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

Title	:	Reporting and Analysis Plan for Study 207187: A Double-Blind (Sponsor Unblinded), Randomized, Placebo-Controlled, Single and Repeated Dose Escalation Study to Investigate the Safety, Tolerability and Pharmacokinetics of GSK3640254 in Healthy Participants
Compound Number	:	GSK3640254
Effective Date	:	08-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 207187.
- This RAP is intended to describe the safety, tolerability, and pharmacokinetic 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.

RAP Author(s):

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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 Protocol: 207187

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

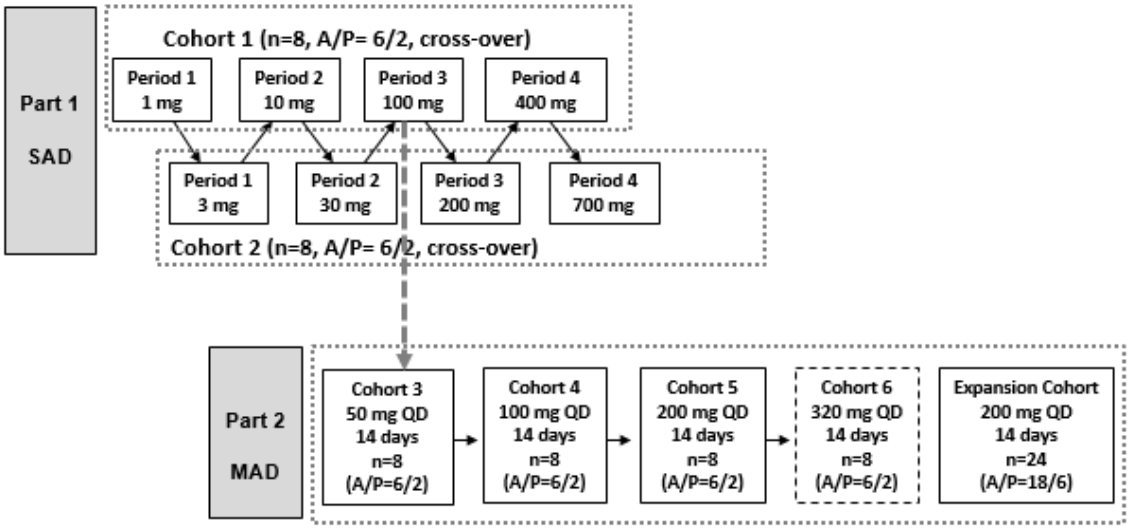
There were no changes or deviations to the originally planned statistical analysis specified in the protocol amendment 3 Dated: 05/DEC/2017.

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

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To investigate the safety and tolerability of GSK3640254 following single and repeated daily administration	• GSK3640254 safety parameters: adverse events; post-baseline values and changes over time of clinical laboratory evaluations (haematology, clinical chemistry, urinalysis), vital signs, and ECG parameters from predose values
Secondary Objectives	**Secondary Endpoints**
• To describe the PK of GSK3640254 following single and repeated daily administration	• GSK3640254 PK parameters: Part 1 (single dose): AUC(0-24), AUC(0-tlast), AUC(0-inf), Cmax, C24, tmax, tlag, t1/2, Clast, tlast, CL/F. Part 2 (Repeated QD doses for 14 days): Day 1: AUC(0-24), Cmax, C24, tmax, tlag Day 14: AUC(0-τ), Cmax, Cτ, tmax, t1/2, and CL/F
• To examine dose proportionality following single and repeated doses of GSK3640254	• GSK3640254 Single dose: AUC(0-inf), Cmax. • Repeat dose AUC(0-τ), Cmax, Cτ
• To assess accumulation of GSK3640254	• Accumulation ratios: R AUC(0-τ), R(Cmax), R (Cτ)
• To assess time to steady-state of GSK3640254	• Pre-dose concentrations on Day 2 -14 (Part 2)
Exploratory Objectives	**Exploratory Endpoints**
• To assess the exposure response relationship between GSK3640254 and safety parameter, including QTcF following single and repeated administration	• Change-from-baseline QTcF (ΔQTcF)
• To investigate the biotransformation of GSK3640254 in plasma and urine	• Provide samples of plasma and urine for the identification of any compound derived metabolite(s)
• As available, to assess the impact of food on the PK of GSK3640254	• GSK3640254 single dose Cmax, AUC(0-inf), and C24

Note: The exploratory endpoints may be analyzed once GSK3640254 clinical development continues.

2.3. Study Design

Overview of Study Design and Key Features	
	
Design Features	• Two part, Phase 1, double-blind (sponsor-unblinded), randomized, placebo controlled, single- and repeat-dose escalation study. **Part 1 (SAD):** • SAD portion will be conducted in an interlocking fashion with 2 separate cohorts of 8 healthy participants each. Each of these 2 cohorts will contain up to 4 escalating doses of GSK3640254. • In each escalating period and Cohort, 6 participants will be randomized to GSK3640254 and 2 participants will be randomized to placebo. • Participants in Cohort 1 and Cohort 2 will follow the same randomization strategy with alternating ascending doses with 4-period crossover, placebo-controlled. **Part 2 (MAD):** • Part 2 consists of 4 ascending repeat-dose cohorts (Cohorts 3 to 6), each with 8 participants (active/PBO=6/2) who will receive a once-daily dose of GSK3640254 or PBO for 14 days. • Part 2 also includes an Expansion Cohort which will be conducted at the conclusion of cohort 5. • The Expansion Cohort will evaluate the rate of GI intolerability in 24 participants (active/PBO =18/6).
Dosing	**Part 1 (SAD):** • The dose for Part 1 Cohort 1 of this study were 1 mg for Period 1, 10 mg for Period 2, 100 mg for Period 3 and 400 mg for Period 4. • The dose for Part 1 Cohort 2 of this study will be 3 mg for Period 1, 30 mg for Period 2, 200 mg for Period 3 and 700 mg for Period 4. **Part 2 (MAD):** • The dose for Part 2 of this study were 50 mg for Cohort 3, 100 mg for Cohort 4, 200 mg for Cohort 5 and the expansion cohort, and 320 mg for cohort 6.

<table>
<tr><th colspan="2">Overview of Study Design and Key Features</th></tr>
<tr><td></td><td>All doses were administered in fed condition.</td></tr>
<tr><td>Time & Events</td><td>• Refer to Appendix 2: Schedule of Activities</td></tr>
<tr><td>Treatment Assignment</td><td>Part 1 (SAD):
• Participants in either Cohort 1 or Cohort 2 will be assigned to 1 of the 4 treatment sequences in a cross-over, and each participant will receive placebo once.
<table>
<tr><th>Cohort 1</th><th>Period 1</th><th>Period 2</th><th>Period 3</th><th>Period 4</th></tr>
<tr><td>Sequence 1</td><td>Placebo</td><td>Dose 3</td><td>Dose 5</td><td>Dose 7</td></tr>
<tr><td>Sequence 2</td><td>Dose 1</td><td>Placebo</td><td>Dose 5</td><td>Dose 7</td></tr>
<tr><td>Sequence 3</td><td>Dose 1</td><td>Dose 3</td><td>Placebo</td><td>Dose 7</td></tr>
<tr><td>Sequence 4</td><td>Dose 1</td><td>Dose 3</td><td>Dose 5</td><td>Placebo</td></tr>
</table>
<table>
<tr><th>Cohort 2</th><th>Period 1</th><th>Period 2</th><th>Period 3</th><th>Period 4</th></tr>
<tr><td>Sequence 1</td><td>Placebo</td><td>Dose 4</td><td>Dose 6</td><td>Dose 8</td></tr>
<tr><td>Sequence 2</td><td>Dose 2</td><td>Placebo</td><td>Dose 6</td><td>Dose 8</td></tr>
<tr><td>Sequence 3</td><td>Dose 2</td><td>Dose 4</td><td>Placebo</td><td>Dose 8</td></tr>
<tr><td>Sequence 4</td><td>Dose 2</td><td>Dose 4</td><td>Dose 6</td><td>Placebo</td></tr>
</table>
Part 2 (MAD):
• In Cohorts 3 to 6, 8 participants per cohort (active/PBO=6/2) will receive a once-daily dose of GSK3640254 or PBO for 14 days.
• In the Expansion Cohort, 24 participants (active/PBO=18/6) will receive a once-daily dose (200 mg) of GSK3640254 or PBO for 14 days</td></tr>
<tr><td>Interim Analysis</td><td>• All preliminary safety, tolerability, and available PK data were reviewed internally at VH/GSK prior to each dose escalation. Safety data (labs, vital signs, ECG, AEs, SAEs) were reviewed by the PI/Sub-I and VH/GSK study team after completion of each dose level.</td></tr>
</table>

2.4. Statistical Hypotheses

The main purpose of this study is to assess the safety, tolerability and PK of single and repeated oral doses of GSK3640254 in healthy volunteers. No formal hypotheses are to be tested and no statistical testing will be performed.

3. PLANNED ANALYSES

3.1. Interim Analyses

All preliminary safety, tolerability, and available PK data were reviewed internally at VH/GSK prior to each dose escalation. Safety data (labs, vital signs, ECG, AEs, SAEs) will be reviewed by the PI/Sub-I and VH/GSK study team after completion of each dose level.
At each dose, the Bayesian probability of an individual exceeding the Cmax stopping criteria in Part 1 and the Bayesian probability of an individual exceeding the AUC stopping criteria in Part 2 will be calculated and compared with 50%. This will be used to help selection of the next dose together with safety and tolerability data. The Bayesian probability will be based on Whitehead's model shown below [Whitehead, 2001] using non-informative prior for model parameters.

$$y_{ij} = \theta_1 + \theta_2 d_{ij} + s_i + \epsilon_{ij} \quad [1]$$

Where y_{ij} is log-PK of i-th participant to j-th dose, d_{ij} is j-th log-dose administered to i-th participant. θ_1 and θ_2 are population intercept and slope, respectively. s_i is random effect of i-th participant and ϵ_{ij} is random error of i-th participant in j-th dose. Note that, from the first to the second dose in Part 1 of the study, we will assume that the PK is dose-proportional for the model.

When intra-participant PK variability cannot be estimated early in Part 1 (i.e., early on in the study when there is not sufficient information to estimate intra-participant variability) and for conducting prediction of all doses in Part 2, the same Whitehead's model will be used for Bayesian probability calculations as below.

$$y_i = \theta_1 + \theta_2 d_i + \epsilon_i \quad [2]$$

Where y_i is log-PK of i-th participant, d_i is the log-dose administered to i-th participant. θ_1 and θ_2 are population intercept and slope, respectively and ε_i is random error of i-th participant. Note that, from the first to the second dose in Part 2 of the study, we will assume that the PK is dose-proportional for the model.

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) has been declared by Data Management.
3. All criteria for unblinding the randomization codes have been met.
4. Randomization codes have been distributed according to RandAll NG procedures.

