CLINICAL TRIAL CONSULTANTS AB

CONFIDENTIAL

Statistical analysis plan (SAP)

Sponsor:	*Gesynta Pharma AB*
Study code:	*GS-1002*
CTC project no:	*276-118-2019*
Study title:	*An open, one-sequence, three-period study in healthy subjects to evaluate pharmacokinetics and food effect after oral single dosing of two different solid formulations of GS-248*
SAP version and date:	*Final version 1.0 04JUN2020*

1 TABLE OF CONTENTS

2 VERSION HISTORY

This statistical analysis plan for study GS-1002 is based on the protocol dated 29JAN2020.

Table 1 SAP Version History Summary

SAP version	Approval Date	Changes	Rationale
0.1	15MAY2020	-	Version for internal review
0.2	20MAY2020	Minor adjustments	Version for Sponsor review
0.3	02JUN2020	Minor adjustments	Version for Sponsor review
1	04JUN2020	NA	Original version

3 INTRODUCTION

This statistical analysis plan gives details regarding the statistical analyses and data presentation outlined in the final clinical study protocol (CSP) for the study *GS-1002.* Any changes from the final CSP are given in Section 9.

4 CLINICAL STUDY DETAILS

4.1 Clinical study objectives and endpoints

Table 2 – Study objectives and endpoints

Objects	Estimands/Endpoints
Primary	
1. To evaluate the pharmacokinetics (PK) of two different solid formulations of oral GS-248 in healthy subjects.	1.1 The PK parameters of a single dose of two different formulations of GS-248 in fasting conditions. The PK parameters to be assessed include, but are not limited to, maximum plasma concentration (C_{max}), time to C_{max} (T_{max}), area under the plasma concentration versus time curve (AUC) from timepoint 0 to the last measured timepoint ($AUC_{0\text{-last}}$), AUC from timepoint 0 to infinity ($AUC_{0\text{-inf}}$), plasma half-life associated with the terminal elimination phase ($T_{½(z)}$), volume of distribution associated with the terminal elimination phase following non-intravenous administration (Vz/F), and total clearance of the drug from plasma following non-intravenous administration (CL/F).
2. To evaluate the effect of food on the PK of one of the two formulations of GS-248.	2.1 The relative bioavailability of GS-248 after a single dose of Formulation A versus Formulation B, and of one of the two formulations in fed versus fasting conditions. 2.2 The PK parameters of a single dose of one of the two formulations of GS-248 in fed conditions.
Secondary	Applicable for both objectives
1a. To evaluate the safety and tolerability of two different solid formulations of oral GS-248 in healthy subjects. **1b. To evaluate the safety and tolerability of one of the two formulations of oral GS-248 given after a standardised high-fat high-calorie breakfast.**	1.1 Frequency, intensity, and seriousness of adverse events (AEs). 1.2 Clinically significant changes in: - Physical examination - Vital signs - Body temperature - Resting 12-lead electrocardiogram (ECG) - Safety laboratory parameters
Tertiary/Exploratory	
NA	NA

4.2 Clinical study design

This was a Phase I, open, one-sequence, three-period study in healthy volunteers to evaluate the PK, safety and tolerability of two different solid formulation of GS-248, as well as the effect of a high-calorie high-fat breakfast on the PK and safety of one of these two formulations.

4.3 Statistical hypotheses

No formal hypothesis was defined in the protocol. However, p-values will be calculated as outlined in this SAP, based on the null hypothesis that there is no difference in systemic exposure with either different formulations or fed/fasting states.

4.4 Number of subjects

A total of 14 subjects were included in the study.

4.5 Randomisation

Not applicable.

4.6 Blinding

This was an open study and thus no blinding was needed.

5 STATISTICAL AND ANALYTICAL PLANS

5.1 Sample size determination

No formal sample size calculation was performed for this study. The proposed sample size was considered sufficient to provide adequate information for the study objectives.
14 subjects were dosed to achieve a total of at least 12 evaluable subjects that completed the study. Subjects were evaluated for safety analysis after receiving one dose of the study drug.

5.2 Definition of analysis sets

5.2.1 Safety analysis set

The safety analysis set will consist of all subjects who received at least one dose of the investigational medical product (IMP).

5.2.2 Pharmacokinetics analysis set (PKAS) - formulation

The PKAS formulation will consist of all subjects who received a single dose of both Formulation A and Formulation B, from whom PK blood samples were collected after IMP dosing, and for whom there were no AEs or protocol deviations judged to affect the analysis of the data.

