Division	:	Worldwide Development
Information Type	:	Reporting and Analysis Plan (RAP)

Title	:	Reporting and Analysis Plan for Randomized, open label, 2-way crossover, single dose bioequivalence study of Paroxetine IR tablets manufactured in GSKT and Mississauga sites in healthy Chinese participants under fasting and fed conditions.
Compound Number	:	BRL29060
Effective Date	:	06-SEP-2018

Description:

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 207652.
- This RAP will be provided to the study team members to convey the content of the final Statistical Analysis Complete (SAC) deliverable.

RAP Author(s):

Approver	Date	Approval Method
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RAP Team Approvals:

Approver	Date	Approval Method
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TABLE OF CONTENTS

PAGE

1. INTRODUCTION

The purpose of this reporting and analysis plan (RAP) is to describe the analyses to be included in the Clinical Study Report for 207652 Protocol:

Revision Chronology:		
2017N312753_00	01-JUN-2017	Original
2017N312753_01	20-JUL-2018	Amendment 1

All decisions regarding final analysis, as defined in this RAP document, have been made prior to Database Freeze (DBF) of the study data.

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

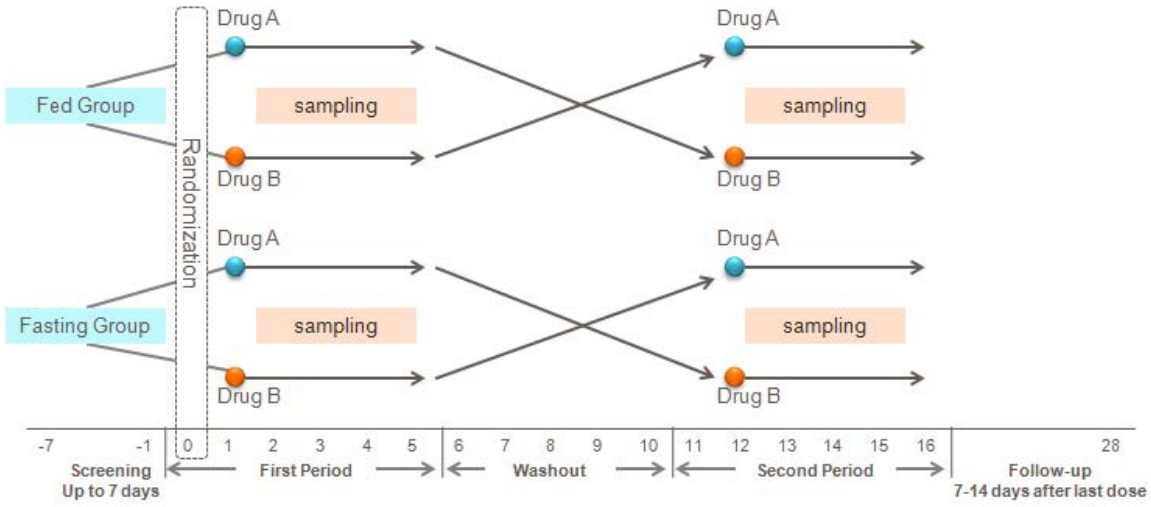
There were no changes or deviations to the Amendment 1 planned statistical analysis specified in the protocol [Dated: 20/JUL/2017].

2.2. Study Objective(s) and Endpoint(s)

Objectives	**Endpoints**
Primary Objectives	**Primary Endpoints**
• To evaluate the bioequivalence of Paroxetine IR tablets manufactured in GSKT and Mississauga sites in healthy Chinese participants under fasting and fed conditions.	• $AUC_{(0-\infty)}$, $AUC_{(0-t)}$ and Cmax of Paroxetine IR tablets
Secondary Objectives	**Secondary Endpoints**
• To assess the safety and tolerability of dosing with Paroxetine IR tablets in healthy Chinese participants.	• Safety and tolerability as measured by adverse events, vital signs, ECG and clinical laboratory measurements.
• To obtain the pharmacokinetic profile of Paroxetine IR tablets in healthy Chinese participants.	• T_{max}, λ_z, and $t_{1/2}$ of Paroxetine IR as data permit.

2.3. Study Design

Overview of Study Design and Key Features



Design Features	• A single dose, open-label, randomized, two-way crossover study to demonstrate the bioequivalence of Paroxetine IR tablets manufactured in GSKT (A) and Mississauga (B) sites in healthy Chinese participants under fasting and fed conditions.
Dosing	• On Day 1, each enrolled participant will take a single dose of Paroxetine IR 40mg (20mg*2 tablets) A or B. • Following a washout from Day 6 to Day 11, participants will be crossed over in Period 2 to receive the treatment that they did not receive in Period 1. Eligible participants will take Paroxetine IR 40mg (20mg*2 tablets) A or B once on Day 12.
Treatment Assignment	• The whole study will be divided into two groups, one for fasting condition and another for fed condition. For each group, eligible participants will be randomized to either AB or BA treatment sequence according to 1:1 ratio. • Participants will be randomly assigned to either regimen sequence (AB or BA) in a balanced manner to ensure similar proportions of participants on each sequence, according to a randomization schedule prepared in advance of the study by Statistics, GlaxoSmithKline, using internal validated software (i.e. RandAll).
Interim Analysis	• No interim analysis is planned.

2.4. Statistical Hypotheses

This study is designed to test the bioequivalence of Paroxetine IR 20mg×2 GSKT tablets and Paroxetine IR 20mg×2 Mississauga tablets in healthy Chinese participants under fasting and fed conditions. The null hypothesis is that the true ratio of the geometric mean of the test treatment (Paroxetine IR 20mg×2 GSKT tablets) to the geometric mean of the reference treatment (Paroxetine IR 20mg×2 Mississauga tablets), μ(test)/μ(reference), for $AUC_{(0-\infty)}$, $AUC_{(0-t)}$ ($AUC_{(0-t)}$ only if $AUC_{(0-\infty)}$ can't be accurately determined) and Cmax

of Paroxetine, is either less than 0.80 or greater than 1.25. The alternate hypothesis is that the true ratio of the test treatment geometric mean to the reference treatment geometric mean is greater than / equal to 0.80 and less than / equal to 1.25. Symbolically, this is expressed as follows:

$$H(0): \mu(test)/\mu(reference) < 0.80 \text{ or } \mu(test)/\mu(reference) > 1.25,$$

i.e., treatments are not bioequivalent.

Versus

$$H(1): 0.80 \leqslant \mu(test)/\mu(reference) \leqslant 1.25,$$

i.e., treatments are bioequivalent.

For each PK parameter designated as a primary endpoint, a two one-sided t-test (TOST) procedure [Schuirmann, 1987] with α=0.05 for each one-sided test will be used to test this set of hypotheses. This is equivalent to requiring that a 90% interval for the true ratio of test to reference geometric means fall entirely within the range of 0.80 to 1.25.

3. PLANNED ANALYSES

3.1. Interim Analyses

No interim analysis is planned.

3.2. Final Analyses

The final planned primary analyses will be performed after the completion of the following sequential steps:

1. All participants have completed the study as defined in the protocol.
2. All required database cleaning activities have been completed and final database release (DBR) and database freeze (DBF) (both the CRF data and PK data) has been declared by Data Management.