Data will be listed and summarized according to GlaxoSmithKline reporting standards, where applicable. Listings will be sorted by subject, day and time, noting treatment; summaries will be presented by treatment, day, and time. Unless stated otherwise, descriptive summaries will include n, mean, standard deviation (SD), coefficient of variation (%CV), median, minimum, and maximum for continuous variables, whereas n and percent will be used as summary statistics for categorical variables, and geometric mean, 95% confidence interval (CI), and the between-participant CV (%CVb) for the log-transformed PK parameters. Baseline or predose assessment is the last available assessment prior to time of the first dose unless it is specified otherwise. If there are multiple assessments collected on the same scheduled time, the average of these assessments will be used. For tabulated safety summaries, only the scheduled assessments will be included in the summary tables. Version 9.3 or higher of the SAS system will be used to analyse the data as well as to generate tables, figures, and listings.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Screened	• All participants who were screened for eligibility	• Study Population
Enrolled	• All participants who passed screening and entered the study. • Note screening failures (who never passed screening even if rescreened) and participants screened but never enrolled into the study (Reserve, Not Used) are excluded from the Enrolled population, as they did not enter the study.	• Study Population
Safety	• All randomized participants who received at least one dose of study treatment. • This population will be based on the treatment the subject actually received for each respective cohort/period .	• Study Population • Safety
Pharmacokinetic (PK) Concentration	• Part 1 (SAD) The PK Concentration Population will include all participants who undergo plasma PK sampling and have at least one evaluable concentration during the single dose phase of the study Part 1. • Part 2 (MAD) The PK Concentration Population will include all participants who undergo plasma PK sampling and have at least one evaluable concentration during the repeat dose phase of the study Part 2.	• PK concentration Listing • PK individual concentration-time data plots
Pharmacokinetic (PK) Parameter	• Part 1 (SAD) The PK Parameter Population will include all participants who undergo plasma PK sampling and have evaluable PK parameters estimated during the single dose phase of the study Part 1. • Part 2 (MAD) The PK Parameter Population will include all	• PK parameter listing • PK mean/median concentration-time data plots • PK parameter

Population	Definition / Criteria	Analyses Evaluated
	participants who undergo plasma PK sampling and have evaluable PK parameters estimated during the repeat dose phase of the study Part 2.	summary • Dose proportionality • Accumulation ratio analysis and steady state analysis for Part 2

Refer to Appendix 12: 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 Version 002 (09-May-2018).

- Data will be reviewed prior to freezing the database to ensure all important deviations 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 listing 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 & Sub-group Display Descriptors

Treatment Group Descriptions				
RandAll NG		Data Displays for Reporting		
Code	Description	Description	Header	Order in TLF
Part 1				
P/PS	Placebo/Placebo Sentinel	Placebo SD	SD PBO	9
D1/ D1S	GSK3640254 Dose Level 1/ GSK3640254 Dose Level 1 sentinel	GSK3640254 1 mg SD	SD 1mg	1
D2/ D2S	GSK3640254 Dose Level 2/ GSK3640254 Dose Level 2 sentinel	GSK3640254 3 mg SD	SD 3mg	2
D3/ D3S	GSK3640254 Dose Level 3/ GSK3640254 Dose Level 3 sentinel	GSK3640254 10 mg SD	SD 10mg	3
D4/ D4S	GSK3640254 Dose Level 4/ GSK3640254 Dose Level 4 sentinel	GSK3640254 30 mg SD	SD 30mg	4
D5/ D5S	GSK3640254 Dose Level 5/ GSK3640254 Dose Level 5 sentinel	GSK3640254 100 mg SD	SD 100mg	5
D6/ D6S	GSK3640254 Dose Level 6/ GSK3640254 Dose Level 6 sentinel	GSK3640254 200 mg SD	SD 200mg	6
D7/ D7S	GSK3640254 Dose Level 7/ GSK3640254 Dose Level 7 sentinel	GSK3640254 400 mg SD	SD 400mg	7
D8/ D8S	GSK3640254 Dose Level 8/ GSK3640254 Dose Level 8 sentinel	GSK3640254 700 mg SD	SD 700mg	8
Part 2				
RP	Placebo Repeated Dose	Placebo RD	RD PBO	5
R1	GSK3640254 Repeat Dose Level 1	GSK3640254 50 mg RD	RD 50mg	1
R2	GSK3640254 Repeat Dose Level 2	GSK3640254 100 mg RD	RD 100mg	2
R3	GSK3640254 Repeat Dose Level 3	GSK3640254 200 mg RD	RD200 mg	3
R4	GSK3640254 Repeat Dose Level 4	GSK3640254 320 mg RD	RD 320mg	4
R5	GSK3640254 Repeat Dose Level for Expansion Cohort	GSK3640254 200 mg RD	RD200 mg	3

NOTES:

- Order represents treatments being presented in TFL, as appropriate.
- Placebo is pooled by part

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 -2	Day -1	Day 1 (Pre-Dose)	
Lab	X	X			Day -2 in each period
ECG	X	X	X	X	Day 1(Pre-Dose) in each period

Parameter	Study Assessments Considered as Baseline				Baseline Used in Data Display
	Screening	Day -2	Day -1	Day 1 (Pre-Dose)	
Vital Signs	X		X		Day -1 in each period

Unless otherwise stated, if baseline data is missing no derivation will be performed and baseline will be set to missing.

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
12.3	Appendix 3: Assessment Windows
12.4	Appendix 4: Study Phases and Treatment Emergent Adverse Events
12.5	Appendix 5: Data Display Standards & Handling Conventions
12.5	Appendix 6: Derived and Transformed Data
12.7	Appendix 7: Reporting Standards for Missing Data
12.8	Appendix 8: 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, unless otherwise specified.

Study population analyses including analyses of subject's disposition, protocol deviations, demographic and baseline characteristics, prior and concomitant medications, and exposure and treatment compliance will be based on GSK Core Data Standards. Details of the planned displays are presented in Appendix 12: List of Data Displays.

Table 1 provides an overview of the planned study population analyses, with full details of data displays being presented in Appendix 12.

Table 1 Overview of Planned Study Population Analyses

Display Type	Data Displays Generated		
	Table	Figure	Listing
Subject Disposition			
Subject Disposition	Y		
Reasons for Screening Failures	Y		Y[1]
Study Treatment Discontinuation	Y		Y
Reasons for Subject Withdrawal			Y
Protocol Deviations			
Important[3] Protocol Deviations	Y		Y
Subjects with Inclusion/Exclusion Criteria Deviations			Y[2]
Populations Analysed			
Study Populations and Exclusions	Y		
Subjects Excluded from Any Population			Y
Subjects for whom the Treatment Blind was Broken			Y[4]
Demographic and Baseline Characteristics			
Demographic Characteristics	Y		Y
Race and Racial Combinations	Y		Y
Summary of Age Ranges	Y		
Concomitant Medications			
Concomitant Medications[5]	Y		Y
Exposure and Treatment Compliance			
Study Treatment Overall Compliance	Y		
Exposure to Study Treatment	Y		Y
Meal data			Y

NOTES :

- Y = Yes display generated.

1. Conditional displays, if data is available listing will be generated.
2. Listing of subjects excluded from any population will be generated only.
3. All protocol deviations will be listed, with important protocol deviations summarized.
4. Listing will be created for part 2 when data is available.
5. Provide summary table if more than 10 conmeds

6.2. Display Details

6.2.1. Subject Disposition

The disposition table will consist of all subjects in the safety population.

The number and percentage of subjects who failed screening and were, therefore, not entered into the study, overall and by reason, will be summarized. A listing of the screen failure record for all subjects who failed screening, including the reasons for screen failure will be produced.

Reasons for study treatment discontinuation will be summarized for each treatment group and overall. A by-subject listing of reasons for study withdrawal and a by-subject listing of reasons for study treatment discontinuation will be produced.

6.2.2. Protocol Deviations

The number and percentage of subjects who had important protocol deviations defined in Section 4.1 will be summarized by treatment group and overall.

A listing of all protocol deviations will be produced.

Subjects with inclusion and exclusion deviations will be listed.

6.2.3. Populations Analysed

The number of subjects who were enrolled into the study, and the number of subjects within each analysis population (Safety and PK) will be summarized for each treatment group and overall.

Subjects excluded from any population and subjects for whom the Treatment Blind was broken will be listed.

6.2.4. Demographic and Baseline Characteristics

The demographic and baseline characteristics age, sex, race, ethnicity, height, weight, BMI will be summarized by treatment group and overall for the safety population. The count, mean, standard deviation, median, minimum, and maximum value will be computed for age, BMI, height, and weight.

A by-subject listing of demographic and baseline characteristics will also be produced.

Summaries of race and racial combinations will be produced for each treatment group and overall. A listing of race by subject will also be produced.

Summaries of age ranges will be produced for each treatment group and overall.

6.2.5. Concomitant Medications

Medications will be coded using the GSK Drug v1.4 coding dictionary.

Concomitant medications will be summarised by GSK-Drug Anatomical Therapeutic Chemical (ATC) classification level 1 (body system) and ingredient if there are more than 10 concomitant medications. Drugs that are composed of a combination of ingredients will be displayed according to the ATC classifications of the ingredients, not of the combination. A by-subject listing will also be conducted.

6.2.6. Exposure and Treatment Compliance

The complete dosing experience will be listed for all subjects for both Part 1 and Part 2. The total duration of exposure (number of days on study drug), and cumulative dose will be summarized by treatment group for Part 2.

For subjects who completed the 14-day treatment period in Part 2 of the study, the expected number of doses is 14. For subjects who permanently discontinued the study treatment and/or withdrew from the study, the expected number of doses during the treatment period will be calculated using "Days on study drug" where "Days on study drug" is Last Dose Date – First Dose Date +1.

A summary of study medication compliance will be produced by treatment group for Part 2: 0%, >0-<100%, 100%, >100%. The compliance will be calculated for the whole study treatment period as the percentage of cumulative dose [100*(actual cumulative dose) / (expected cumulative dose for the subject's treatment duration)]. For subjects who completed the 14-day treatment period in Part 2, the expected cumulative dose of GSK3640254 taken during the treatment period is as follows:

- For subjects who received 50 mg GSK3640254, the expected cumulative dose is 700 mg GSK3640254
- For subjects who received 100 mg GSK3640254, the expected cumulative dose is 1400 mg GSK3640254
- For subjects who received 200 mg GSK3640254, the expected cumulative dose is 2800 mg GSK3640254
- For subjects who received 320 mg GSK3640254, the expected cumulative dose is 4480 mg GSK3640254

For subjects who permanently discontinued study treatment or withdrew early from the study, the expected cumulative dose of GSK3640254 taken during the treatment period will be calculated as follows:

- For subjects who received 50 mg GSK3640254, the expected cumulative dose is 50 mg*(Last Dose Date – First Dose Date +1)
- For subjects who received 100 mg GSK3640254, the expected cumulative dose is 100 mg*(Last Dose Date – First Dose Date +1)
- For subjects who received 200 mg GSK3640254, the expected cumulative dose is 200 mg*(Last Dose Date – First Dose Date +1)

- For subjects who received 320 mg GSK3640254, the expected cumulative dose is 320 mg*(Last Dose Date – First Dose Date +1)

The actual cumulative dose of GSK3640254 for all subjects is the sum of all doses, in mg, of study drug consumed for the duration of the study.

A by-participant listing of the meal data will also be generated including start and stop date and time of meal, dosing time, type of meal and whether the totality of the meal was ingested.

7. SAFETY ANALYSES

7.1. Overview of Planned Safety Analysis

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

Safety data are the primary endpoints of the study, will be presented in tabular and summarized and listed descriptively accordingly to GSK's Integrated Data Standards Library (IDSL)standards. Details of the planned displays are presented in Appendix 12: List of Data Displays.

