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

Title	:	Reporting and Analysis Plan for A Phase I, Randomized, Double-Blind (Sponsor Unblinded), Single-Center, Placebo-Controlled, Three-Part Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of Ascending Single and Repeat Intravenous Doses of GSK3342830 in Healthy Adult Subjects
Compound Number	:	GSK3342830
Effective Date	:	17-AUG-2017

Description :

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 204847.
- This RAP is intended to describe the safety, tolerability, and pharmacokinetic analyses required for the study.
- This RAP is updated based upon Protocol Amendment 1. However,, Part 3 (Japanese subjects) that was added in Protocol Amendment 1 will not be conducted.
- This RAP will be provided to the study team members to convey the content of the Dose Escalation (DE) and Statistical Analysis Complete (SAC) deliverable.

Author's Name and Functional Area:

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1. REPORTING & ANALYSIS PLAN SYNOPSIS

Overview	Key Elements of the RAP
Purpose	The purpose of this reporting and analysis plan (RAP) is to describe: • Any planned analyses and output to be included in the clinical study report for Protocol 204847.
Protocol	• This RAP is based on the original protocol (Dated: 18-FEB-2016) of study 204847 (GSK Document No. : 2015N257523_00).
Primary Objective	• For Part 1, to investigate the safety and tolerability of GSK3342830 after administration of single IV doses in healthy adult subjects • For Part 2, to investigate the safety and tolerability of GSK3342830 after administration of repeat IV doses in healthy adult subjects • For Part 3, to investigate the safety and tolerability of GSK3342830 after administration of a single IV dose in healthy adult Japanese subjects
Primary Endpoint	• Clinical safety data from adverse events (AEs), clinical laboratory tests, vital signs (blood pressure, heart rate, temperature, and respiration rate), and 12-lead electrocardiogram (ECG) readings
Study Design	• This is a Phase I, first-time-in-human (FTIH), randomized, double-blind (sponsor unblinded), single-center, placebo-controlled, dose-escalation study to determine the safety, tolerability, and pharmacokinetic (PK) profile of GSK3342830 after administration of single (Part 1) and repeat (Part 2) IV doses in healthy adult subjects, and after administration of a single IV dose in healthy adult Japanese subjects (Part 3). • Dose escalation will be conducted only if it is supported by the preliminary safety, tolerability, and PK results from the preceding dose levels in the study. This is the first administration of GSK3342830 in humans; therefore, as preliminary safety, tolerability, and PK results are reviewed internally at GSK and with the clinical study site, study design adjustments may be made based on emerging data from each dose cohort. • The repeat dose escalation component (Part 2) of this study is planned to be initiated after completion and evaluation of the all single dose cohorts up to and including 4000 mg. Initiation of Part 2 will be based on the evaluation of preliminary safety, tolerability, and PK data from the single dose escalation (Part 1) cohorts once safety at an exposure that exceeds the daily exposure predicted for the Part 2 planned starting dose of 1000 mg TID is demonstrated, which is predicted to occur at the 4000 mg single dose. • The single dose administration in Japanese subjects component (Part 3) of this study is planned to be conducted in parallel with Part 2. The dose for the Part 3 cohort will be based on preliminary safety and tolerability results of doses determined to be safe and well tolerated in subjects of non-Japanese heritage after completion of the single escalation dose cohorts (Part 1).
Planned	• Safety and PK data will be presented in tabular and/or graphical format and

Overview	Key Elements of the RAP
Analyses	summarized descriptively according to GSK's Integrated Data Standards Library (IDSL) standards.
Analysis Populations	• Safety Population – defined as all subjects who receive at least 1 dose of study drug and have at least 1 post-dose safety assessment. • PK Population - defined as all subjects who receive at least 1 dose of GSK3342830 and have evaluable PK data for GSK3342830. • PK Parameter Population - defined as all subjects in the PK population for whom valid and evaluable PK parameters were derived.
Hypothesis	• No inferential hypothesis testing will be performed on the safety variables. • Dose proportionality of AUC(0-∞) and Cmax on Day 1 and for repeat dose groups AUC(0-τ) and Cmax of GSK3342830 on Day 15 will be assessed separately by day using the following power model: $y = a * dose^{\beta}$. where y denotes the PK parameter being analyzed and a depends on the random error in the repeat dose phase where subjects take the study drug in a parallel-group fashion. Dose proportionality implies that β=1 and will be assessed by estimating β along with its 90% CI. The exponent, β, in the power model will be estimated by regressing the loge-transformed PK parameter on loge-transformed dose. $\log(y)=\log(\alpha) + \beta * \log(dose)$ The power model will be fitted by restricted maximum likelihood (REML) using Statistical Analysis Software (SAS) Proc Mixed, with a fixed effect term for dose. The PK parameter endpoint and the factor dose will be loge-transformed prior to the analysis. • For the repeat dose cohorts (Part 2), the time invariance ratio will be assessed by fitting a mixed effect model for AUC(0-∞) on Day 1 and AUC(0-τ) on Day 15 data with subject as a random effect and group (group=1 for AUC(0-∞) on Day 1, and group=2 for AUC(0-τ) on Day 15) as a fixed effect for each cohort. • For the repeat dose cohorts (Part 2), the accumulation ratio (Ro) will be calculated as the ratio of AUC(0-τ) on Day 15 to AUC(0-τ) on Day 1 for each subject. The dosing interval (τ) will be equal to 8 hours. Following log-transformation, AUC(0-τ) of GSK3342830 on Days 1 and 15 will be analyzed by a mixed effect model, fitting dose, day, and dose-by-day interaction as fixed effects and subject as a random effect. For each dose, point estimate and 90% CI for the difference "AUC(0-τ) on Day 15 - AUC(0-τ) on Day 1" will be constructed using the appropriate error term. The point estimate and associated 90% CI will then be exponentially back-transformed to provide point and 90% CI estimates for the ratios "AUC(0-τ) on Day 15: AUC(0-τ) on Day 1." If dose-by-day interaction is not significant, then a single point estimate and 90% CI pooled across all doses for the ratio AUC(0-τ) on Day 15: AUC(0-τ) on Day 1

Overview	Key Elements of the RAP
	may be constructed with all estimates for each dose. • To evaluate whether steady state was achieved, statistical analysis of steady-state Cτ will be performed after log-transformation of Cτ on Days 3, 6, 9, 12, 13, and 15. A mixed effect model will be fitted by dose and day (as a continuous covariate) as a fixed effect term and subject as a random effect term. Distributional assumptions underlying the statistical analyses will be assessed by visual inspection of residual plots. Normality will be examined by normal probability plots, while homogeneity of variance will be assessed by plotting the residuals against the predicted values for the model. Alternative analyses of the data will be performed if any of the model assumptions appear to be violated.

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

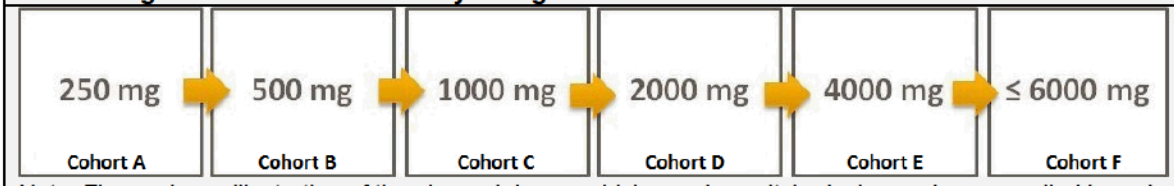
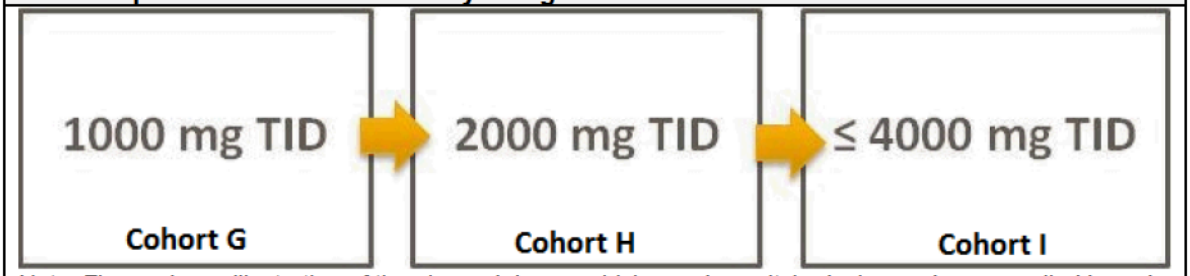
Not applicable.

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

Objectives	Endpoints
Part 1	
Primary Objectives	**Primary Endpoints**
• To investigate the safety and tolerability of GSK3342830 after administration of single IV doses in healthy adult subjects	• Clinical safety data from AEs, clinical laboratory tests, vital signs (blood pressure, heart rate, temperature, and respiration rate), and 12-lead ECG readings
Secondary Objectives	**Primary Objectives**
• To determine the pharmacokinetics of GSK3342830 after administration of single IV doses in healthy adult subjects	• Plasma and urine concentrations PK endpoints include AUC(0-t), AUC(0-∞), Cmax, Tmax, CL, Vss, t1/2, Feu(t1-t2), Ae, and CLr of GSK3342830, as data permit
• To assess dose proportionality of GSK3342830 after administration of single IV doses in healthy adult subjects	• Pharmacokinetic endpoints include AUC(0-t), AUC(0-∞), and Cmax of GSK3342830 after administration of single IV doses for the assessment of dose proportionality, as data permit
Exploratory Objectives	**Exploratory Endpoints**
• To correlate PK parameters (AUC[0-t], AUC[0-∞], and Cmax) of GSK3342830 with safety findings after administration of single IV doses in healthy adult subjects	• Exposure-response analyses, as data permit
• To evaluate the production of any GSK3342830 metabolites in plasma and urine and determine the need to perform a more detailed analysis of any metabolites	• Metabolite characterization in plasma and urine and estimation of observed drug-related material in plasma to determine the presence of any metabolite >10%, and estimate the percentage dose eliminated via urine
Part 2	
Primary Objectives	**Primary Endpoints**
• To investigate the safety and tolerability of GSK3342830 after administration of repeat IV doses in healthy adult subjects	• Clinical safety data from AEs, clinical laboratory tests, vital signs (blood pressure, heart rate, temperature, and respiration rate), and 12-lead ECG readings
Secondary Objectives	**Secondary Endpoints**
• To determine the pharmacokinetics of GSK3342830 after administration of repeat IV doses in healthy adult subjects	• Plasma and urine concentrations and PK endpoints include AUC(0-t) and AUC(0-∞) on Day 1 only, AUC(0-τ), Cmax, Tmax, CL, Vss, t1/2, Cτ, Feu(t1- t2), Ae, and CLr of GSK3342830, as data permit
• To assess dose proportionality of GSK3342830 after administration of repeat IV doses in healthy adult subjects	• Pharmacokinetic endpoints include AUC(0-τ) and Cmax of GSK3342830 after administration of repeat IV doses for the assessment of dose proportionality, as data permit

Objectives	Endpoints
• To examine the extent of accumulation, time invariance, and achievement of steady-state of GSK3342830 after administration of repeat IV doses in healthy adult subjects	• Observed accumulation ratio (Ro) based on AUC and Cmax of GSK3342830 after administration of repeat IV doses, as data permit • Steady-state ratio (Rss) of GSK3342830 to assess time invariance, as data permit • Trough plasma concentrations at the end of the dosing interval (Cτ) to assess the achievement of steady-state of GSK3342830 after administration of repeat IV doses, as data permit
Exploratory Objectives	**Exploratory Endpoints**
• To correlate PK parameters (AUC[0-t], AUC[0-∞], AUC[0-τ], and Cmax) of GSK3342830 with safety findings in healthy adult subjects after administration of repeat IV doses	• Exposure-response analyses, as data permit
• To evaluate the production of any GSK3342830 metabolites in plasma and urine and determine the need to perform a more detailed analysis of any metabolites	• Metabolite characterization in plasma and urine and estimation of observed drug-related material in plasma to determine the presence of any metabolite >10%, and estimate the percentage dose eliminated via urine
Part 3	
Primary Objectives	**Primary Endpoints**
• To investigate the safety and tolerability of GSK3342830 after administration of a single IV dose in healthy adult Japanese subjects	• Clinical safety data from AEs, clinical laboratory tests, vital signs (blood pressure, heart rate, temperature, and respiration rate), and 12-lead ECG readings
Secondary Objectives	**Secondary Endpoints**
• To determine the pharmacokinetics of GSK3342830 after administration of a single IV dose in healthy adult Japanese subjects	• Plasma and urine concentrations PK endpoints include AUC(0-t), AUC(0-∞), Cmax, Tmax, CL, Vss, t1/2, Feu(t1-t2), Ae, and CLr of GSK3342830, as data permit
Exploratory Objectives	**Exploratory Endpoints**
• To correlate PK parameters (AUC[0-t], AUC[0-∞], and Cmax) of GSK3342830 with safety findings in healthy adult Japanese subjects after administration of repeat IV doses	• Exposure-response analyses, as data permit
• To evaluate the production of any GSK3342830 metabolites in plasma and urine and determine the need to perform a more detailed analysis of any metabolites	• Metabolite characterization in plasma and urine and estimation of observed drug-related material in plasma to determine the presence of any metabolite >10%, and estimate the percentage dose eliminated via urine

2.3. Study Design

Overview of Study Design and Key Features	
Part 1 Single Dose Escalation Study Design Schematic	
 Note: Figure shows illustration of the planned doses, which may be switched, changed, or cancelled based on preliminary safety, tolerability, and pharmacokinetic data from preceding cohorts.	
Part 2 Repeat Dose Escalation Study Design Schematic	
 Note: Figure shows illustration of the planned doses, which may be switched, changed, or cancelled based on preliminary safety, tolerability, and pharmacokinetic data from preceding cohorts.	
Design Features	• Part 1 is planned to include 6 dose level cohorts. Up to 2 additional doses (1 per cohort) may be evaluated to further understand the study drug. The planned starting GSK3342830 dose in Part 1 is 250 mg administered as a single IV infusion. The dose is planned to increase in subsequent cohorts to 500, 1000, 2000, 4000, and ≤6000 mg IV. In Part 1, subjects will remain confined to the clinical unit from admission on Day –1 until all scheduled safety and PK assessments have been completed on Day 3. The duration of study (from Screening to the Follow-up visit) for each subject will be up to approximately 43 days. • Part 2 is planned to include a sequential panel of up to 3 dose level cohorts. Additional repeat dose cohorts may be evaluated to further assess the safety, tolerability, and pharmacokinetics of GSK3342830. The planned starting GSK3342830 dose in Part 2 is 1000 mg administered as a single IV infusion on Day 1, TID IV infusions on Days 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, and 14, and a single IV infusion on Day 15. The dose is planned to increase in subsequent cohorts to 2000 and 4000 mg TID. In Part 2, subjects will remain confined to the clinical unit from admission on Day –1 until after all scheduled safety assessments have been completed on Day 16. The duration of study (from Screening to the Follow-up visit) for each subject will be up to approximately 56 days. • Part 3 is planned to include 1 cohort (Cohort J). The planned GSK3342830 dose in Part 3 will be either 250, 500, 1000, 2000, 4000, or ≤6000 mg based on preliminary safety and tolerability results of doses determined to be safe and well tolerated in subjects of non-Japanese heritage after completion of the single escalation dose cohorts (Part 1). The dose in Part 3 will be

Overview of Study Design and Key Features	
	administered as a single IV infusion on Day 1. In Part 3, subjects will remain confined to the clinical unit from admission on Day –1 until all scheduled safety and PK assessments have been completed on Day 3. The duration of study (from Screening to the Follow-up visit) for each subject will be up to approximately 43 days.
Dosing	• For Part 1, doses are planned to escalate in a sequential fashion contingent on the safety, tolerability, and PK profile of approximately 4 subjects who received active treatment in the previous cohort. The evaluated subjects should be followed for a minimum of 48 hours after dosing. Dose escalations or reductions will progress with modifications based on the preliminary safety, tolerability, and PK data from the preceding cohorts. • For Part 2, doses are planned to escalate in a sequential fashion based on the preliminary safety, tolerability, and PK data from Part 1 and at least 14 days of repeat dosing in approximately 5 subjects who received active treatment in the previous cohort in Part 2. The evaluated subjects should be followed for a minimum of 24 hours after dosing on Day 15. The dosing frequency, duration of dosing, and decision to dose in the next dose level may be changed based on the safety, tolerability, or PK findings in Part 1 or earlier doses in Part 2. • The dose in Part 3 will be administered as a single IV infusion on Day 1.
Treatment Assignment	• For Part 1 on Day 1, before study drug administration, subjects will be randomized to treatment with either GSK3342830 or placebo in a 3:1 ratio. As a safety precaution, all Part 1 cohorts will be split into 2 sub-cohorts for sentinel dosing. In each cohort, the first 2 subjects will receive either GSK3342830 or placebo (1 active/1 placebo). Dosing in the remaining 6 subjects (5 active/1 placebo) in that cohort will occur at least 24 hours later based on the safety results from the first sub-cohort. • For Part 2 on Day 1, before study drug administration, subjects will be randomized to treatment with either GSK3342830 or placebo in a 4:1 ratio. • For Part 3 on Day 1, before study drug administration, subjects will be randomized to treatment with either GSK3342830 or placebo in a 4:1 ratio.
Interim Analysis	• No formal interim analysis. However, during dose escalation, Bayesian analysis is performed to produce inferences about model parameters and the predictive probability that an individual will have certain PK parameters larger than prespecified thresholds at for each dose level to aid the next dose selection.

2.4. Statistical Hypotheses

No inferential hypothesis testing will be performed.

3. PLANNED ANALYSES

3.1. Interim Analyses

No formal interim analysis is planned for this study. However, one may be conducted in the event of clinically significant safety or PK findings. All preliminary safety, tolerability, and available PK data will be reviewed internally at GSK and with the clinical study site before each dose escalation in Part 1, before initiation of Part 2, and before each dose escalation in Part 2.

The relationship between dose and plasma GSK3342830 exposure, and associated variability will be characterized by a power model once data are available from 3 dose levels. Prior to that, prediction of the human exposure at the next dose will be based on population PK modeling (if feasible) or on the assumption of dose–exposure proportionality (i.e., doubling the dose gives an approximate doubling of exposure). If prior PK results show less than proportional increase in exposure with increasing dose, the prediction will be based on the assumption that the fold exposure increase to fold dose increase ratio will be the same with the current dose escalation as it was with the previous one. If prior PK results show more than proportional increase in exposure with dose, subsequent dose escalations will not be higher than 3-fold. The power model will be updated as data become available throughout the study. During dose escalation, Bayesian inferential probability that a group mean will have AUCs (AUC[0-t] for single dose and AUC[0-8]x3 as AUC[0-24] for repeat dose) and Cmax values greater than 2875 h•μg/mL and 2270 μg/mL (mean exposures at the NOAEL dose in the rat and monkey), respectively, and Bayesian predictive probability that an individual will have AUC(0-24) and Cmax values greater than 3460 h•μg/mL and 2590 μg/mL (maximum exposures at the NOAEL dose in the rat for AUC and the monkey for Cmax), respectively, may be calculated for the next dose level and used together with safety and tolerability data to aid the next dose selection.

3.2. Final Analyses

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

1. All subjects have completed the study as defined in the protocol.
2. All required database cleaning activities have been completed and final database release and database freeze has been declared by Data Management.
3. All criteria for unblinding the randomisation codes have been met.
4. Randomisation codes have been distributed according to PPD procedures.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Safety	• Defined as all subjects who receive at least 1 dose of study drug and have at least 1 post-dose safety assessment.	• Study Population • Safety

Population	Definition / Criteria	Analyses Evaluated
	• This population will be based on the treatment the subject was randomized to receive.	
Pharmacokinetic	• Defined as all subjects who receive at least 1 dose of GSK3342830 and have evaluable PK data for GSK3342830.	• PK
Pharmacokinetic Parameter	• Defined as all subjects in the PK population for whom valid and evaluable PK parameters were derived	• PK Parameter

NOTES :

- Please refer to Appendix 11: List of Data Displays which details the population to be used for each displays being generated.

4.1. Protocol Deviations

- Important protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, patient management or patient assessment) will be summarised and listed.
- Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan.
    - Data will be reviewed prior to unblinding and freezing the database to ensure all important deviations and deviations which may lead to exclusion from the analysis are captured and categorised on the protocol deviations dataset.
    - This dataset will be the basis for the summaries and listings of protocol deviations.
- A separate summary and listing of all inclusion/exclusion criteria deviations will also be provided. This summary will be based on data as recorded on the inclusion/exclusion page of the eCRF.

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

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

Table 1 Overview of Appendices

Section	Component
10.1	Appendix 1: Time & Events
10.2	Appendix 2: Treatment States and Phases
10.3	Appendix 3: Data Display Standards & Handling Conventions
10.4	Appendix 4: Derived and Transformed Data
10.5	Appendix 5: Premature Withdrawals & Handling of Missing Data
10.6	Appendix 6: Values of Potential Clinical Importance
10.6	Appendix 7: DMID Adult Toxicity Tables for Adverse Event Assessment
10.8	Appendix 8: Multiple Comparisons & Multiplicity
10.9	Appendix 9: Model Checking and Diagnostics for Statistical Analyses.
10.10	Appendix 10: Abbreviations & Trade Marks.
10.11	Appendix 11: List of Data Displays.

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Analyses

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

Table 2 provides an overview of the planned study population analyses, with full details of data displays being presented in Appendix 11: List of Data Displays.

Table 2 Overview of Planned Study Population Analyses

Display Type	Data Displays Generated		
	Table	Figure	Listing
Randomisation			
Randomisation			Y
Subject Disposition			
Subject Disposition	Y		Y
Reason for Screening Failures	Y		Y
Reason for Withdrawals	Y		Y
Inclusion and Exclusion Criteria Deviations			Y
Demography			
Demographic Characteristics	Y		Y
Medical Conditions and Concomitant Medications			
Concomitant Medication	Y		Y
Medical Conditions (Current/Past)	Y		Y

NOTES :
Y = Yes display generated.

7. PRIMARY STATISTICAL ANALYSES

7.1. Safety Analyses

7.1.1. Overview of Planned Safety Analyses

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

Table 3 provides an overview of the planned Safety analyses, with full details of data displays being presented in Appendix 11: List of Data Displays.

Table 3 Overview of Planned Safety Analyses

Display Type	Absolute				Change from Baseline			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
Exposure								
Extent of Exposure	Y			Y				
Adverse Events								
All AEs	Y			Y				
All Drug-Related AEs	Y			Y				
Serious AEs				Y				
Withdrawal AEs				Y				
Laboratory Values								
Clinical Chemistry	Y			Y	Y			
Hematology	Y			Y	Y			
Urinalysis (Dipstick)	Y			Y				
ECGs								
ECG Findings	Y			Y				
ECG Values	Y			Y	Y			
Vital Signs								
Vital Signs	Y			Y	Y			
Cardiac Telemetry								
Cardiac Telemetry				Y				
Liver								
Liver Events [1]				Y				
Cardiovascular								
Cardiovascular Events [1]				Y				
Injection Site Reactions								
Injection Site Reaction Events [1]				Y				
Rash								
Rash Events [1]				Y				
Biomarker								
Cytokines			Y	Y				

NOTES :

1. Conditional displays, they will only be produced when an event has occurred.

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

8. SECONDARY STATISTICAL ANALYSES

8.1. Pharmacokinetic Analyses

8.1.1. Overview of Planned Pharmacokinetic Analyses

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

Table 4 provides an overview of the planned PK analyses, with further details of data displays being presented in Appendix 11: List of Data Displays.

Table 4 Overview of Planned Pharmacokinetic Analyses

Endpoint / 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 Plasma Concentrations				Y	Y[1] [2]	Y[1]	Y							
PK Urine Concentrations							Y							
PK Plasma Parameters	Y			Y		Y	Y	Y			Y			
PK Urine Parameters				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.

[1] Linear and Semi-Log plots will be created on the same display.

[2] Separate mean, median, and median trough (Part 2 only) concentration plots will be generated.

8.1.2. Drug Concentration Measures

Refer to Appendix 3: Data Display Standards & Handling Conventions (Section 10.3.3 Reporting Process & Standards).

8.1.3. Pharmacokinetic Parameters

8.1.3.1. Deriving Pharmacokinetic Parameters

- Refer to Appendix 3: Data Display Standards & Handling Conventions (Section 10.3.3 Reporting Process & Standards).
- The pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using Phoenix WinNonlin Version 6.2.1 or higher.

- All calculations of non-compartmental parameters will be based on actual sampling times.
- Pharmacokinetic parameters described in Table 5 will be determined from the plasma GSK3342830 concentration-time data, as data permits.
- Pharmacokinetic parameters described in Table 6 will be determined from the urinary GSK3342830 concentration data, as data permits.

Table 5 Derived Plasma Pharmacokinetic Parameters

Parameter	Parameter Description
Cmax	Maximum plasma concentration
Tmax	Time to Cmax
AUC(0-t)	AUC from time zero to the last quantifiable concentration after dosing
AUC(0-∞)	AUC extrapolated from time 0 to infinity (estimated for single dose in Part 1 and Part 3 and on Day 1 for repeat dose in Part 2)
AUC(0-τ)	AUC over the dosing interval τ
t1/2	Terminal elimination half-life
CL	Total systemic clearance
Vss	Steady-state volume of distribution
Cτ	Trough concentration
Ratio of invariance	Time invariance ratio, calculated by (AUC(0-τ) on Day 15)/(AUC(0-∞) on Day 1)
Ratio of accumulation	Accumulation ratio, calculated by (AUC(0-τ) on Day 15)/(AUC(0-τ) on Day 1)

NOTES:

- Additional parameters may be included as required.

Table 6 Derived Urinary Pharmacokinetic Parameters

Parameter	Parameter Description
Feu(t1-t2)	Urinary excretion ratio relative to dose
CLr	Renal clearance
Ae	Amount excreted in urine

8.1.3.2. Statistical Analysis of Pharmacokinetic Parameters

The following pharmacokinetic statistical analyses will only be performed, if sufficient data is available (i.e. if subjects have well defined plasma profiles).

Pharmacokinetic Statistical Analyses
Assessment
• Dose proportionality of GSK3342830.

Pharmacokinetic Statistical Analyses

Endpoint(s)

- An estimate of slope (with corresponding 90% CI).

Model Specification

- Dose proportionality of AUC(0-∞) and Cmax on Day 1 after single dose (Part 1) and for repeat dose groups (Day 15 in Part 2), AUC(0-τ) and Cmax of GSK3342830 on Day 15 will be assessed separately by day using the following power model:

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

  where y denotes the PK parameter being analyzed and α depends on the random error in the repeat dose phase where subjects take the study drug in a parallel-group fashion. Dose proportionality implies that β=1 and will be assessed by estimating β along with its 90% CI. The exponent, β, in the power model will be estimated by regressing the $\log_e$-transformed PK parameter on $\log_e$-transformed dose.

  $$\log(y)=\log(\alpha) + \beta * \log(dose)$$

  The power model will be fitted by restricted maximum likelihood (REML) using Statistical Analysis Software (SAS) Proc Mixed, with a fixed effect term for dose. The PK parameter endpoint and the factor dose will be $\log_e$-transformed prior to the analysis.
- In the case where dose proportionality is not established over the entire dosing range, secondary analysis of dose proportionality will be assessed for select doses over the higher dosing range with the power model or by pair-wise analysis of variance (ANOVA) using the SAS mixed models procedure. If the secondary analysis using the pair-wise ANOVA approach is performed, a reference dose would be chosen based on the lowest clinically relevant dose over which the pharmacokinetics can be adequately described and the other doses would be treated as test doses.

Model Checking & Diagnostics

- Refer to Appendix 9: Model Checking and Diagnostics for Statistical Analyses.

Model Results Presentation

- An estimate of slope (with corresponding 90% CI) will be provided as a measure of potential dose proportionality (i.e. a slope of approximately 1 implies dose proportionality) will be produced in tabular format.

Assessment

- Time invariance of GSK3342830.

Endpoint(s)

- An estimate of time invariance ratio (with corresponding 90% CI).

Model Specification

For the repeat dose cohorts (Part 2), the time invariance ratio will be assessed by fitting a mixed effect model for AUC(0-∞) on Day 1 and AUC(0-τ) on Day 15 data with subject as a random effect and group (group=1 for AUC(0-∞) on Day 1, and group=2 for AUC(0-τ) on Day 15) as a fixed effect for each cohort.

Model Checking & Diagnostics

- Refer to Appendix 9: Model Checking and Diagnostics for Statistical Analyses.

Model Results Presentation

- The time invariance ratio of GSK3342830 will be estimated by calculating the ratio of the geometric least squares means of group 1 (AUC(0-τ) on Day 15) to group 2 (AUC(0-∞) on Day 1) and the corresponding 90% CI for each cohort.

Assessment

Pharmacokinetic Statistical Analyses
• Accumulation ratio of GSK3342830.
Endpoint(s)
• An estimate of accumulation ratio (with corresponding 90% CI).
Model Specification
• For the repeat dose cohorts (Part 2), the accumulation ratio (Ro) will be calculated as the ratio of AUC(0-τ) on Day 15 to AUC(0-τ) on Day 1 for each subject. The dosing interval (τ) will be equal to 8 hours. Following log-transformation, AUC(0-τ) of GSK3342830 on Days 1 and 15 will be analyzed by a mixed effect model, fitting dose, day, and dose-by-day interaction as fixed effects and subject as a random effect. For each dose, point estimate and 90% CI for the difference "AUC(0-τ) on Day 15 - AUC(0-τ) on Day 1" will be constructed using the appropriate error term. The point estimate and associated 90% CI will then be exponentially back-transformed to provide point and 90% CI estimates for the ratios "AUC(0-τ) on Day 15: AUC(0-τ) on Day 1." If dose-by-day interaction is not significant, then a single point estimate and 90% CI pooled across all doses for the ratio AUC(0-τ) on Day 15: AUC(0-τ) on Day 1 may be constructed with all estimates for each dose.
Model Checking & Diagnostics
• Refer to Appendix 9: Model Checking and Diagnostics for Statistical Analyses.
Model Results Presentation
• The point estimate and 90% CI for the accumulation ratios of AUC(0-τ) on Day 15 to AUC(0-τ) on Day 1 will be calculated.
Assessment
• Steady state assessment of GSK3342830.
Endpoint(s)
• An estimate of the slope (with corresponding 90% CI).
Model Specification
• To evaluate whether steady state was achieved, statistical analysis of steady-state Cτ will be performed after log-transformation of Cτ on Days 3, 6, 9, 12, 13, and 15. A mixed effect model will be fitted by dose and day (as a continuous covariate) as a fixed effect term and subject as a random effect term. Distributional assumptions underlying the statistical analyses will be assessed by visual inspection of residual plots. Normality will be examined by normal probability plots, while homogeneity of variance will be assessed by plotting the residuals against the predicted values for the model. Alternative analyses of the data will be performed if any of the model assumptions appear to be violated.
Model Checking & Diagnostics
• Refer to Appendix 9: Model Checking and Diagnostics for Statistical Analyses.
Model Results Presentation
• The coefficients for the slope of the day effect on the log-scale will be used to evaluate steady-state for each dose group. Using the pooled estimate of variance, the 90% CIs for the slope will be calculated.
Model Results Presentation
• The least squares geometric mean ratio and 90% CI for the comparison of AUC(0-t), AUC(0-∞) and Cmax from Japanese subjects (Part 3) to subjects of non-Japanese heritage of the same dose level (Part 1) will be calculated.
Assessment
• Assessment of GSK3342830 PK in healthy adult Japanese subjects vs the same dose level of

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healthy adult subjects in Part 1.
Endpoint(s)
• The geometric mean ratio and associated 90% CI for Part 3 vs Part 1.
Model Specification
• To evaluate whether there is a difference in the PK parameters in healthy adult Japanese subjects, a fixed effect model will be fitted with Study Part as fixed effect.
Model Checking & Diagnostics
• Refer to Appendix 9: Model Checking and Diagnostics for Statistical Analyses.
Model Results Presentation
• The geometric mean ratio and associated 90% CI will be presented in a table.