All the analyses will be displayed separately for each group (Fasting or Fed).

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
All participants	• All participants who signed the ICF.	• Subject population • Screen failures
Safety Population	• All randomized participants who take at least one dose of study treatment. • Participants will be analysed according to the treatment they actually received.	• Study Population • Safety
Pharmacokinetic (PK) Population	• All randomized participants who take at least one dose of study treatment and provide at least one evaluable pharmacokinetic concentration data. • Participants will be analysed according to the treatment they actually received.	• PK
Bioequivalence (BE) Analysis Population	• All randomized participants who complete all the planned treatments and provide at least one evaluable primary PK parameter data from both period 1 and period 2. • Participants will be analysed according to the treatment they actually received.	• Bioequivalence analysis

Refer to Appendix 7: List of Data Displays which details the population used for each display.

4.1. Protocol Deviations

Important protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, patient management or patient assessment) will be summarised and listed.

Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan.

- Data will be reviewed prior to freezing the database to ensure all important deviations and deviations which may lead to exclusion from the analysis are captured and categorised on the protocol deviations dataset.
- This dataset will be the basis for the summaries and listings of protocol deviations.

A separate summary and listing of all inclusion/exclusion criteria deviations will also be provided. This summary will be based on data as recorded on the inclusion/exclusion page of the eCRF.

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

5.1. Study Treatment

Treatment Group Descriptions			
Randomization System		**Data Displays for Reporting**	
Code	**Description**	**Description**	**Order in TLF**
A	Paroxetine IR GSKT tablets 20mg*2 tablets	40mg GSKT	1
B	Paroxetine IR Mississauga tablets 20mg*2 tablets	40mg Mississauga	2

Treatment comparisons will be displayed as A vs B.

5.2. Baseline Definitions

For all endpoints (except as noted in baseline definitions), the baseline value will be the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. If time is not collected, Day 1 assessments are assumed to be taken prior to first dose and used as baseline.

Parameter	**Study Assessments Considered as Baseline**			**Baseline Used in Data Display**
	Screening	**Day 0**	**Day 1 (Pre-Dose)**	
Safety				
Laboratory	X			Screening
Vital Signs	X	X	X	Latest available pre-dose assessment
Weight, Height	X	X		Latest available pre-dose assessment
12-Lead ECG	X			Screening

Unless otherwise stated, if baseline data is missing no derivation will be performed and baseline will be set to missing. The mean of replicate assessments at any given time point will be used as the value for that time point.

Definition	**Reporting Details**
Change from Baseline	= Post-baseline Value – Baseline
% Change from Baseline	= 100 x [(Post-baseline Value – Baseline) / Baseline]

5.3. Other Considerations for Data Analyses and Data Handling Conventions

Other considerations for data analyses and data handling conventions are outlined in the appendices:

Section	Component
10.1	Appendix 1: Study Phases and Adverse Events
10.2	Appendix 2: Data Display Standards & Handling Conventions
10.3	Appendix 3: Derived and Transformed Data
10.4	Appendix 4: Reporting Standards for Missing Data
10.5	Appendix 5: Values of Potential Clinical Importance

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Study Population Analyses

The study population analyses will be based on the "Safety" population, and displayed separately for each group (Fasting or Fed), unless otherwise specified. Screen failures will be listed based on the "All participants" population.

Study population analyses including analyses of subject's disposition, protocol deviations, demographic and baseline characteristics and prior and concomitant medications will be based on GSK Core Data Standards. Details of planned study population data displays will be presented in Appendix 7: List of Data Displays of Full RAP.

6.2. Subject's Disposition

The number and percentage of subjects who completed the study as well as subjects who withdrew prematurely from the study will be summarized by completion status and reason for withdrawal. A listing of the subjects who withdrew from the study prematurely will be provided.

The number of subjects included in the safety population, and those included in the PK population will be summarized. Subjects who are excluded from the safety population and those who are excluded from PK population will be listed with the corresponding reason.

Subject's disposition summary will be displayed by "Total".

6.3. Protocol Deviations

A listing of the inclusion/exclusion criteria deviation record for all subjects with deviations will be provided. Other deviations will be noted as applicable, including use of prohibited concomitant medications during the study, incorrect study drug administration, and any other deviations deemed to have the potential for notably influencing the study results. A summary of important protocol deviations and by-subject listing of important protocol deviations will be provided.

The summary will be displayed by "Total".

6.4. Demographic and Baseline Characteristics

6.4.1. Demographic characteristics

Demographic characteristics listed below will be summarized either with descriptive statistics for continuous variables or with frequencies and percentages for categorical variables. A by-subject listing of these characteristics will be provided.

- Continuous variables: Age, Height, Weight, and Body mass index (BMI)
- Categorical Variables: Sex, Ethnicity and Geographic Ancestry

The summary will be displayed by "Total" for demographic characteristics.

6.4.2. Substance Use

Substance use, including smoking, alcohol consumption and drug abuse, will be summarized and listed.

The summary will be displayed by "Total".

6.4.3. Medical Conditions

The CRF texts for medical conditions will be coded using Medical Dictionary for Regulatory Activities (MedDRA), and will be reported using System Organ Class (SOC) and preferred term (PT). A by-subject listing of medical conditions will be provided.

6.5. Concomitant Medications

The CRF texts for concomitant medications will be coded using the WHO Drug Dictionary. A by-subject listing of concomitant medications will be provided.

7. SAFETY ANALYSES

The safety analyses will be based on the "Safety" population and displayed separately for each group (Fasting or Fed). Treatment A/B were assigned using safety assessment date or adverse event start date.

The analyses of safety data will be based on GSK Core Data Standards. The details of the planned safety displays are provided in Appendix 7: List of Data Displays of Full RAP.

7.1. Extent of Exposure

A by-subject listing of study treatment dosing information will be provided separately.

7.2. Adverse Events Analyses

Adverse events analyses include the analysis of adverse events (AEs) and Serious (SAEs).

Adverse events (AEs) will be coded using Medical Dictionary for Regulatory Activities (MedDRA) and grouped by system organ classes (SOCs) and preferred term (PT). AEs will be summarized and grouped by SOC and by PT within SOC. Results will be displayed in the order of decreasing frequency both across SOC and within SOC. In the summary of AEs, the incidence of AEs will be the number of subjects reporting AEs and not the number of AEs reported. Multiple occurrences of the same AE in one individual will be based on each treatment, so subjects will appear in more than one treatment category.

The following summaries and listings will be provided:

- Overview of AEs
- Summary of all AEs
- Summary of all adverse events by maximum intensity
- Summary of all drug-related AEs
- Summary of adverse events leading to withdrawals from study
- Summary of serious adverse events
- Summary of non-serious AEs by system organ class and preferred term
- Listing of all AEs
- Listing of serious adverse events (overall, fatal, non-fatal)
- Listing of all drug-related AEs

- Listing of adverse events leading to withdrawals from study
- Listing of subject numbers for individual adverse events
- Listing of hierarchical relationship of adverse event system organ class, preferred term and verbatim text

The summary will be displayed by treatment group A/B/Total (A: Paroxetine IR 40 mg GSKT tablet; B: Paroxetine IR 40 mg Mississauga tablet).

