Statistical Analysis Plan J2A-MC-GZGO 2.0

A Single-Group, Open-Label, Single-Period, Phase 1 Study to Determine the Absolute Bioavailability of LY3502970 in Healthy Participants

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STATISTICAL ANALYSIS PLAN

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2. ABBREVIATIONS

Abbreviations pertain to the Statistical Analysis Plan (SAP) only (not the tables, figures and listings [TFLs]).

%AUC(t_{last}-∞)	Percentage of AUC(0-∞) extrapolated
AE	Adverse event
AUC	Area under the concentration versus time curve
AUC(0-∞)	Area under the concentration versus time curve from time zero to infinity
AUC(0-t_{last})	Area under the concentration versus time curve from time zero to time t, where t is the last time point with a measurable concentration
BQL	Below the quantifiable lower limit of the assay
CI	Confidence interval
CL	Total body clearance of drug calculated after intravenous administration
CL/F	Apparent total body clearance of drug calculated after extra-vascular administration
C_{last}	Last quantifiable drug concentration
C_{max}	Maximum observed drug concentration
CRF	Case Report Form
CRU	Clinical Research Unit
CSR	Clinical Study Report
CV	Coefficient of variation
DMP	Data Management Plan
ECG	Electrocardiogram
ED	Early discontinuation
F	Bioavailability
ICF	Informed consent form
ICH	International Conference on Harmonisation
IV	Intravenous
LLOQ	Lower limit of quantification
MedDRA	Medical Dictionary for Regulatory Activities
MRE	Magnetic resonance elastography

PK	Pharmacokinetic
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SD	Standard deviation
$t_{1/2}$	Half-life associated with the terminal rate constant (λ_z) in non-compartmental analysis
TEAE	Treatment-emergent adverse event
TFLs	Tables, Figures, and Listings
t_{last}	last time point where the concentration is above the limit of quantitation
t_{max}	Time of maximum observed drug concentration
V_{ss}/F	Apparent volume of distribution at steady state after extravascular administration
V_z/F	Apparent volume of distribution during the terminal phase after extra-vascular administration
WHO	World Health Organization

3. INTRODUCTION

This SAP has been developed after review of the Clinical Study Protocol (final version dated 28 June 2023).

This Statistical Analysis Plan (SAP) describes the planned analysis of the safety, tolerability, and pharmacokinetic (PK) data from this study. A detailed description of the planned Tables, Figures, and Listings (TFLs) to be presented in the clinical study report (CSR) is provided in the accompanying TFL shell document.

The intent of this document is to provide guidance for the statistical and PK analyses of data. In general, the analyses are based on information from the protocol, unless they have been modified by agreement with Eli Lilly and Company. A limited amount of information concerning this study (e.g., objectives, study design) is given to help the reader's interpretation. This SAP must be finalized prior to first participant visit. When the SAP and TFL shells are agreed upon and finalized, they will serve as the template for this study's CSR.

This SAP supersedes the statistical considerations identified in the protocol; where considerations are substantially different, they will be so identified. If additional analyses are required to supplement the planned analyses described in this SAP, they may be performed and will be identified in the CSR. Any substantial deviations from this SAP will be agreed upon with Eli Lilly and Company and identified in the CSR. Any minor deviations from the TFLs may not be documented in the CSR.

This SAP is written with consideration of the recommendations outlined in the International Conference on Harmonisation (ICH) E9 Guideline entitled Guidance for Industry: Statistical Principles for Clinical Trials[1] and the ICH E3 Guideline entitled Guidance for Industry: Structure and Content of Clinical Study Reports[2].

4. STUDY OBJECTIVES AND ENDPOINTS

Objectives	Endpoints
Primary	
To determine the absolute bioavailability of LY3502970 following a single oral dose of CCI mg LY3502970 and an intravenous (IV) dose of less than CCI-µg [^{14}C]-LY3502970 (hemicalcium salt) in healthy participants.	Absolute bioavailability (F) of LY3502970.
Secondary	
To evaluate the PK of LY3502970, [^{14}C]-LY3502970, and total radioactivity following a single oral dose of CCI mg	Area under the concentration versus time curve from zero to infinity (AUC[0-∞]) and maximum observed drug concentration

LY3502970 and an IV dose of [^{14}C]-LY3502970 (hemicalcium salt) in healthy participants.	(C_{max}) for plasma total radioactivity, [^{14}C]-LY3502970, and LY3502970.
To describe the safety of LY3502970 following a single oral dose of [redacted] mg LY3502970 and an IV dose of [^{14}C]-LY3502970 (hemicalcium salt) in healthy participants.	Number and incidence of treatment-emergent adverse event (TEAEs) and serious adverse event (SAEs).

