Statistical Analysis Plan

A Phase 1, Randomized, Double-Blind, Placebo-Controlled, Single Ascending Dose Study to Assess the Safety, Tolerability, Pharmacokinetics, and Food Effect of SXC-2023 when Administered Orally to Healthy Adult Subjects

Protocol No: PRO-101
Final Protocol Date: 17 July 2017
Amendment #1 Date: 02 November 2017
Amendment #2 Date: 05 January 2018

Compound Name: SXC-2023

Celerion Project CA22427
Draft Version 1.0
Date: 28 February 2018

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Statistical Analysis Plan Signature Page

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Issue Date: 28 February 2018

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1. INTRODUCTION

The following statistical analysis plan (SAP) provides the framework for the summarization of the data from this study. The SAP may change due to unforeseen circumstances. Any changes made from the planned analysis within protocol, after the unblinding, or locking of the database will be documented in the clinical study report (CSR). The section referred to as Table Shells within this SAP describes the traceability of the tables, figures, and listings (TFLs) back to the data. Note that the header for this page will be the one used for the main body of the CSR.

Any additional exploratory analyses not addressed within this SAP and/or driven by the data, or requested by Promentis Pharmaceuticals, will be considered out of scope and must be described in the CSR.

2. OBJECTIVES AND ENDPOINTS

2.1 Objectives

Primary:

To assess the safety and tolerability of SXC-2023 following administration of single ascending doses (SAD) to healthy adult subjects.

Secondary:

Objective 1: To assess the pharmacokinetics (PK) of SXC-2023 in plasma, red blood cells (RBC), if applicable, and urine following administration of single ascending doses to healthy adult subjects.

Objective 2: To compare the single-dose PK of SXC-2023 in plasma, RBCs (if applicable), and urine following oral administration under fed and fasting conditions.

Objective 3: To assess the PK of SXC-2023's primary metabolites, N-acetylcysteine (NAC), and *p*-toluic acid, as available, in plasma, RBCs (if applicable), and urine, following administration of a single dose to healthy adult subjects.

2.2 Endpoints

Primary:

The primary endpoints of the study will be the number and severity of treatment-emergent adverse events (TEAEs) following single doses of SXC-2023 and placebo.

Secondary:

The secondary endpoints of the study are the PK parameters following SXC-2023 administration under fasted and fed conditions. The following PK parameters will be computed, as appropriate:

SXC-2023:

- Plasma: AUC0-t, AUC0-inf, Cmax, Tmax, CL/F, Vz/F, Kel, and T½.
- Urine: Aet1-t2, Ae0-72, CLr, and %Fe.
- RBC (if applicable): AUC0-t, AUC0-inf, Cmax, Tmax, CL/F, Vz/F, Kel, and T½.

NAC and *p*-toluic acid:

- Plasma: AUC0-t, AUC0-inf, Cmax, Tmax, Kel, and T½.
- Urine: Aet1-t2, Ae0-72, and CLr.
- RBC (if applicable): AUC0-t, AUC0-inf, Cmax, Tmax, and T½.

The effect of food on a single oral dose of SXC-2023 will be assessed by comparing AUC0-t, AUC0-inf, and Cmax under fed versus fasting conditions using an ANOVA.

3. STUDY DESIGN

This is a randomized, double-blind, placebo-controlled, SAD and food-effect (FE) study.

Up to 48 healthy, adult male and female subjects are planned to be enrolled in 6 cohorts of 8 subjects each (6 active and 2 placebo). Subjects will participate in only one cohort. Attempts will be made to enroll 50% of each sex in each cohort.

Screening of subjects will occur within 28 days prior to dosing. Each subject will be assigned a unique identification number upon screening. Subjects who complete the study screening assessments and meet all the eligibility criteria will be assigned a unique randomization identification number at the time of dosing, different from the screening number, and will receive the corresponding dose of study drug/placebo, according to a randomization scheme generated at Celerion.

Each cohort will include a sentinel group (1 active and 1 placebo) who will be dosed at least 24 hours before the remaining 6 subjects (5 active and 1 placebo). Dosing of the remaining 6 subjects will be conducted following a safety evaluation of the sentinel group by the Principal Investigator (PI), Medical Monitor, and Sponsor.

In each cohort, subjects will receive a single oral dose of SXC-2023 or placebo under fasting conditions, with one cohort crossing over to receive the same dose of

SXC-2023 or placebo for a second time under fed conditions. There will be a washout period of at least 7 days between dosing under fasting conditions and dosing under fed conditions (high-fat breakfast).

Blood and urine samples will be collected predose and through 72 hours postdose for the PK assessment of SXC-2023, NAC, and *p*-toluic acid, as appropriate.

Safety will be monitored throughout the study by repeated clinical and laboratory evaluations. Discontinued subjects may be replaced at the discretion of the Sponsor.

Dose escalation to the next dose level (i.e., next cohort) will not take place until a PI, Medical Monitor, and Sponsor representative have determined that adequate safety, tolerability, and PK plasma have been demonstrated regarding the previous cohort(s) to permit proceeding to the next cohort.

The dose level (i.e., cohort) to be used for the assessment of a FE will be determined based on the safety, tolerability, and PK plasma evaluations of previous cohorts. At least one dose level higher than the dose level selected for the FE cohort, may be evaluated for safety and tolerability of the dose at least.

Subjects will be housed on Day -1, at the time indicated by the clinical research unit (CRU), until after the 72-hour blood draw and/or end of treatment procedures on Day 4. Subjects from one cohort will be confined for a second, similar, period for the FE arm of the study. A subject may be required to remain at the CRU for longer at the discretion of the PI or designee. All subjects who received a dose of study drug/placebo (including subjects who terminate the study early) will return to the CRU approximately 7 days after the last study drug/placebo administration for follow-up procedures and to determine if any adverse events (AEs) have occurred since the last study visit.

The total planned duration of subject participation is approximately 35 days from screening to follow-up, with CRU confinement from check-in on Day -1 to Day 4. The total planned duration of subject participation is approximately 42 days for subjects enrolled to receive a second dose under fed conditions.

4. ANALYSIS POPULATIONS

4.1 Analysis Populations

Safety Population

All subjects who received any dose of the study drug or placebo will be included in the safety evaluations.

Pharmacokinetic Population

The PK population will include data from all subjects who received at least one dose

of active treatment (SXC-2023) and completed at least one PK blood draw resulting in at least one quantifiable plasma concentration. All available data will be included in the concentration tables to the extent possible. Data for each subject will be included in the concentration summary statistics with the exceptions described as follows:

- Data from subjects who experience emesis at or before 2 times median Tmax for SXC-2023 during the PK sampling period time course may be excluded from the summary statistics.
- Data from subjects who significantly violate a protocol inclusion or exclusion criteria, deviate significantly from the protocol, or have unavailable or incomplete data, which may influence the PK analysis, will be excluded from the PK analysis population.

Any subject or data excluded from the analysis will be identified, along with their reason for exclusion, in the CSR.

Pharmacokinetic Evaluable Population

The PK evaluable population will include all subjects in the PK population who comply sufficiently with the protocol and display an evaluable PK profile (e.g., exposure to treatment, availability of measurements and absence of major protocol violations). PK evaluable population will be used in the PK parameter summary statistics and in statistical comparisons. For the FE cohort subject must have sufficient data in both periods (fed and fasted) to be included in the PK evaluable population.

4.2 Preliminary Data and Interim Analysis

4.2.1 Blinding

This is a double-blind, randomized, placebo controlled study. One set of sealed envelopes containing the randomization code will be supplied to the PI or designee at the start of the study.

Breaking of the blind is expressly forbidden except in the event of a medical emergency where the identity of the drug must be known in order to properly treat the subject or in the event of an interim analysis.

In the event of a medical emergency, it is requested that the PI or designee make every effort to contact the Study Monitor or designee prior to breaking the blind. If breaking the blind is required because of a medical emergency, the treatment identity will be revealed by the PI or designee, for that subject only. In the event that the emergency is one, in which it appears that the other subjects may be at imminent risk, the blind may be broken for all subjects dosed at that dose level. The unblinding will be properly documented in the study file.

In all cases where the blind is broken, the PI or designee should record the date and reason for blind breaking.

At the end of the study, envelopes will be retained or destroyed according to site procedures unless specified otherwise by the Sponsor.

In the absence of a medical emergency, the blinded randomization for this study will not be revealed until all data are entered in the database, edits checks are performed, queries closed, and the database is officially locked.

4.2.2 Interim Analysis

Safety: the PI, Medical Monitor, and Sponsor representative will review all available blinded safety data prior to dose escalation and to determine the dose level for the FE cohort.

At the Sponsor's request, unblinded safety tables, figures, and data listings may be presented to the Sponsor for the purposes of planning the next clinical studies prior to database lock. These interim analyses will be performed on data that will be edit-checked and monitored.

A safety data analyst and a biostatistician at Celerion who are not involved with the present study and are not located at the Celerion's Phoenix site will be unblinded to prepare unblinded safety tables, figures, and data listings, if needed. All the personnel related to the present study will remain blinded.

Pharmacokinetics: Preliminary PK analysis will be performed for all cohorts. PK plasma analysis data will be used to guide the dose escalation decision and may be used to evaluate the sampling time points as the study progresses. PK plasma analysis data will also be used to determine the dose level for the FE cohort.

Interim PK analysis will not use the actual subject numbers in order to avoid breaking the blind. The bioanalytical personnel will scramble subject numbers before sending to Celerion for analysis. PK analysis will be performed on SXC-2023, NAC, and *p*-toluic acid plasma concentration-time data using Phoenix® WinNonlin® Version 6.3 or higher. The parameters listed in Section 6.5 will be calculated. The following interim tables and figures will be generated using Phoenix® WinNonlin® Version 6.3 or higher: Concentration tables, PK parameter tables, mean graphs and superimposed (spaghetti) plots generated by cohort and analyte. The interim analysis populations will be the same as the analysis populations described in Section 4.1.

5. TREATMENT DESCRIPTIONS

SXC-2023 will be supplied as 50 and 200 mg capsules.

Placebo will be provided as matching placebo capsules.

Subjects will be instructed not to crush, split or chew the study drug/placebo.

Subjects in each cohort will receive a single oral dose of SXC-2023 or placebo, under fasting conditions.

Planned doses will be as follows:

Cohort 1: 50 mg (1 x 50 mg capsule) SXC-2023 or matching placebo

Cohort 2: 100 mg (2 x 50 mg capsules) SXC-2023 or matching placebo

Cohort 3: 200 mg (1 x 200 mg capsule) SXC-2023 or matching placebo

Cohort 4: 400 mg (2 x 200 mg capsules) SXC-2023 or matching placebo

Cohort 5: 800 mg (4 x 200 mg capsules) SXC-2023 or matching placebo

Cohort 6: 1600 mg (8 x 200 mg capsules) SXC-2023 or matching placebo

Treatments will be described as follows:

Treatment	**Short Description (Legends, Columns Headers, Report Text)**	**Long Description (Titles, Footnotes)**
Placebo	Pooled Placebo	A single oral dose of Placebo (Cohorts 1-6)
Treatment A	50 mg SXC-2023 Fasted	A single oral dose of 50 mg SXC-2023 administered under fasted conditions (Cohort 1)
Treatment B	100 mg SXC-2023 Fasted	A single oral dose of 100 mg SXC-2023 administered under fasted conditions (Cohort 2)
Treatment C	200 mg SXC-2023 Fasted	A single oral dose of 200 mg SXC-2023 administered under fasted conditions (Cohort 3)
Treatment D	400 mg SXC-2023 Fasted	A single oral dose of 400 mg SXC-2023 administered under fasted conditions (Cohort 4)
Treatment E	800 mg SXC-2023 Fasted	A single oral dose of 800 mg SXC-2023 administered under fasted conditions (Cohort 5)
Treatment F*	800 mg SXC-2023 Fed	A single oral dose of 800 mg SXC-2023 administered under fed conditions (Cohort 5)

Treatment	Short Description (Legends, Columns Headers, Report Text)	Long Description (Titles, Footnotes)
Treatment G	1600 mg SXC-2023 Fed	A single oral dose of 1600 mg SXC-2023 administered under fed conditions (Cohort 6)

**Programmer's note: Treatment letters may change depending on which cohort is selected for the FE evaluation. The Description for Treatments F and G will also be updated accordingly then.*

All doses of study drug/placebo will be administered with approximately 240 mL of water. When administered under fed conditions, SXC-2023 or placebo will be administered orally following a high-fat breakfast.

6. PHARMACOKINETIC ANALYSIS

6.1 Measurements and Collection Schedule

For all subjects, blood samples for the determination of plasma SXC-2023, NAC, and *p*-toluic acid will be collected at the following time points: predose and 0.083, 0.167, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, 16, 24, 48, and 72 hours postdose. For doses equal or greater than 200 mg, analytes may also be determined in RBC samples collected at selected time points, as necessary.

All concentration data will be included in the calculation of the individual PK parameters, in the individual and superimposed concentration-time plots (based on actual sample times), and in the mean concentration-time plots (based on nominal sample times). However, if there are any significant deviations from nominal sample times, some concentration data may be excluded from mean concentration-time plots and/or additional concentration-time plots of the mean data may be provided. All deviations and excluded data will be provided and discussed in the CSR.

For all subjects, urine samples for the determination of urine SXC-2023, NAC, and *p*-toluic acid will be collected at the following intervals: predose, and 0-1, 1-2, 2-4, 4-8, 8-12, 12-24, 24-48, and 48-72 hours postdose.

6.2 Bioanalytical Method

6.2.1 SXC-2023

Plasma and urine concentrations of SXC-2023 will be determined using high performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS) methods validated with respect to accuracy, precision, linearity, sensitivity, and

specificity at Covance BioAnalytic (Salt Lake City, Utah). The lower limit of quantitation (LLOQ) for SXC-2023 in plasma and urine will be 50.0 ng/mL. Method development in RBC is ongoing but concentration will be determined using qualified methods with a targeted LLOQ of 50.0 ng/mL. This could vary depending on the success/limitations of the on-going bioanalytical method development work.

6.2.2 N-acetylcysteine

Plasma and urine concentrations of NAC will be determined using HPLC-MS/MS methods validated with respect to accuracy, precision, linearity, sensitivity, and specificity at Covance BioAnalytic (Salt Lake City, Utah). The LLOQ for NAC in plasma and urine will be 100 ng/mL. Method development in RBC is ongoing but concentration will be determined using qualified methods with a targeted LLOQ of 100 ng/mL. This could vary depending on the success/limitations of the on-going bioanalytical method development work.

6.2.3 *p*-Toluic Acid

Plasma and urine concentrations of *p*-toluic acid will be determined using HPLC-MS/MS methods validated with respect to accuracy, precision, linearity, sensitivity, and specificity at Covance BioAnalytic (Salt Lake City, Utah). The LLOQ for *p*-toluic acid in plasma and urine will be 50 ng/mL. Method development in RBC is ongoing but concentration will be determined using qualified methods with a targeted LLOQ of 50 ng/mL. This could vary depending on the success/limitations of the on-going bioanalytical method development work.

6.3 Investigational Product and PK Analyte Information

6.3.1 SXC-2023

Plasma, RBC, and urine will be analyzed for SXC-2023 concentrations. The analyte can be described with the following structure and a molecular weight (MW) of 281.33 g/mol (Figure A). SXC-2023 capsules are an oral dosage form available in 50 mg and 200 mg unit dose strengths.

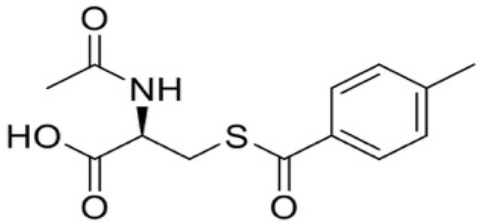


Figure A: SXC-2023 (free acid MW = 281.33 g/mol)

The nominal dose will be administered in the form of the free acid therefore, MW adjustment will not be needed for the calculation of dose-dependent PK parameters since SXC-2023 is dosed in the same form it is measured in.

6.3.2 N-Acetylcysteine

Plasma, RBC, and urine will be analyzed for NAC concentrations. Dose-dependent PK parameters will not be calculated for NAC; therefore, no MW adjustments will be necessary for PK calculations. Molecular weights and structures are contained in the Investigator's Brochure (IB).

6.3.3 *p*-Toluic Acid

Plasma, RBC, and urine will be analyzed for *p*-toluic acid concentrations. Dose-dependent PK parameters will not be calculated for *p*-toluic acid; therefore, no MW adjustments will be necessary for PK calculations. Molecular weights and structures are contained in the IB.

6.4 Pharmacokinetic Concentrations

Plasma, RBC, and urine concentrations of SXC-2023, NAC, and *p*-toluic acid, as determined at the collection times and per the bioanalytical methods described in Section 6.1 and Section 6.2, respectively, will be used for the calculation of the plasma, RBC, and urine PK parameters. Concentrations reported from subjects who received the placebo treatment will be listed in the concentration tables only.

6.5 NonCompartmental Pharmacokinetic Analysis and Parameter Calculation

6.5.1 Plasma and RBC Pharmacokinetic Parameters

The appropriate noncompartmental PK parameters will be calculated from the plasma SXC-2023, NAC, and *p*-toluic acid concentration-time data as well as from the RBC (if applicable) SXC-2023, NAC, and *p*-toluic acid concentration-time data using Phoenix® WinNonlin® Version 6.3 or higher. Actual sample times will be used in the calculations of the PK parameters. The calculation of the actual time for all analytes will be in respect to the start of dose administration time of SXC-2023. All PK parameters included in the protocol are listed in Table 6.1 below, and are defined as appropriate for study design.