8.2. Bayesian Dose Escalation Analyses

8.2.1. Overview of Planned Bayesian Dose Escalation Analyses

The Bayesian Dose Escalation analyses will be based on the PK population, unless otherwise specified.

Table 7 provides an overview of the planned Bayesian analyses, with further details of data displays being presented in Appendix 11: List of Data Displays.

Table 7 Overview of Planned Bayesian Analyses

Endpoint / 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
AUC[0-t], AUC[0-24], AUC[0-8]x3, Cmax				Y	Y		Y	Y	Y					

NOTES :

- T = Table, F = Figure, L = Listing, Y = Display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TF related to any summaries (i.e. descriptive statistics) of the observed raw data, posterior distribution data and predictive data about future hypothetical subjects.
- Individual = Represents FL related to any displays of individual subject observed raw data.

8.2.2. Planned Bayesian Statistical Analyses

Table 8 Bayesian Statistical Analyses

Bayesian Statistical Analyses
Endpoint(s)
• AUC[0-t] where t varies depending dose and Cmax for Part 1 single dose phase • AUC[0-24] which is calculated as AUC[0-8]x3, Cmax for Part 2 repeat dose phase
Model Specification
To guide dose selection, Bayesian posterior inferences about population probability distributions of model parameters of PK parameters will be assessed by using the following power model: $y = \exp(\theta_1+\varepsilon)\cdot \text{dose}^{\theta 2}$ where y denotes the PK parameter being analyzed. The θ_s, s=1,2, in the power model will be estimated by linear regression of the $\log_e$-transformed PK parameters on $\log_e$ dose levels. $\log(y_{ij}) = \theta_1 + \theta_2\cdot \log(d_{ij}) + \varepsilon_{ij}$ (1) where • y_{ij} is the observed or predicted log-PK variable of the j-th dose d_{ij} administered to the i-th subject. In particular, it is an AUC (AUC[0-t] for single dose, and AUC[0-24] for repeat dose) or a Cmax, as applicable. • θ_1, θ_2 are population intercept and slope, respectively.

Bayesian Statistical Analyses

- ϵ_{ij} is a random error term, with mean zero and variance σ^2.

In general, Bayesian inference seeks to quantify the probability distributions of model parameters such as the ($\theta_1, \theta_2, \sigma$) defined in Equation (1). The present inference will incorporate a normal-Half-Normal prior distribution, to express the prior information about the parameters ($\theta_1, \theta_2, \sigma$). Due to limited information available about the GSK3342830 compound, an informative prior with large variance will be used. For ease of parameterization for the normal distribution in computer programming, use $\nu = \sigma^{-2}$ as the precision. Model parameters are assumed *a priori* to be independent.

Table 9 Prior Distributions

Model Parameter	Prior
θ_1 (intercept)	~ Normal(-1, precision=10^{-6})*
θ_2 (slope of log-dose)	~ Half-Normal(0, precision=10^{-5}, lower=0)*
ν (precision)	~ Gamma(1, iscale=5)*

All model parameters are *a prioiri* independent.

*SAS Version 9.4 will be used for the Bayesian analysis, specifying the normal distribution using mean and precision. Because of the assumption that population mean PK parameter values increase as a higher dose is administered, let θ_2 have a Half Normal prior distribution truncated at 0 to guarantee the positivity of θ_2. Simple linear regression, with maximum likelihood estimation, on available data at dose escalation will be used to estimate the model parameters (θ_1, θ_2, ν),thus providing the initial values for model parameter estimation by Bayesian approach; however, if insufficient data are available for estimation, (1, -1, 0.2) will be used as the initial values for (θ_1, θ_2, v). Furthermore, the scale and shape parameters of the precision prior Gamma function are chosen to attain E(ν)=0.2 and Var(ν)=0.04. Two chains will be run for the estimation of each parameter.

Model Checking & Diagnostics

The Gibbs sampling chains will be run using the following conventions:

1. The burn-in period, the number of iterations judged necessary for the Markov Chain Monte Carlo (MCMC) algorithm to achieve convergence, will be assessed after each 5,000 iteration increment until convergence is achieved. Convergence of the chains to the posterior distribution will be assessed using:

- Gelman-Rubin statistic
- MCMC error of the chains
- Autocorrelation plot to assess autocorrelation within each chain
- Visual inspection of the chain trace plots for proper chain mixing after the application of thinning

2. The burn-in samples must meet all the following convergence criteria, before we accept

Bayesian Statistical Analyses

the MCMC output as a sample from the posterior distribution:

1) The Gelman-Rubin statistic will indicate convergence provided the Brooks-Gelman Ratio (Brooks and Gelman 1998) for all parameters is within the interval (0.8, 1.2). The SAS procedure diagnostic tool will generate the necessary output.

2) All MCMC chains will be run until each parameter has estimated MCMC error of less than 5% of its associated standard deviation. This calculation will be performed as the ratio of the MCMC error divided by the parameter's estimated posterior standard deviation.

3) Autocorrelation plots will be generated for all chains and accepted provided the estimated autocorrelation for each chain is within ±0.10 by lag 10. In the event that any chain's autocorrelations for any one parameter are outside that range after 10 iterations, the number of iterations will be increased by 5000.

4) All chains' trace plots will be inspected visually, to assess the mixing of each chain. Convergence is indicated when all chains appear to be mixing well (to be clear: No chain's convergence is indicated until the chains of all model parameters appear well-mixed). Mixing is defined as "each chain is sampling independently values similar to those the other chains have sampled." This will appear in the trace plots as all chains overlapping each other randomly.

The burn-in period will end at the iteration which convergence is reached as determined using the above criteria. Upon convergence a sample size of 10,000 will be obtained from the posterior from each chain. Estimated density plots will be created and inspected for smoothness. If the estimated density plots are not smooth, then an additional sample size of 10,000 iterations, 10,000 from each chain, will be gathered until the estimated density plots are smooth. Estimates for each parameter will include mean, standard deviation, MCMC error, median, and the centred 90% credible sets (the 5th and 95th percentiles) along with the estimated MCMC error for the chain. We will also obtain the Deviance Information Criteria for the model and display this with the associated output.

Poor fit for the model will be indicated by the following, possibly among other findings:

1) Patterns in the residuals.

2) The model requires more than 10,000 iterations for the burn-in period, after thinning, and an acceptable reparameterisation of the model is not found or it is determined that the chains will not reach convergence.

Model Results Presentation

Once the posterior distributions have been estimated using SAS, the following key interim analysis inferences and predictions will be estimated using the associated posteriors:

- Univariate features of the posterior probability distribution (mean, StdDev, MCMC error, ratio of MCMC error/StdDev, median, and 5th and 95th percentiles used for 90% equal-tailed credible intervals (CrI)) will be calculated for each model parameter. The estimated dose response curve with a 90% CrI will be graphically displayed, and overlaid on the

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observed data.

- The range of possible doses: 250, 500, 1000, 2000, 4000 and 6000 mg for Part 1 and 1000, 2000, 4000 mg for Part 2.
- At each chain of the MCMC algorithm in the SAS program (as described above), we will obtain an estimate for the mean AUC[0-t] or Cmax at each dosing level (as in the previous bullet for Part 1) with a 90% CrI using the 5th and 95th percentiles. This will be calculated as found in the model formulation (1) using the sampled parameter values.
- These point estimates will be displayed on a figure with the dots connected. If the associated posterior distributions for the predicted responses at the dose levels are skewed then the point estimates used to generate the dose response curve plot will be generated using the median as a measure of central tendency. The 5th and 95th percentiles will still be used for the 90% CrI about the parameter.
- The observed data will be overlaid on this curve at the doses which were explored.

- The Bayesian inferential probability that mean AUC[0-t] and Cmax values will be greater than 2875 h.µg/mL and 2270 µg/mL (maximum exposures at the NOAEL dose in the rat for AUC and the monkey for Cmax), respectively, will be calculated for each dose level in Part 1.
- The Bayesian predictive probability that an individual subject will have AUC[0-t] and Cmax values greater than 3460 h.µg/mL and 2590 µg/mL (maximum exposures at the NOAEL dose in the rat for AUC and the monkey for Cmax), respectively, will be calculated for each dose level in Part 1.

All the outputs discussed above and listed below are used together with safety and tolerability data to aid the next dose selection.

The mean, median, and 5th and 95th percentiles (90% CrI) for each model parameter and prediction will be tabulated.

Figures will be produced for posterior dose-response model for AUC[0-t], and Cmax (with 90% CrI), respectively as discussed above in inference bullet.

A Listing for PK parameters AUC[0-t] and Cmax in Part I single dose phase will be provided.

In addition, the above listed inferences and predictions will be performed for PK parameters AUC[0-24] and Cmax in Part 2 repeat dose phase. The corresponding tables, figure and listing listed above will also be produced.

Sensitivity and Supportive Statistical Analyses

Not applicable.

8.2.3. Deviations from RAP Planned Analysis

To ensure transparency, any deviations from the above analyses will be documented in a log appended to the CSR. These deviations may include (although are not limited to) algebraically different model parameterizations or changes in the prior structure to support convergence of the parameter estimations in SAS. These possible issues and solutions for them are discussed above in the appropriate sections.

9. REFERENCES

GlaxoSmithKline Document Number 2015N257523_01 (Amendment 1 – 01-NOV-2016): A Phase I, Randomized, Double-Blind (Sponsor Unblinded), Single-Center, Placebo-Controlled, Three-Part Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of Ascending Single and Repeat Intravenous Doses of GSK3342830 in Healthy Adult Subjects.

10. APPENDICES

Section	Appendix
RAP Section 5 : General Considerations for Data Analyses & Data Handling Conventions	
Section 10.1	Appendix 1: Time and Events
Section 10.2	Appendix 2: Treatment States & Phases
Section 10.3	Appendix 3: Data Display Standards & Handling Conventions • Study Treatment & Sub-group Display Descriptors • Baseline Definitions & Derivations • Reporting Process & Standards
Section 10.4	Appendix 4: Derived and Transformed Data • General, Study Population & Safety • Efficacy • Pharmacokinetic • Pharmacodynamic and or Biomarkers
Section 10.5	Appendix 5: Premature Withdrawals & Handling of Missing Data • Premature Withdrawals • Handling of Missing Data
Section 10.6	Appendix 6: Values of Potential Clinical Importance
Section 10.8	Appendix 7: DMID Adult Toxicity Tables for Adverse Event Assessment
Section 10.8	Appendix 8: Multiple Comparisons and Multiplicity
Section 10.9	Appendix 9: Model Checking and Diagnostics for Statistical Analyses
Other RAP Appendices	
Section 10.10	Appendix 10: Abbreviations & Trade Marks
Section 10.11	Appendix 11: List of Data Displays

10.1. Appendix 1: Time & Events

10.1.1. Protocol Defined Time & Events

Time and Events Table: Screening and Day –1; Single and Repeat Dose Escalation (Part 1 and Part 2) and Single Dose (Part 3)

Procedure	Screening (up to 30 days before Day 1)	Day –1	Notes
Informed consent	X		
Inclusion and exclusion criteria	X	X	
Demography	X		
Medical history (includes substance usage and family history of premature cardiovascular disease)	X	X	Substances: drugs, alcohol, tobacco and caffeine.
Past and current medical conditions including cardiovascular medical history	X	X	
Safety and Laboratory Assessments			
SAE review	X	X	Serious AEs will be collected from the signing of informed consent.
Concomitant medication review	X	X	
Full physical examination including height and weight	X		
Brief physical examination		X	
Vital signs (BP, HR, oral temperature, respiration rate)	X	X	
12-lead electrocardiogram	X	X	
Continuous cardiac monitoring		X	Continuous dual-lead telemetry will be initiated on Day –1 at least 8 hours before study drug administration on Day 1.
Urine cotinine and drug and breath alcohol screens	X	X	
β-hCG pregnancy test/estradiol/FSH	X	X	Pregnancy test (if female of child-bearing age; serum at screening and urine at Day –1); estradiol and FSH at screening as appropriate. Only women of non-child-bearing potential may participate.
Human immunodeficiency virus antibody, hepatitis B surface antigen, and hepatitis C antibody screen	X		
Table is continued on the next page.			

Procedure	Screening (up to 30 days before Day 1)	Day –1	Notes
Clinical chemistry (including liver chemistries), hematology, and urinalysis	X	X	The albumin to creatinine ratio will be determined at Screening using the first morning void urine as described in protocol Section 7.3.7. An aliquot of the urine sample will be collected for NGAL and KIM-1 at Day –1. These samples may be analyzed after the end of the study if a clinical signal is detected. Instructions for collection and storage of these urine samples are included in the Study Reference Manual. Hematology assessments on Day –1 will also include total iron, total binding iron capacity, ferritin, and reticulocytes.
Genetic sample		X	Collect a pharmacogenomics sample only if the subject has a signed consent specific for this purpose. The pharmacogenomics sample can be collected anytime, but Day –1 is recommended. Informed consent for optional sub-studies (e.g., genetics research) must be obtained before collecting a sample.
Admission to clinical unit		X	

β-hCG = beta human chorionic gonadotropin, BP = blood pressure, FSH = follicle-stimulating hormone, HR = heart rate, KIM-1 = kidney injury molecule 1, NGAL = neutrophil gelatinase-associated lipocalin, SAE = serious adverse event.

Time and Events Table: Part 1 - Single Dose Escalation and Part 3 – Single Dose

Procedure	Day 1																	Day 2		Day 3
	Hours relative to treatment administration																			
	Pre-dose	0	0.5	1	1.25	1.5	2	3	3.5	4	4.5	5	6	8	10	12	16	24	36	48
Randomization	X																			
12-lead ECG[1]	X		X	X		X	X	X		X			X			X		X		X
Vital signs (BP, HR, oral temperature, respiration rate)	X		X	X		X	X	X		X			X			X		X		X
Fasting clinical chemistry, hematology, and urinalysis[2]																		X		
Treatment administration[3]		X																		
Blood collection for pharmacokinetics[4]	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Urine collection for pharmacokinetics[5]	X-- ---------X----------X----------X----------X----------X----------X----------X																			
Continuous cardiac monitoring[6]	X←----------Continuous review----------→																			
AE review		X←----------Continuous review----------→																		
SAE review	X←----------Continuous review----------→																			
Concomitant medication review	X←----------Continuous review----------→																			
Discharge from inpatient unit[7]																				X

AE = adverse event, BP = blood pressure, ECG = electrocardiogram, HR = heart rate, SAE = serious adverse event.

NOTES:

1. Triplicate 12-lead ECGs to be obtained at least 5 minutes apart within 1 hour before dosing. Single ECGs will be obtained at all other time points.
2. An aliquot of the urine sample will be collected for neutrophil gelatinase-associated lipocalin (NGAL) and kidney injury molecule 1 (KIM-1). These samples may be analyzed after the end of the study if a clinical signal is detected. Instructions for collection and storage of these urine samples are included in the Study Reference Manual. The albumin to creatinine ratio will be determined using the first morning void urine on Day 2.
3. GSK3342830 or placebo will be administered as a single IV infusion in the morning on Day 1. The planned infusion duration time is 1 hour.
4. Pharmacokinetic blood samples will be collected for GSK3342830 and potential metabolites. At the end of the study the saved blood samples from a predicted therapeutically-relevant dose level and higher dose level for plasma PK analysis of parent and the highest dose level completed for metabolite profile, will be transferred to a GSK specified laboratory. Details of PK sample collection and storage will be provided in the Study Reference Manual.
5. Pooled urine samples will be collected over the following time intervals: pre-dose (within a 24-hour period before dosing, may begin on Day –1) and 0 to 4, 4 to 8, 8 to 12, 12 to 24, and 24 to 48 hours post-dose. Two aliquots of urine samples for baseline analysis may be collected from any time after admission to just before dosing on Day 1. At the end of the study, the saved urine samples from a predicted therapeutically-relevant dose level and higher dose level for urinary PK analysis of parent and the highest dose level completed for potential metabolite profile, will be transferred to a GSK specified laboratory. Urine will be collected in opaque bottles to maintain blind of blinded study site personnel. Details of urine sample collection and storage will be provided in the Study Reference Manual.
6. Continuous dual-lead telemetry will be initiated on Day –1 at least 8 hours before treatment administration on Day 1 and will continue until 48 hours post dose.
7. Subjects will be discharged from the clinical unit after the 48-hour post-dose assessments are complete.

Time and Events Table: Part 2 - Repeat Dose Escalation

Procedure	Study Day															
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Randomization	X															
12-lead ECG[1]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Vital signs (BP, HR, oral temperature, respiration rate)[2]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Fasting clinical chemistry, hematology, and urinalysis tests[3]		X			X					X					X	
Treatment administration[4]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Blood collection for pharmacokinetics[5]	X		X			X			X			X	X		X	
Urine collection for pharmacokinetics[6]	X	X													X	X
Continuous cardiac monitoring[7]	X←Continuous review→															
AE review	X←---------- ----------Continuous review----------→															
SAE review	X←----------Continuous review----------→															
Concomitant medication review	X←----------Continuous review----------→															
Discharge from inpatient unit[8]																X

AE = adverse event, BP = blood pressure, ECG = electrocardiogram, HR = heart rate, SAE = serious adverse event.

NOTES:

1. Triplicate 12-lead ECGs will be obtained at least 5 minutes apart within 1 hour before the start of infusion (pre-dose) on Day 1. Single ECGs will be obtained at 0.5, 1, 1.5, 2, 3, 4, 6, and 12 hours after the start of infusion on Day 1 and Day 15, within 1 hour before the start of the morning infusion on Days 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, and 14, and in the morning on Day 16.
2. Vital signs will be measured within 1 hour before the start of infusion (pre-dose) and at 0.5, 1, 1.5, 2, 3, 4, 6, and 12 hours after the start of infusion on Days 1 and 15, within 1 hour before the start of the morning infusion and on Days 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, and 14, and in the morning on Day 16.
3. An aliquot of the urine sample will be collected for neutrophil gelatinase-associated lipocalin (NGAL) and kidney injury molecule 1 (KIM-1). These samples may be analyzed after the end of the study if a clinical signal is detected. Instructions for collection and storage of these urine samples are included in the Study Reference Manual. Hematology assessments on Days 5 and 15 will also include total iron, total iron binding capacity, ferritin, and reticulocytes. The albumin to creatinine ratio will be determined using the first morning void urine on Days 5 and 15.
4. GSK3342830 or placebo will be administered as a single IV infusion in the morning on Day 1, TID IV infusions (approximately every 8 hours) on Days 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, and 14, and as a single IV infusion in the morning on Day 15. The planned infusion duration time is 1 hour.

Footnotes are continued on the next page.

5. Pharmacokinetic samples for GSK3342830 and potential metabolites will be collected on Day 1 at the following time points: pre-dose (within 15 minutes before dosing) and 0.5, 1 (end of infusion), 1.25, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 6, 8, 10, 12, 16, and 24 hours after the start of infusion. Single pre-dose trough samples will be taken on the mornings of Days 3, 6, 9, 12, and 13. Serial samples will be collected on Day 15 at the following time points: pre-dose (within 15 minutes before dosing) and 0.5, 1 (end of infusion), 1.25, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 6, and 8 hours after the start of infusion. At the end of the study, the saved blood samples from a predicted therapeutically-relevant dose level and higher dose level for plasma PK analysis of parent and from the highest dose level completed for potential metabolite profile will be transferred to a GSK specified laboratory. Details of PK sample collection and storage will be provided in the Study Reference Manual.
6. Pooled urine samples will be collected on Day 1 and Day 15 over the following time intervals: pre-dose (within a 24-hour period before dosing, may begin on Day –1) and 0 to 8 and 8 to 24 hours post-dose. Two aliquots of urine samples for baseline analysis may be collected from any time after admission to just before dosing on Day 1. At the end of the study, the saved urine samples from a predicted therapeutically-relevant dose level and higher dose level for urinary PK analysis of parent and from the highest dose-level completed for potential metabolite profile, will be transferred to a GSK specified laboratory. Urine will be collected in opaque bottles to maintain blind of blinded study site personnel. Details of urine sample collection and storage will be provided in the Study Reference Manual.
7. Continuous dual-lead telemetry will be initiated on Day –1 at least 8 hours before treatment administration on Day 1 and will continue until 48 hours post dose.
8. Subjects will be discharged from the clinical unit after the Day 16 assessments are complete.

Time and Events Table: Follow-up Visit; Single and Repeat Dose Escalation (Part 1 and Part 2) and Single Dose (Part 3)

Procedure	Follow-up Visit (7 to 10 days post last dose or early termination)
Adverse event/serious adverse event review	X
Concomitant medication review	X
Brief physical examination	X
12-lead electrocardiogram	X
Vital signs	X
Urine β-human chorionic gonadotropin pregnancy test (women of child-bearing age)	X
Clinical chemistry, hematology, and urinalysis tests[1]	X

NOTE:

1. An aliquot of the urine sample will be collected for neutrophil gelatinase-associated lipocalin (NGAL) and kidney injury molecule 1 (KIM-1). These samples may be analyzed after the end of the study if a clinical signal is detected. Instructions for collection and storage of these urine samples are included in the Study Reference Manual. Hematology assessments will also include total iron, total iron binding capacity, ferritin, and reticulocytes. The albumin to creatinine ratio will be determined using the first morning void urine as described in protocol Section7.3.7.

10.2. Appendix 2: Treatment States and Phases

10.2.1. Treatment Phases

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

Treatment Phase	Definition
Pre-Treatment	Date < Study Treatment Start Date
On-Treatment	Study Treatment Start Date ≤ Date ≤ Study Treatment Stop Date
Post-Treatment	Date > Study Treatment Stop Date

10.2.2. Treatment States

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

10.2.2.1. Treatment States for Safety Data

Treatment State	Definition
Pre-Treatment	Date/time < Study Treatment Start Date/time
On-Treatment	Study Treatment Start Date/time ≤ Date/time ≤ Study Treatment Stop Date/time + 2 days
Post-Treatment	Date/time > Study Treatment Stop Date/time + 2 days

NOTES:

- If the study treatment stop date is missing then the assessment will be considered to be On-Treatment

10.2.2.2. Treatment States for AE Data

Treatment State	Definition
Pre-Treatment	AE Start Date/time < Study Treatment Start Date/time
On-Treatment	If AE onset date/time is on or after treatment start date & on or before treatment stop date/time. Study Treatment Start Date/time ≤ AE Start Date/time ≤ Study Treatment Stop Date/time + 2 days
Post-Treatment	If AE onset date/time is after the treatment stop date/time. AE Start Date/time > Study Treatment Stop Date/time + 2 days
Onset Time Since 1st Dose (Days)	If Treatment Start Date/time > AE Onset Date/time, = AE Onset Date - Treatment Start Date If Treatment Start Date/time ≤ AE Onset Date/time, = AE Onset Date - Treatment Start Date +1 Missing otherwise.
Duration (Days)	AE Resolution Date – AE Onset Date + 1
Drug-related	If relationship is marked 'YES' on CRF OR value is missing.

NOTES:

- If the study treatment stop date is missing then the AE will be considered to be On-Treatment.

10.3. Appendix 3: Data Display Standards & Handling Conventions

10.3.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions				
Randomization Schedule			Data Displays for Reporting	
Part	Code	Description	Description	Order [1]
1	A1	Cohort A GSK3342830	GSK3342830 250 mg	1
1	A2	Cohort B GSK3342830	GSK3342830 500 mg	2
1	A3	Cohort C GSK3342830	GSK3342830 1000 mg	3
1	A4	Cohort D GSK3342830	GSK3342830 2000 mg	4
1	A5	Cohort E GSK3342830	GSK3342830 4000 mg	5
1	A6	Cohort F GSK3342830	GSK3342830 6000 mg	6
1	A7	Cohort X1 GSK3342830	GSK3342830 XXXX[3] mg	7
1	A8	Cohort X2 GSK3342830	GSK3342830 XXXX[3] mg	8
1	P	Placebo	Placebo	9
2	A9	Cohort G GSK3342830	GSK3342830 1000 mg TID	10
2	A10	Cohort H GSK3342830	GSK3342830 2000 mg TID	11
2	A11	Cohort I GSK3342830	GSK3342830 4000 mg TID	12
2	A12	Cohort Y1 GSK3342830	GSK3342830 XXXX[3] mg TID	13
2	A13	Cohort Y2 GSK3342830	GSK3342830 XXXX[3] mg TID	14
2	P	Placebo	Placebo	15
3	AJ1	Cohort J GSK3342830	GSK3342830 XXXX[4] mg	16
3	PJ	Placebo	Placebo	17
3	AJ2	Cohort Z1 GSK3342830	GSK3342830 XXXX[4] mg	18
3	PJ	Placebo	Placebo	19

NOTES:

1. Order represents treatments being presented in TFL, as appropriate.
2. Cohort X1, X2, Y1, and Y2 are created per protocol to allow 2 additional doses which may be evaluated to further understand the study drug. The Randomization Schedule does not contain the actual dose levels but instead refers to the Cohort dose level. Dose levels may change from the protocol defined levels. The TLFs will display the actual dose levels used in the study.
3. The dose for Cohort X1, X2, Y1, and Y2 will be determined once the decision is made to enroll those optional cohorts.
4. The dose for Cohort J will either 250, 500, 1000, 2000, 4000 or ≤6000 mg based on preliminary safety and tolerability results of doses determined to be safe and well tolerated in subjects of non-Japanese heritage after completion of the single escalation dose cohorts (Part 1).

10.3.2. Baseline Definition & Derivations

10.3.2.1. Baseline Definitions

For all endpoints (expect as noted in baseline definitions) the baseline value will be the latest pre-dose assessment.

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

NOTES :

- Unless otherwise stated, the mean of replicate assessments at any given time point will be used as the value for that time point.

10.3.2.2. Derivations and Handling of Missing Baseline Data

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

NOTES :

- Unless otherwise specified, the baseline definitions specified in Section 10.3.2.1 Baseline Definitions will be used for derivations for endpoints / parameters and indicated on summaries and listings.
- Unless otherwise stated, if baseline data is missing no derivation will be performed and will be set to missing.
- The baseline definition will be footnoted on all change from baseline displays.

10.3.3. Reporting Process & Standards

Reporting Process
Software
• The currently supported versions of SAS software [Insert Other Software as Required] will be used.
Analysis Datasets
• Analysis datasets will be created according to CDISC standards (SDTM IG Version 3.1.3 & AdaM IG Version 1.0. • For creation of ADaM datasets (ADCM/ADAE), the same version of dictionary datasets will be implemented for conversion from SI to SDTM.
Generation of RTF Files
• RTF files will be generated for all reporting efforts described in the RAP.

Reporting Standards
General

Reporting Standards	
• The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated: o 4.03 to 4.23: General Principles o 5.01 to 5.08: Principles Related to Data Listings o 6.01 to 6.11: Principles Related to Summary Tables o 7.01 to 7.13: Principles Related to Graphics	
Formats	
• All data will be reported according to the actual treatment the subject received unless otherwise stated. • GSK IDSL Statistical Principles (5.03 & 6.06.3) for decimal places (DP's) will be adopted for reporting of data based on the raw data collected. • 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. • Visits outside the protocol defined time-windows (i.e. recorded as protocol deviations) will be included in listings but omitted from figures, summaries and statistical analyses.	
Unscheduled Visits	
• Unscheduled visits will not be included in summary tables. • Unscheduled visits will not be included in figures. • All unscheduled visits will be included in listings.	
Descriptive Summary Statistics	
Continuous Data	Refer to IDSL Statistical Principle 6.06.1
Categorical Data	N, n, frequency, %
Reporting of Pharmacokinetic Concentration Data	
Descriptive Summary Statistics	Refer to IDSL Statistical Principle 6.06.1 Assign zero to NQ values (Refer to GUI_51487 for further details)
Reporting of Pharmacokinetic Parameters	
Descriptive Summary Statistics (Log Transformed)	N, n, geometric mean, 95% CI of geometric mean, standard deviation (SD) of logged data and between geometric coefficient of variation (CVb- (%)) will be reported. CV_b (%) = $\sqrt{}$ (exp(SD^2) - 1) * 100 (SD = SD of log transformed data)

Reporting Standards	
Parameters Not Being Log Transformed	Tmax, %AUCex, tlast, lambda_z, lambda_z_lower, lambda_z_upper, lambda_z_no. of points, Ratio of time invariance, Ratio of accumulation, Feu(t1-t2), CLr, Ae
Listings	Include all following PK parameters: Cmax, AUC0-∞, AUC0-t, AUC(0-τ), t1/2, CL, Vss, Cτ, Ratio of time invariance, Ratio of accumulation, Tmax, %AUCex, tlast, lambda_z, lambda_z_lower, lambda_z_upper, lambda_z_no. of points, Feu(t1-t2), CLr, Ae.
Graphical Displays	
• Refer to IDSL Statistical Principals 7.01 to 7.13.	