5.2.3 PKAS – food interaction set

The PKAS food interaction set will consist of all subjects who received all three IMP doses, from whom PK blood samples were collected after IMP dosing, and for whom there were no AEs or protocol deviations judged to affect the analysis of the data.

5.2.4 Use of analysis set

The safety analysis set population will be used for the safety evaluation and the PKAS will only be used for the PK evaluations.

If any of the analysis populations are identical, only one will be used.

5.3 Definition of baseline

Baseline measurement will be defined as the latest measurement prior to first dose of the IMP.

5.4 Summary statistics

In general, all data collected will be presented with summary statistics and given in subject data listings. Summary statistics will include at least the number of subjects, mean, standard deviation, median, minimum, and maximum for continuous data. Summary statistics for categorical data will consist of at least frequency and percentage. Tables with summary statistics will be divided by treatment group and assessment time, where applicable. Subject data listings will be sorted by treatment, subject, and timing of assessments.

5.5 Significance level

See section 8.1.

5.6 Multiple comparisons/multiplicity

No adjustment for multiple comparison/multiplicity will be performed. All significant findings must be reviewed for medical relevance.

5.7 Handling of dropouts, missing data, and outliers

Outliers will be included in summary tables and listings and will not be handled separately in any analyses. No imputation of data will be performed.

5.8 Adjustment for covariates

No adjustments for covariates are planned to be performed.

5.9 Multicentre studies

Not applicable.

5.10 Examination of subgroups

No examination of subgroups is planned to be performed.

5.11 Blind review

Not applicable.

6 SUBJECTS

6.1 Subject disposition

The subject disposition table will include the number of screened subjects, reasons for withdrawal prior to dose, number of subjects in the treatment arms, reasons for withdrawal during the study, and number of completed subjects in the study. The table will also summarise the number of subjects at each visit and the number of subjects in each study population. See tables and listings in the statistical output layout, section **Fel! Hittar inte referenskälla.**.

6.2 Baseline characteristics and demographics

The following baseline characteristics will be summarised by treatment:

- Gender
- Age
- Ethnicity
- Race
- Weight
- Height
- BMI
- Medical/surgical history
- Prior and concomitant medication
- HIV and Hepatitis B/C
- Pregnancy test
- Urine drug screen
- Alcohol breath test

7 TREATMENT INFORMATION AND EXTENT OF EXPOSURE

7.1 Active Treatment

The number of subjects on each formulation of the IMP will be tabulated using listings and summary statistics.

7.2 Prior and concomitant medications

Prior and concomitant medications will be coded according to the World Health Organization (WHO) Anatomical Therapeutic Chemical (ATC) classification system. Prior and concomitant medication data will be listed and tabulated by ATC code.

8 STATISTICAL METHODOLOGY

All parameters will be presented by treatment and visit using summary statistics. Additional statistical analyses are specified below.

8.1 Primary endpoint(s) analysis

8.1.1 Definition of endpoint(s)

8.1.1.1 Pharmacokinetics

The PK analysis will be based on the PKAS and performed by CTC. The PK parameters will be calculated by non-compartmental analysis (NCA) using the software Phoenix WinNonlin® version 8.1 or later (Certara, U.S.A.).

The NCA PK parameters to be assessed include, but are not limited to:

- C_{max} – The maximum observed plasma concentration.
- T_{max} – The time from dosing to reach C_{max}.
- $AUC_{0\text{-}last}$ – The AUC from timepoint 0 to t hours, where t is the time of the last detectable plasma concentration.
- $AUC_{0\text{-}inf}$ – The $AUC_{0\text{-}last}$ extended to infinity using $lambda_z$.
- $AUC_{0\text{-}24}$ – The AUC from timepoint 0 to 24 hours for profiles with time of last detectable plasma concentration ≥ 24 hours
- $T_{½(z)}$ – The plasma half-life associated with the terminal elimination phase
- CL/F – The total plasma clearance after oral administration.
- V_z/F – The apparent volume of distribution associated with the terminal elimination
- Relative bioavailability for Formulation A versus Formulation B and for one of the two formulations in fed versus fasting conditions.
- Comparisons of all relevant PK parameters (*e.g.,* AUC:s, T_{max}, C_{max}) for Formulation A versus B and for one of the two formulations in fed versus fasting conditions.

