
UPSIT Score Summary
Full Analysis Set

		Remdesivir (N=xx)					
		Infected (N=xx)		Uninfected (N=xx)		All (N=xx)	
Visit	Sum Total Symptoms Score	Absolute	Change from Baseline	Absolute	Change from Baseline	Absolute	Change from Baseline
Day -1	n	XX		XX		XX	
	Mean (SD)	XX.X (XX.XX)		XX.X (XX.XX)		XX.X (XX.XX)	
	GM	XX.X		XX.X		XX.X	
	%CV	XX.X		XX.X		XX.X	
	SE	XX.XX		XX.XX		XX.XX	
	Median	XX.X		XX.X		XX.X	
	Q1, Q3	XX.X, XX.X		XX.X, XX.X		XX.X, XX.X	
	Min, Max	XX, XX		XX, XX		XX, XX	
Baseline (Day 0 Pre-Challenge)	n	XX		XX		XX	
	Mean (SD)	XX.X (XX.XX)		XX.X (XX.XX)		XX.X (XX.XX)	
	GM	XX.X		XX.X		XX.X	
	%CV	XX.X		XX.X		XX.X	
	SE	XX.XX		XX.XX		XX.XX	
	Median	XX.X		XX.X		XX.X	
	Q1, Q3	XX.X, XX.X		XX.X, XX.X		XX.X, XX.X	
	Min, Max	XX, XX		XX, XX		XX, XX	
Day 1	n	XX	XX	XX	XX	XX	XX
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
	GM	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	%CV	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SE	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
	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

[Repeat for Day 2 to Day 14, Day 28, Day 90, Day 180, Day 270, Day 360]

Programming Note: Repeat the above for No Remdesivir (Infected, Uninfected, All) and 'All Subjects'

Table 14.2.8.2
UPSIT: Shift Table of Olfactory Index of Absolute Dysfunction
Full Analysis Set

		Remdesivir (N=xx)				
		Infected (N=xx)				
Visit Olfactory Index of Absolute Dysfunction [1]		Baseline Olfactory Index of Absolute Dysfunction [1]				
		0	1	2	3	4
Day 1						
0	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
1	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
2	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
3	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
4	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
Missing	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
Day 2						
0	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
1	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
2	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
3	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
4	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
Missing	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
[Repeat for Day 3 to Day 14, Day 28, Day 90, Day 180, Day 270, Day 360] *[Repeat for each Dose Group]*						

[1] 0 = Normosmia, 1 = Mild Microsmia, 2 = Microsmia, 3=Severe Microsmia, 4 = Anosmia

Programming Note: Repeat the above for Remdesivir (Uninfected, All) No Remdesivir (Infected, Uninfected, All) and All Subjects

Table 14.3.1.1
Overall Viral-Challenge Emergent Adverse Events up to Day 28
Safety Analysis Set

	Infected (N=xx)		Uninfected (N=xx)		All Subjects (N=xx)		Remdesivir (N=xx)		No Remdesivir (N=xx)	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Number of Events	XX		XX		XX		XX		XX	
Number of Subjects with any Adverse Event	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Mild	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Moderate	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Severe	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Number of Subjects with any Serious Adverse Event	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Number of Subjects with any Related Adverse Event	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Number of Subjects 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)

The AEs summarised here are those that occurred from Viral Challenge until Day 28 visit.
If a subject experiences more than one event, then the event with the worst severity or strongest relationship is included in the relevant level of summarisation.
Percentages are based on the safety analysis set.
'Related' = 'Possibly related', 'Probably related', 'Definitely related', 'Not Assessed'.
'Adverse Event Leading to Withdrawal from the Study' = Subject withdrew from the study due to an adverse event.
Percentages are based on the safety analysis set.

This table layout will also be used for Tables 14.3.2.1, 14.3.5.1

Programming note: Adapt footnotes to the appropriate AE groupings.
Programming Note: adapt footnotes for time period covered by the table as appropriate.

Table 14.3.1.2
Viral-Challenge Emergent Adverse Events up to Day 28 by SOC and PT
Safety Analysis Set

System Organ Class/ Preferred Term [1]	Infected (N=xx) n	(%)	Uninfected (N=xx) n	(%)	All Subjects (N=xx) n	(%)	Remdesivir (N=xx) n	(%)	No Remdesivir (N=xx) n	(%)
Number of Events	XX		XX		XX		XX		XX	
Number of Subjects 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)	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)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Preferred Term 1										
Preferred Term 2	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)
Preferred Term 1	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Preferred Term 2	XX	(XX.X)	XX	XX	XX	(XX.X)	(XX.X)	(XX.X)	XX	(XX.X)

[1] MedDRA Version 24.0.
The AEs summarised here are those that occurred from viral challenge until Day 28 visit..
Table shows distinct number of subjects with events for each system organ class/preferred term.
Percentages are based on the safety analysis set.

The table template should be used for Table 14.3.1.4, 14.3.1.5, 14.3.2.2, 14.3.2.4, 14.3.2.5, 14.3.5.2, 14.3.5.4, 14.3.5.5

Table 14.3.1.3
Viral-Challenge Emergent Adverse Events up to Day 28 by SOC and PT and severity
Safety Analysis Set

	Infected (N=xx)		Uninfected (N=xx)		All Subjects (N=xx)		Remdesivir (N=xx)		No Remdesivir (N=xx)	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
System Organ Class 1	XX		XX		XX		XX		XX	
Mild										
Moderate	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Severe	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)
Preferred Term 1	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Mild										
Moderate	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Severe										
	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Preferred Term 2										
Mild	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Moderate	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
Severe	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX

[1] MedDRA Version 24.0.
This table shows distinct number of subjects with events for each system organ class/preferred term/severity.
If a subject experienced a specific event more than once then the event with the worst severity is summarised.
Note: Percentages are based on the safety analysis set.

