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

Title	:	Reporting and Analysis Plan for 204678 A single centre, open-label, parallel-group, single oral dose study to evaluate the pharmacokinetic, safety and tolerability of Pyrimethamine in healthy Japanese and Caucasian male subjects
Compound Number	:	GR99352
Effective Date	:	15-SEP-2017

Description :

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 204678.
- This RAP is intended to describe the Pharmacokinetic (PK) and safety analyses required for the study.
- This RAP will be provided to the study team members to convey the content of the Statistical Analysis Complete (SAC) deliverable.

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1. REPORTING & ANALYSIS PLAN SYNOPSIS

Overview	Key Elements of the RAP
Purpose	• The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 204678.
Protocol	• This RAP is based on the original protocol Dated:19/JUL/2017 of study204678 (GSK Document Number.: 2017N318316_00).
Primary Objective	• To investigate PK following a single oral dose of Pyrimethamine 50 mg in fasted healthy Japanese male subjects.
Primary Endpoint	• Cmax, AUC(0-t), AUC(0-inf), AUC(0-24), tmax, t1/2, CL/F, Vd/F from the plasma concentrations of Pyrimethamine in healthy Japanese male subjects, as data permit.
Study Design	• This study will be a single centre, open-label, parallel-group, single oral dose study to evaluate the pharmacokinetic (PK), safety and tolerability of Pyrimethamine in healthy Japanese and Caucasian male subjects. • Sufficient Japanese and Caucasian healthy male volunteer subjects will be enrolled such that 6 subjects of each population complete dosing and critical assessments.
Analysis Populations	• Screened: Consisting of all participants screened in the study. • Screening Failure: Participants who sign the ICF in the study but are never subsequently administered study treatment. • Safety: All participants who take at least one dose of study treatment. • Pharmacokinetic: This population is defined as all participants administered at least one dose of study treatment and who have PK sample taken and analyzed.
Hypothesis	• The objectives of this study are to evaluate safety and tolerability of Pyrimethamine and to estimate Pyrimethamine pharmacokinetic parameters in healthy male Japanese and Caucasian subjects. No formal statistical hypotheses will be tested. Descriptive statistics will be used to assess safety and tolerability objectives. An estimation approach will be used to address the pharmacokinetic study objectives, where point estimates and corresponding 95% confidence intervals will be constructed, unless otherwise stated.

Overview	Key Elements of the RAP
Pharmacokinetic Analyses	• Individual Pyrimethamine plasma concentration-time profiles (by group, and subject) and median/mean (±SD) profiles by group will be plotted and listed. • Plasma concentration time data for Pyrimethamine will be analyzed by non-compartmental methods using Phoenix WinNonlin (version 6.3 or higher) and all derived PK parameters will be graphically presented, summarised and listed. No formal statistical analyses will be conducted.
Safety Analyses	• Safety data will be presented in tabular and/or graphical format and summarised descriptively.

1.1. History

Version	Issue Date	Amendments	Reason
00	15-SEP-2017	Original (New document)	-

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

There were no changes or deviations to the originally planned statistical analysis specified in the protocol (Dated: 19/JUL/2017).

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

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To investigate PK following single dose of Pyrimethamine 50 mg in fasted status in healthy Japanese male subjects.	• Cmax, AUC(0-t), AUC(0-inf), AUC(0-24), tmax, t1/2, CL/F, Vd/F of the plasma concentration of Pyrimethamine in healthy Japanese male subjects, as data permit.
Secondary Objectives	**Secondary Endpoint**
• To investigate PK following single dose of Pyrimethamine 50 mg in fasted status in healthy Caucasian male subjects.	• Cmax, AUC(0-t), AUC(0-inf), AUC(0-24), tmax, t1/2, CL/F, Vd/F of the plasma concentration of Pyrimethamine in healthy Caucasian male subjects, as data permit.
• To assess safety and tolerability following single dose of Pyrimethamine in fasted status in healthy Japanese and Caucasian male subjects.	• AE and change from the baseline of clinical laboratory values, vital signs and ECG.

2.3. Study Design

Overview of Study Design and Key Features	
Design Features	• This study will be a single centre, open-label, parallel-group, single oral dose study to evaluate the PK, safety and tolerability of Pyrimethamine in healthy male Japanese and Caucasian subjects.
Dosing	• Subjects will have a screening visit within 30 days prior to the first dose of study treatment, one treatment period, and re-visits 15 (±1) and 22 (±1) days after the dose for follow-up assessments including PK sampling. • Subjects will be housed in the Clinical Research Unit from Day -1 through Day 8, and return to the unit on Day 15 (±1) and 22 (±1) for the remaining PK samples and safety assessments post dose. • During the treatment period, subjects will receive single dose of Pyrimethamine 50 mg in the fasted state after overnight fast (at least 10 hours). Calcium folinate 15 mg will be coadministered with Pyrimethamine at Day 1, and will continue to be administered once a day until Day 8. • Blood sampling for PK analysis and safety assessments will be performed prior to dosing and over 22 days after dosing. The duration of each subject's participation will be approximately 2 months from screening to the follow-up.
Treatment Assignment	• Sufficient Japanese and Caucasian healthy male subjects will be enrolled such that 6 subjects of each population complete dosing and critical assessments.
Interim Analysis	• No interim analyses will be planned.

2.4. Statistical Hypotheses

The objectives of this study are to evaluate safety and tolerability of Pyrimethamine and to estimate Pyrimethamine pharmacokinetic parameters in healthy Japanese and Caucasian male subjects. No formal statistical hypotheses will be tested. Descriptive statistics will be used to assess safety and tolerability objectives by group (Japanese, Caucasian). An estimation approach will be used to address the pharmacokinetic study objectives, where point estimates and corresponding 95% confidence intervals will be constructed, unless otherwise stated.

3. PLANNED ANALYSES

3.1. Interim Analyses

An interim analysis is not planned.

3.2. Final Analyses

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

1. All subjects have completed the study as defined in the protocol.
2. All required database cleaning activities have been completed and final database release and database freeze has been declared by Data Management.
3. Even though single arm study, randomisation codes have been distributed according to RandAll NG procedures.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Screened	• Consisting of all participants screened in the study	• Study Population
Screening Failure	• Participants who sign the ICF in the study but are never subsequently administered study treatment. All participants who sign the ICF have the screening test in the study.	• Study Population
Safety	• All participants who take at least one dose of study treatment.	• Study Population • Safety
Pharmacokinetic	• This population is defined as all participants administered at least one dose of study treatment and who have PK sample taken and analysed.	• PK

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

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

Table 1 provides an overview of appendices within the RAP for outlining general considerations for data analyses and data handling conventions.