C_{max} and T_{max} will be derived from the observed plasma concentration data. Plasma concentrations below the quantification limit will be set to 0 before T_{max} and missing thereafter. The pre-dose sampling time will be set to 0. All other timepoints used for calculations of PK parameters will be based on actual timepoints. The area under the plasma concentration versus time curve will be calculated according to the linear up-log down trapezoidal method.

$AUC_{0\text{-}last}$ will be calculated from time 0 to the time t of the last detectable plasma concentration. For $AUC_{0\text{-}inf,}$ the area will be calculated to the last point showing a measurable plasma concentration and then extrapolated to infinity using the concentration in the last quantifiable sample and $lambda_z$. CL/F and Vz/F will be calculated based on the $AUC_{0\text{-}inf}$ described above.

$Lambda_z$, the first order rate constant associated with the terminal portion of the curve, will be determined by lin-logarithmic regression of the terminal elimination phase of individual plasma concentration vs time curves. $T_{½}$ will be calculated by ln 2 / $lambda_z$. Determination of $lambda_z$ requires identification of a sufficiently linear terminal phase (as determined by

visual inspection of the lin-log plasma concentration versus time plot with the regression line) consisting of at least 3 terminal concentration values (not including C_{max}). If this is not achieved, $lambda_z$ and its dependent PK parameters will not be reported for that profile. In the following cases, $lambda_z$ dependent PK parameters will be flagged in listings and tables as potentially unreliable:

- $Lambda_z$ estimation is based on a period of less than 1.5 times the resulting $T_{½}$.
- The adjusted R^2 value of the regression line is < 0.85.
- The estimated % extrapolated AUC is > 20% ($AUC_{0\text{-}inf}$ -$AUC_{0\text{-}t}$ / $AUC_{0\text{-}inf}$).

If a subject has measurable pre-dose plasma levels that is equal to or less than 5% of their measured C_{max}, their data will be included in the analysis without adjustment. If a subject has pre-dose plasma levels that is greater than 5% of the measured C_{max} value from the same profile, the impact of this will be individually assessed for the potential need for data exclusion for the specific analyte and period. Data will not be excluded in cases where the lower limit of quantification is more than 5% of the respective C_{max} if pre-dose values are below the limit of quantification.

If a subject experiences emesis outside 2 x the median T_{max} of the respective treatment condition (i.e. the formulation used and fasting or fed state) , the PK parameters will be included in the analysis without adjustments. In case of emesis within 2 x the median T_{max}, data from that analyte and period will be excluded from the PK analysis set.

If there is a confirmed dosing error during the study, the PK data for that period will be excluded from statistical analyses and descriptive statistics. Available individual data from excluded periods will be presented in relevant listings.

In case of missed blood samples, potential impact on PK parameters should be assessed for each individual case. PK parameters with a high degree of uncertainty due to missing samples (e.g., multiple samples missing around C_{max}) will be flagged as unreliable in the report and may in rare cases be excluded from summary tables and statistical analysis.

Summary statistics for the PK parameters will be presented with the number of measurements, arithmetic mean, SD, CV, median, minimum, maximum, geometric mean, geometric CV%, except for T_{max} for which only median, minimum, and maximum will be presented.

The relative bioavailability of GS-248 will be analysed with a 90% confidence interval (CI) for the ratio of Formulation A to Formulation B, and for the ratio of the selected formulation in fed to fasting conditions using a mixed model approach with treatment, and subject as factors in the model.

Geometric mean ratio (GMR) will be calculated for GS-248, Formulation A and Formulation B, and for the selected formulation in fed and fasting conditions. The GMR will be estimated using an analysis of covariance (ANCOVA) model in SAS (PROC MIXED). Subject and treatment will be included as fixed effects the calculated comparisons. Confidence intervals at 90% for the comparison. The CI will be presented for the GMR (obtained from logarithmic

transformed data) and p-values for the difference between the treatments will be estimated from the model.

The table for the comparisons between the formulations will include PK parameters, 90% CI lower bound, ratio of geometric mean, 90% CI upper bound, p-value, %CV (within subject), and %CV (between subject).

All data will be listed by subject. See tables and listings in the statistical output layout, section 14.

8.2 Sensitivity analysis

No sensitivity analyses are planned to be performed.

8.3 Supplementary analyses

No supplementary analyses are planned to be performed.

Secondary endpoint(s) analysis

8.4 Definition of endpoint(s)

8.4.1.1 Adverse events

This section refers to secondary objective #1 and endpoint 1.1.