Reporting Standards

10.4. Appendix 4: Derived and Transformed Data

10.4.1. General

Multiple Measurements at One Time Point
• Mean of the measurements will be calculated and used in any derivation of summary statistics but if listed, all data will be presented. • If there are two values within a time window the value closest to the target day for that window will be used. If values are the same distance from the target then the mean will be taken. • Subjects having both High and Low values for Normal Ranges at any post-baseline visits for safety parameters will be counted in both the High and Low categories of "Any visit post-baseline" row of related summary tables. This will also be applicable to relevant Potential Clinical Importance summary tables.
Study Day

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

10.4.2. 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**

10.4.3. Safety

ECG Parameters
RR Interval
• IF ECG values are machine read and RR interval (msec) is not provided directly, then RR interval can be derived as : [1] If QTcB is machine read & RR is not provided, then : $$RR = \left[\left(\frac{QT}{QTcB}\right)^2\right] * 1000$$ [2] If QTcF is machine read and RR is not provided, then:

ECG Parameters
$$RR = \left[\left(\frac{QT}{QTcF}\right)^{3}\right] * 1000$$ • If ECGs are manually read, the RR value preceding the measurement QT interval should be a collected value THEN do not derive. • Important Note: Machine read values of RR should not be replaced with re-derived values.
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 : $$QTcB = \frac{QT}{\sqrt{\frac{RR}{1000}}} \qquad QTcF = \frac{QT}{\sqrt[3]{\frac{RR}{1000}}}$$ • Important Note: Machine read values of QTcB and QTcF should not be replaced with re-derived values. If neither machine read QTcB or QTcF are available but QT and RR are collected, then a QTcB and QTcF can be derived however this should be discussed and agreed with the study team and the TLFs must have an appropriate footnote denoting those parameters are derived.

Adverse Events
AE'S OF Special Interest
• Liver events • CV events • Infusion site reactions • Potential systemic allergic reactions • Hematologic events • Rash Events

10.5. Appendix 5: Premature Withdrawals and Handling of Missing Data

10.5.1. Premature Withdrawals

Element	Reporting Detail
General	• Subject study completion (i.e. as specified in the protocol) was defined as one who has completed all phases of the study including the follow-up visit. • Withdrawn subjects may be replaced in the study. • All available data from subjects who were withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified.

10.5.2. Handling of Missing Data

Element	Reporting Detail
General	• Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument : o These data will be indicated by the use of a "blank" in subject listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table. o Answers such as "Not applicable" and "Not evaluable" are not considered to be missing data and should be displayed as such.
Outliers	• Any subjects excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report.

10.5.2.1. Handling of Missing 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: o 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 2: Treatment States and Phases. o 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. Consequently, time to onset and duration of such events will be missing.

Element	Reporting Detail
	• Start or end dates which are completely missing (i.e. no year specified) will remain missing, with no imputation applied.

10.5.2.2. Handling of Partial Dates

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

Adverse Events	• Any partial dates for adverse events will be raised to data management. If the full date cannot be ascertained, the following assumptions will be made: o If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month. o However, if these results in a date prior to Week 1 Day 1 and the event could possibly have occurred during treatment from the partial information, then the Week 1 Day 1 date will be assumed to be the start date. o The AE will then be considered to start on-treatment (worst case). o If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month. • The recorded partial date will be displayed in listings.

10.6. Appendix 6: Values of Potential Clinical Importance

10.6.1. ECG

ECG Parameter	Units	Potential Clinical Importance Range	
		Lower	Upper
Absolute			
Absolute QTc Interval	msec	> 450 [1]	
		> 450 [2]	≤ 479[2]
		≥ 480[2]	≤ 499[2]
		≥ 500[2]	
Absolute PR Interval	msec	< 110 [1]	> 220 [1]
Absolute QRS Interval	msec	< 75 [1]	> 110 [1]
Change from Baseline			
Increase from Baseline QTc	msec	≤30[2]	
	msec	> 30[2]	≤ 59[2]
	msec	≥ 60 [1]	

NOTES:

1. Represent standard ECG values of PCI for HV studies.
2. Represent further subdivisions of ECG values for analysis.

10.6.2. Vital Signs

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

10.7. Appendix 7: DMID Adult Toxicity Tables for Adverse Event Assessment

10.7.1. Laboratory Values

Parameter values are converted to use SI units.

HEMATOLOGY

	Grade 1	Grade 2	Grade 3	Grade 4
Hemoglobin	95 to 105 G/L	80 to 94 G/L	65 to 79 G/L	<65 G/L
Absolute neutrophil count	1.0 to 1.5 10^9/L	0.75 to 0.999 10^9/L	0.5 to 0.749 10^9/L	<0.5 10^9/L
Platelets	75 to 99.999 10^9/L	50 to 74.999 10^9/L	20 to 49.999 10^9/L	<20 10^9/L
White Blood Cells	11 to 13 10^9/L	13 to 15 10^9/L	15 to 30 10^9/L	>30 or <1 10^9/L
% Polymorphonuclear leukocytes + band cells	>80%	90 to 95%	>95%	N/A
Abnormal Fibrinogen	Low: 1 to 2 G/L High: 4 to 6 G/L	Low: <1 G/L High: >6 G/L	Low: <0.5 G/L High: N/A	Fibrinogen associated with gross bleeding or with disseminated coagulation
Fibrin Split Product	0.020 to 0.040 G/L	0.041 to 0.050 G/L	0.051 to 0.060 G/L	>0.060 G/L
Prothrombin Time	1.01 to 1.25 × ULN	1.26 to 1.5 × ULN	1.51 to 3.0 × ULN	>3 × ULN
Activated Partial Thromboplastin	1.01 to 1.66 × ULN	1.67 to 2.33 × ULN	2.34 to 3 × ULN	>3 × ULN
Methemoglobin	5.0 to 9.9%	10.0 to 14.9%	15.0 to 19.9%	>20%

N/A = not applicable; ULN = upper limit of normal.

CHEMISTRIES

	Grade 1	Grade 2	Grade 3	Grade 4
Hyponatremia	130 to 135 MMOL/L	123 to 129 MMOL/L	116 to 122 MMOL/L	<116 MMOL/L or abnormal sodium *with* mental status changes or seizures
Hypernatremia	146 to 150 MMOL/L	151 to 157 MMOL/L	158 to 165 MMOL/L	>165 MMOL/L or abnormal sodium *with* mental status changes or seizures
Hypokalemia	3.0 to 3.4 MMOL/L	2.5 to 2.9 MMOL/L	2.0 to 2.4 MMOL/L or intensive replacement therapy of hospitalization required	<2.0 MMOL/L or abnormal potassium *with* paresis, ileus, or life-threatening arrhythmia
Hyperkalemia	5.6 to 6.0 MMOL/L	6.1 to 6.5 MMOL/L	6.6 to 7.0 MMOL/L	>7.0 MMOL/L or abnormal potassium *with*

				life-threatening arrhythmia
Hypoglycemia	3.0 to 3.55 MMOL/L	2.22 to 2.99 MMOL/L	1.67 to 2.21 MMOL/L	<1.67 MMOL/L or abnormal glucose *with* mental status changes or coma
Hyperglycemia (nonfasting and no prior diabetes)	6.44 to 8.88 MMOL/L	8.89 to 13.88 MMOL/L	13.89 to 27.75 MMOL/L	>27.76 MMOL/L or abnormal glucose *with* ketoacidosis or seizures
Hypocalcemia (corrected for albumin)	2.10 to 1.95 MMOL/L	1.94 to 1.75 MMOL/L	1.74 to 1.52 MMOL/L	<1.52 MMOL/L or abnormal calcium *with* life-threatening arrhythmia or tetany
Hypercalcemia (corrected for albumin)	2.64 to 2.87 MMOL/L	2.88 to 3.12	3.13 to 3.37 MMOL/L	>3.37 MMOL/L or abnormal calcium *with* life-threatening arrhythmia
Hypomagnesemia	0.7 to 0.6 MMOL/L	0.59 to 0.45 MMOL/L	0.44 to 0.3 MMOL/L	<0.3 MMOL/L or abnormal magnesium *with* life-threatening arrhythmia
Hypophosphatemia	0.7 to 0.8 MMOL/L	0.5 to 0.6 MMOL/L or replacement Rx required	0.3 to 0.4 MMOL/L intensive therapy or hospitalization required	<0.3 MMOL/L or abnormal phosphate *with* life-threatening arrhythmia
Hyperbilirubinemia (when accompanied by any increase in other liver function test)	1.1 to <1.25 × ULN	1.25 to <1.5 × ULN	1.5 to 1.75 × ULN	>1.75 × ULN
Hyperbilirubinemia (when other liver function tests are in the normal range)	1.1 to <1.5 × ULN	1.5 to <2.0 × ULN	2.0 to 3.0 × ULN	>3.0 × ULN
Blood urea nitrogen	1.25 to 2.5 × ULN	2.6 to 5 × ULN	5.1 to 10 × ULN	>10 × ULN
Hyperuricemia (uric acid)	446 to 595 UMOL/L	596 to 714 UMOL/L	715 to 892 UMOL/L	>892 UMOL/L
Creatinine	1.1 to 1.5 × ULN	1.6 to 3.0 × ULN	3.1 to 6.0 × ULN	>6 × ULN or dialysis required

Rx = therapy; ULN = upper limit of normal.

ENZYMES				
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**
Aspartate aminotransferase	1.1 to <2.0 × ULN	2.0 to <3.0 × ULN	3.0 to 8.0 × ULN	>8.0 × ULN
Alanine aminotransferase	1.1 to <2.0 × ULN	2.0 to <3.0 × ULN	3.0 to 8.0 × ULN	>8.0 × ULN
Gamma to glutamyl transferase	1.1 to <2.0 × ULN	2.0 to <3.0 × ULN	3.0 to 8.0 × ULN	>8.0 × ULN
Alkaline Phosphatase	1.1 to <2.0 × ULN	2.0 to <3.0 × ULN	3.0 to 8.0 × ULN	>8.0 × ULN
Amylase	1.1 to 1.5 × ULN	1.6 to 2.0 × ULN	2.1 to 5.0 × ULN	>5.1 × ULN
Lipase	1.1 to 1.5 × ULN	1.6 to 2.0 × ULN	2.1 to 5.0 × ULN	>5.1 × ULN

ULN = upper limit of normal.

URINALYSIS				
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**
Proteinuria	1+ or 200 MG to 1 GM loss/day	2 to 3+ or 1 to 2 GM loss/day	4+ or 2 to 3.5 GM loss/day	Nephrotic syndrome or >3.5 GM loss/day
Hematuria	Microscopic only <10 RBC/HPF	Gross, no clots >10 RBC/HPF	Gross, with or without clots, or red blood cells casts	Obstructive or required transfusion

HPF = high-powered field; RBC = red blood cells.

10.8. Appendix 8: Multiple Comparisons & Multiplicity

10.8.1. Handling of Multiple Comparisons & Multiplicity

No adjustments for multiplicity will be made.

10.9. Appendix 9: Model Checking and Diagnostics for Statistical Analyses

10.9.1. Statistical Analysis Assumptions

Endpoint(s)	• PK endpoints AUC and Cmax
Analysis	• Mixed Effects

- Model assumptions will be applied, but appropriate adjustments maybe made based on the data.
- The Kenward and Roger method for approximating the denominator degrees of freedom and correcting for bias in the estimated variance-covariance of the fixed effects will be used.
- Distributional assumptions underlying the statistical analyses will be assessed by visual inspection of residual plots. Normality will be examined by normal probability plots, while homogeneity of variance will be assessed by plotting the residuals against the predicted values for the model.

10.10. Appendix 10 – Abbreviations & Trade Marks

10.10.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
Ae	Amount excreted in urine
AUC	Area under the curve
AUC(0-t)	AUC from time zero to the time of last quantifiable concentration
AUC(0-∞)	AUC from time zero to infinity
AUC(0-τ)	AUC over the dosing interval τ
A&R	Analysis and Reporting
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CL	Total systemic clearance
CLr	Renal clearance
Cmax	Concentration at maximum
Cτ	Trough concentration
CPMS	Clinical Pharmacology Modelling & Simulation
CrI	Credible interval
CS	Clinical Statistics
CSR	Clinical Study Report
CTR	Clinical Trial Register
CV_b / CV_w	Coefficient of Variation (Between) / Coefficient of Variation (Within)
DOB	Date of Birth
DP	Decimal Places
eCRF	Electronic Case Record Form
Feu(t1-t2)	Urinary excretion ratio relative to dose
IA	Interim Analysis
ICH	International Conference on Harmonisation
IDSL	Integrated Data Standards Library
IMMS	International Modules Management System
IP	Investigational Product
GUI	Guidance
MCMC	Markov Chain Monte Carlo
PCI	Potential Clinical Importance
PDMP	Protocol Deviation Management Plan
PK	Pharmacokinetic
PP	Per Protocol
QC	Quality Control
QTcF	Frederica's QT Interval Corrected for Heart Rate
QTcB	Bazett's QT Interval Corrected for Heart Rate
RAP	Reporting & Analysis Plan

Abbreviation	Description
Ratio of accumulation	Accumulation ratio, calculated by AUC(0-τ) on day 15/ AUC(0-τ) on day 1
Ratio of time invariance	Time invariance ratio, calculated by AUC(0-τ) on day 15/ AUC(0-∞) on day 1
SAC	Statistical Analysis Complete
SDTM	Study Data Tabulation Model
SOP	Standard Operation Procedure
TA	Therapeutic Area
TFL	Tables, Figures & Listings
t1/2	Terminal elimination half-life
Tmax	Time of maximum concentration
Vss	Steady-state volume of distribution
GSK	GlaxoSmithKline

10.10.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
NONE

Trademarks not owned by the GlaxoSmithKline Group of Companies
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SAS

10.11. Appendix 11: List of Data Displays

10.11.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.9	
Safety	2.1 to 2.17	2.1
Pharmacokinetic	3.1 to 3.22	3.1 to 3.22
Section	**Listings**	
ICH Listings	1 to 47	

10.11.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required an example mock-up displays provided in the TLF Specification documents.

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

NOTES:

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

10.11.3. Deliverable [Priority]

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

NOTES:

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

10.11.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition and Analysis Sets					
1.1	Safety	NS	Summary of Number of Subjects Enrolled by Country and Site ID		SAC [1]
1.2	Safety	ES1	Summary of Subject Disposition		SAC [1]
1.3	Screened	ES6	Summary of Reasons for Screening Failures		SAC [1]
1.4	Screened	DV1	Summary of Important Protocol Deviations		SAC [1]
Demographics and Baseline Characteristics					
1.5	Safety	DM1	Summary of Demographic Characteristics		SAC [1]
1.6	Safety	DM11	Summary of Age Ranges		SAC [1]
1.7	Safety	DM5	Summary of Race and Racial Combinations		SAC [1]
1.8	Safety	DM6	Summary of Race and Racial Combinations Details		SAC [1]
Medical Conditions					
1.9	Safety	MH1	Summary of Cardiovascular Related Medical Conditions		SAC [1]

10.11.5. Safety Tables

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events					
2.1	Safety	AE2	Relationship of Adverse Event System Organ Classes, Preferred Terms and Verbatim Text		SAC [1]
2.2	Safety	AE1	Summary of All Adverse Events		SAC [1]
2.3	Safety	AE1	Summary of Drug-Related Adverse Events		SAC [1]
2.4	Safety	A15	Summary of Common (>=5%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)		SAC [1]
2.5	Safety	A16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)		SAC [1]
Laboratory Measurements					
2.6	Safety	LB1	Summary of Clinical Chemistry Values		SAC [1]
2.7	Safety	LB1	Summary of Clinical Chemistry Change from Baseline		SAC [1]
2.8	Safety	LB1	Summary of Haematology Values		SAC [1]
2.9	Safety	LB1	Summary of Haematology Change from Baseline		SAC [1]
2.10	Safety	UR3b	Summary of Urinalysis Dipstick Results		SAC [1]
Electrocardiograms					
2.11	Safety	EG1	Summary of ECG Findings		SAC [1]
2.12	Safety	EG2	Summary of ECG Values		SAC [1]
2.13	Safety	EG2	Summary of Change from Baseline in ECG Values		SAC [1]
2.14	Safety	SAFE_T1	Summary of Frequency of Maximum Post-Dose ECG Parameter Corrected QTc Interval		SAC [1]

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.15	Safety	SAFE_T2	Summary of Frequency of Maximum Change from Baseline for ECG Parameter Corrected QTc Interval		SAC [1]
Vital Signs					
2.16	Safety	VS1	Summary of Vital Signs		SAC [1]
2.17	Safety	VS1	Summary of Vital Signs Change from Baseline		SAC [1]

10.11.6. Safety Figures

Safety : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Cytokine Plots					
2.1	Safety	SAFE_F1	Boxplot of Cytokine Data		SAC [1]
2.2	Safety	SAFE_F2	Individual Cytokine Plot		SAC [1]

10.11.7. Pharmacokinetic Tables

Pharmacokinetic : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK Concentration Data					
3.01	PK	PK01	Summary of GSK3342830 Single Dose Plasma Pharmacokinetic Concentration-Time Data (units) by Treatment in Part 1 and Part 3		SAC [1]
3.02	PK	PK01	Summary of GSK3342830 Plasma Pharmacokinetic Concentration-Time Data (units) by Treatment in Part 2		SAC [1]
PK Parameters					
3.03	PK Parameter	PKPT1	Summary of Untransformed GSK3342830 Single Dose Plasma Pharmacokinetic Parameters in Part 1 and Part 3	Tmax, %AUCex, tlast, lambda_z, lambda_z_lower, lambda_z_upper, lambda_z_no. of points	SAC [1]
3.04	PK Parameter	PKPT3	Summary of Log-transformed GSK3342830 Single Dose Plasma Pharmacokinetic Parameters in Part 1 and Part 3	Cmax, AUC(0-t), AUC(0-∞), t1/2, CL, Vss	SAC [1]
3.05	PK Parameter	PKPT1	Summary of Untransformed GSK3342830 Single Dose Urine Pharmacokinetic Parameters in Part 1 and Part 3	Feu(t1-t2), CLr, Ae	SAC [1]
3.06	PK Parameter	PKPT1	Summary of Untransformed GSK3342830 Plasma Pharmacokinetic Parameters in Part 2	Cmax, AUC(0-t), AUC(0-∞), AUC(0-τ), t1/2, CL, Vss, Cτ, Ratio of time invariance, Ratio of accumulation, Tmax, %AUCex, tlast, lambda_z, lambda_z_lower, lambda_z_upper, lambda_z_no. of points	SAC [1]
3.07	PK Parameter	PKPT3	Summary of Log-transformed GSK3342830 Plasma Pharmacokinetic Parameters in Part 2	Cmax, AUC(0-t), AUC(0-∞), AUC(0-τ), t1/2, CL, Vss, Cτ	SAC [1]

Pharmacokinetic : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.08	PK Parameter	PKPT1	Summary of Untransformed GSK3342830 Urine Pharmacokinetic Parameters in Part 2	Feu(t1-t2), CLr, Ae	SAC [1]
PK Analysis Tables					
3.09	PK Parameter	PK_T1	Summary of Statistical Analysis of GSK3342830 Plasma Dose Proportionality in Part 1	Cmax, AUC(0-∞)	SAC [1]
3.10	PK Parameter	PK_T1	Summary of Statistical Analysis of GSK3342830 Plasma Dose Proportionality in Part 2	Cmax, AUC(0-τ)	SAC [1]
3.11	PK Parameter	PK_T1	Summary of Statistical Analysis of GSK3342830 Plasma Time Invariance in Part 2	AUC(0-∞) on Day 1 and AUC(0-τ) on Day 15	SAC [1]
3.12	PK Parameter	PK_T1	Summary of Statistical Analysis of GSK3342830 Plasma Accumulation Ratio in Part 2	AUC(0-τ)	SAC [1]
3.13	PK Parameter	PK_T1	Summary of Statistical Analysis of GSK3342830 Plasma Steady State Assessment in Part 2	Cτ	SAC [1]
Bayesian Dose Escalation					
3.14	PK Parameter	PK_T2	Summary of Model Parameters for Part 1 - Posterior Distributions		DE [1]
3.15	PK Parameter	PK_T2	Summary of Model Parameters for Part 2 - Posterior Distributions		DE [1]
3.16	PK Parameter	PK_T3	Summary of PK Parameters for Part 1 - Bayesian Prediction of Individual Subjects		DE [1]
3.17	PK Parameter	PK_T3	Summary of PK Parameters for Part 2 - Bayesian Prediction of Individual Subjects		DE [1]
3.18	PK Parameter	PK_T4	Summary of PK Parameters for Part 1 - Bayesian Predictive Probability		DE [1]

Pharmacokinetic : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.19	PK Parameter	PK_T4	Summary of PK Parameters for Part 2 - Bayesian Predictive Probability		DE [1]
3.20	PK Parameter	PK_T4	Summary of PK Parameters for Part 1 - Bayesian Inferential Probability		DE [1]
3.21	PK Parameter	PK_T4	Summary of PK Parameters for Part 2 - Bayesian Inferential Probability		DE [1]
3.22	PK Parameter	PK_T1	Summary of Statistical Analysis of GSK3342830 Single Dose Plasma Pharmacokinetic Parameters in Part 1 and Part 3 Subjects		SAC [1]

10.11.8. Pharmacokinetic Figures

Pharmacokinetic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Concentration Plots					
3.01	PK	PKCF4	Mean (SD) GSK3342830 Single Dose Plasma Concentration-Planned Time Plots for Part 1 and Part 3 (Linear and Semi-Log)		SAC [1]
3.02	PK	PKCF5	Median (range) GSK3342830 Single Dose Plasma Concentration-Planned Time Plots for Part 1 and Part 3 (Linear and Semi-Log)		SAC [1]
3.03	PK	PKCF4	Mean (SD) GSK3342830 Plasma Concentration-Planned Time Plots for Part 2 (Linear and Semi-Log)		SAC [1]
3.04	PK	PKCF5	Median (range) GSK3342830 Plasma Concentration-Planned Time Plots for Part 2 (Linear and Semi-Log)		SAC [1]
3.05	PK	PKCF5	Median (range) GSK3342830 Plasma Pre-dose Concentration versus Day for Part 2 (Linear and Semi-Log)		SAC [1]
3.06	PK	PKCF1P	Individual GSK3342830 Single Dose Plasma Concentration-Planned Time Plots for Part 1 and Part 3 (Linear and Semi-Log)		SAC [1]
3.07	PK	PKCF1P	Individual GSK3342830 Plasma Concentration-Planned Time Plots for Part 2 (Linear and Semi-Log)		SAC [1]
PK Parameters					
3.08	PK Parameter	PKPF3	Comparative Plot of Individual GSK3342830 Plasma AUC(0-t) Versus Dose for Part 1		SAC [1]
3.09	PK Parameter	PKPF3	Comparative Plot of Individual GSK3342830 Plasma AUCinf Versus Dose for Part 1		SAC [1]

Pharmacokinetic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.10	PK Parameter	PKPF3	Comparative Plot of Individual GSK3342830 Plasma Cmax Versus Dose for Part 1		SAC [1]
3.11	PK Parameter	PKPF3	Comparative Plot of Individual GSK3342830 Plasma Ae Versus Dose for Part 1		SAC [1]
3.12	PK Parameter	PKPF3	Comparative Plot of Individual GSK3342830 Plasma AUC(0-t) Versus Dose on Day 1 for Part 2		SAC [1]
3.13	PK Parameter	PKPF3	Comparative Plot of Individual GSK3342830 Plasma AUC(0-∞) Versus Dose on Day 1 for Part 2		SAC [1]
3.14	PK Parameter	PKPF3	Comparative Plot of Individual GSK3342830 Plasma Cmax Versus Dose on Day 1 for Part 2		SAC [1]
3.15	PK Parameter	PKPF3	Comparative Plot of Individual GSK3342830 Plasma Ae Versus Dose on Day 1 for Part 2		SAC [1]
3.16	PK Parameter	PKPF3	Comparative Plot of Individual GSK3342830 Plasma AUCtau Versus Dose on Day 15 for Part 2		SAC [1]
3.17	PK Parameter	PKPF3	Comparative Plot of Individual GSK3342830 Plasma Cmax Versus Dose on Day 15 for Part 2		SAC [1]
3.18	PK Parameter	PKPF3	Comparative Plot of Individual GSK3342830 Plasma Ae Versus Dose on Day 15 for Part 2		SAC [1]
Bayesian Dose Escalation					
3.19	PK Parameter	PK_F1	AUC[0-t] (µg.h/mL) in Part 1 - Dose Response Curve		DE [1]
3.20	PK Parameter	PK_F1	Cmax (µg/mL) in Part 1 - Dose Response Curve		DE [1]
3.21	PK Parameter	PK_F1	AUC[0-24] (µg.h/mL) in Part 2 - Dose Response Curve		DE [1]
3.22	PK Parameter	PK_F1	Cmax (µg/mL) in Part 2 - Dose Response Curve		DE [1]

10.11.9. ICH Listings

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Randomisation					
1	Safety	TA1	Listing of Randomized and Actual Treatments		SAC [1]
Subject Disposition					
2	Safety	ES2	Listing of Reasons for Study Withdrawal		SAC [1]
3	Screened	ES7	Listing of Reasons for Screening Failure		SAC [1]
4	Screened	DV2	Listing of Important Protocol Deviations		SAC [1]
5	Safety	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations		SAC [1]
Demographics					
6	Safety	DM2	Listing of Demographic Characteristics	Include height, weight, BMI, Smoking History, Alcohol History, Caffeine History, and Drug Use History	SAC [1]
7	Safety	DM9	Listing of Race		SAC [1]
Medical Conditions and Concomitant Medications					
8	Safety	MH2	Listing of Medical Conditions		SAC [1]
9	Safety	CM3	Listing of Concomitant Medications		SAC [1]
Exposure					
10	Safety	SAFE_L1	Listing of Exposure Data		SAC [1]
Safety					
11	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events		SAC [1]

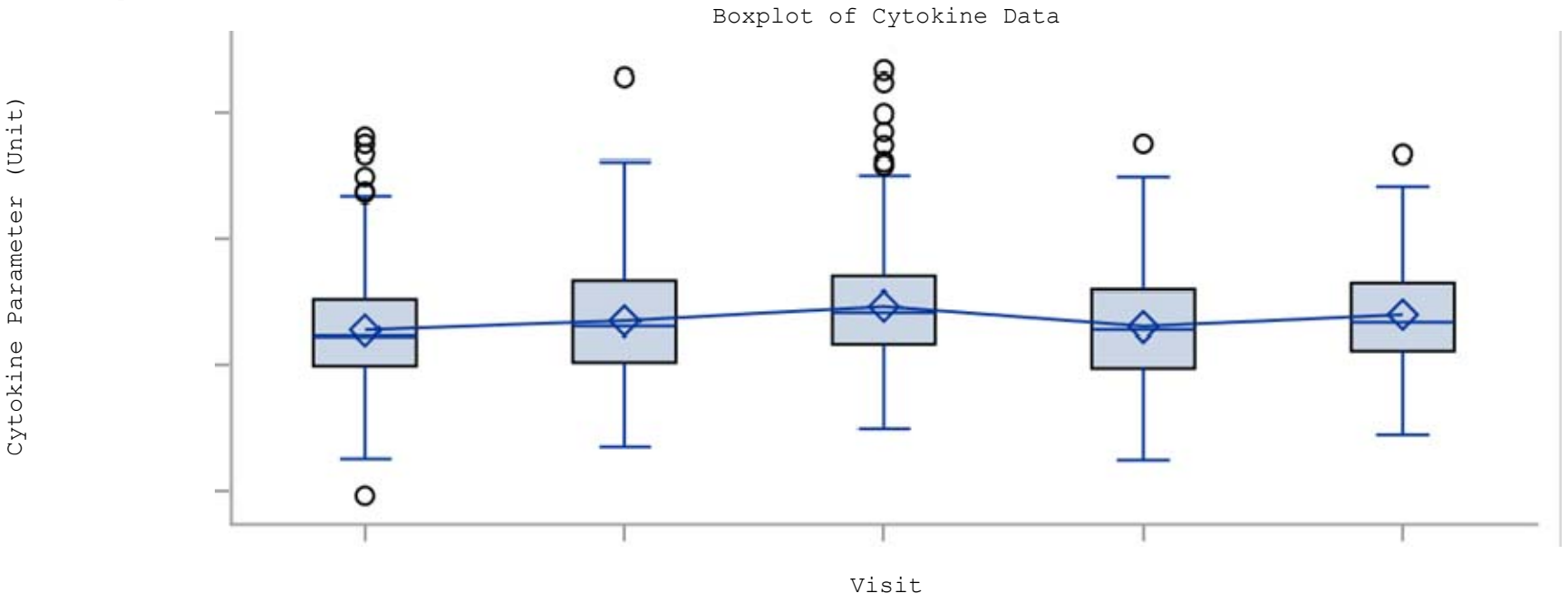
ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
12	Safety	AE8	Listing of All Adverse Events		SAC [1]
13	Safety	AE8	Listing of Drug-Related Adverse Events		SAC [1]
14	Safety	SAFE_L2	Listing of Serious Adverse Events		SAC [1]
15	Safety	AE8	Listing of Adverse Events Leading to Withdrawal from Study		SAC [1]
16	Safety	SAFE_L3	Listing of Infusion Site Reaction Adverse Events	Conditional display	SAC [1]
17	Safety	SAFE_L4	Listing of Liver Adverse Events	Conditional display	SAC [1]
18	Safety	SAFE_L5	Listing of Cardiovascular Adverse Events	Conditional display	SAC [1]
19	Safety	SAFE_L8	Listing of Rash Events	Conditional display	SAC [1]
Laboratory Measurements					
20	Safety	LB5	Listing of Clinical Chemistry Toxicities of Grade 3 or Higher		SAC [1]
21	Safety	LB5	Listing of All Clinical Chemistry Data for Subjects with Toxicities of Grade 3 or Higher		SAC [1]
22	Safety	LB5	Listing of Haematology Toxicities of Grade 3 or Higher		SAC [1]
23	Safety	LB5	Listing of All Haematology Data for Subjects with Toxicities of Grade 3 or Higher		SAC [1]
24	Safety	UR2a	Listing of Urinalysis Toxicities of Grade 3 or Higher		SAC [1]
25	Safety	UR2a	Listing of Urinalysis Data for Subjects with Toxicities of Grade 3 or Higher		SAC [1]
ECGs					
26	Safety	EG5	Listing of Abnormal ECG Findings		SAC [1]
27	Safety	EG5	Listing of All ECG Findings for Subjects with an Abnormal Finding		SAC [1]
28	Safety	EG3	Listing of ECG Values of Potential Clinical Importance		SAC [1]