7.3. Clinical Laboratory Analyses

Laboratory evaluations include the analyses of haematology laboratory tests, chemistry laboratory tests and urinalysis.

The haematology and chemistry data will be summarized and listed separately. Each laboratory test will be summarized at every assessed time point. Parameter values and change from baseline will be summarized separately. The shift tables with respect to normal range will be used to summarize the abnormal laboratory values. By-subject listings of all laboratory data for subjects who had any value of potential clinical importance during the study will be provided. By-subject listings of laboratory values of potential clinical importance only will also be provided.

The urinalysis analysis data will be summarized at every assessed time point.

A listing of laboratory test normal ranges will be provided. A by-subject listing of all laboratory values (including haematology, chemistry and urinalysis analysis) outside the normal reference range will be provided.

The summary will be displayed overall for Screening and by treatment group A/B for post-baseline timepoint (A: Paroxetine IR 40 mg GSKT tablet; B: Paroxetine IR 40 mg Mississauga tablet).

7.4. Other Safety Analyses

The analyses of non-laboratory safety test results include vital signs, ECGs, pregnancy test and Columbia Suicide-Severity Rating Scale (C-SSRS).

7.4.1. Vital Signs

Each vital sign parameter at every assessed time point will be summarized. The change from baseline for each vital sign parameter will also be summarized.

A listing of all vital sign values for subjects who had any value of potential clinical importance during the study will be provided. A listing of vital sign values of potential clinical importance only will also be provided.

The summary will be displayed overall for Screening, Day 0 and Day 11, and by treatment group A/B (A: Paroxetine IR 40 mg GSKT tablet; B: Paroxetine IR 40 mg Mississauga tablet) for other time points.

7.4.2. 12-Lead Electrocardiogram

Each ECG parameter at every assessed time point will be summarized. A summary of mean change from baseline in ECG values will also be provided. A by-subject listing of all ECG values for subjects who had any value of potential clinical importance during the study will be provided. A listing of ECG values of potential clinical importance only will also be provided.

A summary of the number and percentage of subjects who had abnormal with/without clinically significant ECG findings will be displayed. A by-subject listing of all ECG data for subjects with an abnormal finding during the study will be provided. A by-subject listing of abnormal ECG findings only will also be provided.

The summary will be displayed overall for Screening and by treatment group A/B for post-baseline time points (A: Paroxetine IR 40 mg GSKT tablet; B: Paroxetine IR 40 mg Mississauga tablet).

7.4.3. Pregnancy

The pregnancy information will be summarized and a listing of all pregnancies will be provided.

7.4.4. Columbia Suicide-Severity Rating Scale (C-SSRS)

The C-SSRS information and possible suicidality-related adverse event will be listed.

8. PHARMACOKINETIC ANALYSES

All the pharmacokinetic analyses will be based on the "Pharmacokinetic" population, and displayed separately for each group (Fasting or Fed).

All the PK summary will be displayed by treatment group A/B (A: Two Paroxetine IR 40mg GSKT tablets; B: Two Paroxetine IR 40mg Mississauga tablets).

Pharmacokinetic analyses will be based on GSK data standards and statistical principles. Details of the planned pharmacokinetic displays will be provided in Appendix 7: List of Data Displays of Full RAP.

8.1. Endpoint / Variables

8.1.1. Drug Concentration Measures

Concentrations of Paroxetine in plasma will be summarized and listed. Standard summary statistics will be calculated (i.e. mean, standard deviation, median, minimum and maximum).

Individual plasma concentration-time profiles and median/mean profiles will be plotted. Each of the figures will contain one plot on the untransformed scale (i.e. a linear plot) and one plot on the log transformed scale (i.e. log-linear plot). Mean profiles will be plotted with standard deviation bar. Median profiles will be plotted with range bar.

Refer to Appendix 2: Data Display Standards & Handling Conventions (Section 10.2.3 Reporting Standards for Pharmacokinetic) for details.

8.1.2. Derived Pharmacokinetic Parameters

Pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using the currently supported version of WinNonlin 6.3 or higher version. All calculations of non-compartmental parameters will be based on actual sampling times. Pharmacokinetic parameters listed will be determined from the plasma concentration-time data for Paroxetine, as data permits.

Parameter	Parameter Description
$AUC_{0-\infty}$	Area under the concentration-time curve from time zero extrapolated to infinite time
$AUC_{(0-t)}$	Area under the concentration-time curve from administration extrapolated to the last time of quantifiable concentration, calculated as logarithm of trapezoid area.
C_{max}	The observed maximum drug concentration
T_{max}	Time to reach Cmax
$t_{1/2}$	Terminal elimination half-time
λ_z	Terminal elimination rate constant
CL/F	Oral clearance
Vd/F	Apparent volume of distribution
MRT	Mean residence time

For each of the derived parameters described above, except T_{max}, the following summary statistics will be calculated: arithmetic mean, 95% confidence interval for the arithmetic mean, standard deviation, median, minimum, maximum of untransformed data, geometric mean, 95% confidence interval for the geometric mean, standard deviation and coefficient of variation of logarithmically transformed data. For T_{max}, arithmetic mean, 95% confidence interval for the arithmetic mean, standard deviation, median, minimum and maximum will be calculated.

8.2. Statistical Analyses / Methods

After $\log_e$-transformation, $AUC_{(0-\infty)}$, $AUC_{(0-t)}$ and C_{max} will be analyzed, each separately, using mixed effect model. The model will include period and treatment as fixed effects, and participant as random effects. The covariance structure of the G matrix will be specified as unstructured, and the Kenward and Roger method for approximating the denominator degrees of freedom will be used.

Point estimates and their associated adjusted 90% confidence interval within A or B will be provided for the above mentioned PK parameters in log scale. All the data will be used to calculate for the within-treatment analysis.

Point estimates and their associated adjusted 90% confidence interval of difference between A and B will be provided for the above mentioned PK parameters in log scale.

If the 90% confidence interval of $AUC_{(0-\infty)}$, $AUC_{(0-t)}$ ($AUC_{(0-t)}$ only if $AUC_{(0-\infty)}$ can't be accurately determined) and Cmax fall in the range of 0.80-1.25, it can be stated that the two formulations are bioequivalent.

```
PROC MIXED data=PK;
   class seq subject trt Period;
   model log(PKParm)= seq trt Period/solution ddfm=satterth;
   random intercept/subject=subject(seq) type=un;
   lsmeans trt/cl diff alpha=0.1;
run;
```

The point estimates and their associated adjusted 90% confidence intervals will then be back-transformed.

Within subject coefficient of variation (%CVw) for transformed data will be calculated according to the following methods:

%CVw = SQRT(exp(mse) – 1) x 100

where mse is the residual error from the model for log-transformed data.

Unless otherwise specified, endpoints / variables defined in Section 8.1 will be summarised using descriptive statistics and listed, and BE population will be used for analysis.

Sensitivity analysis will be performed on BE population excluding the subjects with I/E violation.