An overview of all AEs, including serious adverse events (SAEs), intensity, relationship to the IMP, and deaths will be presented by system organ class (SOC) and preferred term (PT).

Incidence of AEs and SAEs will be summarised by SOC and PT.

All AE data will be listed by subject and include the verbatim term entered by the investigator. See tables and listings in the statistical output layout, section 14.

8.4.1.2 Physical examinations

This section refers to secondary objective #1 and endpoint 1.2.

Clinically significant and non-clinically significant abnormal findings will be specified and presented by subject and summarised.

All data will be listed by subject. See tables and listings in the statistical output layout, section 14.

8.4.1.3 Vital signs

This section refers to secondary objective #1 and endpoint 1.2.

Vital signs (systolic/diastolic BP, pulse) and body temperature will be summarised. Data will be presented with absolute and percent change from baseline at each visit. Clinical evaluation of vital signs will be summarised in frequency tables.

All data will be listed by subject. See tables and listings in the statistical output layout, section 14.

8.4.1.4 ECG resting 12-lead

This section refers to secondary objective #1 and endpoint 1.2.

All ECGs will be categorised as “normal”, “abnormal, not clinically significant”, or “abnormal, clinically significant” (as judged by the investigator) and summarised using frequency tables. Changes over time will be presented using shift tables, if considered applicable.

All data will be listed by subject. See tables and listings in the statistical output layout, section 14.

8.4.1.5 Safety laboratory analyses

This section refers to secondary objective #1 and endpoint 1.2.

Safety laboratory data will be summarised with absolute and percent change from baseline at each visit. Abnormal, clinically significant values will be summarised separately if considered appropriate.

All data will be listed by subject. See tables and listings in the statistical output layout, section 14.

8.5 Sensitivity analysis

No sensitivity analyses are planned to be performed.

8.6 Supplementary analyses

No supplementary analyses are planned to be performed.

8.7 Tertiary/exploratory endpoint(s) analysis

Not applicable.

8.8 Discontinuation

Patients who discontinue from IMP treatment will be tabulated. The reason for discontinuation will be given. For discontinuation due to AE, the AEs will be given.

8.9 Other analyses

Not applicable.

8.10 Interim analysis

Not applicable.

9 CHANGES FROM THE CSP

10 STATISTICAL DELIVERABLES

The following documents will be delivered:

- SAP
- Statistical analyses and summary tables

11 SOFTWARE

All statistical analyses will be performed using SAS Version 9.4 (SAS institute, Cary, NC) and all PK parameters will be calculated by non-compartmental analysis (NCA) using the software Phoenix WinNonlin® version 8.1 or later (Certara, U.S.A.).

12 APPROVAL

Issued by:

Responsible Biostatistician
CTC Representative

Date (dd-Mmm-yyyy)

Approved by:

Sponsor Representative
C Edenius
Head Clin. R&D

04JUN2020
Date (dd-Mmm-yyyy)

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13 SUPPORTIVE DOCUMENTATION

13.1 Appendix 1 – list of abbreviations

Abbreviation of term	Explanation
AE	Adverse event
ANCOVA	Analysis of covariance
ATC	Anatomical therapeutic chemical
AUC	Area under the plasma concentration versus time curve
$AUC_{0\text{-inf}}$	Area under the curve from timepoint 0 to infinity
$AUC_{0\text{-last}}$	Area under the curve from timepoint 0 to the sampling time of the last sample with quantifiable concentration
CF	Clean file
C_{max}	Maximum plasma concentration
CRF	Case report form
CSP	Clinical study protocol
FAS	Full analysis Set
IMP	Investigational medical product
MedDRA	Medical dictionary for regulatory affairs
NCA	Non-compartmental analysis
PK	Pharmacokinetic
PKAS	Pharmacokinetics analysis set
SAE	Serious adverse event
SAP	Statistical analysis plan
SAS	Statistical analysis system
SD	Standard deviation
T_{max}	Time to C_{max}
$T_{½(z)}$	Plasma half-life associated with the terminal elimination phase
WHO	World Health Organization

13.2 Appendix 2 – changes to protocol-planned analyses

14 STATISTICAL OUTPUT LAUOUT

14.1 Tables

Table 14.1.1 Baseline characteristics and demographics (analysis set)