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
29	Safety	EG3	Listing of All ECG Values for Subjects with Any Value of Potential Clinical Importance		SAC [1]
Vital Signs					
30	Safety	VS4	Listing of Vital Signs of Potential Clinical Importance		SAC [1]
31	Safety	VS4	Listing of All Vital Signs for Subjects with Potential Clinical Importance Values		SAC [1]
Liver Events					
32	Safety	LIVER5	Listing of Liver Monitoring/Stopping Event Reporting	Conditional display	SAC [1]
33	Safety	MH3	Listing of Medical Conditions for Subjects with Liver Stopping Events	Conditional display	SAC [1]
34	Safety	SAFE_L9	Listing of Alcohol Intake at Onset of Liver Event	Conditional display	SAC [1]
35	Safety	PKCL1X	Listing of Plasma Concentration Data for Subjects with Liver Stopping Events	Conditional display	SAC [1]
36	Safety	LIVER7	Listing of Liver Biopsy Details	Conditional display	SAC [1]
37	Safety	LIVER8	Listing of Liver Imaging Details	Conditional display	SAC [1]
Cardiac Telemetry					
38	Safety	SAFE_L10	Listing of Cardiac Telemetry Monitoring		SAC [1]
39	Safety	SAFE_L11	Listing of Cytokine Data		SAC [1]
Pharmacokinetic Concentration					
40	PK	PKCL1X	Listing of GSK3342830 Pharmacokinetic Plasma Concentration-Time Data by Treatment in Part 1 and Part 3		SAC [1]
41	PK	PKUL1P	Listing of GSK3342830 Pharmacokinetic Urine Concentration-Time Data by Treatment in Part 1 and Part 3		SAC [1]

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
42	PK	PKCL1X	Listing of GSK3342830 Pharmacokinetic Plasma Concentration-Time Data by Treatment in Part 2		SAC [1]
43	PK	PKUL1P	Listing of GSK3342830 Pharmacokinetic Urine Concentration-Time Data by Treatment in Part 2		SAC [1]
Pharmacokinetic Parameter					
44	PK Parameter	PLPL1X	Listing of GSK3342830 Plasma Pharmacokinetic Parameters by Treatment in Part 1 and Part 3		SAC [1]
45	PK Parameter	PLPL1X	Listing of GSK3342830 Urine Pharmacokinetic Parameters by Treatment in Part 1 and Part 3		SAC [1]
46	PK Parameter	PLPL1X	Listing of GSK3342830 Plasma Pharmacokinetic Parameters by Treatment in Part 2		SAC [1]
47	PK Parameter	PLPL1X	Listing of GSK3342830 Urine Pharmacokinetic Parameters by Treatment in Part 2		SAC [1]

Figure 2.1

Part: xx
Cytokine Parameter (Unit)

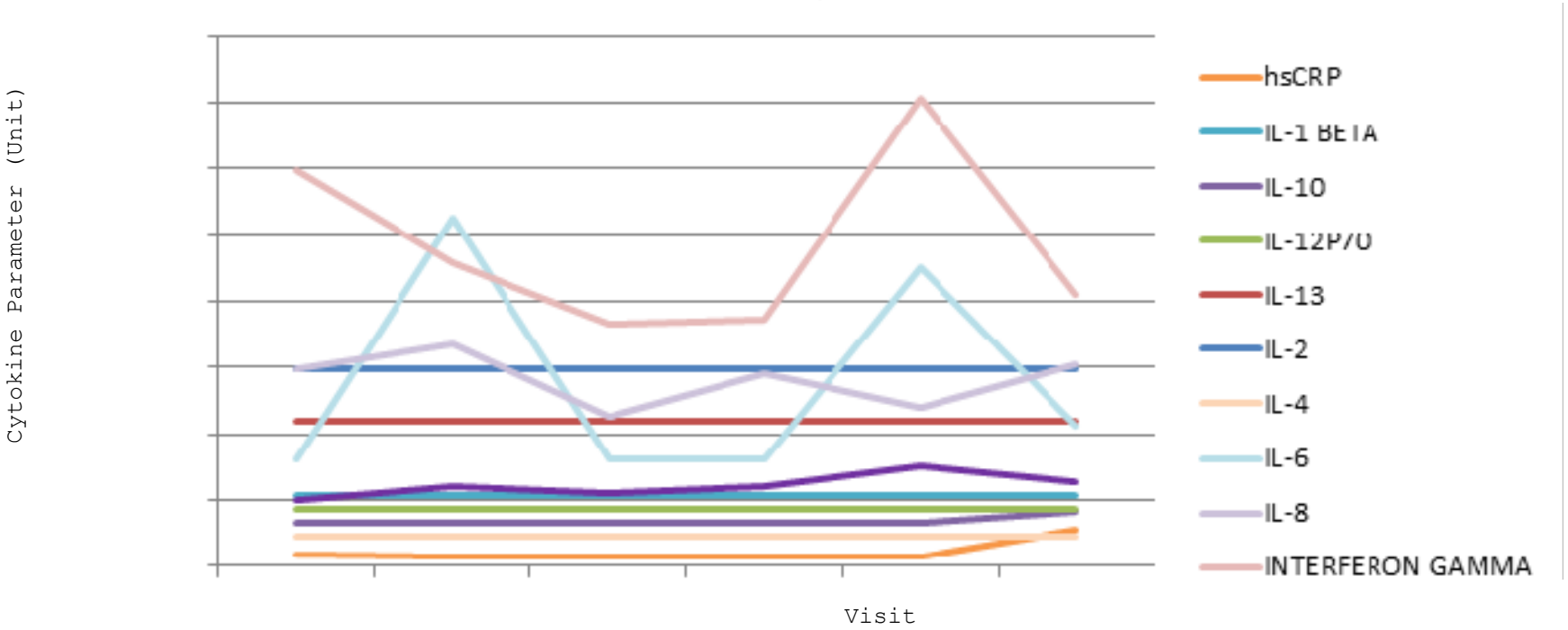


Programming notes: Present each cytokine parameter on a separate page for all scheduled visits. Include a separate line for each treatment and use different symbols for each treatment. Include a legend to describe the treatments.

Figure 2.2

Part: xx

Individual Cytokine Plot
Subject = xxxxx



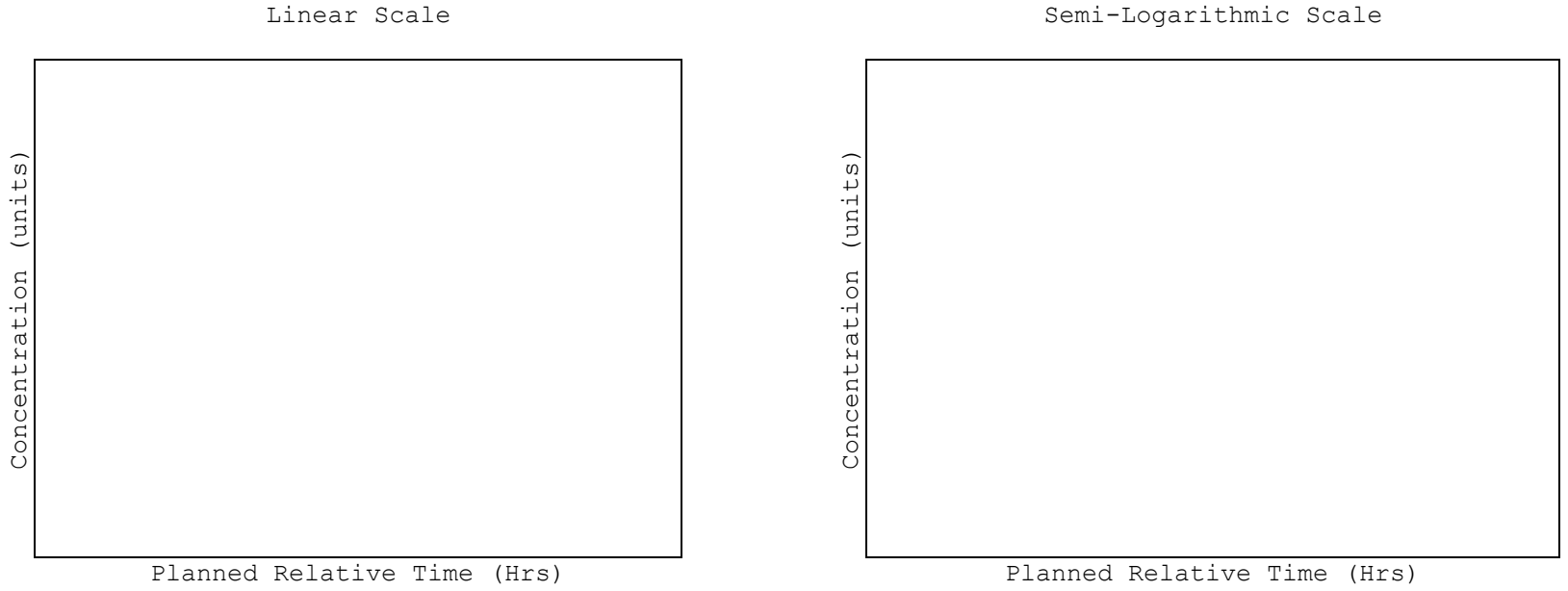
Source Data: Listing 39

Programming notes: Present each subject separately (one per page) and then present all cytokine parameters on the same page for that subject. Include a separate line for each parameter and use different symbols for each parameter. Include a legend to describe the parameters and the units.
Present all scheduled results by visit for the x-axis.

Figure 3.01

Mean (SD) GSK3342830 Single Dose Plasma Concentration-Planned Time Plots for Part 1 and Part 3 (Linear and Semi-Log)

Part: Part 1



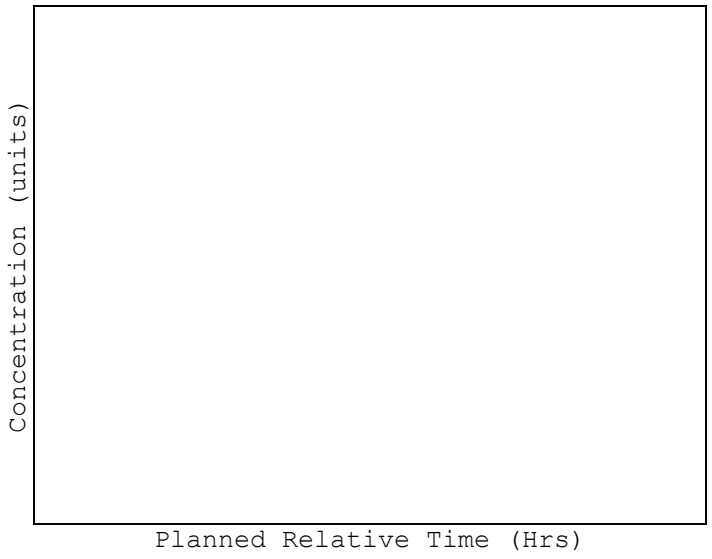
Note to Programmer: Present Part 1 first, then Part 3. Dashed line represents the LLQ. Present all dose levels by part in the same plots. Add legend for doses at the bottom.

Source Data: Listing 39

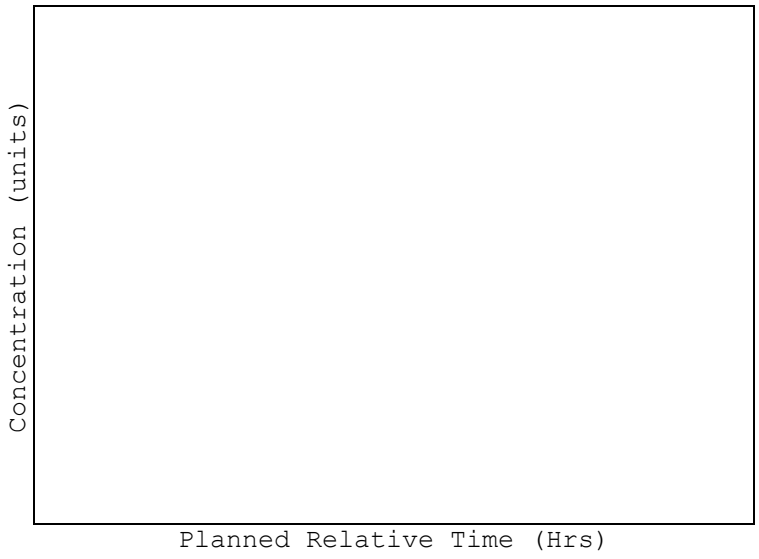
Figure 3.02
Median (range) GSK3342830 Single Dose Plasma Concentration-Planned Time Plots
for Part 1 and Part 3
(Linear and Semi-Log)

Part: Part 1

Linear Scale



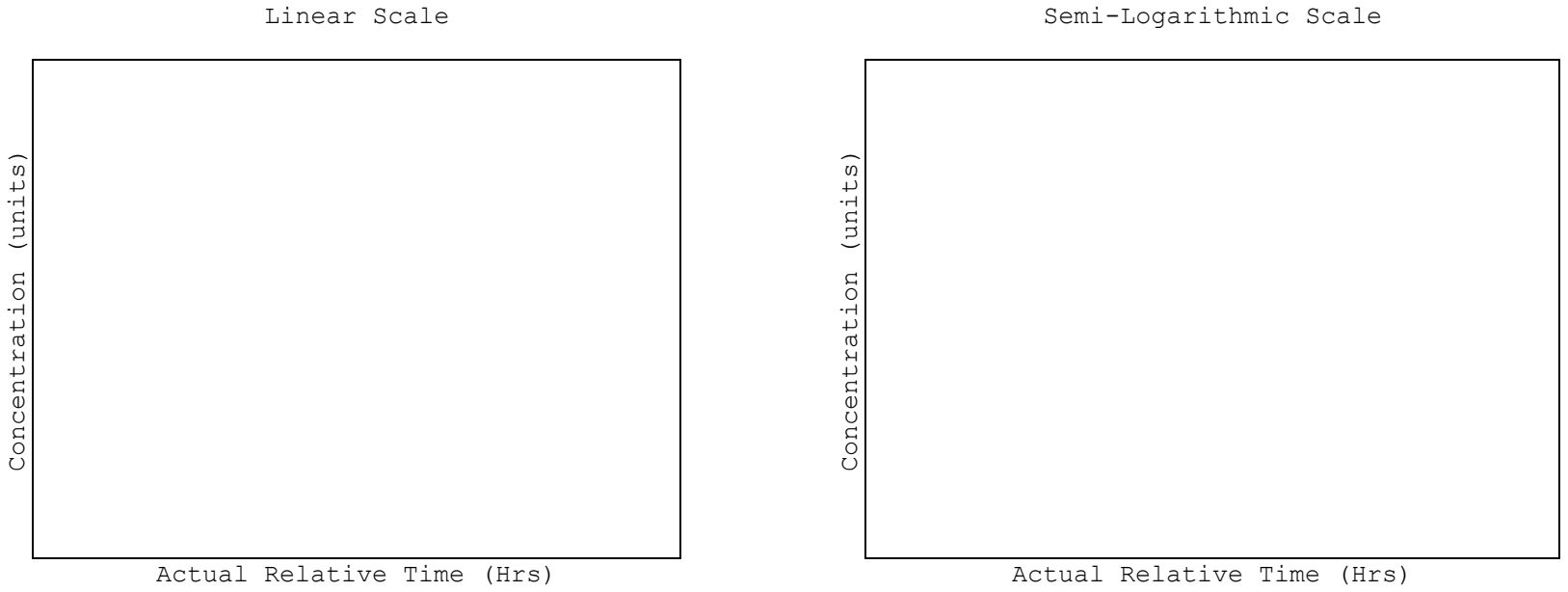
Semi-Logarithmic Scale



Note to Programmer: Present Part 1 first, then Part 3. Display dashed line to represent the LLQ. Present all cohort groups in the same plots. Add legend for doses at the bottom.

Note: LLQ = xx units
Source Data: Listing 39

Figure 3.03
Mean (SD) GSK3342830 Plasma Concentration-Planned Time Plots for Part 2 (Linear and Semi-Log)
Day: 1

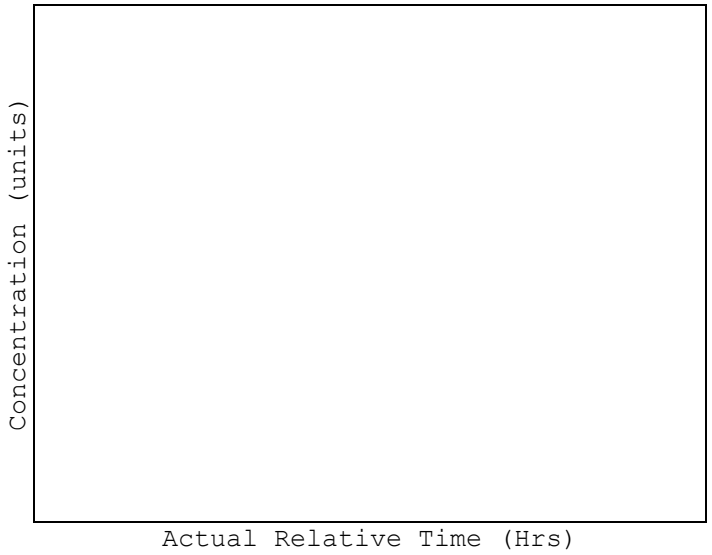


Note to Programmer: Display dashed line to represent the LLQ. Present all cohort groups in the same plots. Add legend for doses at the bottom. Repeat for Day 15.

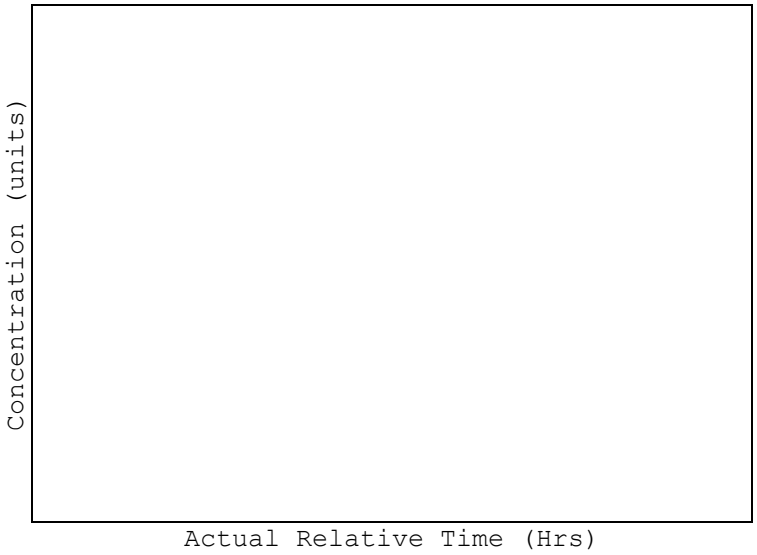
Note: LLQ = xx units
Source Data: Listing 41

Figure 3.04
Median (range) GSK3342830 Plasma Concentration-Planned Time Plots for Part 2 (Linear and Semi-Log)
Day : 1

Linear Scale



Semi-Logarithmic Scale

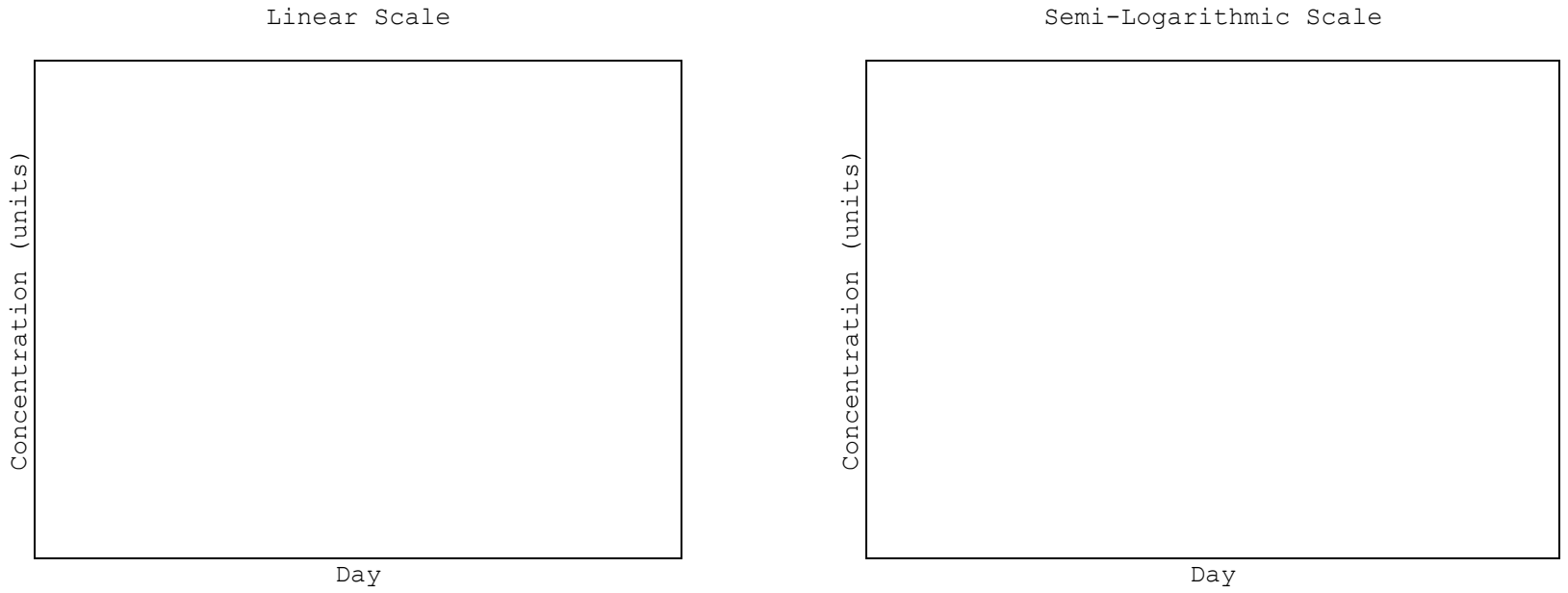


Note to Programmer: Display dashed line to represent the LLQ. Present all cohort groups in the same plots. Add legend for doses at the bottom. Repeat for Day 15.

Note: LLQ = xx units
Source Data: Listing 41

Figure 3.05

Median (range) GSK3342830 Plasma Pre-dose Concentration versus Day for Part 2 (Linear and Semi-Log)

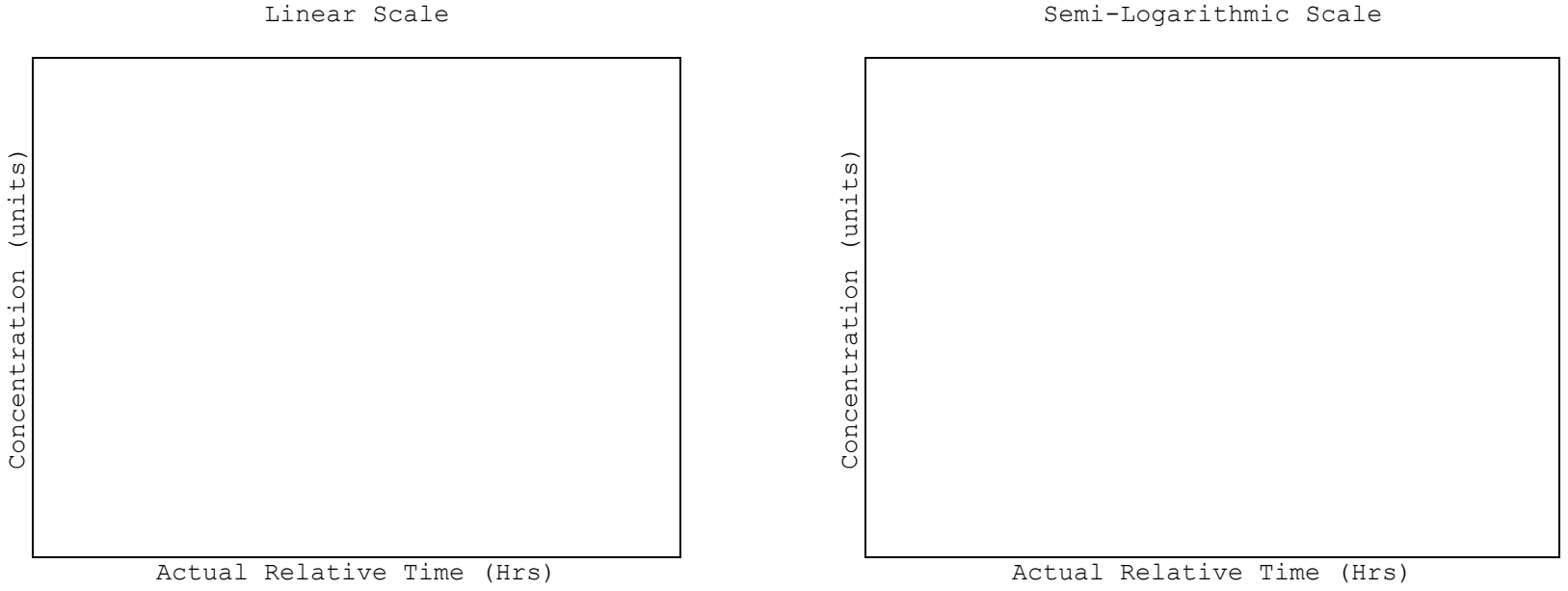


Note to Programmer: Display dashed line to represent the LLQ. Present all cohort groups in the same plots. Add legend for doses at the bottom.

Note: LLQ = xx units
Source Data: Listing 41

Figure 3.06
Individual GSK3342830 Single Dose Plasma Concentration-Planned Time Plots for Part 1 and Part 3 (Linear and Semi-Log)
Subject ID: XXXX

Part: Part 1



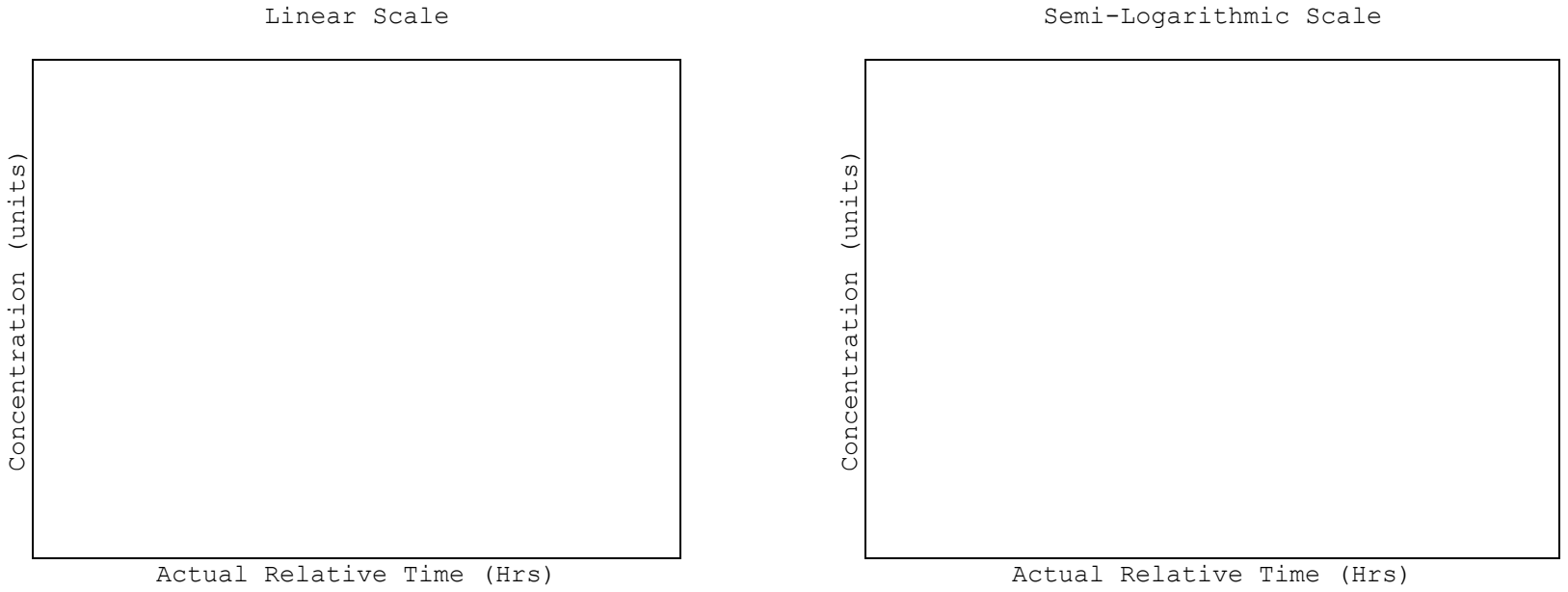
Note to Programmer: Present Part 1 first, then Part 3. Display dashed line to represent the LLQ.

Note: LLQ = xx units
Source Data: Listing 39

Figure 3.07

Individual GSK3342830 Plasma Concentration-Planned Time Plots for Part 2 (Linear and Semi-Log)

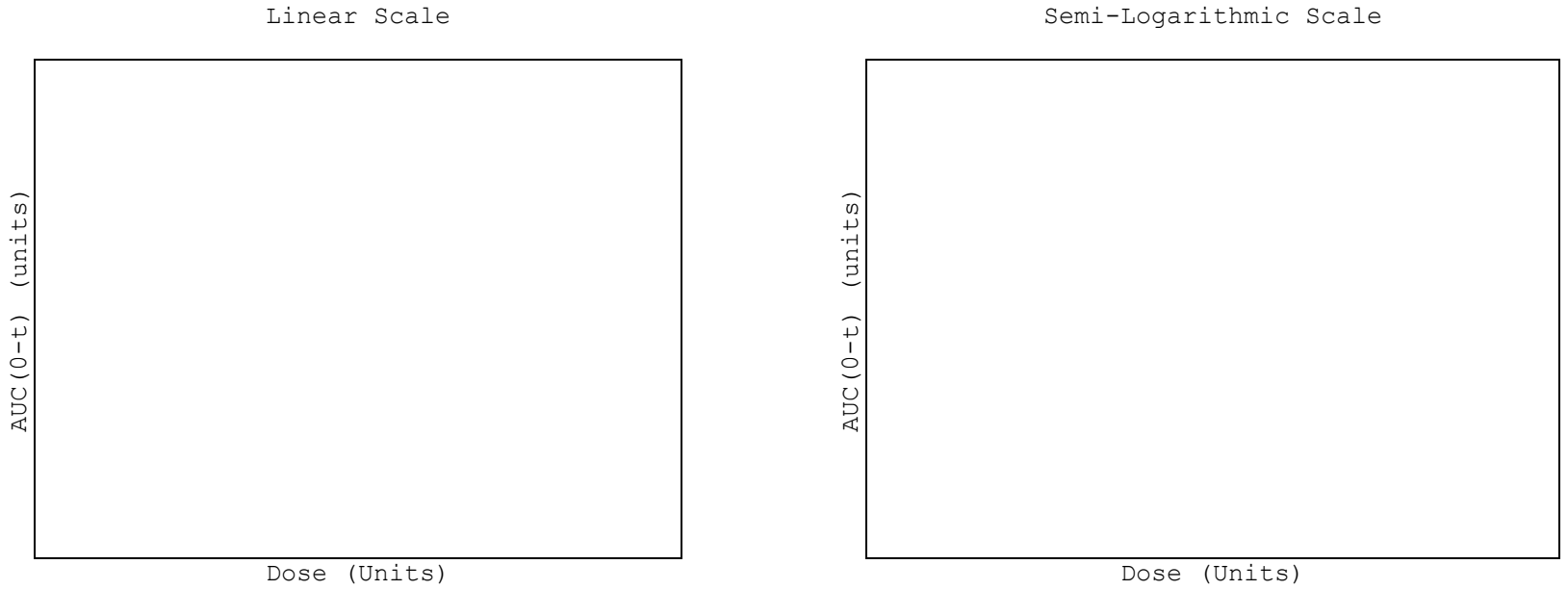
Subject ID: XXXX



Note to Programmer: Display dashed line to represent the LLQ. Display Day 1 and Day 15 on the same figure.