9. REFERENCES

Schuirmann DJ. 1987. A comparison of the two one-sided tests procedure and the power approach for assessing the equivalence of average bioavailability. J Pharmacokinet and Biopharm, 15, 657-680.

10. APPENDICES

10.1. Appendix 1: Study Phases and Adverse Events

10.1.1. Treatment States for AE data

Treatment State	Definition
Onset Time Since First Dose (Days)	If Treatment Start Date > AE Onset Date, onset time since first dose= AE Onset Date - Treatment Start Date If Treatment Start Date ≤ AE Onset Date, onset time since first dose = AE Onset Date - Treatment Start Date +1 Missing otherwise
Duration (Days)	AE Resolution Date – AE Onset Date + 1
Drug-related	If relationship is marked 'YES' on eCRF or value is missing

NOTES:

- If AE onset is during one period and worsens during a later period it would be counted in both periods.

10.2. Appendix 2: Data Display Standards & Handling Conventions

10.2.1. Reporting Process

Software
• The currently supported versions of SAS software will be used.
Analysis Datasets
• Analysis datasets will be created according to CDISC standards (SDTM IG Version 3.2 & ADaM IG Version 1.0).
Generation of RTF Files
• Both RTF and bookmarked PDF files will be generated.

10.2.2. Reporting Standards

General

• The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated (IDSL Standards Location: https://spope.gsk.com/sites/IDSLLibrary/SitePages/Home.aspx):
  • 4.03 to 4.23: General Principles
  • 5.01 to 5.08: Principles Related to Data Listings
  • 6.01 to 6.11: Principles Related to Summary Tables
  • 7.01 to 7.13: Principles Related to Graphics

Formats
• All data will be reported according to the actual treatment the subject received unless otherwise stated. • GSK IDSL Statistical Principles (5.03 & 6.06.3) for decimal places (DP's) will be adopted for reporting of data based on the raw data collected, unless otherwise stated. • Numeric data will be reported at the precision collected on the eCRF. • The reported precision from non eCRF sources will follow the IDSL statistical principles but may be adjusted to a clinically interpretable number of DP's.
Planned and Actual Time

• Reporting for tables, figures and formal statistical analyses:
  • Planned time relative to dosing will be used in figures, summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated.
  • The impact of any major deviation from the planned assessment times and/or scheduled visit days on the analyses and interpretation of the results will be assessed as appropriate.
• Reporting for Data Listings:
  • Planned and actual time relative to study drug dosing will be shown in listings (Refer to IDSL Statistical Principle 5.05.1).
  • Unscheduled or unplanned readings will be presented within the subject's listings.

Unscheduled Visits
• Unscheduled visits will not be included in by-visit summary tables and figures. • All unscheduled visits will be included in listings.

Descriptive Summary Statistics	
Continuous Data	Refer to IDSL Statistical Principle 6.06.1
Categorical Data	N, n, frequency, %
Graphical Displays	
• Refer to IDSL Statistical Principals 7.01 to 7.13.	

10.2.3. Reporting Standards for Pharmacokinetic

Pharmacokinetic Concentration Data	
PC WinNonlin (WNL) File	PC WNL file (CSV format) for the non compartmental analysis by Clinical Pharmacology Modelling and Simulation function will be created according to current working practices. Note: Concentration values will be imputed as per GUI_51487
Descriptive Summary Statistics, Graphical Displays and Listings	Refer to IDSL PK Display Standards. Refer to IDSL Statistical Principle 6.06.1. Note: Concentration values will be imputed as per GUI_51487 for descriptive summary statistics/analysis and summarized graphical displays only.
Pharmacokinetic Parameter Derivation	
PK Parameter to be Derived by Clinical Pharmacology Modelling and Simulation team	All the PK parameters will be derived by the Clinical Pharmacology Modelling and Simulation team
Pharmacokinetic Parameter Data	
Descriptive Summary Statistics, Graphical Displays and Listings	Refer to IDSL PK Display Standards. N, n, arithmetic mean, median, min, max, SD, 95% CI of arithmetic mean will be provided for untransformed data. For log-transformed data, N, n, geometric mean, 95% CI of geometric mean, standard deviation (SD) and between subject coefficient of variation (CVb (%)) of log-transformed data will be reported. $CVb\ (\%) = SQRT(\exp(SD^2)-1) * 100$ Where SD is the standard deviation of the $\log_e$-transformed data.
Parameters Not Being Log Transformed	T_{max}

10.3. Appendix 3: Derived and Transformed Data

10.3.1. General

Multiple Measurements at One Analysis Time Point
• Mean of the measurements will be calculated and used in any derivation of summary statistics but if listed, all data will be presented. • Participants having both High and Low values for Normal Ranges at any post-baseline visit for safety parameters will be counted in both the High and Low categories of "Any visit post-baseline" row of related summary tables. This will also be applicable to relevant Potential Clinical Importance summary tables.
Study Day

• Calculated as the number of days from First Dose Date:
  • Ref Date = Missing → Study Day = Missing
  • Ref Date < First Dose Date → Study Day = Ref Date – First Dose Date
  • Ref Data ≥ First Dose Date → Study Day = Ref Date – (First Dose Date) + 1

10.3.2. Study Population

Age
GSK standard IDSL algorithms will be used for calculating age where birth date is imputed as: • Any subject with a missing day will have this imputed as day '15'. • Any subject with a missing date and month will have this imputed as '30th June'. • Birth date will be presented in listings as 'YYYY'.
Body Mass Index (BMI)
• Calculated as Weight (kg) / [Height (m)2]

10.3.3. Safety

Laboratory Parameters
• If a laboratory value which is expected to have a numeric value for summary purposes, has a non-detectable level reported in the database, where the numeric value is missing, but typically a character value starting with '<x' or '>x' (or indicated as less than x or greater than x in the comment field) is present, the number of significant digits in the observed values will be used to determine how much to add or subtract in order to impute the corresponding numeric value. • Example 1: 2 Significant Digits = '< x ' becomes x – 0.01 • Example 2: 1 Significant Digit = '> x' becomes x + 0.1 • Example 3: 0 Significant Digits = '< x' becomes x – 1

10.3.4. Pharmacokinetic

PK
• Plasma sample analysis will be carried out by Bioanalytical Service at Wuxi AppTec. Paroxetine plasma concentrations will be determined using the currently validated methodology. The actual sampling times, if different from protocol, will be used in the PK calculations. Please refer to the rules in Section 10.4.1 for the plasma concentrations below Limit of quantification (LOQ). • Paroxetine plasma concentration-time data will be analyzed by non-compartmental methods with WinNonlin 6.3 or above and derived PK parameters will be summarised and listed. Derived Pharmacokinetic parameters will be summarized by treatment group. Mean, Median, Min, Max, SD, GeoMean, log SD, CVb, 95% CI will be provided; Individual and mean, median PK concentration-time curves will be provided.

10.4. Appendix 4: Reporting Standards for Missing Data

10.4.1. Premature Withdrawals

Element	Reporting Detail
General	• Subject study completion (i.e. as specified in the protocol) was defined as completion of all phases of the study including the follow-up visit. • Withdrawn subjects will not be replaced in the study. • All participants who withdraw prematurely from the study will be documented and the reason for their withdrawal recorded in the final Clinical Pharmacology Study Report (CPSR). • All available data from participants who were withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified. • In the event that the study is prematurely discontinued, all available data will be listed and a review carried out by the study team to assess which statistical analyses are still considered appropriate.