		Total (N=X)
Age (years)	n/nmiss	x/x
	Mean (SD)	x.x (x.x)
	Median (Min, Max)	x.x (x,x)
Body Mass Index (kg/m2)	n/nmiss	x/x
	Mean (SD)	x.xx (x.xx)
	Median (Min, Max)	x.xx (x.x, x.x)
Height (cm)	n/nmiss	x/x
	Mean (SD)	x.x (x.x)
	Median (Min, Max)	x.x (x,x)
Weight (kg)	n/nmiss	x/x
	Mean (SD)	x.xx (x.xx)
	Median (Min, Max)	x.xx (x.x,x.x)
Sex	Female	x (x.x%)
	Male	x (x.x%)
Ethnicity	Hispanic Or Latino	x (x.x%)
	Not Hispanic Or Latino	x (x.x%)
Race	American Indian Or Alaska Native	x (x.x%)
	Asian	x (x.x%)

	Total (N=X)
Black or African American	x (x.x%)
Native Hawaiian or other Pacific Islander	x (x.x%)
White	x (x.x%)

```
[STUDYID] Summarised demographics data.
Data based on the [analysis set].
SAS program: summary_demographics.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]
```

Table 14.1.2 Subject disposition (all subject)

	Total
Screened subjects	x
Withdrawn prior to [dose]	x
--- Withdrawal reason x	x
--- Withdrawal reason x	x
--- Withdrawal reason x	x
Included subjects	x
--- [Formulation A]	x
--- [Formulation B]	x
--- [Formulation A/B fed]	x
Withdrawn subjects	x
--- Withdrawal reason x	x
--- Withdrawal reason x	x
--- Withdrawal reason x	x
Completed subjects	x
--- [Formulation A]	x
--- [Formulation B]	x
--- [Formulation A/B fed]	x
Included in [Safety analysis set]	x
Included in [PK analysis set (fed)]	x
Included in [PK analysis set (food interaction)]	x
Subjects at [VISIT 1]	x

	Total
Subjects at [VISIT 2]	x
Subjects at [VISIT 3]	x
Subjects at [VISIT 4]	x
Subjects at [VISIT 5]	x
Subjects at [VISIT 6]	x
Subjects at [VISIT 7]	x

```
[STUDYID] Disposition, SAS program: disposition.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]
```

Table 14.1.3. Medical history events by system organ class and preferred term (analysis set)

System organ class Preferred term	Total N=X n(%)	m
Total	**x(x.x%)**	**x**
SOC 1	**x(x.x%)**	**x**
SOC 1 PT 1	x(x.x%)	x
SOC 1 PT 2	x(x.x%)	x
SOC 1 PT 3	x(x.x%)	x
SOC 2	**x(x.x%)**	**x**
SOC 2 PT 1	x(x.x%)	x
SOC 2 PT 2	x(x.x%)	x

n, number of subjects; m, number of events
Percentages are based on the number of subjects in the treatment period included in the [analysis set]
[STUDYID] Medical history events by system organ class and preferred term, [analysis set], SAS program: mh_summary_by_soc_and_pt.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]

Table 14.1.4. Concomitant medications by ATC levels 4 and 5 (analysis set)

	Formulation A N=X		Formulation B N=X		Formulation A/B fed N=X		Total N=X	
ATC level 4 ATC level 5	n(%)	m	n(%)	m	n(%)	m	n(%)	m
Total	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**
ATC 4	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**
ATC 5	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x

n, number of subjects; m, number of events;

Percentages are based on the number of subjects in the full analysis set

Table 14.2.x.x PK variables (analysis set)

Assessment (unit)		Formulation A	Formulation B	Formulation A/B fed
[Parameter 1] (unit)	n	X	x	X
	Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
	Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
	Geometric Mean (CV%)	xx.xx (xx.x)	xx.xx (xx.x)	xx.xx (xx.x)
[Parameter 2] (unit)	n	X	x	x
	Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
	Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
	Geometric Mean (CV%)	xx.xx (xx.x)	xx.xx (xx.x)	xx.xx (xx.x)

Data based on [ANALYSIS SET]
[STUDYID] [DOMAIN]: [PARAMETER CATEGORY], SAS program: descriptive_stat_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]

Table 14.2.x.x PK concentration (analysis set)

Assessment (unit)	Assessment timepoint		Formulation A	Formulation B	Formulation A/B fed
[Parameter 1] (unit)	[Assessment timepoint 1]	n/BLQ/ULQ	x/x/x	x/x/x	x/x/x
		Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
		Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
		Geometric Mean (CV%)	xx.xx (xx.x)	xx.xx (xx.x)	xx.xx (xx.x)
	[Assessment timepoint 2]	n/BLQ/ULQ	x/x/x	x/x/x	x/x/x
		Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
		Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
		Geometric Mean (CV%)	xx.xx (xx.x)	xx.xx (xx.x)	xx.xx (xx.x)