Table 6.1. Noncompartmental Pharmacokinetic Parameters to be Calculated

Parameter	Definition	Method of Determination
AUC0-t	Area under the concentration-time curve from time 0 to the time of the last observed/measured non-zero concentration	Calculated using the Linear Trapezoidal with Linear Interpolation Method

Parameter	Definition	Method of Determination
AUC0-inf	Area under the concentration-time curve from time 0 extrapolated to infinity	AUC0-∞ = AUC0-t + (Clast/kel) where Clast is the last observed/measured plasma or RBC concentration
Cmax	The maximum observed concentration	Taken directly from bioanalytical data
Tmax	The time to reach Cmax	Taken from clinical database as the difference in the time of administration and the time of the blood draw which is associated with the Cmax.
t1/2	Apparent first-order terminal elimination half-life	Calculated as 0.693/Kel
Kel	Apparent first-order terminal elimination rate constant calculated from a semi-log plot of the plasma or RBC concentration versus time curve	Calculated by linear least-squares regression analysis using the maximum number of points in the terminal log-linear phase (e.g., 3 or more non-zero plasma concentrations).
CL/F	The apparent total plasma or RBC clearance after extravascular administration (Calculated for SXC-2023 only)	Calculated as Dose/(AUC0-inf)
Vz/F	The apparent volume of distribution during the terminal elimination phase after extravascular administration (Calculated for SXC-2023 only)	Calculated as Dose/(AUC0-inf x Kel)

Pharmacokinetic parameters will not be calculated for subjects with less than 3 consecutive postdose time points with quantifiable concentrations. Subjects for whom there are insufficient data to calculate the PK parameters will be included in the concentration tables only and excluded from the statistical analysis.

Plasma or RBC concentrations below the limit of quantitation (BLQ) prior to the first quantifiable concentration will be set to zero (0) and plasma or RBC concentrations BLQ after the first quantifiable concentration will be treated as missing.

The Kel will be determined using linear regressions composed of least 3 data points. The Kel will not be assigned if 1) the terminal elimination phase is not apparent, 2) if Tmax is one of the 3 last data points, or 3) if the R^2 value is less than 0.8. In cases where the Kel interval is not assigned, the values of t½, AUC0-inf, CL/F, and Vz/F are considered not calculable and will not be reported. Wherever the resulting t½ is more than half as long as the sampling interval, the Kel values and associated parameters (t½, AUC0-inf, CL/F, and Vz/F) may not be presented as judged appropriate and in accordance with Celerion SOPs.

Subjects who vomit within twice the median Tmax value for SXC-2023 may be excluded from the PK Evaluable population.

6.5.2 Urine Pharmacokinetic Parameters

The following PK parameters will be calculated from urine SXC-2023, NAC, and *p*-toluic acid data using SAS® Version 9.3 or higher.

Table 6.2. Noncompartmental Urine Pharmacokinetic Parameters to be Calculated

Parameter	Definition	Method of Determination
Conct1-t2	Drug concentration in the urine during the urine collection interval from t1 to t2	Taken directly from bioanalytical data
Volt1-t2	Sum of volume of urine collected over the entire urine collection interval from t1-t2	Taken directly from CRF data
Aet1-t2	Amount of analyte excreted in the urine collection interval from t1 to t2	Calculated as (Curt1-t2 x Vurt1-t2)
CumAe (Ae0-72)	Total amount of analyte excreted in the urine over the entire period of sample collection, obtained by adding the amounts excreted over each collection interval	Calculated as: $Ae = \sum_{i=1}^{n-1} Ae_i (t_i - t_{i+1})$ where t1 = 0 and tn = t and Aei is measured between ti and ti+1, i=1,…,nth interval
CLr	Renal clearance	calculated as : Ae(t'-t")/AUC(t'-t") where t'-t" is the longest interval of time during which Ae and AUC are both obtained
%Dose	The percent of dose excreted into urine during a urine collection interval (Calculated for SXC-2023 only)	Calculated as: [Aet1-t2]/Dose x 100
Cum%Dose (%Fe)	The percent of dose excreted into urine over the entire period of sample collection (Calculated for SXC-2023 only)	Calculated as: [CumAe]/Dose x 100

For the calculation of descriptive statistics and urine PK parameters, urine concentrations that are BLQ will be set to zero. Cumulative urine PK parameters (e.g., CumAe) and derived parameters (e.g., %Dose and Cum%Dose) after a missing sample (e.g., lost part of void, volume not recorded, etc.) will continue to be presented, but will be excluded from the summary statistics.

6.6 Data Summarization and Presentation

All SXC-2023, NAC, and *p*-toluic acid PK concentrations and/or PK parameters descriptive statistics will be generated using SAS®.

The plasma, RBC, and urine concentrations of SXC-2023, NAC, and *p*-toluic acid will be listed and summarized by analyte, treatment (dose level) and time point or collection interval for all subjects in the PK Population. Plasma, RBC, and urine concentrations of SXC-2023, NAC, and *p*-toluic acid will be presented with the same level of precision as received from the bioanalytical laboratory. Summary statistics, including sample size (n), arithmetic mean (Mean), standard deviation (SD), coefficient of variation (CV%), standard error of the mean (SEM), minimum, median, and maximum will be calculated for all nominal concentration time points. Excluded subjects will be included in the concentration listings, but will be excluded from the summary statistics and noted as such in the tables. All BLQ values will be presented as "BLQ" in the concentration listings and footnoted accordingly.

Mean and individual concentration-time profiles will be presented on linear and semi-log scales. Linear mean plots will be presented with and without SD. Superimposed profiles (spaghetti plots) will be presented per treatment on linear scale.

Plasma, RBC (if applicable), and urine PK parameters for SXC-2023, NAC, and *p*-toluic acid will be listed and summarized by analyte and treatment (dose level) for all subjects in the PK Evaluable Population. Cmax will be presented with the precision of the bio data. AUCs will be reported to 3-4 significant figures (to be determined by the PKist once bio data are received). Tmax and t1/2 will be presented with 2 decimal places. Kel, Vz/F, and CL/F will be presented with 3 significant figures. Summary statistics (n, arithmetic mean, SD, CV%, SEM, minimum, median, maximum, geometric mean [Geom Mean] and geometric CV% [Geom CV%]) will be calculated for plasma, RBC, and urine SXC-2023, NAC, and *p*-toluic acid PK parameters. Excluded subjects will be listed in the PK parameter tables, but will be excluded from the summary statistics and noted as such in the tables.

The level of precision for each concentration and PK parameter statistic will be presented as follows: minimum/maximum in same precision as in bioanalytical data and/or parameter output, mean/median/Geom.Mean in one more level of precision than minimum/maximum, SD/SEM in one more level of precision than mean/median, n will be presented as an integer and CV% and Geom CV will be presented to the nearest tenth.

6.7 Statistical Analysis of PK Parameters

6.7.1 Food Effect Assessment

A comparison will be performed on the natural-log (ln)-transformed SXC-2023 plasma and RBC (if applicable) PK parameters Cmax, AUC0-t, and AUC0-inf to

evaluate the relative bioavailability of fed versus fasted conditions, by performing an analysis of variance (ANOVA) model using PROC MIXED of SAS®. The ANOVA model will include treatment (fed or fasted) as a fixed effect and subject as a random effect. The inferential results (least-squares means [LSMs], difference between LS means, and 90% CIs of the difference) will be exponentiated to the original scale. Geometric LSM, geometric mean ratios (GMRs) and 90% CIs will be presented. The ratios and 90% CIs will be expressed as a percentage relative to the fasting conditions.

The ANOVA will be performed using the following SAS® code:

PROC MIXED;

CLASS TREATMENT SUBJECT;

MODEL PK_PARAMETER = TREATMENT;

RANDOM SUBJECT;

*ESTIMATE “FED vs. FASTED” TREATMENT -1 1/ cl alpha=0.1 e;

* Programmer Note: Please only include data from the food effect cohort in this model. Prior to running the model, please contact biostatistician to confirm coefficients for the ESTIMATE statement.

6.7.2 Dose Proportionality Analysis

Dose proportionality will be evaluated for SXC-2023, NAC, and *p*-toluic AUC0-t, AUC0-inf, and Cmax plasma PK parameters following administration of single doses (fasted cohorts). To evaluate dose proportionality, a regression approach will be used. A statistical linear relationship between the ln-transformed PK parameters AUC and Cmax and the ln-transformed dose will be fitted by using a regression model with ln-transformed dose as a covariate.

$Ln(Y) = \beta 0 + \beta \text{ Ln Dose} + \varepsilon$ (Model 1)

where Y represents the PK parameter, AUCs and Cmax.

This approach is usually referred to as a power model because after exponentiation:

$Y = \alpha (\text{Dose})\beta$

where α only depends on $\beta 0$ and error.

Dose proportionality requires that $\beta = 1$ for dose-dependent parameters.

As a first step, the statistical linear relationship between the ln-transformed PK parameters AUC and Cmax and the ln-transformed dose will be verified by including the $(\ln \text{Dose})^2$ and $(\ln \text{Dose})^3$ terms in Step 1 (see below), which corresponds to the quadratic and cubic effects. A 5% level of significance will be used to test the quadratic and/or cubic effects. The statistical linear relationship will be concluded if the quadratic and cubic terms are not statistically significant or if the effects are statistically significant, but of small magnitude (not clinically relevant).

The following SAS® PROC MIXED code will be used:

Step 1: Test of a quadratic and cubic effects:

```
PROC MIXED;
MODEL LN_PKPARAMETER = LNDOSE  LNDOSE2 LNDOSE3   /DDFM=KR
                       HTYPE = 1 SOLUTION;
RUN;
```

Where LNDOSE = Ln(Dose) and LNDOSEN = $[\text{Ln(dose)-Mean(Ln(dose))}]^N$. The centralized quadratic and cubic terms are used to avoid multicollinearity and estimation problems.

If the statistical linear relationship is established in step 1, a second step (see below) will be performed. As a second step, model will be used to calculate the 95% CIs for the slope of the ln-transformed PK parameters, AUC and Cmax.

Dose proportionality will be established if a statistical linear relationship is demonstrated and if the 95% CIs for these parameters include the value of 1 for dose-dependent parameters (AUC and Cmax). The above assessments of dose proportionality will be performed the following SAS® PROC MIXED code:

Step 2: Test for a linear effect and obtaining a 95% CI for the slope parameter:

```
PROC MIXED;
MODEL LPARM = LNDOSE / DDFM = KR SOLUTION CL ALPHA=0.05;
RUN;
```

Where LNDOSE = Ln(Dose)

7. SAFETY

All case report form (CRF) data will be listed by subject and chronologically by assessment time points. This will include rechecks, unscheduled assessments, and early termination.

Applicable continuous variables will be summarized using n, arithmetic mean, SD, minimum, median, and maximum. Data from subjects who received the placebo

treatment (fasted or fed) will be pooled across cohorts. Therefore, for subjects in the food effect cohort, the placebo treatment received in Periods 1 and 2 will be summarized under the same treatment.

The level of precision will be presented as follows: minimum/maximum in the same precision as in the database, mean/median in one more precision level than minimum/maximum, SD in one more precision level than mean/median, and n will be presented as an integer.

Where individual data points are missing because of dropouts or other reasons, the data will be summarized based on reduced denominators.

No inferential statistics will be performed for safety assessments.

7.1 Subject Discontinuation

Subjects will be summarized by number of subjects enrolled, completed, and discontinued the study with discontinuation reasons by randomized treatment (including pooled placebo) and overall. Subjects enrolled in the food effect cohort will be summarized according to the treatment they were randomized to receive in Period 1.

7.2 Demographics

Descriptive statistics will be calculated for continuous variables (age, weight, height, and body mass index [BMI]) by randomized treatment (including pooled placebo) and overall. Weight, height, and BMI will be summarized at screening. Age will be derived from date of birth to date of first dosing (Day 1 of Period 1). Frequency counts will be provided for categorical variables (race, ethnicity, and sex) by randomized treatment (including pooled placebo) and overall. Subjects enrolled in the food effect cohort will be summarized according to the treatment they were randomized to receive in Period 1.

7.3 Adverse Events

All AEs occurring during this clinical trial will be coded using the Medical Dictionary for Regulatory Activities (MedDRA®), Version 20.0.

All AEs captured in the database will be listed in by-subject data listings including verbatim term, coded term, treatment, severity, relationship to study medication, and actions; however, only TEAEs will be summarized.

A TEAE is defined as an AE that is starting or worsening at the time of or after study drug administration. Each TEAE will be attributed to a treatment based on the onset date and time of the AE. For subjects enrolled in the food effect cohort, an AE that

occurs during the washout period between drugs will be considered treatment-emergent to the treatment administered in Period 1.

If an AE increases in severity, that AE will be given a resolution date and time and a new record will be initiated with the new severity. If the severity of an AE remains the same or decreases, the AE will be kept open through to resolution.

If the onset date and/or time of an AE is/are missing, the AE will be treated as TEAE to the randomized treatment, unless the onset date of the AE is known to have occurred prior to dosing. For subjects enrolled in the food effect cohort, if the onset time of an AE is missing and the onset date is the same as the treatment dosing date, then the AE will be considered treatment emergent to both treatments. If onset time of an AE is missing and the onset date does not fall on a dosing date, then the AE will be considered treatment emergent for the last treatment administered. If the onset date of an AE is missing, then the AE will be considered treatment emergent and attributed to both treatments, unless the onset date is known to have occurred within or between specific treatment periods.

TEAEs will be tabulated by System Organ Class (SOC) and Preferred Term. Summary tables will include number of subjects reporting the AE and as percent of number of subjects dosed by treatment (including pooled placebo), and overall. The number of AEs will be tabulated in a similar manner. Tables which tabulate the number of TEAEs by severity and relationship to study treatment will also be included.

Serious adverse events (SAEs), if present, will also be listed. Applicable narratives will be included in the CSR.

7.4 Clinical Laboratory Tests (Serum Chemistry, Hematology, Urinalysis)

All clinical laboratory test results will be presented in by-subject data listings; however, only serum chemistry (including Total testosterone, LH, and FSH), hematology, and urinalysis values will be summarized.

Serum chemistry (including Total testosterone, LH, and FSH), hematology, and urinalysis tests will be performed at the following time points:

Table 7-1 Clinical Laboratory Collection Time Points

Test*	Period	Day	Time Point
Serum Chemistry, Hematology, Urinalysis	Screen		
	1,2**	-1	Check-in
		2	Hour 24
		4 / ET	Hour 72 or Early Termination
*Coagulation, HIV/Hepatitis and urine cotinine tests will also be performed at Screening. Serum pregnancy tests will be performed at Screening, Day -1 and Day 4 of each period. Urine cotinine screen will be performed at Screening and Urine alcohol and drug screens will be performed at Screening and Day -1 of each period.			

** Period 2 assessments will only be performed for subjects included in the food effect cohort.

Out-of-normal-range flags will be recorded as follows: high (H) and low (L) for numerical results and did-not-match (*) for categorical results. If a value fails the reference range, it will automatically be compared to a computer clinically significant (CS) range. If the value falls within the computer CS range, it will be noted as “N” for not clinically significant. If the value fails the computer CS range (i.e., falls outside of the CS range), it will be flagged with a “Y”, which prompts the PI to determine how the out-of-range value should be followed using 4 Investigator flags: "N", not clinically significant; "R", requesting a recheck; "^", checking at the next scheduled visit; or "Y", clinically significant. To distinguish the PI flag from the computer CS range flags, the PI flags of “N” and “Y” will be presented as “-” and “+”, respectively, in the data listing. Additionally, a derived flag based on a search of the PI comments for a comment of “CS” or “Clinically Significant” will be used. The derived flag will be populated with “+” if the positive clinically significant determination is found in the comments for cases when the PI flag is populated with a “^” or an “R”.

Out-of-range values and corresponding recheck results will be listed. Results that are indicated as CS by the PI (either in the PI flag or in PI comments) will be listed in the table.

For all numeric laboratory values, descriptive statistics will be presented for each laboratory test by assessment time point and treatment. Change from baseline will be summarized in a similar manner. Baseline is defined as the result closest and prior to dose which may include unscheduled or recheck results. This will typically be the result collected on Day -1 in each period. Postdose unscheduled events or rechecks will not be included in summaries. Similarly, early termination results will not be included in summaries.

For each laboratory test, a shift table will be developed to compare the frequency of the results at baseline (above reference, within reference, or below reference) with the respective postdose results. For urinalysis tests, the categories are normal and outside normal.

7.5 Vital Signs

Single measurements of oral body temperature, respiratory rate, blood pressure and heart rate will be performed with subjects in a seated position at the following time points:

Table 7-2 Vital Signs Collection Time Points

Vital Sign Measurement	Period	Day	Time Point
Blood Pressure (Systolic, Diastolic), Heart Rate, Body Temperature, Respiratory Rate	Screen		
	1, 2**	-1	Predose
		1	Hour 2, Hour 4
		2	Hour 24
		3	Hour 48
		4 / ET	Hour 72 or Early Termination
		FU*	Follow-Up
*The follow-up measurements will be collected approximately 7 days after the last study drug/placebo administration. ** Period 2 assessments will only be performed for subjects included in the food effect cohort.			

All vital signs data will be listed by subject. Descriptive statistics will be reported for all vital signs measurements by treatment and time point. Change from baseline will be summarized in a similar way. Baseline is defined as the result closest and prior to first dosing in each period, which may include unscheduled or recheck results. This will typically be the predose measurement collected within 24 hours prior to dosing in each period. For subjects in the food effect cohort, baseline for the follow-up time point will be the predose measurement collected in Period 2. Postdose unscheduled events, rechecks, or early termination records will not be included in summaries.

7.6 Electrocardiogram

Single 12-lead ECG parameters (i.e., HR, PR, QRS, QT, and QTcF [QT corrected for heart rate using Fridericia's equation]) will be collected with subjects in supine position at the following time points:

Table 7-3 12-lead ECG Collection Time Points

ECG Parameter	Period	Day	Time Point
HR, PR, QRS, QT, QTcF	Screen		
	1, 2*	-1	Predose
		1	Hour 2
		2	Hour 24
		4 / ET	Hour 72 or Early Termination
*Period 2 assessments will only be performed for subjects included in the food effect cohort.			

Descriptive statistics will be reported for ECG parameters by treatment and time point. Change from baseline will be summarized in a similar way. Baseline is defined as the result closest and prior to dosing, which may include unscheduled or recheck results. This will typically be the predose measurement collected within 24 hours prior to dosing in each period. Postdose unscheduled events or rechecks will not be

included in summaries. Similarly, early termination results will not be included in summaries. QTcF values greater than 450 and QTcF changes from baseline greater than 30 msec will be flagged in the data listing.