Table 1 Overview of Appendices

Section	Component
10.1	Appendix 1: Protocol Deviation Management
10.2	Appendix 2: Time & Events
10.3	Appendix 3: Treatment States and Phases
10.4	Appendix 4: Data Display Standards & Handling Conventions
10.5	Appendix 5: Derived and Transformed Data
10.6	Appendix 6: Premature Withdrawals & Handling of Missing Data
10.7	Appendix 7: Values of Potential Clinical Importance

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Analyses

The study population analyses will be based on the Safety population, unless otherwise specified.

Table 2 provides an overview of the planned study population analyses, with full details of data displays being presented in Appendix 9: List of Data Displays.

Table 2 Overview of Planned Study Population Analyses

Display Type	Data Displays Generated		
	Table	Figure	Listing
Subject Disposition			
Subject Disposition and Reason for Study Withdrawal	Y		Y
Screening Status and Reasons for Screen Failure	Y		Y
Protocol Deviations			
Important Protocol Deviations	Y		Y
Subjects with Inclusion/Exclusion Criteria Deviations			Y
Populations Analysed			
Study Populations	Y		
Subjects Excluded from Any Population			Y
Demographic and Baseline Characteristics			
Demographic Characteristics	Y		Y
Demographic Characteristics for Screening Failure			Y
Age Ranges	Y		
Race and Racial Combinations	Y		Y
Race and Racal Combination for Failure			Y
Medical Conditions and Concomitant Medications			
Medical Conditions			Y
Concomitant Medications			Y
Exposure and Treatment Compliance			
Exposure to Study Treatment			Y

NOTES :

- Y = Yes display generated.

7. SAFETY ANALYSES

The safety analyses will be based on the Safety population, unless otherwise specified.

7.1. Overview of Planned Analyses

Table 3 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 9: List of Data Displays.

Table 3 Overview of Planned Safety Analyses

Display Type	Absolute		
	Summary		Individual
	T	F	L
Adverse Events (AEs)			
All AEs by SOC and PT	Y		Y
All AEs by Maximum Intensity	Y		
Drug-Related AEs by SOC and PT	Y		
Drug-Related AEs by Maximum Intensity	Y		
Subject Numbers for Individual AEs			Y
Relationship Between AE SOCs, PT and Verbatim Text			Y
Serious and Other Significant AEs			
Serious AEs			Y
AEs Leading to Withdrawal from Study			Y

NOTES:

- T = Table, F = Figures, L = Listings, Y = Yes display generated, SOC = System Organ Class, PT = Preferred Term.
- Summary = Represents TF related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

7.2. Overview of Planned Clinical Laboratory Analyses

Table 4 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 9: List of Data Displays.

Table 4 Overview of Planned Clinical Laboratory Analyses

Display Type	Absolute			Change from BL		
	Summary		Individual	Summary		Individual
	T	F	L	T	F	L
Chemistry						
Chemistry Data	Y		Y	Y		Y
Chemistry Results Relative to Normal Range				Y		
All Chemistry Data for Subjects with any Value of Potential Clinical Concern/PCI			Y			

Display Type	Absolute			Change from BL		
	Summary		Individual	Summary		Individual
	T	F	L	T	F	L
Hematology						
Hematology Data	Y		Y	Y		Y
Hematology Results Relative to Normal Range				Y		
All Hematology Data for Subjects with any Value of Potential Clinical Concern/PCI			Y			
Urinalysis						
Dipstick Data (Glucose, Protein, Blood, Ketones, Bilirubin, Urobilinogen)	Y		Y*			
Gravity and pH	Y		Y			
Hepatobiliary (Liver)						
Liver Monitoring/Stopping Event Reporting			Y			
Medical Conditions for Subjects with Liver Stopping Events			Y			
Substance Use for Subjects with Liver Stopping Events			Y			

NOTES:

- T = Table, F = Figures, L = Listings, Y = Yes display generated, PCI = Potential Clinical Importance
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
  Individual = Represents FL related to any displays of individual subject observed raw data.

*: If blood or protein is abnormal, microscopic examination will be included.

7.3. Overview of Planned Other Safety Analyses

Table 5 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 9: List of Data Displays.

Table 5 Overview of Planned Other Safety Analyses

Display Type	Absolute			Change from BL		
	Summary		Individual	Summary		Individual
	T	F	L	T	F	L
ECG						
ECG Findings	Y		Y			
ECG Values	Y		Y	Y		Y
All ECG Values for Subjects with any Value of PCI			Y			
Vital Signs						
Vitals Values	Y		Y	Y		Y
All Vital Signs for Subjects with any Value of PCI			Y			

NOTES:

- T = Table, F = Figures, L = Listings, Y = Yes display generated, PCI = Potential Clinical Importance
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

8. PHARMACOKINETIC ANALYSES

8.1. Overview of Planned Pharmacokinetic Analyses

The pharmacokinetic (PK) analyses will be based on the Pharmacokinetic population, unless otherwise specified.

Table 6 provides an overview of the planned analyses, with full details being presented in Appendix 9: List of Data Displays.

Table 6 Overview of Planned Pharmacokinetic Analyses

Display Type	Untransformed				Log-Transformed			
	Summary		Individual		Summary		Individual	
	F	T	F	L	F	T	F	L
Plasma Drug Concentrations	Y [1] [2]	Y	Y [1]	Y				
Derived PK Parameters	Y	Y		Y		Y		

NOTES :

- T = Table, F = Figures, L = Listings, Y = Yes display generated.
- Summary = Represents TFL related to any summaries (descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

1. Linear and Semi-Log plots will be created on the same display.
2. Separate Mean (± SD) and Median plots will be generated.

8.2. Drug Concentration Measures

Plasma concentrations of Pyrimethamine at each nominal time will be listed and summarised by group. Standard summary statistics will be calculated (i.e. mean, standard deviation, median, minimum and maximum).

Individual plasma concentration-time profiles and median/mean profiles by group 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).

All individual plasma concentration-time 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).

Refer to Appendix 4: Data Display Standards & Handling Conventions (Section 10.4.3 Reporting Process & Standards).