Data based on [ANALYSIS SET].
[STUDYID] [DOMAIN]: [PARAMETER CATEGORY], SAS program: descriptive_stat_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]

Figure 14.2.x.x PK concentration (analysis set)

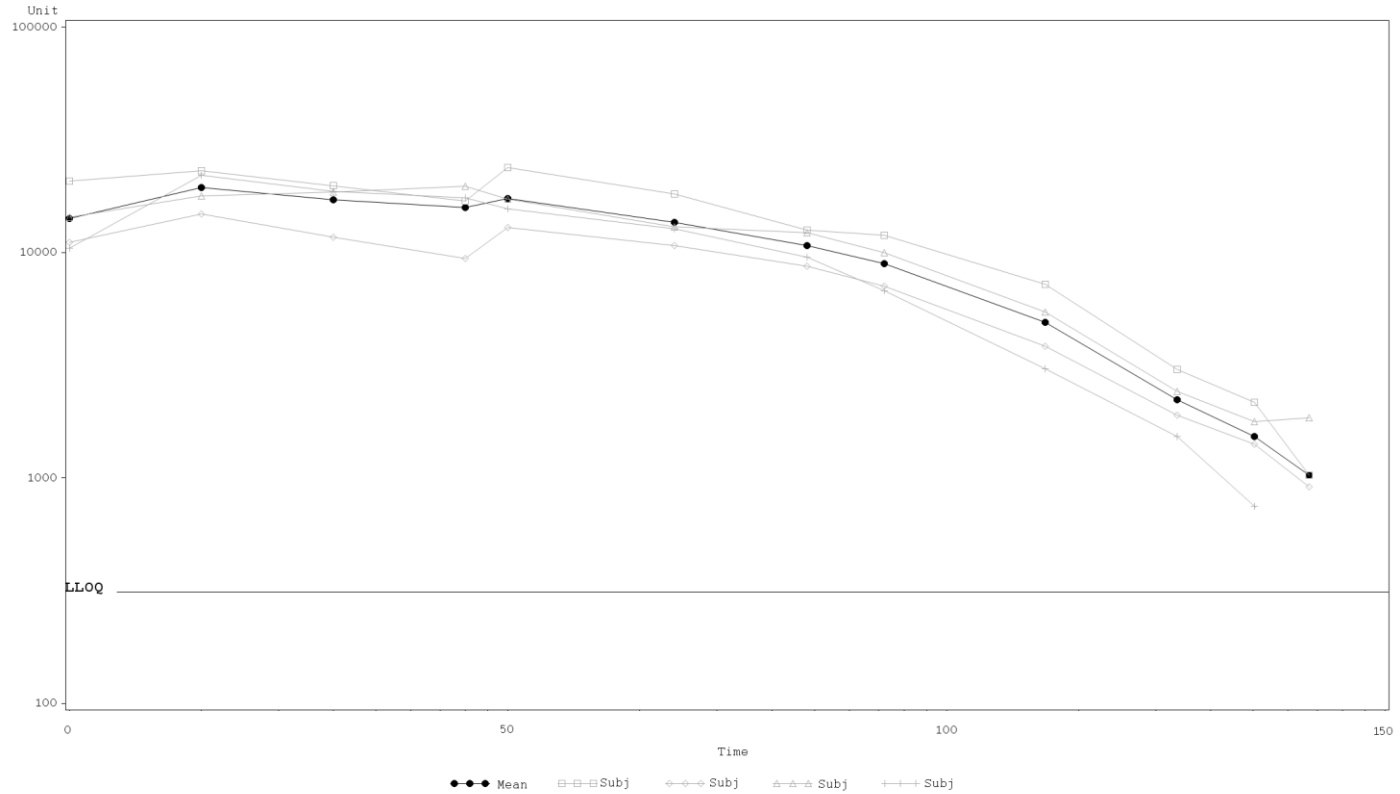

Figure 14.2.x.x Geometric mean PK concentration (analysis set)

[Plot for geometric mean, all dose groups overlaid, with lin-lin and lin-log axes]

Figure 14.2.x.x Spaghetti plot PK concentration (analysis set)

[Spaghetti plot with lin-lin and lin-log axes]