10.4.2. Handling of Missing Data

Element	Reporting Detail
General	• Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument: o These data will be indicated by the use of a "blank" in subject listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table. o Answers such as "Not applicable" and "Not evaluable" are not considered to be missing data and should be displayed as such.
Outliers	• Any participants excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report.
PK	• Concentrations which are below the LLQ ("lower limit of quantification" for the analyte in question) are listed as NQ in the raw concentration data provided by DMPK. Several derived variables exist for the imputation of these concentrations. • The following variables exist in the PKCNC dataset for different imputations of the raw concentration data; PCORRES: Original result PCSTRESN: Original result in standard units PCSTIMPN: Imputed result for use in the calculation of summary statistics PCSTIMSN: Imputed result for individual concentration plots PCWNLN: Imputed result for use in WinNonlin analysis • The imputation of NQs for variables in the PKCNC file will be based on that defined in GUI_51487, under the section "How to Handle Values Below the Quantification Limit". A brief summary is provided in the table below.

Element	Reporting Detail

Variable	Leading NQ	Single NQ between measurable concentrations	More than one consecutive NQ between measurable concentrations	Measurable concentrations after more than one consecutive mid-profile NQ*	Trailing NQ (consecutive NQs in the tail)
PCSTIMPN	0	NULL	0	NULL	0
PCSTIMSN	0	NULL	0	No Action	NULL
PCWNLN	0	NULL	NULL	NULL	NULL

* a mid-profile NQ is defined as any NQ where measurable concentrations exist both before and after that NQ in the profile

10.4.2.1. Handling of Missing and Partial Dates

Element	Reporting Detail
General	• Partial dates will be displayed as captured in subject listing displays.
Adverse Events	• The eCRF allows for the possibility of partial dates (i.e., only month and year) to be recorded for AE start and end dates; that is, the day of the month may be missing. • Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing. • The recorded partial date will be displayed in the listings
Concomitant Medications/ Medical History	• Partial dates for any concomitant medications recorded in the CRF will not be imputed. • The recorded partial date will be displayed in listings.

10.5. Appendix 5: Values of Potential Clinical Importance

10.5.1. Laboratory Values

Haematology				
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (>x)**
Hematocrit	Ratio of 1	Male	0.03	0.54
		Female	0.04	0.54
Haemoglobin	g/L	Male	110	180
		Female	100	170
Red Blood Cell Count	$x10^{12}$/L	Male	4.5	5.5
		Female	4	5
Platelet Count	$x10^{9}$/ L		80	400

Clinical Chemistry				
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (>x)**
Albumin	g/L		30	
Calcium	mmol/L		2	2.75
Creatinine	umol/L			133
Glucose	mmol/L		3	9
Potassium	mmol/L		3	5.5
Sodium	mmol/L		130	150
ALP	IU/L		20	200
ALT/SGPT	U/L	High		≥ 2x ULN
AST/SGOT	U/L	High		≥ 2x ULN

10.5.2. ECG

ECG Parameter	Units	Clinical Concern Range	
		Lower	Upper
Absolute			
Heart Rate	bpm	< 50	> 110
Absolute QT Interval	msec		> 400
Absolute QTc Interval	msec		> 450
Absolute PR Interval	msec	< 110	> 220
Absolute QRS Interval	msec	<60	>120
Change from Baseline			
Increase from Baseline QTc	msec		>10

10.5.3. Vital Signs

Vital Sign Parameter (Absolute)	Units	Clinical Concern Range	
		Lower	Upper
Systolic Blood Pressure	mmHg	< 85	> 160
Diastolic Blood Pressure	mmHg	< 50	> 100

10.6. Appendix 6: Abbreviations & Trade Marks

10.6.1. Abbreviations

Abbreviation	Description
AE	adverse event
ALP	alkaline phosphatase
ALT	alanine aminotransferase
$AUC_{0-\infty}$	Area under the concentration-time curve from time zero extrapolated to infinite time
AUC_{0-t}	Area under the concentration-time curve from administration extrapolated to the last time of quantifiable concentration
BE	bioequivalence
BMI	body mass index
BQL	Below quantifiable level
CFDA	China Food and Drug Administration
CL/F	Oral clearance
Cmax	The observed maximum serum drug concentration
CONSORT	Consolidated Standards of Reporting Trials
CPMS	Clinical Pharmacology Modeling and Simulation
CRF	case report form
C-SSRS	Columbia Suicide Severity Rating Scale
DC	direct compression
ECG	Electrocardiogram
GSK	GlaxoSmithKline
GSKT	GlaxoSmithKline Tianjin
hCG	human chorionic gonadotropin
ICF	informed consent form
IDSL	Integral Data Standard Library
IEC	Independent Ethics Committees
IR	immediate release
IRB	Institutional Review Boards
MAOIs	monoamine oxidase inhibitors
MDD	major depressive disorder
MRT	mean residence time
MSDS	Material Safety Data Sheet
OCD	obsessive compulsive disorder
OTC	over the counter
PD	panic disorder
PK	pharmacokinetic
PSRAE	Possible Suicidality-related Adverse Event
PT	preferred term
QTcB	QT interval corrected for heart rate according to Bazett's formula
QTcF	QT interval corrected for heart rate according to Fridericia's formula
RAP	Reporting and Analysis Plan
SAD	social anxiety disorder

Abbreviation	Description
SAE	serious adverse event
SIADH	syndrome of inappropriate antidiuretic hormone secretion
SOA	Schedule of Activities
SOC	system organ class
SRM	Study Reference Manual
SSRI	selective serotonin reuptake inhibitor
SUSAR	suspected unexpected serious adverse reactions
$t_{1/2}$	Terminal elimination half-time
T_{max}	Time to reach Cmax
TSKF	Tianjin SmithKline & French
ULN	upper limit of normal
Vd/F	Apparent volume of distribution
WG	wet granulation
λ_z	Terminal elimination rate constant

10.6.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
HARP
RANDALL

Trademarks not owned by the GlaxoSmithKline Group of Companies
SAS
WinNonlin

10.7. Appendix 7: List of Data Displays

10.7.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.n	1.1 to 1.n
Safety	2.1 to 2.n	2.1 to 2.n
Pharmacokinetic	3.1 to 3.n	3.1 to 3.n
Section	**Listings**	
ICH Listings	1 to x	
Other Listings	y to z	

10.7.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required example mock-up displays provided in Appendix 8: Example Mock Shells for Data Displays.

Section	Figure	Table	Listing
Study Population	POP_Fn	POP_Tn	POP_Ln
Safety	SAFE_Fn	SAFE_Tn	SAFE_Ln
Pharmacokinetic	PK_Fn	PK_Tn	PK_Ln

NOTES:

- Non-Standard displays are indicated in the 'IDSL / Example Shell' or 'Programming Notes' column as '[Non-Standard] + Reference.'