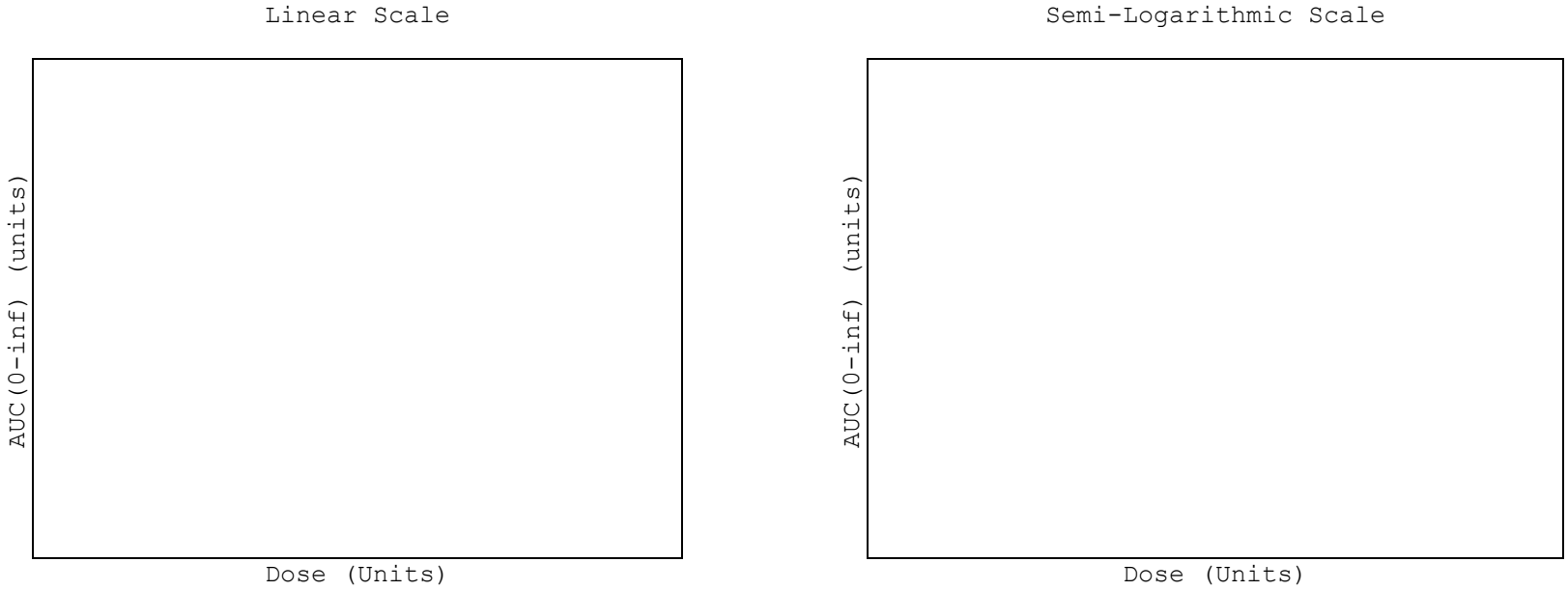
Note: LLQ = xx units
Source Data: Listing 41

Figure 3.08
Comparative Plot of Individual GSK3342830 Plasma AUC(0-t) Versus Dose for Part 1 and Part 3



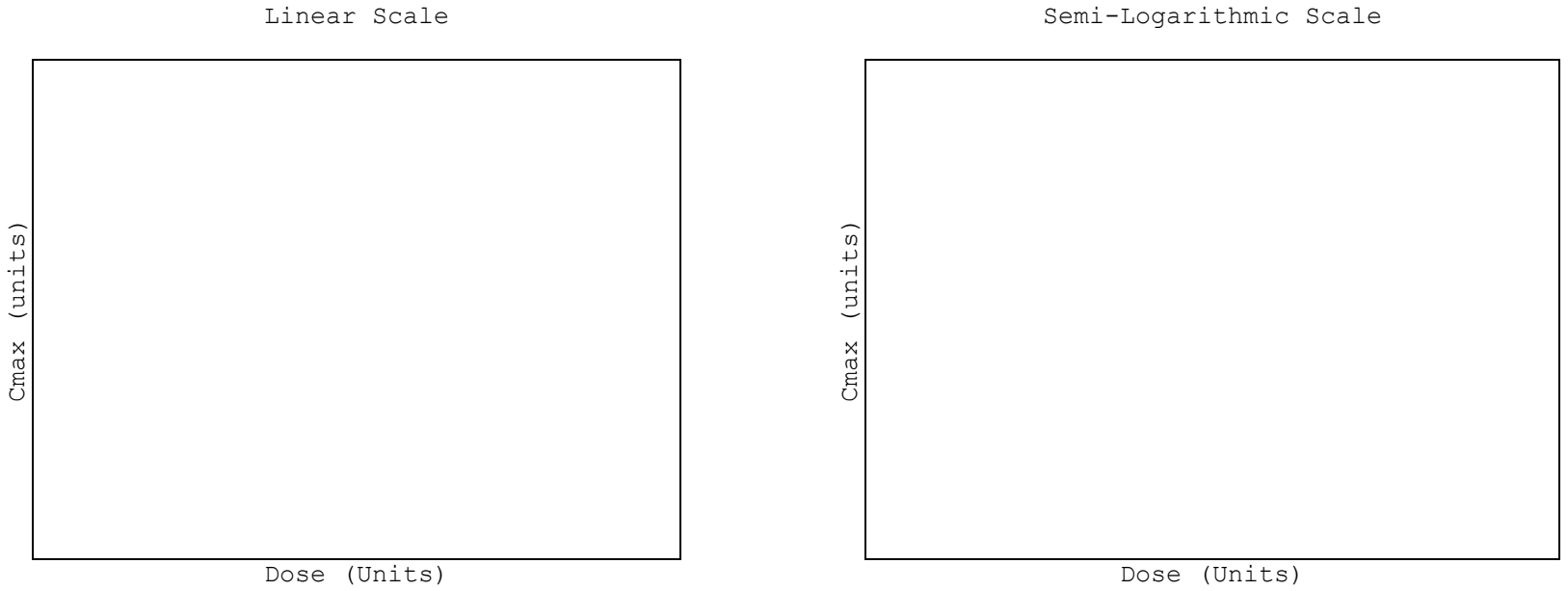
Note to Programmer: Present box plot for all cohort groups in the same plot. Place Part 3 at the right end of the axis, footnote will be added for the Part 3 dose.
Source Data: Listing 43

Figure 3.09
Comparative Plot of Individual GSK3342830 Plasma AUC(0-inf) Versus Dose for Part 1 and Part 3



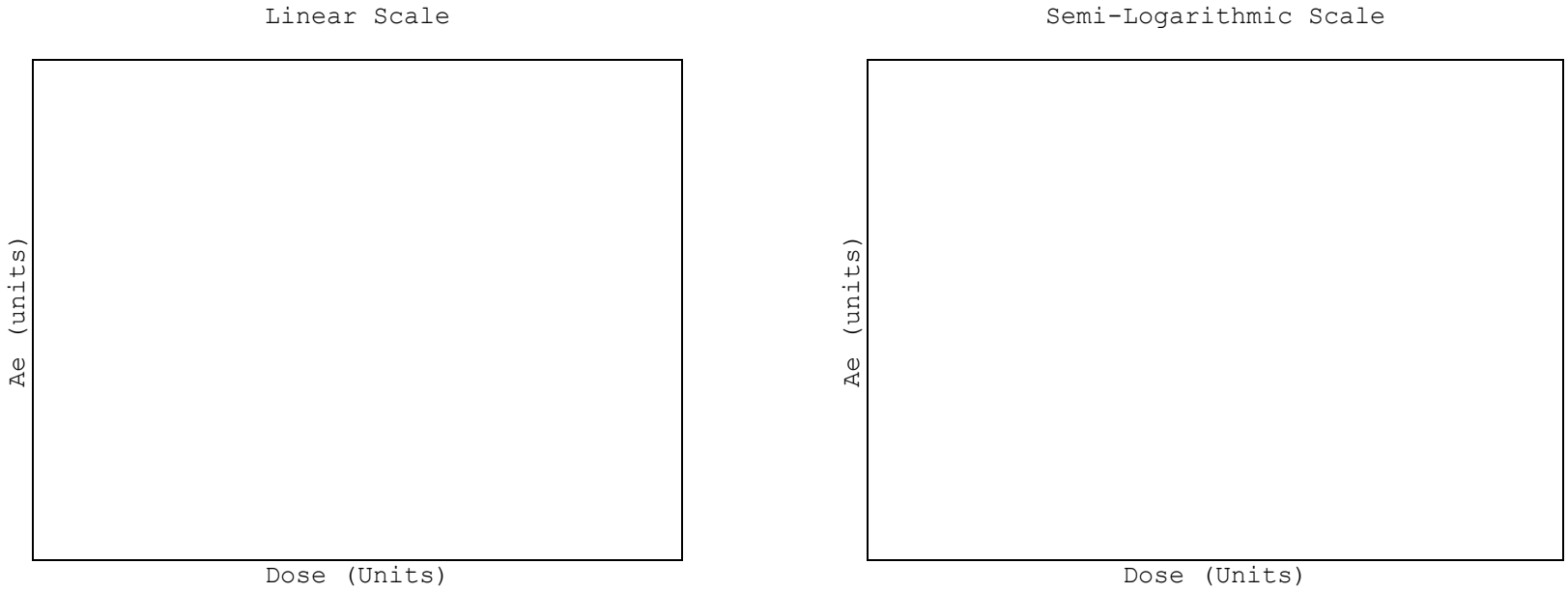
Note to Programmer: Present box plot for all cohort groups in the same plot. Place Part 3 at the right end of the axis, footnote will be added for the Part 3 dose.3
Source Data: Listing 41

Figure 3.10
Comparative Plot of Individual GSK3342830 Plasma Cmax Versus Dose for Part 1 and Part 3



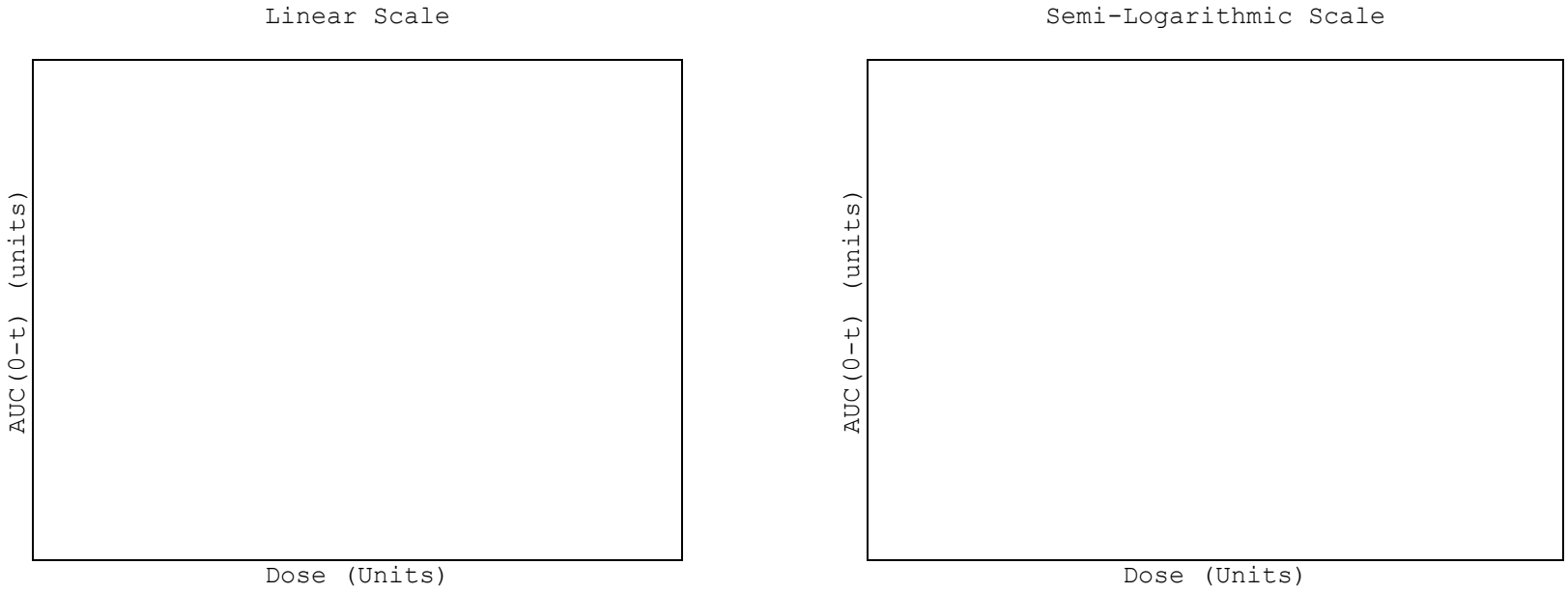
Note to Programmer: Present box plot for all cohort groups in the same plot. Place Part 3 at the right end of the axis, footnote will be added for the Part 3 dose.
Source Data: Listing 43

Figure 3.11
Comparative Plot of Individual GSK3342830 Plasma Ae Versus Dose for Part 1



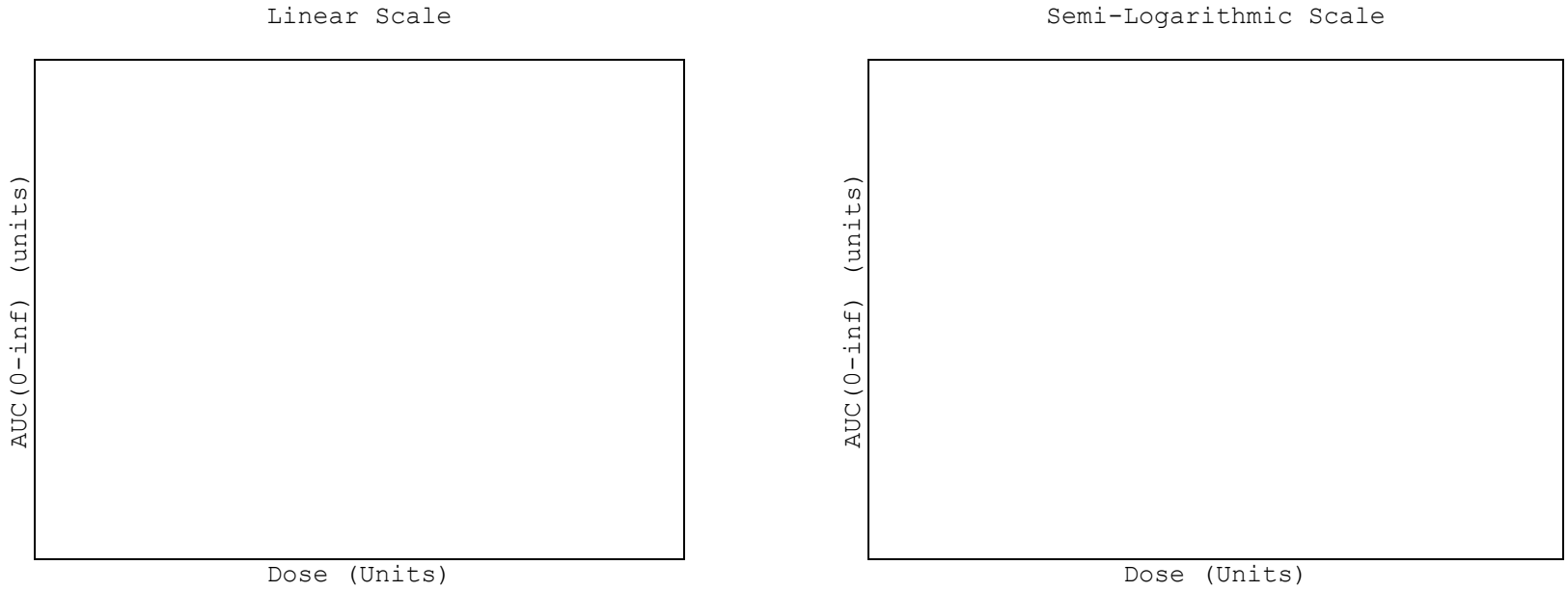
Note to Programmer: Present all cohort groups in the same plots.
Source Data: Listing 44

Figure 3.12
Comparative Plot of Individual GSK3342830 Plasma AUC(0-t) Versus Dose on Day 1 for Part 2



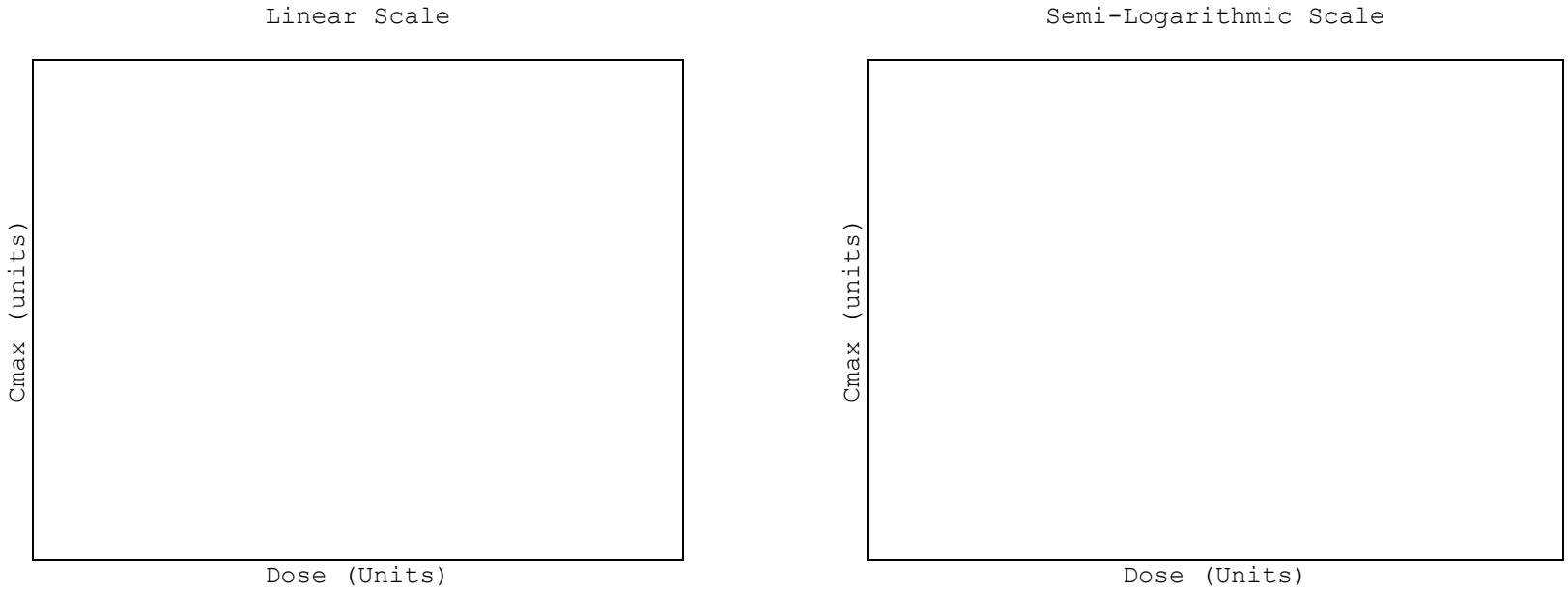
Note to Programmer: Present all cohort groups in the same plots.
Source Data: Listing 45

Figure 3.13
Comparative Plot of Individual GSK3342830 Plasma AUC(0-inf) Versus Dose on Day 1 for Part 2



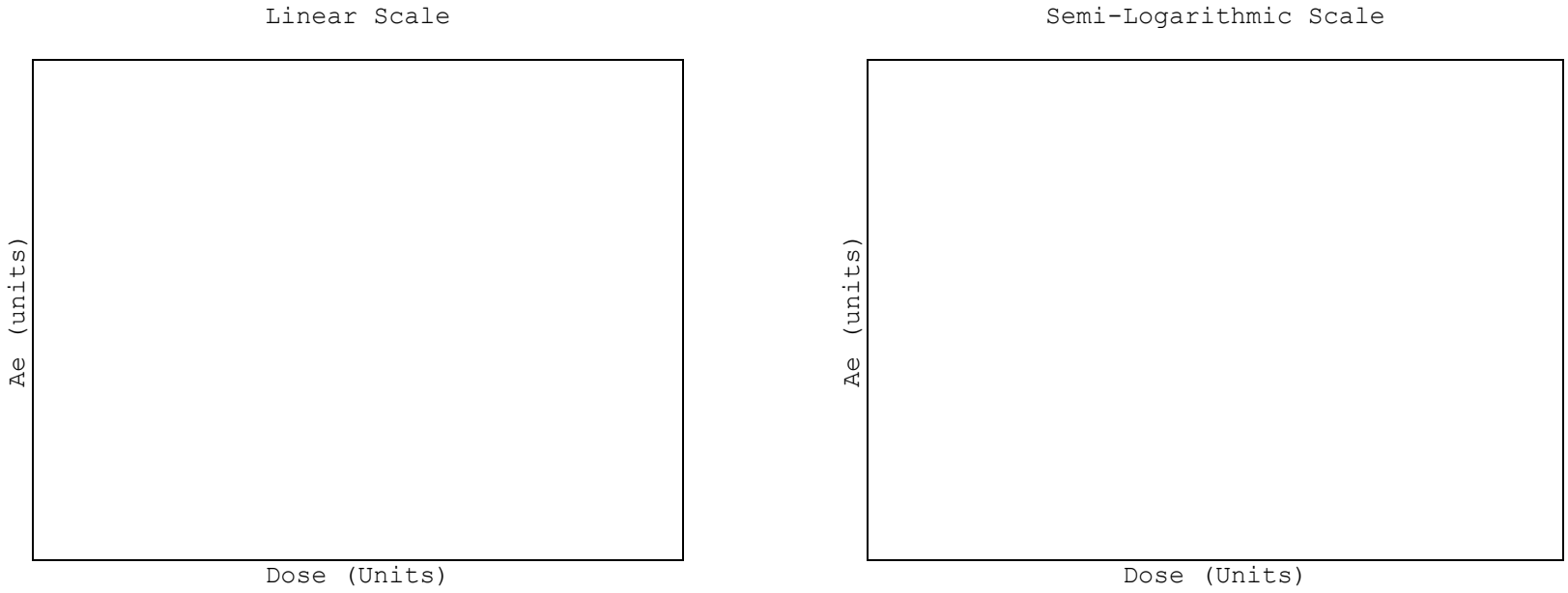
Note to Programmer: Present all cohort groups in the same plots.
Source Data: Listing 45

Figure 3.14
Comparative Plot of Individual GSK3342830 Plasma Cmax Versus Dose on Day 1 for Part 2



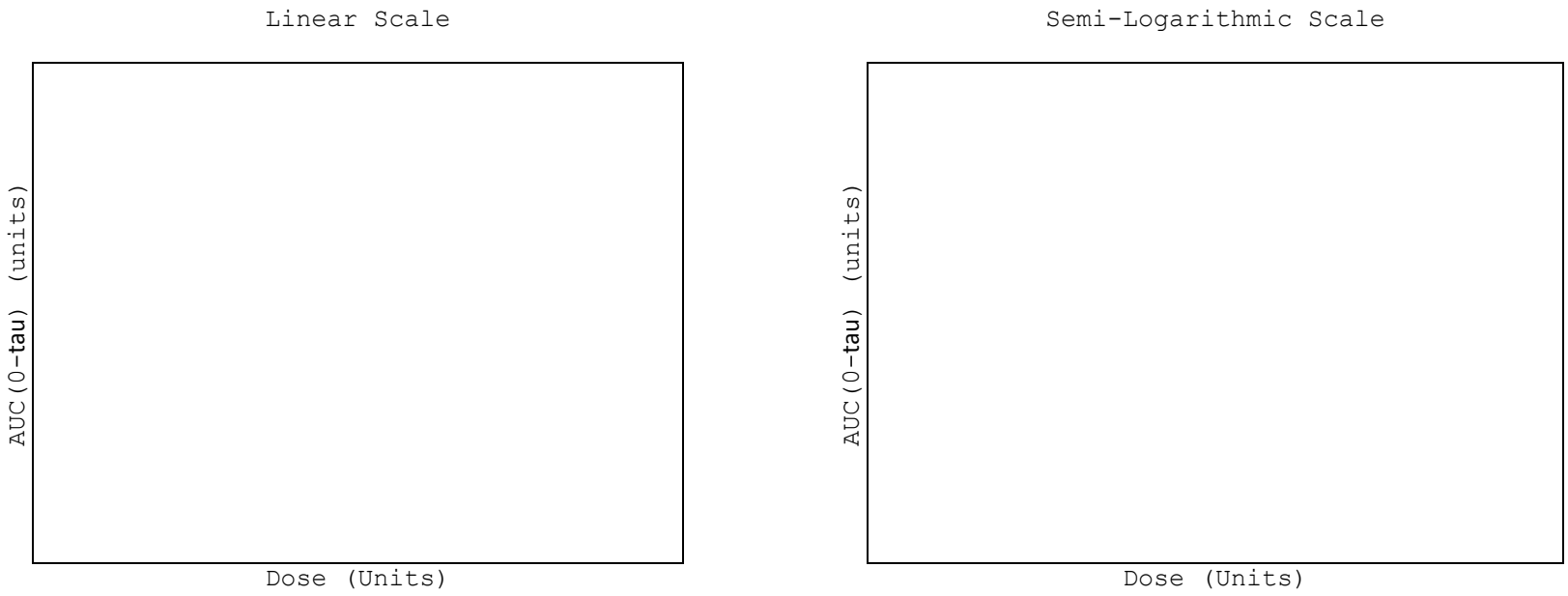
Note to Programmer: Present all cohort groups in the same plots.
Source Data: Listing 45

Figure 3.15
Comparative Plot of Individual GSK3342830 Plasma Ae Versus Dose on Day 1 for Part 2



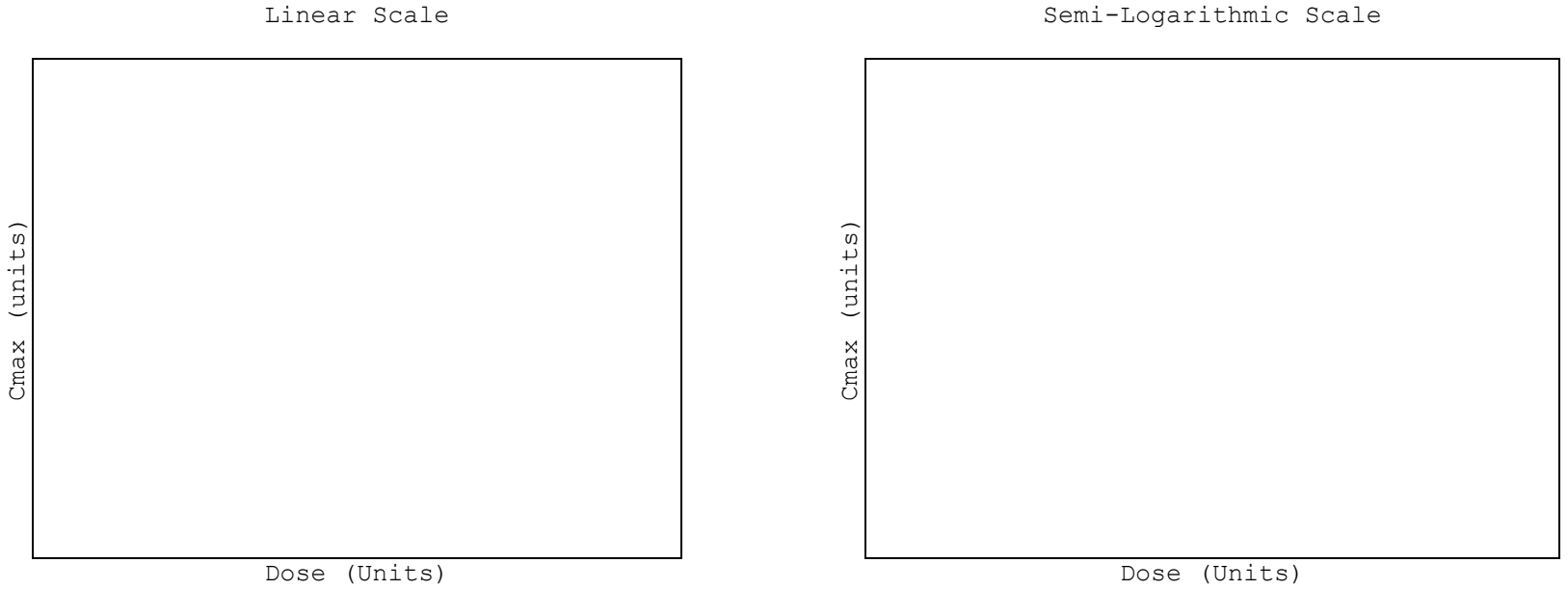
Note to Programmer: Present all cohort groups in the same plots.
Source Data: Listing 46

Figure 3.16
Comparative Plot of Individual GSK3342830 Plasma AUC(0-tau) Versus Dose on Day 15 for Part 2