Table 14.2.x.x Comparison between formulations for selected PK variables (analysis set)

PK variable	Test product	Reference product	90% CI lower bound	Ratio of geometric mean	90% CI upper bound	P-value	Inter subject CV (%)	Intra subject CV (%)
Parameter (unit)	Xxx	xxx	x.xxx	x.xxxx	x.xxx	x.xxxx	xx	xx
xxx	Xxx	xxx	x.xxx	x.xxxx	x.xxx	x.xxxx	xx	xx
xxx	Xxx	xxx	x.xxx	x.xxxx	x.xxx	x.xxxx	xx	xx

```
Data based on [ANALYSIS SET]
[STUDYID][TITLE],SAS program:[SAS PROGRAM]. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]
```

Table 14.3.x.x. Overview of adverse events (analysis set)

	Formulation A N=X		Formulation B N=X		Formulation A/B fed N=X		Total N=X	
	n(%)	m	n(%)	m	n(%)	m	n(%)	m
Any AE	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
Any SAE	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
Any AE leading to withdrawal	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
Any AE leading to death	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
Causality								
Possibly Related	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
Probably Related	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
Severity								
Mild	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
Moderate	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
Severe	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x

n, number of subjects; m, number of events
Percentages are based on the number of subjects in the treatment period included in the [analysis set].
Adverse events that occurred during [ELEMENTS] are omitted from summary.
[STUDYID] Overview of adverse events, [analysis set], SAS program: ae_summary_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]

Table 14.3.x.x. Adverse events by system organ class and preferred term (analysis set)

	Formulation A N=X		Formulation B N=X		Formulation A/B fed N=X		Total N=X	
System organ class Preferred term	n(%)	m	n(%)	m	n(%)	m	n(%)	m
Total	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**
SOC 1s	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**
SOC 1 PT 1	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
SOC 1 PT 2	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
SOC 1 PT 3	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
SOC 2	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**	**x(x.x%)**	**x**
SOC 2 PT 1	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x
SOC 2 PT 2	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x	x(x.x%)	x

n, number of subjects; m, number of events
Percentages are based on the number of subjects in the treatment period included in the [analysis set]
[STUDYID] Medical history events by system organ class and preferred term, [analysis set], SAS program: mh_summary_by_soc_and_pt.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]

Table 14.3.x.x. Physical examinations (analysis set)

Assessment	Assessment timepoint	Result	Formulation A	Formulation B	Formulation A/B fed
[Parameter 1]	[Assessment timepoint 1]	[RESULT 1]	x(x.x%)/X	x(x.x%)/X	x(x.x%)/X
		[RESULT 2]	x(x.x%)/X	x(x.x%)/X	x(x.x%)/X
	[Assessment timepoint 2]	[RESULT 1]	x(x.x%)/X	x(x.x%)/X	x(x.x%)/X
		[RESULT 2]	x(x.x%)/X	x(x.x%)/X	x(x.x%)/X

Data based on [ANALYSIS SET].
[STUDYID] [DOMAIN]: [PARAMETER CATEGORY], SAS program: descriptive_stat_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]

Table 14.3.x.x. Vital signs (analysis set)

				Formulation A	Formulation B	Formulation A/B fed
Assessment (unit)	Result Category	Assessment timepoint				
[Parameter 1] (unit)	Measured value	[Assessment timepoint 1]	n	x	x	x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
		[Assessment timepoint 2]	n	x	x	x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
	Absolute change from baseline	[Assessment timepoint 2]	n	x	x	x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
	Relative change from baseline (%)	[Assessment timepoint 2]	n	x	x	x
			Mean (SD)	x.x (x.x)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.x (x, x)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)

```
Data based on [ANALYSIS SET].
[STUDYID] [DOMAIN]: [PARAMETER CATEGORY], SAS program: descriptive_stat_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]
```

Table 14.3.x.x. ECG (analysis set)

				Formulation A	Formulation B	Formulation A/B fed
Assessment (unit)	Result Category	Assessment timepoint				
[Parameter 1] (unit)	Measured value	[Assessment timepoint 1]	n	x	x	x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
		[Assessment timepoint 2]	n	x	x	x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
	Absolute change from baseline	[Assessment timepoint 2]	n	x	x	x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
	Relative change from baseline (%)	[Assessment timepoint 2]	n	x	x	x
			Mean (SD)	x.x (x.x)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.x (x, x)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)

```
Data based on [ANALYSIS SET].
[STUDYID] [DOMAIN]: [PARAMETER CATEGORY], SAS program: descriptive_stat_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]
```