Table 2 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 12.

Table 2 Overview of Planned Safety Analyses

Display Type	Absolute				Change from Baseline			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
Adverse Events (AEs)								
AEs Overview	Y							
All AEs				Y				
All Adverse Events by Maximum Grade and SOC and PT	Y							
All Drug-Related AEs				Y				
Drug-Related Adverse Events by Maximum Grade and SOC and PT	Y							
Serious AEs				Y				
Serious AEs by SOC and PT (Subjects & No. of Occurrences)	Y							
Drug Related Serious Adverse Events				Y				
Fatal AEs				Y				
Non-Fatal SAEs				Y				

Display Type	Absolute				Change from Baseline			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
Grade 2- 4 Adverse Events				Y				
AEs of Special Interest	Y			Y				
Adverse Events Leading to Withdrawal from Study/Permanent Discontinuation of Study Treatment	Y			Y				
Subject Numbers for Individual AEs				Y				
Common Adverse Events and Common Non-Serious Adverse Events By Overall Frequency	Y							
Relationship of Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text				Y				
Laboratory Values								
Clinical Chemistry	Y			Y	Y			
Hematology	Y			Y	Y			
Urinalysis	Y			Y				
Clinical Chemistry Value of Potential Clinical Importance				Y				
Hematology Values of Potential Clinical Importance				Y				
Urinalysis Values of Potential Clinical Importance				Y				
Worst Case Chemistry Lab Results by Maximum Grade Post-Baseline Relative to Baseline	Y							
Worst Case Hematology Lab Results by Maximum Grade Post-Baseline Relative to Baseline	Y							
Worst Case Urine Lab Results by Maximum Grade Post-Baseline Relative to Baseline	Y							
Lab Results Identified				Y				

Display Type	Absolute				Change from Baseline			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
as Adverse Events								
Treatment Emergent Laboratory Toxicities	Y							
Subjects with grades 2 or higher laboratory toxicities				Y				
ECG								
ECG Findings	Y			Y				
Abnormal ECG Findings				Y				
ECG Values	Y				Y			
All ECG Values for Subjects with a Value of PCI				Y				
Maximum Increase in QTc Values Post-Baseline Relative to Baseline by Category					Y			
Mean (95% CI) Change from Baseline in QTc interval by Time and Treatment						Y		
Vital Signs								
Vital Values	Y			Y	Y			
All Vital Signs for Subjects with Values of PCI				Y				
Hepatobiliary (Liver)								
Liver Monitoring/Stopping Event Reporting	Y							
Summary of Hepatobiliary Laboratory Abnormalities	Y							

NOTES :

- T = Table, F = Figure, L = Listing, 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.

7.2. Display Details

7.2.1. Adverse Events Analysis

All adverse event (AE) data will be summarized, sorted by the system organ class and preferred term assigned by MedDRA version 21.0, and presented by treatment group. The following summaries will be provided:

- Adverse events overview
- All adverse events by maximum grade and SOC and PT
- Drug related adverse events by maximum grade and SOC and PT
- Serious adverse events by SOC and PT (Subjects & No. of Occurrences)
- Adverse events of Special Interest
- Adverse events leading to withdrawal from study/permanent discontinuation of study treatment
- Common (>= 5%) adverse events by overall frequency
- Common (>= 5%) non-serious adverse events by overall frequency

The following listings will be provided:

- All adverse events
- Drug related adverse events
- Serious adverse events
- Drug related serious adverse events
- Fatal adverse events
- Non-fatal serious adverse events
- Grade 2 - 4 Adverse Events
- Adverse events of special interest
- Adverse events leading to withdrawal from study/permanent discontinuation of study treatment
- Subject Numbers for Individual AEs
- Relationship of Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text

Adverse Events of Special Interest:

A comprehensive list of MedDRA terms based on clinical review will be used to identify each type of GI event (Nausea and Vomiting, Dyspepsia etc.). [Changes to the MedDRA dictionary may occur between the start of the study and the time of reporting and/or emerging data from on-going studies may highlight additional adverse events of special interest, therefore the list of terms to be used for each event of interest and the specific events of interest will be based on the safety review team (SRT) agreements in place at the time of reporting.]

7.2.2. Clinical Laboratory Safety Analyses

Laboratory evaluations including the analyses of chemistry laboratory tests, hematology laboratory tests and urinalysis will be based on GSK Core Data Standards.

Haematology, clinical chemistry and urinalysis parameters collected are listed below.

Protocol Required Safety Laboratory Assessments

Laboratory Assessments	Parameters			
Hematology	Platelet Count RBC Count Hemoglobin Hematocrit	RBC Indices: MCV MCH %Reticulocytes	WBC count with Differential: Neutrophils Lymphocytes Monocytes Eosinophils Basophils	
Clinical Chemistry	BUN	Potassium	Aspartate Aminotransferase (AST)/ Serum Glutamic-Oxaloacetic Transaminase (SGOT)	Total bilirubin
	Creatinine	Sodium, Chloride, Bicarb	Alanine Aminotransferase (ALT)/ Serum Glutamic-Pyruvic Transaminase (SGPT)	Total Protein
	Glucose (non-fasting)	Calcium, Magnesium, Phosphate	Alkaline phosphatase	Fasting Lipid Panel (Cholesterol, Triglycerides, HDL, LDL)
Routine Urinalysis	• Specific gravity • pH, glucose, protein, blood, ketones, bilirubin, urobilinogen, nitrite, leukocyte esterase by dipstick • Microscopic examination (if blood or protein is abnormal)			

The following summaries will be provided:

- Laboratory values for hematology, clinical chemistry, and urinalysis by visit and by treatment
- Laboratory values change from baseline for hematology and clinical chemistry by visit and by treatment group
- The number and percentage of subjects with on-treatment laboratory abnormalities worsened from baseline by maximum grade for haematology, clinical chemistry and urinalysis.
- Treatment emergent laboratory toxicities

The following listings will be provided:

- Laboratory values for haematology, clinical chemistry, and urinalysis
- Laboratory values of potential clinical importance for hematology, clinical chemistry and urinalysis (potential clinical importance criteria are specified in Section 12.8.1)
- Laboratory results identified as adverse events
- Subjects with grades 2 or higher laboratory toxicities

7.2.3. Other Safety Analyses

7.2.3.1. Electrocardiograms

A summary of the number and percentage of subjects of all ECG findings will be displayed by treatment. Additionally, summary statistics of ECG values and change from baseline in ECG values will be presented. Maximum QTc values and maximum increase in QTc values post-baseline relate to baseline will be summarized by category. Mean (95% CI) change from baseline in QTcF interval will be plotted by time and treatment. A by-subject listing of ECG findings for all subjects will be listed. Abnormal ECG findings and all ECG values for subjects with a value of potential clinical importance will be listed (potential clinical importance criteria are specified in Section 12.8.2).

7.2.3.2. Vital Signs

Vital sign values and change from baseline will be summarized. A by-subject listing of vital signs for all subjects will be produced. All vital signs for subjects with values of potential clinical importance will be listed (potential clinical importance criteria are specified in Section 12.8.3)

7.2.3.3. Hepatobiliary (Liver)

Liver monitoring/stopping event reporting will be summarized by treatment group. A summary of hepatobiliary laboratory abnormalities will be produced.

8. PHARMACOKINETIC ANALYSES

8.1. Pharmacokinetic Analyses

The pharmacokinetic (PK) analyses will be based on the "PK Concentration" and "PK Parameter" population, unless otherwise specified.

As an overview, individual, mean and median plasma GSK3640254 concentration-time profiles will be plotted by treatment and day (linear and semi-linear profiles). PK sampling times will be related to the start of the dosing date/time. Actual sampling times will be used to calculate all of the non-compartmental pharmacokinetic parameters. Individual concentrations of GSK3640254 in plasma will be listed and summarised by treatment and nominal time. Details of the planned displays are presented in Appendix 12: List of Data Displays.

Table 3 provides an overview of the planned analyses, with full details being presented in Appendix 12.

Table 3 Overview of Planned Pharmacokinetic Analyses

Display Type	Untransformed							Log-Transformed						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
PK Concentrations														
Plasma Drug Concentrations				Y	Y	Y	Y					Y	Y	
PK Parameters														
PK Parameters				Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	

NOTES :

- T = Table, F = Figure, L = Listings, Y = Display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- 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.

8.1.1. Endpoint / Variables

8.1.1.1. Drug Concentration Measures

Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 12.5.3 Reporting Standards for Pharmacokinetic)

8.1.1.2. 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. 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, as data permits.

Parameter	Parameter Description

AUC(0-inf)	Area under the concentration-time curve extrapolated to infinity will be calculated as: **AUC = AUC(0-t) + C(t) / λ_z**
AUC(0-tlast)	Area under the concentration-time curve from time zero to the time of the last quantifiable concentration (C(t)) will be calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid.
AUC(0-24)	Area under the plasma concentration time curve from zero to 24
AUC(0-τ)	Area under the curve (Area under the plasma drug concentration-time curve from pre-dose to the end of the dosing interval at steady state)
%AUCex	The percentage of AUC (0-inf) obtained by extrapolation (%AUCex) will be calculated as: **[AUC(0-inf) – AUC(0-t)] / AUC(0-inf) x 100**
Cmax	Maximum observed concentration, determined directly from the concentration-time data.
C24	Concentration at 24 hours post-dose on Day 1
Clast	Last quantifiable concentration
Cτ	Pre-dose (trough) concentration at the end of the dosing interval
tmax	Time to reach Cmax, determined directly from the concentration-time data.
t½	Apparent terminal half-life will be calculated as: **t½ = ln2 / λ _z**
tlag	Absorption lag time
tlast	Time of last quantifiable concentration
CL/F	Apparent oral clearance

NOTES:

- Additional parameters may be included as required.

8.1.2. Summary Measure

- Part 1 (single dose): AUC (0-24), AUC(0-tlast), AUC (0-inf), Cmax, C24, tmax, tlag, t1/2, Clast, tlast, CL/F.
- Part 2 (Repeated QD doses for 14 days):
  - Day 1: AUC(0-24), Cmax, C24, tmax, tlag
  - Day 14: AUC(0-τ), Cmax, Cτ, tmax, t1/2, and CL/F.

8.1.3. Population of Interest

The primary pharmacokinetic analyses will be based on the Pharmacokinetic Parameter population, unless otherwise specified.

8.1.4. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 12: List of Data Displays and will be based on GSK Data Standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 8.1.1 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

8.1.4.1. Statistical Methodology Specification

Dose Proportionality-Power model:

Part 1, and 2:

Dose proportionality of GSK3640254 following single-dose administration in Part

1 and following single-dose and repeat-dose administration inPart 2 of the study will be assessed separately using the power model (Smith, 2000) as

described below:

$y = \alpha * dose^{\beta}$

where y denotes the PK parameter being analyzed [for Part 1: AUC(0-∞), AUC(0-24),

and Cmax. For Part 2: AUC(0-24), Cmax on Day1;

AUC(0-τ), Cmax, C_{τ} on Day 14] . Dose proportionality implies that β=1 and will be

assessed by estimating β along with its confidence interval. The exponent, β, in the

power model will be estimated by regressing the log_e-transformed PK parameter on log_e

dose.

log(y) = log(α) + β * log(dose)

The power model will be fitted by restricted maximum likelihood (REML) using SAS

Proc Mixed. For Part 1, a power model with subject as the random effect will be fitted. If the model does not converge then a fixed effect power model will be fitted. For Part 2, a fixed effect power model will be fitted. The mean slope will be estimated from the power model and the corresponding 90% confidence interval calculated. Intra-subject CV% calculated from the model will be presented in the table. Point estimates and confidence intervals for the slope will be reported to 4 decimal places with no rounding.