8.3. Pharmacokinetic Parameters

8.3.1. Derived Pharmacokinetic Parameters

- Derivation of pharmacokinetic parameters will be performed by, or under the direct auspices of, Clinical Pharmacology & Science Promotion Office, GlaxoSmithKline K.K.
- Refer to Appendix 4: Data Display Standards & Handling Conventions (Section 10.4.3 Reporting Process & Standards).
- The pharmacokinetic parameters will be calculated by non-compartmental analysis using Phoenix WinNonlin (version 6.3 or higher)
- All calculations of non-compartmental parameters will be based on actual sampling times recorded during the study.

Pharmacokinetic parameters described in Table 7 will be determined from plasma Pyrimethamine concentration-time data, as data permits.

Table 7 Derived Pharmacokinetic Parameters

Parameter	Parameter Description
AUC(0-24)	Area under the concentration-time curve will be calculated to fixed nominal time 24 hours after administration (AUC(0-24)),using the combination of linear and logarithmic trapezoidal methods (i.e., Linear Up/Log Down calculation method in Phoenix WinNonlin) . If a sampling time deviation occurred at nominal time 24 hours after administration (and 24 < t), AUC(0-24) will be calculated using the concentration at time 24 hours after administration post-dose estimated by the method of interpolation. If nominal time 24 hours after administration > t (or if the concentration at time 24 hours after administration was below the limit of quantification), then the concentration (y) at time 24 hours after administration is estimated using λz and last observed Ct according to the formula: $y=Ct(obser) \times e^{-lambda\_z(24-t)}$ Then the following equation will be used to calculate AUC(0-24) where t is the time of last quantifiable plasma concentration. **AUC(0-24) = AUC(0-t) + AUC(t-24)** If lambda_z is not estimable, AUC(0-24) is not calculated (when 24 > t).
AUC(0-t)	Area under the concentration-time curve from time zero time (pre-dose) to the time of last quantifiable concentration (AUC(0-t)) will be calculated by a combination of linear and logarithmic trapezoidal methods. The linear trapezoidal method will be employed for all incremental trapezoids arising from increasing concentrations and the logarithmic trapezoidal method will be used for those arising from decreasing concentrations (i.e., Linear Up/Log Down calculation method in Phoenix WinNonlinl).
AUC(0-inf)	Area under the concentration-time curve from zero time (pre-dose) extrapolated to infinite time (AUC(0-inf)) will be calculated as follows: **AUC(0-inf) = AUC(0-t) + C(t) / lambda_z**
%AUCex	The percentage of AUC (0-∞) obtained by extrapolation (%AUCex) will be calculated as: **%AUCex = [AUC(0-inf) – AUC(0-t)] / AUC(0-inf) x 100**
Cmax	Maximum observed concentration will be obtained directly from the concentration-time data.
Tmax	Time to first occurrence of Cmax will be obtained directly from the concentration-time data.
t½	Apparent terminal phase half-life will be calculated as: **t½ = ln2 / lambda_z**
Tlast	The time of the last measurable (positive) concentration.
lambda_z	The first order rate constant associated with the terminal (log-linear) portion of the curve.
lambda_z lower	The lower limit on time for values to be included in the calculation of lambda_z.
lambda_z upper	The upper limit on time for values to be included in the calculation of lambda_z.
#pts	The number of time points used in computing lambda_z.
R-square	Square of the correlation coefficient.
CL/F	Apparent clearance following oral dosing will be calculated as: **CL/F = Dose / AUC (0-inf)**
Vd/F	Apparent volume of distribution following oral dosing will be calculated as: **Vd/F = Dose / lambda_z * AUC(0-inf)**

NOTES:

- Additional parameters may be included as required.
- Lambda_z is the terminal phase rate constant.
- Ct is the last observed quantifiable concentration.

8.3.2. Summary of Pharmacokinetic Parameters

- For each of these parameters, except for tmax, the following summary statistics will be calculated for each treatment:
    - Non-transformed: median, maximum, minimum, arithmetic mean, 95% confidence interval for the arithmetic mean and standard deviation
    - Loge-transformed: geometric mean, 95% confidence interval for the geometric mean, standard deviation of logarithmically transformed data and between geometric coefficient of variation (CVb (%))
- For tmax, median, maximum, minimum, arithmetic mean, standard deviation and 95% Confidence Interval (CI) for the arithmetic mean will be calculated.
- An exploratory analysis will be performed using PK parameter plots in order to assess the results in Japanese and Caucasian subjects. Plots of AUC(0-t), AUC(0-inf), Cmax and T1/2 versus group (Japanese, Caucasian) will be produced.

9. REFERENCES

GlaxoSmithKline Document Numbers 2017N318316_00 Study Protocol of 204678. A single centre, open-label, parallel, single oral dose study to evaluate the pharmacokinetic, safety and tolerability of Pyrimethamine in healthy Japanese and Caucasian subjects (Effective date: 19-JUL-17)

10. APPENDICES

Section	Appendix
RAP Section 4 : Analysis Populations	
Section 10.1	Appendix 1: Protocol Deviation Management
RAP Section 5 : General Considerations for Data Analyses & Data Handling Conventions	
Section 10.2	Appendix 2: Time and Events
Section 10.3	Appendix 3: Treatment States & Phases
Section 10.4	Appendix 4: Data Display Standards & Handling Conventions • Study Treatment & Sub-group Display Descriptors • Baseline Definitions & Derivations • Reporting Process & Standards
Section 10.5	Appendix 5: Derived and Transformed Data • General • Study Population • Safety • Pharmacokinetic
Section 10.6	Appendix 6: Premature Withdrawals & Handling of Missing Data • General • Study Population & Safety
Section 10.7	Appendix 7: Values of Potential Clinical Importance • Laboratory Values • ECG • Vital Signs
Other RAP Appendices	
Section 10.8	Appendix 8: Abbreviations & Trade Marks
Section 10.9	Appendix 9: List of Data Displays
Section 10.10	Appendix 10: Example Mock Shells for Data Displays

10.1. Appendix 1: Protocol Deviation Management

Details will be referred latest Protocol Deviation Management Plan and data handling will be decided prior to final data base release.