A normal-abnormal shift from baseline table will be presented for the ECG overall interpretation by treatment and time point.

7.7 Concomitant Medications

All concomitant medications recorded during the study will be coded with the WHO Dictionary Version 01MAR2017 and listed.

7.8 Physical Examination

A full physical examination will be performed at Screening. Symptom-driven physical examinations may be performed at other times, if deemed necessary by the PI or designee. Abnormal findings will be reported as medical history or adverse events. All data found in the CRF will be listed.

8. SUMMARY OF CHANGES FROM PROTOCOL-PLANNED ANALYSIS

The analyses described in this SAP are aligned with those analyses described in the protocol.

9. SUMMARY TABLES AND FIGURES

Summary tables and figures are numbered following the International Conference on Harmonization (ICH) structure but may be renumbered as appropriate during the compilation of the tables and figures for the CSR. Note that all PK and safety summary tables and figures will be generated using SAS® Version 9.3 or higher.

9.1 In-text Summary Tables and Figures

The following is a list of table and figure titles that will be included in the text of the CSR. Tables and figures will be numbered appropriately during compilation of the CSR.

Section 10:

Table 10-1 Summary of Disposition

Section 11:

Table 11-1 Demographic Summary

SXC-2023 In-Text Tables and Figures

Table 11-2 Summary of Plasma SXC-2023 Pharmacokinetics Following Single Oral Doses of SXC-2023 Administered Under Fasted or Fed Conditions

Table 11-3 Summary of Statistical Comparisons of Plasma SXC-2023 Pharmacokinetic Parameters Following Single Oral Doses of SXC-2023 Administered Under Fed Versus Fasted Conditions

Table 11-4 Dose Proportionality Analysis of Plasma SXC-2023 Pharmacokinetic Parameters Following Single Oral Doses of SXC-2023 Administered Under Fasted Conditions

Table 11-5 Summary of RBC SXC-2023 Pharmacokinetics Following Single Oral Doses of SXC-2023 Administered Under Fasted or Fed Conditions

Table 11-6 Summary of Statistical Comparisons of RBC SXC-2023 Pharmacokinetic Parameters Following Single Oral Doses of SXC-2023 Administered Under Fed Versus Fasted Conditions

Table 11-7 Summary of Urine SXC-2023 Pharmacokinetics Following Single Oral Doses of SXC-2023 Administered Under Fasted or Fed Conditions

Figure 11-1 Arithmetic Mean Plasma SXC-2023 Concentration-Time Profiles Following Administration of Single Oral Doses of SXC-2023 Under Fasted or Fed Conditions

Figure 11-2 Arithmetic Mean Urine SXC-2023 Amount Excreted-Time Profiles Following Administration of Single Oral Doses of SXC-2023 Under Fasted or Fed Conditions

Figure 11-3 Arithmetic Mean Percent of SXC-2023 Dose Excreted in Urine-Time Profiles Following Administration of Single Oral Doses of SXC-2023 Under Fasted or Fed Conditions

NAC In-Text Tables and Figures

Table 11-8 Summary of Plasma NAC Pharmacokinetics Following Single Oral Doses of SXC-2023 Administered Under Fasted or Fed Conditions

Table 11-9 Dose Proportionality Analysis of Plasma NAC Pharmacokinetic Parameters Following Single Oral Doses of SXC-2023 Administered Under Fasted Conditions

Table 11-10 Summary of RBC NAC Pharmacokinetics Following Single Oral Doses of SXC-2023 Administered Under Fasted or Fed Conditions

Table 11-11 Summary of Urine NAC Pharmacokinetics Following Single Oral Doses of SXC-2023 Administered Under Fasted or Fed Conditions

Figure 11-4 Arithmetic Mean Plasma NAC Concentration-Time Profiles Following Administration of Single Oral Doses of SXC-2023 Under Fasted or Fed Conditions

Figure 11-5 Arithmetic Mean Urine NAC Amount Excreted-Time Profiles Following Administration of Single Oral Doses of SXC-2023 Under Fasted or Fed Conditions

p-Toluic Acid In-Text Tables and Figures

Table 11-12 Summary of Plasma *p*-Toluic Acid Pharmacokinetics Following Single Oral Doses of SXC-2023 Administered Under Fasted or Fed Conditions

Table 11-13 Dose Proportionality Analysis of Plasma *p*-Toluic Acid Pharmacokinetic Parameters Following Single Oral Doses of SXC-2023 Administered Under Fasted Conditions

Table 11-14 Summary of RBC *p*-Toluic Acid Pharmacokinetics Following Single Oral Doses of SXC-2023 Administered Under Fasted or Fed Conditions

Table 11-15 Summary of Urine *p*-Toluic Acid Pharmacokinetics Following Single Oral Doses of SXC-2023 Administered Under Fasted or Fed Conditions

Figure 11-6 Arithmetic Mean Plasma *p*-Toluic Acid Concentration-Time Profiles Following Administration of Single Oral Doses of SXC-2023 Under Fasted or Fed Conditions

Figure 11-7 Arithmetic Mean Urine *p*-Toluic Acid Amount Excreted-Time Profiles Following Administration of Single Oral Doses of SXC-2023 Under Fasted or Fed Conditions

Programmer's note if no parameters can be determined in RBC Tables 11-5, 11-6, 11-10, and 11-14, as appropriate, will not be generated and table numbers will be updated accordingly.

Section 12:

Table 12-1 Treatment-Emergent Adverse Event Frequency by Treatment - Number of Subjects Reporting the Event (% of Subjects Dosed)

9.2 Section 14 Summary Tables and Figures

The following is a list of table and figure titles that will be included in Section 14 of the report. Table and figure titles may be renumbered as appropriate during the compilation of the report.

14.1 Demographic Data Summary Tables

Table 14.1.1 Summary of Disposition (Safety Population)
Table 14.1.2 Demographic Summary (Safety Population)

14.2 Pharmacokinetic Data Summary Tables and Figures

14.2.1 SXC-2023 Tables and Figures

14.2.1.1 Plasma SXC-2023 Tables

Table 14.2.1.1.1 Plasma SXC-2023 Concentrations (<units>) Following a Single Oral Dose of 50 mg SXC-2023 Administered Under Fasted Conditions (Cohort 1 - Treatment A) (Pharmacokinetic Population)
Table 14.2.1.1.2 Plasma SXC-2023 Concentrations (<units>) Following a Single Oral Dose of 100 mg SXC-2023 Administered Under Fasted Conditions (Cohort 2 - Treatment B) (Pharmacokinetic Population)
Table 14.2.1.1.3 Plasma SXC-2023 Concentrations (<units>) Following a Single Oral Dose of 200 mg SXC-2023 Administered Under Fasted Conditions (Cohort 3 - Treatment C) (Pharmacokinetic Population)
Table 14.2.1.1.4 Plasma SXC-2023 Concentrations (<units>) Following a Single Oral Dose of 400 mg SXC-2023 Administered Under Fasted Conditions (Cohort 4 - Treatment D) (Pharmacokinetic Population)
Table 14.2.1.1.5 Plasma SXC-2023 Concentrations (<units>) Following a Single Oral Dose of 800 mg SXC-2023 Administered Under Fasted Conditions (Cohort 5 - Treatment E) (Pharmacokinetic Population)
Table 14.2.1.1.6 Plasma SXC-2023 Concentrations (<units>) Following a Single Oral Dose of 800 mg SXC-2023 Administered Under Fed Conditions (Cohort 5 - Treatment F) (Pharmacokinetic Population)
Table 14.2.1.1.7 Plasma SXC-2023 Concentrations (<units>) Following a Single Oral Dose of 1600 mg SXC-2023 Administered

Under Fasted Conditions (Cohort 6 - Treatment G) (Pharmacokinetic Population)

Table 14.2.1.1.8 Plasma SXC-2023 Concentrations (<units>) Following a Single Oral Dose of Placebo Administered under Fasted Conditions (Cohorts 1-6 – Pooled Placebo)

Table 14.2.1.1.9 Plasma SXC-2023 Pharmacokinetic Parameters Following a Single Oral Dose of 50 mg SXC-2023 Administered Under Fasted Conditions (Cohort 1 - Treatment A) (Pharmacokinetic Evaluable Population)

Table 14.2.1.1.10 Plasma SXC-2023 Pharmacokinetic Parameters Following a Single Oral Dose of 100 mg SXC-2023 Administered Under Fasted Conditions (Cohort 2 - Treatment B) (Pharmacokinetic Evaluable Population)

Table 14.2.1.1.11 Plasma SXC-2023 Pharmacokinetic Parameters Following a Single Oral Dose of 200 mg SXC-2023 Administered Under Fasted Conditions (Cohort 3 - Treatment C) (Pharmacokinetic Evaluable Population)

Table 14.2.1.1.12 Plasma SXC-2023 Pharmacokinetic Parameters Following a Single Oral Dose of 400 mg SXC-2023 Administered Under Fasted Conditions (Cohort 4 - Treatment D) (Pharmacokinetic Evaluable Population)

Table 14.2.1.1.13 Plasma SXC-2023 Pharmacokinetic Parameters Following a Single Oral Dose of 800 mg SXC-2023 Administered Under Fasted Conditions (Cohort 5 - Treatment E) (Pharmacokinetic Evaluable Population)

Table 14.2.1.1.14 Plasma SXC-2023 Pharmacokinetic Parameters Following a Single Oral Dose of 800 mg SXC-2023 Administered Under Fed Conditions (Cohort 5 - Treatment F) (Pharmacokinetic Evaluable Population)

Table 14.2.1.1.15 Plasma SXC-2023 Pharmacokinetic Parameters Following a Single Oral Dose of 1600 mg SXC-2023 Administered Under Fasted Conditions (Cohort 6 - Treatment G) (Pharmacokinetic Evaluable Population)

Table 14.2.1.1.16 Intervals (Hours) Used for Determination Plasma SXC-2023 Kel Values (Pharmacokinetic Population)

Table 14.2.1.1.17 Statistical Comparisons of Plasma SXC-2023 Pharmacokinetic Parameters: Fed Versus Fasted Conditions (Cohort 5 - Pharmacokinetic Evaluable Population)

Table 14.2.1.1.18 Dose Proportionality Analysis of Plasma SXC-2023 Pharmacokinetic Parameters Under Fasted Conditions (Pharmacokinetic Evaluable Population)

14.2.1.2 Plasma SXC-2023 Figures

Figure 14.2.1.2.1 Mean (SD) Plasma SXC-2023 Concentration Versus Time Profiles Following Administration of Single Oral Doses of SXC-2023 (Linear Scale) (Treatments A-G - Pharmacokinetic Evaluable Population)

Figure 14.2.1.2.2 Mean Plasma SXC-2023 Concentration Versus Time Profiles Following Administration of Single Oral Doses of SXC-2023 (Linear Scale) (Treatments A-G - Pharmacokinetic Evaluable Population)

Figure 14.2.1.2.3 Mean Plasma SXC-2023 Concentration Versus Time Profiles Following Administration of Single Oral Doses of SXC-2023 (Semi-Log Scale) (Treatments A-G Pharmacokinetic Evaluable Population)

Figure 14.2.1.2.4 Superimposed Plasma SXC-2023 Concentration Versus Time Profiles Following Administration a Single Oral Dose of 50 mg SXC-2023 Administered Under Fasted Conditions (Treatment A) (Linear Scale)

Figure 14.2.1.2.5 Superimposed Plasma SXC-2023 Concentration Versus Time Profiles Following Administration a Single Oral Dose of 100 mg SXC-2023 Administered Under Fasted Conditions (Treatment B) (Linear Scale)

Figure 14.2.1.2.6 Superimposed Plasma SXC-2023 Concentration Versus Time Profiles Following Administration a Single Oral Dose of 200 mg SXC-2023 Administered Under Fasted Conditions (Treatment C) (Linear Scale)

Figure 14.2.1.2.7 Superimposed Plasma SXC-2023 Concentration Versus Time Profiles Following Administration a Single Oral Dose of 400 mg SXC-2023 Administered Under Fasted Conditions (Treatment D) (Linear Scale)

Figure 14.2.1.2.8 Superimposed Plasma SXC-2023 Concentration Versus Time Profiles Following Administration a Single Oral Dose of 800 mg SXC-2023 Administered Under Fasted Conditions (Treatment E) (Linear Scale)

Figure 14.2.1.2.9 Superimposed Plasma SXC-2023 Concentration Versus Time Profiles Following Administration a Single Oral Dose of 800 mg SXC-2023 Administered Under Fed Conditions (Treatment F) (Linear Scale)

Figure 14.2.1.2.10 Superimposed Plasma SXC-2023 Concentration Versus Time Profiles Following Administration a Single Oral Dose of 1600 mg SXC-2023 Administered Under Fasted Conditions (Treatment G) (Linear Scale)

Programmer's note: Figures 14.2.1.2.4 through 14.2.1.2.10 will be spaghetti plots.

14.2.1.3 RBC SXC-2023 Tables

Table 14.2.1.3.1 RBC SXC-2023 Concentrations (<units>) Following a Single Oral Dose of 200 mg SXC-2023 Administered Under Fasted Conditions (Cohort 3 - Treatment C) (Pharmacokinetic Population)

Table 14.2.1.3.2 RBC SXC-2023 Concentrations (<units>) Following a Single Oral Dose of 400 mg SXC-2023 Administered Under Fasted Conditions (Cohort 4 - Treatment D) (Pharmacokinetic Population)

Table 14.2.1.3.3 RBC SXC-2023 Concentrations (<units>) Following a Single Oral Dose of 800 mg SXC-2023 Administered Under Fasted Conditions (Cohort 5 - Treatment E) (Pharmacokinetic Population)

Table 14.2.1.3.4 RBC SXC-2023 Concentrations (<units>) Following a Single Oral Dose of 800 mg SXC-2023 Administered Under Fed Conditions (Cohort 5 - Treatment F) (Pharmacokinetic Population)

Table 14.2.1.3.5 RBC SXC-2023 Concentrations (<units>) Following a Single Oral Dose of 1600 mg SXC-2023 Administered Under Fasted Conditions (Cohort 6 - Treatment G) (Pharmacokinetic Population)

Table 14.2.1.3.6 RBC SXC-2023 Concentrations (<units>) Following a Single Oral Dose of Placebo Administered under Fasted Conditions (Cohorts 1-6 – Pooled Placebo)

Table 14.2.1.3.7 RBC SXC-2023 Pharmacokinetic Parameters Following a Single Oral Dose of 200 mg SXC-2023 Administered Under Fasted Conditions (Cohort 3 - Treatment C) (Pharmacokinetic Evaluable Population)

Table 14.2.1.3.8 RBC SXC-2023 Pharmacokinetic Parameters Following a Single Oral Dose of 400 mg SXC-2023 Administered Under Fasted Conditions (Cohort 4 - Treatment D) (Pharmacokinetic Evaluable Population)

Table 14.2.1.3.9 RBC SXC-2023 Pharmacokinetic Parameters Following a Single Oral Dose of 800 mg SXC-2023 Administered Under Fasted Conditions (Cohort 5 - Treatment E) (Pharmacokinetic Evaluable Population)

Table 14.2.1.3.10 RBC SXC-2023 Pharmacokinetic Parameters Following a Single Oral Dose of 800 mg SXC-2023 Administered

Under Fed Conditions (Cohort 5 - Treatment F) (Pharmacokinetic Evaluable Population)

Table 14.2.1.3.11 RBC SXC-2023 Pharmacokinetic Parameters Following a Single Oral Dose of 1600 mg SXC-2023 Administered Under Fasted Conditions (Cohort 6 - Treatment G) (Pharmacokinetic Evaluable Population)

Table 14.2.1.3.12 Intervals (Hours) Used for Determination RBC SXC-2023 Kel Values (Pharmacokinetic Population)

Table 14.2.1.3.13 Statistical Comparisons of RBC SXC-2023 Pharmacokinetic Parameters: Fed Versus Fasted Conditions (Cohort 5 - Pharmacokinetic Evaluable Population)

Programmer's note: if RBC PK parameters cannot be determined tables 14.2.1.3.7 through 14.2.1.3.13 will not be generated.

14.2.1.4 RBC SXC-2023 Figures

Figure 14.2.1.4.1 Mean (SD) RBC SXC-2023 Concentration Versus Time Profiles Following Administration of Single Oral Doses of SXC-2023 (Linear Scale) (Treatments C-G - Pharmacokinetic Evaluable Population)

Figure 14.2.1.4.2 Mean RBC SXC-2023 Concentration Versus Time Profiles Following Administration of Single Oral Doses of SXC-2023 (Linear Scale) (Treatments C-G - Pharmacokinetic Evaluable Population)

Figure 14.2.1.4.3 Mean RBC SXC-2023 Concentration Versus Time Profiles Following Administration of Single Oral Doses of SXC-2023 (Semi-Log Scale) (Treatments C-G - Pharmacokinetic Evaluable Population)

Figure 14.2.1.4.4 Superimposed RBC SXC-2023 Concentration Versus Time Profiles Following Administration a Single Oral Dose of 200 mg SXC-2023 Administered Under Fasted Conditions (Treatment C) (Linear Scale)

Figure 14.2.1.4.5 Superimposed RBC SXC-2023 Concentration Versus Time Profiles Following Administration a Single Oral Dose of 400 mg SXC-2023 Administered Under Fasted Conditions (Treatment D) (Linear Scale)

Figure 14.2.1.4.6 Superimposed RBC SXC-2023 Concentration Versus Time Profiles Following Administration a Single Oral Dose of 800 mg SXC-2023 Administered Under Fasted Conditions (Treatment E) (Linear Scale)

Figure 14.2.1.4.7 Superimposed RBC SXC-2023 Concentration Versus Time Profiles Following Administration a Single Oral Dose of

800 mg SXC-2023 Administered Under Fed Conditions (Treatment F) (Linear Scale)

Figure 14.2.1.4.8 Superimposed RBC SXC-2023 Concentration Versus Time Profiles Following Administration a Single Oral Dose of 1600 mg SXC-2023 Administered Under Fasted Conditions (Treatment G) (Linear Scale)

Programmer's note: Figures 14.2.1.4.4 through 14.2.1.4.8 will be spaghetti plots.