Part 1,

An example of SAS code is included here for the power model approach.

ODS output solutionf=stat

Proc Mixed;

class subject;

model logPKvar = logdose /cl alpha=0.1 solution ddfm=kr;

random intercept /subject=subject type=un;

run;

If the above model still does not converge, then use:

ODS output solutionf=stat

Proc Mixed;

model logPKvar = logdose /cl alpha=0.1 solution ddfm=kr;

run;

Part 2,

ODS output solutionf=stat

Proc Mixed;

model logPKvar = logdose /cl alpha=0.1 solution ddfm=kr;

run;

Dose Proportionality-ANOVA Model

Part 1, and 2:

Additionally, dose proportionality may be assessed by pair-wise analysis of variance (ANOVA) using the SAS Mixed model procedure if power model does not show dose proportionality. A reference dose of 3 mg for all parts, and will be used and the other doses would be treated as test dose. PK parameters will be normalized to the reference dose and then log-transformed prior to the analysis. Point estimates and 90% confidence intervals for AUC and Cmax will be reported to 4 decimal places with no rounding.

An example of SAS code is also included here for the ANOVA approach.

ODS output solutionf=stat;

Proc Mixed;

class treatment; / treatments are different dose groups */*

model logdnPKvar = treatment/ddfm=kr;

lsmeans treatment; / assuming one ref and four test treatments */*

estimate 'test1 vs ref' treatment -1 1 0 0 0 /cl alpha=0.1;

estimate 'test2 vs ref' treatment -1 0 1 0 0/cl alpha=0.1;

run;

Individual and box plot of dose-normalized plasma GSK3640254 PK parameters by treatment will be generated.

Accumulation Ratio Analysis

Part 2:

An ANOVA with a random effect term for subject and fixed effect terms for day will be performed by dose on the loge-transformed PK parameters (AUC(0-τ), Cτ, and Cmax). Day will be treated as a class variable in the model. The accumulation ratio of GSK3640254 will be estimated by calculating the ratio of the geometric least squares (GLS) means of PK parameters between Day 14 and Day 1 for Cohort 3,4,5, 6 and expansion, and the corresponding 90% CI for each dose.

An example of SAS code is included here.

ODS output solutionf=stat;

Proc Mixed;

by dose;

class subject day;

model logPKpar = day / ddfm=kr;

random subject;

lsmeans day;

estimate 'Day X vs Day 1' day -1 1/cl alpha=0.1;

run;

Comparative plots of individual plasma GSK3640254 PK estimates will be generated by dose group [AUC(0-τ)), Cτ, and Cmax on Day 14 versus AUC(0-24), C24 and Cmax on Day 1] on linear and semi-logarithmic scales. The accumulation ratio will also be listed and summarized along with other PK parameters.

Steady State Assessment

Part 2

Predose concentrations on Day 2 through 14 and Cτ on day 14 from Cohort 3, 4, 5, 6 and expansion of Part 2 of the study will be plotted versus day by treatment (dose). An ANOVA with terms for subject as a random effect and day as a fixed effect will be performed by dose

on the loge-transformed C0 and Cτ. Day will be treated as a continuous variable in the model. Achievement of plasma GSK3640254 steady state will be assessed by visual inspection of plots and calculating the point estimate and 90% CI of the slope of the linear regression of Days 2-14 for Cohort 3, 4, 5,6 and expansion of Part 2 of pre-dose C0 and Cτ versus Day by dose group. To claim that steady state is reached, the pre-dose

concentration slope estimate is close to zero or the 90% CI for the slope estimate includes zero.

An example of SAS code to assess achievement of steady-state is included here.

```
ODS output solutionf=stat;
Proc Mixed;
by dose;
where (Day in (10,11,12,13,14, 15));
class subject;
model logCtau = Day/cl alpha=0.1 solution;
random intercept/subject=subject type=un;
run;
```

The same analysis will be repeated with C0 data by dropping one earlier day at time between day 2-14, and the results will be presented in the same table.

8.1.5. Food Effect Assessment

As the study did not administer GSK in fasted conditions, the food effect evaluation can't be performed.

9. POPULATION PHARMACOKINETIC (POPPK) ANALYSES

The population PK analysis and pharmacodynamic analyses will be presented separately from the main clinical study report (CSR).

10. REFERENCES

- GlaxoSmithKline Document Number 2016N297505_00: A Double-Blind (Sponsor Unblinded), Randomized, Placebo-Controlled, Single and Repeated Dose Escalation Study to Investigate the Safety, Tolerability and Pharmacokinetics of GSK3640254 in Healthy Participants. Effective Date: 03-MAY-2017
- Whitehead J. et al., Easy-to-implement Bayesian methods for dose-escalation studies in healthy participants, Biostatistics, 2, 47cs, 2, 47v 2001

11. APPENDICES

11.1. Appendix 1: Protocol Deviation Management and Definitions for PK Parameter Population

A subject meeting any of the following criteria will be excluded from the PK Parameter Summary Population:

Number	Exclusion Description
01	Failure of any inclusion/exclusion criteria, but subject is still enrolled

11.2. Appendix 2: Schedule of Activities

11.2.1. Protocol Defined Schedule of Events

SAD Cohorts 1 and 2 Screening

Procedure	Screening (up to 28 days before Day 1)
Outpatient Visit	X
Informed Consent	X
Inclusion/Exclusion Criteria and Demography	X
Medical/medication/ drug/alcohol history	X
Full Physical Exam[1]	X
Columbia Suicide Severity Rating Scale (CSSRS)	X
Height, Weight, BMI	X
Vital signs	X
12 Lead ECG	X
Screening Holter	X
Pregnancy Test	X
Drug/alcohol/cotinine screen	X
HbsAg, HCV, HIV tests	X
Hem/Chem/Urine tests	X

SAD Cohorts 1 and 2 On-Treatment: Before, During, and After Dosing in Each Period

Procedure	Periods 1 through 4																					Follow-up (7-14 days post last dosing)
	Day -2	Day -1	Day 1															Day 2	Day 3	Day 4	Day 5	
			Pre-dose	0 h	0.5 h	1 h	1.5 h	2 h	2.5 h	3 h	3.5 h	4 h	4.5 h	5 h	6 h	8 h	12 h	24 h	48 h	72 h	96 h	
Admission to Unit	X																					
Outpatient Visit																						X
Full Physical Exam[1]		X																	X			X
Weight, BMI		X																				
Vital signs		X				X		X					X		X		X	X	X	X	X	X
12-lead safety ECGs	X	X	X			X		X				X			X		X	X	X	X	X	X
Continuous ECG (full time matched baseline on Day-1)[2]		X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X				
Pregnancy Test	X																					X[3]
Drug/alcohol/cotinine screen	X																					
Hem/Chem/Urine tests	X																	X	X		X	X
Single Dosing with GSK3640254 following moderate fat meal				X																		
Plasma PK Sampling[4]			X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Adverse Event Review	<==========																					==========>
Con Med Review	<==========																					==========>
Furlough from Unit																					X	

HCV=Hepatitis C; BMI= Body mass index; ECG= Electrocardiogram; PK= Pharmacokinetic, SAD=single ascending dose

Note:

1. A Full Physical Exam will include at a minimum, assessments of the Skin, Cardiovascular, Respiratory, Gastrointestinal and Neurological systems.
2. Additional safety ECGs may be printed at the discretion of the PI if prolongation in QT interval is suspected. The frequency of ECGs will support an exploratory endpoint (should clinical development continue) to evaluate the exposure-response relationship between GSK3640254 and QTcF. Once human PK data (e.g. Cmax) are available, the number of ECG time points may be reduced in subsequent dosing groups. At timepoints for ECG extraction, subjects will be supinely resting for at least 10 minutes. When ECG extractions coincide with safety ECGs, vital signs assessment and blood draws, procedures should be carried out in said order.
3. This pregnancy test will be obtained approximately 37 days after the last dose of study treatment
4. The number of PK sampling time points may be reduced in subsequent dosing groups once human PK data are available.

MAD Cohorts 3, 4, 5 and the Expansion Cohort Screening

Procedure	Screening (up to 28 days before Day 1)
Outpatient Visit	X
Informed Consent	X
Inclusion/Exclusion Criteria and Demography	X
Medical/medication/ drug/alcohol history	X
Full Physical Exam[1]	X
CSSRS	X
Height, Weight, BMI	X
Vital signs	X
12 Lead ECG	X
Screening Holter	X
Drug/alcohol/cotinine screen	X
HbsAg, HCV, HIV tests	X
Hem/Chem/Urine tests	X
Pregnancy Test	X

1. A Full Physical Exam will include at a minimum, assessments of the Skin, Cardiovascular, Respiratory, Gastrointestinal and Neurological systems.

MAD Cohorts 3, 4, 5 and the Expansion Cohort On-Treatment

Procedure	Day -2	Day -1	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	Day 15	Day 16	Day 17	Day 18	Follow-up (7-14 days post last dosing)
																0h	24h	48h	72h	96h	
Admission to Unit	X																				
Outpatient Visit																					X
Full Physical Exam[1]		X						X						X			X			X	X
CSSRS						X														X	
Weight, BMI		X																			
Vital signs		X	X	X		X		X		X		X		X		X			X		X
12-lead safety ECGs	X	X	X	X	X	X		X		X		X		X		X	X	X	X	X	X
Continuous ECG (full time matched baseline on Day-1)[2]		X	X	X												X	X				
Drug/alcohol/cotinine screen	X																				
Hem/Chem/Urine tests	X			X		X		X		X		X		X		X		X		X	X
Pregnancy Test	X																				X[3]
QD Dosing with GSK3640254 following moderate fat meal			X	X	X	X	X	X	X	X	X	X	X	X	X	X					
Plasma PK Sampling[4]			X	X	X	X		X		X		X		X		X	X	X	X	X	
Plasma Metabolite Sampling[5]			X	X												X	X				

Procedure	Day -2	Day -1	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	Day 15	Day 16	Day 17	Day 18	Follow-up (7-14 days post last dosing)
																0h	24h	48h	72h	96h	
Urine PK and Metabolite Sampling[6]			X	X												X	X				
PGx Sampling (if participant consents)	X																				
Adverse Event Review	<==========																				==========>
Con Med Review	<==========																				==========>
Furlough from Unit																				X	

Note:

1. A Full Physical Exam will include at a minimum, assessments of the Skin, Cardiovascular, Respiratory, Gastrointestinal and Neurological systems.
2. ECG data extracted from the Continuous ECG will be assessed before PK sampling, prior to dosing and 0.5,1, 1.5, 2, 2.5, 3, 3.5, 4.5, 5, 5.5, 6, 8, 12 h, and 24 h post dose on Day 1 and Day 14 and on corresponding timepoints on Day -1. At timepoints for ECG extraction, subjects will be supinely resting for at least 10 minutes. When ECG extractions coincide with safety ECGs, vital signs assessment and blood draws, procedures should be carried out in said order. The frequency of EKGs will support an exploratory endpoint to evaluate (should clinical development continue) the ER relationship between GSK3640254 and QTcF. Once human data (eg Cmax) is known, the number of EKG time points may be reduced.
3. This pregnancy test will be obtained approximately 37 days after the last dose of study treatment
4. Plasma PK samples for bioanalysis for GSK3640254 will be collected pre-dose (within 15 minutes prior to dosing) and 0.5,1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 8, 12 h on Day 1 and Day 14. On dosing days, plasma PK will be collected pre-dose. The number of PK sampling time points may be reduced in the initial MAD cohort as well as further in subsequent MAD dosing groups once human PK data are available in the SAD as well as in the initial MAD cohorts.
5. Plasma Metabolite samples for metabolite identification will be collected pre-dose (within 15 minutes prior to dosing) and at the same time points as for plasma PK samples on Day 1, Day 2 and Day 14, and Day 15. Plasma metabolite samples will not be collected in the expansion cohort.