10.2. Appendix 2: Time & Events

10.2.1. Protocol Defined Time & Event

	Scr	Day -1	Day 1							Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 15 [4]	Follow-up Day 22 [4]
			Pre	0 h	1 h	2 h	4 h	6 h	12 h	24 h	48 h	72 h	96 h	120 h	144 h	168 h	336 h	504 h
Admission to Unit		X																
Informed consent	X																	
Subject demography/Medical history	X																	
Physical examination	X	X								X	X	X	X	X	X	X		X
12-lead ECG	X		X				X		X	X	X							X
Vital signs	X		X				X		X	X	X	X	X	X	X	X	X	X
Urine drug screen	X	X																
Alcohol breath test	X	X																
CO breath test	X	X																
Serological test	X																	
Haematology, clinical chemistry and urinalysis	X	X								X			X			X	X	X
Study treatment dosing				X														
Calcium folinate dosing				X [1]						X	X	X	X	X	X	X		
PK Sampling			X		X	X	X	X	X	X	X	X		X		X	X	X
SAEs [2]	←==========→																	
AEs [3]				←==========→														
Con Med review	←==========→																	
Discharge																X		
Outpatient Visit	X																X	X

1. Calcium folinate will be coadministered with Pyrimethamine on Day 1.
2. All SAEs will be collected from the signing of the ICF until the follow-up visit at the time points specified.
3. All AEs will be collected from the start of treatment until the follow-up visit at the time points specified.
4. Subjects will return to the unit on Day 15 (±1) and 22 (±1) for the remaining PK samples and safety assessments post dose.

10.3. Appendix 3: Treatment States and Phases

10.3.1. Treatment Phases

Assessments and events will be classified according to the time of occurrence relative to the assessment date.

10.3.1.1. Treatment States for AE Data

Treatment State	Definition
Pre-Treatment	AE Start Date < Study Treatment Start Date and Time
On treatment	Dosing Start Date and Time in each group ≤ AE Start Date and Time
Onset Time Since First Dose (Minute)	If Dosing Start Date and Time > AE Onset Date and Time = AE Onset Date and Time – Dosing Start Date and Time If dosing Start Date and Time ≤ AE Onset Date and Time = AE Onset Date and Time - Dosing Start Date and Time +1 Missing otherwise
Onset Time Since Last Dose (Minute)	AE Start Date and Time – Most Recent Treatment Start Date and Time + 1
Duration (Minute)	AE Resolution Date and Time – AE Onset Date and Time + 1
Drug-related	If relationship is marked 'YES' on eCRF

10.4. Appendix 4: Data Display Standards & Handling Conventions

10.4.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions			
RandAll NG		Data Displays for Reporting	
Schedule	Description	Description	Order [1]
1	D	Caucasian	2
2	D	Japanese	1

NOTES:

1. Order represents treatments being presented in TFL, as appropriate.

10.4.2. Baseline Definition & Derivations

10.4.2.1. Baseline Definitions

Parameter	Study Assessments Considered As Baseline			Baseline Used in Data Display
	Screening	Day -1	Day 1 (Pre-Dose)	
Safety				
12 Lead ECG & Vital Signs	X		X	Day 1 (Pre Dose)
Haematology	X	X		Day -1
Clinical Chemistry	X	X		Day -1

10.4.2.2. Derivations and Handling of Missing Baseline Data

Definition	Reporting Details
Change from Baseline	= Post-Dose Visit Value – Baseline

NOTES :

- Unless otherwise specified, the baseline definitions specified in Section 10.4.2.1 Baseline Definitions will be used for derivations for endpoints / parameters and indicated on summaries and listings.
- Unless otherwise stated, if baseline data is missing no derivation will be performed and will be set to missing.

10.4.3. Reporting Process & Standards

Reporting Area	
Software	
• The currently supported versions of SAS software will be used.	
Reporting Area	
HARP Server	N/A

Reporting Area	
HARP Area	N/A
QC Spreadsheet	N/A

Analysis Datasets

- Analysis datasets will be created according to CDISC standards (SDTM IG Version 3.1.3 & AdaM IG Version 1.0).

Generation of RTF Files

- N/A

Reporting Standards

General

- The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated:
  - 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 (4.24) for decimal places (DP's) will be adopted for reporting of data based on the raw data collected.
- 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..
  - For PK parameters derivation, actual times are used.
  - 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.
  - Visits outside the protocol defined time-windows (i.e. recorded as protocol deviations) will be included in listings but omitted from figures, summaries and statistical analyses.

Unscheduled Visits

- Unscheduled visits will not be included in summary tables.
- Unscheduled visits will not be included in figures.

Reporting Standards	
• 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, %
Reporting of Pharmacokinetic Concentration Data	
Descriptive Summary Statistics	Refer to IDSL Statistical Principle 6.06.1 Assign zero to NQ values (Refer to GUI_51487 for further details)
Reporting of Pharmacokinetic Parameters	
Descriptive Summary Statistics (Log Transformed)	N, n, geometric mean, 95% CI of geometric mean, standard deviation (SD) of logged data and between geometric coefficient of variation (CVb (%)) will be reported. CV_b (%) = $\sqrt{}$ (exp(SD^2) - 1) * 100 (SD = SD of log transformed data)
Parameters Not Being Log Transformed	Tmax
Parameters Not Being Summarised	The following PK parameters will not be summarised but listed: %AUCex, Tlast, lambda_z, lambda_z_lower, lambda_z_upper, #pts, R2
Graphical Displays	
• Refer to IDSL Statistical Principals 7.01 to 7.13.	

10.5. Appendix 5: Derived and Transformed Data

10.5.1. General

Multiple Measurements at One 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. • If there are two values within a time window the value closest to the target day for that window will be used. If values are the same distance from the target then the mean will be taken. • Subjects having both High and Low values for Normal Ranges at any post-baseline visits 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 study day of start of dosing date : o Ref Date = Missing → Study Day = Missing o Ref Date < Dosing Start Date → Study Day = Ref Date – Dosing Start Date o Ref Data ≥ Dosing Start Date → Study Day = Ref Date – (Dosing Start Date) + 1

10.5.2. Study Population

Demographics
Age
• GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as: o Any subject with a missing day will have this imputed as day '15'. o Any subject with a missing date and month will have this imputed as '30th June'. • Birth date will be presented in listings as 'YYYY'. • Reference date for calculation of age at screening will be from visit 1 (Screening visit) date, however this will be from screen failure date for a screen failure subject. • Analysis age group will be categorized (Years): <=18, 19-64, 65-74, >=75 • Age will be categorized for EudraCT: Adults (18-64 years)
Body Mass Index (BMI)
• Calculated as **Weight (kg) / [Height (m)^2**

10.5.3. Safety

ECG Parameters

RR Interval

- IF RR interval (msec) is not provided directly, then RR can be derived as :

  [1] If QTcB is machine read & QTcF is not provided, then :

$$RR = \left[\left(\frac{QT}{QTcB}\right)^2\right] * 1000$$

  [2] If QTcF is machine read and QTcB is not provided, then:

$$RR = \left[\left(\frac{QT}{QTcF}\right)^3\right] * 1000$$

- If ECGs are manually read, the RR value preceding the measurement QT interval should be a collected value THEN do not derive.