5. STUDY DESIGN

Study J2A-MC-GZGO is an open-label, single-center study to determine the absolute bioavailability of LY3502970 in healthy participants following a single oral dose of [redacted] mg LY3502970 and an IV dose of less than CCI-µg [^{14}C]-LY3502970 (hemicalcium salt) containing approximately CCI nCi.

Approximately 10 participants will be enrolled to target at least 6 participants complete the study. Participants will undergo screening procedures up to 42 days prior to enrollment and will be admitted to the clinical research unit (CRU) on Day -1. Participants will be administered a single dose of [redacted] mg LY3502970 and an IV dose of [^{14}C]-LY3502970 (hemicalcium salt) on Day 1 and will remain in the CRU until after completion of assessments on Day 9. Participants may stay longer in the CRU at the investigator's discretion. Participants will return a final follow-up visit or early discontinuation (ED) visit on Day 16, ±3 days.

Clinical laboratory tests, physical examination, vital signs, single 12-lead electrocardiograms (ECGs), and adverse events (AEs) will be monitored to assess safety and tolerability. Blood samples for PK analysis will be collected predose through the follow-up visit.

6. BLINDING

This is a non-randomized, open-label study.

The Fortrea biometrics and Eli Lilly study teams will be unblinded throughout the study.

7. TREATMENT

The following is the study treatment that will be used in the TFLs.

Study Treatment Name	Treatment order in TFL
[redacted] mg LY3502970 + CCI µg [^{14}C]-LY3502970 IV	1

8. SAMPLE SIZE JUSTIFICATION

Approximately 10 participants will be enrolled to target at least 6 participants complete the study. No formal statistical assessment of sample size has been conducted as this study does not have a hypothesis. The sample size chosen for this study is common in human radiolabeled studies and is considered sufficient to achieve the objectives of the study.

9. DEFINITION OF ANALYSIS POPULATIONS

The "Enrolled" population will consist of all participants who were assigned to LY3502970, regardless of whether they take any doses.

The "Safety" population will consist of all participants who receive at least 1 dose of LY3502970 whether or not they completed all protocol requirements.

The "Pharmacokinetic" population will consist of all participants who receive at least 1 dose of LY3502970 or [^{14}C]-LY3502970 and have evaluable PK data. Participants may be excluded from the LY3502970 PK summary statistics if a participant has an AE of vomiting that occurs at or before 2 times median time of maximum observed drug.

All protocol deviations that occur during the study will be considered for their severity/impact and will be taken into consideration when participants are assigned to analysis populations.

10. STATISTICAL METHODOLOGY

10.1 General

Data listings will be provided for all data that is databased. Summary statistics and statistical analysis will only be presented for data where detailed in this SAP. For continuous data, summary statistics will include the arithmetic mean, arithmetic standard deviation (SD), median, minimum, maximum and number of observations; for log-normal data (e.g. the PK parameters: area under the concentration versus time curves [AUCs] and C_{max}) the geometric mean and geometric coefficient of variation (CV%) will also be presented. For categorical data, frequency count and percentages will be presented. Data listings will be provided for all participants up to the point of withdrawal, with any participants excluded from the relevant population highlighted. Summary statistics and statistical analyses will generally only be performed for participants included in the relevant analysis population. For the calculation of summary statistics and statistical analysis, unrounded data will be used.

For change from baseline summary statistics, each individual change from baseline will be calculated by subtracting the individual participant's baseline value from the value at that time point. The individual participants' change from baseline values will be used to calculate the summary statistics (arithmetic mean, arithmetic SD, median, minimum, maximum and number of observations) using a SAS procedure such as Proc Univariate.

Data analysis will be performed using SAS® Version 9.4 or greater.

10.2 Demographics and Participant Disposition

Participant disposition will be listed. The demographic variables age, sex, race, ethnicity, body weight, height and body mass index will be summarized and listed. All other demographic variables will be listed only.

10.3 Pharmacokinetic Assessment

10.3.1 Pharmacokinetic Analysis

Noncompartmental methods applied with a validated software program (WinNonlin Phoenix v8.3.5 or later) to the plasma concentrations of LY3502970, [^{14}C]-LY3502970 and total radioactivity will be used to determine the following PK parameters, when possible.

Extravascular Administration (LY3502970):

Parameter	Units	Definition
AUC(0-∞)	ng.h/mL	area under the concentration versus time curve from time zero to infinity
AUC(0-t_{last})	ng.h/mL	area under the concentration versus time curve from time zero to time t, where t is the last time point with a measurable concentration
%AUC(t_{last}-∞)	%	percentage of AUC(0-∞) extrapolated
C_{max}	ng/mL	maximum observed drug concentration
t_{max}	h	time of maximum observed drug concentration
t_{last}	h	last time point where the concentration is above the limit of quantitation
t½	h	half-life associated with the terminal rate constant (λ_z) in non-compartmental
CL/F	L/h	apparent total body clearance of drug calculated after extra-vascular administration
V_z/F	L	apparent volume of distribution during the terminal phase after extra-vascular administration
V_{ss}/F	L	apparent volume of distribution at steady state after extra-vascular administration

F	%	absolute bioavailability

Intravenous Administration ([^{14}C]-LY3502970 and total radioactivity)

Parameter	Units*	Definition
AUC(0-∞)	ng.h/mL	area under the concentration versus time curve from time zero to infinity
AUC(0-t_{last})	ng.h/mL	area under the concentration versus time curve from time zero to time t, where t is the last time point with a measurable concentration
%AUC(t_{last}-∞)	%	percentage of AUC(0-∞) extrapolated
C_{max}	ng/mL	maximum observed drug concentration
t_{max}	h	time of maximum observed drug concentration
t_{last}	h	last time point where the concentration is above the limit of quantitation
t½	h	half-life associated with the terminal rate constant (λ_z) in non-compartmental
CL	L/h	total body clearance of drug calculated after IV administration ([^{14}C]-LY3502970 only)
V_z	L	volume of distribution during the terminal phase following IV administration ([^{14}C]-LY3502970 only)
V_{ss}	L	volume of distribution at steady state following IV administration ([^{14}C]-LY3502970 only)
AUC(0-∞) Plasma [^{14}C]-LY3502970: AUC(0-∞) Plasma Total Radioactivity	NA	the AUC of plasma [^{14}C]-LY3502970 to plasma total radioactivity ratio

* For radioactivity, AUC and C_{max} will be presented in mass equivalent units. Where the total radioactivity data is received in ng Eq/g, total radioactivity AUC and C_{max} will be reported using ng Eq*h/mL and ng Eq/mL, respectively, as a density of 1 g/mL will be assumed.

Additional PK parameters may be calculated, as appropriate.

Evaluation of absolute bioavailability (F) will be estimated using the AUC(0-∞) values from each individual participant based on IV dosed [^{14}C]-LY3502970 compared to oral dosed LY3502970:

$$F = \frac{\text{Dose}_{IV} * \text{Gmean AUC}(0-\infty)_{EV}}{\text{Dose}_{EV} * \text{Gmean AUC}(0-\infty)_{IV}}$$

The concentration ratios of plasma [^{14}C]-LY3502970 : plasma total radioactivity will be calculated for each time point. In addition, the ratios of exposure of plasma [^{14}C]-LY3502970 to plasma total radioactivity will be calculated based on AUC(0-∞).

An alternative AUC measure, such as AUC to a common time point, may be calculated if AUC(0-∞) and its ratios cannot be reliably calculated.

The software and version used for the final analyses will be specified in the clinical study report. Any exceptions or special handling of data will be clearly documented within the final study report.

Formatting of tables, figures and abbreviations will follow the Eli Lilly Global PK/PD/TS Tool: NON-COMPARTMENTAL PHARMACOKINETIC STYLE GUIDE. The version of the tool effective at the time of PK analysis will be followed.

General PK Parameter Rules

- Actual sampling times will be used in the final analyses of individual PK parameters, except for non-bolus pre-dose sampling times which will be set to zero.

- C_{max} and time of maximum observed drug concentration (t_{max}) will be reported from observed values. If C_{max} occurs at more than one time point, t_{max} will be assigned to the first occurrence of C_{max}.