6. Urine PK and Metabolite Sampling for bioanalysis and metabolite identification will be collected pre-dose (within 1 hour prior to dosing) and from time 0 up to 24 hours on Day 1 and Day 14. Urine samples will not be collected in the expansion cohort.

11.3. Appendix 3: Assessment Windows

Not applicable.

11.4. Appendix 4: Study Phases and Treatment Emergent Adverse Events

11.4.1. Study Phases

Assessments and events will be classified according to the time of occurrence relative to start and/or stop date of the study treatment.

Study Phase	Definition
Pre-Treatment	Date ≤ (First) Study Treatment Start Date
On-Treatment	(First) Study Treatment Start Date < Date ≤ (Last) Study Treatment Stop Date + 5 days
Post-Treatment	Date > (Last) Study Treatment Stop Date + 5 days

Study epoch of follow-up data for Part 1will be summarized in following way:
Follow-up from Period 1will be counted in Period 1 summary;
Follow-up from Period 2 will be counted in Period 2 summary;
Follow-up from Period 3 will be counted in Period 3 summary;
Follow-up from final follow-up will be counted in Period 4 summary.

11.4.1.1. Study Phases for Concomitant Medication

Study Phase	Definition
Prior	If medication end date is not missing and is before 28 days prior to screening visit
Concomitant	Any medication that is not a prior

NOTES:

- Please refer to Appendix 7: Reporting Standards for Missing Data for handling of missing and partial dates for concomitant medication. Use the rules in this table if concomitant medication date is completely missing.

11.4.2. Treatment Emergent Flag for Adverse Events

Flag	Definition
Treatment Emergent	• If AE onset date is on or after treatment start date & on or before treatment stop date. • Study Treatment Start Date ≤ AE Start Date ≤ Study Treatment Stop Date • For Part 1: AE onset is during one period and worsens during a later period it would be counted in both periods. For the initial period, the logic would be as above. For the later period the logic would use the treatment dates associated with the later period • Treatment Period Start Date ≤ AE Worsening Date ≤ Study Treatment Stop Date

NOTES:

- If the study treatment stop date is missing, then the AE will be considered to be On-Treatment.
- Time of study treatment dosing and start/stop time of AEs should be considered, if collected.

11.4.3. Adverse Events Assignment to Treatment Period for Part 1

Adverse events (AEs) will be assigned to a treatment period and corresponding treatment received in that treatment period after the imputations defined in RAP section 12.7.2 have been performed.

- Treatment Period 1: all AEs with start date/time at the time of or after administration in Treatment Period 1 and before administration in Treatment Period 2
- Treatment Period 2: all AEs with start date/time at the time of or after administration in Treatment Period 2 and before administration in Treatment Period 3
- Treatment Period 3: all AEs with start date/time at the time of or after administration in Treatment Period 3 and before administration in Treatment Period 4
- Treatment Period 4: all AEs with start date/time at the time of or after administration in Treatment Period 4

Thus, AEs occurring during the 1st washout will be assigned to the treatment received in Treatment Period 1, AEs occurring during the 2th washout will be assigned to the treatment received in Treatment Period 2, AEs occurring during the 3rd washout will be assigned to the treatment received in Treatment Period 3 and AEs occurring during final follow-up will be assigned to the treatment received in Treatment Period 4.

11.4.4. Concomitant Medication Assignment to Treatment Period for Part 1

Concomitant medications (CMs) will be assigned to a treatment period and corresponding treatment received in that treatment period after the imputations defined in RAP section 12.7.2 have been performed.

- Treatment Period 1: all CMs with start date/time at the time of or after administration in Treatment Period 1 and before administration in Treatment Period 2
- Treatment Period 2: all CMs with start date/time at the time of or after administration in Treatment Period 2 and before administration in Treatment Period 3
- Treatment Period 3: all CMs with start date/time at the time of or after administration in Treatment Period 3 and before administration in Treatment Period 4
- Treatment Period 4: all CMs with start date/time at the time of or after administration in Treatment Period 4

Thus, CMs occurring during the 1st washout will be assigned to the treatment received in Treatment Period 1, CMs occurring during the 2th washout will be assigned to the treatment received in Treatment Period 2, CMs occurring during the 3rd washout will be assigned to the treatment received in Treatment Period 3, and CMs occurring during follow-up will be assigned to the treatment received in Treatment Period 4.

11.5. Appendix 5: Data Display Standards & Handling Conventions

11.5.1. Reporting Process

Software	
• The currently supported versions of SAS software will be used.	
Reporting Area	
HARP Server	: US1SALX00259
HARP Compound	: 3640254
Analysis Datasets	
• Analysis datasets will be created according to CDISC standards (SDTM IG Version 3.13 & ADaM IG Version 1.0]. If the Study Data Standardization Plan (SDSP) exists for a study, ensure the CDISC versions are consistent.	
Generation of RTF Files	
• RTF files will be generated for SAC.	

11.5.2. 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
• Do not include subject level listings in the main body of the GSK Clinical Study Report. All subject level listings should be located in the modular appendices as ICH or non-ICH listings
• Statistical analyses of the pharmacokinetic parameter data will be the responsibility of Clinical Statistics, GSK.

Formats
• 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 summary tables and/or 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.
Plasma GSK3640254 concentrations and PK data
• Will be summarized by treatment and listed by participant. Unless stated otherwise, descriptive summaries will include number (n), mean, standard deviation (SD), coefficient of variation (%CV), median, minimum, and maximum for continuous variables, n and percent (%) for categorical variables, and geometric mean, 95% confidence interval (CI), and the between-participant CV (%CVb) for the log-transformed PK parameters.
Between-subject coefficient of variation (%CVb)
• Untransformed Data: 100 * (SD/Mean) • Transformed Data: 100 * (sqrt(exp(SDlog2)-1)), where SDlog indicates the standard deviation of log-transformed data. • Within subject coefficient of variation (%CVw) will be calculated according to the following method: CVw(%) = SQRT(exp(MSE) – 1)×100 and MSE is the residual mean squared error from the model. CVw represents a pooled measure of within-subject variability across the treatments.

11.5.3. Reporting Standards for Pharmacokinetic

Pharmacokinetic Concentration Data	
PC Windows Non-Linear (WNL) File	PC WNL file (CSV format) for the non-compartmental analysis by Clinical Pharmacology Modelling and Simulation function will be created according to [Insert document name]. 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.
NONMEM/Pop PK File	Not applicable.
Pharmacokinetic Parameter Derivation	
PK Parameter to be Derived by Programmer	The following PK parameters will be derived by the Programmer: C24, AUC/Dose, Cmax/Dose, Ratio of accumulation
Pharmacokinetic Parameter Data	
Is NQ impacted PK Parameters Rule Being Followed	[Modify as required] No. OR Yes, refer to [Standards for Handling NQ Impacted PK Parameters].
Descriptive Summary	Refer to IDSL PK Display Standards.

Statistics, Graphical Displays and Listings	Refer to [Insert document name]

11.6. Appendix 6: Derived and Transformed Data

11.6.1. 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

11.6.2. Study Population

Demographics
Age

• GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as follows:
  ○ 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**

Extent of Exposure
• Number of days of exposure to study drug will be calculated based on the formula: **Duration of Exposure in Days = Treatment Stop Date – (Treatment Start Date) + 1** • Subjects who were randomized but did not report a treatment start date will be categorised as having zero days of exposure. • The cumulative dose will be based on the formula: **Cumulative Dose = Sum of (Number of Days x Total Daily Dose)** • If there are any treatment breaks during the study, exposure data will be adjusted accordingly.

11.6.3. Safety

Adverse Events
• Gastrointestinal nonspecific symptoms and therapeutic procedures
Abdominal discomfort

Abdominal distension
Abdominal pain
Abdominal pain lower
Abdominal pain upper
Abdominal symptom
Abdominal tenderness
Abnormal faeces
Aerophagia
Anorectal discomfort
Bowel movement irregularity
Change of bowel habit
Constipation
Defaecation disorder
Defaecation urgency
Diarrhoea
Discoloured vomit
Epigastric discomfort
Eructation
Faecal volume decreased
Faecal volume increased
Faeces hard
Faeces soft
Flatulence
Frequent bowel movements
Gastrointestinal pain
Gastrointestinal sounds abnormal
Gastrointestinal toxicity
Infrequent bowel movements
Nausea
Non-cardiac chest pain
Oesophageal discomfort
Oesophageal pain
Vomiting
Anorectal swelling
Antacid therapy
Antidiarrhoeal supportive care
Antiemetic supportive care
Breath odour
Chest pain
Colonic lavage
Dysphagia
Early satiety
Gastritis prophylaxis
Gastrointestinal disorder therapy

Gastrointestinal tract irritation
Gastrooesophageal reflux prophylaxis
Glycogenic acanthosis
Hypovolaemia
Laxative supportive care
Malabsorption
Mucous stools
Pernicious anaemia
Post procedural constipation
Post procedural diarrhoea
Post-tussive vomiting
Probiotic therapy
Procedural nausea
Procedural vomiting
Prophylaxis against diarrhoea
Prophylaxis of nausea and vomiting
Regurgitation
Retching
Steatorrhoea
Vomiting projectile

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 :

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

11.6.4. Pharmacokinetic

General
• The PK Plasma Concentration Population will include all subjects who undergo plasma PK sampling and have evaluable PK assay results for the study drug. • Data from subjects who have major protocol deviations will be excluded from PK concentration summary, PK parameter summary and statistical comparisons but will be included in the Listing and flagged. • This population will be used for listing PK concentrations, parameters, calculating PK parameters and plotting of individual concentration-time files. • If during clinical phase, 3 consecutive samples in any phase i.e.(Absorption, Distribution and Metabolism / Excretion) are found to be missing then data for that subject will not be included in PK and statistical analysis and only the concentration data of that subject(s) will be presented
• **Calculation of Pharmacokinetic Parameter Values Not Described in Section 9** (refer to GUI_51487 for pharmacokinetic analysis information)

11.6.5. Pharmacodynamic (and / or Biomarker)

Not applicable.

11.7. Appendix 7: Reporting Standards for Missing Data

11.7.1. Premature Withdrawals

Element	Reporting Detail
General	• Subject study completion was defined as complete all phases of the study including the follow-up visit. • Withdrawn subjects may be replaced in the study, if applicable, at the discretion of the sponsor in consultation with the investigator. • 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. • All subjects who withdraw prematurely from the study/study drug will be documented and the reason for their withdrawal recorded in the final Clinical Pharmacology Study Report (CPSR). • 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.