Corrected QT Intervals

- When not entered directly in the eCRF, corrected QT intervals by Bazett's (QTcB) and Fredericia's (QTcF) formulas will be calculated, in msec, depending on the availability of other measurements.
- IF RR interval (msec) is provided then missing QTcB and/or QTcF will be derived as :

$$QTcB = \frac{QT}{\sqrt{\frac{RR}{1000}}} \qquad QTcF = \frac{QT}{\sqrt[3]{\frac{RR}{1000}}}$$

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

Laboratory Assessments	
Haematology	Platelet Count, RBC Count, Haemoglobin, Hematocrit, RBC Indices (MCV, MCH, MCH, %Reticulocytes), WBC count with Differential (Neutrophils, Lymphocytes, Monocytes, Eosinophils, Basophils)
Clinical Chemistry	BUN, Creatinine, Glucose (fasting), Potassium, Sodium, Calcium, Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Alkaline phosphatise, Total and direct bilirubin, Total Protein
Routine Urinalysis	Specific gravity, pH (assessed by dipstick) • glucose, protein, blood, ketones, bilirubin, urobilinogen, nitrite, leukocyte esterase by dipstick

Laboratory Assessments	
	• Microscopic examination (if blood or protein is abnormal)

ECG (12-lead ECG)
ECG findings, ECG values (Heart rate, PR interval, QRS duration, QT interval, and QTcF intervals)

Vital Signs
Pulse rate, Blood pressure (Systolic, Diastolic), respiratory rate, Temperature

10.5.4. Pharmacokinetic

PK Parameters
• If one or more non-quantifiable (NQ) values occur in a profile before the first measurable concentration, they will be assigned a value of zero concentration. For linear plots, zero concentration value(s) before the first measurable concentration will be included in the plot. For log-linear plots, zero concentration value(s) before the first measurable concentration will be assigned a missing value. • If a single NQ value occurs between measurable concentrations in a profile, the NQ should generally be set to missing in the derivation of pharmacokinetic parameters, statistical analysis, and the individual subject plots. • If two or more NQ values occur in succession between measurable concentrations, the profile will be deemed to have terminated at the last measurable concentration prior to these NQs. For the purpose of individual subject plots, these NQs will be set to 0, and the subsequent measurable concentrations will be retained. For the derivation of pharmacokinetic parameters, these NQs and any subsequent measurable concentrations will be set to missing. • NQs which occur after the last measurable concentration will be omitted (set to missing) in the derivation of pharmacokinetic parameters and from the individual subject plots. • Individual's PK parameters reported as 'NC' (Not Calculable) or 'ND' (Not Determined) will be included in listings but omitted (set to missing) from figures, summaries and statistical analyses.

10.6. Appendix 6: Premature Withdrawals & Handling of Missing Data

10.6.1. Premature Withdrawals

Element	Reporting Detail
General	• Subject study completion was defined as a participant has completed all phases of the study including the last visit or the last scheduled procedure (Follow-up) as described in the protocol. • Withdrawn subjects maybe replaced in the study. • All available data from subjects 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.

10.6.2. 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.

10.6.2.1. Handling of Partial Dates

Element	Reporting Detail
Concomitant Medications	• Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention: o If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month o If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month. • The recorded partial date will be displayed in listings.

10.7. Appendix 7: Values of Potential Clinical Importance

10.7.1. Laboratory Values

Haematology				
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (>x)**
Hematocrit	Ratio of 1	Male		0.54
		Female		0.54
		Δ from BL	↓0.075	
Hemoglobin	g/L	Male		180
		Female		180
		Δ from BL	↓25	
Lymphocytes	$x10^9$/ L		0.8	
Neutrophil Count	$x10^9$/ L		1.5	
Platelet Count	$x10^9$/ L		100	550
While Blood Cell Count (WBC)	$x10^9$/ L		3	20

Clinical Chemistry				
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (>x)**
Calcium	mmol/L		2	2.75
Creatinine	µmol/L	Δ from BL		↑ 44.2
Glucose	mmol/L		3	9
Potassium	mmol/L		3	5.5
Sodium	mmol/L		130	150

Liver Function			
Test Analyte	**Units**	**Category**	**Clinical Concern Range**
ALT/SGPT	U/L	High	≥ 2x ULN
AST/SGOT	U/L	High	≥ 2x ULN
AlkPhos	U/L	High	≥ 2x ULN
T Bilirubin	µmol/L	High	≥ 1.5xULN
T. Bilirubin + ALT	µmol/L U/L	High	1.5xULN T. Bilirubin + ≥ 2x ULN ALT

10.7.2. ECG

ECG Parameter	Units	Clinical Concern Range	
		Lower	Upper
Absolute			
Absolute QTc Interval	msec		> 450 [1]
Absolute PR Interval	msec	< 110 [1]	> 220 [1]
Absolute QRS Interval	msec	< 75 [1]	> 110 [1]
Change from Baseline			
Increase from Baseline QTc	msec		> 60 [1]

NOTES:

1. Represent standard ECG values of PCI for HV studies

10.7.3. Vital Signs

Vital Sign Parameter (Absolute)	Units	Clinical Concern Range	
		Lower	Upper
Systolic Blood Pressure	mmHg	< 85	> 160
Diastolic Blood Pressure	mmHg	< 45	> 100
Heart Rate	bpm	< 40	> 110

10.8. Appendix 8 – Abbreviations & Trade Marks

10.8.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
A&R	Analysis and Reporting
AUC	Area under the concentration-time curve
AUC(0-inf)	Area under the concentration-time curve from time 0 to infinity
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
Cmax	Maximum observed concentration
CSR	Clinical Study Report
CV_b	Coefficient of Variation (Between)
eCRF	Electronic Case Record Form
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
IDSL	Integrated Data Standards Library
GUI	Guidance
PCI	Potential Clinical Importance
PDMP	Protocol Deviation Management Plan
PK	Pharmacokinetic
QTcF	Frederica's QT Interval Corrected for Heart Rate
QTcB	Bazett's QT Interval Corrected for Heart Rate
RAP	Reporting & Analysis Plan
SAC	Statistical Analysis Complete
SDTM	Study Data Tabulation Model
TFL	Tables, Figures & Listings
GSK	GlaxoSmithKline

10.8.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
NONE

Trademarks not owned by the GlaxoSmithKline Group of Companies
SAS
WinNonlin

10.9. Appendix 9: List of Data Displays

10.9.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.7	N/A
Safety	2.1 to 2.17	N/A
Pharmacokinetic	3.1 to 3.3	4.1 to 4.13
Section	**Listings**	
ICH Listings	1 to 36	
Other Listings	N/A	

10.9.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required an example mock-up displays provided in Appendix 10: 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 / TST ID / Example Shell' or 'Programming Notes' column as '[Non-Standard] + Reference.'