- AUC parameters will be calculated using a combination of the linear and logarithmic trapezoidal methods (linear-log trapezoidal rule). The linear trapezoidal method will be applied up to t_{max} and then the logarithmic trapezoidal method will be used after t_{max}. The minimum requirement for the calculation of AUC will be the inclusion of at least three consecutive plasma concentrations above the lower limit of quantification (LLOQ), with at least one of these concentrations following C_{max}. AUC(0-∞) values where the percentage of the total area extrapolated is more than 20% will be flagged. Any AUC(0-∞) value excluded from summary statistics will be noted in the footnote of the summary table.

- Half-life ($t_{1/2}$) will be calculated, when appropriate, based on the apparent terminal log-linear portion of the concentration-time curve. The start of the terminal elimination phase for each subject will be defined by visual inspection and generally will be the first point at which there is no systematic deviation from the log-linear decline in plasma concentrations. Half-life will only be calculated when a reliable estimate for this

parameter can be obtained comprising of at least 3 data points. If $t_{1/2}$ is estimated over a time window of less than 2 half-lives, the values will be flagged in the data listings. Any $t_{1/2}$ value excluded from summary statistics will be documented in the footnote of the summary table.

- A uniform weighting scheme will be used in the regression analysis of the terminal log-linear portion of the concentration-time curve.

- The parameters based on observed last quantifiable drug concentration (C_{last}) will be reported.

Individual PK Parameter Rules

- Only quantifiable concentrations will be used to calculate PK parameters with the exception of special handling of certain concentrations reported below the lower limit of quantitation (BQL). Concentrations reported as BQL will be set to a value of zero when all of the following conditions are met:

    - The compound is non-endogenous.

    - The samples are from the initial dose period for a subject or from a subsequent dose period following a suitable wash-out period.

    - The time points occur before the first quantifiable concentration.

- All other BQL concentrations that do not meet the above criteria will be set to missing.

- Also, where two or more consecutive concentrations are BQL towards the end of a profile, the profile will be deemed to have terminated and therefore any further quantifiable concentrations will be set to missing for the calculation of the PK parameters unless it is considered to be a true characteristic of the profile of the drug.

Individual Concentration vs. Time Profiles

- Individual concentrations will be plotted utilizing actual sampling times.

- The terminal point selections will be indicated on a semi-logarithmic plot.

Average Concentration vs. Time Profiles

- The average concentration profiles will be graphed using scheduled (nominal) sampling times.

- The average concentration profiles will be graphed using arithmetic average concentrations.

- The pre-dose average concentration for single-dose data from non-endogenous compounds will be set to zero. Otherwise, only quantifiable concentrations will be used to calculate average concentrations.

- Concentrations at a sampling time exceeding the sampling time window specified in the protocol, or ± 10%, will be excluded from the average concentration profiles.

- Concentrations excluded from the mean calculation will be documented in the final study report.

- A concentration average will be plotted for a given sampling time only if 2/3 of the individual data at the time point have quantifiable measurements that are within the sampling time window specified in the protocol or ± 10%. An average concentration estimated with less than 2/3 but more than 3 data points may be displayed on the mean concentration plot if determined to be appropriate and will be documented within the final study report.

Treatment of Outliers during Pharmacokinetic Analysis

Application of this procedure to all PK analyses is not a requirement. Rather, this procedure provides justification for exclusion of data when scientifically appropriate. This procedure describes the methodology for identifying an individual value as an outlier for potential exclusion but does not require that the value be excluded from analysis. The following methodology will not be used to exclude complete profiles from analysis.

Data within an Individual Profile

A value within an individual profile may be excluded from analysis if any of the following criteria are met:

- For PK profiles during single dosing of non-endogenous compounds, the concentration in a pre-dose sample is quantifiable.

- For any questionable datum that does not satisfy the above criteria, the profile will be evaluated, and results reported with and without the suspected datum.

Data between Individual Profiles

1. If $n<6$, then the dataset is too small to conduct a reliable range test. Data will be analyzed with and without the atypical value, and both sets of results will be reported.

2. If $n\geq6$, then an objective outlier test will be used to compare the atypical value to other values included in that calculation:

    a. Transform all values in the calculation to the logarithmic domain.

b. Find the most extreme value from the arithmetic mean of the log transformed values and exclude that value from the dataset.

c. Calculate the lower and upper bounds of the range defined by the arithmetic mean ±3*SD of the remaining log-transformed values.

d. If the extreme value is within the range of arithmetic mean ±3*SD, then it is not an outlier and will be retained in the dataset.

e. If the extreme value is outside the range of arithmetic mean ±3*SD, then it is an outlier and will be excluded from analysis.

If the remaining dataset contains another atypical datum suspected to be an outlier and $n \geq 6$ following the exclusion, then repeat step 2 above. This evaluation may be repeated as many times as necessary, excluding only one suspected outlier in each iteration, until all data remaining in the dataset fall within the range of arithmetic mean ±3*SD of the log-transformed values.

Reporting of Excluded Values

Individual values excluded as outliers will be documented in the final report. Approval of the final report will connote approval of the exclusion.

10.3.2 Pharmacokinetic Statistical Methodology

PK parameters will be summarized using descriptive methodology. No formal statistical analysis will be performed.

A sensitivity analysis will be performed if there are an excessive number of participant exclusions due to an AE of vomiting, in which excluded participants will be included in the analyses.

10.4 Safety and Tolerability Assessments

10.4.1 Adverse events

Where changes in severity are recorded in the case report form (CRF), each separate severity of the AE will be reported in the listings, only the most severe will be used in the summary tables. A pre-existing condition is defined as a condition that starts before the participant has provided written informed consent and is ongoing at consent. A non-treatment emergent AE is defined as an AE which starts after informed consent but prior to dosing. A TEAE is defined as an AE which occurs postdose or which is present prior to dosing and becomes more severe postdose. Onset time will be calculated relative to the [redacted] mg LY3502970 dose.

All AEs will be listed. TEAEs will be summarized by severity and relationship to the study drug. The frequency (the number of AEs, the number of participants experiencing an AE and the percentage of participants experiencing an AE) of TEAEs will be summarized by Medical

Dictionary for Regulatory Activities (MedDRA) (version is documented in the Data Management Plan [DMP]) system organ class and preferred term. The summary and frequency AE tables will be presented for all causalities and those considered related to the study drug by the investigator. Any SAEs will be listed.

AEs of special interest will be listed separately, and are as follows:

- hepatic disorders
- severe GI AEs including nausea, vomiting, and diarrhea
- arrhythmias and cardiac conduction disorders
- major adverse cardiovascular events
- hypotension, orthostatic hypotension, and syncope
- hypoglycemia
- hypersensitivity reaction
- pancreatitis
- acute renal events, and
- gallbladder and biliary tract disorders.

Discontinuations due to AEs will be listed.

10.4.2 Glucose Monitoring and Hypoglycemia

During the study, blood glucose concentrations will be monitored for safety assessments. Glucose data will be listed and summarized together with changes from baseline, where baseline is defined as Day 1 predose.

Hypoglycemic events will be appropriately recorded in the CRF. In the case of a hypoglycemic event, the actual blood glucose value, if measured, will be recorded in the CRF, together with any treatments administered. Each category of hypoglycemic events (defined below) will be listed and summarized. Hypoglycemia is defined as follows:

- **Level 1 hypoglycemia:**

Glucose less than 70 mg/dL (3.9 mmol/L) and greater than or equal to 54 mg/dL (3.0 mmol/L): Level 1 hypoglycemia can alert a person to take action such as treatment with fast-acting carbohydrates. Providers should continue to counsel participants to treat hypoglycemia at this glucose alert value.

- **Level 2 hypoglycemia:**

Glucose less than 54 mg/dL (3.0 mmol/L): Level 2 hypoglycemia is also referred to as documented or blood glucose confirmed hypoglycemia with glucose less than 54 mg/dL

(3.0 mmol/L). This glucose threshold is clinically relevant regardless of the presence or absence of symptoms of hypoglycemia.

- **Level 3 hypoglycemia:**

Severe hypoglycemia: A severe event characterized by altered mental or physical status requiring assistance for treatment of hypoglycemia. For example, participants had altered mental status, and could not assist in their own care, or were semiconscious or unconscious, or experienced coma with or without seizures, and the assistance of another person was needed to actively administer carbohydrate, glucagon, or other resuscitative actions. Glucose measurements may not be available during such an event, but neurological recovery attributable to the restoration of glucose concentration to normal is considered sufficient evidence that the event was induced by a low glucose concentration.

The determination of a hypoglycemic event as an episode of severe hypoglycemia, as defined above, is made by the investigator based on the medical need of the participant to have required assistance and is not predicated on the report of a participant simply having received assistance.

If a hypoglycemic event meets the criteria of severe hypoglycemia, the investigator must record the event as serious on the AE CRF and report it to Lilly as an SAE.