11.7.2. 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:
	  ○ 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.
	  ○ 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.

11.7.2.1. 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. In such a case, the following conventions will be applied for calculating the time to onset and the duration of the event:
	  ○ Missing Start Day: First of the month will be used unless this is before the start date of study treatment; in this case the study treatment start date will be used and hence the event is considered On-treatment as per Appendix 4: Study Phases and Treatment Emergent Adverse Events.
	  ○ Missing Stop Day: Last day of the month will be used, unless this is after the stop date of study treatment; in this case the study treatment stop date will be used.
	• Completely missing start or end dates will remain missing, with no imputation applied.

Element	Reporting Detail
	Consequently, time to onset and duration of such events will be missing.

Concomitant Medications	• Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention:
	  ○ If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month
	  ○ 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.

11.8. Appendix 8: Values of Potential Clinical Importance

11.8.1. Laboratory Values

Division of AIDS (DAIDS, Version 2.0, November 2014)AE grade 2 and above of lab abnormalities will be listed by subject, period/treatment, visit, and actual date and time.

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
White Blood Cell Count (WBC)	$x10^9$/ L		3	12
Clinical Chemistry				
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (>x)**
Albumin	g/L		30	
Bicarbonates	mmol/L		18	32
BUN	mmol/L			>9
Creatinine	µmol/L	Δ from BL		↑ 44.2
Glucose	mmol/L		3	9
Potassium	mmol/L		3	5.5
Sodium	mmol/L		130	150
Total CO2	mmol/L		18	32
Total Protein	g/L	Δ from BL	< -15	>15
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	
Total Bilirubin	µmol/L	High	≥ 1.5xULN	

11.8.2. ECG

ECG Parameter	**Units**	**Clinical Concern Range**	
		Lower	**Upper**
Absolute			

ECG Parameter	Units	Clinical Concern Range	
		Lower	Upper
PR Interval	msec	< 120	> 200
QRS Duration	msec	< 60	> 120
QT Interval	msec	< 320	> 450
QTc Interval (Bazett)	msec	< 320	> 450
QTc Interval (Fridericia)	msec	< 320	> 450
RR Interval	msec	< 600	> 1200
Change from Baseline			
Increase from Baseline QTc	msec		>60

11.8.3. Vital Signs

Vital Sign Parameter (Absolute)	Units	Clinical Concern Range	
		Lower	Upper
Systolic Blood Pressure	mmHg	< 85	> 140
Diastolic Blood Pressure	mmHg	< 45	> 90
Heart Rate	bpm	< 40	> 100

11.9. Appendix 9: Population Pharmacokinetic (PopPK) Analyses

Not Appicable.

11.10. Appendix 10: Pharmacokinetic / Pharmacodynamic Analyses

The PK/PD analysis will be conducted if data is available.

11.11. Appendix 11: Abbreviations & Trade Marks

11.11.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CPMS	Clinical Pharmacology Modelling & Simulation
CSR	Clinical Study Report
CTR	Clinical Trial Register
CV_b / CV_w	Coefficient of Variation (Between) / Coefficient of Variation (Within)
DBF	Database Freeze
DBR	Database Release
DP	Decimal Places
eCRF	Electronic Case Record Form
GSK	GlaxoSmithKline
IA	Interim Analysis
ICH	International Conference on Harmonization
IDSL	Integrated Data Standards Library
IP	Investigational Product
PCI	Potential Clinical Importance
PD	Pharmacodynamic
PDMP	Protocol Deviation Management Plan
PK	Pharmacokinetic
PopPK	Population PK
QC	Quality Control
QTcF	Fridericia's QT Interval Corrected for Heart Rate
QTcB	Bazett's QT Interval Corrected for Heart Rate
RAP	Reporting & Analysis Plan
SAC	Statistical Analysis Complete
SDSP	Study Data Standardization Plan
SDTM	Study Data Tabulation Model
TFL	Tables, Figures & Listings
VH	ViiV healthcare

11.11.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
None

Trademarks not owned by the GlaxoSmithKline Group of Companies
DAIDS
Phoenix
WinNonlin
SAS

11.12. Appendix 12: List of Data Displays

11.12.1. 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	3.1 to 3.n	3.1 to 3.n
Pharmacokinetic	4.1 to 4.n	4.1 to 4.n
Phamacokinetic/Pharmacodynamic		5.1 to 5.n
Section	**Listings**	
ICH Listings	1 to x	
Other Listings	y to z	

11.12.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required example mock-up displays provided in 2: 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.'

11.12.3. Deliverables

Delivery	Description
SAC	Final Statistical Analysis Complete

11.12.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Part 1					
Subject Disposition					
1.1.	Safety	ES4	Summary of Subject Disposition at Each Study Epoch - Part 1	ICH E3	SAC
1.2.	Safety	ES1A	Summary of Subject Status and Reason for Study Withdrawal – Part 1	ICH E3, FDAAA, EudraCT	SAC
1.3.	Safety	ES6	Summary of Screening Status and Reasons for Screen Failure - Part 1	ICH E3	SAC
1.4.	Safety	SD1	Summary of Treatment Status and Reasons for Discontinuation of Study – Part 1	The treatment group column will indicate the treatment that the subject was taking at the time of discontinuation	SAC
Protocol Deviation					
1.5.	Safety	DV1	Summary of Important Protocol Deviations - Part 1	ICH E3, Only the total column will appear	SAC
Population Analysed					
1.6.	Safety	SP1	Summary of Study Populations - Part 1		SAC
Demographic and Baseline Characteristics					
1.7.	Safety	DM3	Summary of Demographic Characteristics - Part 1	ICH E3, FDAAA, EudraCT	SAC
1.8.	Enrolled	DM11	Summary of Age Ranges - Part 1	EudraCT, only the total column will appear	SAC

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
1.9.	Safety	DM5	Summary of Race and Racial Combinations - Part 1	ICH E3, FDA, FDAAA, EudraCT, only the total column will appear	SAC
Prior and Concomitant Medications					
1.10.	Safety	CM1	Summary of Concomitant Medications – Part 1	only the total column will appear	SAC
Exposure and Treatment Compliance					
1.11.	Safety	EX1	Summary of Exposure to Study Drug– Part 1	ICH E3 For ClinPharm, a listing often substitutes for a table.	SAC
Part 2					
Subject Disposition					
1.12.	Safety	ES4	Summary of Subject Disposition at Each Study Epoch - Part 2	ICH E3	SAC
1.13.	Safety	ES1	Summary of Subject Status and Reason for Study Withdrawal – Part 2	ICH E3, FDAAA, EudraCT	SAC
1.14.	Safety	ES6	Summary of Screening Status and Reasons for Screen Failure - Part 2	ICH E3	SAC
1.15.	Safety	SD1	Summary of Treatment Status and Reasons for Discontinuation of Study– Part 2		SAC
Protocol Deviation					
1.16.	Safety	DV1	Summary of Important Protocol Deviations - Part 2	ICH E3	SAC
Population Analysed					
1.17.	Safety	SP1	Summary of Study Populations - Part 2	IDSL	SAC

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Demographic and Baseline Characteristics					
1.18.	Safety	DM1	Summary of Demographic Characteristics - Part 2	ICH E3, FDAAA, EudraCT	SAC
1.19.	Enrolled	DM11	Summary of Age Ranges - Part 2	EudraCT	SAC
1.20.	Safety	DM5	Summary of Race and Racial Combinations - Part 2	ICH E3, FDA, FDAAA, EudraCT	SAC
Prior and Concomitant Medications					
1.21.	Safety	CM1	Summary of Concomitant Medications – Part 2	ICH E3	SAC
Exposure and Treatment Compliance					
1.22.	Safety	EX1	Summary of Exposure to Study Drug – Part 2		SAC