This table template should be used for table 14.3.2.3, 14.3.5.3

Table 14.3.3
Listing of Subjects with Serious Adverse Events
Safety Analysis Set

Subject	MedDRA SOC / Preferred Term [1] / Adverse Event (verbatim)	Start Date / Time (Study Day)	Stop Date / Time (Study Day)	Relationship to Viral Challenge	Severity	VE [2]

[1] MedDRA Version 24.0
[2] VE = Viral Challenge Emergent. An AE occurring on or after the date of viral challenge

Table 14.3.4
Listing of Subjects with Adverse Events Directly Resulting in Withdrawal from the Study
Safety Analysis Set

Subject	MedDRA SOC / Preferred Term [1] / Adverse Event (verbatim)	Start Date / Time (Study Day)	Stop Date / Time (Study Day)	Relationship to Viral Challenge	Severity	VE [2]

[1] MedDRA Version 24.0
[2] VE = Viral Challenge Emergent. An AE occurring on or after the date of viral challenge

Table 14.3.6.1.1
Haematology: Platelet Count Summary
Safety Analysis Set

		All Subjects (N=xx)	
Platelet Count (X10^9/L)		Absolute	Change from Baseline
Screening	n	xx	
	Mean	xx.x	
	SD	xx.xx	
	%CV	xx.xx	
	SE	xx.xx	
	Median	xx.x	
	Q1	xx.x	
	Q3	xx.x	
	Min	xx	
	Max	xx	
Admission	n	xx	
	Mean	xx.x	
	SD	xx.xx	
	%CV	xx.xx	
	SE	xx.xx	
	Median	xx.x	
	Q1	xx.x	
	Q3	xx.x	
	Min	xx	
	Max	xx	
Baseline (Day 0 Pre-Challenge)	n	xx	
	Mean	xx.x	
	SD	xx.xx	
	%CV	xx.xx	
	SE	xx.xx	
	Median	xx.x	
	Q1	xx.x	
	Q3	xx.x	
	Min	xx	
	Max	xx	
Day 1	n	xx	xx
	Mean	xx.x	xx.x
	SD	xx.xx	xx.xx
	%CV	xx.xx	xx.xx
	SE	xx.xx	xx.xx
	Median	xx.x	xx.x
	Q1	xx.x	xx.x
	Q3	xx.x	xx.x
	Min	xx	xx
	Max	xx	xx

[Repeat for each timepoint]

This table template should be used for Table 14.3.6.1.2 - 14.3.6.1.7, Table 14.3.7.1.1 - 14.3.7.1.2, Table 14.3.8, 14.3.9.1, 14.3.9.2
Baseline should be updated for each set of parameters – Haematology, Biochemistry and Cardiac Enzymes this should be Day 0 pre-Challenge. For Thyroid function and Coagulation this should be Admission.

Table 14.3.6.2
Haematology Parameters: Toxicity Grade Shift Table
Safety Analysis Set

		All Subjects (N=xx)				
Parameter / Visit / Toxicity Grade [1]		Baseline Toxicity Grade				
		Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Parameter 1						
Day 1						
Grade 0	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
Grade 1	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
Grade 2	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
Grade 3	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
Grade 4	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
Missing	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
Day 2						
Grade 0	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
Grade 1	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
Grade 2	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
Grade 3	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
Grade 4	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
Missing	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
Day 3						
Grade 0	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
Grade 1	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
Grade 2	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
Grade 3	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
Grade 4	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
Missing	n (%)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)	X (X.XX)
[Repeat for visits Day 4-Day 14, Day 28, Day 90, Day 180, Day 270 Day 360]						
[Repeat for each Haematology parameter for which toxicity grade available]						
[Repeat for each dose group]						

[1] Grade 0=None, Grade 1=Mild, Grade 2=Moderate, Grade 3=Severe, Grade 4=Potentially life-threatening.
Note: Baseline is Day 0 Pre-Challenge

Programming Note: If toxicity criteria available for parameter and toxicity grade missing (and aval not missing) then assume toxicity grade is 0 (none).

Toxicity criteria and grades are shown in Appendix 1.

This table template should be used for Table 14.3.7.2

Table 14.3.10.1
Vital Signs: Heart Rate Summary
Safety Analysis Set

Heart Rate (BPM)		All Subjects (N=xx) Absolute	Change from Baseline
Screening	n	xx	
	Mean	xx.x	
	SD	xx.xx	
	%CV	xx.xx	
	SE	xx.xx	
	Median	xx.x	
	Q1	xx.x	
	Q3	xx.x	
	Min	xx	
	Max	xx	
Admission	n	xx	
	Mean	xx.x	
	SD	xx.xx	
	%CV	xx.xx	
	SE	xx.xx	
	Median	xx.x	
	Q1	xx.x	
	Q3	xx.x	
	Min	xx	
	Max	xx	
Baseline (Day 0 Pre-Challenge)	n	xx	
	Mean	xx.x	
	SD	xx.xx	
	%CV	xx.xx	
	SE	xx.xx	
	Median	xx.x	
	Q1	xx.x	
	Q3	xx.x	
	Min	xx	
	Max	xx	
Day 1	n	xx	xx
	Mean	xx.x	xx.x
	SD	xx.xx	xx.xx
	%CV	xx.xx	xx.xx
	SE	xx.xx	xx.xx
	Median	xx.x	xx.x
	Q1	xx.x	xx.x
	Q3	xx.x	xx.x
	Min	xx	xx
	Max	xx	xx

[Repeat for each timepoint]

This table template should be used for Table 14.3.10.2 – 14.3.10.5, 14.3.11

Table 14.3.12.1
Spirometry: FEV1 Summary
Safety Analysis Set

		All Subjects (N=xx)	
		Absolute	Change from Baseline
Screening	n	XX	
	Mean (SD)	XX.X (XX.XX)	
	%CV	XX.X	
	SE	XX.XX	
	Median	XX.X	
	Q1, Q3	XX.X, XX.X	
	Min, Max	XX, XX	
Admission	n	XX	
	Mean (SD)	XX.X (XX.XX)	
	%CV	XX.X	
	SE	XX.XX	
	Median	XX.X	
	Q1, Q3	XX.X, XX.X	
	Min, Max	XX, XX	
Day 0 (Pre-Challenge)	n	XX	
	Mean (SD)	XX.X (XX.XX)	
	%CV	XX.X	
	SE	XX.XX	
	Median	XX.X	
	Q1, Q3	XX.X, XX.X	
	Min, Max	XX, XX	
Day 1	n	XX	XX
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
	%CV	XX.X	XX.X
	SE	XX.XX	XX.XX
	Median	XX.X	XX.X
	Q1, Q3	XX.X, XX.X	XX.X, XX.X
	Min, Max	XX, XX	XX, XX