14.2.1.5 Urine SXC-2023 Tables

Table 14.2.1.5.1 Urinary Excretion of SXC-2023 Following a Single Oral Dose of 50 mg SXC-2023 Administered Under Fasted Conditions (Cohort 1 - Treatment A) (Pharmacokinetic Population)

Table 14.2.1.5.2 Urinary Excretion of SXC-2023 Following a Single Oral Dose of 100 mg SXC-2023 Administered Under Fasted Conditions (Cohort 2 - Treatment B) (Pharmacokinetic Population)

Table 14.2.1.5.3 Urinary Excretion of SXC-2023 Following a Single Oral Dose of 200 mg SXC-2023 Administered Under Fasted Conditions (Cohort 3 - Treatment C) (Pharmacokinetic Population)

Table 14.2.1.5.4 Urinary Excretion of SXC-2023 Following a Single Oral Dose of 400 mg SXC-2023 Administered Under Fasted Conditions (Cohort 4 - Treatment D) (Pharmacokinetic Population)

Table 14.2.1.5.5 Urinary Excretion of SXC-2023 Following a Single Oral Dose of 800 mg SXC-2023 Administered Under Fasted Conditions (Cohort 5 - Treatment E) (Pharmacokinetic Population)

Table 14.2.1.5.6 Urinary Excretion of SXC-2023 Following a Single Oral Dose of 800 mg SXC-2023 Administered Under Fed Conditions (Cohort 5 - Treatment F) (Pharmacokinetic Population)

Table 14.2.1.5.7 Urinary Excretion of SXC-2023 Following a Single Oral Dose of 1600 mg SXC-2023 Administered Under Fasted Conditions (Cohort 6 - Treatment G) (Pharmacokinetic Population)

Table 14.2.1.5.8 Urinary Excretion of SXC-2023 Following a Single Oral Dose of Placebo Administered Under Fasted Conditions

(Cohorts 1-6 – Pooled Placebo) (Pharmacokinetic Population)

14.2.1.6 Urine SXC-2023 Figures

Figure 14.2.1.6.1 Mean (SD) Cumulative Urine SXC-2023 Amounts Excreted Following Administration of Single Oral Doses of SXC-2023 (Linear Scale) (Treatments A-G) (Pharmacokinetic Population)

Figure 14.2.1.6.2 Mean Cumulative Urine SXC-2023 Amounts Excreted Following Administration of Single Oral Doses of SXC-2023 (Linear Scale) (Treatments A-G) (Pharmacokinetic Population)

Figure 14.2.1.6.3 Mean (SD) Cumulative Percent of SXC-2023 Dose Excreted in Urine Following Administration of Single Oral Doses of SXC-2023 (Linear Scale) (Treatments A-G) (Pharmacokinetic Population)

Figure 14.2.1.6.4 Mean Cumulative Percent of SXC-2023 Dose Excreted in Urine Following Administration of Single Oral Doses of SXC-2023 (Linear Scale) (Treatments A-G) (Pharmacokinetic Population)

Programmer's note: Figures 14.2.1.6.1 through 14.2.1.6.4 will present cumulative amount (CumAe)/fraction excreted (Cum%Dose) versus the nominal end of the collection interval (0, 1, 2, 4, 8, 12, 24, 48, and 72 hours postdose).

14.2.2 N-acetylcysteine Tables and Figures

14.2.2.1 Plasma N-acetylcysteine Tables

Table 14.2.2.1.1 Plasma N-acetylcysteine Concentrations (<units>) Following a Single Oral Dose of 50 mg SXC-2023 Administered Under Fasted Conditions (Cohort 1 - Treatment A) (Pharmacokinetic Population)

Programmer's note: Tables 14.2.2.1.1 through 14.2.2.1.17 will present plasma NAC data and will follow the same format as Tables 14.2.1.1.1 through 14.2.1.1.18 (with the exception that the statistical comparisons for FE, corresponding to SXC-2023 Table 14.2.1.1.17, will not be presented).

14.2.2.2 Plasma N-acetylcysteine Figures

Figure 14.2.2.2.1 Mean (SD) Plasma N-acetylcysteine Concentration Versus Time Profiles Following Administration of Single Oral Doses of SXC-2023 (Linear Scale) (Treatments A-G - Pharmacokinetic Evaluable Population)

Programmer's note: Figures 14.2.2.2.1 through 14.2.2.2.10 will present plasma NAC data and will follow the same format as Figures 14.2.1.2.1 through 14.2.1.2.10.

Programmer's note: Figures 14.2.2.2.4 through 14.2.2.2.10 will be spaghetti plots.

14.2.2.3 RBC N-acetylcysteine Tables

Table 14.2.2.3.1 RBC N-acetylcysteine Concentrations (<units>) Following a Single Oral Dose of 200 mg SXC-2023 Administered Under Fasted Conditions (Cohort 3 - Treatment C) (Pharmacokinetic Population)

Programmer's note: Tables 14.2.2.3.1 through 14.2.2.3.12 will present RBC NAC data and will follow the same format as Tables 14.2.1.3.1 through 14.2.1.3.12

Programmer's note: if RBC PK parameters cannot be determined tables 14.2.2.3.7 through 14.2.2.3.12 will not be generated.

14.2.2.4 RBC N-acetylcysteine Figures

Figure 14.2.2.4.1 Mean (SD) RBC N-acetylcysteine Concentration Versus Time Profiles Following Administration of Single Oral Doses of SXC-2023 (Linear Scale) (Treatments C-G - Pharmacokinetic Evaluable Population)

Programmer's note: Figures 14.2.2.4.1 through 14.2.2.4.8 will present RBC NAC data and will follow the same format as Figures 14.2.1.4.1 through 14.2.1.4.8.

Programmer's note: Figures 14.2.2.4.4 through 14.2.2.4.8 will be spaghetti plots.

14.2.2.5 Urine N-acetylcysteine Tables

Table 14.2.2.5.1 Urinary Excretion of N-acetylcysteine Following a Single Oral Dose of 50 mg SXC-2023 Administered Under Fasted Conditions (Cohort 1 - Treatment A) (Pharmacokinetic Population)

Programmer's note: Tables 14.2.2.5.1 through 14.2.2.5.8 will present urine NAC data and will follow the same format as Tables 14.2.1.5.1 through 14.2.1.5.8.

14.2.2.6 Urine N-acetylcysteine Figures

Figure 14.2.2.6.1 Mean (SD) Cumulative Urine N-acetylcysteine Amounts Excreted Following Administration of Single Oral Doses of SXC-2023 (Linear Scale) (Treatments A-G) (Pharmacokinetic Population)

Figure 14.2.2.6.2 Mean Cumulative Urine N-acetylcysteine Amounts Excreted Following Administration of Single Oral Doses of SXC-2023 (Linear Scale) (Treatments A-G) (Pharmacokinetic Population)

Programmer's note: Figures 14.2.2.6.1 and 14.2.2.6.2 will present urine NAC data and will follow the same format as Figures 14.2.1.6.1 and 14.2.1.6.2.

Programmer's note: Figures 14.2.1.6.1 and 14.2.1.6.2 will present cumulative amounts excreted (CumAe) versus the nominal end of the collection interval (0, 1, 2, 4, 8, 12, 24, 48, and 72 hours postdose).

14.2.3 *p*-Toluic Acid Tables and Figures

14.2.3.1 Plasma *p*-Toluic Acid Tables

Table 14.2.3.1.1 Plasma *p*-Toluic Acid Concentrations (<units>) Following a Single Oral Dose of 50 mg SXC-2023 Administered Under Fasted Conditions (Cohort 1 - Treatment A) (Pharmacokinetic Population)

Programmer's note: Tables 14.2.3.1.1 through 14.2.3.1.17 will present plasma p-toluic acid data and will follow the same format as Tables 14.2.1.1.1 through 14.2.1.1.18 (with the exception that the statistical comparison for FE, corresponding to SXC-2023 Table 14.2.1.1.17, will not be presented.

14.2.3.2 Plasma *p*-Toluic Acid Figures

Figure 14.2.3.2.1 Mean (SD) Plasma *p*-Toluic Acid Concentration Versus Time Profiles Following Administration of Single Oral Doses of SXC-2023 (Linear Scale) (Treatments A-G - Pharmacokinetic Evaluable Population)

Programmer's note: Figures 14.2.3.2.1 through 14.2.3.2.10 will present plasma p-Toluic Acid data and will follow the same format as Figures 14.2.1.2.1 through 14.2.1.2.10.

Programmer's note: Figures 14.2.3.2.4 through 14.2.3.2.10 will be spaghetti plots.

14.2.3.3 RBC *p*-Toluic Acid Tables

Table 14.2.3.3.1 RBC *p*-Toluic Acid Concentrations (<units>) Following a Single Oral Dose of 200 mg SXC-2023 Administered Under Fasted Conditions (Cohort 3 - Treatment C) (Pharmacokinetic Population)

Programmer's note: Tables 14.2.3.3.1 through 14.2.3.3.12 will present RBC p-toluic acid data and will follow the same format as Tables 14.2.1.3.1 through 14.2.1.3.12

Programmer's note: if RBC PK parameters cannot be determined tables 14.2.3.3.7 through 14.2.3.3.12 will not be generated.

14.2.3.4 RBC *p*-Toluic Acid Figures

Figure 14.2.3.4.1 Mean (SD) RBC *p*-Toluic Acid Concentration Versus Time Profiles Following Administration of Single Oral Doses of SXC-2023 (Linear Scale) (Treatments C-G - Pharmacokinetic Evaluable Population)

Programmer's note: Figures 14.2.3.4.1 through 14.2.3.4.8 will present RBC p-toluic acid data and will follow the same format as Figures 14.2.1.4.1 through 14.2.1.4.8.

Programmer's note: Figures 14.2.3.4.4 through 14.2.3.4.8 will be spaghetti plots.

14.2.3.5 Urine *p*-Toluic Acid Tables

Table 14.2.3.5.1 Urinary Excretion of *p*-Toluic Acid Following a Single Oral Dose of 50 mg SXC-2023 Administered Under Fasted Conditions (Cohort 1 - Treatment A) (Pharmacokinetic Population)

Programmer's note: Tables 14.2.3.5.1 through 14.2.3.5.8 will present urine p-Toluic Acid data and will follow the same format as Tables 14.2.1.5.1 through 14.2.1.5.8.

14.2.3.6 Urine *p*-Toluic Acid Figures

Figure 14.2.3.6.1 Mean (SD) Cumulative Urine *p*-Toluic Acid Amounts Excreted Following Administration of Single Oral Doses of SXC-2023 (Linear Scale) (Treatments A-G) (Pharmacokinetic Population)

Figure 14.2.3.6.2 Mean Cumulative Urine *p*-Toluic Acid Amounts Excreted Following Administration of Single Oral Doses of SXC-2023 (Linear Scale) (Treatments A-G) (Pharmacokinetic Population)

Programmer's note: Figures 14.2.3.6.1 and 14.2.3.6.2 will present urine p-toluic acid data and will follow the same format as Figures 14.2.1.6.1 and 14.2.1.6.2.

Programmer's note: Figures 14.2.3.6.1 and 14.2.3.6.2 will present amount excreted (CumAe) versus the nominal end of the collection interval (0, 1, 2, 4, 8, 12, 24, 48, and 72 hours postdose).

14.3 Safety Data Summary Tables

14.3.1 Displays of Adverse Events

Table 14.3.1.1 Treatment-emergent Adverse Event Frequency by Treatment – Number of Subjects Reporting the Event (% of Subject Dosed) (Safety Population)

Table 14.3.1.2 Treatment-emergent Adverse Event Frequency by Treatment – Number of Adverse Events (% of Total Adverse Events) (Safety Population)

Table 14.3.1.3 Treatment-emergent Adverse Event Frequency by Treatment, Severity, and Relationship to Study Drug – Number of Adverse Events (Safety Population)

14.3.2 Listings of Deaths, other Serious and Significant Adverse Events

Table 14.3.2.1 Serious Adverse Events (Safety Population)

14.3.3 Narratives of Deaths, other Serious and Certain other Significant Adverse Events

14.3.4 Abnormal Laboratory Value Listing (each patient)

Table 14.3.4.1 Out-of-Range Values and Recheck Results – Serum Chemistry (Safety Population)

Table 14.3.4.2 Out-of-Range Values and Recheck Results – Hematology (Safety Population)
Table 14.3.4.3 Out-of-Range Values and Recheck Results – Urinalysis (Safety Population)
Table 14.3.4.4 Clinically Significant Values and Recheck Results (Safety Population)

14.3.5 Displays of Other Laboratory, Vital Signs, Electrocardiogram, Physical Examination, and Other Safety Data

Table 14.3.5.1.1 Clinical Laboratory Summary – Serum Chemistry (Safety Population)
Table 14.3.5.1.2 Clinical Laboratory Change From Baseline – Serum Chemistry (Safety Population)
Table 14.3.5.1.3 Clinical Laboratory Shift From Baseline – Serum Chemistry (Safety Population)
Table 14.3.5.2.1 Clinical Laboratory Summary – Hematology (Safety Population)
Table 14.3.5.2.2 Clinical Laboratory Change From Baseline – Hematology (Safety Population)
Table 14.3.5.2.3 Clinical Laboratory Shift From Baseline – Hematology (Safety Population)
Table 14.3.5.3.1 Clinical Laboratory Summary – Urinalysis (Safety Population)
Table 14.3.5.3.2 Clinical Laboratory Change From Baseline – Urinalysis (Safety Population)
Table 14.3.5.3.3 Clinical Laboratory Shift From Baseline – Urinalysis (Safety Population)
Table 14.3.5.4.1 Vital Sign Summary (Safety Population)
Table 14.3.5.4.2 Vital Sign Change From Baseline (Safety Population)
Table 14.3.5.5.1 12-Lead Electrocardiogram Summary (Safety Population)
Table 14.3.5.5.2 12-Lead Electrocardiogram Change From Baseline (Safety Population)
Table 14.3.5.5.3 12-Lead Electrocardiogram Shift From Baseline (Safety Population)

9.3 Section 16 Data Listings

Note: Hepatitis and HIV results that are provided by the clinical laboratory will not be presented in subject data listings and will not be included in any database transfer.

Data listings are numbered following the ICH structure but may be renumbered as appropriate during the compilation of the TFLs for the CSR. The following is a list of appendix numbers and titles that will be included as data listings:

16.1 Study Information

Appendix 16.1.9 Statistical Methods

Appendix 16.1.10.1 Clinical Laboratory Reference Ranges

16.2 Subject Data Listings

16.2.1 Subject Discontinuation

Appendix 16.2.1 Subject Discontinuation (Safety Population)

16.2.2 Protocol Deviations

Appendix 16.2.2 Protocol Deviations

16.2.3 Subjects Excluded from Pharmacokinetic Analysis

Appendix 16.2.3 Subjects Excluded from Pharmacokinetic Analysis

Note: Appendices 16.2.2 and 16.2.3 are generated in MS Word for inclusion in the study report.

16.2.4 Demographic Data

Appendix 16.2.4.1 Demographics (Safety Population)
Appendix 16.2.4.2 Physical Examination (Safety Population)
Appendix 16.2.4.3 Medical and Surgical History (Safety Population)
Appendix 16.2.4.4 Substance Use (Safety Population)

16.2.5 Compliance and/or Drug Concentration Data

Appendix 16.2.5.1.1 Inclusion Criteria
Appendix 16.2.5.1.2 Exclusion Criteria
Appendix 16.2.5.2 Subject Eligibility (Safety Population)
Appendix 16.2.5.3.1 Check-in and Return Criteria

Appendix 16.2.5.3.2 Check-in and Return Responses (Safety Population)
Appendix 16.2.5.4.1 Test Compound Description (Safety Population)
Appendix 16.2.5.4.2 Test Compound Administration Times (Safety Population)
Appendix 16.2.5.5 Blood Draw Times (Safety Population)
Appendix 16.2.5.6 Urine Collection Times (Safety Population)
Appendix 16.2.5.7 Meal Times (Safety Population)
Appendix 16.2.5.8 Prior and Concomitant Medications (Safety Population)

16.2.6 Individual Pharmacokinetic Response Data

Appendix 16.2.6.1 Plasma SXC-2023 Concentrations Versus Time (Linear and Semi-Log Scale) for Subject #

Appendix 16.2.6.2 RBC SXC-2023 Concentrations Versus Time (Linear and Semi-Log Scale) for Subject #

Appendix 16.2.6.3 Urine SXC-2023 Amounts Excreted Versus Time (Linear Scale) for Subject #

Appendix 16.2.6.4 Percent of SXC-2023 Dose Excreted in urine Versus Time (Linear Scale) for Subject #

Appendix 16.2.6.5 Plasma NAC Concentrations Versus Time (Linear and Semi-Log Scale) for Subject #

Appendix 16.2.6.6 RBC NAC Concentrations Versus Time (Linear and Semi-Log Scale) for Subject #

Appendix 16.2.6.7 Urine NAC Amounts Excreted Versus Time (Linear Scale) for Subject #

Appendix 16.2.6.8 Plasma *p*-Toluic Acid Concentrations Versus Time (Linear and Semi-Log Scale) for Subject #

Appendix 16.2.6.9 RBC *p*-Toluic Acid Concentrations Versus Time (Linear and Semi-Log Scale) for Subject #

Appendix 16.2.6.10 Urine *p*-Toluic Acid Amounts Excreted Versus Time (Linear Scale) for Subject #

16.2.7 Adverse Events Listings

Appendix 16.2.7.1.1 Adverse Events (I of II) (Safety Population)
Appendix 16.2.7.1.2 Adverse Events (II of II) (Safety Population)

Appendix 16.2.7.2 Adverse Event Non-Drug Therapy (Safety Population)

Appendix 16.2.7.3 Adverse Event Preferred Term Classification (Safety Population)

16.2.8 Listings of Individual Laboratory Measurements and Other Safety Observations

Appendix 16.2.8.1.1 Clinical Laboratory Report - Serum Chemistry (Safety Population)

Appendix 16.2.8.1.2 Clinical Laboratory Report - Hematology (Safety Population)

Appendix 16.2.8.1.3 Clinical Laboratory Report - Urinalysis (Safety Population)

Appendix 16.2.8.1.4 Clinical Laboratory Report - Urine Drug Screening (Safety Population)

Appendix 16.2.8.1.5 Clinical Laboratory Report - Comments (Safety Population)

Appendix 16.2.8.2 Vital Signs (Safety Population)

Appendix 16.2.8.3 12-Lead Electrocardiogram (Safety Population)

10. TABLE AND FIGURE SHELLS

The following table shells provide a framework for the display of data from this study. The shells may change due to unforeseen circumstances. These shells may not be reflective of every aspect of this study, but are intended to show the general layout of the tables that will be presented and included in the final report. Unless otherwise noted, all tables will be presented in Times New Roman font size 8. These tables will be generated off of the Celerion ADaM Model 2.1 and ADaM Implementation Guide 1.1.