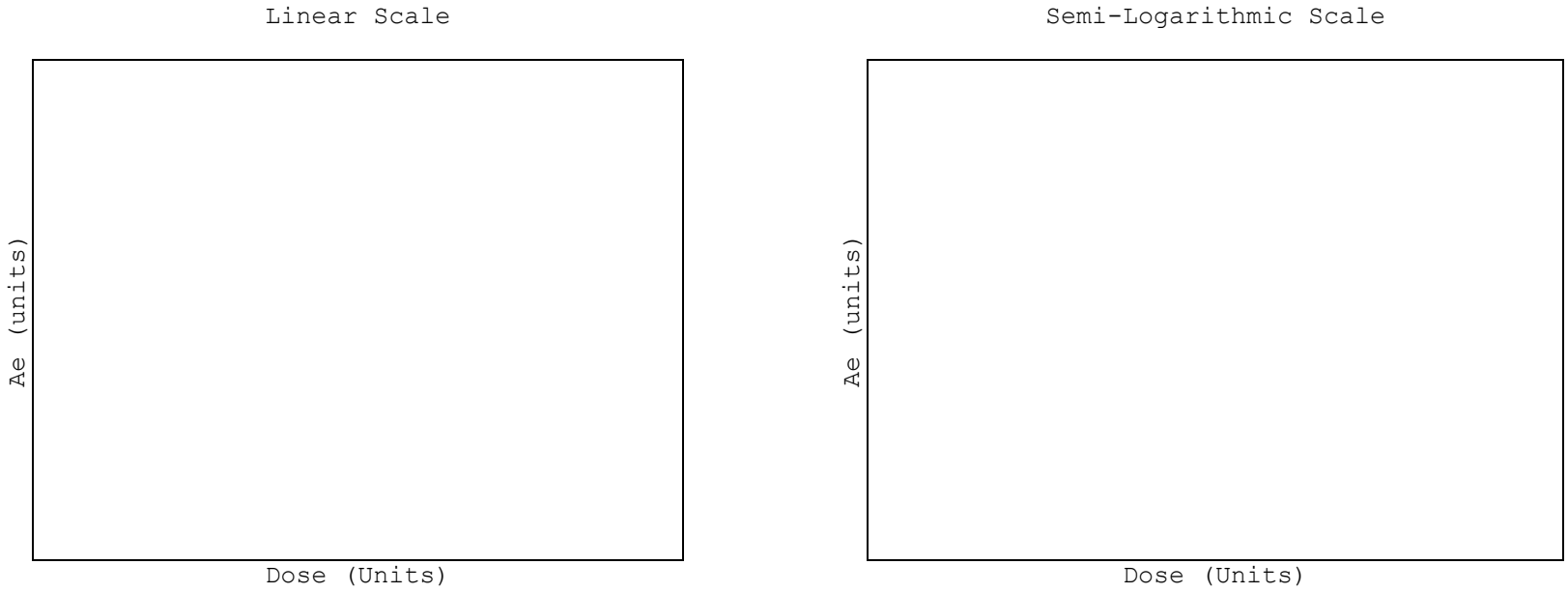
Note to Programmer: Present all cohort groups in the same plots.
Source Data: Listing 45

Figure 3.17
Comparative Plot of Individual GSK3342830 Plasma Cmax Versus Dose on Day 15 for Part 2



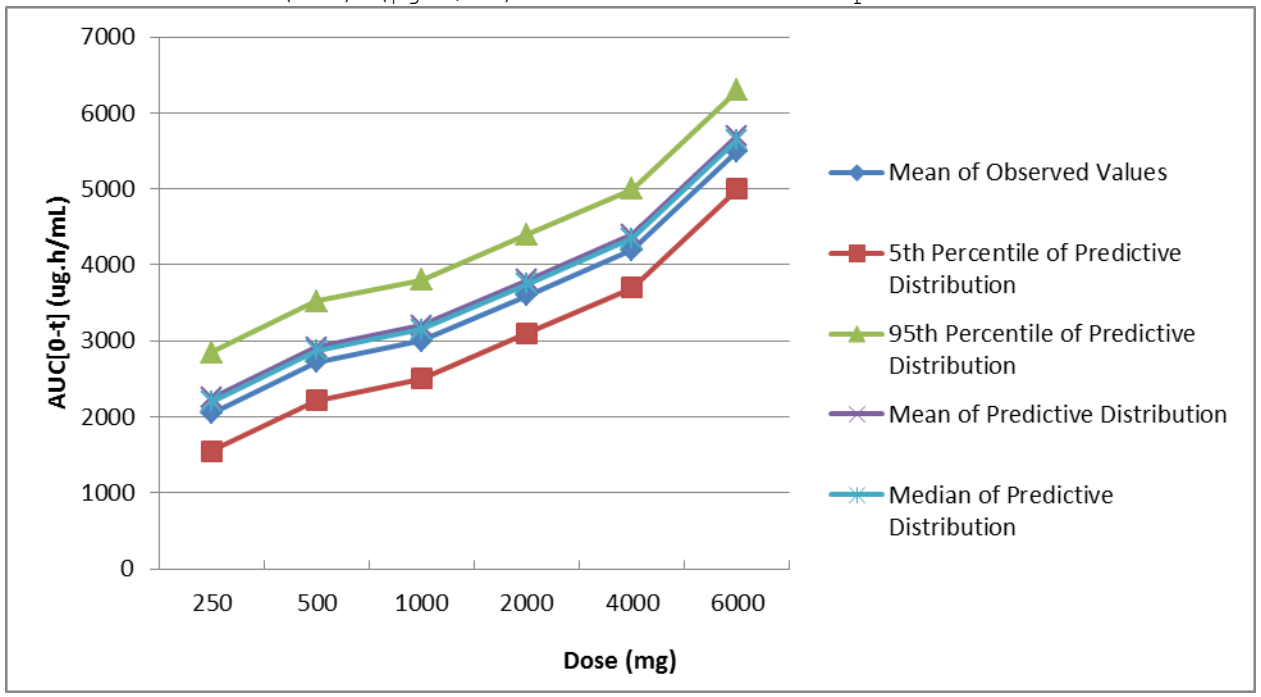
Note to Programmer: Present all cohort groups in the same plots.
Source Data: Listing 45

Figure 3.18
Comparative Plot of Individual GSK3342830 Plasma Ae Versus Dose on Day 15 for Part 2



Note to Programmer: Present all cohort groups in the same plots.
Source Data: Listing 46

Figure 3.19
AUC(0-t) (µg.h/mL) in Part 1 - Dose Response Curve



Note: The predictive distributions are derived from linear model log-PK-parameter = intercept + slope*log-dose + error term.
Source Table: T3.16

Programming notes:

Figure 3.20
Cmax (µg/mL) in Part 1 - Dose Response Curve

Note: The predictive distributions are derived from linear model log-PK-parameter = intercept + slope*log-dose + error term.

Programming notes: repeat figure 3.19 for Cmax (µg/mL)

Figure 3.21
AUC(0-8)x3 (µg.h/mL) in Part 2 - Dose Response Curve

Note: The predictive distributions are derived from linear model log-PK-parameter = intercept + slope*log-dose + error term.
Source Table: T3.17

Programming notes: repeat figure 3.19 for AUC[0-8]x3 with X-axis only has 3 dose levels: 1000, 2000, 4000 mg

Figure 3.22
Cmax (µg/mL) in Part 2 - Dose Response Curve

Note: The predictive distributions are derived from linear model log-PK-parameter = intercept + slope*log-dose + error term.
Source Table: T3.17

Programming notes: repeat figure 3.19 for Cmax (µg/mL) with X-axis only has 3 dose levels: 1000, 2000, 4000 mg

Example : TA1
Protocol : 204847
Population : Randomized

Listing 1
Listing of Randomized and Actual Treatments

Part: xx

Subject ID.	Cohort	Randomisation Number	Randomization Date	Randomised Treatment	Actual Treatment
xxx	x	xxxxxx	DDMMMYYYY	xxxxxxxxxxxx	xxxxxxxxxxxx
xxx	x	xxxxxx	DDMMMYYYY	xxxxxxxxxxxx	xxxxxxxxxxxx

Example : ES2
Protocol : 204847
Population : Safety

Listing 2
Listing of Reasons for Study Withdrawal

Part: xx
Treatment: xxxx

Subject ID.	Date of Withdrawal	Study Day	Primary Reason
xxx	DDMMMYYYY	x	xxxxxxxxxxxxx
xxx	DDMMMYYYY	x	xxxxxxxxxxxxxxx
xxx	DDMMMYYYY	x	xxxxxxxxxxxxx
xxx	DDMMMYYYY	x	xxxxxxxxxxxxxx

Example : ES7
Protocol : 204847
Population : Screened

Listing 3
Listing of Reasons for Screening Failure

Subject ID.	Date of Screen Failure	Reason
xxx	DDMMMYYYY	xxxxxxxxxxxxxx
xxx	DDMMMYYYY	xxxxxxxxxxxxxxxx
xxx	DDMMMYYYY	xxxxxxxxxxxxxx
xxx	DDMMMYYYY	xxxxxxxxxxxxxxxx

Example : DV2
Protocol : 204847
Population : Screened

Listing 4
Listing of Important Protocol Deviations

Part: xx
Treatment: xxxx

Subject ID.	Date of Deviation/ Study day	Category/ Subcategory	Description	Outcome
xxxxxx/ xxxxxx	ddmmmyyyy/ xx	xxxxxxxxxx/ xxxxxxxxxx	xxxxxxxxxxxxxxxxxxxxxx	xxxxxxxx
	ddmmmyyyy/ xx	xxxxxxxxxx/ xxxxxxxxxx	xxxxxxxxxxxxxx	xxxxxxxx
xxxxxx/ xxxxxx	ddmmmyyyy/ xx	xxxxxxxxxxxxxxxxx	xxxxxxxxxxxxxx	xxxxxxxx
xxxxxx/ xxxxxx	ddmmmyyyy/ xx	xxxxxxxxxx/ xxxxxxxxxx	xxxxxxxxxxxxxx	xxxxxxxx

Example : IE3
Protocol : 204847
Population : Safety

Listing 5
Listing of Subjects with Inclusion/Exclusion Criteria Deviations

Part: xx
Treatment: xxxx

Subject ID.	Type	Criterion
xxx	Inclusion	xxxxxxxxxxxxxx
xxx	Exclusion	xxxxxxxxxxxxxxxx
xxx	xxxxxxxxxx	xxxxxxxxxxxxxx
xxx	xxxxxxxxxx	xxxxxxxxxxxxxxxx

Example : DM2
Protocol : 204847
Population : Safety

Listing 6
Listing of Demographic Characteristics

Part: xx
Treatment: xxxx

Subject ID.	Year of Birth	Age (yrs)	Sex	Ethnicity	Height (cm)	Weight (kg)	BMI (kg/m^2)	History of Smoking/Date Last Smoked	Subject Consume Alcohol/Avg. Consumed Weekly	Subject Consume Caffeine/Avg. Servings per Day	Subjects History of Drug Use
xxxx	YYYY	xx	Female	Hispanic/Latino	xxx.x	xxx.x	xxx.x	Yes	xx	xx	xx
xxxx	YYYY	xx	Female	Not Hispanic/Latino	xxx.x	xxx.x	xxx.x	Yes	xx/DDMMYYYY	xxx/xx	xx

…

Example : DM9
Protocol : 204847
Population : Safety

Listing 7
Listing of Race

Part: xx
Treatment: xxxx

Subject ID.	Race
xxxx	XXXXXXXXXXXXXXXXXX
	XXXXXXXXXXXXXXXX
xxxx	XXXXXXXXXXXXXXXXXXXXX
…	XXXXXXXXXXXXXXXXXX
	XXXXXXXXXXXXXXXX

Example : MH2
Protocol : 204847
Population : Randomized

Listing 8
Listing of Medical Conditions

Part: xx
Treatment: xxxx

Subject	Classification	Condition	Status
PPD - This section has been excluded to protect patient privacy.			

Example : CM3
Protocol : 204847
Population : Randomized

Listing 9
Listing of Concomitant Medications

Part: xx
Treatment: xxxx

Subj. ID	ATC Level 1/ Ingredient/ Verbatim Text/ Indication	Dose/ Units/ Freq/ Route	Start Date/Time Study Day/ Period Day	Stop Date/Time Study Day/ Period Day	Started Pre-Trial?	Ongoing Medication?
XXXX	Endocrine & metabolic/ Fluticasone propionate/ FLIXOTIDE/ Asthma	2/ MG/ 2XD/ IH	27SEP1999/ 12:30/ 15/ 7			Y

Example : SAFE_L1
Protocol : 204847
Population : Safety

Listing 10
Listing of Exposure Data

Part: xx
Treatment: xxxx

Subject ID.	Treatment	Start Date/Time of Dose	End Date/Time of Dose	Dose	Dose Unit	Was infusion interrupted?/ Reason/ Interrupt Date/Time/ Restart Date/Time	Was infusion discontinued?/ Reason/ Discontinuation Date/Time	Did subject receive correct treatment?/ Comment
xxx	XXXXXXX	DDMMMYYYY/ hh:mm	DDMMMYYYY/ hh:mm	xx	xx	No	No	Yes
	XXXXXXX	DDMMMYYYY/ hh:mm	DDMMMYYYY/ hh:mm	xx	xx	Yes/xxxxxxxxxx DDMMMYYYY/hh:mm/ DDMMMYYYY/hh:mm	Yes/xxxxxxxxx DDMMMYYYY/hh:mm	No/xxxxxxxx
	…							

Example : AE7
Protocol : 204847
Population : Safety

Listing 11
Listing of Subject Numbers for Individual Adverse Events

Part: xx
Treatment: xxxx

System Organ Class Preferred Term	Group	No. with Event	Subject Numbers
SOC #1			
Preferred Term #1	xxxxxx	X	xxxx, xxxxx, xxxxxxx
	xxxxxx	X	xxxx, xxxxx, xxxxxxx xxxx, xxxxx, xxxxxxx
Preferred Term #2	xxxxxx	X	xxxx, xxxxx, xxxxxxx
	xxxxxx	X	xxxx, xxxxx, xxxxxxx xxxx, xxxxx, xxxxxxx

Example : AE8
Protocol : 204847
Population : Safety

Listing 12
Listing of All Adverse Events

Part: x
Treatment: xxxxx

Subj. ID	Age(y)/ Sex/ Race/ Weight (kg)	System Organ Class/ Preferred Term/ VERBATIM TEXT	Outcome/ Onset Date/Time Date/Time of Resolution/ Duration	Time Since 1st Dose/ Time Since Last Dose	Maximum Intensity/ Maximum Serious/ Withdrawal	Frequency/ Action Taken/ Relation to Study Drug
xxxxx	xx/ xxxx/xxx/ xx.x	xxxxxxxxxxxxxx/ xxxxxxxxxxxxxx/ xxxxxxxxxxxxx	Resolved/ DDMMMYYYY/hh:mm DDMMMYYYY/hh:mm 1 d	19 d/ 19 d/ 1 d	Mild/ No/ No	xxxxxxx/ Dose reduced/ No
		xxxxxxxxxxxxxx/ xxxxxxxxxxxxxx/ xxxxxxxxxxxxx	Resolving/ DDMMMYYYY/hh:mm DDMMMYYYY/hh:mm 1 d	21 d/ 1 d/ 1 d	Moderate/ No/ No	xxxxxxx/ Dose inter-rupted/ No
		xxxxxxxxxxxxxx/ xxxxxxxxxxxxxx/ xxxxxxxxxxxxx	Not resolved/ DDMMMYYYY/hh:mm DDMMMYYYY/hh:mm 120 d	36 d/ 16 d/ 16 d	Severe/ No/ Yes	xxxxxxx/ Withdrawn/ No
		xxxxxxxxxxxxxx/ xxxxxxxxxxxxxx/ xxxxxxxxxxxxx	Resolved with sequelae/ DDMMMYYYY/hh:mm DDMMMYYYY/hh:mm 85 d	99 d/ 79 d/ 1 d	Mild/ No/ No	xxxxxxx/ None/ Possible

Example : AE8
Protocol : 204847
Population : Safety

Listing 13
Listing of Drug-Related Adverse Events

Note to programmer: Use the same shell as Listing 12.

Example : SAFE_L1
Protocol : 204847
Population : Safety

Listing 14
Listing of Serious Adverse Events

Part: x
Treatment: xxxxx
Outcome: xxxxxxxxxxxxxx

Subj. ID	Age(y)/ Sex/ Race/ Weight (kg)	System Organ Class/ Preferred Term/ VERBATIM TEXT	Onset Date/Time Date/Time of Resolution/ Duration	Time Since 1st Dose/ Time Since Last Dose	Maximum Intensity/ Maximum Serious/ Withdrawal	Frequency/ Action Taken/ Relation to Study Drug
xxxxx	xx/ xxxx/xxx/ xx.x	xxxxxxxxxxxxxx/ xxxxxxxxxxxxxx/ xxxxxxxxxxxxx	DDMMMYYYY/hh:mm DDMMMYYYY/hh:mm 1 d	19 d/ 19 d/ 1 d	Mild/ No/ No	xxxxxxx/ Dose reduced/ No
		xxxxxxxxxxxxxx/ xxxxxxxxxxxxxx/ xxxxxxxxxxxxx	DDMMMYYYY/hh:mm DDMMMYYYY/hh:mm 1 d	21 d/ 1 d/ 1 d	Moderate/ No/ No	xxxxxxx/ Dose inter-rupted/ No
		xxxxxxxxxxxxxx/ xxxxxxxxxxxxxx/ xxxxxxxxxxxxx	DDMMMYYYY/hh:mm DDMMMYYYY/hh:mm 120 d	36 d/ 16 d/ 16 d	Severe/ No/ Yes	xxxxxxx/ Withdrawn/ No
		xxxxxxxxxxxxxx/ xxxxxxxxxxxxxx/ xxxxxxxxxxxxx	DDMMMYYYY/hh:mm DDMMMYYYY/hh:mm 85 d	99 d/ 79 d/ 1 d	Mild/ No/ No	xxxxxxx/ None/ Possible

Listing 14
Listing of Serious Adverse Events

Part: x
Treatment: xxxxx
Outcome: xxxxxxxxxxxxxx

Subj. ID	Age(y)/ Sex/ Race/ Weight (kg)	System Organ Class/ Preferred Term/ VERBATIM TEXT	Reason Considered SAE/Recur After Invetigational Product Administered?	Possible Causes of SAE	Relevant Medical Conditions/Onset Date/Present at Time of SAE	Relevant Risk Factors
xxxxx	xx/ xxxx/xxx/ xx.x	xxxxxxxxxxxxxx/ xxxxxxxxxxxxxx/ xxxxxxxxxxxxx	xxxxxxxxxxxx/xx	xxxx: xxxxxxxxx	xxxxxxxxxxxx (DDMMMYYYY)xxx/	xxxxx
		xxxxxxxxxxxxxx/ xxxxxxxxxxxxxx/ xxxxxxxxxxxxx	xxxxxxxxxxxx/xx	xxxx: xxxxxxxxx	xxxxxxxxxxxx (DDMMMYYYY)xxx/	xxxxxxxxxxxx
		xxxxxxxxxxxxxx/ xxxxxxxxxxxxxx/ xxxxxxxxxxxxx	xxxxxxxxxxxx/xx	xxxx: xxxxxxxxx	xxxxxxxxxxxx (DDMMMYYYY)xxx/	
		xxxxxxxxxxxxxx/ xxxxxxxxxxxxxx/ xxxxxxxxxxxxx	xxxxxxxxxxxx/xx	xxxx: xxxxxxxxx	xxxxxxxxxxxx (DDMMMYYYY)xxx/	xxxxxxxx

Listing 14
Listing of Serious Adverse Events

Part: x
Treatment: xxxxx
Outcome: xxxxxxxxxxxxxx

Subj. ID	Age(y)/ Sex/ Race/ Weight (kg)	System Organ Class/ Preferred Term/ VERBATIM TEXT	Relevant Concomitant Medications/ Dose/Frequency/Route/Taken Prior to Study/ Start Date/Stop Date/Ongoing/ Reason	Details of Investigational Product	Relevant Assessments	Narrative Remarks
xxxxx	xx/ xxxx/xxx/ xx.x	xxxxxxxxxxxxxx/ xxxxxxxxxxxxxx/ xxxxxxxxxxxxx	xxxxxxxxxx/xxx (unit)/xxxxx/ xxxxxxx/xxx/ DDMMMYYYY/DDMMMYYY/ xxxxxxxxx	xxxxxxxxxx	xxxxxxxxxx	xxxxxxxxxx
		xxxxxxxxxxxxxx/ xxxxxxxxxxxxxx/ xxxxxxxxxxxxx	xxxxxxxxxx/xxx (unit)/xxxxx/ xxxxxxx/xxx/ DDMMMYYYY/Ongoing/ xxxxxxxxx	xxxxxxxxxx	xxxxxxxxxx	xxxxxxxxxx
		xxxxxxxxxxxxxx/ xxxxxxxxxxxxxx/ xxxxxxxxxxxxx		xxxxxxxxxx	xxxxxxxxxx	xxxxxxxxxx
		xxxxxxxxxxxxxx/ xxxxxxxxxxxxxx/ xxxxxxxxxxxxx		xxxxxxxxxx	xxxxxxxxxx	xxxxxxxxxx

Example : AE8
Protocol : 204847
Population : Safety

Listing 15
Listing of Adverse Events Leading to Withdrawal from Study

Note to programmer: Use the same shell as Listing 11.

Example : SAFE_L2
Protocol : 204847
Population : Safety

Listing 16
Listing of Infusion Site Reaction Adverse Events

Part: xx
Treatment: xxxx

Subject ID.	AE/SAE Number	Date of Infusion	Date/Time of Reaction	Reaction Details/ Skin Rash Type	Reaction Time/ Inter-vention/ Treatment?	Require Management?/ Photographs Taken? Reaction Length, Width (cm)	Biopsy Taken?/ Interp-retation/ Diagnostic Tests	Recent exposure?/ Allergic Reactions Other Drugs?/ History of Allergic Reaction/
xxx	xxxxx	DDMMMYYYY	DDMMMYYYY/ hh:mm	xxxxx/ xxxxx	xxxxx/ xxxxx	xx/ xx/ xx, xx cm	xx/ xxxxxxx/ xxxxxxxx	xx/ xx/ NONE

Example : SAFE_L3
Protocol : 204847
Population : Safety

Listing 17
Listing of Liver Adverse Events

Note to programmer: Use the same shell as Listing 11. Present all applicable variables recorded on the eCRF.

Example : SAFE_L4
Protocol : 204847
Population : Safety

Listing 18
Listing of Cardiovascular Adverse Events

Note to programmer: Use the same shell as Listing 15. Present all applicable variables recorded on the eCRF.

Example : SAFE_L5
Protocol : 204847
Population : Safety

Listing 19
Listing of Rash Events

Part: xx
Treatment: xxxx

Subject ID.	Rash Onset Date/Time	Rash Symptoms/ Type	Description/ Appearance/ Appearance/ Site	Require Management?/ Photographs Taken? Reaction Length, Width (cm)	Biopsy Taken?/ Interp- retation/ Diagnostic Tests	Recent exposure?/ Allergic Reactions Other Drugs?/ History of Allergic Reaction/
xxx	DDMMMYYYY/hh:mm	xxxxxxxx/	xxxxxxx/	xx/ xx/ xx, xx cm	xx/ xxxxxxx/ xxxxxxxx	xx/ xx/ NONE
		xxxxxxxxxxxxxx	xxxxxxxxxx/ xxxxxxxxx/ xxxxxxxxx			

Example : LB5
Protocol : 204847
Population : Safety

Listing 20
Listing of Clinical Chemistry Toxicities of Grade 3 or Higher

Part: xx
Treatment: xxxx

Subj. ID	Age(y)/ Sex/ Race	Lab test (units)	Planned Relative Time	Date	Study Day	Converted Data Value	Converted Data Normal Range	Flag[1] NR	Flag[1] TG	Flag[1] BL
xxxxx	xx/ xxxx/ xxxxxx	xxxxxx (xxx)	xxxxxxx	DDMMMYYYY	x	xx.x	xx.x-xx.x			
			xxxxxxx	DDMMMYYYY	x	xx.x	xx.x-xx.x			
		xxxxxx (xxx)	xxxxxxxxx	DDMMMYYYY	x	xx.x	xx.x-xx.x			
			xxxxxxxxx	DDMMMYYYY	x	xx.x	xx.x-xx.x	H	x	H

[1] NR for Normal Range flag, TG for Toxicity flag; BL for Change from Baseline flag. H=Above range, L=Below range

Example : LB5
Protocol : 204847
Population : Safety

Listing 21
Listing of All Clinical Chemistry Data for Subjects with Toxicities of Grade 3 or Higher

Note to programmer: Use the shell from Listing 20.

Example : LB5
Protocol : 204847
Population : Safety

Listing 22
Listing of Haematology Toxicities of Grade 3 or Higher

Note to programmer: Use the shell from Listing 20.

Example : LB5
Protocol : 204847
Population : Safety

Listing 23
Listing of Haematology Data for Subjects with Toxicities of Grade 3 or Higher

Note to programmer: Use the shell from Listing 20.

Example : UR2a
Protocol : 204847
Population : Safety

Listing 24
Listing of Urinalysis Toxicities of Grade 3 or Higher

Part: xx
Treatment: xxxx

Subject ID.	Visit	Sample Date	Sample Time	Study Day	Urinalysis Test	Result	Toxicity Grade
xxxxxx	xxxxx	DDMMMYYYY	HH:MM	1	Blood	++ or 2+	x
	xxxxx	DDMMMYYYY	HH:MM	1	Blood	+ or 1+	
xxxxxx	xxxxx	DDMMMYYYY	HH:MM	1	Blood	+ or 1+	
					Protein	+++ or 3+	x
	xxxxx	DDMMMYYYY	HH:MM	1	Blood	+ or 1+	

Example : UR2a
Protocol : 204847
Population : Safety

Listing 25
Listing of Urinalysis for Subjects with Toxicities of Grade 3 or Higher

Note to programmer: Use the shell from Listing 24.

Example : EG5
Protocol : 204847
Population : Safety

Listing 26
Listing of Abnormal ECG Findings

Part: xx
Treatment: xxxx

Subj. ID	Age/ Sex/ Race	Planned Rel Time/ ECG Date/ Time	Study Day	ECG Finding	Clinically Significant Change from Baseline?	Clinically Significant Abnormality
xxxxx	xx/ xxxxx/ xxxx	xxxxxxx/ DDMMMYYYY /hh:mm	xx	Abnormal-not clinically significant	No	
		xxxxxxx/ DDMMMYYYY /hh:mm	xx	Abnormal-not clinically significant	No	
		xxxxxxx/ DDMMMYYYY /hh:mm	xx	Abnormal-clinically significant	Yes	Sinus tachycardia
		xxxxxxx/ DDMMMYYYY /hh:mm	xx	Abnormal-not clinically significant	No	
xxxxx	xx/ xxxxx/ xxxx	xxxxxxx/ DDMMMYYYY /hh:mm	xx	Abnormal-clinically significant	Yes	Ectopic ventricular beats
		xxxxxxx/ DDMMMYYYY /hh:mm	xx	Abnormal-clinically significant	No	Ectopic ventricular beats

Example : EG5
Protocol : 204847
Population : Safety

Listing 27
Listing of All ECG Findings for Subjects with an Abnormal Finding

Note to programmer: Use the shell from Listing 26.

Example : EG3
Protocol : 204847
Population : Safety

Listing 28
Listing of ECG Values of Potential Clinical Importance

Part: xx
Treatment: xxxx

Subj. ID	Age/ Sex/ Race	Planned Rel Time	ECG Date/ Time	Study Day	Heart Rate (beats/ min.)	PR Interval (msec)	QRS Duration (msec)	QRS Axis (deg)	QT Interval (msec)	QTc Interval (msec)	QTc (Bazett) (msec)	QTc (Fridericia) (msec)	RR Interval (msec)
xxxxxx	xx/ xxxxxx/ xxxxx	xxxxxxx	DDMMMYYYY/hh:mm	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
		xxxxxxx	DDMMMYYYY/hh:mm	xx	xx	xx L	xx	xx	xx	xx	xx	xx	xx
		xxxxxxx	DDMMMYYYY/hh:mm	xx	80	xx	xx	xx	xx	xx	xx	xx	xx
		xxxxxxx	DDMMMYYYY/hh:mm	xx	xx	xx	xx	xx	xx	xx H	xx	xx	xx
xxxxx	xx/ xxxxxx/ xxxxx	xxxxxxx	DDMMMYYYY/hh:mm	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
		xxxxxxx	DDMMMYYYY/hh:mm	xx	xx	xx	xx	xx	xx	xx I	xx	xx	xx

Note: L=Low, H=High, I=Increase, D=Decrease

Example : EG3
Protocol : 204847
Population : Safety

Listing 29

Listing of All ECG Values for Subjects with Any Value of Potential Clinical Importance

Note to programmer: Use shell for Listing 28.

Example : VS4
Protocol : 204847
Population : Safety

Listing 30
Listing of Vital Signs of Potential Clinical Importance

Part: xx
Treatment: xxxx

Subj. ID	Age(y)/ Sex/ Race	Planned Relative Time	Actual Date/Time	Body Position	Study Day	Systolic Blood Pressure (mmHg)	Diastolic Blood Pressure (mmHg)	Pulse (beats/ min)	Temper- ature (C)	Comment
xxx	xx/ xxxxxx/ xxxxx	xxxxxxx	DDMMMYYYY/hh:mm	xxxxxxx	x	xxx	xxx	xxx	xxx	
		xxxxxxx	DDMMMYYYY/hh:mm	xxxxxxx	x	xxx	xxx	xxx		
		xxxxxxx	DDMMMYYYY/hh:mm	xxxxxxx	x	Xxx H	Xxx H	xxx		xxxxxxxxxx
		xxxxxxx	DDMMMYYYY/hh:mm	xxxxxxx	x	xxx	xxx	xxx		
		xxxxxxx	DDMMMYYYY/hh:mm	xxxxxxx	x	xxx	xxx	xxx		
		xxxxxxx	DDMMMYYYY/hh:mm	xxxxxxx	x	xxx	xxx	xxx		
		xxxxxxx	DDMMMYYYY/hh:mm	xxxxxxx	x	xxx	xxx	xxx L		
xxx	xx/ xxxxxx/ xxxxx	xxxxxxx	DDMMMYYYY/hh:mm	xxxxxxx	x	xxx	xxx	xxx	xxx	
		xxxxxxx	DDMMMYYYY/hh:mm	xxxxxxx	x	xxx	xxx	xxx		

Note: L=Low, H=High

Example : VS4 Page 1 of n
Protocol : 204847
Population : Safety

Listing 31
Listing of All Vital Signs for Subjects with Potential Clinical Importance Values

Note to programmer: Use shell for Listing 30.

Example : LIVER5
Protocol : 204847
Population : Safety

Listing 32
Listing of Liver Monitoring/Stopping Event Reporting

Part: xxxxx
Treatment: xxxxxx

Site Id./ Unique Subject Id.	Age(YEARS)/ Sex/ Race Detail	Maximum Status of the Liver Event	Date First Detected/ Study Day	Time Since First Dose (days)	Time Since Last Dose (days)	Restart/Re-challenge After Stopping Criteria Was Met	Resolved?/ Date resolved
PPD - This section has been excluded to protect patient privacy.							