11.12.5. Safety Tables

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Part 1					
Adverse Events (AEs)					
3.1.	Safety	AE13	Adverse Event Overview – Part 1	the counting of events and the percentages will be based on the number of subjects on each treatment, so subjects will appear in more than one treatment category	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.2.	Safety	AE5A	Summary of All Adverse Events by Maximum Grade by System Organ Class and Preferred Term - Part 1	ICH E3	SAC
3.3.	Safety	AE5A	Summary of All Drug-Related Adverse Events by Maximum Grade by System Organ Class and Preferred Term – Part 1	ICH E3, 3.2.	SAC
Serious and Other Significant Adverse Events					
3.4.	Safety	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Participants and Occurrences) – Part 1	FDAAA, EudraCT	SAC
3.5.	Safety	AE5A	Summary of Adverse Events of Special Interest by Maximum Grade by System Organ Class and Preferred Term – Part 1		SAC
3.6.	Safety	AE1	Summary of Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study – Part 1	IDSL	SAC
3.7.	Safety	AE3	Summary of Common (>=5%) Adverse Events by Overall Frequency – Part 1	ICH E3	SAC
3.8.	Safety	AE15	Summary of Common (>=5%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences) – Part 1	FDAAA, EudraCT	SAC
Laboratory: Chemistry					
3.9.	Safety	LB1	Summary of Clinical Chemistry Data – Part 1	Will have Non-fasting Glucose and fasting Glucose results separately.	SAC
3.10.	Safety	LB1	Summary of Clinical Chemistry Changes from Baseline – Part 1	ICH E3, Non-fasting Glucose test results will not be included since the baseline values are fasting results.	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.11.	Safety	LB16	Summary of Worst Case Clinical Chemistry Results by Maximum Grade Increase Post-Baseline Relative to Baseline – Part 1	ICH E3, (reference study 204953 Table 2.11)	SAC
3.12.	Safety	LB2	Summary of Treatment Emergent Clinical Chemistry Toxicities – Part 1	(reference study mid200207 Table 2.16)	SAC
Laboratory: Hematology					
3.13.	Safety	LB1	Summary of Hematology Data – Part 1		SAC
3.14.	Safety	LB1	Summary of Hematology Changes from Baseline – Part 1	ICH E3	SAC
3.15.	Safety	LB16	Summary of Worst Case Hematology Results by Maximum Grade Increase Post-Baseline Relative to Baseline – Part 1	ICH E3, 3.11	SAC
3.16.	Safety	LB2	Summary of Treatment Emergent Hematology Toxicities – Part 1		SAC
Laboratory: Urinalysis					
3.17.	Safety	UR1	Summary of Urine Data – Part 1		SAC
3.18.	Safety	LB1	Summary of Urine Concentration Changes from Baseline– Part 1	ICH E3	SAC
3.19.	Safety	LB16	Summary of Worst Case Urinalysis by Maximum Grade Increase Post-Baseline Relative to Baseline – Part 1	ICH E3	SAC
Laboratory: Hepatobiliary (Liver)					
3.20.	Safety	LIVER1	Summary of Liver Monitoring/Stopping Event Reporting – Part 1		SAC
3.21.	Safety	LIVER10	Summary of Hepatobiliary Laboratory Abnormalities – Part 1		SAC
ECG					
3.22.	Safety	EG1	Summary of ECG Findings – Part 1		SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.23.	Safety	EG10	Summary of Maximum QTc Values Post-Baseline Relative to Baseline by Category – Part 1	ICH E14	SAC
3.24.	Safety	EG2	Summary of Change from Baseline for ECG Values – Part 1		SAC
3.25.	Safety	EG11	Summary of Maximum Increase in QTc Values Post Baseline Relative to Baseline by Category – Part 1	ICH E14	SAC
Vital Signs					
3.26.	Safety	VS1	Summary of Change from Baseline in Vital Signs – Part 1	ICH E 3, 3.11	SAC
3.27.	Safety	VS6	Summary of Vital Sign Results by Maximum Grade Increases Post-Baseline Relative to Baseline – Part 1	IDSL	SAC
Part 2					
Adverse Events (AEs)					
3.28.	Safety	AE13	Adverse Event Overview – Part 2		SAC
3.29.	Safety	AE5A	Summary of All Adverse Events by Maximum Grade by System Organ Class and Preferred Term - Part 2	ICH E3	SAC
3.30.	Safety	AE5A	Summary of All Drug-Related Adverse Events by Maximum Grade by System Organ Class and Preferred Term – Part 2	ICH E3, 3.2.	SAC
Serious and Other Significant Adverse Events					
3.31.	Safety	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Participants and Occurrences) – Part 2	FDAAA, EudraCT	SAC
3.32.	Safety	AE5A	Summary of Adverse Events of Special Interest by Maximum Grade by System Organ Class and Preferred Term – Part 2		SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.33.	Safety	AE1	Summary of Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study – Part 2	IDSL	SAC
3.34.	Safety	AE3	Summary of Common (>=5%) Adverse Events by Overall Frequency – Part 2	ICH E3	SAC
3.35.	Safety	AE15	Summary of Common (>=5%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences) – Part 2	FDAAA, EudraCT	SAC
Laboratory: Chemistry					
3.36.	Safety	LB1	Summary of Clinical Chemistry Data – Part 2	Will have Non-fasting Glucose and fasting Glucose results separately.	SAC
3.37.	Safety	LB1	Summary of Clinical Chemistry Changes from Baseline – Part 2	Non-fasting Glucose test results will not be included since the baseline values are fasting results.	SAC
3.38.	Safety	LB16	Summary of Worst Case Clinical Chemistry Results by Maximum Grade Increase Post-Baseline Relative to Baseline – Part 2	(reference study 204953 Table 2.11)	SAC
3.39.	Safety	LB2	Summary of Treatment Emergent Clinical Chemistry Toxicities – Part 2	(reference study mid200207 Table 2.16)	SAC
Laboratory: Hematology					
3.40.	Safety	LB1	Summary of Hematology Data – Part 2		SAC
3.41.	Safety	LB1	Summary of Hematology Changes from Baseline – Part 2		SAC
3.42.	Safety	LB16	Summary of Worst Case Hematology Results by Maximum Grade Increase Post-Baseline Relative to Baseline – Part 2	3.11	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.43.	Safety	LB2	Summary of Treatment Emergent Hematology Toxicities – Part 2		SAC
Laboratory: Urinalysis					
3.44.	Safety	UR1	Summary of Urine Data – Part 2		SAC
3.45.	Safety	LB1	Summary of Urine Concentration Changes from Baseline– Part 2	ICH E3	SAC
3.46.	Safety	LB16	Summary of Worst Case Urinalysis by Maximum Grade Increase Post-Baseline Relative to Baseline – Part 2	ICH E3	SAC
Laboratory: Hepatobiliary (Liver)					
3.47.	Safety	LIVER1	Summary of Liver Monitoring/Stopping Event Reporting – Part 2		SAC
3.48.	Safety	LIVER10	Summary of Hepatobiliary Laboratory Abnormalities – Part 2		SAC
ECG					
3.49.	Safety	EG1	Summary of ECG Findings – Part 2		SAC
3.50.	Safety	EG10	Summary of Maximum QTc Values Post-Baseline Relative to Baseline by Category – Part 2	ICH E14	SAC
3.51.	Safety	EG2	Summary of Change from Baseline for ECG Values – Part 2		SAC
3.52.	Safety	EG11	Summary of Maximum Increase in QTc Values Post Baseline Relative to Baseline by Category – Part 2	ICH E14	SAC
Vital Signs					
3.53.	Safety	VS1	Summary of Change from Baseline in Vital Signs – Part 2	3.11	SAC
3.54.	Safety	VS6	Summary of Vital Sign Results by Maximum Grade Increases Post-Baseline Relative to Baseline – Part 2	IDSL	SAC

11.12.6. Safety Figures

Safety : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Part 1					
ECG					
3.1.	Safety	mid200207 Figure 2.6	Plot of Mean (95% CI) Change from Baseline in QTcF Interval by Treatment and Time – Part 1	(reference study mid200207 Figure 2.6)	SAC
Part 2					
ECG					
3.2.	Safety	mid200207 Figure 2.6	Plot of Mean (95% CI) Change from Baseline in QTcF Interval by Treatment and Time – Part 2	(reference study mid200207 Figure 2.6)	SAC

11.12.7. Pharmacokinetic Tables

Pharmacokinetic : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Part 1					
PK Concentration Data					
4.1.	PK Concentration	PKCT1	Summary of Plasma GSK3640254 PK Concentration-Time Data by Treatment and by Day – Part 1		SAC
PK Derived Parameters					
4.2.	PK Parameter	PKPT1	Summary of Untransformed Derived Plasma GSK3640254 PK Parameters by Treatment – Part 1		SAC

Pharmacokinetic : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
4.3.	PK Parameter	PKPT3	Summary of Log_e-transformed Derived Plasma GSK3640254 PK Parameters by Treatment – Part 1		SAC
PK Statistical Analysis Table					
4.4.	PK Parameter	mid200207 Table 3.5	Summary Results of Single Dose Proportionality Assessment Using Power Model – Part 1	(reference study mid200207 Table 3.5)	SAC
4.5.	PK Parameter	mid200207 Table 3.5	Summary Results of Single Dose Proportionality Assessment Using ANOVA – Part 1	(reference study mid200207 Table 3.5)	SAC
Part 2					
PK Concentration Data					
4.6.	PK Concentration	PKCT1	Summary of Plasma GSK3640254 PK Concentration-Time Data by Treatment and by Day – Part 2		SAC
PK Derived Parameters					
4.7.	PK Parameter	PKPT1	Summary of Untransformed Derived Plasma GSK3640254 PK Parameters by Treatment – Part 2		SAC
4.8.	PK Parameter	PKPT3	Summary of Log_e-transformed Derived Plasma GSK3640254 PK Parameters by Treatment – Part 2		SAC
PK Statistical Analysis Table					
4.9.	PK Parameter	mid200207 Table 3.5	Summary Results of Repeat Dose Day 1 Dose Proportionality Assessment Using Power Model – Part 2		SAC
4.10.	PK Parameter	mid200207 Table 3.5	Summary Results of Repeat Dose Day 14 Dose Proportionality Assessment Using Power Model – Part 2		SAC
4.11.	PK Parameter	mid200207, Table 3.7	Summary Results of Repeat Dose Day 1 Dose Proportionality Assessment Using ANOVA – Part 2		SAC

Pharmacokinetic : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
4.12.	PK Parameter	mid200207, Table 3.7	Summary Results of Repeat Dose Day 14 Dose Proportionality Assessment Using ANOVA – Part 2		SAC
4.13.	PK Parameter	mid200207, Table 3.9	Summary Results of Steady-State GSK3640254 Concentrations Assessment – Part 2	One for each treatment	SAC
4.14.	PK Parameter	mid200207, Table 3.10	Summary Results of GSK3640254 PK Parameter Treatment Comparisons – Accumulation Ratio – Part 2	One for each treatment	SAC

11.12.8. Pharmacokinetic Figures

Pharmacokinetic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Part 1					
PK Concentration Plots					
4.1.	PK Concentration	PKCF6	Individual Plasma GSK3640254 Concentration-Time Plots (Linear and Semi-Log) by Treatment – Part 1	Overlay all individual profile within each treatment with all days profiles	SAC
4.2.	PK Parameter	PKCF2	Mean Plasma GSK3640254 Concentration-Time Plots (Linear and Semi-Log) – Part 1		SAC
4.3.	PK Parameter	PKCF3	Median Plasma GSK3640254 Concentration-Time Plots (Linear and Semi-Log) – Part 1		SAC
PK Derived Parameters Plots					
4.4.	PK Parameter	mid200207 Figure 3.4	Individual and Box Plot of Plasma GSK3640254 PK Parameters (Linear and Semi-Log) by Treatment– Part 1	Include all treatments & all of the PK parameters.	SAC
4.5.	PK Parameter	GSK1265744/ LAI117020, Figure 3.6	Comparative Plots of Individual Plasma GSK3640254 PK Parameters (Linear and Semi-Log) by Treatment – Part 1	By Treatment, connect individual data. Also geometric mean overlay with a thicker line for Part 1 subjects	SAC
Part 2					
PK Concentration Plots					
4.6.	PK Concentration	PKCF6	Individual Plasma GSK3640254 Concentration-Time Plots (Linear and Semi-Log) by Treatment and by Day – Part 2	Overlay all individual profile within each treatment with all days profiles	SAC
4.7. .	PK Parameter	PKCF2	Mean Plasma GSK3640254 Concentration-Time Plots (Linear and Semi-Log) by Day – Part 2		SAC
4.8.	PK Parameter	PKCF3	Median Plasma GSK3640254 Concentration-Time Plots (Linear and Semi-Log) by Day – Part 2		SAC
PK Derived Parameters Plots					

Pharmacokinetic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
4.9.	PK Parameter	mid200207 Figure 3.4	Individual and Box Plot of Plasma GSK3640254 PK Parameters (Linear and Semi-Log) by Treatment and by Day – Part 2	Include all treatments & all of the PK parameters.	SAC
4.10.	PK Parameter	GSK1265744/ LAI117020, Figure 3.6	Comparative Plots of Individual Plasma GSK3640254 PK Parameters (Linear and Semi-Log) by Treatment – Part 1	By Treatment, connect individual data. Also geometric mean overlay with a thicker line for Part 1 subjects	SAC

11.12.9. Pharmacokinetic / Pharmacodynamic Figures

Pharmacokinetic / Pharmacodynamic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK Concentration Data/ECG					
5.1.	PK Concentration	mid200207, Figure 3.6	Scatter Plot of Individual QTcF Change from Baseline vs Time Matched GSK3640254 PK Concentration	All Subjects assume the placebo subjects with 0 concentrations All Time-matched Concentrations	SAC

11.12.10. ICH Listings

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Part 1					
Subject Disposition					
1.	Screening	ES7	Listing of Reasons for Screen Failure – Part 1		SAC
2.	Safety	ES3	Listing of Reasons for Study Withdrawal – Part 1	ICH E3	SAC
Protocol Deviations					
3.	Safety	DV2A	Listing of Important Protocol Deviations – Part 1	ICH E3	SAC
4.	Safety	IE4	Listing of Subjects with Inclusion/Exclusion Criteria Deviations – Part 1	ICH E3, Listing also includes analysis population exclusions.	SAC
Populations Analysed					
5.	Screening	SP3A	Listing of Subjects Excluded from Any Population – Part 1	ICH E3	SAC
6.	Safety	BL2	Listing of Subjects for Whom the Treatment Blind was Broken – Part 1	ICH E3	SAC
Demographic and Baseline Characteristics					
7.	Safety	DM4	Listing of Demographic Characteristics – Part 1	ICH E3	SAC
8.	Safety	DM10	Listing of Race – Part 1	ICH E3	SAC
Concomitant Medications					
9.	Safety	CM2	Listing of Concomitant Medications – Part 1		SAC
Exposure and Treatment Compliance					
10.	Safety	EX3	Listing of Exposure Data – Part 1	ICH E3	SAC
11.	Safety	Non-Standard	Listing of Meal Data – Part 1		SAC
Adverse Events					