Table 14.3.x.x. ECG interpretation (analysis set)

			Formulation A	Formulation B	Formulation A/B
Assessment	Assessment timepoint	Result			
[Parameter 1]	[Assessment timepoint 1]	[RESULT 1]	x(x.x%)/X	x(x.x%)/X	x(x.x%)/X
		[RESULT 2]	x(x.x%)/X	x(x.x%)/X	x(x.x%)/X
	[Assessment timepoint 2]	[RESULT 1]	x(x.x%)/X	x(x.x%)/X	x(x.x%)/X
		[RESULT 2]	x(x.x%)/X	x(x.x%)/X	x(x.x%)/X

Data based on [ANALYSIS SET].
[STUDYID] [DOMAIN]: [PARAMETER CATEGORY], SAS program: descriptive_stat_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]

Table 14.3.x.x. ECG – shift table (analysis set)

Assessment	Assessment timepoint	Result	NORMAL n (%)	ABNORMAL CS n (%)	ABNORMAL NCS n (%)	MISSING n (%)	TOTAL n (%)
[Parameter 1]	[Assessment timepoint 1]	NORMAL	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)
		ABNORMAL CS	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)
		ABNORMAL NCS	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)
		MISSING	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)
		TOTAL	x (x%)	x (x%)	x (x%)	x (x%)	x (x%)

Data based on [ANALYSIS SET].
[STUDYID] [DOMAIN]: [PARAMETER CATEGORY], SAS program: descriptive_stat_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]

Table 14.3.x.x. Safety laboratory results (analysis set)

Assessment (unit)	Result Category	Assessment timepoint		Formulation A	Formulation B	Formulation A/B fed
[Parameter 1] (unit)	Measured value	[Assessment timepoint 1]	n	x	x	x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
		[Assessment timepoint 2]	n	x	x	x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
	Absolute change from baseline	[Assessment timepoint 2]	n	x	x	x
			Mean (SD)	x.xxx (x.xxx)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)
	Relative change from baseline (%)	[Assessment timepoint 2]	n	x	x	x
			Mean (SD)	x.x (x.x)	x.xxx (x.xxx)	x.xxx (x.xxx)
			Median (Min, Max)	x.x (x, x)	x.xxx (x.xx, x.xx)	x.xxx (x.xx, x.xx)

```
Data based on [ANALYSIS SET].
[STUDYID] [DOMAIN]: [PARAMETER CATEGORY], SAS program: descriptive_stat_tables.sas. Run by: [USERNAME], [USER EMAIL] [TIMESTAMP]
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Clinical chemistry, haematology, coagulation, and urinalysis

14.2 Listings

Listing 16.2.1.1. Discontinued subjects (All subjects)

Listing 16.2.2.1. Protocol deviations (All subjects)

Listing 16.2.3.1 Subjects excluded from PKAS (All subjects)

Listing 16.2.3.2 Population definitions (All subjects)

Listing 16.2.3.3. Non-eligible subjects (All subjects)

Listing 16.2.4.1. Demography (Full analysis set)

Listing 16.2.4.2 Medical history (Full analysis set)

Listing 16.2.5. Prior and concomitant medications (Full analysis set)

Listing 16.2.6. Exposure (Full analysis set)

Listing 16.2.7.x. Plasma concentration (Full analysis set) including actual relative sampling times presented

Listing 16.2.8. x. PK parameters (Full analysis set)

Listing 16.2.9.1. Adverse events, part 1 (Full analysis set)

Listing 16.2.9.2. Adverse events, part 2 (Full analysis set)

Listing 16.2.9.3. Serious adverse events, part 1 (Full analysis set)

Listing 16.2.9.4. Serious adverse events, part 2 (Full analysis set)

Listing 16.2.9.5. Serious adverse events, seriousness criteria (Full analysis set)

Listing 16.2.10.x. Physical examinations (Full analysis set)

Listing 16.2.11. x. Vital signs (Full analysis set)

Listing 16.2.12.x. ECG (Full analysis set)

Listing 16.2.13.1 Laboratory values (Full analysis set)

Listing 16.2.13.2 Abnormal laboratory values (Full analysis set)

Listing 16.2.14. x. Meals (Full analysis set)

Listing 16.2.15. x. Disposition (All subjects)

Listing 16.2.16. x. Subject visits (All subjects)

Listing 16.2.17. x. Subject elements (All subjects)