Example : MH2
Protocol : 204847
Population : Safety

Listing 33
Listing of Medical Conditions for Subjects with Liver Stopping Events

Part: xx
Treatment: xxxx

Subject ID	Classification	Condition	Status
xxxx	xxxxxxxxxxxx	XXXXXXXXXXXX	Current
	xxxxxxxxx	XXXXXXXXXXXXXXXXXXXXX	Past
xxxx	xxxx	XXXXXXXXXXXXXXXXX	Current
xxxx	xxxxxxxxxxxx	XXXXXXXXXXXXXXXXXXX	Current

Example : SAFE_L9
Protocol : 204847
Population : Safety

Listing 34
Listing of Alcohol Intake at Onset of Liver Event

Part: xx
Treatment: xxxx

Subject ID	Age(y)/ Sex/ Race	Exam Date/Time	Consume Alcohol?	Average Number Units Consumed per Week?
xxxx	xx/xx/xxxxxxx	DDMMMYYYY/hh:mm	xxx	x
xxxx	xx/xx/xxxxxxx	DDMMMYYYY/hh:mm	xx	xx
xxxx	xx/xx/xxxxxxx	DDMMMYYYY/hh:mm	xx	x

Example : PKCL1X
Protocol : 204847
Population : Safety

Listing 35
Listing of Plasma Concentration Data for Subjects with Liver Stopping Events

Note to programmer: Use shell for Listing 40.

Example : LIVER7
Protocol : 204847
Population : Safety

Listing 36
Listing of Liver Biopsy Details

Part: xx
Treatment: xxxx

Subject ID	Age(y)/ Sex/ Race	Biopsy Date/ Study Day	Biopsy Size	Liver Biopsy Test	Liver Biopsy Result
xxxx	xx/ xxxxxx/ xxxxx	DDMMMYYYY/ xx	xx	xxxxxxxxxxxxx	xxxxxxxxxxxxxxxxxxxxx
				xxxxxxxxxxxxx	xxxxxxxxxxxxxxxxxxxxx
				xxxxxxxxxxxxx	xxxxxxxxxxxxxxxxxxxxx
				xxxxxxxxxxxxx	xxxxxxxxxxxxxxxxxxxxx
				xxxxxxxxxxxxx	xxxxxxxxxxxxxxxxxxxxx

Example : LIVER8
Protocol : 204847
Population : Safety

Listing 37
Listing of Liver Imaging Details

Part: xx
Treatment: xxxx

Subject ID	Age(y)/ Sex/ Race	Imaging Date/ Study Day	Liver Imaging Method	Are Images Technically Adequate	Liver Imaging Test	Liver Imaging Result
xxxx	xx/ xxxxxx/ xxxxx	DDMMMYYYY/ xx	xx	xxxx	xxxxxxxxxxxxx	xxxxxxxxxxxxxxxxxxxx
					xxxxxxxxxxxxx	xxxxxxxxxxxxxxxxxxxx
					xxxxxxxxxxxxx	xxxxxxxxxxxxxxxxxxxx
					xxxxxxxxxxxxx	xxxxxxxxxxxxxxxxxxxx
					xxxxxxxxxxxxx	xxxxxxxxxxxxxxxxxxxx

Example : SAFE_L10
Protocol : 204847
Population : Safety

Listing 38
Listing of Cardiac Telemetry Monitoring

Part: xx
Treatment: xxxx

Subject ID	Start Date/Time	End Date/Time	Overall Interpretation	Specify Abnormality/Comments
xxxx	DDMMMYYYY/hh:mm	DDMMMYYYY/hh:mm	xxxxxxxxxxx	xxxxxxxxxxx/xxxxxx
xxxx	DDMMMYYYY/hh:mm	DDMMMYYYY/hh:mm	xxxxxxxxx	
xxxx	DDMMMYYYY/hh:mm	DDMMMYYYY/hh:mm	xxxxxxxxxxxxx	

Example : LB5
Protocol : 204847
Population : Safety

Listing 39
Listing of Cytokine Data

Note to programmer: Use the shell from Listing 20. Do not present toxicity (TG) column.

Example : PKCL1X
Protocol : 204847
Population : PK

Listing 40
Listing of GSK3342830 Pharmacokinetic Plasma Concentration-Time Data by Treatment in Part 1 and Part 3

Part: Part 1
Dose: XXXX mg

Subject ID.	Age (y)/ Sex/ Race xx/ xxxx/ xxxxx	Visit	Date	Study Day	Planned Relative Time	Actual Time	Time Deviation (h)	Actual Relative Time (h)	Concentration (units)
xxxx		xxxx	MMDDYYYY	1	pre-dose	HH:MM	xx	0h 0m 0s	xx.xx
					0.5h	HH:MM	xx	0h 0m 0s	xx.xx
					1h	HH:MM	xx	0h 0m 0s	xx.xx
					1.25h	HH:MM	xx	0h 0m 0s	xx.xx
					1.5h	HH:MM	xx	0h 0m 0s	xx.xx
					2h	HH:MM	xx	0h 0m 0s	xx.xx
					3h	HH:MM	xx	0h 0m 0s	xx.xx
					3.5h	HH:MM	xx	0h 0m 0s	xx.xx
					4h	HH:MM	xx	0h 0m 0s	xx.xx
					4.5h	HH:MM	xx	0h 0m 0s	xx.xx
					5h	HH:MM	xx	0h 0m 0s	xx.xx
					6h	HH:MM	xx	0h 0m 0s	xx.xx
					8h	HH:MM	xx	0h 0m 0s	xx.xx
					10h	HH:MM	xx	0h 0m 0s	xx.xx
					12h	HH:MM	xx	0h 0m 0s	xx.xx
					16h	HH:MM	xx	0h 0m 0s	xx.xx
				2	24h	HH:MM	xx	0h 0m 0s	xx.xx
					36h	HH:MM	xx	0h 0m 0s	xx.xx
				3	48h	HH:MM	xx	0h 0m 0s	xx.xx

Note to Programmer: Present all Part 1 first, then repeat for Part 3. Please list all the concentration data including unscheduled.

LLOQ = xx.x (units)
NQ=Not quantifiable

Example : PKUL1P
Protocol : 204847
Population : PK

Listing 41
Listing of GSK3342830 Pharmacokinetic Urine Concentration-Time Data by Treatment in Part 1 and Part 3

Part: Part 1
Dose: XXXX mg

Subject ID.	Age (y)/ Sex/ Race	Visit	Date	Study Day	Planned Relative Time	Actual Midpt. of Collection	Actual Duration (h)	Urine Conc. (units)	Total Sample Volume (units)
xxxx	xx/ xxxx/ xxxxx	xxxx	MMDDYYYY	xxxx	0-4h	HH MM	HH MM	xx.xx	xx.xx
					4-8h	HH MM	HH MM	xx.xx	xx.xx
					8-12h	HH MM	HH MM	xx.xx	xx.xx
					12-24h	HH MM	HH MM	xx.xx	xx.xx
					24-48h	HH MM	HH MM	xx.xx	xx.xx

Note to Programmer: Present all Part 1 first, then repeat for Part 3. Please list all the concentration data including unscheduled.

LLOQ = xx.x (units)
NQ=Not quantifiable

Example : PKCL1X
Protocol : 204847
Population : PK

Listing 42
Listing of GSK3342830 Pharmacokinetic Plasma Concentration-Time Data by Treatment in Part 2

Dose: XXXX mg

Subject ID.	Age (y)/ Sex/ Race xx/ xxxx/	Visit	Date	Study Day	Planned Relative Time	Actual Time	Time Deviation (h)	Actual Relative Time (h)	Concentration (units)
xxxx	xxxxx	xxxx	MMDDYYYY	1	pre-dose	HH:MM	xx	0h 0m 0s	xx.xx
					0.5h	HH:MM	xx	0h 0m 0s	xx.xx
					1h	HH:MM	xx	0h 0m 0s	xx.xx
					1.25h	HH:MM	xx	0h 0m 0s	xx.xx
					1.5h	HH:MM	xx	0h 0m 0s	xx.xx
					2h	HH:MM	xx	0h 0m 0s	xx.xx
					…	…	..	…	…
					16h	HH:MM	xx	0h 0m 0s	xx.xx
				2	24h	HH:MM	xx	0h 0m 0s	xx.xx
				3	pre-dose	HH:MM	xx	0h 0m 0s	xx.xx
				6	pre-dose	HH:MM	xx	0h 0m 0s	xx.xx
				9	pre-dose	HH:MM	xx	0h 0m 0s	xx.xx
				12	pre-dose	HH:MM	xx	0h 0m 0s	xx.xx
				13	pre-dose	HH:MM	xx	0h 0m 0s	xx.xx
				15	pre-dose	HH:MM	xx	0h 0m 0s	xx.xx
					0.5h	HH:MM	xx	0h 0m 0s	xx.xx
					1h	HH:MM	xx	0h 0m 0s	xx.xx
					1.25h	HH:MM	xx	0h 0m 0s	xx.xx
					…	…	…	…	…
					6h	HH:MM	xx	0h 0m 0s	xx.xx
					8h	HH:MM	xx	0h 0m 0s	xx.xx

Note to Programmer: Please list all the concentration data including unscheduled.
Timepoints on day 1 is Pre-dose, 0.5, 1.25,1.5, 2,2.5,3,3.5,4,4.5,5,6,8,10,12,16 and 24. Timepoints on day 15 is Pre-dose,0.5,1,1.25,1.5,2,2.5,3,3.5,4,4.5, 5, 6 and 8.

LLOQ = xx.x (units)
NQ=Not quantifiable

Example : PKUL1P
Protocol : 204847
Population : PK

Listing 43
Listing of GSK3342830 Pharmacokinetic Urine Concentration-Time Data by Treatment in Part 2

Dose: XXXX mg

Subject ID.	Age (y)/ Sex/ Race	Visit	Date	Study Day	Planned Relative Time	Actual Midpt. of Collection	Actual Duration (h)	Urine Conc. (units)	Total Sample Volume (units)
xxxx	xx/ xxxx/ xxxxx	xxxx	MMDDYYYY	1	0-8h	HH MM	HH MM	xx.xx	xx.xx
					8-24h	HH MM	HH MM	xx.xx	xx.xx
				15	0-8h	HH MM	HH MM	xx.xx	xx.xx
					8-24h	HH MM	HH MM	xx.xx	xx.xx

Note to Programmer: Please list all the concentration data including unscheduled.

LLOQ = xx.x (units)
NQ=Not quantifiable

Example : PLPL1X
Protocol : 204847
Population : PK Parameter

Listing 44
Listing of GSK3342830 Plasma Pharmacokinetic Parameters by Treatment in Part 1 and Part 3

Part: Part 1
Dose: XXX mg

Subject ID.	Age (y)/ Sex/ Race	AUC(0-t) (units)	AUC(0-∞) (units)	Cmax (units)	Tmax (unit)
xxxx	xx/ xxxx/ xxxxx	xx.xx	xx.xx	xx.xx	xx.xx
xxxx	xx/ xxxx/ xxxxx	xx.xx	xx.xx	xx.xx	xx.xx
xxxx	xx/ xxxx/ xxxxx	xx.xx	NC	xx.xx	xx.xx
xxxx	xx/ xxxx/ xxxxx	xx.xx	xx.xx	xx.xx	xx.xx

Note to Programmer: Present all Part 1 first, then repeat for Part 3
Additional parameters include t1/2, CL, Vss, %AUCex, tlast, lambda_z, lambda_z_lower, lambda_z_upper, lambda_z_no. of points

Source Data: Listing 40

Example : PLPL1X
Protocol : 204847
Population : PK Parameter

Listing 45
Listing of GSK3342830 Urine Pharmacokinetic Parameters by Treatment in Part 1 and Part 3

Part: Part 1
Dose: XXX mg

Subject ID.	Age (y)/ Sex/ Race	Ae (units)	CLr (units)	Feu(0-4) (units)
xxxx	xx/ xxxx/ xxxxx	xx.xx	xx.xx	xx.xx
xxxx	xx/ xxxx/ xxxxx	xx.xx	xx.xx	xx.xx
xxxx	xx/ xxxx/ xxxxx	xx.xx	xx.xx	xx.xx
xxxx	xx/ xxxx/ xxxxx	xx.xx	xx.xx	xx.xx

Note to Programmer: Present all Part 1 first, then repeat for Part 3
Additional parameters include Feu(4-8) (units), Feu(8-12) (units), Feu (12-24) (units), Feu (24-48) (units)

Source Data: Listing 40

Example : PLPL1X
Protocol : 204847
Population : PK Parameter

Listing 46
Listing of GSK3342830 Plasma Pharmacokinetic Parameters by Treatment in Part 2

Dose: XXX mg

Subject ID.	Age (y)/ Sex/ Race	Day	AUC(0-t) (units)	AUC(0-∞) (units)	AUC(0-τ) (units)	Cmax (unit)
xxxx	xx/ xxxx/ xxxxx	1	xx.xx	xx.xx	xx.xx	xx.xx
		15	xx.xx	xx.xx	xx.xx	xx.xx
xxxx	xx/ xxxx/ xxxxx	1	xx.xx	xx.xx	xx.xx	xx.xx
		15	xx.xx	xx.xx	xx.xx	xx.xx
xxxx	xx/ xxxx/ xxxxx	1	xx.xx	NC	xx.xx	xx.xx
		15	xx.xx	NC	xx.xx	xx.xx
xxxx	xx/ xxxx/ xxxxx	1	xx.xx	xx.xx	xx.xx	xx.xx
		15	xx.xx	xx.xx	xx.xx	xx.xx

Note to Programmer:
Additional parameters include Tmax, t1/2, CL, Vss, Cτ, Ratio of time invariance, Ratio of accumulation, %AUCex, tlast, lambda_z, lambda_z_lower, lambda_z_upper, lambda_z_no. of points

Source Data: Listing 41

Example : PLPL1X
Protocol : 204847
Population : PK Parameter

Listing 47
Listing of GSK3342830 Urine Pharmacokinetic Parameters by Treatment in Part 2

Dose: XXX mg

Subject ID.	Age (y)/ Sex/ Race	Day	Ae (units)	CLr (units)	Feu(0-8) (units)
xxxx	xx/ xxxx/ xxxxx	1	xx.xx	xx.xx	xx.xx
		15	xx.xx	xx.xx	xx.xx
xxxx	xx/ xxxx/ xxxxx	1	xx.xx	xx.xx	xx.xx
		15	xx.xx	xx.xx	xx.xx
xxxx	xx/ xxxx/ xxxxx	1	xx.xx	xx.xx	xx.xx
		15	xx.xx	xx.xx	xx.xx
xxxx	xx/ xxxx/ xxxxx	1	xx.xx	xx.xx	xx.xx
		15	xx.xx	xx.xx	xx.xx

Note to Programmer:
Additional parameters include Feu(8-24) (units).

Source Data: Listing 42

Table 1.1
Summary of Number of Subjects Enrolled by Country and Site ID

Study Part: 1

Country	Site ID	Investigator Name	GSK3342830 250 mg (N=xx)	GSK3342830 500 mg (N=xx)	… …	Placebo (N=xx)	Total (N=xx)
xxxxxxxxxxx	xxxxxxxxx	xxxxxxxxxx	xx (xx.x%)	xx (xx.x%)		xx (xx.x%)	xx (xx.x%)
xxxxxxxxxxx	xxxxxxxxx	xxxxxxxxxx	xx (xx.x%)	xx (xx.x%)		xx (xx.x%)	xx (xx.x%)

Note to programmer: Continue for all treatments in Part 1, Part 2, and Part 3. Present Part 2 and Part 3 on separate pages.

Table 1.2
Summary of Subject Disposition

Study Part: 1

	GSK3342830 250 mg (N=xx)	GSK3342830 500 mg (N=xx)	… …	Placebo (N=xx)	Total (N=xx)
Subject Status					
Completed	xx (xx.x%)	xx (xx.x%)		xx (xx.x%)	xx (xx.x%)
Withdrawn	xx (xx.x%)	xx (xx.x%)		xx (xx.x%)	xx (xx.x%)
Primary reason for study withdrawal					
Adverse Event	xx (xx.x%)	xx (xx.x%)		xx (xx.x%)	xx (xx.x%)
Protocol Deviation	xx (xx.x%)	xx (xx.x%)		xx (xx.x%)	xx (xx.x%)
Subject reached protocol-defined stopping criteria	xx (xx.x%)	xx (xx.x%)		xx (xx.x%)	xx (xx.x%)
Study closed/terminated	xx (xx.x%)	xx (xx.x%)		xx (xx.x%)	xx (xx.x%)
Lost to Follow-up	xx (xx.x%)	xx (xx.x%)		xx (xx.x%)	xx (xx.x%)
Investigator discretion	xx (xx.x%)	xx (xx.x%)		xx (xx.x%)	xx (xx.x%)
Withdrew Consent	xx (xx.x%)	xx (xx.x%)		xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)		xx (xx.x%)	xx (xx.x%)

Note to programmer: Continue for all treatments in Part 1, Part 2, and Part 3. Present Part 2 and Part 3 on separate pages.

Table 1.3
Summary of Reasons for Screening Failures

	Screened Subjects (N=xx)
Screening Status	
Enrolled	xx (xx.x%)
Failed	xx (xx.x%)
Reason for failure	
Did not meet inclusion/exclusion criteria	xx (xx.x%)
Adverse event	xx (xx.x%)
Protocol deviation	xx (xx.x%)
Medical or Surgical Condition Exclusion	xx (xx.x%)
Investigator discretion	xx (xx.x%)
Participant withdrew consent	xx (xx.x%)
Lost to follow up	xx (xx.x%)
Other	xx (xx.x%)

Table 1.4
Summary of Important Protocol Deviations

Study Part: 1

Category/Subcategory	GSK3342830 250 mg (N=xx)	GSK3342830 500 mg (N=xx)	…	Placebo (N=xx)	Total (N=xx)
Any protocol deviations	xx (xx.x%)	xx (xx.x%)	…	xx (xx.x%)	xx (xx.x%)
Informed Consent					
xxxxxxxxxxxxxx					
xxxxxxxxxxxxx					
…					
Eligibility criteria not met	xx (xx.x%)	xx (xx.x%)	…	xx (xx.x%)	xx (xx.x%)
xxxxxxxxxxxxxx					
Not withdrawn after developing withdrawal criteria	xx (xx.x%)	xx (xx.x%)	…	xx (xx.x%)	xx (xx.x%)
Excluded medication, vaccine, or device	xx (xx.x%)	xx (xx.x%)	…	xx (xx.x%)	xx (xx.x%)
Visit Completion	xx (xx.x%)	xx (xx.x%)	…	xx (xx.x%)	xx (xx.x%)
Assessment or time point completion					
Wrong study treatment/administration/dose or incorrect dose	xx (xx.x%)	xx (xx.x%)	…	xx (xx.x%)	xx (xx.x%)
Study Procedures	xx (xx.x%)	xx (xx.x%)	…	xx (xx.x%)	xx (xx.x%)
Failure to report safety events per protocol	xx (xx.x%)	xx (xx.x%)	…	xx (xx.x%)	xx (xx.x%)
…					

Note to programmer: Continue for all treatments in Part 1, Part 2, and Part 3. Present Part 2 and Part 3 on separate pages. Present all Categories and Subcategories on the eCRF for which there is non-zero count.

Table 1.5
Summary of Demographic Characteristics

Study Part: 1

		GSK3342830 250 mg (N=xx)	GSK3342830 500 mg (N=xx)	…	Total (N=xx)
Sex	n	xx	xx	…	xx
	Male	xx (xx.x%)	xx (xx.x%)	…	xx (xx.x%)
	Female	xx (xx.x%)	xx (xx.x%)	…	xx (xx.x%)
Age (YEARS)[1]	n	xx	xx	…	xx
	Mean	xx.x	xx.x	…	xx.x
	SD	xx.xx	xx.xx	…	xx.xx
	Median	xx.x	xx.x	…	xx.x
	Min.	xx.x	xx.x	…	xx.x
	Max.	xx.x	xx.x	…	xx.x
Ethnicity	n	xx	xx	…	xx
	Hispanic/Latino	xx (xx.x%)	xx (xx.x%)	…	xx (xx.x%)
	Not Hispanic/Latino	xx (xx.x%)	xx (xx.x%)	…	xx (xx.x%)
Height (cm)	n	xx	xx	…	xx
	Mean	xx.x	xx.x	…	xx.x
	SD	xx.xx	xx.xx	…	xx.xx
	Median	xx.x	xx.x	…	xx.x
	Min.	xx.x	xx.x	…	xx.x
	Max.	xx.x	xx.x	…	xx.x
Weight (kg)	n	xx	xx	…	xx
	Mean	xx.x	xx.x	…	xx.x
	SD	xx.xx	xx.xx	…	xx.xx
	Median	xx.x	xx.x	…	xx.x
	Min.	xx.x	xx.x	…	xx.x
	Max.	xx.x	xx.x	…	xx.x
BMI (kg/m2)	n	xx	xx	…	xx
	Mean	xx.x	xx.x	…	xx.x
	SD	xx.xx	xx.xx	…	xx.xx
	Median	xx.x	xx.x	…	xx.x
	Min.	xx.x	xx.x	…	xx.x
	Max.	xx.x	xx.x	…	xx.x

Note to programmer: Continue for all treatments in Part 1, Part 2, and Part 3. Present Part 2 and Part 3 on separate pages.

[1] Age is imputed when full date of birth is not provided.

Table 1.6
Summary of Age Ranges

Study Part: 1

	GSK3342830 250 mg (N=xx)	GSK3342830 500 mg (N=xx)	…	Total (N=xx)
Age Ranges [1]				
Adult (18-64 years)	xx (xx.x%)	xx (xx.x%)	…	xx (xx.x%)

Note to programmer: Continue for all treatments in Part 1, Part 2, and Part 3. Present Part 2 and Part 3 on separate pages.

[1] Age is imputed when full date of birth is not provided.

Table 1.7
Summary of Race and Racial Combinations

Race	GSK3342830 250 mg (N=xx)	GSK3342830 500 mg (N=xx)	…	Total (N=xx)
n	xx	xx		xx
AMERICAN INDIAN OR ALASKA NATIVE	xx (xx.x%)	xx (xx.x%)		xx (xx.x%)
ASIAN	xx (xx.x%)	xx (xx.x%)		xx (xx.x%)
BLACK OR AFRICAN AMERICAN	xx (xx.x%)	xx (xx.x%)		xx (xx.x%)
NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER	xx (xx.x%)	xx (xx.x%)		xx (xx.x%)
WHITE	xx (xx.x%)	xx (xx.x%)		xx (xx.x%)
MULTIPLE	xx (xx.x%)	xx (xx.x%)		xx (xx.x%)
	xx (xx.x%)	xx (xx.x%)		xx (xx.x%)
	xx (xx.x%)	xx (xx.x%)		xx (xx.x%)
	xx (xx.x%)	xx (xx.x%)		xx (xx.x%)
	xx (xx.x%)	xx (xx.x%)		xx (xx.x%)
…				

Programmer's note: Do not display "MULTIPLE" unless present in the data. Percentages will add up to 100.
Continue for all treatments in Part 1, Part 2, and Part 3. Present Part 2 and Part 3 on separate pages.

Table 1.8
Summary of Race and Racial Combinations Details

		GSK3342830 250 mg (N=xx)	GSK3342830 500 mg (N=xx)	…	Total (N=xx)
Race	n	xx	xx		xx
	AMERICAN INDIAN OR ALASKA NATIVE	xx (xx.x%)	xx (xx.x%)		xx (xx.x%)
	ASIAN	xx (xx.x%)	xx (xx.x%)		xx (xx.x%)
	BLACK OR AFRICAN AMERICAN	xx (xx.x%)	xx (xx.x%)		xx (xx.x%)
	NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER	xx (xx.x%)	xx (xx.x%)		xx (xx.x%)
	WHITE	xx (xx.x%)	xx (xx.x%)		xx (xx.x%)

Programmer's note: A subject may be displayed more than once, ie. percentages may add up to more than 100.
Continue for all treatments in Part 1, Part 2, and Part 3. Present Part 2 and Part 3 on separate pages.

Table 1.9
Summary of Cardiovascular Related Medical Conditions

Study Part: 1

Classification	GSK3342830 250 mg (N=xx)	GSK3342830 500 mg (N=xx)	…	Placebo (N=xx)	Total (N=xx)
Any condition	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Angina pectoris	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Myocardial infarction	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Stroke	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
...	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Note to programmer: Continue for all treatments in Part 1, Part 2, and Part 3. Present Part 2 and Part 3 on separate pages.

Table 2.1
Relationship of Adverse Event System Organ Classes, Preferred Terms and Verbatim Text

System Organ Class	Preferred Term	Verbatim Text
SOC #1	Preferred Term # 1	XXXXXXXXX
	Preferred Term # 2	XXXXXXXXX
	Preferred Term # 3	XXXXXXXXX
	Preferred Term # 4	XXXXXXXXX
SOC #2	Preferred Term # 1	XXXXXXXXX
	Preferred Term # 2	XXXXXXXXX
	Preferred Term # 3	XXXXXXXXX
	Preferred Term # 4	XXXXXXXXX

Table 2.2
Summary of All Adverse Events

Study Part: 1

System Organ Class Preferred Term	GSK3342830 250 mg (N=xx)	GSK3342830 500 mg (N=xx)	…	Total (N=xx)
Any Event	xx (xx.x%)	xx (xx.x%)	…	xx (xx.x%)
System Organ Class #1	xx (xx.x%)	xx (xx.x%)	…	xx (xx.x%)
Preferred Term #1	xx (xx.x%)	xx (xx.x%)	…	xx (xx.x%)
Preferred Term #2	xx (xx.x%)	xx (xx.x%)	…	xx (xx.x%)
Preferred Term #3	xx (xx.x%)	xx (xx.x%)	…	xx (xx.x%)

...
Note to programmer: System Organ Class (SOC) is displayed in descending order of frequency for 'Overall' then alphabetically.
Preferred Term is displayed in descending order of frequency for 'Overall' then alphabetically within SOC.
Continue for all treatments in Part 1, Part 2, and Part 3. Present Part 2 and Part 3 on separate pages.

At each level of subject summarization, a subject is counted once if the subject reported one or more events.

Table 2.3
Summary of Drug-Related Adverse Events

Study Part: 1

System Organ Class Preferred Term	GSK3342830 250 mg (N=xx)	GSK3342830 500 mg (N=xx)	…	Total (N=xx)
Any Event	xx (xx.x%)	xx (xx.x%)	…	xx (xx.x%)
System Organ Class #1	xx (xx.x%)	xx (xx.x%)	…	xx (xx.x%)
Preferred Term #1	xx (xx.x%)	xx (xx.x%)	…	xx (xx.x%)
Preferred Term #2	xx (xx.x%)	xx (xx.x%)	…	xx (xx.x%)
Preferred Term #3	xx (xx.x%)	xx (xx.x%)	…	xx (xx.x%)

...

Note to programmer: System Organ Class (SOC) is displayed in descending order of frequency for 'Overall' then alphabetically.
Preferred Term is displayed in descending order of frequency for 'Overall' then alphabetically within SOC.
Continue for all treatments in Part 1, Part 2, and Part 3. Present Part 2 and Part 3 on separate pages.

At each level of subject summarization, a subject is counted once if the subject reported one or more events.

Table 2.4
Summary of Common (>=5%) Non-serious Adverse Events by System Organ Class and Preferred Term
(Number of Subjects and Occurrences)

Study Part: 1

System Organ Class Preferred Term		GSK3342830 250 mg (N=xx)	GSK3342830 500 mg (N=xx)	…	Total (N=xx)
Any Event	Number of Subject with AEs	xx (xx.x%)	xx (xx.x%)	…	xx (xx.x%)
	Number of AEs	xx	xx		xx
System Organ Class #1					
Preferred Term #1	Number of Subject with AEs	xx (xx.x%)	xx (xx.x%)	…	xx (xx.x%)
...	Number of AEs	xx	xx		xx

Note to programmer: System Organ Class (SOC) is displayed in descending order of frequency for 'Overall' then alphabetically.
Preferred Term is displayed in descending order of frequency for 'Overall' then alphabetically within SOC.
Continue for all treatments in Part 1, Part 2, and Part 3. Present Part 2 and Part 3 on separate pages.

At each level of subject summarization, a subject is counted once if the subject reported one or more events.

Table 2.5
Summary of Serious Adverse Events by System Organ Class and Preferred Term
(Number of Subjects and Occurrences)

Study Part: 1

System Organ Class Preferred Term		GSK3342830 250 mg (N=xx)	GSK3342830 500 mg (N=xx)	…	Total (N=xx)
Any Event	Number of Subjects with SAEs	xx (xx.x%)	xx (xx.x%)	…	xx (xx.x%)
	Number of SAEs	xx	xx		xx
	Number of Drug-related SAEs	xx	xx		xx
	Number of Fatal SAEs	xx	xx		xx
	Number of Drug-related Fatal SAEs	xx	xx		xx
System Organ Class #1					
Preferred Term #1	Number of Subjects with SAEs	xx (xx.x%)	xx (xx.x%)	…	xx (xx.x%)
...	Number of SAEs	xx	xx		xx
	Number of Drug-related SAEs	xx	xx		xx
	Number of Fatal SAEs	xx	xx		xx
	Number of Drug-related Fatal SAEs	xx	xx		xx

Note to programmer: System Organ Class (SOC) is displayed in descending order of frequency for 'Overall' then alphabetically.
Preferred Term is displayed in descending order of frequency for 'Overall' then alphabetically within SOC.
Continue for all treatments in Part 1, Part 2, and Part 3. Present Part 2 and Part 3 on separate pages.

At each level of subject summarization, a subject is counted once if the subject reported one or more events.

Table 2.6
Summary of Clinical Chemistry Values

Study Part: 1

Lab Test	Treatment	N	Planned Relative Time	n	Mean	SD	Median	Min.	Max.
XXXXXXXX (XXX)	GSK3342830 250 mg	XXX	Baseline	xx	xx.x	xx.xx	xx	xx	xx
			Day 2	xx	xx.x	xx.xx	xx	xx	xx
			Follow-Up	xx	xx.x	xx.xx	xx	xx	xx
	GSK3342830 500 mg	XXX	Baseline	xx	xx.x	xx.xx	xx	xx	xx
			Day 2	xx	xx.x	xx.xx	xx	xx	xx
			Follow-Up	xx	xx.x	xx.xx	xx	xx	xx
	…	XXX	Baseline	xx	xx.x	xx.xx	xx	xx	xx
			Day 2	xx	xx.x	xx.xx	xx	xx	xx
			Follow-Up	xx	xx.x	xx.xx	xx	xx	xx
			...						