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
12.	Safety	AE9CP	Listing of All Adverse Events – Part 1	ICH E3	SAC
13.	Safety	AE9CP	Listing of All Drug Related Adverse Events – Part 1		SAC
14.	Safety	AE9CP	Listing of Serious Adverse Events – Part 1		SAC
15.	Safety	AE9CP	Listing of Drug Related Serious Adverse Events – Part 1		SAC
16.	Safety	AE9CP	Listing of Fatal Adverse Events – Part 1	ICH E3	SAC
17.	Safety	AE9CP	Listing of non-Fatal Serious Adverse Events – Part 1	ICH E3	SAC
18.	Safety	AE14	Listing of Reasons for Considering as a Serious Adverse Event – Part 1	ICH E3	SAC
19.	Safety	AE9CP	Listing of Grade 2 ~4 Adverse Events – Part 1		SAC
20.	Safety	AE9CP	Listing of Adverse Event of Special Interest – Part 1		SAC
21.	Safety	AE9CP	Listing of Adverse Events Leading to Permanent Discontinuation of Study Drug or Withdrawal from Study – Part 1	ICH E3	SAC
22.	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events – Part 1	ICH E3	SAC
23.	Safety	AE2	Relationship of Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text – Part 1	IDSL	SAC
Laboratory Values					
24.	Safety	LB6	Listing of Clinical Chemistry Data – Part 1	Glucose (non-fasting) results will be shown in listings with the fasting/non-fasting flag.	SAC
25.	Safety	LB6	Listing of Hematology Data – Part 1		SAC
26.	Safety	UR2a	Listing of Urinalysis Data – Part 1		SAC
27.	Safety	LB6	Listing of All Clinical Chemistry Data for Subjects with Any Value of Potential Clinical Importance – Part 1	ICH E3	SAC

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
28.	Safety	LB6	Listing of All Hematology Data for Subjects with Any Value of Potential Clinical Importance –Part 1	ICH E3	SAC
29.	Safety	UR2a	Listing of Urinalysis Data for Subjects with Abnormalities of Potential Clinical Concern – Part 1	ICH E3	SAC
30.	Safety	LB6	Listing of Clinical Chemistry Values of Potential Clinical Importance – Part 1	IDSL	SAC
31.	Safety	LB6	Listing of Hematology Values of Potential Clinical Importance – Part 1	IDSL	SAC
32.	Safety	UR2a	Listing of Urinalysis Values of Potential Clinical Concern – Part 1	IDSL	SAC
33.	Safety	LB14	Listing of Laboratory Data with Character Results – Part 1	ICH E3	SAC
34.	Safety	HAI114885 Table 10.14	Listing of Lab Results Identified as Adverse Events – Part 1		SAC
35.	Safety	mid200207 Table 2.17	Listing of Grade 2 or Higher Treatment Emergent Clinical Chemistry Data Toxicities – Part 1		SAC
36.	Safety	mid200207 Table 2.17	Listing of Grade 2 or Higher Treatment Emergent Hematology Data Toxicities – Part 1		SAC
ECG					
37.	Safety	EG6	Listing of ECG Findings – Part 1		SAC
38.	Safety	EG6	Listing of Abnormal ECG findings –Part 1		SAC
39.	Safety	EG4	Listing of All ECG Values for Subjects with a Value of Potential Clinical Importance – Part 1		SAC
Vital Signs					
40.	Safety	VS5	Listing of Vital Signs – Part 1		SAC

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
41.	Safety	VS5	Listing of All Vital Signs for Subjects with Values of Potential Clinical Importance – Part 1		SAC
Part 2					
Subject Disposition					
42.	Screening	ES7	Listing of Reasons for Screen Failure – Part 2		SAC
43.	Safety	ES2	Listing of Reasons for Study Withdrawal – Part 2		SAC
Protocol Deviations					
44.	Safety	DV2	Listing of Important Protocol Deviations – Part 2		SAC
45.	Safety	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations – Part 2	Listing also includes analysis population exclusions.	SAC
Populations Analysed					
46.	Screening	SP3	Listing of Subjects Excluded from Any Population – Part 2		SAC
47.	Safety	BL1	Listing of Subjects for Whom the Treatment Blind was Broken – Part 2		SAC
Demographic and Baseline Characteristics					
48.	Safety	DM2	Listing of Demographic Characteristics – Part 2		SAC
49.	Safety	DM9	Listing of Race – Part 2		SAC
Concomitant Medications					
50.	Safety	CM2	Listing of Concomitant Medications – Part 2		SAC
Exposure and Treatment Compliance					
51.	Safety	EX3	Listing of Exposure Data – Part 2		SAC
52.	Safety	Non-Standard	Listing of Meal Data – Part 1		SAC
Adverse Events					

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
53.	Safety	AE8CP	Listing of All Adverse Events – Part 2		SAC
54.	Safety	AE8CP	Listing of All Drug Related Adverse Events – Part 2		SAC
55.	Safety	AE8CP	Listing of Serious Adverse Events – Part 2		SAC
56.	Safety	AE8CP	Listing of Drug Related Serious Adverse Events – Part 2		SAC
57.	Safety	AE8CP	Listing of Fatal Adverse Events – Part 2	ICH E3	SAC
58.	Safety	AE8CP	Listing of non-Fatal Serious Adverse Events – Part 2	ICH E3	SAC
59.	Safety	AE14	Listing of Reasons for Considering as a Serious Adverse Event – Part 2	ICH E3	SAC
60.	Safety	AE8CP	Listing of Grade 2 ~ 4 Adverse Events – Part 2		SAC
61.	Safety	AE8CP	Listing of Adverse Event of Special Interest – Part 2		SAC
62.	Safety	AE8CP	Listing of Adverse Events Leading to Permanent Discontinuation of Study Drug or Withdrawal from Study – Part 2	ICH E3	SAC
63.	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events – Part 2	ICH E3	SAC
64.	Safety	AE2	Relationship of Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text – Part 2	IDSL	SAC
Laboratory Values					
65.	Safety	LB6	Listing of Clinical Chemistry Data – Part 2	Glucose (non-fasting) results will be shown in listings with the fasting/non-fasting flag.	SAC
66.	Safety	LB6	Listing of Hematology Data – Part 2		SAC
67.	Safety	UR2a	Listing of Urinalysis Data – Part 2		SAC
68.	Safety	LB6	Listing of All Clinical Chemistry Data for Subjects with Any Value of Potential Clinical Importance – Part 2	ICH E3	SAC

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
69.	Safety	LB6	Listing of All Hematology Data for Subjects with Any Value of Potential Clinical Importance – Part 2	ICH E3	SAC
70.	Safety	UR2a	Listing of Urinalysis Data for Subjects with Abnormalities of Potential Clinical Concern – Part 2	ICH E3	SAC
71.	Safety	LB6	Listing of Clinical Chemistry Values of Potential Clinical Importance – Part 2	IDSL	SAC
72.	Safety	LB6	Listing of Hematology Values of Potential Clinical Importance – Part 2	IDSL	SAC
73.	Safety	UR2a	Listing of Urinalysis Values of Potential Clinical Concern – Part 2	IDSL	SAC
74.	Safety	LB14	Listing of Laboratory Data with Character Results – Part 2	ICH E3	SAC
75.	Safety	HAI114885 Table 10.14	Listing of Lab Results Identified as Adverse Events – Part 2		SAC
76.	Safety	mid200207 Table 2.17	Listing of Grade 2 or Higher Treatment Emergent Clinical Chemistry Data Toxicities – Part 2		SAC
77.	Safety	mid200207 Table 2.17	Listing of Grade 2 or Higher Treatment Emergent Hematology Data Toxicities – Part 2		SAC
ECG					
78.	Safety	EG5	Listing of ECG Findings – Part 2		SAC
79.	Safety	EG5	Listing of Abnormal ECG findings –Part 2		SAC
80.	Safety	EG3	Listing of All ECG Values for Subjects with a Value of Potential Clinical Importance – Part 2		SAC
Vital Signs					
81.	Safety	VS4	Listing of Vital Signs – Part 2		SAC
82.	Safety	VS4	Listing of All Vital Signs for Subjects with Values of Potential Clinical Importance – Part 2		SAC

11.12.11. Non-ICH Listings

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Part 1					
PK Concentration Data					
83.	PK Concentration	PKCL1X	Listing of Plasma GSK3640254 PK Concentration-Time Data – Part 1		SAC
84.	PK Parameter	PKPL1X	Listing of Derived Plasma GSK3640254 PK Parameters – Part 1		SAC
PK Statistical Analysis					
85.	PK Parameter	SAS output of Table 4.4	SAS Output of Summary Results of Single Dose Day 1 Dose Proportionality Assessment Using Power Model – Part 1		SAC
86.	PK Parameter	SAS output of Table 4.5	SAS Output of Summary Results of Single Dose Day 1 Dose Proportionality Assessment Using ANOVA – Part 1		SAC
Part 2					
PK Concentration Data					
87.	PK Concentration	PKCL1X	Listing of Plasma GSK3640254 PK Concentration-Time Data – Part 2		SAC
88.	PK Parameter	PKPL1X	Listing of Derived Plasma GSK3640254 PK Parameters – Part 2		SAC
PK Statistical Analysis					
89.	PK Parameter	SAS output of Table 4.9	SAS Output of Summary Results of Repeat Dose Day 1 Dose Proportionality Assessment Using Power Model – Part 2		SAC
90.	PK Parameter	SAS output of Table 4.10	SAS Output of Summary Results of Repeat Dose Day 14 Dose Proportionality Assessment Using Power Model – Part 2		SAC

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
91.	PK Parameter	SAS output of Table 4.11	SAS Output of Summary Results of Repeat Dose Day 1 Dose Proportionality Assessment Using ANOVA – Part 2		SAC
92.	PK Parameter	SAS output of Table 4.12	SAS Output of Summary Results of Repeat Dose Day 14 Dose Proportionality Assessment Using ANOVA – Part 2		SAC
93.	PK Parameter	SAS output of Table 4.13	SAS Output of Summary Results of Steady-State GSK3640254 Concentrations Assessment – Part 2		SAC
94.	PK Parameter	SAS output of Table 4.14	SAS Output of Summary Results of GSK3640254 PK Parameter Treatment Comparisons – Accumulation Ratio – Part 2		SAC

Example Shells

Non-Standard 1

Protocol: AAA111111
of xx
Population: Safety

Listing x
Listing of Meal Data (Safety Population)

{Inv./} Subj.	{Age(y)/ Sex/ Race}	Trt.	Visit/Pl. Time	Start Date/Start Time of Meal	Stop Date/Stop Time of Meal	Start Date/Start Time of Dosing	Meal Type	Totality of the Meal been Ingested ?	Proportional of the Meal Consumed ?
PPD	36/ M/ Mixed Race	A	PART1 P1D1/PREDOSE	PPD /09:00	9/09:10	/09:30	High Fat Meal	No	76-100%