10.7.3. Deliverables

Delivery [Priority] [1]	Description
SAC [1]	Final Statistical Analysis Complete

NOTES:

1. Indicates priority (i.e. order) in which displays will be generated for the reporting effort

10.7.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.1.	Safety	ES1	Summary of Subject Disposition - Fed		SAC [1]
1.2.	Safety	ES1	Summary of Subject Disposition - Fasting		SAC [1]
1.3.	All Participants	ES6	Summary of Screening Failures - Fed		SAC [1]
1.4.	All Participants	ES6	Summary of Screening Failures - Fasting		SAC [1]
Protocol Deviation					
1.5.	Safety	DV1A	Summary of Important Protocol Deviations - Fed		SAC [1]
1.6.	Safety	DV1A	Summary of Important Protocol Deviations - Fasting		SAC [1]
1.7.	Safety	DV1A	Summary of Other Protocol Deviation - Fed		SAC [1]
1.8.	Safety	DV1A	Summary of Other Protocol Deviation - Fasting		SAC [1]
1.9.	Safety	DV1A	Summary of Inclusion/Exclusion Criteria Deviations - Fed		SAC [1]
1.10.	Safety	IE1	Summary of Inclusion/Exclusion Criteria Deviations - Fasting		SAC [1]
Population Analysed					
1.11.	All Participants	POP_T1	Summary of Study Populations - Fed		SAC [1]
1.12.	All Participants	POP_T1	Summary of Study Populations - Fasting		SAC [1]
Demographic and Baseline Characteristics					
1.13.	Safety	DM1	Summary of Demographic Characteristics - Fed		SAC [1]
1.14.	Safety	DM1	Summary of Demographic Characteristics - Fasting		SAC [1]
1.15.	Safety	DM5	Summary of Race and Racial Combinations - Fed		SAC [1]
1.16.	Safety	DM5	Summary of Race and Racial Combinations - Fasting		SAC [1]

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Substance Use					
1.17.	Safety	SU1	Summary of Substance Use - Fed		SAC [1]
1.18.	Safety	SU1	Summary of Substance Use - Fasting		SAC [1]

10.7.5. Safety Tables

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events (AEs)					
2.1.	Safety	AE13	Adverse Event Overview - Fed		SAC [1]
2.2.	Safety	AE13	Adverse Event Overview - Fasting		SAC [1]
2.3.	Safety	CP_AE1x	Summary of All Adverse Events - Fed		SAC [1]
2.4.	Safety	CP_AE1x	Summary of All Adverse Events - Fasting		SAC [1]
2.5.	Safety	CP_AE1x	Summary of all Adverse Events by Maximum Intensity - Fed		SAC [1]
2.6.	Safety	CP_AE1x	Summary of all Adverse Events by Maximum Intensity - Fasting		SAC [1]
2.7.	Safety	CP_AE1x	Summary of Drug-Related Adverse Events - Fed		SAC [1]
2.8.	Safety	CP_AE1x	Summary of Drug-Related Adverse Events - Fasting		SAC [1]
2.9.	Safety	CP_AE1x	Summary of Adverse Events Leading to Withdrawals from Study - Fed		SAC [1]
2.10.	Safety	CP_AE1x	Summary of Adverse Events Leading to Withdrawals from Study - Fasting		SAC [1]
2.11.	Safety	CP_AE1x	Summary of Serious Adverse Events - Fed		SAC [1]

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.12.	Safety	CP_AE1x	Summary of Serious Adverse Events - Fasting		SAC [1]
2.13.	Safety	CP_AE1x	Summary of Non-Serious Adverse Events - Fed		SAC [1]
2.14.	Safety	CP_AE1x	Summary of Non-Serious Adverse Events - Fasting		SAC [1]
Laboratory: Chemistry					
2.15.	Safety	LB1	Summary of Change from Baseline in Chemistry Laboratory Values - Fed		SAC [1]
2.16.	Safety	LB1	Summary of Change from Baseline in Chemistry Laboratory Values - Fasting		SAC [1]
2.17.	Safety	LB2	Summary of Chemistry Laboratory Values Relative to Potential Clinical Importance Criteria, Day 16 or Early Withdrawal - Fed		SAC [1]
2.18.	Safety	LB2	Summary of Chemistry Laboratory Values Relative to Potential Clinical Importance Criteria, Day 16 or Early Withdrawal - Fasting		SAC [1]
2.19.	Safety	LB4	Summary of Chemistry Laboratory Shifts From Baseline with Respect to the Normal Range - Fed		SAC [1]
2.20.	Safety	LB4	Summary of Chemistry Laboratory Shifts From Baseline with Respect to the Normal Range - Fasting		SAC [1]
Laboratory: Hematology					
2.21.	Safety	LB1	Summary of Change from Baseline in Hematology Laboratory Values - Fed		SAC [1]
2.22.	Safety	LB1	Summary of Change from Baseline in Hematology Laboratory Values - Fasting		SAC [1]
2.23.	Safety	LB2	Summary of Hematology Laboratory Values Relative to Potential Clinical Importance Criteria, Day 16 or Early Withdrawal - Fed		SAC [1]

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.24.	Safety	LB2	Summary of Hematology Laboratory Values Relative to Potential Clinical Importance Criteria, Day 16 or Early Withdrawal - Fasting		SAC [1]
2.25.	Safety	LB4	Summary of Hematology Laboratory Shifts From Baseline with Respect to the Normal Range - Fed		SAC [1]
2.26.	Safety	LB4	Summary of Hematology Laboratory Shifts From Baseline with Respect to the Normal Range - Fasting		SAC [1]
Laboratory: Urinalysis					
2.27.	Safety	LB1	Summary of Urinalysis Dipstick Results - Fed		SAC [1]
2.28.	Safety	LB1	Summary of Urinalysis Dipstick Results - Fasting		SAC [1]
2.29.	Safety	LB4	Summary of Urinalysis Laboratory Shifts From Baseline with Respect to the Normal Range - Fed		SAC [1]
2.30.	Safety	LB4	Summary of Urinalysis Laboratory Shifts From Baseline with Respect to the Normal Range - Fasting		SAC [1]
ECG					
2.31.	Safety	EG1	Summary of ECG Findings - Fed		SAC [1]
2.32.	Safety	EG1	Summary of ECG Findings - Fasting		SAC [1]
2.33.	Safety	EG2	Summary of ECG Values - Fed		SAC [1]
2.34.	Safety	EG2	Summary of ECG Values - Fasting		SAC [1]
2.35.	Safety	EG2	Summary of Mean Change from Baseline in ECG Values - Fed		SAC [1]
2.36.	Safety	EG2	Summary of Mean Change from Baseline in ECG Values - Fasting		SAC [1]
2.37.	Safety	EG1	Summary of the Number and Percentage of Subjects Who Had Abnormal ECG Findings - Fed		SAC [1]
2.38.	Safety	EG1	Summary of the Number and Percentage of Subjects Who Had Abnormal ECG Findings - Fasting		SAC [1]