10.9.3. Deliverable [Priority]

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

NOTES:

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

10.9.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.1.	Safety	ES1	Summary of Subject Disposition	Completed or withdrawn and the reason for withdrawal.	SAC [1]
1.2.	Screened	ES6	Summary of Screening Status and Reasons for Screen Failure	The number (%) of Randomized or screening failure subjects as the screening status, and the reason for screening failure.	SAC [1]
Protocol Deviation					
1.3.	Safety	DV1	Summary of Important Protocol Deviations	Data is from DV dataset.	SAC [1]
Population Analysed					
1.4.	Safety	SP1	Summary of Study Populations		SAC [1]
Demographic and Baseline Characteristics					
1.5.	Safety	DM1	Summary of Demographic Characteristics		SAC [1]
1.6.	Screened	DM11	Summary of Age Ranges	Adults (18-64 years)	
1.7.	Safety	DM5	Summary of Race and Racial Combinations		SAC [1]

10.9.5. Safety Tables

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events (AEs)					
2.1.	Safety	AE1	Summary of All Adverse Events by System Organ Class and Preferred Term		SAC [1]
2.2.	Safety	AE5A	Summary of All Adverse Events by Maximum Intensity		SAC [1]
2.3.	Safety	AE1	Summary of All Drug-Related Adverse Events by System Organ Class and Preferred Term		SAC [1]
2.4.	Safety	AE5A	Summary of All Drug-Related Adverse Events by Maximum Intensity		SAC [1]
Laboratory: Chemistry					
2.5.	Safety	LB1	Summary of Chemistry		SAC [1]
2.6.	Safety	LB1	Summary of Chemistry Changes from Baseline		SAC [1]
2.7.	Safety	LB4	Summary of Chemistry Data Shifts from Baseline with Respect to the Normal Range		SAC [1]
Laboratory: Hematology					
2.8.	Safety	LB1	Summary of Hematology		SAC [1]
2.9.	Safety	LB1	Summary of Hematology Changes from Baseline		SAC [1]
2.10.	Safety	LB4	Summary of Hematology Data Shifts from Baseline with Respect to the Normal Range		SAC [1]

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Laboratory: Urinalysis					
2.11.	Safety	UR3b	Summary of Urinalysis (Glucose, Protein, Blood, Ketones, Bilirubin, Urobilinogen nitrite, leukocyte esterase) Data		SAC [1]
2.12.	Safety	LB1	Summary of Urinalysis (Specific Gravity and pH)		SAC [1]
ECG					
2.13.	Safety	EG1	Summary of ECG Findings		SAC [1]
2.14.	Safety	EG2	Summary of ECG Value		SAC [1]
2.15.	Safety	EG2	Summary of Change from Baseline in ECG Values by Visit		SAC [1]
Vital Signs					
2.16.	Safety	VS1	Summary of Vital Signs		SAC [1]
2.17.	Safety	VS1	Summary of Change from Baseline in Vital Signs		SAC [1]

10.9.6. Pharmacokinetic Tables

Pharmacokinetic : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.1.	PK	PK01: PKCT1	Summary of Pyrimethamine Plasma Concentration		SAC [1]
3.2.	PK	PK03: PKPT1	Summary of Pyrimethamine Pharmacokinetic Parameters (non-transformed)		SAC [1]
3.3.	PK	PK05: PKPT3	Summary of Pyrimethamine Pharmacokinetic Parameters (loge-transformed)		SAC [1]

10.9.7. Pharmacokinetic Figures

Pharmacokinetic: Figures					
IDSL / TST ID / Example Shell	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
4.1.	PK	PK16a: PKCF1p	Individual Pyrimethamine Plasma Concentration-Time Plots by Subject (from Pre-Dose to Day 22)	by Subject (Linear and Semi-Log) Time: from Pre-dose to Day 22	SAC [1]
4.2.	PK	PK24: pkcf6	Individual Pyrimethamine Plasma Concentration-Time Plots by group (from Pre Dose to Day 22)	By group (Linear and Semi-Log) Time: from Pre-dose to Day 22	SAC [1]
4.3.	PK	PK19: PKCF4	Mean (+SD) Pyrimethamine Concentration-Time Plots (from Pre Dose to Day 22)	Time: from Pre-dose to Day 22	SAC [1]
4.4.	PK	PK18: PKCF3	Median Pyrimethamine Plasma Concentration-Time Plots (from Pre Dose to Day 22)	Time: from Pre-dose to Day 22	SAC [1]
4.5.	PK	PK16a: PKCF1p	Individual Pyrimethamine Plasma Concentration-Time Plots by Subject (from Pre Dose to 72 hr)	by Subject (Linear and Semi-Log) Time: from Pre-dose to 72 hr	SAC [1]
4.6.	PK	PK24: pkcf6	Individual Pyrimethamine Plasma Concentration-Time Plots by group (from Pre Dose to 72 hr)	By rgroup (Linear and Semi-Log) Time: from Pre-dose to 72 hr	SAC [1]
4.7.	PK	PK19: PKCF4	Mean (+SD) Pyrimethamine Concentration-Time Plots (from Pre Dose to 72 hr)	Time: from Pre-dose to 72 hr	SAC [1]
4.8.	PK	PK18: PKCF3	Median Pyrimethamine Plasma Concentration-Time Plots (from Pre Dose to 72 hr)	Time: from Pre-dose to 72 hr	SAC [1]
4.9.	PK	PK28	Plot of Pyrimethamine Treatment and PK Parameters	AUC(0-t), AUC(0-inf), Cmax, t1/2 Plot and Mean with 95%CI X axis: Japanese, Caucasian Y axis: PK parameters	SAC [1]