10.1 In-text Summary Tables Shells

In-text Table 10-1 will be in the following format:

Table 10-1 Summary of Disposition

	Randomized Treatment						
Disposition	**A**	**B**	**C**	**…**	**G**	**Placebo**	**Overall**
Enrolled	XX (1000%)	XX (100.0%)	XX (100.0%)	XX (100.0%)	XX (100.0%)	XX (100.0%)	XX (100.0%)
Completed	X (X.X%)	X (X.X%)	X (X.X%)	X (X.X%)	X (X.X%)	X (X.X%)	X (X.X%)
Discontinued Early	X (X.X%)	X (X.X%)	X (X.X%)	X (X.X%)	X (X.X%)	X (X.X%)	X (X.X%)
<Reason1>	X (X.X%)	X (X.X%)	X (X.X%)	X (X.X%)	X (X.X%)	X (X.X%)	X (X.X%)
<Reason2>	X (X.X%)	X (X.X%)	X (X.X%)	X (X.X%)	X (X.X%)	X (X.X%)	X (X.X%)

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >
<AE =Adverse event >
Subjects enrolled in the food effect cohort are summarized according to the treatment they were randomized to receive in Period 1.

Source: Table 14.1.1.1
Program: /CAXXXXX/sas_prg/stsas/intexttest/t_disp.sas DDMMMYYYY HH:MM

In-text Table 11-1 will be in the following format:

Table 11-1 Demographic Summary

		Treatment						
Trait	**Category/Statistics**	**A**	**B**	**C**	**…**	**G**	**Placebo**	**Overall**
Sex	Male	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	Female	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Race	Asian	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	Black or African American	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	White	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Ethnicity	Hispanic or Latino	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	Not Hispanic or Latino	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Age* (yrs)	n	XX	XX	XX	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX	XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Maximum	XX	XX	XX	XX	XX	XX	XX

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >
BMI = Body mass index
*Age is derived from birth date to date of first dose.
Subjects enrolled in the food effect cohort are summarized according to the treatment they are randomized to receive in Period 1.

Source: Table 14.1.1.2
Program: /CAXXXXX/sas_prg/stsas/intexttest/t_dem.sas DDMMMYYYY HH:MM

Programmer Notes: Height (cm), Weight(cm), and BMI (kg/m²) will be also summarized in the table above. Weight will be summarized at screening.

In-text Tables 11-2, 11-5, 11-7, 11-8, 11-10, 11-11, 11-12, 11-14, and 11-15 will be in the following format:

Table 11-2 Summary of Plasma SXC-2023 Pharmacokinetics Following Single Oral Doses of SXC-2023 Administered Under Fasted or Fed Conditions

Pharmacokinetic Parameters	Treatment <Y>	Treatment <X>
Param1 (units)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
Param2 (units)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
Param3 (units)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
Param4 (units)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
Treatment <Y>: <Label for Second Treatment> Treatment <X>: <Label for First Treatment> AUCs and Cmax values are presented as geometric mean and geometric CV%. Tmax values are presented as median (min, max). Other parameters are presented as arithmetic mean (± SD). Source: Tables <XXXX> and <YYYY>		

Notes for Generating the Actual Table:

Presentation of Data:

- The following plasma and RBC PK parameters (In-Text Tables 11-2, 11-5, 11-9, 11-12, 11-16, and 11-19) will be presented in the following order and with following units: AUC0-t (ng*hr/mL), AUC0-inf ng*hr/mL), Cmax (ng/mL), Tmax (hr), Kel (1/hr), t½ (hr), CL/F (L/hr), and Vz/F (L). CL/F and Vz/F will not be presented for NAC and p-toluic acid plasma and RBC PK tables (In-text Tables 11-9, 11-12, 11-16 and 11-19).
- The following urine PK parameters (In-Text Tables 11-8, 11-15, and 11-22) will be presented in the following order and with following units: Ae0-72 (mg), CLr (L/hr or mL/hr), and %Fe (%). %Fe will not be presented for NAC and p-toluic acid urine PK tables (In-text Tables 11-15 and 11-22).
- Summary statistics will be presented with same precision as defined in post-text shells.
- Internal template: ITPar1

Celerion Note: Per study design needs, the following changes are made to this table relative to Celerion's standard shell: 6 columns will be presented instead of 2. Column headers will be: '50 mg Fasted', '100 mg Fasted', '200 mg Fasted', '400 mg Fasted', '800 mg Fasted', and 'XX mg Fed'.

Program: /CAXXXXX/sas_prg/pksas/intext-pk-tables.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_intext_pkparam.sas DDMMMYYYY HH:MM

In-text Tables 11-3 and 11-6 will be in the following format:

Table 11-3 Summary of Statistical Comparisons of Plasma SXC-2023 Pharmacokinetic Parameters Following Single Oral Doses of SXC-2023 Administered Under Fed Versus Fasted Conditions

Parameter	Treatment <X> (Test)		Treatment <Y> (Reference)		GMR (%)	90% Confidence Interval	Intra subject CV%
	Geometric LSMs	n	Geometric LSMs	n			
param1 (units)	XXX.X	XX	XXX.X	XX	XX.XX	XX.XX - XX.XX	X.XX
param2 (units)	XXX.X	XX	XXX.X	XX	XX.XX	XX.XX - XX.XX	X.XX
param3 (units)	XXX.X	XX	XXX.X	XX	XX.XX	XX.XX - XX.XX	X.XX

Treatment <X>: <Label for Test Treatment>
Treatment <Y>: <Label for Reference Treatment>
Geometric least-squares means (LSMs) are calculated by exponentiating the LSMs derived from the ANOVA.
Geometric Mean Ratio (GMR) = 100*(test/reference)
Intra-subject CV% was calculated as 100 x square root(exp[MSE]-1), where MSE = Residual variance from ANOVA.
Source: Table XXXX

Notes for Generating the Actual Table:

Presentation of Data:

- The following PK parameters will be presented in the following order and with following units: AUC0-t (ng*hr/mL), AUC0-inf ng*hr/mL), and Cmax (ng/mL);
- n will be presented as an integer (with no decimal);
- All statistics will be presented with same precision as defined in post-text shells;
- The test treatment will be the fed condition and the reference treatment will be the fasted condition for the cohort selected for FE;
- Treatment Labels will be updated depending on the cohort selected for FE;
- Internal template: Table ITPStat1.

Celerion Note: Per study design needs, the following changes are made to this table relative to Celerion's standard shell: None.

Program: /CAXXXXX/sas_prg/pksas/intext-pk-tables.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_intext_pkparam.sas DDMMMYYYY HH:MM

In-text Tables 11-4, 11-9, and 11-13 will be in the following format:

Table 11-4 Dose Proportionality Analysis of Plasma SXC-2023 Pharmacokinetic Parameters Following Single Oral Doses of SXC-2023 Administered Under Fasted Conditions

Pharmacokinetic Parameters	Estimate of Slope (b)	Standard Error	95% Confidence Interval for Slope
Param1	X.XXXX	X.XXXX	X.XXXX - X.XXXX
Param2	X.XXXX	X.XXXX	X.XXXX - X.XXXX
Param3	X.XXXX	X.XXXX	X.XXXX - X.XXXX

Presentation of Data:

- Slope will be presented to 4 decimal places
- Standard error will be presented to 4 decimal places
- 95% CI will be presented to 4 decimal places
- Internal template: CPDProp1

Notes for Generating the Actual Table:

Programmers Note:
PK Parameters are AUC0-t (ng*hr/mL), AUC0-inf ng*hr/mL), and Cmax (ng/mL)
Biostat Note:
Please use the footnote below if it is power model:
Parameters were ln-transformed prior to analysis.
The following statistical model using PROC MIXED of SAS was used to test dose proportionality: Parameter = a * Dose^b which was equivalent to ln(Parameter) = ln(a) + b[ln(Dose)]
Dose proportionality is not rejected if the 95% CI for b contains 1.

Per study design needs, the following changes are made to this table relative to Celerion standard: None
Program: /CAXXXXX/sas_prg/pksas/doseprop-mixed.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_dosepropmixed.sas DDMMMYYYY HH:MM

In-text Table 12-1 will be in the following format:

Table 12-1 Treatment-Emergent Adverse Event Frequency by Treatment – Number of Subjects Reporting the Event (% of Subjects Dosed)

	Treatment							
Adverse Event*	**A**	**B**	**C**	**D**	**…**	**G**	**Placebo**	**Overall**
Number of Subjects Dosed	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Number of Subjects With TEAEs	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Number of Subjects Without TEAEs	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
System Organ Class 1	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Preferred Term 1	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Preferred Term 2	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
System Organ Class 2	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Preferred Term 1	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Preferred Term 2	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)

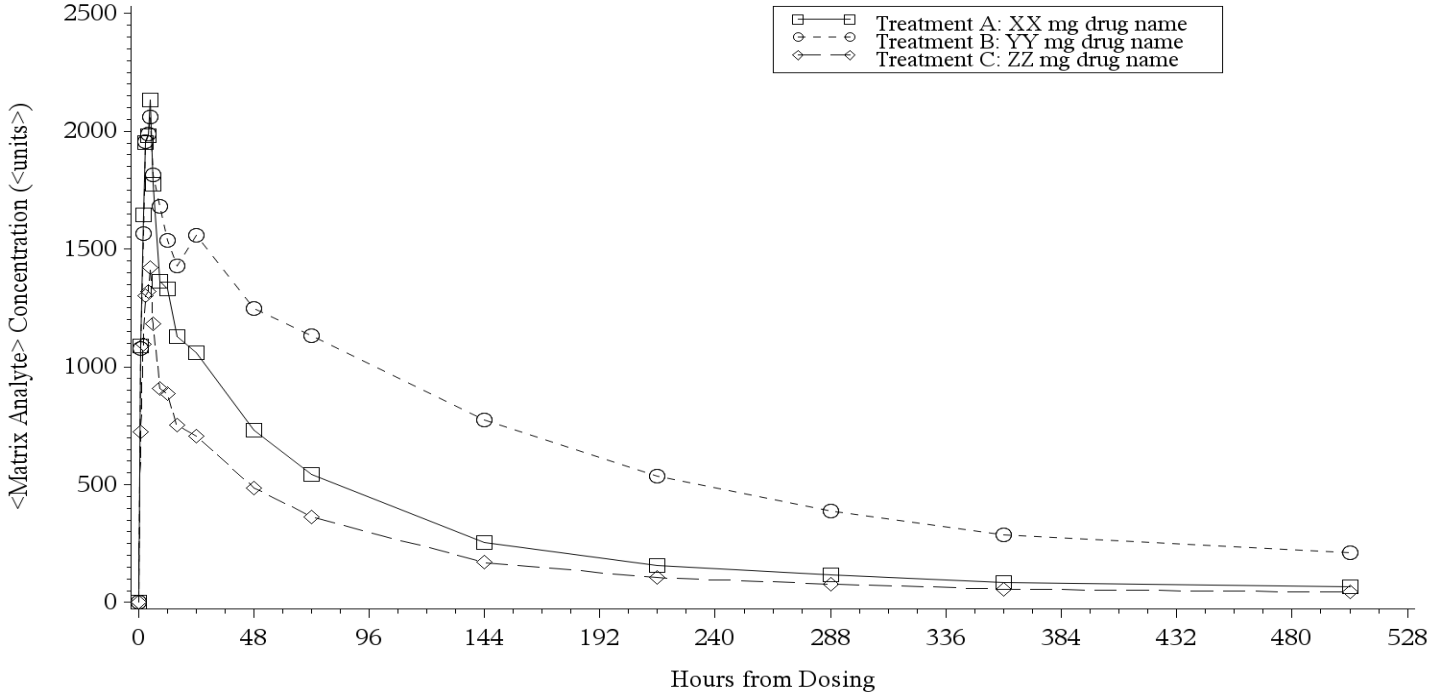
Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >
*Adverse events are coded using MedDRA® Version 20.0.
If a subject has 2 or more clinical adverse events, the subject is counted only once within a category. The same subject may appear in different categories.
TEAEs = Treatment-emergent adverse events

Source: Table 14.3.1.1.1
Program: /CAXXXXX/sas_prg/stsas/intexttest/t_ae.sas DDMMMYYYY HH:MM

10.2 Figures Shells

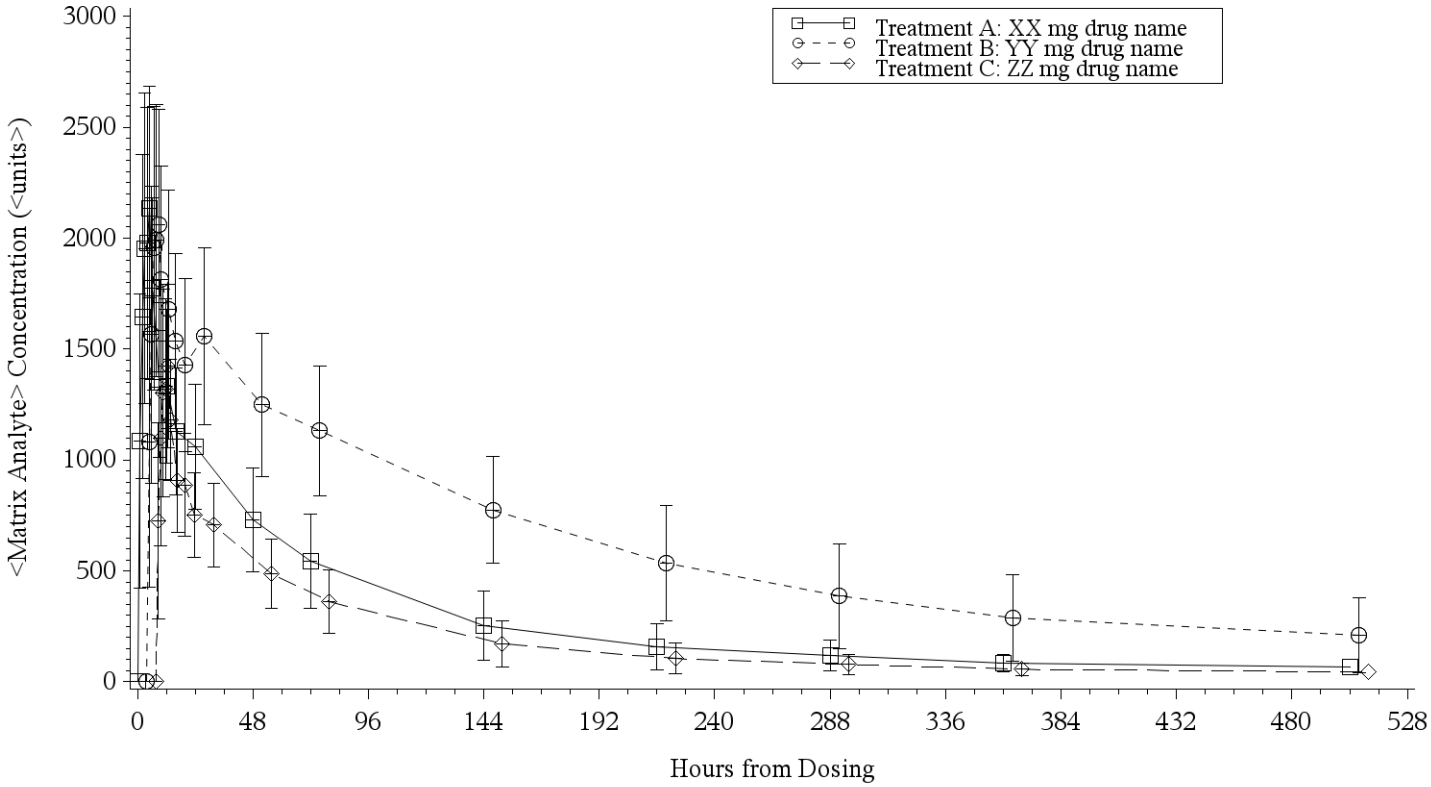
In-text Figures 11-1 through 11-7 and Figures 14.2.1.2.2, 14.2.1.4.2, 14.2.1.6.2, 14.2.1.6.4, 14.2.2.2.2, 14.2.2.4.2, 14.2.2.6.2, 14.2.3.2.2, 14.2.3.4.2, and 14.2.3.6.2 will be in the following format (Internal template: PFPConc2):

Figure 11-1 Arithmetic Mean Plasma SXC-2023 Concentration-Time Profiles Following Administration of Single Oral Doses of SXC-2023 Under Fasted or Fed Conditions



Figures 14.2.1.2.1, 14.2.1.4.1, 14.2.1.6.1, 14.2.1.6.3, 14.2.2.2.1, 14.2.2.4.1, 14.2.2.6.1, 14.2.3.2.1, 14.2.3.4.1, and 14.2.3.6.1 will be in the following format (Internal template: PFPConc1):