- **Other hypoglycemia categories:**
  - **Nocturnal hypoglycemia** is a hypoglycemia event, including severe hypoglycemia, that occurs at night and presumably during sleep.

Investigator review of glucose results clinically indicative of hypoglycemia will be required.

10.4.3 Concomitant medication

Concomitant medication will be coded using the WHO drug dictionary (version is documented in the DMP). Concomitant medication will be listed.

10.4.4 Clinical laboratory parameters

All clinical chemistry, hematology and urinalysis data will be summarized by timepoint and listed. Additionally, clinical chemistry, hematology and urinalysis data outside the reference ranges will be listed and flagged on individual participant data listings.

Values recorded as $<x$, $\leq x$, $>x$, or $\geq x$ will be displayed in the listings as recorded, these values will be excluded from summary statistics.

10.4.5 Vital signs

Where supine blood pressure and pulse rate are measured in triplicate, the mean value will be calculated and used in all subsequent calculations. When triplicate blood pressure or pulse rate measurements precede a standing measurement, the last supine blood pressure or pulse rate measurement will be used for orthostatic calculations.

Vital signs data will be summarized by time point together with changes from baseline, where baseline is defined as the mean of the triplicate Day 1 predose assessment.

Values for individual participants will be listed.

10.4.6 Electrocardiogram

ECGs will be performed for safety monitoring purposes only and will not be presented. Any clinically significant findings from ECGs will be reported as an AE.

10.4.7 Hepatic Monitoring

If a participant experiences elevated laboratory parameters, as detailed in Section 8.2.5.1 of the protocol, additional tests will be performed to confirm the abnormality. Additional safety data may be collected if required, as defined in the protocol. Where applicable, the following will be presented.

The participants' liver disease history and associated person liver disease history data will be listed. Use of acetaminophen during the study, which has potential for hepatotoxicity, will be listed. Results from any hepatic monitoring procedures, such as a magnetic resonance elastography (MRE) scan, and biopsy assessments will be listed, if performed.

Hepatic risk factor assessment data will be listed. Liver related signs and symptoms data will be summarized by treatment, if deemed appropriate, and listed. Alcohol and recreational drug use data will also be listed.

All hepatic chemistry, hematology, coagulation, and serology data will be listed. Values outside the reference ranges will be flagged on the individual participant data listings.

10.4.8 Hypersensitivity reactions

For all drug hypersensitivity reactions that occur, additional follow-up data will be collected to assess the participant's medical history, alternative causes, and symptoms.

These data will be listed.

10.4.9 Pancreatic Monitoring

The frequency of pancreatic amylase or fasting lipase values ≥3× upper limit of normal will be listed.

10.4.10 Other assessments

All other safety assessments not detailed in this section will be listed but not summarized or statistically analyzed.

10.4.11 Safety and Tolerability Statistical Methodology

No inferential statistical analyses are planned.

11. INTERIM ANALYSES

No interim statistical analyses are planned.

12. CHANGES FROM THE PROTOCOL SPECIFIED STATISTICAL ANALYSES

There were no changes from the protocol specified statistical analyses.

13. REFERENCES

1. International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, ICH Harmonized Tripartite Guideline, Statistical Principles for Clinical Trials (E9), 5 February 1998.

2. International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, ICH Harmonized Tripartite Guideline, Structure and Content of Clinical Study Reports (E3), 30 November 1995.

14. DATA PRESENTATION

14.1 Derived Parameters

Individual derived parameters (e.g. PK parameters) and appropriate summary statistics will be reported to three significant figures. Observed concentration data, e.g. C_{max}, should be reported as received. Observed time data, e.g. t_{max}, should be reported as received. Number of observations and percentage values should be reported as whole numbers. Median values should be treated as an observed parameter and reported to the same number of decimal places as minimum and maximum values.

14.2 Missing Data

Missing data will not be displayed in listings.

14.3 Insufficient Data for Presentation

Some of the TFLs may not have sufficient numbers of participants or data for presentation. If this occurs, the blank TFL shell will be presented with a message printed in the center of the table, such as, “No serious adverse events occurred for this study.”

15. APPENDICES

Appendix 1: Document History

Status and Version	Date of Change	Summary/Reason for Changes
Final Version 1.0	NA	NA; the first version.

NA = not applicable

Signature Page for VV-CLIN-144463 v1.0

Approval	PPD PKPDPMx 09-Feb-2024 17:45:56 GMT+0000

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