Pharmacokinetic: Figures					
IDSL / TST ID / Example Shell	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
4.10.	PK	Study Specifics (PK_F1)	Individual Pyrimethamine Plasma Concentration-Time Plots (from Pre-Dose to Day 22)	Japanese & Caucasian (Linear and Semi-Log) Time: from Pre-dose to Day 22	SAC [1]
4.11.	PK	Study Specifics (PK_F1)	Individual Pyrimethamine Plasma Concentration-Time Plots (from Pre-Dose to 72 hr)	Japanese & Caucasian (Linear and Semi-Log) Time: from Pre-dose to 72 hr	SAC [1]
4.12.	PK	Study Specifics (PK_F2)	Mean (+SD) Pyrimethamine Concentration-Time Plots (from Pre Dose to Day 22)	Japanese & Caucasian Time: from Pre-dose to Day 22	SAC [1]
4.13.	PK	Study Specifics (PK_F2)	Mean (+SD) Pyrimethamine Concentration-Time Plots (from Pre Dose to 72 hr)	Japanese & Caucasian Time: from Pre-dose to 72 hr	SAC [1]

10.9.8. ICH Listings

Note: 'Inv.' in the standard displays will be replaced to 'Centre'.

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.	Screening Failure	ES7	Listing of Reasons for Screen Failure		SAC [1]
2.	Safety	ES2	Listing of Reasons for Study Withdrawal		SAC [1]
Protocol Deviations					
3.	Safety	DV2	Listing of Important Protocol Deviations		SAC [1]
4.	Screened	IE4	Listing of Subjects with Inclusion/Exclusion Criteria Deviations		SAC [1]
Populations Analysed					
5.	Safety	Study Specifics (SP_T1)	Listing of Subjects Excluded from PK Population		SAC [1]
Demographic and Baseline Characteristics					
6.	Safety	DM2	Listing of Demographic Characteristics	"Age at Screening" is added.	SAC [1]
7.	Screening Failure	DM2	Listing of Demographic Characteristics for Screening Failure Subjects		SAC [1]
8.	Safety	DM9	Listing of Race		SAC [1]
9.	Screening Failure	DM9	Listing of Race for Screening Failure Subjects		SAC [1]
Medical Conditions and Concomitant Medications					
10.	Screened	MH3	Listing of Medical Conditions		SAC [1]

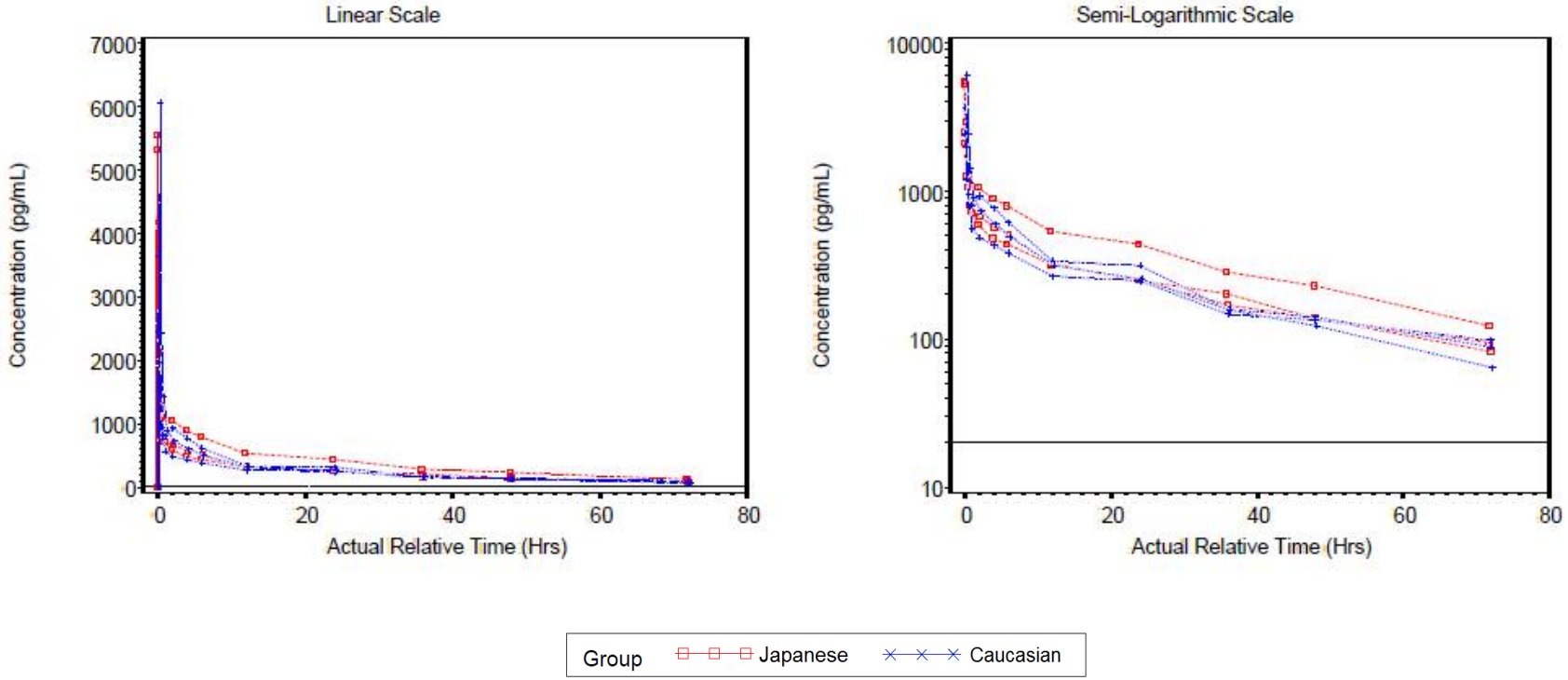
ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
11.	Safety	CM5	Listing of Concomitant Medications		SAC [1]
12.	Safety	CM6	Relationship between ATC Level 1, Ingredient and Verbatim Text		SAC [1]
Exposure and Treatment Compliance					
13.	Safety	EX3	Listing of Exposure Data		SAC [1]
Adverse Events					
14.	Safety	CP_AE8	Listing of All Adverse Events		SAC [1]
15.	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events		SAC [1]
16.	Screened	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text		SAC [1]
Serious and Other Significant Adverse Events					
17.	Safety	CP_AE8	Listing of Serious Adverse Events		SAC [1]
18.	Screening Failure	CP_AE8	Listing of Serious Adverse Events for Screening Failure Subject		SAC [1]
19.	Safety	CP_AE8	Listing of Adverse Events Leading to Withdrawal from Study		SAC [1]
Laboratory (Chemistry Data)					
20.	Safety	CP_LB5	Listing of All Chemistry Data	Change from baseline is included.	SAC [1]
21.	Safety	CP_LB5	Listing of All Chemistry Data for Subjects with Any Value of Potential Clinical Importance		SAC [1]
Laboratory (Hematology Data)					
22.	Safety	CP_LB5	Listing of All Hematology Data	Change from baseline is included.	SAC [1]
23.	Safety	CP_LB5	Listing of All Hematology Data for Subjects with Any Value of Potential Clinical Importance		SAC [1]