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Vital Signs					
2.39.	Safety	VS1	Summary of Vital Signs - Fed		SAC [1]
2.40.	Safety	VS1	Summary of Vital Signs - Fasting		SAC [1]
2.41.	Safety	VS1	Summary of Change from Baseline in Vital Signs - Fed		SAC [1]
2.42.	Safety	VS1	Summary of Change from Baseline in Vital Signs - Fasting		SAC [1]
Pregnancy					
2.43.	Safety	Standard	Summary of Pregnancy - Fed		SAC [1]
2.44.	Safety	Standard	Summary of Pregnancy - Fasting		SAC [1]

- The requirements for each display (i.e. IDSL, ICH, FDAAA etc) specified in the programming notes may be retained, all other red reference notes should be deleted.
- Select appropriate standard based on study design (i.e. parallel vs cross-over), when applicable.
- Suggested IDSL shells are noted in the third column, but other IDSL shells may be used, as appropriate
- The ADaM datasets for the Core Study Population/Safety displays can be found in the IDSL Library under Reference →Statistical Displays →ADaM Datasets for Core RAP Displays

10.7.6. Pharmacokinetic Tables

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK Concentration Data					
3.1.	PK	PKCT1	Summary of Paroxetine Plasma Pharmacokinetic Concentration-Time Data - Fed		SAC [1]
3.2.	PK	PKCT1	Summary of Paroxetine Plasma Pharmacokinetic Concentration-Time Data - Fasting		SAC [1]
PK Parameter Data					
3.3.	PK	PKPT1	Summary of Derived Paroxetine Plasma Pharmacokinetic Parameters - Fed		SAC [1]
3.4.	PK	PKPT1	Summary of Derived Paroxetine Plasma Pharmacokinetic Parameters - Fasting		SAC [1]
3.5.	PK	PKPT3	Summary of Log-Transformed Derived Paroxetine Plasma Pharmacokinetic Parameters - Fed		SAC [1]
3.6.	PK	PKPT3	Summary of Log-Transformed Derived Paroxetine Plasma Pharmacokinetic Parameters - Fasting		SAC [1]
3.7.	PK	Non-Standard	Summary of Results from Statistical Analysis of Derived Paroxetine Plasma Pharmacokinetic Parameters to Assess Bioequivalence - Fed		SAC [1]
3.8.	PK	Non-Standard	Summary of Results from Statistical Analysis of Derived Paroxetine Plasma Pharmacokinetic Parameters to Assess Bioequivalence - Fasting		SAC [1]
3.9.	PK	Non-Standard	Summary of Results from Statistical Analysis of Derived Paroxetine Plasma Pharmacokinetic Parameters to Assess Bioequivalence (Sensitivity Analysis) - Fed		
3.10.	PK	Non-Standard	Summary of Results from Statistical Analysis of Derived Paroxetine Plasma Pharmacokinetic Parameters to Assess Bioequivalence (Sensitivity Analysis) - Fasting		

10.7.7. Pharmacokinetic Figures

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK Concentration Data					
3.1.	PK	PKCF1P	Individual Paroxetine Plasma Concentration-Time Plot by Subject (Linear and Semi-Log) - Fed		SAC [1]
3.2.	PK	PKCF1P	Individual Paroxetine Plasma Concentration-Time Plot by Subject (Linear and Semi-Log) - Fasting		SAC [1]
3.3.	PK	PKCF2	Mean (+SD) Paroxetine Plasma Concentration-Time Plots by Visit (Linear and Semi-log) - Fed		SAC [1]
3.4.	PK	PKCF2	Mean (+SD) Paroxetine Plasma Concentration-Time Plots by Visit (Linear and Semi-log) - Fasting		SAC [1]
3.5.	PK	PKCF2	Median (Range) Paroxetine Plasma Concentration-Time Plots by Visit (Linear and Semi-log) - Fed		SAC [1]
3.6.	PK	PKCF2	Median (Range) Paroxetine Plasma Concentration-Time Plots by Visit (Linear and Semi-log) - Fasting		SAC [1]

10.7.8. ICH Listings

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.	All Participants	ES7	Listing of Reasons for Screening Failure - Fed		SAC [1]
2.	All Participants	ES7	Listing of Reasons for Screening Failure - Fasting		SAC [1]
3.	Safety	ES2	Listing of Reasons for Study Withdrawal - Fed		SAC [1]
4.	Safety	ES2	Listing of Reasons for Study Withdrawal - Fasting		SAC [1]
Protocol Deviations					
5.	Safety	DV2	Listing of Important Protocol Deviations - Fed		SAC [1]
6.	Safety	DV2	Listing of Important Protocol Deviations - Fasting		SAC [1]
7.	Safety	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations - Fed		SAC [1]
8.	Safety	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations - Fasting		SAC [1]
9.	Safety	DV2	Listing of Other Protocol Deviations - Fed		SAC [1]
10.	Safety	DV2	Listing of Other Protocol Deviations - Fasting		SAC [1]
Populations Analysed					
11.	All Participants	Standard	Listing of Study Population - Fed		SAC [1]
12.	All Participants	Standard	Listing of Study Population - Fasting		SAC [1]

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Demographic and Baseline Characteristics					
13.	Safety	DM4	Listing of Demographic Characteristics - Fed		SAC [1]
14.	Safety	DM4	Listing of Demographic Characteristics - Fasting		SAC [1]
15.	Safety	DM10	Listing of Race and Racial Combinations - Fed		SAC [1]
16.	Safety	DM10	Listing of Race and Racial Combinations - Fasting		SAC [1]
Substance Use					
17.	Safety	SU2	Listing of Substance Use - Fed		SAC [1]
18.	Safety	SU2	Listing of Substance Use - Fasting		SAC [1]
Medical Conditions					
19.	Safety	MH3	Listing of Medical Conditions - Fed		SAC [1]
20.	Safety	MH3	Listing of Medical Conditions - Fasting		SAC [1]
Prior and Concomitant Medications					
21.	Safety	CP_CM5	Listing of Concomitant Medications - Fed		SAC [1]
22.	Safety	CP_CM5	Listing of Concomitant Medications - Fasting		SAC [1]
Exposure and Treatment Compliance					
23.	Safety	EX4	Listing of Exposure and Overdose - Fed		SAC [1]
24.	Safety	EX4	Listing of Exposure and Overdose - Fasting		SAC [1]
Adverse Events					
25.	Safety	CP_AE9	Listing of All Adverse Events - Fed		SAC [1]
26.	Safety	CP_AE9	Listing of All Adverse Events - Fasting		SAC [1]
27.	Safety	CP_AE9a	Listing of Serious Adverse Events (Overall) - Fed		SAC [1]
28.	Safety	CP_AE9a	Listing of Serious Adverse Events (Overall) - Fasting		SAC [1]