Note to programmer: Continue for all treatments in Part 1, Part 2, and Part 3. Present Part 2 and Part 3 on separate pages. Timepoints for Part 1 and Part 3 are Baseline, Day 2, Follow-Up. Timepoints for Part 2 are Baseline, Day 2, Day 5, Day 10, Day 15, and Follow-Up.

Note: For subjects Baseline is defined as the last nonmissing measurement before dosing.
Unscheduled measurements are not included in this summary table except when calculating baseline.

Table 2.7
Summary of Clinical Chemistry Change from Baseline

Note to programmer: Please use the shell from Table 2.6 and include only Planned Relative Time after Baseline.

Table 2.8
Summary of Haematology Values

Note to programmer: Please use the shell from Table 2.6.

Table 2.9
Summary of Haematology Change from Baseline

Note to programmer: Please use the shell from Table 2.6 and include only Planned Relative Time after Baseline.

Table 2.10
Summary of Urinalysis Dipstick Results

Study Part: 1

Test	Planned Relative Time	Result	GSK3342830 250 mg (N=xx)	GSK3342830 500 mg (N=xx)	... (N=xx)	Placebo (N=xx)
Urine General Dipstick	Baseline	Positive	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		Negative	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		No Result	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		Not Done	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Day 2	...	...	...	...	...
	Follow-up	...	...	...	...	...
Urine Occult Blood (Dipstick)	Baseline	None	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		Trace	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		1+	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		2+	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		3+	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		4+	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		5+	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		No Result	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		Not Done	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
...	...	...	...	...	...	...

Note to Programmer: Continue for all treatments in Part 1, Part 2, and Part 3. Present Part 2 and Part 3 on separate pages.

Table 2.11
Summary of ECG Findings

Study Part: 1

	GSK3342830 250 mg (N=XX)	GSK3342830 500 mg (N=XX)	...	Total (N=XX)
Baseline				
n	xx	xx	...	xx
Normal	xx (xx%)	xx (xx%)	...	xx (xx%)
Abnormal, not clinically significant	xx (xx%)	xx (xx%)	...	xx (xx%)
Abnormal, clinically significant	xx (xx%)	xx (xx%)	...	xx (xx%)
Day 1 - 0.5 HR				
n	xx	xx	...	xx
Normal	xx (xx%)	xx (xx%)	...	xx (xx%)
Abnormal, not clinically significant	xx (xx%)	xx (xx%)	...	xx (xx%)
Abnormal, clinically significant	xx (xx%)	xx (xx%)	...	xx (xx%)
...	...	...		...

Note to Programmer: Continue for all treatments in Part 1, Part 2, and Part 3. Present Part 2 and Part 3 on separate pages. Timepoints for Part 1 and Part 3 are Baseline, Day 1 - 0.5 HR, Day 1 - 1 HR, Day 1 - 1.5 HR, Day 1 - 2 HR, Day 1 - 3 HR, Day 1 - 4 HR, Day 1 - 6 HR, Day 1 - 12 HR, Day 2, Day 3, Follow-Up. Timepoints for Part 2 are Baseline, Day 1 - 0.5 HR, Day 1 - 1 HR, Day 1 - 1.5 HR, Day 1 - 2 HR, Day 1 - 3 HR, Day 1 - 4 HR, Day 1 - 6 HR, Day 1 - 12 HR, Day 2 through Day 14, Day 15 - 0.5 HR, Day 15 - 1 HR, Day 15 - 1.5 HR, Day 15 - 2 HR, Day 15 - 3 HR, Day 15 - 4 HR, Day 15 - 6 HR, Day 15 - 12 HR, Day 16, and Follow-Up.

Note: Baseline is defined as the last nonmissing measurement before dosing.
Unscheduled measurements are not included in this summary table except when calculating baseline.

Table 2.12
Summary of ECG Values

Study Part: 1

ECG Test	Group	N	Planned Relative Time	n	Mean	SD	Median	Min.	Max.
XXXXXXXX (XXX)	GSK3342830 250 mg	XXX	Baseline	xx	xx.x	xx.xx	xx	xx	xx
			Day 1 - 0.5 HR	xx	xx.x	xx.xx	xx	xx	xx
			...						
			Follow-Up	xx	xx.x	xx.xx	xx	xx	xx
XXXXXXXX (XXX)	GSK3342830 500 mg	XXX	Baseline	xx	xx.x	xx.xx	xx	xx	xx
			...						
XXXXXXXX (XXX)	...	XXX	Baseline	xx	xx.x	xx.xx	xx	xx	xx
			...						

Note to Programmer: Continue for all treatments in Part 1, Part 2, and Part 3. Present Part 2 and Part 3 on separate pages. Timepoints for Part 1 and Part 3 are Baseline, Day 1 - 0.5 HR, Day 1 - 1 HR, Day 1 - 1.5 HR, Day 1 - 2 HR, Day 1 - 3 HR, Day 1 - 4 HR, Day 1 - 6 HR, Day 1 - 12 HR, Day 2, Day 3, Follow-Up. Timepoints for Part 2 are Baseline, Day 1 - 0.5 HR, Day 1 - 1 HR, Day 1 - 1.5 HR, Day 1 - 2 HR, Day 1 - 3 HR, Day 1 - 4 HR, Day 1 - 6 HR, Day 1 - 12 HR, Day 2 through Day 14, Day 15 - 0.5 HR, Day 15 - 1 HR, Day 15 - 1.5 HR, Day 15 - 2 HR, Day 15 - 3 HR, Day 15 - 4 HR, Day 15 - 6 HR, Day 15 - 12 HR, Day 16, and Follow-Up.
ECG measurements summarized are: Heart Rate (beats/min), PR Interval (msec), QT Interval (msec), QTc Interval (msec), QTcB Interval (msec), QTcF Interval (msec), QRS Duration (msec), QRS Axis (deg), and RR Interval (msec).

Note: Baseline is defined as the last nonmissing measurement before dosing for the respective treatment period
Unscheduled measurements are not included in this summary table except when calculating baseline.

Table 2.13
Summary of Change from Baseline in ECG Values

Note to programmer: Please use the shell from Table 2.12 and include only Planned Relative Time after Baseline.

Table 2.14
Summary of Frequency of Maximum Post-Dose ECG Parameter Corrected QTc Interval

Study Part: 1

	GSK3342830 250 mg (N=XX)	GSK3342830 550 mg (N=XX)	… (N=XX)	Placebo (N=XX)
QTcB (msec)				
n	xx	xx	xx	xx
<=450	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
>450-<=479	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
>=480-<=499	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
>=500	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
QTcF (msec)				
n	xx	xx	xx	xx
<=450	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
>450-<=479	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
>=480-<=499	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
>=500	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)

Note to Programmer: Continue for all treatments in Part 1, Part 2, and Part 3. Present Part 2 and Part 3 on separate pages.

Table 2.15
Summary of Frequency of Maximum Change from Baseline for ECG Parameter Corrected QTc Interval

Study Part: 1

	GSK3342830 250 mg (N=XX)	GSK3342830 550 mg (N=XX)	… (N=XX)	Placebo (N=XX)
QTcB (msec)				
n	xx	xx	xx	xx
<=30	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
>30-<=59	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
>=60	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
QTcF (msec)				
n	xx	xx	xx	xx
<=30	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
>30-<=59	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
>=60	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)

Note to Programmer: Continue for all treatments in Part 1, Part 2, and Part 3. Present Part 2 and Part 3 on separate pages.

Note: Baseline is defined as the last nonmissing measurement before dosing for the respective treatment period.
Unscheduled measurements are not included in this summary table except when calculating baseline.

Table 2.16
Summary of Vital Signs

Study Part: 1

Vital Sign	Group	N	Planned Relative Time	n	Mean	SD	Median	Min.	Max.
XXXXXXXX (XXX)	GSK3342830 250 mg	XXX	Baseline	xx	xx.x	xx.xx	xx	xx	xx
			Day 1 - 0.5 HR	xx	xx.x	xx.xx	xx	xx	xx
			...						
			Follow-Up	xx	xx.x	xx.xx	xx	xx	xx
XXXXXXXX (XXX)	GSK3342830 500 mg	XXX	Baseline	xx	xx.x	xx.xx	xx	xx	xx
			...						
XXXXXXXX (XXX)	...	XXX	Baseline	xx	xx.x	xx.xx	xx	xx	xx
			...						

Note to Programmer: Continue for all treatments in Part 1, Part 2, and Part 3. Present Part 2 and Part 3 on separate pages. Timepoints for Part 1 and Part 3 are Baseline, Day 1 - 0.5 HR, Day 1 - 1 HR, Day 1 - 1.5 HR, Day 1 - 2 HR, Day 1 - 3 HR, Day 1 - 4 HR, Day 1 - 6 HR, Day 1 - 12 HR, Day 2, Day 3, Follow-Up. Timepoints for Part 2 are Baseline, Day 1 - 0.5 HR, Day 1 - 1 HR, Day 1 - 1.5 HR, Day 1 - 2 HR, Day 1 - 3 HR, Day 1 - 4 HR, Day 1 - 6 HR, Day 1 - 12 HR, Day 2 through Day 14, Day 15 - 0.5 HR, Day 15 - 1 HR, Day 15 - 1.5 HR, Day 15 - 2 HR, Day 15 - 3 HR, Day 15 - 4 HR, Day 15 - 6 HR, Day 15 - 12 HR, Day 16, and Follow-Up.
Vital sign measurements summarized are: Systolic Blood Pressure (mmHg), Diastolic Blood Pressure (mmHg), Oral Temperature (C), and Pulse Rate (beats per min).

Note: Baseline is defined as the last nonmissing measurement before dosing.
Unscheduled measurements are not included in this summary table except when calculating baseline.

Table 2.17
Summary of Change from Baseline in Vital Signs

Note to programmer: Please use the shell from Table 2.14 and include only Planned Relative Time after Baseline.

Table 3.01
Summary of GSK3342830 Single Dose Plasma Pharmacokinetic Concentration-Time Data (units) by Treatment in Part 1 and Part 3

Part: Part 1

Dose	Study Day	N	Planned Relative Time	n	No. Imputed	Mean	SD	CV%	Median	Min.	Max.
xxx mg	1	xx	pre-dose	xx	xx	NQ	.	.	.	.	.
			0.5h	xx	0	xxxx.x	xx.xx	xx.x	xxxx.x	xxxx	xxxx
			1h	xx	0	xxxx.x	xx.xx	xx.x	xxxx.x	xxxx	xxxx
			1.25h	xx	0	xxxx.x	xx.xx	xx.x	xxxx.x	xxxx	xxxx
			1.5h	xx	0	xxxx.x	xx.xx	xx.x	xxxx.x	xxxx	xxxx
			…	…	…	…	…	…	…	…	…
			…	…	…	…	…	…	…	…	…

Note to Programmer: Present all part 1 first then repeat for Part 3. Blood samples for PK analysis will be collected at predose time point and 0.5, 1,1.25,1.5, 2, 2.5, 3,3.5, 4, 4.5, 5, 6, 8, 10, 12, 16, 24 ,36 and 48 hours after dosing.If mean is below the level of quantification, report the mean value as NQ.

Note: NQ=Not quantifiable.

Source Data: Listing 40

Table 3.02
Summary of GSK3342830 Plasma Pharmacokinetic Concentration-Time Data (units) by Treatment in Part 2

Dose	Day	N	Planned Relative Time	n	No. Imputed	Mean	SD	CV%	Median	Min.	Max.
xxx mg	1	xx	pre-dose	xx	xx	NQ	·	·	·	·	·
			0.5h	xx	0	xxxx.x	xx.xx	xx.x	xxxx.x	xxxx	xxxx
			1h	xx	0	xxxx.x	xx.xx	xx.x	xxxx.x	xxxx	xxxx
			1.25h	xx	0	xxxx.x	xx.xx	xx.x	xxxx.x	xxxx	xxxx
			1.5h	xx	0	xxxx.x	xx.xx	xx.x	xxxx.x	xxxx	xxxx
			…	…	…	…	…	…	…	…	…
	15	xx	pre-dose	xx	xx	NQ	·	·	·	·	·
			0.25h	xx	0	xxxx.x	xx.xx	xx.x	xxxx.x	xxxx	xxxx
			…	…	…	…	…	…	…	…	…

Note to Programmer: Blood samples for PK analysis on day 1 will be collected at predose, 0.5, 1.25,1.5, 2,2.5,3,3.5,4,4.5,5,6,8,10,12,16 and 24. Timepoints on day 15 is Pre-dose,0.5,1,1.25,1.5,2,2.5,3,3.5,4,4.5, 5,6 and 8.If mean is below the level of quantification, report the mean value as NQ.

Note: NQ=Not quantifiable.

Source Data: Listing 42

Table 3.03
Summary of Untransformed GSK3342830 Single Dose Plasma Pharmacokinetic Parameters in Part 1 and Part 3

Part: Part 1

Parameter	Summary Statistics	Dose level					
		XX mg	XX mg	XX mg	XX mg	XX mg	XX mg
Cmax (units)	N	xx	xx	xx	xx	xx	xx
	n	xx	xx	xx	xx	xx	xx
	Arithmetic Mean	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx
	95% CI	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)
	SD	xxxx.xxx	xxxx.xxx	xxxx.xxx	xxxx.xxx	xxxx.xxx	xxxx.xxx
	Median	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx
	Min	xxx	xxx	xxx	xxx	xxx	xxx
	Max	xxx	xxx	xxx	xxx	xxx	xxx

Note to Programmer: Present all Part 1 first, then repeat for Part 3
Additional untransformed parameters include AUC(0-t), AUC(0-∞), Tmax, t1/2, CL, Vss, %AUCex, tlast, lambda_z, lambda_z_lower, lambda_z_upper, lambda_z_no. of points.

Note: NQ=Not quantifiable.
Source Data: Listing 44

Table 3.04
Summary of Log-transformed GSK3342830 Single Dose Plasma Pharmacokinetic Parameters in Part 1 and Part 3

Part: Part 1

Parameter	Summary Statistics	Dose level					
		XX mg	XX mg	XX mg	XX mg	XX mg	XX mg
Cmax (units)	N	xx	xx	xx	xx	xx	xx
	n	xx	xx	xx	xx	xx	xx
	Geometric Mean	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx
	95% CI	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)
	Geometric SD	xxxx.xxx	xxxx.xxx	xxxx.xxx	xxxx.xxx	xxxx.xxx	xxxx.xxx
	%CVb	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx

Note to Programmer: Present all Part 1 first, then repeat for Part 3
Additional untransformed parameters include AUC(0-t), AUC(0-∞), t1/2, CL, Vss.

Note: NQ=Not quantifiable.
Source Data: Listing 45

Table 3.05
Summary of Untransformed GSK3342830 Single Dose Urine Pharmacokinetic Parameters in Part 1 and Part 3

Part: Part 1

Parameter	Summary Statistics	Dose level					
		XX mg	XX mg	XX mg	XX mg	XX mg	XX mg
Ae (units)	N	xx	xx	xx	xx	xx	xx
	n	xx	xx	xx	xx	xx	xx
	Geometric Mean	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx
	95% CI	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)
	Geometric SD	xxxx.xxx	xxxx.xxx	xxxx.xxx	xxxx.xxx	xxxx.xxx	xxxx.xxx
	%CVb	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx

Note to Programmer: Present all Part 1 first, then repeat for Part 3
Additional untransformed parameters include Clr, Feu(0-4) (units), Feu(4-8) (units), Feu(8-12) (units), Feu (12-24) (units), Feu (24-48) (units).

Note: NQ=Not quantifiable.
Source Data: Listing 45

Table 3.06
Summary of Untransformed GSK3342830 Plasma Pharmacokinetic Parameters in Part 2

Day	Parameter	Summary Statistics	Dose level					
			XX mg	XX mg	XX mg	XX mg	XX mg	XX mg
1	Cmax (units)	N	xx	xx	xx	xx	xx	xx
		n	xx	xx	xx	xx	xx	xx
		Arithmetic Mean	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx
		95% CI	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)
		SD	xxxx.xxx	xxxx.xxx	xxxx.xxx	xxxx.xxx	xxxx.xxx	xxxx.xxx
		Median	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx
		Min	xxx	xxx	xxx	xxx	xxx	xxx
		Max	xxx	xxx	xxx	xxx	xxx	xxx

Note to Programmer:
Additional untransformed parameters include AUC(0-t), AUC(0-∞), AUC(0-τ), Tmax, t1/2, CL, Vss, %AUCex, tlast, lambda_z, lambda_z_lower, lambda_z_upper, lambda_z_no. of points, Cτ, Ratio of time invariance, Ratio of accumulation. Repeat for day 15

Note: NQ=Not quantifiable.
Source Data: Listing 46

Table 3.07
Summary of Log-transformed GSK3342830 Plasma Pharmacokinetic Parameters in Part 2

Day	Parameter	Summary Statistics	Dose level					
			XX mg	XX mg	XX mg	XX mg	XX mg	XX mg
1	Cmax (units)	N	xx	xx	xx	xx	xx	xx
		n	xx	xx	xx	xx	xx	xx
		Geometric Mean	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx
		95% CI	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)
		Geometric SD	xxxx.xxx	xxxx.xxx	xxxx.xxx	xxxx.xxx	xxxx.xxx	xxxx.xxx
		%CVb	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx

Note to Programmer:
Additional untransformed parameters include AUC(0-t), AUC(0-∞), AUC(0-τ), t1/2, CL, Vss, Cτ. Repeat for Day 15.

Note: NQ=Not quantifiable.
Source Data: Listing 46

Table 3.08
Summary of Untransformed GSK3342830 Urine Pharmacokinetic Parameters in Part 2

		Summary Statistics					
Day	Parameter	XX mg	XX mg	XX mg	XX mg	XX mg	XX mg
1	Ae (units)	xx	xx	xx	xx	xx	xx
		xx	xx	xx	xx	xx	xx
		xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx
		(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)	(xxxx.x,xxxx.x)
		xxxx.xxx	xxxx.xxx	xxxx.xxx	xxxx.xxx	xxxx.xxx	xxxx.xxx
		xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx	xxxx.xx

Note to Programmer:
Additional untransformed parameters include Clr, Feu(0-8) (units), Feu(8-24) (units). Repeat for Day 15.

Note: NQ=Not quantifiable.
Source Data: Listing 47

Table 3.09
Summary of Statistical Analysis of GSK3342830 Plasma Dose Proportionality in Part 1

Dose (units)	Parameter	Estimated Slope for log(dose)	Standard Error	90% CI Lower-Upper	P-Value (b=1)
XX mg	Cmax (units)	x.xxx	x.xxx	x.xxxx-x.xxxx	x.xxxx
		x.xxx	x.xxx	x.xxxx-x.xxxx	x.xxxx

Note: The power model, log(parameter) = log(a) + b*log(dose), was used to estimate the slope, corresponding 90% confidence interval, and the p-value testing dose proportionality (b=1). Natural log-transformation was used.
Source Data: Listing 44.

Note to programmer: In the case where dose proportionality is not established over the entire dosing range, secondary analysis of dose proportionality will be assessed for select doses over the higher dosing range with the power model or by pair-wise analysis of variance (ANOVA) using the SAS mixed models procedure. If the secondary analysis using the pair-wise ANOVA approach is performed, a reference dose would be chosen based on the lowest clinically relevant dose over which the pharmacokinetics can be adequately described and the other doses would be treated as test doses.

Table 3.10
Summary of Statistical Analysis of GSK3342830 Plasma Dose Proportionality in Part 2

Day	Dose (Units)	Parameter	Estimated Slope for log(dose)	Standard Error	90% CI Lower–Upper	P-Value (b=1)
15	XX mg	Cmax (units)	x.xxx	x.xxx	x.xxxx–x.xxxx	x.xxxx
			x.xxx	x.xxx	x.xxxx–x.xxxx	x.xxxx

Note: The power model, log(parameter) = log(a) + b*log(dose), was used to estimate the slope, corresponding 90% confidence interval, and the p-value testing dose proportionality (b=1). Natural log-transformation was used.
Source Data: Listing 46.

Note to programmer: In the case where dose proportionality is not established over the entire dosing range, secondary analysis of dose proportionality will be assessed for select doses over the higher dosing range with the power model or by pair-wise analysis of variance (ANOVA) using the SAS mixed models procedure. If the secondary analysis using the pair-wise ANOVA approach is performed, a reference dose would be chosen based on the lowest clinically relevant dose over which the pharmacokinetics can be adequately described and the other doses would be treated as test doses.

Table 3.11
Summary of Statistical Analysis of GSK3342830 Plasma Time Invariance in Part 2

Dose: XX mg

Parameter (Unit)	Day	N	Geometric LS Means	Regimen Comparison	Ratio of Geometric LS Means (%)	90% Confidence Interval of Ratio (%)	CVw(%)
AUC(0-inf) (Unit)	1	xx	x.xxx	15/1	x.xxx	(x.xxx, x.xxx)	x.xxx
AUC(0-tau) (Unit)	15	xx	x.xxx				

Notes to programmer: Repeat for each dose level.

Note: A linear mixed-effect model with group (group=1 for AUC(0-inf) on Day 1, and group=2 for AUC(0-tau) on Day 15) as a fixed effect and subject as a random effect was fitted to the natural log transformed PK parameters.
Source Data: Listing 46.

Table 3.12
Summary of Statistical Analysis of GSK3342830 Plasma Accumulation Ratio in Part 2

Parameter (Unit)	Dose* (mg)	Day	N	Geometric LS Means	Regimen Comparison	Ratio of Geometric LS Means (%)	90% Confidence Interval of Ratio (%)	CVw(%)
AUC(0-tau) (Unit)	xx	1	xx	x.xxx	15/1	x.xxx	(x.xxx, x.xxx)	x.xxx
		15	xx	x.xxx				
	yy	1	xx	x.xxx	15/1	x.xxx	(x.xxx, x.xxx)	
		15	xx	x.xxx				
	zz	1	xx	x.xxx	15/1	x.xxx	(x.xxx, x.xxx)	
		15	xx	x.xxx				

Note: A linear mixed-effect model with dose, day, and dose-by-day interaction as fixed effects and subject as a random effect was fitted to the natural log transformed PK parameters.
* If dose-by-day interaction is significant (p-value less then 0.05), then point estimate and 90% CI will be reported for each dose level.
Source Data: Listing 46.

Table 3.13
Summary of Statistical Analysis of GSK3342830 Plasma Steady State Assessment in Part 2

Parameter	Days Included	Estimated Slope for Day	90% CI Lower-Upper
Ctrough (units)	3, 6, 9, 12, 13, 15	x.xxx	x.xxxx-x.xxxx

Note to programmer: If the 90% CI does not include zero, repeat the analysis without the data for the earliest day used in the previous analysis. Display the results for all models run.

Note: A mixed effect model will be fitted by dose and day (as a continuous covariate) as a fixed effect term and subject as a random effect term. No formal statistical hypothesis tested. Steady state is estimated to be achieved by the earliest day included in the analysis when the 90% CI of the slope includes 0.
Source Data: Table 3.06.

Table 3.14
Summary of Model Parameters for Part 1 - Posterior Distributions

PK Parameter on log scale Model Parameter	Mean	SD	MC error	5th Percentile	Median	95th Percentile
AUC[0-t](µg.h/mL)						
Intercept	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x
Slope of log dose	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x
Precision	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x
Cmax (µg/mL)						
Intercept	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x
Slope of log dose	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x
Precision	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x

Note: The posterior distributions are derived from linear model log-PK-parameter = intercept + slope*log-dose + error term.

Programmer note: Decimals will be adjusted to include approximately 5 significant digits.

Table 3.15
Summary of Model Parameters for Part 2 - Posterior Distributions

PK Parameter on log scale Model Parameter	Mean	SD	MC error	5th Percentile	Median	95th Percentile
AUC[0-8]x3(µg.h/mL)						
Intercept	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x
Slope of log dose	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x
Precision	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x
Cmax (µg/mL)						
Intercept	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x
Slope of log dose	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x
Precision	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x

Note: The posterior distributions are derived from linear model log-PK-parameter = intercept + slope*log-dose + error term.

Programmer note: Decimals will be adjusted to include approximately 5 significant digits.

Table 3.16
Summary of PK Parameters for Part 1 - Bayesian Prediction of Individual Subjects

PK Parameter Statistics	250 mg	500 mg	1000 mg	2000 mg	4000 mg	6000 mg
AUC[0-t] (µg.h/mL)						
n	xxx	xxx	xxx	xxx	xxx	xxx
Observed Mean	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x
Predictive Distribution						
Mean	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x
5th Percentile	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x
Median	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x
95th Percentile	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x
Cmax (µg/mL)						
Observed Mean	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x
Predictive Distribution						
Mean	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x
5th Percentile	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x
Median	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x
95th Percentile	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x	xxxx.x

Note: The predictive distributions are derived from linear model log-PK-parameter = intercept + slope*log-dose + error term.

Programming notes:
1. Decimals will be adjusted to include approximately 5 significant digits as a guideline not as a requirement.
2. If no observed values available for some doses, use 'NA' for the observed mean/n.

Table 3.17
Summary of PK Parameters for Part 2 - Bayesian Prediction of Individual Subject

PK Parameter Statistics	1000 mg	2000 mg	4000 mg
AUC[0-8]x3 (µg.h/mL)			
n	xxx	xxx	xxx
Observed Mean	xxxx.x	xxxx.x	xxxx.x
Predictive Distribution			
Mean	xxxx.x	xxxx.x	xxxx.x
5th Percentile	xxxx.x	xxxx.x	xxxx.x
Median	xxxx.x	xxxx.x	xxxx.x
95th Percentile	xxxx.x	xxxx.x	xxxx.x
Cmax (µg/mL)			
Observed Mean	xxxx.x	xxxx.x	xxxx.x
Predictive Distribution			
Mean	xxxx.x	xxxx.x	xxxx.x
5th Percentile	xxxx.x	xxxx.x	xxxx.x
Median	xxxx.x	xxxx.x	xxxx.x
95th Percentile	xxxx.x	xxxx.x	xxxx.x

Note: The predictive distributions are derived from linear model log-PK-parameter = intercept + slope*log-dose + error term.

Programming notes: Decimals will be adjusted to include approximately 5 significant digits.

Table 3.18
Summary of PK Parameters for Part 1 - Bayesian Predictive Probability

PK Parameter	Threshold on actual scale	Probability (greater than threshold | observed data)					
		250 mg	500 mg	1000 mg	2000 mg	4000 mg	6000 mg
AUC[0-t] (µg.h/mL)	3460	x.xx%	x.xx%	x.xx%	x.xx%	xx.xx%	xx.xx%
Cmax (µg/mL)	2590	x.xx%	x.xx%	x.xx%	x.xx%	xx.xx%	xx.xx%

Note: The predictive distributions are derived from linear model log-PK-parameter = intercept + slope*log-dose + error term.

Note: Each probability is the posterior predictive probability of the PK parameter exceeding the threshold, for a hypothetical future study subject.

Programming notes:
Please keep at least 4 decimal points for each probability value. If prob <0.0001, please display as <0.0001. If prob > 0.9999, then display as > 0.9999.

Table 3.19
Summary of PK Parameters for Part 2 – Bayesian Predictive Probability

PK Parameter	Threshold on actual scale	Probability (greater than threshold | observed data)		
		1000 mg	2000 mg	4000 mg
AUC[0-8]x3 (µg.h/mL)	3460	x.xx%	x.xx%	xx.xx%
Cmax (µg/mL)	2590	x.xx%	x.xx%	xx.xx%

Note: The predictive distributions are derived from linear model log-PK-parameter = intercept + slope*log-dose + error term.
Note: Each probability is the posterior predictive probability of the PK parameter exceeding the threshold, for a hypothetical future study subject.

Programming notes:
Please keep at least 4 decimal points for each probability value. If prob <0.0001, please display as <0.0001. If prob > 0.9999, then display as > 0.9999.

Table 3.20
Summary of PK Parameters for Part 1 - Bayesian Inferential Probability

PK Parameter	Threshold on actual scale	Probability (greater than threshold | observed data)					
		250 mg	500 mg	1000 mg	2000 mg	4000 mg	6000 mg
AUC[0-t] (µg.h/mL)	2875	0.xxxx	0.xxxx	0.xxxx	0.xxxx	0.xxxx	0.xxxx
Cmax (µg/mL)	2270	0.xxxx	0.xxxx	0.xxxx	0.xxxx	0.xxxx	0.xxxx

Note: The inferential probability are derived from linear model log-PK-parameter = intercept + slope*log-dose + error term.

Note: Each probability is the posterior inferential probability of the mean PK parameter exceeding the threshold.

Programming notes:
Please keep at least 4 decimal points for each probability value. If prob <0.0001, please display as <0.0001. If prob > 0.9999, then display as > 0.9999.

Table 3.21
Summary of PK Parameters for Part 2 - Bayesian Inferential Probability

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PK Parameter	Threshold on actual scale	Probability (greater than threshold | observed data)		
		1000 mg	2000 mg	4000 mg
AUC[0-8]x3 (µg.h/mL)	2875	0.xxxx	0.xxxx	0.xxxx
Cmax (µg/mL)	2270	0.xxxx	0.xxxx	0.xxxx

Note: The inferential distributions are derived from linear model log-PK-parameter = intercept + slope*log-dose + error term.
Note: Each probability is the posterior inferential probability of the mean PK parameter exceeding the threshold.

Programming notes:
Please keep at least 4 decimal points for each probability value. If prob <0.0001, please display as <0.0001. If prob > 0.9999, then display as > 0.9999.

Table 3.22
Summary of Statistical Analysis of GSK3342830 Single Dose Plasma Pharmacokinetic Parameters in Part 1 and Part 3 Subjects

Parameter (Unit)	Dose (mg)	Study Part	N	Geometric LS Means	Regimen Comparison	Ratio of Geometric LS Means (%)	90% Confidence Interval of Ratio (%)
AUC(0-t) (Unit)	xx	Part 1	xx	x.xxx	Part 3/Part 1	x.xxx	(x.xxx, x.xxx)
		Part 3	xx	x.xxx			
AUC(0-inf) (Unit)	yy	Part 1	xx	x.xxx	Part 3/Part 1	x.xxx	(x.xxx, x.xxx)
		Part 3	xx	x.xxx			
Cmax (Unit)	zz	Part 1	xx	x.xxx	Part 3/Part 1	x.xxx	(x.xxx, x.xxx)
		Part 3	xx	x.xxx			

Note: A linear mixed-effect model with study part as fixed effect was fitted to the natural log transformed PK parameters.
Part 1 subjects were normal healthy volunteers and Part 3 subjects were Japanese healthy volunteers.
Source Data: Listing 44.