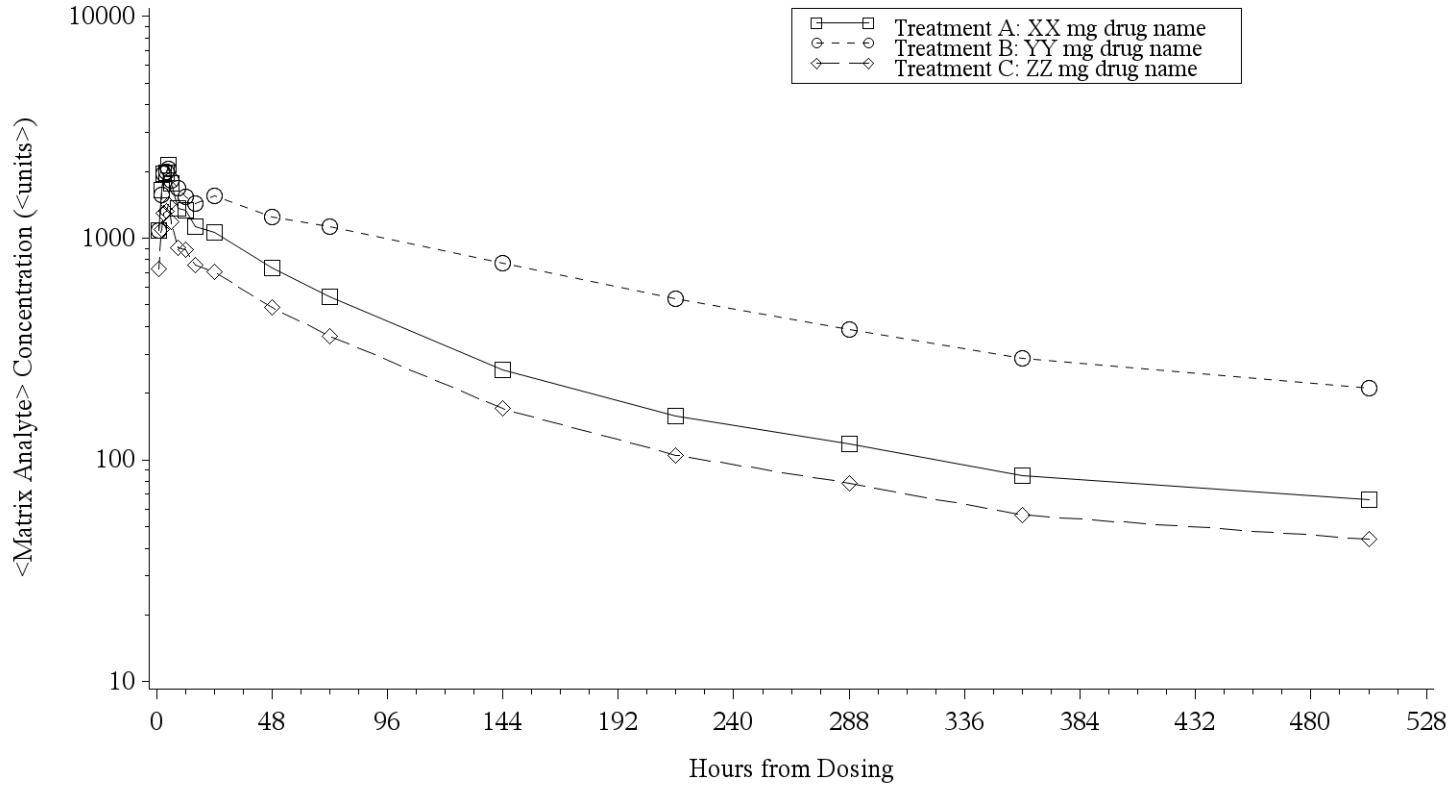
Figure 14.2.1.2.1 Mean (SD) Plasma SXC-2023 Concentration Versus Time Profiles Following Administration of Single Oral Doses of SXC-2023 (Linear Scale) (Treatments A-G - Pharmacokinetic Evaluable Population)



Treatments B and C are shifted to the right for ease of reading
Program: /CAXXXXX/sas_prg/pksas/adam_meangraph.sas DDMMMYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/meangraph.sas DDMMMYYY HH:MM

Figures 14.2.1.2.3, 14.2.1.4.3, 14.2.2.2.3, 14.2.2.4.3, 14.2.3.2.3, and 14.2.3.4.3 will be in the following format (Internal template: PFPConc3):

Figure 14.2.2.3 Mean Plasma SXC-2023 Concentration Versus Time Profiles Following Administration of Single Oral Doses of SXC 2023 (Semi-Log Scale) (Treatments A-G Pharmacokinetic Evaluable Population)



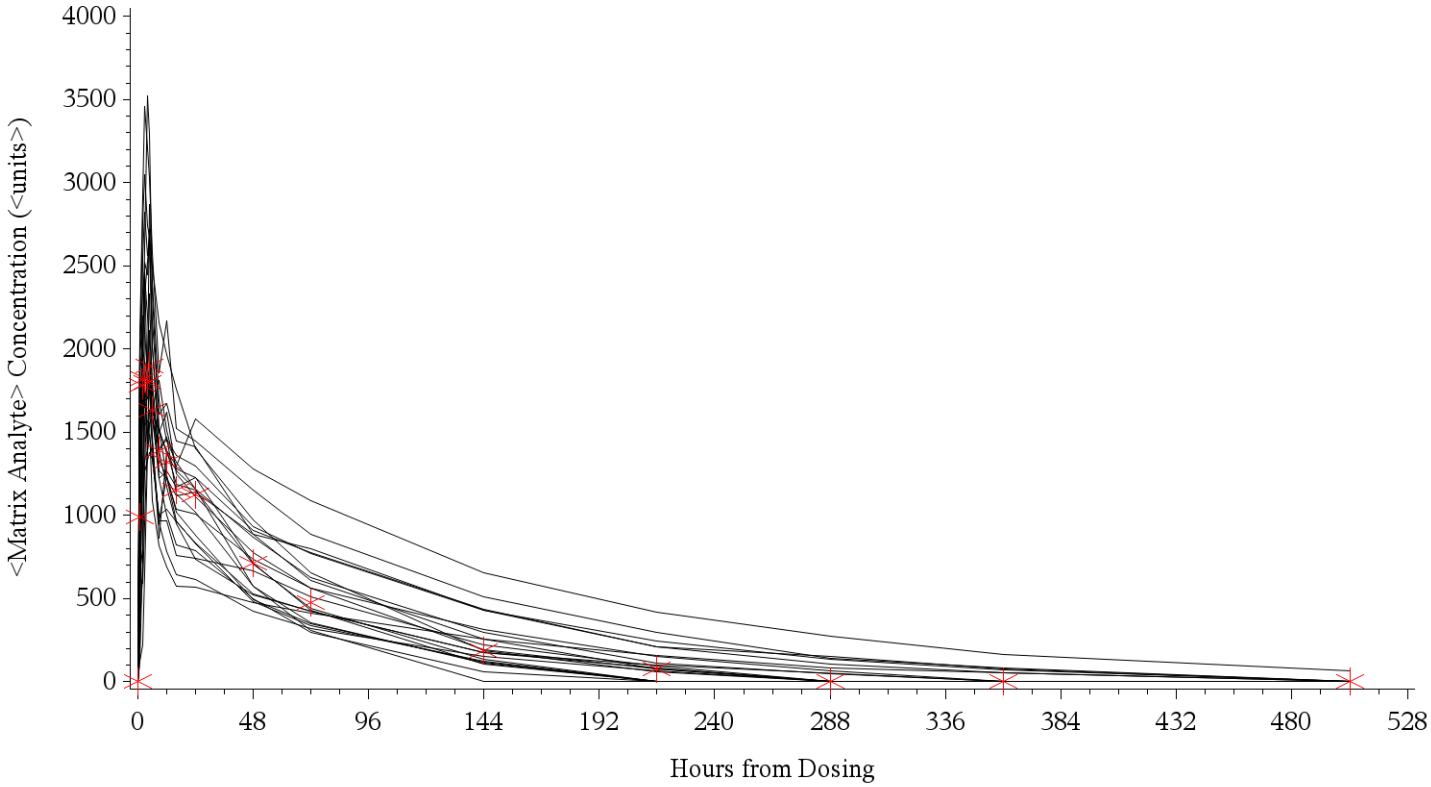
Notes for Generating the Actual Mean Figure:

- Legends will be: **'50 mg Fasted', '100 mg Fasted', '200 mg Fasted', '400 mg Fasted', '800 mg Fasted', and 'XX mg Fed';**
- Y axis label will be Plasma <Analyte> Concentration (ng/mL)for Figures 11-1, 11-4, and 11-6, Amount Excreted (mg) for Figures 11-2, 11-5, and 11-7, or Percent of Dose Excreted (%)for Figure 11-3;
- X axis label will be "Hours From Dosing".
- 3 treatments will be shifted to the right for ease of reading

Program: /CAXXXXX/sas_prg/pksas/meangraph.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_meangraph.sas DDMMMYYYY HH:MM

Figures 14.2.1.2.4 through 14.2.1.2.10, 14.2.1.4.4 through 14.2.1.4.8, 14.2.2.2.4 through 14.2.2.2.10, 14.2.2.4.4 through 14.2.2.4.8, 14.2.3.2.4 through 14.2.3.2.10, and 14.2.3.4.4 through 14.2.3.4.8 will be in the following format (Internal template: PFPConc6):

Figure 14.2.2.1 Superimposed Plasma SXC-2023 Concentration Versus Time Profiles Following Administration a Single Oral Dose of 50 mg SXC-2023 Administered Under Fasted Conditions (Treatment A) (Linear Scale)



Individual lines in the plot are individual subject values and the red stars are the median values.
Program: /CAXXXXX/sas_prg/pksas/adam_spaggraph.sas DDMMMYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/spaggraph.sas DDMMMYYY HH:MM

Notes for Generating the Actual Spaghetti Plots Figure:

- All profiles will be presented with the same line type (with or without color)
- Y axis label will be <Matrix> <Analyte> Concentration (<units>)
- X axis label will be "Hours From Dosing"
- Reference line will not be included for the LOQ
- Mean or median values will not be presented, the descriptive footnote will be removed and no median or mean (red stars) will be presented – only individual lines representing subject values will be shown

Program: /CAXXXXX/sas_prg/pksas/spaggraph.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_spaggraph.sas DDMMMYYYY HH:MM

10.3 Section 14 Summary Tables Shells

Table 14.1.1.1 will be in the following format:

Part 1 of X

Table 14.1.1.1 Summary of Disposition (Safety Population)

	Randomized Treatment						
Category	A	B	C	…	G	Placebo	Overall
Enrolled	XX (100%)	XX (100%)	XX (100%)	XX (100%)	XX (100%)	XX (100%)	XX (100%)
Completed	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Discontinued Early	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
<Reason1>	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
<Reason2>	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >
<AE = Adverse event>
Subjects included in the food effect cohort are summarized according to the treatment they were randomized to receive in Period 1.

Program: /CAXXXXX/sas_prg/stsas/tab programname.sas DDMMMYYYY HH:MM

Table 14.1.1.2 will be in the following format:

Table 14.1.1.2 Demographic Summary (Safety Population)

		Treatment						
Trait		A	B	C	…	G	Placebo	Overall
Sex	Male	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Female	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Race	Asian	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Black or African American	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	White	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Ethnicity	Hispanic or Latino	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	Not Hispanic or Latino Latino	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Age* (yrs)	n	X	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX	XX

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >
* Age is derived from birth date to date of first dose.
Subjects included in the food effect cohort are summarized according to the treatment they were randomized to receive in Period 1.
BMI = Body mass index

Programmer Notes: Weight (kg), Height (cm) and BMI (kg/m^2) will also be summarized in the table above. Weight will be summarized at screening.

Program: /CAXXXXX/sas_prg/stsas/tab programname.sas DDMMMYYYY HH:MM

Concentration tables: Tables 14.2.1.1.1 through 14.2.1.1.8, Tables 14.2.1.3.1 through 14.2.1.3.6, Tables 14.2.2.1.1 through 14.2.2.1.8, Tables 14.2.2.3.1 through 14.2.2.3.6, Tables 14.2.3.1.1 through 14.2.3.1.8, and Tables 14.2.3.3.1 through 14.2.3.3.6 will be in the following format:

Table 14.2.1.1.1 Plasma SXC-2023 Concentrations ng/mL) Following a Single Oral Dose of 50 mg SXC-2023 Administered Under Fasted Conditions (Cohort 1 - Treatment A) (Pharmacokinetic Population)

Subject Number	Treatment Sequence	Study Period	Sample Times (hr) Predose	XX	XX	XX	XX	XX	XX	XX	XX
X	XXX	X	BLQ	XX	XX	XX	XX	XX	XX	XX	XX
X	XXX	X	BLQ	XX	XX	XX	XX	XX	XX	XX	XX
X	XXX	X	BLQ	XX	XX	XX	XX	XX	XX	XX	XX
n			XX	XX	XX	XX	XX	XX	XX	XX	XX
Mean			XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SD			XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
CV%			.	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SEM			XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Minimum			XX	XX	XX	XX	XX	XX	XX	XX	XX
Median			XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Maximum			XX	XX	XX	XX	XX	XX	XX	XX	XX

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of XX are treated as 0 before the first quantifiable concentration and as missing elsewhere.
. = Value missing or not reportable.

Notes for Generating the Actual Table:

Presentation of Data:
Concentrations will be presented to same precision as in bio data.
Summary statistics presentation with respect to the precision of the bio data: n = integer; Mean and Median +1; SD and SEM +2, Min and Max +0, CV% to 1 decimal
Internal template: Table CPConc1

Programmer Note:
PK Time points are from Protocol: i.e. predose and 0.083, 0.167, 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, 16, 24, 48, and 72 hours postdose.

Per study design needs, the following changes are made to this table relative to Celerion standard: Columns 'Treatment Sequence' and 'Study Period' will be removed except for the food effect cohort where the 'Study Period' column will be presented.

```
Program:  /CAXXXXX/sas_prg/pksas/pk-conc-tables.sas         DDMMMYYYY  HH:MM
Program:  /CAXXXXX/sas_prg/pksas/pk-conc-tables-sig.sas     DDMMMYYYY  HH:MM
Program:  /CAXXXXX/sas_prg/pksas/adam_conc.sas          DDMMMYYYY  HH:MM
```

PK parameter tables: Tables 14.2.1.1.9 through 14.2.1.1.15, Tables 14.2.1.3.7 through 14.2.1.3.11, Tables 14.2.2.1.9 through 14.2.2.1.15, Tables 14.2.2.3.7 through 14.2.2.3.11, Tables 14.2.3.1.9 through 14.2.3.1.15, and Tables 14.2.3.3.7 through 14.2.3.3.11 will be in the following format:

Table 14.2.1.1.9 Plasma SXC-2023 Pharmacokinetic Parameters Following a Single Oral Dose of 50 mg SXC-2023 Administered Under Fasted Conditions (Cohort 1 - Treatment A) (Pharmacokinetic Evaluable Population)

			Parameters					
Subject Number	Treatment Sequence	Study Period	param1 (units)	param2 (units)	param3 (units)	param4 (units)	param5 (units)	param6 (units)
X	XXX	X	XXX	X.XX	XXX	XXX	XX.X	X.XXX
X	XXX	X	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
X	XXX	X	XXX	X.XX	XXX	XXX	XX.X	X.XXX
X	XXX	X	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
X	XXX	X	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
X	XXX	X	X.XX	X.XX	XXX	XXX	XX.X	X.XXX
X	XXX	X	XXX	X.XX	XXX	XXX	XX.X	X.XXX
n			XX	XX	XX	XX	XX	XX
Mean			XXX.X	X.XXX	XXX.X	XXX.X	XX.XX	X.XXXX
SD			XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
CV%			XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SEM			XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Minimum			XX.X	X.XX	XXX	XXX	XX.X	X.XXX
Median			XX.XX	X.XXX	XXX.X	XXX.X	XX.XX	X.XXXX
Maximum			XXX	X.XX	XXX	XXX	XX.X	X.XXX
Geom Mean			XXX.X	X.XXX	XXX.X	XXX.X	XX.XX	X.XXXX
Geom CV%			XX.X	XX.X	XX.X	XX.X	XX.X	XX.X

. = Value missing or not reportable.

Notes for Generating the Actual Table:

Presentation of Data:

- PK Parameters will be presented in the following order and with following units: AUC0-t (ng*hr/mL), AUC0-inf ng*hr/mL), Cmax (ng/mL), Tmax (hr), Kel (1/hr), t½ (hr), CL/F (L/hr), and Vz/F (L). CL/F and Vz/F will not be presented for plasma and RBC NAC and p-toluic

acid PK tables (Tables 14.2.2.1.8 through 14.2.2.1.13, Tables 14.2.2.3.6 through 14.2.2.3.9, Tables 14.2.3.1.8 through 14.2.3.1.13, and Tables 14.2.3.3.6 through 14.2.3.3.9);

- n will be presented as an integer (with no decimal);
- Parameter values for Cmax will be presented with the precision of the bio data,
- Parameter values for AUCs will be presented with 3-4 significant figures (to be determined by the PKist once bio data are received),
- Parameter values for Kel,Vz/F, and CL/F will be presented with 3 significant figures,
- Values for time-based parameters (i.e. Tmax and t1/2) will be presented with 2 decimals,
- Summary statistics for all parameters will be presented as: Mean, Median, and Geom Mean +1; SD and SEM +2, Min and Max +0;
- CV% and Geom CV% for all parameters will be presented with 1 decimal;
- Internal template: Table CPPar1.

Per study design needs, the following changes are made to this table relative to Celerion standard: Columns 'Treatment Sequence' and 'Study Period' will be removed except for the food effect cohort where the 'Study Period' column will be presented.>

Program: /CAXXXXX/sas_prg/pksas/pk-tables.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_pkparam.sas DDMMMYYYY HH:MM

Kel Interval tables: Tables 14.2.1.1.16, 14.2.1.3.12, 14.2.2.1.16, 14.2.2.3.12, 14.2.3.1.16, and 14.2.3.3.12 will be in the following format:

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Table 14.2.1.1.16 Intervals (Hours) Used for Determination of Plasma SXC 2023 Kel Values (Pharmacokinetic Population)

Subject Number	Treatment	Interval	R2	n
X	X	XX.X - XX.X	X.XXX	X
X	X	XX.X - XX.X	X.XXX	X
X	X	XX.X - XX.X	X.XXX	X
X	X	XX.X - XX.X	X.XXX	X
X	X	XX.X - XX.X	X.XXX	X
X	X	XX.X - XX.X	X.XXX	X

Treatment <X>: <Label for First Treatment>
Treatment <Y>: <Label for Second Treatment>
R2 = Coefficient of determination
n = Number of points used in Kel calculation
. = Kel value not reportable.