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Laboratory (Urinalysis Data)					
24.	Safety	UR2a	Listing of All Urinalysis Dipstick and Microscopy Data	Time will be displayed after 'Date'.	SAC [1]
25.	Safety	CP_LB5	Listing of Urinalysis Data (Gravity and pH)		SAC [1]
Hepatobiliary (Liver)					
26.	Safety	LIVER5	Listing of Liver Monitoring/Stopping Event Reporting		SAC [1]
27.	Safety	MH2	Listing of Medical Conditions for Subjects with Liver Stopping Events		SAC [1]
28.	Safety	SU2	Listing of Substance Use for Subjects with Liver Stopping Events		SAC [1]
ECG					
29.	Safety	EG3	Listing of All ECG Values		SAC [1]
30.	Safety	EG3	Listing of Change from Baseline in ECG Values		SAC [1]
31.	Safety	EG5	Listing of ECG Findings		SAC [1]
32.	Safety	CP_EG3	Listing of All ECG Data for Subjects with Any Value of Potential Clinical Importance		SAC [1]
Vital Signs					
33.	Safety	VS4	Listing of All Vital Signs	Change from baseline is included.	SAC [1]
34.	Safety	CP_VS4	Listing of All Vital Signs Data for Subjects with Any Value of Potential Clinical Importance		SAC [1]
PK					
35.	PK	PK07: PKCL1p	Listing of Pyrimethamine Plasma Concentration		SAC [1]
36.	PK	PK13: PKPL1p	Listing of Pyrimethamine Pharmacokinetic Parameters		SAC [1]

10.10. Appendix 10: Example Mock Shells for Data Displays

Example: PK_F1
Protocol: 12345
Population: PK

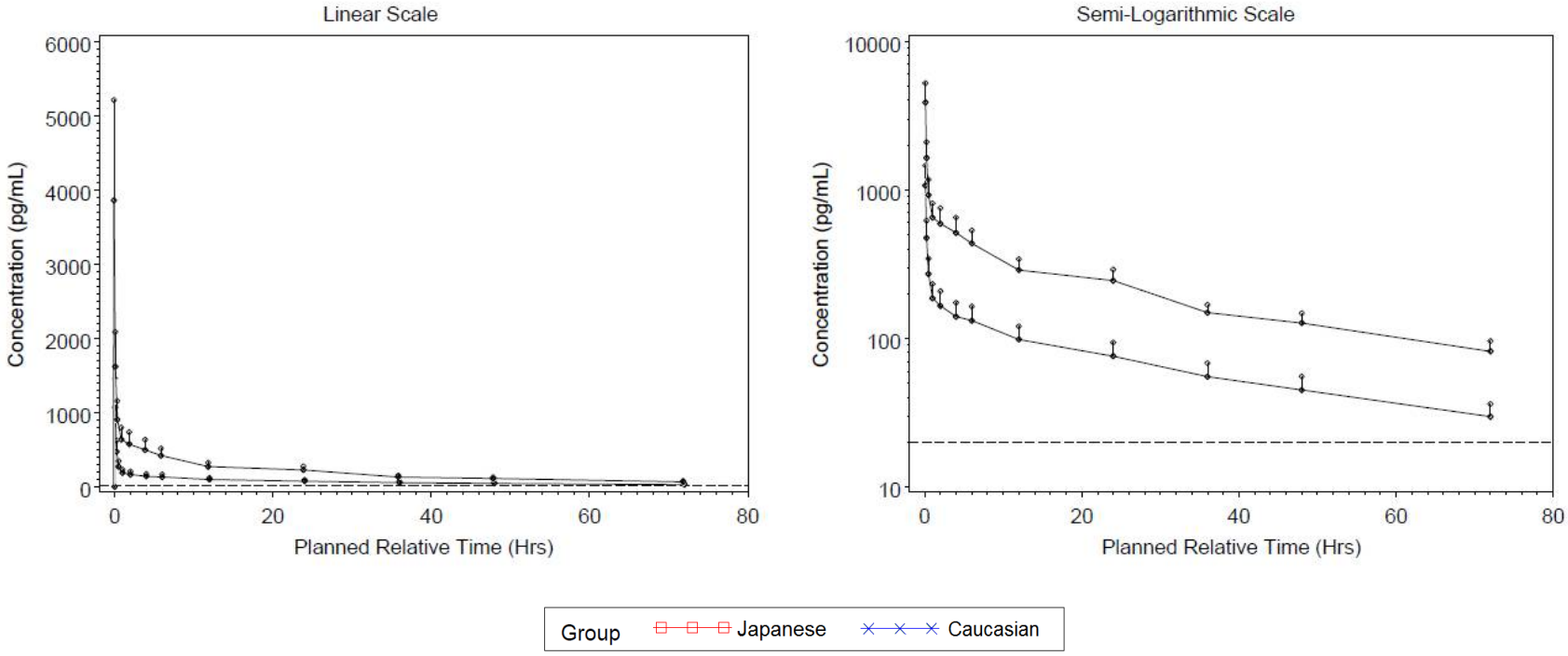
Table X
Individual Plasma Concentration-Time Plots



NOTE: LLQ = *XX unit*
USER ID:directory/program.sas 27JUN2014 12:00

Example: PK_F2
Protocol: 12345
Population: PK

Table X
Mean + SD Concentration-Time Plots (Linear and Semi-log)



NOTE: LLQ = *XX unit*
USER ID:directory/program.sas 27JUN2014 12:00