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
29.	Safety	CP_AE9a	Listing of Serious Adverse Events (Fatal) - Fed		SAC [1]
30.	Safety	CP_AE9a	Listing of Serious Adverse Events (Fatal) - Fasting		SAC [1]
31.	Safety	CP_AE9a	Listing of Serious Adverse Events (Non-Fatal) - Fed		SAC [1]
32.	Safety	CP_AE9a	Listing of Serious Adverse Events (Non-Fatal) - Fasting		SAC [1]
33.	Safety	CP_AE9	Listing of All Drug-Related Adverse Events - Fed		SAC [1]
34.	Safety	CP_AE9	Listing of All Drug-Related Adverse Events - Fasting		SAC [1]
35.	Safety	CP_AE9	Listing of Adverse Events Leading to Withdrawal from Study - Fed		SAC [1]
36.	Safety	CP_AE9	Listing of Adverse Events Leading to Withdrawal from Study - Fasting		SAC [1]
37.	Safety	AE7	Listings of Subject Numbers for Individual Adverse Events - Fed		SAC [1]
38.	Safety	AE7	Listings of Subject Numbers for Individual Adverse Events - Fasting		SAC [1]
39.	Safety	AE2	Listing of Hierarchical Relationship of Adverse Event System Organ Class, Preferred Term and Verbatim Text - Fed		SAC [1]
40.	Safety	AE2	Listing of Hierarchical Relationship of Adverse Event System Organ Class, Preferred Term and Verbatim Text - Fasting		SAC [1]
All Laboratory					
41.	Safety	LB6	Listing of Clinical Chemistry Abnormalities of Potential Clinical Importance - Fed		SAC [1]
42.	Safety	LB6	Listing of Clinical Chemistry Abnormalities of Potential Clinical Importance - Fasting		SAC [1]
43.	Safety	LB6	Listing of Hematology Abnormalities of Potential Clinical Importance - Fed		SAC [1]
44.	Safety	LB6	Listing of Hematology Abnormalities of Potential Clinical Importance - Fasting		SAC [1]

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
45.	Safety	LB6	Listing of All Clinical Chemistry Data for Subjects with Potential Clinical Abnormalities - Fed		SAC [1]
46.	Safety	LB6	Listing of All Clinical Chemistry Data for Subjects with Potential Clinical Abnormalities - Fasting		SAC [1]
47.	Safety	LB6	Listing of All Hematology Data for Subjects with Potential Clinical Abnormalities - Fed		SAC [1]
48.	Safety	LB6	Listing of All Hematology Data for Subjects with Potential Clinical Abnormalities - Fasting		SAC [1]
49.	Safety	LB13	Listing of Laboratory Tests and Associated Reference Ranges		SAC [1]
50.	Safety	LB6	Listing of All Laboratory Values Outside the Normal Reference Range - Fed		SAC [1]
51.	Safety	LB6	Listing of All Laboratory Values Outside the Normal Reference Range - Fasting		SAC [1]
ECG					
52.	Safety	CP_EG4	Listing of ECG Values of Potential Clinical Importance - Fed		SAC [1]
53.	Safety	CP_EG4	Listing of ECG Values of Potential Clinical Importance - Fasting		SAC [1]
54.	Safety	CP_EG4	Listing of All ECG Values for Subjects with a Value of Potential Clinical Importance - Fed		SAC [1]
55.	Safety	CP_EG4	Listing of All ECG Values for Subjects with a Value of Potential Clinical Importance - Fasting		SAC [1]
56.	Safety	CP_EG6	Listing of Abnormal ECG findings - Fed		SAC [1]
57.	Safety	CP_EG6	Listing of Abnormal ECG findings - Fasting		SAC [1]
58.	Safety	CP_EG6	Listing of ECG Findings for Subjects with a Value of Abnormal Finding - Fed		SAC [1]
59.	Safety	CP_EG6	Listing of ECG Findings for Subjects with a Value of Abnormal Finding - Fasting		SAC [1]

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Vital Signs					
60.	Safety	CP_VS5	Listing of Vital Sign Values of Potential Clinical Importance - Fed		SAC [1]
61.	Safety	CP_VS5	Listing of Vital Sign Values of Potential Clinical Importance - Fasting		SAC [1]
62.	Safety	CP_VS5	Listing of All Vital Sign Values for Subjects with a Value of Potential Clinical Importance - Fed		SAC [1]
63.	Safety	CP_VS5	Listing of All Vital Sign Values for Subjects with a Value of Potential Clinical Importance - Fasting		SAC [1]
Pregnancy					
64.	Safety	Non-Standard	Listing of Pregnancy - Fed		SAC [1]
65.	Safety	Non-Standard	Listing of Pregnancy - Fasting		SAC [1]
Liver Event					
66.	Safety	LIVER5	Listing of Liver Monitoring/Stopping Event Reporting - Fed		SAC [1]
67.	Safety	LIVER5	Listing of Liver Monitoring/Stopping Event Reporting - Fasting		SAC [1]
68.	Safety	LIVER6	Listing of Liver Stopping Event Information for RUCAM Score - Fed		SAC [1]
69.	Safety	LIVER6	Listing of Liver Stopping Event Information for RUCAM Score - Fasting		SAC [1]
70.	Safety	SAFE_L2	Listing of Medical Conditions at Onset of Liver Event - Fed		SAC [1]
71.	Safety	SAFE_L2	Listing of Medical Conditions at Onset of Liver Event - Fasting		SAC [1]
72.	Safety	LIVER7	Listing of Liver Biopsy Details - Fed		SAC [1]
73.	Safety	LIVER7	Listing of Liver Biopsy Details - Fasting		SAC [1]
74.	Safety	LIVER8	Listing of Liver Imaging Details - Fed		SAC [1]
75.	Safety	LIVER8	Listing of Liver Imaging Details - Fasting		SAC [1]

10.7.9. Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK Concentration Data					
76.	PK	PK08	Listing of Paroxetine Plasma Concentration-Time Data - Fed		SAC [1]
77.	PK	PK08	Listing of Paroxetine Plasma Concentration-Time Data - Fasting		SAC [1]
78.	PK	Non-standard	Listing of Paroxetine Plasma Concentration Data (Transposed) - Fed		SAC [1]
79.	PK	Non-standard	Listing of Paroxetine Plasma Concentration Data (Transposed) - Fasting		SAC [1]
PK Parameter Data					
80.	PK	PK13	Listing of Derived Paroxetine Plasma Pharmacokinetic Parameters - Fed		SAC [1]
81.	PK	PK13	Listing of Derived Paroxetine Plasma Pharmacokinetic Parameters - Fasting		SAC [1]
C-SSRS					
82.	Safety	PSRAE2	Listing of Possible Suicidality-Related Adverse Event Data: Event and Description (Section 1-Section 2) - Fed		SAC [1]
83.	Safety	PSRAE2	Listing of Possible Suicidality-Related Adverse Event Data: Event and Description (Section 1-Section 2) - Fasting		SAC [1]
84.	Safety	PSRAE2	Listing of C-SSRS Suicidal Ideation and Behaviour Data - Fed		SAC [1]
85.	Safety	PSRAE2	Listing of C-SSRS Suicidal Ideation and Behaviour Data - Fasting		SAC [1]

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Meals					
86.	Safety	CP_ML1x	Listing of Dosing Times, Meal Start and End Times on Fed Treatment Days - Fed		SAC [1]
87.	Safety	CP_ML1x	Listing of Dosing Times, Meal Start and End Times on Fed Treatment Days - Fasting		SAC [1]

10.8. Appendix 8: Example Mock Shells for Data Displays

The data display shells are contained in separate documents which are available on request.