Notes for Generating the Actual Table:

Presentation of Data:

- Interval start and stop times will be presented to 1 decimal or 3 sig figures min;
- R2 will be presented to 3 decimals;
- n will be presented as an integer (with no decimal)
- Internal template: CPKel2

Per study design needs, the following changes are made to this table relative to Celerion standard: 6 treatments will be presented

Program: /CAXXXXX/sas_prg/pksas/kel-tables-parallel.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_kel.sas DDMMMYYYY HH:MM

Statistical comparison (ANOVA) tables: Tables 14.2.1.1.17 and 14.2.1.3.13 will be in the following format:

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Table 14.2.1.1.17 Statistical Comparisons of Plasma SXC-2023 Pharmacokinetic Parameters: Fed Versus Fasted Conditions (Cohort X - Pharmacokinetic Evaluable Population)

		Treatment ------- Geometric LSMs -------				Geometric Mean	90 %	Intra-subject
Parameter	(unit)	<X>	(n)	<Y>	(n)	Ratio	Confidence Intervals	CV%
Param1	(unit)	X.XX	(n)	X.XX	(n)	X.XX	XX.XX - XXX.XX	X.XX
Param2	(unit)	X.XX	(n)	X.XX	(n)	X.XX	XX.XX - XXX.XX	X.XX
Param3	(unit)	X.XX	(n)	X.XX	(n)	X.XX	XX.XX - XXX.XX	X.XX

Treatment <Y>: <Label for Second Treatment> (test)
Treatment <X>: <Label for First Treatment> (reference)
Parameters were ln-transformed prior to analysis.
Geometric least-squares means (LSMs) are calculated by exponentiating the LSMs from ANOVA.
Geometric Mean Ratio = 100*(test/reference)
Intra-subject CV% = 100 x (square root (exp[MSE]-1), where MSE = Residual variance from ANOVA.

Notes for Generating the Actual Table:

Presentation of Data:

- PK parameters will be: AUC0-t (ng*hr/mL), AUC0-inf ng*hr/mL), and Cmax (ng/mL);
- Geometric LSMs be presented to same precision as Mean in the PK parameter table CPPar1;
- Geometric Mean Ratio, 90% CI and intra-subject CV% will be presented to 2 decimal places;
- Internal template: CPStat1

Per study design needs, the following changes are made to this table relative to Celerion standard: None

Program: /CAXXXXX/sas_prg/pksas/stats-tables-mixed.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_statsmixed.sas DDMMMYYYY HH:MM

Dose proportionality analysis tables: Tables 14.2.1.1.18, 14.2.2.1.17, and 14.2.3.1.17 will be in the following format:

Table 14.2.1.1.18. Dose Proportionality Analysis of Plasma SXC-2023 Pharmacokinetic Parameters Under Fasted Conditions (Pharmacokinetic Evaluable Population)

Pharmacokinetic Parameters	Estimate of Slope (b)	Standard Error	95% Confidence Interval for Slope
Param1	X.XXXX	X.XXXX	X.XXXX - X.XXXX
Param2	X.XXXX	X.XXXX	X.XXXX - X.XXXX
Param3	X.XXXX	X.XXXX	X.XXXX - X.XXXX

Presentation of Data:

- Slope will be presented to 4 decimal places
- Standard error will be presented to 4 decimal places
- 95% CI will be presented to 4 decimal places
- Internal template: CPDProp1

Notes for Generating the Actual Table:

Programmers Note:
PK Parameters are AUC0-t (ng*hr/mL), AUC0-inf ng*hr/mL), and Cmax (ng/mL)
Biostat Note:
Please use the footnote below if it is power model:
Parameters were ln-transformed prior to analysis.
The following statistical model using PROC MIXED of SAS was used to test dose proportionality: Parameter = a * Dose^b which was equivalent to ln(Parameter) = ln(a) + b[ln(Dose)]
Dose proportionality is not rejected if the 95% CI for b contains 1.

Per study design needs, the following changes are made to this table relative to Celerion standard: None

Program: /CAXXXXX/sas_prg/pksas/doseprop-mixed.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_dosepropmixed.sas DDMMMYYYY HH:MM

Urine excretion tables: Tables 14.2.1.5.1 through 14.2.1.5.8, Tables 14.2.2.5.1 through 14.2.2.5.8, and Tables 14.2.3.5.1 through 14.2.3.5.8 will be in the following format:

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Table 14.2.1.5.1 Urinary Excretion of SXC-2023 Following a Single Oral Dose of 50 mg SXC-2023 Administered Under Fasted Conditions (Cohort 1 - Treatment A) (Pharmacokinetic Population)

			Parameters								
			Predose		X - X Hours						
Subject Number	Treatment Sequence	Study Period	Conc (units)	Vol (units)	Conc (units)	Vol (units)	Ae (units)	CumAe (units)	%Dose (%)	Cum%Dose (%)	CLr (units)
X	XXX	X	X.XX	X.XX	XX.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
X	XXX	X	X.XX	X.XX	XX.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
X	XXX	X	X.XX	X.XX	XX.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
n			X	X	X	X	X	X	X	X	X
Mean			X.XXX	X.XXX	XX.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
SD			X.XXXX	X.XXXX	XX.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX
CV%			X.X	X.X	XX.X	X.X	X.X	X.X	X.X	X.X	X.X
SEM			X.XXXX	X.XXXX	XX.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX
Minimum			X.XX	X.XX	XX.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
Median			X.XXX	X.XXX	XX.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
Maximum			X.XX	X.XX	XX.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
Geom Mean			X.XXX	X.XXX	XX.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
Geom CV%			X.X	X.X	XX.X	X.X	X.X	X.X	X.X	X.X	X.X

. = Value missing or not reportable.

Notes for Generating the Actual Table:

Presentation of Data:

- Concentrations and amounts will be presented to same precision as the bio concentration data. Volume will be presented to same precision as on the CRF. Cum%Dose will be presented to 2 decimal places. Clr and all other parameters will be presented to 3 significant figures.
- Summary statistics presentation: n = integer; Mean Median and Geom Mean +1; SD and SEM +2, Min/Max +0, CV% and Geom CV% to 1 decimal.

Programmers Note:
Intervals are predose, and 0-1, 1-2, 2-4, 4-8, 8-12, 12-24, 24-48, and 48-72 hours postdose, and 0-72 (Overall).
PK Parameters for each postdose interval are: Conc, Vol, Ae, CumAe, %Dose, Cum%Dose; predose: Conc, Vol, Overall: CumAe, Cum%Dose, CLr

Internal template: Appendix Table C(A)UPar3

Per study design needs, the following changes are made to this table relative to Celerion standard: Columns 'Treatment Sequence' and 'Study Period' will be removed except for the food effect cohort where the 'Study Period' column will be presented.

Notes for preparation of standard programs (to be deleted after standard programs are updated):
Update standard program name to include C(A)UPar3 shell name

Program: DM_PX:[HLXXXXX.PKSAS]URINE-CONC-TABLES.SAS DDMMMYYYY HH:MM

Table 14.3.1.1 will be in the following format:

Table 14.3.1.1 Treatment-Emergent Adverse Event Frequency by Treatment – Number of Subjects Reporting the Event (% of Subjects Dosed) (Safety Population)

	Treatment							
Adverse Event*	A	B	C	D	…	G	Placebo	Overall
Number of Subjects Dosed	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX(XXX%)
Number of Subjects With TEAEs	X (X%)	X (XX%)	X (XX%)	X (XX%)	X (XXX%)	X (XXX%)	X (XXX%)	X(XXX%)
Number of Subjects Without TEAEs	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX(XXX%)
Eye disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X(X%)
Vision blurred	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X(X%)
Gastrointestinal disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X(X%)
Dyspepsia	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X(X%)
Nausea	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X(X%)
Musculoskeletal and connective tissue disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X(X%)
Back pain	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X(X%)
Muscle cramps	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X(X%)
Musculoskeletal pain	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X(X%)

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >
* Adverse events are coded using MedDRA Version 20.0.
If a subject has 2 or more clinical adverse events, the subject is counted only once within a category. The same subject may appear in different categories.
TEAEs = Treatment-emergent adverse events

Programmer Notes: Should all treatments not be able to fit on the same page, then present the following treatments on a separate page: E, F, G, Placebo, Overall.

Program: /CAXXXXX/sas_prg/stsas/tab programname.sas DDMMMYYYY HH:MM

Tables 14.3.1.2 will be in the following format:

Table 14.3.1.2 Treatment-Emergent Adverse Event Frequency by Treatment –Number of Adverse Events (% of Total Adverse Events) (Safety Population)

	Treatment							
Adverse Event*	A	B	C	D	…	G	Placebo	Overall
Number of TEAEs	X (100%)	X (100%)	X (100%)	X (100%)	X (100%)	X (100%)	X (100%)	X(100%)
Eye disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X(X%)
Vision blurred	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X(X%)
Gastrointestinal disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X(X%)
Dyspepsia	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X(X%)
Nausea	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X(X%)
Musculoskeletal and connective tissue disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X(X%)
Back pain	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X(X%)
Muscle cramps	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X(X%)
Musculoskeletal pain	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X(X%)

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >
* Adverse events are coded using MedDRA Version 20.0.
TEAEs = Treatment-emergent adverse events

Programmer Notes: Should all treatments not be able to fit on the same page, then present the following treatments on a separate page: E, F, G, Placebo, Overall.

Program: /CAXXXXX/sas_prg/stsas/tab programname.sas DDMMMYYYY HH:MM

Table 14.3.1.3 will be in the following format:

Table 14.3.1.3 Treatment-Emergent Adverse Event Frequency by Treatment, Severity, and Relationship to Study Drug - Number of Adverse Events (Safety Population)

Adverse Event*	Treatment	Number of Subjects With TEAEs	Number of TEAEs	Severity Grade**				Relationship to Study Drug				
				1	2	3	4	Unrelated	Unlikely	Possibly	Probably	Likely
Abdominal pain	A	X	X	X	X	X	X	X	X	X	X	X
Constipation	F	X	X	X	X	X	X	X	X	X	X	X
Dry throat	B	X	X	X	X	X	X	X	X	X	X	X
Dysmenorrhoea	C	X	X	X	X	X	X	X	X	X	X	X
Dyspepsia	B	X	X	X	X	X	X	X	X	X	X	X
Headache	A	X	X	X	X	X	X	X	X	X	X	X
	E	X	X	X	X	X	X	X	X	X	X	X
Myalgia	G	X	X	X	X	X	X	X	X	X	X	X
Nasal congestion	C	X	X	X	X	X	X	X	X	X	X	X
Skin laceration	F	X	X	X	X	X	X	X	X	X	X	X
Treatment A		X	X	X	X	X	X	X	X	X	X	X
Treatment B		X	X	X	X	X	X	X	X	X	X	X
Treatment C		X	X	X	X	X	X	X	X	X	X	X
Treatment D		X	X	X	X	X	X	X	X	X	X	X
Treatment E		X	X	X	X	X	X	X	X	X	X	X
Treatment F		X	X	X	X	X	X	X	X	X	X	X
Treatment F		X	X	X	X	X	X	X	X	X	X	X
Treatment Placebo		X	X	X	X	X	X	X	X	X	X	X
Overall		X	X	X	X	X	X	X	X	X	X	X

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >
* Adverse events are coded using MedDRA Version 20.0.
** Severity Grade: 1 = Mild, 2 = Moderate, 3 = Severe or medically significant but not immediately life-threatening, 4 = Life-threatening consequences

```
TEAEs = Treatment-emergent adverse events

Program:  /CAXXXXX/sas_prg/stsas/tab programname.sas  DDMMMYYYY HH:MM
```

Table 14.3.2.1 will be in the following format:

Table 14.3.2.1 Serious Adverse Events (Safety Population)

Programmer Note: Will match 16.2.7 or contain the following statement: "There were no serious adverse events recorded during the study."

Program: /AAXXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMMYYYY HH:MM

Tables 14.3.4.1 to 14.3.4.3 will have the following format:

Table 14.3.4.1 Out-of-Range Values and Recheck Results - Serum Chemistry (Safety Population)

Cohort	Subject Number	Age#/ Sex	Study Period	Treatment	Day	Hour	Date	Time	Parameter1 <Range> (Unit)	Parameter2 <Range> (Unit)	Parameter3 <Range> (Unit)	Parameter4 <Range> (Unit)	Parameter5 <Range> (Unit)
X	X	XX/X	Screen		.	.	DDMMMYYYY	HH:MM:SS	XX HN				XX HN
			1	X	-X	-XX.XX	DDMMMYYYY	HH:MM:SS	XX LY-	XX LN		XX LYR+	
			Recheck				DDMMMYYYY	HH:MM:SS				XX	

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >
# Age is calculated at the time of first dosing. F = Female, M = Male
H = Above reference range, L = Below reference range
Computer: N = Not clinically significant, Y = Clinically significant
PI Interpretation: - = Not clinically significant, R = Recheck requested, ^ = Will be retested later, + = Clinically significant

Programmer Notes: Replace Parameter1, 2 etc. with actual lab tests in the study. Sort unscheduled assessment and early termination records chronologically with other scheduled assessments and rechecks. Recheck should be sorted with the scheduled time point the recheck is for.

Clinically significant lab values generally will be captured as AEs, some of which the PI may indicate in Appendix 16.2.8.1.6 lab comments (as per GPG.03.0028 sections 2.9 and 2.10). Derive an additional flag for PI flag -/+ based on comments (i.e. NCS/CS). Present this derived 4th column in all tables, and list only PI-determined out-of-range clinically significant lab values in Table 14.3.4.5.

Program: /CAXXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMMYYYY HH:MM

Page 1 of X

Table 14.3.4.4 Clinically Significant Values and Recheck Results (Safety Population)

Cohort	Subject Number	Age#/ Sex	Study Period	Treatment	Day	Hour	Date	Time	Department	Test	Result		Reference Range	Unit
X	X	XX/X	X	X	1	-X.XX	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX		X - X	mg/dL
					2	XX.XX	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX	HYR+	X - X	mg/dL
					3	XX.XX	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX	HY+	X - X	mg/dL
					4	XX.XX	DDMMMYYYY	HH:MM:SS	Serum Chemistry	Cholesterol	XXX	HN	X - X	mg/dL

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >
# Age is calculated at the time of first dosing. F = Female, M = Male
H = Above reference range
Computer: Y = Clinically significant
PI Interpretation: R = Recheck requested, + = Clinically significant

Programmer Notes: All time points for a subject/test with at least one value deemed as CS by the PI will be presented in this table. If there were no CS values as deemed by PI (i.e., no "CS" or "Clinically Significant" in the PI comment field in the laboratory dataset), then this table will contain the following statement: "There were no laboratory values documented as clinically significant by the PI in the study."

Program: /CAXXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMMYYYY HH:MM

Tables 14.3.5.1.1, 14.3.5.1.2, 14.3.5.2.1, 14.3.5.2.2, 14.3.5.3.1, and 14.3.5.3.2 will be in the following format:

Table 14.3.5.1.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

Laboratory Test (unit)	Reference Range	Time Point	Statistic	Treatment A	B	C	D	…	G	Placebo
Testname (unit)	< - >	Baseline*	n	X	X	X	X	X	X	X
			Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X
			SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			Minimum	XX	XX	XX	XX	XX	XX	XX
			Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X
			Maximum	XX	XX	XX	XX	XX	XX	XX
		Day 2	n	X	X	X	X	X	X	X
			Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X
			SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			Minimum	XX	XX	XX	XX	XX	XX	XX
			Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X
			Maximum	XX	XX	XX	XX	XX	XX	XX
		Day 4	n	X	X	X	X	X	X	X
			Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X
			SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
			Minimum	XX	XX	XX	XX	XX	XX	XX
			Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X
			Maximum	XX	XX	XX	XX	XX	XX	XX

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >
* Baseline is the last non-missing assessment prior to dosing (Day -1 Check-in), including rechecks and unscheduled assessments.
# = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.

Programmer Notes: Similar for all time points and laboratory tests. For the change from baseline tables 14.3.5.1.2, 14.3.5.2.2, and 14.3.5.3.2, please remove the baseline time point, keep the baseline definition footnote and change the 'Treatment' header to 'Change From Baseline'.

Program: /CAXXXXX/sas_prg/stsas/tab programname.sas DDMMMYYYY HH:MM

Tables 14.3.5.1.3, 14.3.5.2.3, and 14.3.5.3.3 will be in the following format:

Table 14.3.5.1.3 Clinical Laboratory Shift From Baseline - Serum Chemistry (Safety Population)

			Baseline* L			Baseline* N			Baseline* H		
			Postdose			Postdose			Postdose		
Laboratory Test (unit)	Treatment	Time Point	L	N	H	L	N	H	L	N	H
Testname (unit)	A	Day 2	X	XX	X	X	XX	X	X	XX	X
		Day 4	X	XX	X	X	XX	X	X	XX	X
	B	Day 2	X	XX	X	X	XX	X	X	XX	X
		Day 4	X	XX	X	X	XX	X	X	XX	X

< - >

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >
* Baseline is the last non-missing assessment prior to dosing (Day -1 Check-in), including rechecks and unscheduled assessments.
N = Within reference range, L = Below reference range, H = Above reference range

Programmer Notes: Similar for all time points and laboratory tests. For urinalysis, the following footnote is used since the categories of N and O will be used instead of L, N, H: N = Within reference range, O = Outside reference range

Program: /CAXXXXX/sas_prg/stsas/tab programame.sas DDMMMYYYY HH:MM

Tables 14.3.5.4.1 and 14.3.5.4.2 will be in the following format:

Table 14.3.5.4.1 Vital Sign Summary (Safety Population)

Vital Sign (unit)	Time Point	Statistic	Treatment A	B	C	D	…	G	Placebo
Testname (unit)	Baseline*	n	X	X	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX	XX	XX
	Day 1 Hour 2	n	X	X	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX	XX	XX
	Day 1 Hour 4	n	X	X	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX	XX	XX

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >
* Baseline is the last non-missing assessment prior to dosing (Predose), including rechecks and unscheduled assessments.
Programmer Notes: Similar for all time points and vital signs. The following time points will be summarized: Baseline, Day 1 Hour 2, Day 1 Hour 4, Day 2, Day 3, Day 4, and Follow-Up. For the change from baseline table 14.3.5.4.2, please remove the baseline time point, keep the baseline definition footnote and change the 'Treatment' header to 'Change From Baseline'.