This table template will be used for Table 14.3.12.2 – 14.3.12.6

Listing 16.2.1.1
Subject Disposition

Subject	Informed Consent Date / Time	Eligible [1]	Quarantine Admission Date	Viral Challenge Date / Time	Discharge Date (Study Day)	Completed Day 28 Visit	Completed Study [2]	Date of Completion/ Withdrawal (Study Day)	Reason for Withdrawal
xxxxxx	ddmmyyyy /hh:mm	Yes/No	ddmmyyyy	ddmmyyyy / hh:mm	ddmmyyyy	Yes / No	Yes / No	ddmmyyyy (xx)	xxxxxxxxxxxxxxxxxxxxxxxxx xxxxxxx

[1] Corresponds to eligibility criteria review at Day 0 Pre-Challenge.
[2] Completed Study = Participating in the study up to and including Day 360 (Follow-up)

Listing 16.2.1.2
Failed Inclusion and Exclusion Criteria

Subject	Reason for Exclusion
xxxxxx	xxxxxxxxxxxxxxxxxxx

Programming note: Listing not required if no subjects fail the criteria.

Listing 16.2.2
Protocol Deviations

Subject	Deviations Reported	Date Occurred (Study Day)	Deviation Category [a]	Other, Specify	Deviation Description	Corrective Action	Serious Breach
xxxxxx	Yes/No	ddmmyyyy (xx)	n	xxxx	xxxxxxxxxx	Xxxxxxxxxx	Yes/No

[a] – Deviation categories: Informed Consent procedure [1] / Subject error [2] / Inclusion/exclusion criteria [3] / Investigational product [4] / Visit window [5] / Concomitant medication/therapy [6] / Study procedure/assessment window [7] / SAE reporting [8] / Study procedure/assessment performance [9] / Missing assessment/sample [11] / Other [12]

Listing 16.2.3
Subject Analysis Sets

Subject	Full Analysis Set [1]	Per Protocol Analysis Set [2]	Safety Analysis Set [3]	Laboratory Confirmed Infection [4]	Received Remdesivir [5]
xxxxxx	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No

[1] Safety Analysis Set = all subjects who were inoculated with wild-type SARS-COV-2 Challenge virus.
[2] Full Analysis Set = all subjects who were inoculated with wild-type SARS-COV-2 Challenge virus.
[3] Per Protocol (PP) Analysis Set = all subjects who were inoculated, had no major protocol deviations and completed the quarantine period (up to Day 14).
[4] Laboratory Confirmed Infection = Two quantifiable (≥LLOQ) RT-PCR measurements from mid turbinate or throat samples, reported on 2 or more consecutive timepoints, starting from Day 2 up to Quarantine discharge.
[5] Received at least one dose of Remdesivir

Listing 6.2.4.1
Demographics

Subject	Age at Time of screening (years)	Sex	Ethnicity	Race	Visit	Date	Height (cm)	Weight (kg)	BMI (kg/m^2)	Comments
xxxxxx	xx	Male / Female	xxxxxxxxxx	xxxxxxxx	Screening / Admission	ddmmyyyy	xxx	xx.xx	xx	xxxxxxxxxxxxxxxxx

Note: NA = Not Applicable. Results for height, weight and BMI are shown for all visits.

Listing 16.2.4.2
Reproductive Status and Contraception Use

Subject	Preg [1]	Child Bearing Potential	Date of Last Period	HSAC [2]	Become HSAC [3]	Agree not To Donate Sperm	SAC [4]	Become SAC [5]	Agree to Use Contraception	Methods [6]	Comment
xxxxxx	Yes / No	Yes / No	ddmmmyyyy	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	x, x	xxxxxxxxxxxxxx

[1] Breast Feeding/Pregnant Recently/Planning Pregnancy
[2] HSAC = Heterosexually Active (female)
[3] Should subject become Heterosexually Active, agree to use Contraception
[4] SAC = Sexually Active (male)
[5] Should subject become Sexually Active, agree to use Contraception
[6] 1 Oral, injected or implanted hormonal methods of contraception (minimum 2 weeks prior to admission).
2 An intrauterine device (IUD) or intrauterine system (IUS), or bilateral tubal ligation.
3 Male Sterilisation
4 Barrier Methods – Condom with spermicide
5 Other method.

Listing 16.2.4.3
Smoking History

Subject	Smoking History	Start Date	Stop Date	Exposure to household smoke	Uses e-cigarettes	Category	Amount	Years	Comments
xxxxxx	xxxxxxxxxxx	ddmmyyyy	ddmmyyyy	Yes / No	Yes / No	Number of cigarettes smoked per day	xx	xx	xxxxxxxxxxx
						Number of cigars smoked per day	xx	xx	xxxxxxxxxxx
						Number of cigarillos smoked per day	xx	xx	xxxxxxxxxxx
						Number of pipe bowls smoked per day	xx	xx	xxxxxxxxxxx
						Tobacco smoked per week (grams)	xx	xx	xxxxxxxxxxx
						Pack years	xx	xx	xxxxxxxxxxx

Note: Comments are collected for the combined smoking, alcohol and drugs of abuse module and hence may relate to any of these parameters.
* Date estimated.

Listing 16.2.4.4
Alcohol Use

Subject	Alcohol Use History	Weekly alcohol intake (units)	Willing to refrain from alcohol intake	Comments
xxxxxx	Never / Current User / Previous User	xx	Yes / No	xxxxxxxxxx

Note: Comments are collected for the combined smoking, alcohol and drugs of abuse module and hence may relate to any of these parameters.

Listing 16.2.4.5
Recreational Drug Use and Abuse

Subject	Current or Recent User	Start Date	Stop Date / Ongoing	Recreational drug(s) used	Volume / amount of Consumption	Route of Administration	Willing to refrain from use?	Comments
xxxxxx	Yes / No	ddmmyyyy	ddmmyyyy	xxxxxxxxxxxx	xxxxxxxxxxxxxxxxxx	xxxxxxxxxxxxxx	Yes / No	xxxxxxxxxx

Note: Comments are collected for the combined smoking, alcohol and drugs of abuse module and hence may relate to any of these parameters.
* Date estimated.

Listing 16.2.4.6
QCovid Risk Assessment

Subject	Visit	Date / Time	Death Risk (Abs)	Death Risk (1 in …)	Hospital Risk (Abs)	Hospital Risk (1 in ….)	Comment
xxxxxx	xxxxx	ddmmyyyy / hh:mm	x.xxxxx	xxxxxx	x.xxxxx	xxxxxx	xxxxxxx

Listing 16.2.4.7
Screening Questionnaires

Subject	Visit	Date / Time	Questionnaire	Score	Comment
xxxxxx	xxxxx	ddmmyyyy / hh:mm	GAD-7 / PHQ-9	xxxxxx	xxxxxxx

Listing 16.2.4.8
Medical History

Subject	Med Hist Line	MedDRA SOC / Preferred Term [1] / Medical Condition	Start Date	End Date	Frequency	Ongoing	Concomitant medication Taken for this condition?
xxxxxx	xxx	Xxxxxxxxxx	ddmmyyyy	ddmmyyyy	Single Episode / Intermittent / Continuous / Other	Yes / No	Yes / No

[1] MedDRA Version 24.0.

Note: * Date estimated.

Listing 16.2.4.9
Prior and Concomitant Medications

Subject	Drug Class (L2) / WHO Drug Preferred Base Name [1] / Medication (verbatim)	Start Date / Time (Study Day)	End Date / Time (Study Day)	Ongoing	Indication / AE / Med History Line	Dose / Dose Units	Freq [2] / Route [3]	P / C28 / C [4]
xxxxxx	xxxxxxxxx	ddmmyyyy / hh:mm (xx)	ddmmyyyy / hh:mm (xx)	Yes / No	xxxxxxxx / AE / MHn	xxx	xxx / xxx	P / C28 / C

[1] WHO Drug Dictionary Global version 2021 (March 1, 2021).
[2] OD = Once a day, BD = Twice a day, PRN = As needed, TDS = Three times a day, QDS = Four times a day, CTS = Continuous.
[3] A = Aural, IM = Intramuscular, INH = Inhalation, IUD = Intrauterine Device, IV = Intravenous, N = Nasal, O = Ocular, PO = Oral, PR = Rectal, PV = Vaginal, SC = Subcutaneous, SL = Sublingual, TOP = Topical.
[4] P=Prior, C28=Concomitant up to Day 28 post-viral challenge, C=Concomitant other.

Note: * Date/Time estimated.

If the medication stop date is before the date of viral challenge, the medication will be assigned as being prior to Viral challenge. In all other cases, the medication is assigned as being concomitant with viral challenge.

Programming notes: Update footnotes 2 and 3 to reflect codes used in actual data.

Listing 16.2.5.1
Inoculation Administration

Subject	Administration Date / Time	Administered Intranasally?	Administered in Both Nostrils?	Administration Successful?	Titre of Virus	Change in Health? [1]	Comments
xxxxxx	ddmmyyyy / hh:mm	Yes / No	Yes / No	Yes / No	xxxxx	Yes / No	xxxxxxxxxxx

[1] Subjects were monitored for 30 minutes post inoculum administration.

Listing 16.2.5.2
Remdesivir Administration

Subject	Dosing Reason [1]	Administration Date / Time (study day)	Dose Number	Full Dose Administered?	Adverse Reaction	Completed Dosing Schedule	Date of Discontinuation	Number of Doses Administered	Reason for Discontinuation
xxxxxx	Infection / Symptoms	ddmmyyyy / hh:mm	x	Yes / No	Yes / No	Yes / No	dmmyyyy	x	xxxxxxxxxxxxxxxxxxxxx

[1] Infection = Confirmation of SARS-COV-2 infection at two consecutive time points.
Symptoms = Immediately after symptoms, signs or investigations suggestive of COVID-19.

Note: Remdesivir only administered during Cohort 1.

Listing 16.2.5.3
Antibodies

Subject	Sample Collection Date / Time (Study Day)	Visit	Presence of SARS-CoV-2	Comments
xxxxxx	ddmmyyyy / hh:mm (xx)	xxxxx	Xxxxx	xxxxxxxxxxx

Listing 16.2.6.1
Viral Load by Mid-Turbinate or Throat Sample Results

Subject	Sample Collection Date / Time (Study Day)	Sample Type	Assessment	qRT-PCR Virus Titre (Log10 Copies/mL)	Viral Culture (Log10 FFU/mL)	Qualitative Viral Culture	Comments
xxxxxx	ddmmyyyy / hh:mm (xx)	Mid-Turbinate / Throat	1 / 2	Xxxxx	xxxxx	Negative / Positive	xxxxxxxxxxx

The Limit of Detection and Lower limit of Quantification will be shown in the footnote.

Listing 16.2.6.2.1
Viral Load by Mid-Turbinate or Throat Sample qRT-PCR Derivations

Subject	Sample Type	AUC (Day 1 to Day 14) (hours*Log10 Copies/mL)	Peak Viral Load (Day 1 to Day 14) (Log10 Copies/mL)	Duration of SARS-CoV-2 (days)	Incubation of SARS-CoV-2 (days)	At Least Two Positive Measurement (>=LLOQ) (Day 1 to Day 14)
xxxxxx	Mid-Turbinate / Throat / Mid-Turbinate or Throat	XX.XX	XX.XX	XX	XX	Yes / No

Listing 16.2.6.2.2
Viral Load by Mid-Turbinate or Throat Sample Viral Culture Derivations

Subject	Sample Type	AUC (Day 1 to Day 14) (hours*Log10 PFU/mL)	Peak Viral Load (Day 1 to Day 14) (Log10 PFU/mL)	Duration of SARS-CoV-2 (days)	Incubation of SARS-CoV-2 (days)	At Least One Positive Measurement (>=LLOQ) (Day 1 to Day 14)
xxxxxx	Mid-Turbinate / Throat / Mid-Turbinate or Throat	XX.XX	XX.XX	XX	XX	Yes / No

Listing 16.2.7.1.1
Symptom Diaries – Individual Symptoms

Subject	Visit	Diary Card Completion Date / Time (Study Day)	Assessment	Type	Sign	Grade	VAS
xxxxxx	xxxxxx	ddmmyyyy / hh:mm (xx)	1 / 2 / 3	LRTI	Cough	x	
					Shortness of Breath	X	
					Chest Tightness	X	
					Wheeze	X	
				URTI	Runny Nose	X	
					Stuffy Nose	X	
					Sneezing	X	
					Sore Throat	X	
					Earache		
					Eye Soreness	X	
					Hoarse Voice	X	
				SI	Headache	X	
					Malaise	X	
					Muscle/Joint ache	X	
					Chilliness/Feverishness	X	
					Dizziness	X	
					Blisters	X	
					Diarrhoea	X	
					Rashes	X	

Listing 16.2.7.1.2
Symptom Diaries – Qualitative

Subject	Visit	Date (Study Day)	Do you have a Cold? [1]	Global Change Since Yesterday [2]	Confusion, disorientation, or drowsiness [3]	Loss of appetite [4]
xxxxxx	xxxxxx	ddmmyyyy (xx)	Yes / No	Very much better / Somewhat better / A little better / The same / A little worse / Somewhat worse / Very much worse	Yes / No	Yes / No

[1] Do you have a cold?
[2] Global Change Since Yesterday: Compared to yesterday I feel that my cold is….
Note: [2] is only answered if subject answers yes to [1]
Note: [1] and [2] are asked in the morning and [3] and [4] are asked in the evening.

Listing 16.2.7.1.3
Individual Total Symptom Scores

Subject	Diary Card Completion Date / Time (Study Day)	Assessment	Total Symptom Score	Daily Total Symptom Score
xxxxxx	ddmmyyyy / hh:mm (xx)	1 / 2 / 3	xx	

Programming Note: Daily total symptom score will be one score per day, shown on the top row for each day.

Listing 16.2.7.1.4
Total Symptom Score Derivations

Subject	Sum Total Symptom Score (Day 1 to Day 14)	Total Symptom Score AUC (Day 1 to Day 14)	Peak Total Symptom Score (Day 1 to Day 14)	Peak Daily Total Symptom Score (Day 2 to Day 13)
xxxxxx	XX	XX	XX	XX

Listing 16.2.7.2.1
Symptoms Grade Derivations

Subject	Grade 1 or Higher on Any Occasion	Grade 1 or Higher on Two Separate Occasions	Grade 2 or Higher on Any Occasion	Grade 2 or Higher on Two Separate Occasions	Grade 3 or Higher on Any Occasion
xxxxxx	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No

Listing 16.2.7.2.2
Illness and Symptomatic Infection Derivations

Subject	Subject has qRT-PCR confirmed (>=LLOQ) symptomatic infection (Variant 1)?	Subject has Culture-lab-confirmed (>=LLOQ) symptomatic infection?	Subject has URTI?	Subject has LRTI?	Subject has SI?	Subject has FI?
xxxxxx	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No

URTI = Upper Respiratory Tract Illness, LRTI = Lower Respiratory Tract Illness, SI = Systemic Illness, FI = Febrile Illness

Listing 16.2.8.1
UPSIT

Subject	UPSIT Test Completion Date / Time (Study Day)	Result	Olfactory Index of Absolute Dysfunction
xxxxxx	ddmmyyyy / hh:mm (xx)	xx	

Listing 16.2.9.1
Adverse Events (Part 1)

Subject	AE Line	MedDRA SOC / Preferred Term [1] / Adverse event (verbatim)	Start Date / Time (Study Day)	Stop Date / Time / (Study Day)	Severity	VE [2]
xxxxxx		xxxxxxxxx	ddmmyyyy / hh:mm (xx)	ddmmyyyy / hh:mm (xx)	Mild / Moderate / Severe / Life-Threatening	Yes / Blank

[1] MedDRA Version 24.0.
[2] VE = Viral Challenge Emergent. An adverse event is Viral Challenge Emergent if the start date is at or after the Viral Challenge.
Note: * Date/Time estimated.

Programming note: Only subjects with AEs will be shown in this listing.

Listing 16.2.9.2
Adverse Events (Part 2)

Subject	MedDRA SOC / Preferred Term [1] / Adverse event (verbatim)	Start Date / Time (Study Day)	Relationship To:[2]				
			Virus	Medication	Procedure	Other	Other Details
xxxxxx	xxxxxxxxx	ddmmyyyy / hh:mm (xx)					

[1] MedDRA Version 24.0

[2] NA = Not Assessed by PI; 1 = Not used in this trial/study; 2 = Not Related; 3 = Unlikely Related; 4 = Possibly Related; 5 = Probably Related; 6 = Definitely Related.

Note: * Date/Time estimated.

Programming note: Only subjects with AEs will be shown in this listing.

Listing 16.2.9.3
Adverse Events (Part 3)

Subject	MedDRA SOC / Preferred Term [1] / Adverse event (verbatim)	Start Date / Time (Study Day)	Freq [2]	Outcome [3]	Action Taken Remdesivir [4]	Action Taken Other [5]	Action Taken Details
xxxxxx	xxxxxxxxx	ddmmyyyy / hh:mm (xx)	x	x	x		xxxxxxxxxxx

[1] MedDRA Version 24.0
[2] Freq = Frequency. For frequency categories, C = Continuous, I = Intermittent, S = Single Episode.
[3] Outcome: 1 = Resolved; 2 = Resolved with Sequelae; 3 = Ongoing; 4 = Fatal; 5 = Unknown.
[4] Action Taken: 1 = Study intervention (Remdesivir) dose not changed; 2 = Study intervention (Remdesivir) dose adjusted; 3 = Study intervention (Remdesivir) administration temporarily interrupted; 4 = Study intervention (Remdesivir) permanently discontinued; 5 = N/A, Study intervention (Remdesivir) not administered
[5] Action Taken: 1 = None; 2 = Non-drug therapy given; 3 = Concomitant medication taken; 4 = Subject withdrawn; 5 = Subject hospitalized; 6 = Other

Note: * Date/Time estimated.

Programming note: Only subjects with AEs will be shown in this listing.

Listing 16.2.9.4
Adverse Events (Part 4)

Subject	MedDRA SOC / Preferred Term [1] / Adverse event (verbatim)	Start Date / Time (Study Day)	SAE	Reason for SAE	Comments
		ddmmyyyy / hh:mm (xx)			
xxxxxx	xxxxxxxxx		Yes / No	xxxxxx	xxxxxxxxxxx

[1] MedDRA Version 24.0.

Note: * Date/Time estimated.

Listing 16.2.10.1
Blood Sample Collection

Treatment Group	Participant	Visit	Sample Collection Date / Time (Study Day)	Sample Type(s) [1]	Clinically Significant Result?	Adverse Event associated with Procedure?	Comments
xxxxxxx	xxxxxx	xxxxx	ddmmyyyy / hh:mm (xx)	x x x x x x	Yes / No	Yes / No	xxxxxxxxxxxxxx

* see Time and Events Schedule.
[1] 1 = Biochemistry, 2 = Cardiac enzymes, 3 = Haematology, 4 = Coagulation, 5 = Thyroid function test, 6 = HIV, hepatitis A, B, & C, 7 = Serum pregnancy test, 8 = Serum FSH, 9, Haemaglobin, 10 = Lipid Profile, 11 = Plasma Markers, 12 = Antibodies, 13 = Paxgene, 14 = PBMC

Listing 16.2.10.2
Haematology

Subject	Visit	Sample Collection Date / Time (Study Day)	Parameter	Result	Change from Baseline	Units	Lower Limit	Upper Limit	Flag	Toxicity Grade	Comments
		ddmmyyyy hh:mm									
xxxxxx	xxxx	(xx)	Basophils (%)	x.xx	x.xx	%	x.xx	x.xx	L / H	0 / 1 / 2 / 3 / 4	xxxxxxxxxxxxxxxxxxx
			Basophils (abs)	x.xx	x.xx	X10^9/L	x.xx	x.xx			
			Eosinophils (%)	x.xx	x.xx	%	x.xx	x.xx			
			Eosinophils (abs)	x.xx	x.xx	X10^9/L	x.xx	x.xx			
			Haematocrit	x.xx	x.xx	%	xx	xx			
			Haemoglobin	xxx	xxx	g/L	xxx	xxx			
			Lymphocytes (%)	x.xx	x.xx	%	x.xx	x.xx			
			Lymphocytes (abs)	x.xx	x.xx	X10^9/L	x.xx	x.xx			
			MCH	x.xx	x.xx	pg	xx.x	xx.x			
			MCHC	xxx	xxx	g/L	xxx	xxx			
			MCV	x.xx	x.xx	fL	xx.x	xx.x			
			Monocytes (%)	x.xx	x.xx	%	xx.x	xx.x			
			Monocytes (abs)	x.xx	x.xx	X10^9/L	xx.x	xx.x			
			Neutrophils (%)	x.xx	x.xx	%	xx.x	xx.x			
			Neutrophils (abs)	x.xx	x.xx	X10^9/L	xx.x	xx.x			
			Platelets	xxx	xxx	X10^9/L	xx.x	xx.x			
			RBC Count	x.xx	x.xx	X10^12/L	x.xx	x.xx			
			Reticulocytes (%)	x.xx	x.xx	%	x.xx	x.xx			
			Reticulocytes (abs)	xx.x	xx.x	X10^9/L	xx.x	xxx.x			
			WBC Count	x.xx	x.xx	X10^9/L	x.x	xx.x			

Note: Flag: L = below lower limit, H = above upper limit. Toxicity Grade: 0=None, 1=Mild, 2=Moderate, 3=Severe, 4=Potentially life-threatening

Same listing template will be used for 16.2.10.3, 16.2.10.4, 16.2.10.5, 16.2.10.6

Listing 16.2.10.7.1
Other Laboratory Tests: TDL (Part 1)

Subject	Visit	Sample Collection Date / Time (Study Day)	HIV 1 and HIV 2 antibodies	HBSAg	HAIgM	Hepatitis C	FSH (IU/L)	Beta HCG (quantitative) (IU/L)
xxxxxx	xxxx	ddmmyyyy hh:mm (xx)	Positive / Negative	Positive / Negative	Positive / Negative	Positive / Negative	xx	xx

Note: L=Low, H=High, ND=Not Done.

Normal Ranges to be displayed in footnote, if available.

Listing 16.2.10.7.2
Other Laboratory Tests: TDL (Part 2)

Subject	Visit	Sample Collection Date / Time (Study Day)	Parameter	Result	Units	Comments
xxxxxx	xxxx	ddmmyyyy hh:mm (xx)	xxxxxxxx	xxx	xxx	xxxxxxxxxx

Programming note: Any other collected TDL lab parameters (that are not contained within previous laboratory listings) will be recorded in this listing (e.g. Globulin, Hematocrit, MPV, RDW, CKMB, Blood film, Globulin).

Note: L=Low, H=High.

Normal Ranges to be displayed in footnote.

Listing 16.2.10.8.1
Other Laboratory Tests: Urine Pregnancy

Subject	Visit	Test Date / Time (Study Day)	Subject has data	Result	Comments
xxxxxx	xxxx	ddmmyyyy / hh:mm (xx)	Yes / No / NA - Male	Positive / Negative	xxxxxxxxxxxxxxxxx

Listing 16.2.10.8.2
Other Laboratory Tests: Drugs of Abuse Screen

Treatment Group	Subject	Visit	Sample Collection Date / Time (Study Day)	Test Performed Time	Drug	Result	Comments
xxxxxxx	xxxxxx	xxxx	ddmmmyyyy hh:mm (xx)	hh:mm		Positive /	
					Cocaine	Negative /	
						Not done	
						Positive /	
					Cannabinoids	Negative /	
						Not done	
						Positive /	
					Methadone	Negative /	
						Not done	
						Positive /	
					Ecstasy	Negative /	
						Not done	
						Positive /	
					Opiates	Negative /	
						Not done	
						Positive /	
					Benzodiazepines	Negative /	
						Not done	
						Positive /	
					Barbituates	Negative /	
						Not done	
						Positive /	
					Amphetamine	Negative /	
						Not done	
						Positive /	
					Methamphetamine	Negative /	
						Not done	
						Positive /	
					Tricyclic	Negative /	
						Not done	

Listing 16.2.10.8.3
Other Laboratory Tests: Urine Cotinine

Subject	Visit	Test Performed Date / Time (Study Day)	Result	Comments
xxxxxx	xxxx	ddmmyyyy / hh:mm (xx)	Positive / Negative	xxxxxxxxxxxxxxxx

Listing 16.2.10.8.4
Other Laboratory Tests: Alcohol Breath Test

Subject	Visit	Test Date / Time (Study Day)	Result	Comments
xxxxxx	xxxx	ddmmyyyy / hh:mm (xx)	Positive / Negative	xxxxxxxxxxxxxxxx

Listing 16.2.10.9.1
Urinalysis

Subject	Visit	Sample Collection Date / Time (Study Day)	Test Performed Time	Parameter	Result [1]
		ddmmyyyy / hh:mm			
xxxxxx	xxxx	(xx)	hh:mm	Appearance	
				Bilirubin	
				Blood - Dip	
				Blood - Haemolysed / Non-Haemolysed	
				Colour	
				Glucose	
				Ketones	
				Leukocytes	
				Nitrite	
				Protein	
				Specific Gravity	
				Urobilinogen	
				pH	
				Interpretation	
				Sent for Microscopy	
				Comments	

[1] NCS = Not clinically significant, CS = Clinically significant.

Programming note: The physician interpretation and microscopy (Yes/No) will be shown as an additional row at the end of each assessment, with the interpretation/microscopy outcome shown in the result column.
Programming note: for Blood parameter there is a Haemolysed/Non-Haemolysed as well as a result.

Listing 16.2.10.9.2
Urinalysis (TDL): Microscopy

Subject	Visit	Sample Collection Date / Time (Study Day)	Urine RBC	Urine WBC	Cellular casts	Granular casts	Hyaline casts	Urine culture
xxxxxx	xxxx	ddmmyyyy / hh:mm (xx)	xxxxxxx	xxxxxxx	xxxxxxx	xxxxxxx	xxxxxxx	xxxxxxxxx

Note: ND=Not Done.

Note: A=Abnormal

Listing 16.2.10.10.1
Vital Signs

Subject	Visit	Date	Assessment	Time Started Supine	Collection Time	Parameter	Result [1]	Change from Baseline	Units	Comments
xxxxxx	xxxx	ddmmyyyy	1 / 2 / 3 / 4	hh:mm	hh:mm	Systolic BP	xxx	xxx	mmHg	
						Diastolic BP	xx	xx	mmHG	
						Heart Rate	xx	xx	bpm	
						Rep. Rate	xx	xx	breaths/min	
						SpO2	xx	xx	%	
						Interpretation	xxxxxxxx			xxxxxxx

[1] NCS = Not clinically significant, CS = Clinically significant.

Note: Comments and Interpretation relate to the complete vital signs module and hence can relate to temperature as well.

Programming note: The physician interpretation will be shown as an additional row at the end of each assessment, with the interpretation outcome shown in the result column.

Listing 16.2.10.10.2
Temperature

Subject	Visit	Date	Assessment	Collection Time	Tympanic Temperature (deg C)	Baseline	Change from Baseline	>=37.9 deg C?	Comments
xxxxxx	xxxx	ddmmyyyy	1 / 2 / 3 / 4	hh:mm	xx.x	xx.xx	xx.xx	Yes / Blank	xxxxxxx

Note: Comments relate to the complete vital signs module and hence relate to one or more vital signs parameters.

Listing 16.2.11
ECG

Subject	Visit	Date	Time Started in Resting Position	Time Performed	Parameter	Result [1]	Change from Baseline	Units	Comments
xxxxxx	xxxx	ddmmyyyy	hh:mm	hh:mm	HR	xxx	xxx	bpm	xxxxxx
					PR	xxx	xxx	ms	
					QRS	xxx	xxx	ms	
					QT	xxx	xxx	ms	
					QTc	xxx	xxx	ms	
					QTcB	xxx	xxx	ms	
					QTcF	xxx	xxx	ms	
					RR	xxx	xxx	ms	
					Interpretation	Normal / Abnormal NCS / Abnormal CS			

[1] NCS = Not clinically significant, CS = Clinically significant.

Programming note: The physician interpretation will be shown as an additional row at the end of each assessment, with the interpretation outcome shown in the result column.

Listing 16.2.12
Spirometry

Subject	Visit	Date	Best Spirometry Time	Parameter	Result [1]	Change from Baseline	Units	Comments
xxxxxx	xxxx	ddmmyyyy	hh:mm	FEV1 (abs)	x.xx	x.xx	L	
				FEV1 (% Pred)	xx	xx	%	
				FEV1/FVC Ratio (abs)	xx	xx		
				FEV1/FVC Ratio (% Pred)	xx	xx	%	
				FVC (abs)	x.xx	x.xx	L	
				FVC (% Pred)	xx	xx	%	
				FEV1 decreased by > 15% from baseline	Yes / No			
				Interpretation	Normal / Abnormal NCS / Abnormal CS			

[1] NCS = Not clinically significant, CS = Clinically significant.

Programming note: The physician interpretation will be shown as an additional row at the end of each assessment, with the interpretation outcome shown in the result column.

Listing 16.2.13
FOT

Subject	Age / Sex / Weight / Height	Test Date (Study Day)	Parameter	Units	Variation	Time	Reference	Result	SD	CV	Z-Score	%Predicted
			R5 / R20 / R5-20 / X5 /									
	xx / xxx / xxx /		X5 in ex / Fres / AX /		Mean / M1 / M2 /							
xxxxxx	xxx	ddmmmyyyy (xx)	VT	xxx	M3	hh:mm:ss	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

Programming Note: The reference, SD, CV and z-score will only be displayed for the mean row of the listing.

Listing 16.2.14
Chest X-ray

Subject	Visit	Date	Time Performed	Interpretation	Comments
xxxxxx	xxxx	ddmmyyyy	hh:mm	Normal / Abnormal NCS / Abnormal CS	xxxxxxxx

[1] NCS = Not clinically significant, CS = Clinically significant.

Listing 16.2.15
Lung CT Scan

Subject	Visit	Date	Time Performed	Interpretation	Comments
xxxxxx	xxxx	ddmmyyyy	hh:mm	Normal / Abnormal NCS / Abnormal CS	xxxxxxxx

[1] NCS = Not clinically significant, CS = Clinically significant.

Listing 16.2.16
Echocardiogram

Subject	Visit	Date	Time Performed	Interpretation	Comments
xxxxxx	xxxx	ddmmyyyy	hh:mm	Normal / Abnormal NCS / Abnormal CS	xxxxxxxx

[1] NCS = Not clinically significant, CS = Clinically significant.

Listing 16.2.17.1
Physical Examination – System Review

Subject	Visit	Date / Time (Study Day)	Physical Type	Parameter	Finding	Comments
xxxxxx	xxxx	ddmmyyyy hh:mm (Study Day)	Directed / Complete	General Appearance Eyes Ears Nose Throat Head and Neck Cranial Nerves/Nervous System Musculoskeletal Skin Cardiovascular Abdomen/GI System Respiratory System Chest – Auscultation Chest – Vocal Resonance Chest – Percussion Other Findings	Normal / Abnormal Not Clinically Significant / Abnormal Clinically Significant / Not Done	

Listing 16.2.17.2
Physical Examination – Upper Respiratory Exam

Subject	Visit	Date / Time (Study Day)	Assessment	Level [1]	Comments
xxxxxx	xxxx	ddmmyyyy hh:mm (Study Day)	Nasal Discharge - Left		
			Nasal Discharge – Right		
			Otitis – Left		
			Otitis – Right		
			Pharyngitis		
			Sinus Tenderness – Left		
			Sinus Tenderness – Right		
			New Wheezes, Rhonchi – Left		
			New Wheezes, Rhonchi – Right		

[1] Nasal Discharge: 0 = None, 1 = Clear, serous; scant but slightly increased, 2 = Clear to white, obvious increased volume, + / - minor blood streaks on tissue, 3 = Frankly prudent (yellow or green), or gross blood.
Otitis: 0 = None, 1 = Dulled tympanic membrane, 2 = Inflamed, injected tympanic membrane, 3 = Retracted or bulging tympanic membrane, obvious air, fluid level.
Pharyngitis: 0 = None, 1 = Mild and / or patchy erythema, 2 = Marked and / or confluent erythema, 3 = Erythema and purulent exudate.
Sinus Tenderness: 0 = None, 1 = Mild tenderness, 2 = Moderate tenderness, 3 = Severe tenderness or overlying erythema.
New Wheezes, Rhonchi: 0 = None, 1 = Mild wheezes or rhonchi, 2 = Scattered wheezes or rhonchi, 3 = Widespread wheezes.

Listing 16.2.18
Visit Dates

Subject	Visit	Date	Source of Unscheduled Visit Comments	Comments
xxxxxx	xxxx	ddmmyyyy	xxxxxxxxxx	xxxxxxxxxxxx

Programming note: Unscheduled visits and visit information will be taken from specific database modules and the "Reason for additional collection" will be placed in the comments column in this listing.

15.APPENDICES

15.1. Appendix 1: Study HVO-vCS-003 assay cut-offs and reporting

Analysis	Assay	Associated units	Assay LLOQ	Assay Reporting		
				Result	Reported result	S-cubed assigned value
Virus titre (Viral Load)	Viral Culture assay (qFFA assay)	Log_{10} FFU/mL	1.57	Quantifiable Titre	Value	Use reported value
				DETECTED	DETECTED	1.0
				NOT DETECTED	NOT DETECTED	0
				INVALID	INVALID	Missing data point
				NOT TESTED	N/A	Missing data point
Virus titre (Viral Load)	qRT-PCR	Log_{10} Copies/mL	3.0	Quantifiable Titre	Value	Use reported value
				DETECTED	DETECTED	1.5
				NOT DETECTED	NOT DETECTED	0
				INVALID	INVALID	Missing data point
				NOT TESTED	N/A	0

15.2. Appendix 2: Toxicity Grade Criteria For Parameters Provided by Central Laboratory (TDL)

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

			LOW			
Analyte	**UK Normal range**	**units**	**1**	**2**	**3**	**4**
Sodium (Hyponatremia)	135-145	mmol/L	132-134	130-131	125-129	<125
Potassium (Hypokalemia)	3.5-5.1	mmol/L	3.2-3.3	3.1	2.5-3.0	<2.5
Albumin (Hypoalbuminemia)	34-50	g/L	28-31	25-27	<25	

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

			HIGH			
Analyte	**UK Normal range**	**units**	**1**	**2**	**3**	**4**
Sodium (Hypernatremia)	135-145	mmol/L	146-147	148-149	150-155	>155
Potassium (Hyperkalemia)	3.5-5.1	mmol/L	5.2-5.3	5.4-5.5	5.6-6.5	>6.5
Urea	1.7-8.3	mmol/L	8.4-9.3	9.4-11.0	>11.0	
Creatinine (Female)	49-92	umol/L	101-138	139-276	>276	
Creatinine (Male)	66-112	umol/L	123-168	169-336	>336	
Total Bilirubin if normal ASL-AST	0-20	umol/L	22-30	31-40	41-60	>60
Total Bilirubin if AST/ ALT elevated	0-20	umol/L	22-25	26-30	31-35	>35
ALP (Male)	40-129	IU/L	142-258	259-387	388-1290	>1290
ALP (Female)	35-104	IU/L	114-208	209-312	313-1040	>1040
AST (Female)	0-31	IU/L	34-78	79-155	156-310	>310
AST (Male)	0-37	IU/L	41-93	94-185	186-370	>370
ALT (Female)	10-35	IU/L	39-88	89-175	176-350	>350
ALT (Male)	10-50	IU/L	55-125	126-250	251-500	>500

Table 6: Toxicity Grade Criteria for Values Below Normal Range (Haematology)

			LOW			
Analyte	**UK Normal range**	**units**	**1**	**2**	**3**	**4**
Haemoglobin (Female)	115-155	g/L	105-113	90-104	80-89	<80
Haemoglobin (Male)	130-170	g/L	115-125	100-114	85-99	<85
Platelets	150-400	x10^9/L	125-140	100-124	25-99	<25
WBC	3.0-10.0	x10^9/L	2.0 -2.99	1.50-1.99	1.0-1.49	<1.0
Neutrophils	2.0-7.5	x10^9/L	1.5-1.99	1.0-1.49	0.5-0.99	<0.5
Lymphocytes	1.2-3.65	x10^9/L	0.75-0.99	0.30-0.74	0.25-0.29	<0.25

Table 7: Toxicity Grade Criteria for Values Above Normal Range (Haematology)

			HIGH			
Analyte	**UK Normal range**	**units**	**1**	**2**	**3**	**4**
WBC	3.0-10.0	x10^9/L	11.5-15.0	15.01-20.0	20.01-25.0	>25.0
Eosinophils	0.0-0.4	x10^9/L	0.65-1.5	1.51-5.0	>5.0	N/A