Program: /CAXXXXX/sas_prg/stsas/tab programname.sas DDMMMYYYY HH:MM

Tables 14.3.5.5.1 and 14.3.5.5.2 will be in the following format:

Table 14.3.5.5.1 12-Lead Electrocardiogram Summary (Safety Population)

Parameter (unit)	Time Point	Statistic	Treatment A	B	C	D	…	G	Placebo
Testname (unit)	Baseline*	n	X	X	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX	XX	XX
	Day 1 Hour 2	n	X	X	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX	XX	XX
	Day 2	n	X	X	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX	XX	XX

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >
* Baseline is the last non-missing assessment prior to dosing (Predose), including rechecks and unscheduled assessments.
Programmer Notes: Similar for all time points and ECG parameters. The following time points will be summarized: Baseline, Day 1 Hour 2, Day 2, and Day 4. For the change from baseline table 14.3.5.5.2, please remove the baseline time point, keep the baseline definition footnote and change the 'Treatment' header to 'Change From Baseline'.

Program: /CAXXXXX/sas_prg/stsas/tab programname.sas DDMMMYYYY HH:MM

Table 14.3.5.5.3 will be in the following format:

Table 14.3.5.5.3 12-Lead Electrocardiogram Shift From Baseline (Safety Population)

		Baseline* N			Baseline* ANCS			Baseline* ACS		
		Postdose			Postdose			Postdose		
Treatment	Time Point	N	ANCS	ACS	N	ANCS	ACS	N	ANCS	ACS
A	Day 1, Hour 2	X	X	X	X	X	X	X	X	X
	Day 2	X	X	X	X	X	X	X	X	X

<similar for all time points and treatments>

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >
* Baseline is the last non-missing assessment prior to dosing (Predose), including rechecks and unscheduled assessments.
N = Normal, ANCS = Abnormal, Not Clinically Significant, ACS = Abnormal, Clinically Significant

Program: /CAXXXXX/sas_prg/stsas/tab programname.sas DDMMMYYYY HH:MM

11. LISTING SHELLS

The following listing shells provide a framework for the display of data from this study. The shells may change due to unforeseen circumstances. These shells may not be reflective of every aspect of this study, but are intended to show the general layout of the listings that will be presented and included in the final report. These listings will be generated off of the Celerion SDTM Tabulation Model 1.4 mapped in accordance with SDTM Implementation Guide 3.2. All listings will be presented in Courier New font size 9.

Appendix 16.1.10.1 Clinical Laboratory Reference Ranges

Laboratory Group	Test Name	Sex	Age Category	Reference Range	Units
Serum Chemistry	Test Name	XXXXXX	XX	XX – XX	units
	Test Name	XXXXXX	XX	XX – XX	units
	Test Name	XXXXXX	XX	XX – XX	units
	Test Name	XXXXXX	XX	XX – XX	units
	Test Name	XXXXXX	XX	XX – XX	units
	Test Name	XXXXXX	XX	XX – XX	units
Hematology	Test Name	XXXXXX	XX	XX – XX	units
	Test Name	XXXXXX	XX	XX – XX	units
	Test Name	XXXXXX	XX	XX – XX	units
	Test Name	XXXXXX	XX	XX – XX	units
	Test Name	XXXXXX	XX	XX – XX	units

<similar for remaining Laboratory Groups and Test Names>

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.1 Subject Discontinuation (Safety Population)

Cohort	Subject Number	Randomized Treatment	Study Period	Date	Completed Study?	Primary Discontinuation Reason
1	1	A	Post	DDMMMYYYY	YES	
	2	A	Post	DDMMMYYYY	YES	
	3	Placebo	Post	DDMMMYYYY	NO	Adverse Event

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >
Subjects included in the food effect cohort are listed according to the treatment they were randomized to receive in Period 1.

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_dis.sas DDMMMYYYY HH:MM

Appendix 16.2.4.1 Demographics (Safety Population)

Cohort	Subject Number	Date Of Birth	Age* (yrs)	Sex	Race	Ethnicity	Height (cm)	Weight (kg)	Body Mass Index (kg/m²)	Informed Consent Date
1	X	DDMMMYYYY	XX	Male	< >	Not Hispanic or Latino	XXX	XX.X	XX.XX	DDMMMYYYY
	X	<similar to above>								

* Age is derived from birth date to date of first dose.

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_dem.sas DDMMMYYYY HH:MM

Appendix 16.2.4.2 Physical Examination (Safety Population)

Cohort	Subject Number	Study Period	Date	Was Physical Exam Performed?	Comment
X	X	Screen	DDMMMYYYY	Yes	XXXXXXXXXXXXXXXXXXXX
	X	Screen	DDMMMYYYY	Yes	

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.4.3 Medical and Surgical History (Safety Population)

Cohort	Subject Number	Any History?	Study Period	Body System	Category	Date Start	Date End	Ongoing?	Condition or Event
X	X	XXX	Screen	XXXXXX XXXXX	Medical	DDMMMYYYY		XXXX	XXXXXXX XXXXXX XX
					Surgical	DDMMMYYYY	DDMMMYYYY		
	X	XXX	Screen	XXXXXXXX XXXXX	Medical	DDMMMYYYY	DDMMMYYYY		

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.4.4 Substance Use (Safety Population)

Cohort	Subject Number	Study Period	Substance	Description of Use	Start Date	End Date
X	X	Screen	XXXXXXXX XXX	XXXXXXXXXX XXXXXX XXXX	DDMMMYYYY	DDMMMYYYY

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.1.1 Inclusion Criteria

X. < >.
X. < >.
X. < >.
X. < >.
X. < >.
X. < >.

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.1.2 Exclusion Criteria

X. < >.
X. < >.
X. < >.
X. < >.
X. < >.
X. < >.
X. < >.

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.2 Subject Eligibility (Safety Population)

Cohort	Subject Number	Study Period	Did subject meet all eligibility criteria?	Specify
X	X	Screen	YES	
	X	Screen	YES	<This column is only presented if data are present.>

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.3.1 Check-in and Return Criteria

X. Did the Subject report any study restriction violations since the last study visit?
X. IF YES TO ANY QUESTION, WAS SUBJECT APPROVED FOR STUDY?

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.3.2 Check-in and Return Responses (Safety Population)

Cohort	Subject Number	Study Period	Day	Hour	Date	Time	Check-in Criteria 1	Check-in Criteria 2	Specify
X	X	X	-X	-XX.X	DDMMMYYYY	HH:MM	No	NA	Will only be present and populated if there is a comment present in the study database.
	X	X	-X	-XX.X	DDMMMYYYY	HH:MM	No	NA	
	X	X	-X	-XX.X	DDMMMYYYY	HH:MM	No	NA	

Please refer to Appendix 16.2.5.3.1 for the Check-in criteria.
NA = Not applicable

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.4.1 Test Compound Description (Safety Population)

Compound	Form	Route
XXXXXXXXXXXXX	< >	XXXX
XXXXXXXXXXXXX	< >	XXXX

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.4.2 Test Compound Administration Times (Safety Population)

Cohort	Subject Number	Study Period	Treatment	Day	Hour	Start		Compound	Dosage	Comments
						Date	Time			
X	X	X	X	X	X.XX	DDMMMYYYY	X:XX:XX	XXXXXXXXX	< >	XXXXXXXXXXXXXXXXXX
	X	X	X	X	X.XX	DDMMMYYYY	X:XX:XX	XXXXXXXXX	< >	
	X	X	X	X	X.XX	DDMMMYYYY	X:XX:XX	XXXXXXXXX	< >	

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.5 Blood Draw Times (Safety Population)

Cohort	Subject Number	Study Period	Treatment	Day	Hour	Date	Actual Time	Bioassay	Comments
1	1	1	A	X	-X.XX	DDMMMYYYY	HH:MM:SS	XXXXXXXX	
				X	XX.XX	DDMMMYYYY	HH:MM:SS	XXXXXXXX	
				X	XX.XX	DDMMMYYYY	HH:MM:SS	XXXXXXXX	
				X	XX.XX	DDMMMYYYY	HH:MM:SS	XXXXXXXX	
				X	XX.XX	DDMMMYYYY	HH:MM:SS	XXXXXXXX	
			<similar for all other time points and subjects>						

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.1.6 Urine Collection Times - SAD (Safety Population)

					Urine Collection						
						Start		Stop			
Cohort	Subject Number	Study Period	Treatment	Collection End Day	Collection Interval	Date	Time	Date	Time	Weight (unit)	Comments
X	X	X	X	1	-X.XX	DDMONYYYY	HH:MM:SS	DDMONYYYY	HH:MM:SS	XXX	
					-.XX	DDMONYYYY	HH:MM:SS	DDMONYYYY	HH:MM:SS		SAMPLE PROCESSING NOT REQUIRED
					-X.XX - X.XX	<similar to above for all time points and subjects>					

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.7 Meal Times (Safety Population)

Cohort	Subject Number	Study Period	Treatment	Day	Hour	Timed Interval (Start HR to Stop HR)	Event	Actual Date	Start Time	Stop Time	Comments
X	X	X	X	-X	-XX.XX		DINNER	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
					-XX.XX		SNACK	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
				X	-X.XX	-X.X TO -X.XX	BREAKFAST	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
					XX.XX		LUNCH	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
					XX.XX		DINNER	DDMMMYYYY	XX:XX:XX	XX:XX:XX	
					XX.XX		SNACK	DDMMMYYYY	XX:XX:XX	XX:XX:XX	

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >
HR = Hour

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.8 Prior and Concomitant Medications (Safety Population)

Cohort	Subject Number	Any Med?	Treat-ment	Medication (WHO DD*)	Dosage	Route	Start Date	Start Time	Stop Date	Stop Time	Frequency	Indication	Continuing?	Prior to Study?
1	1	NO		None										
	2	NO		None										
	3	YES		CETIRIZINE (CETIRIZINE)	X MG	BY MOUTH	DDMMMYYYY	UNK	DDMMMYYYY	HH:MM	XXXXXXX	XXXXXXX	NO	Yes
			X	PARACETAMOL (PARACETAMOL)	X MG	XXXXXXXXX	DDMMMYYYY	HH:MM	DDMMMYYYY	HH:MM	XXXXXXXX	XXXXXXXX	XX	

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >
*Concomitant medications are coded with WHO Dictionary Version 01Mar2017.
Med = Medication, UNK = Unknown, WHO DD = World Health Organization Drug Dictionary

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.7.1.1 Adverse Events (I of II) (Safety Population)

Cohort	Subject Number	Treatment	TE?	Adverse Event	Preferred Term*	Time From Last Dose (DD:HH:MM)	Onset Date	Onset Time	Resolved Date	Resolved Time	Duration (DD:HH:MM)
1	1			None							
	2			None							
	3		No	XXXXXXXXXXXXX XXXXXXXXXXXXXXXXX	XXXXXXXXXXXXXXXXX XXXXXXXXXXX	DD:HH:MM	DDMMMYYYY	HH:MM	DDMMMYYYY	HH:MM	DD:HH:MM
		X	Yes	XXXXXXXXXXXXXXXXX	XXXXXXXXXXXXXXXXXXXXX	<similar to above>					

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >
* Adverse events are coded using MedDRA Version 20.0.
TE = Treatment-emergent

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.7.1.2 Adverse Events (II of II) (Safety Population)

Cohort	Subject Number	Treatment	Adverse Event	Onset Date	Onset Time	Freq^	Severity Grade*	Ser**	Outcome	Relationship to Study Drug	Action
1	1		None								
	2		None								
	3		XXXXXXXXXXXXXXXXXXXX	DDMMMYYYY	HH:MM	Cont.	1	NS	Resolved	Unrelated	None
		X	XXXXXXXXXXXXXXXXXXXX	DDMMMYYYY	HH:MM	<similar to above>					

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >
^ Freq represents Frequency: SE = Single Episode, Inter. = Intermittent, Cont. = Continuous
* Ser represents Serious: NS = Not Serious
** Severity Grade: 1 = Mild, 2 = Moderate, 3 = Severe or medically significant but not immediately life-threatening, 4 = Life-threatening consequences

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_ae2.sas DDMMMYYYY HH:MM

Appendix 16.2.7.2 Adverse Event Non-Drug Therapy (Safety Population)

Cohort	Subject Number	Treatment	Adverse Event	Onset		Procedure Given		
				Date	Time	Date	Time	Description
X	X	X	< >	DDMMMYYYY	HH:MM	DDMMMYYYY	HH:MM	TRENDELENBURG POSITION

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >

Program: /CAXXXXX/sas_prg/stsas/lis_dev/cdash_lis_ae3.sas DDMMMYYYY HH:MM

Appendix 16.2.7.3 Adverse Event Preferred Term Classification (Safety Population)

Cohort	Subject Number	Treatment	Adverse Event	Preferred Term*	System Organ Class	Onset Date	Onset Time
1	1		None				
	2		None				
	3	X	XXXXXXXXXXXXXXX	XXXXXXXXXXXXXXXXXXXXX	XXXXXXXXXXXXXXXXXXXX	DDMMMYYYY	HH:MM
			XXXXXXXXXXXXXXXXXXXXXXXX	XXXXXXXXXXXXXXXXXXXXX	XXXXXXXXXXXXXXXXXXXXXXXX	DDMMMYYYY	HH:MM

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >
* Adverse events are coded using MedDRA Version 20.0.

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_ae4.sas DDMMMYYYY HH:MM

Appendices 16.2.8.1.1 – 16.2.8.1.4 will be in the following format:

Appendix 16.2.8.1.1 Clinical Laboratory Report - Serum Chemistry (Safety Population)

Cohort	Subject Number	Age#/ Sex	Study Period	Treat-ment	Day	Hour	Date	Time	Parameter1 < Range> (Unit)	Parameter2 < Range> (Unit)	Parameter3 < Range> (Unit)	Parameter4 < Range> (Unit)	Parameter5 < Range> (Unit)	Parameter6 < Range> (Unit)
X	X	XX	Screen		.		DDMMMYYYY	HH:MM:SS	XX HN	XX	XX	XX	XX HN	XX
			X	X	-X	-XX.X	DDMMMYYYY	HH:MM:SS	XX LYR+	XX LN	XX	XX LY-	XX	XX

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >
# Age is calculated at the time of first dosing. F = Female, M = Male
H = Above reference range, L = Below reference range
Computer: N = Not clinically significant, Y = Clinically significant
PI Interpretation: - = Not clinically significant, R = Recheck requested, ^ = Will be retested later, + = Clinically significant

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Programmer Notes: Replace Parameter1, 2 etc. with actual lab tests in the study. Sort unscheduled assessment and early term chronologically with other scheduled assessments and rechecks. Recheck should be sorted with the scheduled time point the recheck is for. Serum Cortisol results will be presented in a separate listing (16.2.8.1.2).
Clinically significant lab values generally will be captured as AEs, some of which the PI may indicate in Appendix 16.2.8.1.6 lab comments (as per GPG.03.0028 sections 2.9 and 2.10). Derive an additional flag for PI flag (+) based on positive CS/Clinically Significant comments. Present this derived 4th column in all tables, and list only PI-determined out-of-range clinically significant lab values in Table 14.3.4.5.

Appendix 16.2.8.1.5 Clinical Laboratory Report – Comments (Safety Population)

Cohort	Subject Number	Age#/ Sex	Study Period	Treatment	Day	Hour	Date	Department	Test	Result	Unit	Comment
X	X	X	X	X	-X	-XX.X	DDMMMYYYY	Other Tests	Fibrinogen	XXX	mg/dL	Not significant in the context of this study.

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >
Age is calculated at the time of first dosing. F = Female, M = Male

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.8.2 Vital Signs (Safety Population)

Cohort	Subject Number	Study Period	Treatment	Day	Hour	Date	Time	Blood Pressure (mmHg) Test	Blood Pressure (mmHg) Sys/Dia	Pulse (bpm)	Respiration (rpm)	Temperature (°C)	Weight (kg)	Comment
X	X	Screen		.	.	DDMMMYYYY	X:XX:XX	SITX	XXX/ XX	XX	XX	XX	XXX.X	
		X	X	-X	-XX.X	DDMMMYYYY	X:XX:XX	SITX	XXX/ XX	XX			XXX.X	
				X	XX.X	DDMMMYYYY	X:XX:XX	SITX		XX				

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >
SITX = X-minute sitting, Sys = Systolic, Dia = Diastolic, R = Recheck value

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.8.3 12-Lead Electrocardiogram (Safety Population)

Cohort	Subject Number	Study Period	Treat-ment	Day	Hour	Date	Time	Result	Heart Rate (bpm)	PR (msec)	QRS (msec)	QT (msec)	QTcF* (msec)	Comments
X	1	Screen				DDMMMYYYY	HH:MM:SS	ANCS	XX	XXX	XX	XXX	XXX	EARLY REPOLARIZATION; LEFT AXIS DEVIATION
		1	X	-X	-XX.XX	DDMMMYYYY	HH:MM:SS	ANCS	XX	XXX	XX	XXX	410	LEFT AXIS DEVIATION
				X	X.XX	DDMMMYYYY	HH:MM:SS							
				X	XX.XX	DDMMMYYYY	HH:MM:SS	< >	XX	XXX	XX	XXX	441 @	SINUS BRADYCARDIA
				X	X.XX	DDMMMYYYY	HH:MM:SS	< >	XX	XXX	XX	XXX	451#@	
				X	XX.XX	DDMMMYYYY	HH:MM:SS	< >	XX	XXX	XX	XXX	XXX	

Treatment A: < >
Treatment B: < >
Treatment C: < >
Treatment D: < >
Treatment E: < >
Treatment F: < >
Treatment G: < >
Treatment Placebo: < >
ANCS = Abnormal, Not Clinically Significant, ACS = Abnormal, Clinically Significant
QTcF* = QT corrected for heart rate using Fridericia's correction.
= QTcF > 450, @ = QTcF change from baseline greater than 30 msec

Program: /AAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM