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

Title	:	Reporting and Analysis Plan for a single-centre, double-blind (sponsor open), placebo controlled two part study to evaluate the safety, tolerability and pharmacokinetics of single and repeat doses of GSK2292767 as a dry powder in healthy participants who smoke cigarettes.
Compound Number	:	GSK2292767
Effective Date	:	23-May-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 202062.
- This RAP is intended to describe the safety, pharmacokinetic and exploratory pharmacodynamic analyses required for the study.
- This RAP will be provided to the study team members to convey the content of the Statistical Analysis Complete (SAC) deliverable.

Author's Name and Functional Area:

Approver	Date	Approval Method
PPD Principal Statistician (Clinical Statistics)	NA (Author)	
PPD Clinical Pharmacology	19-May-2017	Approval via E-mail

RAP Team Approvals:

Approver	Date	Approval Method
PPD Programming Manager (Respiratory Clinical Programming)	15-May-2017	E-mail
PPD Data Quality Lead (Respiratory CPSSO Data Management)	19-May-2017	E-mail
PPD Programmer/Analyst (Respiratory Clinical Programming)	18-May-2017	E-mail
PPD Clinical Development Manager (Respiratory R&D Projects Clinical Platforms and Sciences)	15-May-2017	E-mail
PPD Director of Human Translational Models and Biomarkers (Respiratory TAU & Flexible Discovery Unit)	17-May-2017	E-mail
PPD Medical Director, SERM (Global Medical)	16-May-2017	E-mail
PPD Head (Respiratory TAU & Flexible Discovery Unit)	18-May-2017	E-mail

Clinical Statistics and Clinical Programming Line Approvals:

Approver	Date	Approval Method
PPD Director, Statistics & Programming	23-May-2017	E-mail
PPD Manager, Programming	22-May-2017	E-mail

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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: • Planned analyses and output for the final data.
Protocol	• This RAP is based on Protocol Amendment 1(Dated: 05/JAN/2017) of study 202062 (GlaxoSmithKline Document Number 2016N288743_01)
Primary Objective	• To assess the safety and tolerability of single and repeat doses of GSK2292767 as a dry powder in healthy cigarette smokers.
Primary Endpoint	• Safety and tolerability of GSK2292767 as assessed by clinical monitoring of: Vital Signs Spirometry Electrocardiogram (ECG) Laboratory safety data Adverse events (AEs)
Study Design	• This is a two part, single site, randomised, double-blind (sponsor open), placebo controlled study in healthy smokers. • Part A will consist of two 3-period interlocking cohorts. • Part B is planned to follow Part A and is a parallel group design. The highest well tolerated dose achieved in Part A will be selected for Part B.
Planned Analyses	• All decisions regarding final analysis, as defined in this RAP document, will be made prior to Database Freeze (unblinding) of the study data.
Primary Analysis Population	• Primary: Safety Population (Comprised of subjects who receive at least one dose of study treatment and will be based on the treatment which the subject actually received).
Estimation	• An estimation and inference approach will be adopted to evaluate the objectives.
Primary Analyses	• Safety data will be presented in tabular and/or graphical format and summarised descriptively according to GSK's Integrated Data Standards Library (IDSL) standards.
Secondary Analyses	• Pharmacokinetic: Individual GSK2292767 plasma concentration-time profiles (by treatment and subject) and median/mean (±SD) profiles by treatment group will be plotted. Plasma concentration time data for GSK2292767 will be analyzed by non-compartmental methods using WinNonlin and derived PK parameters will be graphically presented, summarised and listed. Data will be analysed for dose proportionality and dose accumulation, peak to trough ratio and steady state. • Pharmacodynamic: All endpoints will be presented in graphical format and/or summarised descriptively and listed.

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

One of the protocol defined endpoints was:

Semi quantitative characterisation of intracellular distribution of GSK2292767 within lung resident cells, binding and lysosomal uptake and retention.

Unfortunately, this binding and lysosomal work failed during preliminary investigation and so only the imaging of the cell for drug will be investigated, though it is uncertain whether the compound ionises sufficiently to allow detection.

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

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To assess the safety and tolerability of single and repeat doses of GSK2292767 as a dry powder in healthy cigarette smokers.	Safety and tolerability of GSK2292767 as assessed by clinical monitoring of: • Vital Signs • Spirometry • ECG • Laboratory safety data • Adverse events (AEs)
Secondary Objectives	**Secondary Endpoints**
• To determine the pharmacokinetic profile of single and repeat doses of GSK2292767 as a dry powder in healthy cigarette smokers	• GSK2292767 plasma concentration data and derived pharmacokinetic parameters including area under the plasma drug concentration versus time curve ($AUC_{(0-t)}$, $AUC_{(0-24)}$, $AUC_{(0-\infty)}$), maximum observed plasma drug concentration (C_{max}), time to maximum observed plasma drug concentration (T_{max}),terminal half-life ($T_{1/2}$) and trough concentrations ($C\tau$) following single and repeated dry powder doses, where data allow.
• To investigate the steady-state trough concentration of GSK2292767 in lung epithelial lining fluid (ELF) and Bronchoalveolar lavage (BAL) cell pellet after repeat inhaled dry powder administration in healthy cigarette smokers.	• BAL concentrations of GSK2292767 and derived lung ELF and cell pellet deposition parameters.

Objectives	Endpoints
Exploratory Objectives	**Exploratory Endpoints**
• To determine the pharmacodynamic effect of GSK2292767 on the biomarker Phosphatidylinositol (3,4,5)-trisphosphate (PIP3) in induced sputum after single and repeat doses of GSK2292767 administered as a dry powder in healthy cigarette smokers.	• PIP3 peak area as a proportion of (PIP3 peak area + Phosphatidylinositol (4,5)-bisphosphate [PIP2] peak area) in induced sputum cells.
• To explore the intracellular distribution, binding and lysosomal disposition of GSK2292767 from lung resident cells derived from bronchoalveolar lavage at steady-state following repeat administration	• Semi quantitative characterisation of intracellular distribution of GSK2292767 within lung resident cells, binding and lysosomal uptake and retention.
• To generate samples that will be used to characterise the metabolic profile of GSK2292767 in plasma, following single and repeat doses of GSK2292767 administered as a dry powder in healthy cigarette smokers.	• Characterisation and quantification of metabolites in plasma.
• To collect urine samples only at the highest proposed dose level to characterise the renal excretion of systemically available drug following inhaled delivery.	• Semi-quantitative characterisation of amount of parent GSK2292767 excreted in urine

3. PLANNED ANALYSES

3.1. Interim Analyses

No formal statistical analysis is planned.

A review of preliminary safety and pharmacokinetic data will be conducted prior to selection of the doses for Part A and before confirmation of the dose for Part B. Safety data will be provided by the site at the end of each dosing session. Pharmacokinetic data will be provided by or under the auspices of Clinical Pharmacokinetics Modelling & Simulation (CPMS) using Phoenix WinNonlin.

The decision to proceed to the next dose level of GSK2292767 in Part A and the selection of the daily dose level to be tested in Part B will be made by the GSK Study Team and the investigator based on blinded safety data (AE, vital signs, ECG and laboratory safety test) and preliminary blinded PK data (up to 24 h) obtained in at least 5 subjects on active

drug at the previous dose level. For a detailed description of the dose justification please refer to protocol Section 10.3.4.

3.2. Final Analyses

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

1. All subjects from both study parts 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 RandAll NG procedures.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Screened	• Comprise of all subjects who were screened	• Listings
Safety	• Comprise of all subjects who receive at least one dose of study treatment. • This population will be based on the treatment the subject actually received.	• Study Population • Safety • Pharmacodynamic
Pharmacokinetic	• Subjects in the 'Safety' population for whom a pharmacokinetic sample was obtained and analysed. • This population will be based on the treatment the subject actually received.	• PK

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.
- 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. 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
Section 10.1	Appendix 1: Time & Events
Section 10.2	Appendix 2: Assessment Windows
Section 10.3	Appendix 3: Treatment States and Phases
Section 10.4	Appendix 4: Data Display Standards & Handling Conventions
Section 10.5	Appendix 5: Derived and Transformed Data
Section 10.6	Appendix 6: Premature Withdrawals & Handling of Missing Data
Section 10.7	Appendix 7: Values of Potential Clinical Importance
Section 10.8	Appendix 8: Model Checking and Diagnostics for Statistical Analyses.
Section 10.9	Appendix 9: Population Pharmacokinetic Analyses
Section 10.10	Appendix 10: Abbreviations and Trademarks
Section 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		
	Figure	Table	Listing
Randomisation			
Randomisation			Y
Subject Disposition			
Subject Disposition		Y	
Reasons for Screening Failures			Y
Important Protocol Deviations		Y	Y
Inclusion and Exclusion Criteria Deviations		Y	Y
Demography			
Demographics Characteristics		Y	Y
Race & Racial Combinations		Y	Y
Study Populations		Y	Y
Medical Condition & Concomitant Medications			
Medical Conditions (Current/Past)		Y	
Concomitant Medication		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.

7.1.2. During the Study

As required, ongoing data reviews will be conducted by the study team of the unblinded safety data, throughout the trial progression.

7.1.2.1. Dose Escalations

- The principal investigator and medical monitor will provide an overall summary of the required safety data for the dose escalation review for progressing to the next cohort, as defined in the protocol.

7.1.3. Final Safety Data

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

Endpoint / Parameter/ 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 (Safety population)	Y			Y				
Drug-related AEs	Y							
Serious AEs				Y				
AEs leading to withdrawal				Y				
Relationship between SOC and verbatim text				Y				
AEs by Preferred Term with Occurrences >=5% in any treatment arm	Y							
Laboratory Data								
Clinical Chemistry				Y[1]	Y			
Haematology				Y[1]	Y			
Urinalysis Data				Y[1]	Y			
ECG								
ECG Values		Y	Y	Y[2]	Y			
ECG Findings	Y			Y				
Frequency of Maximum ECG Values by Pre-Specified Categories	Y							
Vital Signs								
Vital Signs Values				Y[3]	Y			
Spirometry								
Lung Function Parameters				Y	Y			

NOTES:

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

[1]Two Listings of chemistry and haematology data will be produced. One will list all abnormalities of PCI and the other will list all chemistry/haematology data for all subjects with any chemistry/haematology abnormalities.

[2]Two listings of ECG data will be produced. One will list all ECG abnormalities of PCI and the other will list all ECG data for all subjects with any ECG PCI values.

[3]Two listings of vital signs data will be produced. One will list all vital signs abnormalities of PCI and the other will list all vital signs data for all subjects with any vital signs PCI values.

8. SECONDARY STATISTICAL ANALYSES

8.1. Pharmacokinetic Analyses

8.1.1. Overview of Planned Pharmacokinetic Analyses

The following PK analyses will only be performed if sufficient data are available (i.e., if subjects have well defined plasma profiles). Analyses will be performed on the Pharmacokinetic Population.

8.1.2. Drug Concentration Measures

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

8.1.2.1. Overview of Planned Pharmacokinetic Analyses for Drug Concentrations

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

Table 4 Overview of Planned Pharmacokinetic Data

Endpoints	Untransformed				Log-Transformed			
	Summary		Individual		Summary		Individual	
	F	T	F	L	F	T	F	L
Plasma Drug Concentrations	Y [1] [2]	Y	Y [1]	Y		Y	Y	
Derived PK Parameters		Y		Y		Y		
Urine PK Data		Y						
Lung ELF and Cell Pellet	Y	Y					Y	

NOTES:

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

1. Linear and Semi-Log plots will be created on the same display.
2. Median plots will be generated.

8.1.3. Pharmacokinetic Parameters

8.1.3.1. Deriving Pharmacokinetic Parameters

- Refer to Appendix 4: Data Display Standards & Handling Conventions (Section 10.4.3 Reporting Process & Standards).
- The pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using Nonlin Pro.
- All calculations of non-compartmental parameters will be based on actual sampling times recorded during the study.

- Pharmacokinetic parameters described in Table 5 will be determined from plasma GSK2292767 concentration-time data, as data permit.

Table 5 Derived Pharmacokinetic Parameters

Parameter	Parameter Description
AUC(0-t)	Area under the concentration-time curve from time zero to the time of the last quantifiable concentration (C(t)) will be calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid.
AUC(0-24)	Area under the concentration-time curve over the dosing interval.
AUC(0-∞)	Area under the concentration-time curve extrapolated to infinity will be calculated as follows: AUC = AUC(0-t) + C(t)/λz.
Cmax	Maximum observed concentration, determined directly from the concentration-time data.
Cτ	Trough concentration
Tmax	Time to reach Cmax, determined directly from the concentration-time data.
T½	Apparent terminal half-life will be calculated as: **t½ = ln2 / Lambda_z** (NOTE: λz is the terminal phase rate constant).

NOTES: Additional parameters may be included as required.

8.1.4. BAL Parameters

No pharmacokinetic parameters will be derived for BAL data. The corrected concentrations will be listed, summarised and plotted.

8.1.5. Single Dose Escalation (Part A)

Table 6 Overview of Dose Proportionality Summaries

Endpoint / Parameter/ 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
Dose Proportionality														
Dose Proportionality: Power Model								Y						
Dose Proportionality: ANOVA Method								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.

Boxplots of dose-normalised AUC(0-t), Ctau and Cmax versus dose will be produced, a separate plot for each PK parameter. To calculate the dose normalised parameters, the derived parameter for each dose will be divided by the relevant dose and multiplied by the chosen nominal dose (100ug). If, in the opinion of the Clinical Pharmacology representative, there are a high number of LLQ values at the 100ug dose then another nominal dose will be agreed prior to DBF.

8.1.5.1. Statistical Analysis of Dose Proportionality

The following pharmacokinetic statistical analyses will only be performed if sufficient data are available (i.e. if more than 6 subjects have well defined plasma profiles). If the dose with limited data is at the lower end of the dose range, the data will be excluded and the appropriate analysis conducted on the rest of the data. However if there are non-calculable PK parameter data at intermittent doses no statistical analyses will be performed. A minimum of 3 doses will be required to assess dose proportionality. The assessment of dose proportionality will utilise Part A data only.

Pharmacokinetic Statistical Analyses for Dose Proportionality: Power Method
Endpoint(s)
• AUC(0-t), Cτ, Cmax • Each endpoint to be assessed separately.
Model Specification
• loge(Y) = β × loge(dose) + loge(α) where Y is the pharmacokinetic parameter and loge(α) is an intercept term.
Model Checking & Diagnostics
• Refer to Appendix 8: Model Checking and Diagnostics for Statistical Analyses.
Model Results Presentation
• The coefficient of the slope with 90% confidence intervals, on the log scale, will be calculated, using the pooled estimate of variance, and used to assess dose proportionality. • Point estimates and confidence intervals for the slope will be reported to 2 decimal places

The ANOVA method will also be used to assess dose proportionality.

Pharmacokinetic Statistical Analyses for Dose Proportionality: ANOVA Method
Endpoint(s)
• AUC(0-t), Cτ, Cmax • Each endpoint to be assessed separately.
Model Specification
• The PK parameter will be dose-normalised prior to loge-transformation by multiplying by reference dose / dose • Dose will be fitted as a fixed effect, subject as a random effect using DDFM=KR. • Separate lines will be fitted for each cohort by including terms for cohort and cohort*$\log_e$(dose). If the slopes are not significantly (p-value<0.05) different from each other, the interaction term will be removed and a single slope estimate obtained. If the slopes are significantly different from each other, a separate slope estimate and associated 90% confidence interval will be reported for each cohort. • The reference dose will be chosen based on the lowest clinically relevant dose over which PK can be adequately described, with each other dose as the test doses in the construction of the ratio μ(test)/μ(reference).
Model Checking & Diagnostics
• Refer to Appendix 8: Model Checking and Diagnostics for Statistical Analyses.
Model Results Presentation
• Point estimates for the adjusted means on the $\log_e$ scale, the mean difference between each dose (test) and the reference dose and associated 90% confidence interval will be constructed using the residual variance. These will not be presented. • The point estimate and confidence interval will then be exponentially back-transformed to allow the presentation of the adjusted (least square) geometric means for each treatment (dose), and point estimates and associated 90% confidence intervals for the ratio test/reference. • Point estimates and 90% confidence intervals for AUC, Cmax and Cτ will be reported to 2 decimal places Treatment ratios and 90% CIs will be plotted by dose. • Plots will also be provided showing the adjusted geometric mean ratio of test to reference treatment (dose) for AUC(0-∞), AUC(0-t), Cτ and Cmax together with 90% confidence interval.

8.1.6. Repeat Dose (Part B)

- If more than 1 cohort is recruited in order to investigate more than 1 repeat dose then cohort will be added as a covariate. Only Part B data will be analysed for the repeat dose assessments.

Table 7 Overview of Repeat Dose Summaries

Endpoint / Parameter/ 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
Repeat Dose														
Dose Accumulation								Y						
Steady State												Y		
Peak to Trough Ratios								Y						

NOTES:

- T = Table, F = Figure, L = Listings, Y = Display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

8.1.6.1. Statistical Analysis of Dose Accumulation and Steady State

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

Pharmacokinetic Statistical Analyses
Endpoint(s)
• Dose Accumulation: AUC(0-24), Cτ, Cmax on Day 14 compared to Day 1 • Each endpoint to be assessed separately following a log-transformation.
Model Specification
• A mixed effect model will be fitted with day as a fixed effect and subject as a random effect. • The Kenward & Roger (KR) degrees of freedom approach will be used. • Day 14 will be compared to Day 1 in order to estimate the accumulation ratio(s) • The accumulation ratio(s) and 90% confidence interval will be calculated by back-transforming the difference between the least square means for the two days and associated 90% confidence interval.
Model Checking & Diagnostics
• Refer to Appendix 8: Model Checking and Diagnostics for Statistical Analyses.
Model Results Presentation
• Point estimates and confidence intervals for the ratios will be reported to 2 decimal places • Scatter plots of each endpoint against day will be produced. The data points for each subject will be joined with straight lines. If there is more than 1 cohort each treatment will be put on a separate page. • Boxplots of each endpoint against day will be produced. If there is more than 1 cohort each treatment will be put on a separate page.

8.1.6.2. Statistical Analysis of Peak to Trough Ratio

Pharmacokinetic Statistical Analyses
Endpoint(s)
• Peak to trough ratio: Cmax/Ctrough.
Model Specification
• A mixed effect model will be fitted with day*parameter as a fixed effect and subject as a random effect. • The Kenward & Roger (KR) degrees of freedom approach will be used. • Response variable will be the logged peak concentrations and the logged trough concentrations. • Indicator variables will be included to distinguish between the peak and trough concentration data. • The differences in lsmeans of the peak and trough concentrations on each day will be back-transformed to obtain estimates of the peak to trough ratios on each day.
Model Checking & Diagnostics
• Refer to Appendix 8: Model Checking and Diagnostics for Statistical Analyses.
Model Results Presentation
• Peak to trough ratios will be tabulated displaying the adjusted mean (and 90% CIs) Cmax and Ctrough values together with the ratios and corresponding 90% CIs.

8.1.7. Population Pharmacokinetic Analyses

A PME/MAP compliant file will be generated for this study to enable population PK model development, if possible (dependent on data). Data from subjects from both study parts (Parts A and B) will be provided in this file, even for subjects who may not have received a full dose. Such subjects may be included in any subsequent POP PK analysis.

An example file structure is provided in the attachments in Section 10.11. The PME/MAP compliant file will be produced by or under the auspices of Clinical Statistics (Programming).

8.2. Pharmacodynamic Analyses (Parts A and B)

8.2.1. Overview of Planned Pharmacodynamic Analyses

Analyses will be performed separately for each study part.

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

Table 8 provides an overview of the planned pharmacodynamic analyses, with full details of data displays being presented in Appendix 11: List of Data Displays.

Table 8 Overview of Planned Pharmacodynamic Analyses

Endpoint / Parameter/ 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
Phospholipid Data														
PIP2 peak area				Y			Y				Y		Y	
PIP3 peak area				Y			Y	Y	Y		Y		Y	
PIP3 peak area proportion (of PIP2 peak area and PIP3 peak area)				Y			Y	Y	Y		Y		Y	

NOTES:

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

8.2.2. Planned Pharmacodynamic Statistical Analyses

Planned Statistical Analyses

Endpoint(s)

- PIP3 Peak Area proportion (calculated as a proportion of the sum of PIP2 Peak Area and PIP3 Peak Area i.e. PIP3 Peak Area / (PIP2 Peak Area + PIP3 Peak Area))

Model Specification

- Repeated measures analysis based on the two replicates for each subject on each study day.
- Replicates are to be modeled using VC (variance components) structure
- Response variable: Loge(PIP3 Peak Area proportion) .
  The following will be included as fixed effects:
  Part A: period, treatment*daytime
  Part B: treatment*daytime*base
  Where daytime can take the values:
  Part A: ‘Day 1 3h’, ‘Day 1 24h’
  Part B: ‘Baseline’, ‘Day 1 3h’, ‘Day 1 24h’, ‘Day 12 3h’, ‘Day 12 24h’
- Daytime and subject will be fitted as random effects

Model Checking

- Refer to Appendix 8: Model Checking and Diagnostics for Statistical Analyses.

Planned Statistical Analyses
Model Results Presentation
• Adjusted geometric means for each treatment group will be presented along with 90% confidence intervals (CIs). • Part A: Point estimates of the treatment differences versus placebo and their associated 90% CIs will be calculated for both timepoints (using the pooled estimate of variance) and back transformed to provide estimates and 90% CIs for the treatment ratios. • Part B: Point estimates of the daytime differences versus placebo and their associated 90% CIs will be calculated (using the pooled estimate of variance) and back transformed to provide estimates and 90% CIs for the treatment ratios at each timepoint. • Bayesian posterior probabilities of seeing differences from placebo less than 0 (ratio less than 1) will be displayed. • Adjusted geometric means (for each treatment group and timepoint) and treatment ratios, along with 90% CIs will be plotted.

9. REFERENCES

GlaxoSmithKline Document Number 2016N288743_01 Study ID 202062. A single-centre, double-blind (sponsor open), placebo controlled two part study to evaluate the safety, tolerability and pharmacokinetics of single and repeat doses of GSK2292767 as a dry powder in healthy participants who smoke cigarettes. Report Date 05-Jan-2017.

Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault JC. Lung Volumes and Forced Ventilatory Flows. *Eur Respir J.* 1993;Suppl 16:5-40.

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: Assessment Windows
Section 10.3	Appendix 3: Treatment States & Phases
Section 10.4	Appendix 4: Data Display Standards & Handling Conventions • Study Treatment & Sub-group Display Descriptors • Baseline Definitions & Derivations • Reporting Process & Standards
Section 10.5	Appendix 5: Derived and Transformed Data • General, Study Population & Safety • Efficacy • Pharmacokinetic • Pharmacodynamic and or Biomarkers
Section 10.6	Appendix 6: Premature Withdrawals & Handling of Missing Data • Premature Withdrawals • Handling of Missing Data
Section 10.7	Appendix 7: Values of Potential Clinical Importance
Section 10.8	Appendix 8: Model Checking and Diagnostics for Statistical Analyses
Section 10.9	Appendix 9: Population Pharmacokinetic 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

10.1.1.1. SOA – Part A (Single Dose)

Procedure	Part A (Single Dose) Treatment Period														Notes
	Day -1	Day 1 (time relative to dosing)													
		Pre dose	0h	5m	30m	45m	1h	2h	3h	4h	6h	8h	12h	24h	
Admission to Unit	X														
Urine Drug/Alcohol breath test	X														
Urine Pregnancy test	X														
Brief Physical Exam	X													X	
Laboratory Assessments	X													X	
Meals	X							X						X	See Section 6.3.1 of protocol
12-lead ECG (single)		X				X				X			X	X	
Vital signs (single)		X			X		X				X		X	X	

Procedure	**Part A (Single Dose) Treatment Period**													**Notes**
	Day -1	**Day 1 (time relative to dosing)**												
		Pre dose	**0h**	**5m**	**30m**	**45m**	**1h**	**2h**	**3h**	**4h**	**6h**	**8h**	**12h**	**24h**	
Telemetry		←==========→													Cardiac telemetry: To start approximately1hr Pre-dose and then continuously for the first 5h post dose.
Spirometry (triplicate)		X					X								
Pharmacokinetic and Metabolite Profile Blood Sample		X		X	X	X	X	X	X	X	X	X	X	X	
Pharmacokinetic Urine Sample		X	←==========→												Only for the maximum proposed dose group if escalated up to (2000 µg).
Inhaler Training	X														
Dosing			X												
Sputum induction									X					X	
Adverse Event Review		←==========→													
Concomitant Medication Review		←==========→													
Discharge														X	

10.1.1.2. SOA – Part B (Repeat Dose)

Procedure	Part B (Repeat Dose) Study Day																			Notes
	D -2 or D -1	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	D14	D15 (D14 +24h)	D16 (D14 +48h	D17 (D14 +72h	D18 (D14 +96h	
Admission to Unit	X																			
Urine Drug/Alcohol	X																			
Urine Pregnancy test	X																			
Brief Physical Exam	X																			
Laboratory Assessments	X		X[1]		X[1]		X[1]		X[1]		X[1]		X[1]		X[1]	X				1. Perform assessment pre dose
Meals	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X				See Section 6.3.1 of protocol
12-lead ECG (single)	X	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X				2. Perform assessments pre dose and at 30 mins post dose.
Vital signs (single)	X	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X[3]	X				3. Perform assessments pre dose.
Spirometry (triplicate)	X	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]	X[4]					4. Perform assessment pre dose and 1h post dose.
Pharmacokinetic Blood Sample		X[6]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[5]	X[6]	X	X[7]	X[7]	X[7]	5. pre-dose and 5 min post dose. 6. pre-dose, 5 mins, 30 mins, 45 mins, 1, 2, 3, 4, 6, 8 and 12h post dose 7. If following Single dose (SD) PK analysis deemed necessary.

Procedure	Part B (Repeat Dose) Study Day																			Notes
	D -2 or D -1	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	D14	D15 (D14 +24h)	D16 (D14 +48h	D17 (D14 +72h	D18 (D14 +96h	
Blood Sample for Metabolic Profiling															X[6]	X	X[7]	X[7]	X[7]	
Urea Blood Sample																X				Collect sample just before bronchoscopy
Inhaler Training	X																			
Dosing		X	X	X	X	X	X	X	X	X	X	X	X	X	X					
Sputum induction	X[11]	X[8]											X[9] [10]							8. 3h post dose 9. 3h and 24h 10. Should sputum induction fail or be insufficient at any time point then the participant will be allowed to return 24h later for a further attempt to obtain an adequate sample 11. Should sputum induction fail or be insufficient then the participant will be allowed to return 24h later for a further attempt to obtain an adequate sample. Failure to produce a baseline sample will result in participant withdrawal.

Procedure	Part B (Repeat Dose) Study Day																			Notes
	D -2 or D -1	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	D14	D15 (D14 +24h)	D16 (D14 +48h	D17 (D14 +72h	D18 (D14 +96h	
Bronchoscopy																X				
Adverse Event Review		←==========→																		
Concomitant Medication Review		←==========→																		
Discharge																X				

10.2. Appendix 2: Assessment Windows

10.2.1. Definitions of Assessment Windows for Analyses

Analysis Set / Domain	Parameter (if applicable)	Target	Analysis Window		Analysis Timepoint
			Beginning Timepoint	Ending Timepoint	
e.g. "Safety", "Efficacy" or list specific domains if required	e.g. "All" or list specific parameters (i.e. tests) if required	The target or most desired relative day or relative time value for a given visit. e.g. "Day 7"	e.g. "Day 1"	e.g. "Day 10"	e.g. VISIT 1
Pharmacodynamic	Sputum PIP data	Day -2 or Day -1 (Part B)	Predose		PREDOSE
		Day 1 3h (Parts A and B)	Day 1 2h45m	Day 1 3h15m	Day 1 3h
		Day 1 24h (Part A)	Day 1 22h30m	Day 1 25h30m	Day 1 24h
		Day12 3h (Part B)	Day 12[1] 2h45m	Day 12[1] 3h15m	Day 12 3h
		Day 12 24h (Part B)	Day 12[1] 22h30m	Day 12[1] 25h30m	Day 12 24h

NOTES :

- All other data will be summarised using the planned timepoint.

[1] Note that if subject is unable to provide a sputum sample on Day 12, then they may have another attempt on Day 13. If this happens then the Day 12 windowing timing will be relative to the Day 13 dose rather than the Day 12 dose.

10.3. Appendix 3: Treatment States and Phases

10.3.1. Treatment Phases

Assessments and events will be classified according to the time of occurrence relative to study treatment unless otherwise specified.

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

10.3.2. 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.

10.3.2.1. Treatment States for Concomitant Medication Data

Treatment State	Definition
Pre-Treatment	Medication End Date ≤ Study Treatment Start Date
On-Treatment	Study Treatment Start Date <= Conmed Start Date ≤ Study Treatment Stop Date Study Treatment Start Date <= Conmed End Date
Post-Treatment	ConMed Start Date > Study Treatment Stop Date

NOTES:

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

10.3.2.2. Treatment States for AE Data

Treatment State	Definition
Pre-Treatment	AE Start Date < Study Treatment Start Date
On-Treatment	If AE onset date is on or after treatment start date & on or before treatment stop date. Study Treatment Start Date ≤ AE Start Date ≤ Study Treatment Stop Date
Post-Treatment	If AE onset date is after the treatment stop date. AE Start Date > Study Treatment Stop Date
Onset Time Since 1st Dose (Days)	If Treatment Start Date > AE Onset Date = AE Onset Date - Treatment Start Date If Treatment Start Date ≤ AE Onset Date = 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 PIMS OR value is missing.

NOTES:

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

10.4. Appendix 4: Data Display Standards & Handling Conventions

10.4.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions			
RandAll NG		Data Displays for Reporting	
Code	Description	Description[2]	Order [1]
A	Placebo inhaled single dose	Placebo	1
B	50ug GSK2292767 inhaled single dose	50ug OD	2
C	Dose Level 2 GSK2292767 inhaled single dose	100ug OD	3
D	Dose Level 3 GSK2292767 inhaled single dose	200ug OD	4
E	Dose Level 4 GSK2292767 inhaled single dose	500ug OD	5
F	Dose Level 5 GSK2292767 inhaled single dose	1000ug OD	6
G	Dose Level 6 GSK2292767 inhaled single dose	2000ug OD	7
H	Placebo inhaled repeat dose	Placebo	1
I	Dose Level 7 GSK2292767 inhaled repeat dose	XXXXug OD	2

NOTES:

1. Order represents treatments being presented in TFL, as appropriate.
2. Replace X's with the actual agreed dose for the cohort and period.

10.4.2. Baseline Definition & Derivations

10.4.2.1. Baseline Definitions

For all endpoints the baseline value will be the latest pre-dose assessment. For Part A, baseline definitions are applicable to each period. Note that no baseline sputum assessments are planned for Part A so any comparisons will be purely versus placebo at the corresponding timepoints.

10.4.2.2. Derivations and Handling of Missing Baseline Data

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

NOTES:

- Unless otherwise specified, the baseline definitions specified in Section 10.4.2. 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.

10.4.3. Reporting Process & Standards

Reporting Process	
Software	
• The currently supported versions of SAS software (Version 9.4) will be used.	
Reporting Area	
HARP Server	: : UK1SALX00175.corpnet2.com
HARP Area	Two reporting efforts will be set up for this study, 1 for Part A (Final_01) and 1 for Part B (Final_02).
QC Spreadsheet	: ARPROD\ GSK 2292767 \202062\Final\Documents
Analysis Datasets	
• Analysis datasets will be created according to Integrated Data Standards Library.	
Generation of RTF Files	
• RTF files will be generated for all tables	

Reporting Standards
General
• The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated: ○ 4.03 to 4.23: General Principles ○ 5.01 to 5.08: Principles Related to Data Listings ○ 6.01 to 6.11: Principles Related to Summary Tables ○ 7.01 to 7.13: Principles Related to Graphics
Formats
• All data will be reported according to the actual treatment the subject received unless otherwise stated. • GSK IDSL Statistical Principles (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.

Reporting Standards	
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 and or within geometric coefficient of variation (CVb/w (%)) will be reported. [1] CV_b (%) = $\sqrt{}$ (exp(SD^2) - 1) * 100 (SD = SD of log transformed data) [2] CV_w (%) = $\sqrt{}$ (exp(MSE) - 1) * 100 (MSE = mean square error from mixed effect model of loge-transformed data).
Parameters Not Being Log Transformed	Tmax
Summary Tables	All provided PK parameters will be summarised except Lamz, lamzUL, LamzLL, LamzNP and AUC % extrapolated area (if calculated).
Listings	Additionally, include the first point, last point and number of points used in the determination of lambda_z for listings.
Graphical Displays	
• Refer to IDSL Statistical Principles 7.01 to 7.13. • All graphics will be done using the SGPLOT/SGPANEL/SG template procedures. • Where possible, n's will be displayed in summary plots.	

10.5. Appendix 5: Derived and Transformed Data

10.5.1. General

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

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

Insert as Required
• Insert as Required

10.5.2. Study Population

Demographics
Age

• Age will be calculated based on year of birth compared to the date of the screening visit.
• GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as follows:
  ○ Any subject with a missing day will have this imputed as day '15'.
  ○ Any subject with a missing date and month will have this imputed as '30th June'.
• Birth date will be presented in listings as 'YYYY'.

Body Mass Index (BMI)
• Calculated as **Weight (kg) / (Height (m))^2**

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

10.5.3. Safety

ECG Parameters
RR Interval
• IF RR interval (msec) is not provided directly, then RR can be derived as: If QTcB is machine read & QTcF is not provided, then: $$RR = \left[\left(\frac{QT}{QTcB}\right)^2\right] * 1000$$ If QTcF is machine read and QTcB is not provided, then: $$RR = \left[\left(\frac{QT}{QTcF}\right)^3\right] * 1000$$ • If ECGs are manually read, the RR value preceding the measurement QT interval should be a collected value THEN do not derive.
Corrected QT Intervals
• When not entered directly in the eCRF, corrected QT intervals by Bazett's (QTcB) and Fridericia'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 : $$QTcB = \frac{QT}{\sqrt{\frac{RR}{1000}}} \qquad QTcF = \frac{QT}{\sqrt[3]{\frac{RR}{1000}}}$$

Adverse Events
AE'S OF Special Interest
• No AE's of special interest have been defined yet. These will not be identified or summarised for SAC.

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

10.5.4. Calculation of Spirometry Screening Parameters

- Derived parameters for spirometry data at screening will be calculated as follows:

Predicted Normal FEV_1

- Predicted Normal FEV_1 will be calculated using the working party of the European Community for Coal and Steel (ECCS) formula [Quanjer, 1993] :

$$Predicted\ Normal\ FEV1 = b_o * Height + b_1 * Age(Yr) + b_2$$

- The coefficients for male and female subjects are shown in Table 9. Note that no race corrections will be made.

Table 9 Predicted Normal FEV_1 Equation: Coefficients for Male and Female Subjects

	Height (b_0)	Age (b_1)	Intercept (b_2)
Male	0.0430	-0.029	-2.49
Female	0.0395	-0.025	-2.60

% Predicted Normal FEV_1

$$\%Predicted\ Normal\ FEV_1 = \frac{MaxFEV_1}{Predicted\ Normal\ FEV_1} * 100$$

10.5.5. Pharmacodynamic

Sputum Data
PIP3 Ratio
• PIP3 is the analyte of primary interest for the phospholipid data in sputum, and Peak Area data from the mass spectrometer is the endpoint of interest. However, it is acknowledged that there will be some degree of variability between sputum samples due to differences in cell counts, and therefore it is favoured to first normalise PIP3 Peak Area values by (PIP2 Peak Area + PIP3 Peak Area); prior to analysis. • More specifically the parameter of interest is: PIP3 Peak Area proportion (calculated as a proportion of the sum of PIP2 Peak Area and PIP3 Peak Area i.e. PIP3 Peak Area / (PIP2 Peak Area + PIP3 Peak Area)). • PIP3 Peak Area, as a proportion of PIP2 Peak Area and PIP3 Peak Area, will be used to calculate the PIP3 Peak Area proportion as follows:

Sputum Data

$$PIP3\ \ Peak\ \ Area\ \ proportion = \frac{PIP3\ Peak\ Area}{PIP2\ Peak\ Area\ + PIP3\ Peak\ Area}$$

- PIP3 peak area, (PIP3) may be standardised by dividing by a PIP3 standard e.g. ISDPIP3. Similarly, PIP2 peak area (PIP2) may be standardised by dividing by a PIP2 standard e.g. D6PIP2. Multiple standards will be included in the PIP dataset. The unstandardised PIP2 and PIP3 peak areas will be used in the derivation of the PIP3 peak area proportion for the SAC outputs. However, the choice of standards to be used in the analysis may be explored e.g. through comparison of distributions, linear regression post SAC.

10.5.6. Derivation of BAL/ELF Drug Concentration Data

- Urea concentration data will be used to calculate the dilution effect of the lavage which is used to extract the epithelial lining fluid (ELF) from the lung. A correction for dilution will be applied to all BAL fluid drug concentrations for each wash as follows:

$$ELF\ Drug\ Concentration\,(pg/mL) = \frac{BAL\ Fluid}{Drug\ Concentration}\,(pg/mL) \times Dilution\ Factor$$

where

$$Dilution\ Factor = \frac{Plasma\ Urea_{pre-bronch}}{BAL\ Urea}$$

- Additionally, for each wash, the Volume of ELF in BAL fluid and the Total Drug in BAL fluid will be calculated as follows:

$$Volume\ of\ ELF\ in\ BAL\ Fluid\ (mL) = BAL\ Fluid\ Volume\ (mL)/Dilution\ Factor$$

$$Drug\ in\ BAL\ Fluid\,(pg) = \frac{BAL\ Fluid}{Drug\ Concentration}\,(pg/mL) \times BAL\ Fluid\ Volume\,(mL)$$

- Data will then be pooled across all three washes as follows:

$$\underset{in\ BAL\ Fluid}{Total\ Volume\ of\ ELF}\,(mL) = \underset{in\ BAL_{WASH1}}{Volume\ of\ ELF} + \underset{in\ BAL_{WASH2}}{Volume\ of\ ELF} + \underset{in\ BAL_{WASH3}}{Volume\ of\ ELF}$$

$$\underset{BAL\ Fluid}{Total\ Drug\ in}\,(pg) = Drug\ in\ BAL_{WASH1} + Drug\ in\ BAL_{WASH2} + Drug\ in\ BAL_{WASH3}$$

$$Pooled\ ELF\ Drug\ Concentration\ (pg/mL) = \frac{Total\ Drug\ in\ BAL\ Fluid\ (pg)}{Total\ Volume\ of\ ELF\ in\ BAL\ Fluid\ (mL)}$$

10.5.7. Derivation of BAL Cell Pellet Drug Concentration Data

- Cell pellet samples are diluted in a 1:5 ratio. Concentrations will be corrected for the dilution before the ratio is calculated on an individual subject level between the raw lavage result for wash 2 and the cell pellet concentration:

$$Derived\ cell\ pellet\ concentration = \frac{cell\ pellet\ concentration\ x\ 5}{wash\ 2\ lavage\ concentration}\ x\ derived\ pooled\ lavage\ ELF\ concentration$$

- Only the derived concentrations will be included in the listing.

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

10.6.1. Premature Withdrawals

Element	Reporting Detail
General	• Subject study completion (i.e. as specified in the protocol) was defined as the completion of 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.

10.6.2. Handling of Missing Data

Element	Reporting Detail
General	• Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument : These data will be indicated by the use of a "blank" in subject listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table. Answers such as "Not applicable" and "Not evaluable" are not considered to be missing data and should be displayed as such.
Outliers	• Any subjects excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report.
PK and PD	• It is possible that not enough data points will be captured for the sputum at baseline (Part B) and/or at a specific post dose time point for all treatment groups. In such a situation, data should only be listed. No attempt should be made to summarise or statistically analyse the data. • The decision for the summary/statistical analysis of PK and PD data should be made once the study team and statistician have reviewed the totality of available data. • Any values below the Lower Limit of Quantification (LLQ) will be assigned a value of ½ LLQ for display purposes in Figures and for computation of summary statistics. Any values above the Upper Limit of Quantification (ULQ) will be assigned to the ULQ for display purposes in Figures and for computation of summary statistics. If multiple LLQ and /or ULQ values are available per assay (for example if multiple runs with different standard curves are utilised) then the LLQ and/or ULQ value used for the above imputation shall be the minimum of the available LLQs and/or the maximum of the ULQs. Where biomarker concentrations are from an assay of an increased dilution factor the LLQ and ULQ will be multiplied by this factor. • If the number of LLQ (and/or ULQ) values is large for an Individual biomarker then alternative analysis methods such as TOBIT analysis may be required. "Large" is hard to define prospectively and may depend upon the dataset in

Element	Reporting Detail
	question. Any such methodology will be documented in the statistical contributions to the study report. • Imputed values will be used in tables and figures, unless the proportion of imputed values at a given time point is large, in which case the summary statistics may not be presented for that time point and/or alternative actions will be taken and documented in the study report. • Where values are imputed, the number of such imputations will be included as a summary statistic in the relevant summary tables.

10.6.2.1. Handling of Missing Dates

PIMS does not capture partial dates, all AEs and con meds will have full dates. Prior medications will have duration and full stop date.

10.6.2.2. Handling of Missing Data for Statistical Analysis

Element	Reporting Detail
PK and PD data	• Missing data will not be imputed

10.7. Appendix 7: Values of Potential Clinical Importance

10.7.1. Laboratory Values

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

Clinical Chemistry				
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (>x)**
Albumin	mmol/L		30	
Calcium	mmol/L		2	2.75
Creatinine	mmol/L	Δ from BL		↑ 44.2
Glucose	mmol/L		3	9
Magnesium	mmol/L		0.5	1.23
Phosphorus	mmol/L		0.8	1.6
Potassium	mmol/L		3	5.5
Sodium	mmol/L		130	150
Total CO2	mmol/L		18	32

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

10.7.2. ECG

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

NOTES: [1] Represent standard ECG values of PCI for HV studies

10.7.3. Vital Signs

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

10.8. Appendix 8: Model Checking and Diagnostics for Statistical Analyses

10.8.1. Statistical Analysis Assumptions

Endpoint(s)	• Dose proportionality, accumulation, peak to trough ratio, PIP3 Ratio
Analysis	• Mixed effects models

- 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.
- An unstructured covariance structure for the R matrix will be used by specifying 'type=UN' on the REPEATED line.
  - In the event that this model fails to converge, alternative correlation structures may be considered such as CSH or CS.
  - Akaike's Information Criteria (AIC) will be used to assist with the selection of covariance structure.
- Distributional assumptions underlying the model used for analysis will be examined by obtaining a normal probability plot of the residuals and a plot of the residuals versus the fitted values (i.e. checking the normality assumption and constant variance assumption of the model respectively) to gain confidence that the model assumptions are reasonable.
- If there are any departures from the distributional assumptions, alternative models will be explored using appropriate transformed data.

10.9. Appendix 9: Population Pharmacokinetic Analyses

10.9.1. POP PK Dataset creation

A POP PK analysis compliant dataset will be created using the following example structure.

The PME/MAP compliant file structure is a space-delimited file with each row containing the following columns of information.

Variable short name	Assessment description	Format	Unit	Valid Values / Format
STUD	Protocol Number	Varchar	-	202062
SUBJ	Subject identifier in study	Varchar	-	Maximum 10 characters (numeric or text). Different identifier for each subject
CENT	Study centre identifier	Varchar	-	
LABL	Indicator field describing the type of assessment in that record	Varchar		LABL=DOSE for a dosing event and LABL=CONC for a concentration event
AMT	Dose	Decimal	Mcg	
TMT	Treatment Identifier	Integer	-	TMT = 0 for placebo and AMT for dose levels
VISIT	Study visit	Integer	-	Maximum 10 characters (numeric or text).
DAY	Study day	Integer	-	numeric , Actual Study Day Number
DATETIME	Date and time of Dose or measurement	YYYY-MM-DD HH:MM:SS	-	Date and time of assessment. The supported range is '1000-01-01 00:00:00' to '9999-12-31 23:59:59'
TIME	Actual time relative to first active dose	Decimal	Hours	Hours since first active dose.
RTLD	Actual time relative to last active dose	Decimal	Hours	When LABL = DOSE, RTLD = 0 Hours since last active dose. For pre-dose sample. For pre-dose sample, TIME is relative to previous morning (am) dose on previous Day X
CONC	Value of the variable captured in the LABL/TIME pair	Decimal (12,4)	As detailed for variable below	
EVID	Event ID	Integer		EVID=1 for a dosing event record (where AMT is also positive number) and EVID=0 otherwise (where AMT is 0)
MDV	Missing Data Variable	Integer	-	MDV=1 when EVID=1 and MDV=0 when EVID=0
NQ	Non Quantifiable Data	Integer		If CONC is NQ then NQ=1 else 0

Variable short name	Assessment description	Format	Unit	Valid Values / Format
IND	BQL indicator	Integer	-	If CONC is NQ then IND=1, else IND=0
LLQ	Lower Limit of quantification	Integer	pg/mL	Lower limit of quantification for specific analyte
II	Interdose interval	Decimal	Hours	Interdose Interval (II) gives the time between doses (24 h for once daily dosing). II should be a positive number if and only if the AMT data item is a positive number and has the same units as the TIME data item. For CONC records, II should be zero.
AGE	Age	Decimal	Yrs	Integer. Age in years at time of screening rounded down to give age at last birthday.
WT	Weight	Decimal	Kg	Weight in kilograms at time of screening.
HT	Height	Decimal	Cm	Height in centimetres at time of screening.
SEX	Subject gender	Integer	-	Integer. One of the following - 1 = male 2 = female
SEXTXT	Subject gender	Varchar	-	MALE (male) or FEMALE (female)
BMI	Body mass index	Decimal	kg/m^2	body mass index calculated as weight divided by height squared
TOBAC	Tobacco Use	Decimal		Number of pack years (=number of cigarettes per day/20))X number years smoked

Example Dataset

ID	SUBJ	CENT	STUD	LABL	AMT	TMT	VISIT	DAY	DATETIME	TIME	RTLD	CONC	EVID	MDV	NQ	IND	LLQ	II
PPD			DB2113361	CONC_UM_361_MO	0	3	2	1	PPD 1:06:12:00	0	0	0	0	0	1	1	10	.
			DB2113361	DOSE_UM_361_MO	125	3	2	1	PPD 1:06:39:00	0	0	.	1	1	0	0	.	.
			DB2113361	CONC_UM_361_MO	0	3	2	1	PPD 1:06:44:00	0.08	0.08	117.2	0	0	0	0	10	.
			DB2113361	CONC_UM_361_MO	0	3	2	1	PPD 1:07:00:00	0.35	0.35	84.4	0	0	0	0	10	.
			DB2113361	CONC_UM_361_MO	0	3	2	1	PPD 1:15:16:00	8.62	8.62	25.5	0	0	0	0	10	.
			DB2113361	CONC_UM_361_MO	0	3	2	2	PPD 1:05:40:00	23.02	23.02	0	0	0	1	1	10	.

ID	SUBJ	CENT	STUD	LABL	AMT	TMT	VISIT	DAY	DATETIME	TIME	RTLD	CONC	EVID	MDV	NQ	IND	LLQ	II
PPD			DB2113361	DOSE_UM_361_MO	125	3	6	85	PPD 1:07:15:00	2016.6	0	.	4	1	0	0	.	24
			DB2113361	CONC_UM_361_MO	0	3	6	85	PPD 1:07:17:00	2016.63	0.03	109.3	0	0	0	0	10	.
			DB2113361	CONC_UM_361_MO	0	3	6	85	PPD 1:07:50:00	2017.18	0.58	49.8	0	0	0	0	10	.
			DB2113361	CONC_UM_361_MO	0	3	6	85	PPD 1:13:17:00	2022.63	6.03	31.9	0	0	0	0	10	.
			DB2113361	CONC_UM_361_MO	0	3	6	85	PPD 1:06:07:00	2015.47	22.87	23.8	0	0	0	0	10	.
			DB2113361	CONC_UM_361_MO	0	3	6	86	PPD 1:06:23:00	2039.73	23.13	25.6	0	0	0	0	10	.
			DB2113361	DOSE_UM_361_MO	125	3	8	169	PPD 1:06:54:00	4032.25	0	.	4	1	0	0	.	24
			DB2113361	CONC_UM_361_MO	0	3	8	169	PPD 1:06:56:00	4032.28	0.03	168	0	0	0	0	10	.
			DB2113361	CONC_UM_361_MO	0	3	8	169	PPD 1:07:29:00	4032.83	0.58	29.9	0	0	0	0	10	.
			DB2113361	CONC_UM_361_MO	0	3	8	169	PPD 1:13:00:00	4038.35	6.1	16.9	0	0	0	0	10	.
			DB2113361	CONC_UM_361_MO	0	3	8	169	PPD 1:06:14:00	4031.58	23.23	0	0	0	0	1	10	.
			DB2113361	CONC_UM_361_MO	0	3	8	170	PPD 1:06:48:00	4056.15	23.9	0	0	0	0	1	10	.
			DB2113361	CONC_UM_361_CO	0	2	2	1	PPD 1:07:08:00	0	0	0	0	0	1	1	10	.
			DB2113361	DOSE_UM_361_CO	125	2	2	1	PPD 1:08:00:00	0	0	.	1	1	0	0	.	.
			DB2113361	CONC_UM_361_CO	0	2	2	1	PPD 1:08:12:00	0.2	0.2	76.2	0	0	0	0	10	.
			DB2113361	CONC_UM_361_CO	0	2	2	1	PPD 1:08:23:00	0.38	0.38	49.6	0	0	0	0	10	.
			DB2113361	CONC_UM_361_CO	0	2	2	1	PPD 1:14:00:00	6	6	19.2	0	0	0	0	10	.

AGE	HT	SEX	SEXTXT	WT	BMI	TOBAC
69	156	2	F	48.6	20	78
69	156	2	F	48.6	20	78
69	156	2	F	48.6	20	78
69	156	2	F	48.6	20	78
69	156	2	F	48.6	20	78
69	156	2	F	48.6	20	78
69	156	2	F	48.6	20	78
69	156	2	F	48.6	20	78
69	156	2	F	48.6	20	78
69	156	2	F	48.6	20	78
69	156	2	F	48.6	20	78
69	156	2	F	48.6	20	78
69	156	2	F	48.6	20	78
69	156	2	F	48.6	20	78
69	156	2	F	48.6	20	78
69	156	2	F	48.6	20	78
69	156	2	F	48.6	20	78
69	156	2	F	48.6	20	78
55	163	2	F	86.3	32.5	40
55	163	2	F	86.3	32.5	40
55	163	2	F	86.3	32.5	40
55	163	2	F	86.3	32.5	40
55	163	2	F	86.3	32.5	40
55	163	2	F	86.3	32.5	40

10.10. Appendix 10 – Abbreviations & Trade Marks

10.10.1. Abbreviations

Abbreviation	Description
AE	Adverse Event
AIC	Akaike's Information Criteria
A&R	Analysis and Reporting
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CPMS	Clinical Pharmacology Modelling & Simulation
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
EMA	European Medicines Agency
IA	Interim Analysis
ICH	International Conference on Harmonisation
IDMC	Independent Data Monitoring Committee
IDSL	Integrated Data Standards Library
IMMS	International Modules Management System
IP	Investigational Product
ITT	Intent-To-Treat
GUI	Guidance
MMRM	Mixed Model Repeated Measures
PCI	Potential Clinical Importance
PD	Pharmacodynamic
PDMP	Protocol Deviation Management Plan
PK	Pharmacokinetic
PP	Per Protocol
QC	Quality Control
QTcF	Fridericia's QT Interval Corrected for Heart Rate
QTcB	Bazett's QT Interval Corrected for Heart Rate
RAP	Reporting & Analysis Plan
RAMOS	Randomization & Medication Ordering System
SAC	Statistical Analysis Complete
SDTM	Study Data Tabulation Model
SOP	Standard Operation Procedure
TFL	Tables, Figures & Listings
GSK	GlaxoSmithKline

10.10.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
HARP

Trademarks not owned by the GlaxoSmithKline Group of Companies
SAS
WinNonlin

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.n	1.1 to 1.n
Safety	2.1 to 2.n	2.1 to 2.n
Pharmacokinetic	3.1 to 3.n	3.1 to 3.n
Pharmacodynamic and / or Biomarker	4.1 to 4.n	4.1 to 4.n
Pharmacokinetic / Pharmacodynamic	5.1 to 5.n	5.1 to 5.n
Section	**Listings**	
ICH Listings	1 to x	
Other Listings	y to z	

10.11.2. Deliverable

Delivery Priority	Description
SAC	Final Statistical Analysis Complete

NOTES:

- Parts A and B will be reported as part of the same SAC deliverable.

10.11.3. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Part A (Single Dose Escalation): Subject Disposition					
1.101	Screened (Part A)	ES1	Summary of Subject Disposition (Single Dose)		SAC
1.102	Screened (Part A)	ES6	Summary of Reasons for Screening Failure (Single Dose)		SAC
1.103	Safety (Part A)	DV1a	Summary of Important Protocol Deviations (Single Dose)		SAC
1.104	Safety (Part A)	DV1a	Summary of All Inclusion/Exclusion Criteria Deviations (Single Dose)		SAC
Part B (Repeat Dose): Subject Disposition					
1.201	Screened (Part B)	ES1	Summary of Subject Disposition (Repeat Dose)		SAC
1.202	Screened (Part B)	ES6	Summary of Reasons for Screening Failure (Repeat Dose)		SAC
1.203	Safety (Part B)	DV1a	Summary of Important Protocol Deviations (Repeat Dose)		SAC
1.204	Safety (Part B)	DV1a	Summary of All Inclusion/Exclusion Criteria Deviations (Repeat Dose)		SAC

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Part A (Single Dose Escalation): Demographics					
1.105	Safety (Part A)	DM1	Summary of Demographic Characteristics (Single Dose)	Include baseline FEV1 and %predicted normal FEV1.	SAC
1.106	Safety (Part A)	DM5	Summary of Race and Racial Combinations (Single Dose)		SAC
1.107	Safety (Part A)	SA1	Summary of Study Populations (Single Dose)		SAC
Part B (Repeat Dose): Demographics					
1.205	Safety (Part B)	DM1	Summary of Demographic Characteristics (Repeat Dose)	Include baseline FEV1 and %predicted normal FEV1.	SAC
1.206	Safety (Part B)	DM5	Summary of Race and Racial Combinations (Repeat Dose)		SAC
1.207	Screened (Part B)	SA1	Summary of Study Populations (Repeat Dose)		SAC
Part A (Single Dose Escalation): Medical Condition & Con Meds					
1.108	Safety (Part A)	MH1	Summary of Current/Past Medical Conditions (Single Dose)		SAC
1.109	Safety (Part A)	CM1	Summary of Concomitant Medications (Single Dose)		SAC

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Part B (Repeat Dose): Medical Condition & Con Meds					
1.208	Safety (Part B)	MH1	Summary of Current/Past Medical Conditions (Repeat Dose)		SAC
1.209	Safety (Part B)	CM1	Summary of Concomitant Medications (Repeat Dose)		SAC

10.11.4. Safety Tables

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Part A (Single Dose Escalation): Exposure					
2.101	Safety (Part A)	EX1	Summary of Extent of Exposure to Study Treatment (Single Dose)		SAC
Part B (Repeat Dose): Exposure					
2.201	Safety (Part B)	EX1	Summary of Extent of Exposure to Study Treatment (Repeat Dose)		SAC
Part A (Single Dose Escalation): Adverse Events					
2.102	Safety (Part A)	CP_AE1x	Summary of All Adverse Events by System Organ Class (Single Dose)	Include total column.	SAC
2.103	Safety (Part A)	CP_AE1x	Summary of Drug-Related Adverse Events by System Organ Class (Single Dose)	Include total column.	SAC

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.104	Safety (Part A)	AE15/EMA_AE	Summary of Common (>=5%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences, Single Dose)		SAC
Part B (Repeat Dose): Adverse Events					
2.202	Safety (Part B)	CP_AE1p	Summary of All Adverse Events by System Organ Class (Repeat Dose)	Include total column.	SAC
2.203	Safety (Part B)	CP_AE1p	Summary of Drug-Related Adverse Events by System Organ Class (Repeat Dose)	Include total column.	SAC
2.204	Safety (Part B)	AE15	Summary of Common (>=5%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences, Repeat Dose)		SAC
Part A (Single Dose Escalation): Labs					
2.105	Safety (Part A)	LB1	Summary of Chemistry Changes from Baseline by Visit (Single Dose)		SAC
2.106	Safety (Part A)	LB3	Summary of Emergent Chemistry Results by Potential Clinical Importance Criteria (Single Dose)		SAC
2.107	Safety (Part A)	LB1	Summary of Haematology Changes from Baseline by Visit (Single Dose)		SAC
2.108	Safety (Part A)	LB3	Summary of Emergent Chemistry Results by Potential Clinical Importance Criteria (Single Dose)		SAC

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Part B (Repeat Dose): Labs					
2.205	Safety (Part B)	LB1	Summary of Chemistry Changes from Baseline by Visit (Repeat Dose)		SAC
2.206	Safety (Part B)	LB3	Summary of Emergent Chemistry Results by Potential Clinical Importance Criteria (Repeat Dose)		SAC
2.207	Safety (Part B)	LB1	Summary of Haematology Changes from Baseline by Visit (Repeat Dose)		SAC
2.208	Safety (Part B)	LB3	Summary of Emergent Chemistry Results by Potential Clinical Importance Criteria (Repeat Dose)		SAC
Part A (Single Dose Escalation): ECGs					
2.109	Safety (Part A)	EG2	Summary of Change from Baseline in ECG Values by Visit. (Single Dose)		SAC
2.110	Safety (Part A)	EG1	Summary of Maximum Emergent QTc Values by Category. (Single Dose)		SAC
2.111	Safety (Part A)	EG1	Summary of 12-Lead ECG Findings (Single Dose)		SAC
Part B (Repeat Dose): ECGs					
2.209	Safety (Part B)	EG2	Summary of Change from Baseline in ECG Values by Visit. (Repeat Dose)		SAC
2.210	Safety (Part B)	EG1	Summary of Maximum Emergent QTc Values by Category. (Repeat Dose)		SAC

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.211	Safety (Part B)	EG1	Summary of 12-Lead ECG Findings (Single Dose)		SAC
Part A (Single Dose Escalation): Vital Signs					
2.112	Safety (Part A)	VS1	Summary of Change from Baseline in Vital Signs by Visit (Single Dose)	Include the Respiration Rate and Tympanic Temperature	SAC
Part B (Repeat Dose): Vital Signs					
2.212	Safety (Part B)	VS1	Summary of Change from Baseline in Vital Signs by Visit (Repeat Dose)	Include the Respiration Rate and Tympanic Temperature	SAC
Part A (Single Dose Escalation): Spirometry					
2.113	Safety (Part A)	PD_PFT1	Summary of Lung Function Data (Single Dose)		SAC
Part B (Repeat Dose): Spirometry					
2.213	Safety (Part B)	PD_PFT1	Summary of Lung Function Data (Repeat Dose)		SAC

10.11.5. Safety Figures

Safety : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Part A (Single Dose Escalation): ECGs					
2.101	Safety (Part A)	Fig 2.1 from /arenv/arprod/gsk2269557/pii116617/part_c/drivers/f_qtc_boxplot_partc.sas	Box Plots of QTcF and QTcB Over Time (Single Dose)	One page for each of QTcB and QTcF	SAC
Part B (Single Dose Escalation): ECGs					
2.201	Safety (Part B)	Fig 2.2 from /arenv/arprod/gsk2269557/pii116617/part_b/drivers/f_qtc_boxplot_partb.sas	Box Plots of QTcF and QTcB Over Time (Repeat Dose)	One page for each of QTcB and QTcF	SAC
2.202	Safety (Part B)	Fig 2.4 from /arenv/arprod/gsk2269557/pii116617/part_b/drivers/f_qtcindiv_partb.sas	Plot of Individual Subject QTcF and QTcB Over Time (Repeat Dose)		SAC

10.11.6. Pharmacokinetic Tables

Pharmacokinetic : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Part A (Single Dose): Pharmacokinetic Concentrations and Parameters					
3.101	PK (Part A)	PKCT1	Summary of Plasma GSK2292767 Pharmacokinetic Concentration-Time Data (Single Dose)		SAC
3.102	PK (Part A)	PKPT1	Summary of Derived Plasma GSK2292767 Pharmacokinetic Parameters (Single Dose)	Only summarise for AUC(0-t), AUC(0-24), AUC(0-∞), Cmax, Ctau, Tmax, Thalf, Lambda_z.	SAC
3.103	PK (Part A)	PKPT3	Summary of Derived Plasma GSK2292767 Pharmacokinetic Parameters (log transformed, Single Dose))		SAC
3.104	PK (Part A)	PKCT1	Summary of GSK2292767 Pharmacokinetic Urine Excretion Rate-Time Data [units] (Single Dose)	Only for the highest dose.	SAC
Part A (Single Dose): Dose Proportionality					
3.105	PK (Part A)	See Table 3.8 in /arenv/arprod/gsk2269557/pii116617/parts_cb/drivers/t_pkpower_partcb.sas	Summary of Results of Statistical Analysis of Plasma GSK2292767 Cmax, AUC(0-t) and Ctau to Assess Dose Proportionality (Single Dose), Power Model		SAC
3.106	PK (Part A)	Fig 3.10 in /arenv/arprod/gsk2269557/pii116617/parts_cb/drivers/t_pkaccum_stat_partcb.sas	Summary of Results of Statistical Analysis of Plasma GSK2292767 Cmax, AUC(0-t) and Ctau to Assess Dose Proportionality (Single Dose), ANOVA Model		SAC

Pharmacokinetic : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Part B (Repeat Dose): Pharmacokinetic Concentrations and Parameters					
3.201	PK (Part B)	PKCT1	Summary of Plasma GSK2292767 Pharmacokinetic Concentration-Time Data (Repeat Dose)		SAC
3.202	PK (Part B)	PKPT1	Summary of Derived Plasma GSK2292767 Pharmacokinetic Parameters (Repeat Dose)	Only summarise for AUC(0-t), AUC(0-24), AUC(0-∞), Cmax, Ctau, Tmax, Thalf, Lambda_z.	SAC
3.203	PK (Part B)	PKPT3	Summary of Derived Plasma GSK2292767 Pharmacokinetic Parameters (log transformed) (Repeat Dose)		SAC
Part B (Repeat Dose) Statistical Analyses					
3.204	PK (Part B)	Similar to Table 3.10 in /arenv/arprod/gsk2269557/pii116617/parts_cb/drivers/t_pkaccum_stat_partcb.sas	Summary of Statistical Analysis of Plasma GSK2292767 AUC(0-24), Cmax and Ctau Accumulation and Peak: Trough Ratios (Day 14 versus Day 1, Repeat Dose)	Each endpoint to be assessed separately.	SAC
Part B (Repeat Dose): Lung ELF and Cell Pellet Data					
3.205	PK (Part B)	See Table 11.16 in PII115517/Part_C_Cohort_5	Summary of Urea Dilution Factor Data (Repeat Dose)		SAC
3.206	PK (Part B)	See Table 11.17 in PII115517/Part_C_Cohort_5	Summary of Derived Lung ELF and Cell Pellet GSK2292767 Pharmacokinetic Concentrations and Volume Data (Repeat Dose)		SAC

10.11.7. Pharmacokinetic Figures

Pharmacokinetic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Part A (Single Dose Escalation): Pharmacokinetic Concentrations					
3.101	PK (Part A)	PKCF1x	Individual Subject Plasma GSK2292767 Concentration-Time Plots (Linear and Semi-log) by Treatment (Single Dose)	One treatment per page (all subjects within a treatment group on one plot). Add a horizontal line at y-axis = 20 pg/mL and footnote: LLQ = 20 pg/mL,Set pre-dose NQs to missing.	SAC
3.102	PK (Part A)	PKCF3	Median Plasma GSK2292767 Concentration-Time Plot (Linear and Semi-Log, Single Dose)		SAC
Part B (Repeat Dose): Pharmacokinetic Concentrations					
3.201	PK (Part B)	PKCF1	Individual Subject Plasma GSK2292767 Concentration-Time Plots (Linear and Semi-log) by Treatment (Repeat Dose)	If more than one cohort, then 1 cohort per page (all subjects within a treatment group on one plot). Add a horizontal line at y-axis = 20 pg/mL and footnote: LLQ = 20 pg/mL,Set pre-dose NQs to missing.	SAC
3.202	PK (Part B)	PKCF3	Median (+ SD) Plasma GSK2292767 Concentration-Time Plot (Linear and Semi-Log, Repeat Dose)		SAC

Pharmacokinetic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Dose Proportionality					
3.103	PK (Part A)	Fig 3.9 in /arenv/arprod/gsk2269557/pii116617/parts_cb/drivers/f_pkcmax_dosenorm_partcb.sas	Box Plot of Dose Normalised Plasma GSK2292767 PK Parameters against Dose (Single Dose)	Separate plots for AUC(0-t), Ctau and Cmax	SAC
3.104	PK (Part A)	Fig 3.10 from /arenv/arprod/gsk2269557/pii116617/parts_cb/drivers/f_pkanova_partcb.sas	Plot of Adjusted Geometric Mean Treatment Ratios and 90% CIs for Plasma GSK2292767 AUC (0-t) to Assess Plasma Dose Proportionality (Single Dose, ANOVA Model)		SAC
Part B (Repeat Dose): Dose Accumulation, Steady State and Peak to Trough Ratios					
3.203	PK (Part B)	Fig 3.11 from /arenv/arprod/gsk2269557/pii116617/parts_cb/drivers/f_pkcmax_boxplot_partcb.sas	Box Plots of GSK2292767 Plasma PK Parameters by Day (Repeat Dose)	Exclude mean value. Raw means. Cmax, Ctrough and peak to trough ratio on separate pages	SAC

Pharmacokinetic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Part B (Repeat Dose): Lung ELF and Cell Pellet Data					
3.204	PK (Part B)	Figure 3.15 in /arenv/arprod/gsk2269557/pii116617/part_b/drivers/fig_3_15_elf.sas	Individual Subject Derived Lung ELF GSK2292767 Concentrations Plot (Semi-Log) – Individual Washes (Repeat Dose)	Exclude placebo data. Minor tick marks on x-axis (actual rel time). Initially don't join subjects. Add legend to identify wash no. To be reviewed dependent on data distribution as it may be useful to join lines and plot planned times if the plot doesn't look too messy.	SAC
3.205	PK (Part B)	Figure 3.16 in /arenv/arprod/gsk2269557/pii116617/part_b/drivers/fig_3_16_elf.sas	Median Plasma and Individual Subject Derived Lung ELF and Cell Pellet GSK2292767 Concentrations Plot (Semi-Log) – Pooled Washes (Repeat Dose)	Exclude placebo data. To only display day 14 data. Minimum y-axis value should be set to 1000 pg/mL Set pre-dose plasma NQs to missing. Legend to identify plasma/ELF and Subjid. Plasma based on planned rel. Time; ELF on actual rel time of Wash 1 Cell Pellet concentration to only be shown for Wash 2 data, ELF data will be the pooled sample. These should be explained within footnote. Jitter these points to the left and right if any of the two sets of points are seen to overlap.	SAC
3.206	PK (Part B)	Figure 3.17 in /arenv/arprod/gsk2269557/pii116617/part_b/drivers/fig_3_17_pelf.sas	Box Plots of Cell Pellet and Pooled ELF GSK2292767 Concentrations (Repeat Dose)	2 box and whisker plots side by side. Would expect plots to look similar to each other.	SAC

10.11.8. Pharmacodynamic Tables

Pharmacodynamic: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Part A (Single Dose): PIP Data					
4.101	Safety (Part A)	See Table 4.4 in /arenv/arprod/gsk2269557/pii116617/parts_cb/drivers/t_pip_partcb.sas	Summary of Phospholipid Data in Sputum (Single Dose)	Only include evaluable data and include footnote if any non-evaluable. Summarise geometric mean of reps. Include PIP3 Peak Area, PIP2 Peak Area and PIP3 Peak Area Proportion.	SAC
4.102	Safety (Part A)	See Table 4.5 in /arenv/arprod/gsk2269557/pii116617/parts_cb/drivers/t_pip_nottfrz_stat_partcb.sas	Summary of Results of Statistical Analysis of Phospholipid Data in Sputum (Single Dose)	Include PIP3 Peak Area and PIP3 Peak Area Proportion if appropriate. List PIP3 Peak Area Proportion first if analysed. Add Bayesian posterior probabilities	SAC

Pharmacodynamic: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Part B (Repeat Dose): PIP Data					
4.201	Safety (Part B)	See Table 4.4 in /arenv/arprod/gsk2269557/pii116617/parts_cb/drivers/t_pip_partcb.sas	Summary of Phospholipid Data in Sputum (Repeat Dose)	Only include evaluable data and include footnote if any non-evaluable. Summarise geometric mean of reps. Include PIP3 Peak Area, PIP2 Peak Area and PIP3 Peak Area Proportion.	SAC
4.202	Safety (Part B)	See Table 4.5 in /arenv/arprod/gsk2269557/pii116617/parts_cb/drivers/t_pip_nottfrz_stat_partcb.sas	Summary of Results of Statistical Analysis of Phospholipid Data in Sputum (Repeat Dose)	Include PIP3 Peak Area and PIP3 Peak Area Proportion if appropriate. List PIP3 Peak Area Proportion first if analysed. Add Bayesian posterior probabilities	SAC

10.11.9. Pharmacodynamic Figures

Pharmacodynamic: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Part A (Single Dose): PIP Data					
4.101	Safety (Part A)	Fig 4.23 in /arenv/arprod/gsk2269557/pii116617/parts_cb/drivers/f_pipratio_indiv_partcb.sas	Plot of Individual Subject Phospholipid Data in Sputum by Treatment (Single Dose)	Plot PIP3 peak area, PIP2 peak area and PIP2+PIP3 Peak Areas (geo means of reps) by treatment (x-axis). Include all subjects on one plot. Y-axis: log scale ; subject data points to be joined for each analyte. Symbols/colour to identify PIP2 peak area, PIP3 peak area etc. in legend.	SAC
4.102	Safety (Part A)	Fig 4.8 in /arenv/arprod/gsk2269557/pii116617/parts_cb/drivers/f_pipratio_nottfrz_mean_partcb.sas	Plot of Adjusted Geometric Means and 90% CIs of Phospholipid Data in Sputum (Single Dose)	Y-axis: log scale PIP3 peak area Proportion and PIP3 Peak area	SAC
Part B (Repeat Dose): PIP Data					
4.201	Safety (Part B)	Fig 4.4 in /arenv/arprod/gsk2269557/pii116617/interim_c/drivers/f_pipratioindiv_partc.sas	Plot of Individual Subject Phospholipid Data in Sputum by Treatment and Time (Repeat Dose)	PIP3 Peak Area Proportion and PIP3 Peak Area	SAC

Pharmacodynamic: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
4.202	Safety (Part B)	Fig 4.9 in /arenv/arprod/gsk2269557/pii116617/parts_cb/drivers/f_pipratio_nottfrz_diff_partcb.sas	Plot of Adjusted Treatment Ratios and 90% CIs of Phospholipid Data in Sputum (Repeat Dose)	Y-axis: log scale PIP3 Peak Area Proportion and PIP3 Peak Area	SAC

10.11.10. Pharmacokinetic / Pharmacodynamic Figures

(Note: No PK/PD Summary Tables are planned)

Pharmacokinetic / Pharmacodynamic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK vs Sputum PIP3 Ratio					
5.101	PK (Part A)	Fig 6.2 in /arenv/arprod/gsk2269557/pii115119/part_b/drivers/f_pcon_vs_biom	Scatter Plot of Plasma GSK2292767 Pharmacokinetic Concentration vs PIP3 Peak Area Proportion (Single Dose)	Use different symbols for Day 1 3h and Day 1 24h.	SAC
5.201	PK (Part B)	Fig 6.2 in /arenv/arprod/gsk2269557/pii115119/part_b/drivers/f_pcon_vs_biom	Scatter Plot of Plasma GSK2292767 Pharmacokinetic Concentration vs PIP3 Peak Area Proportion (Repeat Dose)	Use different symbols for Day 1 3h Day 12 3h and Day 12 24h.	SAC

10.11.11. ICH Listings: Part A (Single Dose Escalation)

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Treatment Information					
1.	Screened (Part A)	CP_TA2	Listing of Randomised and Actual Treatments (Single Dose)	To include CENTREID (labelled as INVID), subject no., randomisation no., period, randomised treatment, actual treatment and deviation. Also include PTYN and PTSUBJID from DMDATA.PRVTRIAL.	SAC
2.	Screened (Part A)	EX4	Listing of Exposure Data (Single Dose)	Dose: extract from actual treatment (if dosing not completed, set to max. possible dose that could have been taken & include footnote). Exclude 'Cumulative Dose' and replace with 'No. Of Inhalations'.	SAC
Disposition					
3.	Screened (Part A)	CP_ES10x	Listing of Reasons for Withdrawal (Single Dose)		SAC
4.	Screened (Part A)	IE4	Listing of Subjects with Inclusion/Exclusion Criteria Deviations (Single Dose)		SAC
5.	Screened (Part A)	DV2	Listing of Protocol Deviations (Single Dose)		SAC
6.	Screened (Part A)	BL2	Listing of Subjects For Whom the Treatment Blind was Broken (Single Dose)		SAC

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Demography					
7.	Screened (Part A)	DM4	Listing of Demographic Characteristics (Single Dose)		SAC
8.	Screened (Part A)	DM10	Listing of Race (Single Dose)		SAC
Concomitant Medications and Adverse Events					
9.	Screened (Part A)	CP_CM4	Listing of Concomitant Medications by Generic Term (Single Dose)		SAC
10.	Screened (Part A)	CP_AE9	Listing of All Adverse Events (Single Dose)		SAC
11.	Screened (Part A)	CP_AE9a	Listing of Serious Adverse Events (Single Dose)		SAC
12.	Screened (Part A)	AE7	Listing of Subject Numbers for Individual Adverse Events (Single Dose)		SAC
13.	Screened (Part A)	CP_AE9	Listing of Adverse Events Leading to Withdrawal from Study (Single Dose)		SAC
Safety Assessments					
14.	Screened (Part A)	CP_LB6	Listing of Clinical Chemistry Abnormalities of Potential Clinical Importance (Single Dose)		SAC
15.	Screened (Part A)	CP_LB6	Listing of All Clinical Chemistry Laboratory Data for Subjects with any Abnormality of Potential Clinical Importance (Single Dose)		SAC
16.	Screened (Part A)	CP_LB6	Listing of Haematology Abnormalities of Potential Clinical Importance (Single Dose)		SAC
17.	Screened (Part A)	CP_LB6	Listing of All Haematology Laboratory Data for Subjects with any Abnormality of Potential Clinical Importance (Single Dose)		SAC
18.	Screened (Part A)	CP_VS5	Listing of Vital Signs of Potential Clinical Importance (Single Dose)		SAC

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
19.	Screened (Part A)	CP_VS5	Listing of All Vital Signs for Subjects with any Value of Potential Clinical Importance (Single Dose)		SAC
20.	Screened (Part A)	CP_EG4	Listing of All 12-Lead ECG Values of Potential Clinical Importance (Single Dose)		SAC
21.	Screened (Part A)	CP_EG4	Listing of All 12-Lead ECG Values for Subjects with any Value of Potential Clinical Importance (Single Dose)		SAC
22.	Screened (Part A)	CP_EG6	Listing of Abnormal 12-Lead ECG Findings (Single Dose)	Clin sig change from baseline should not be populated for screening and pre-dose timepoints	SAC
23.	Screened (Part A)	UR2b	Listing of All Urinalysis Data (Single Dose)		SAC

10.11.12. ICH Listings: Part B (Repeat Dose)

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Treatment Information					
24.	Screened (Part B)	CP_TA1	Listing of Randomised and Actual Treatments (Repeat Dose)	To include CENTREID (labelled as INVID), subject no., randomisation no., randomised treatment, actual treatment and deviation	SAC
25.	Screened (Part B)	EX3	Listing of Exposure Data (Repeat Dose)	Dose: extract from actual treatment (if dosing not completed, set to max. possible dose that could have been taken & include footnote). Include cumulative dose and insert extra column containing 'No. Of Inhalations'.	SAC
Disposition					
26.	Screened (Part B)	ES2	Listing of Reasons for Withdrawal (Repeat Dose)		SAC
27.	Screened (Part B)	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations (Repeat Dose)		SAC
28.	Screened (Part B)	DV2	Listing of Protocol Deviations (Repeat Dose)		SAC
29.	Screened (Part B)	BL1	Listing of Subjects For Whom the Treatment Blind was Broken (Repeat Dose)		SAC
Demography					
30.	Screened (Part B)	DM2	Listing of Demographic Characteristics (Repeat Dose)		SAC
31.	Screened (Part B)	DM9	Listing of Race (Repeat Dose)		SAC

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Concomitant Medications and Adverse Events					
32.	Screened (Part B)	CP_CM3	Listing of Concomitant Medications by Generic Term (Repeat Dose)		SAC
33.	Screened (Part B)	CP_AE8 (Part B)	Listing of All Adverse Events (Repeat Dose)		SAC
34.	Screened (Part B)	CP_AE8a (Part B)	Listing of Serious Adverse Events (Repeat Dose)		SAC
35.	Screened (Part B)	AE7 (Part B)	Listing of Subject Numbers for Individual Adverse Events (Repeat Dose)		SAC
36.	Screened (Part B)	CP_AE8 (Part B)	Listing of Adverse Events Leading to Withdrawal from Study (Repeat Dose)		SAC
Safety Assessments					
37.	Screened (Part B)	CP_LB5	Listing of Clinical Chemistry Abnormalities of Potential Clinical Importance (Repeat Dose)		SAC
38.	Screened (Part B)	CP_LB5	Listing of All Clinical Chemistry Laboratory Data for Subjects with any Abnormality of Potential Clinical Importance (Repeat Dose)		SAC
39.	Screened (Part B)	CP_LB5	Listing of Haematology Abnormalities of Potential Clinical Importance (Repeat Dose)		SAC
40.	Screened (Part B)	CP_LB5	Listing of All Haematology Laboratory Data for Subjects with any Abnormality of Potential Clinical Importance (Repeat Dose)		SAC

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
41.	Screened (Part B)	CP_VS4	Listing of Vital Signs of Potential Clinical Importance (Repeat Dose)		SAC
42.	Screened (Part B)	CP_VS4	Listing of All Vital Signs for Subjects with any Value of Potential Clinical Importance (Repeat Dose)		SAC
43.	Screened (Part B)	CP_EG3	Listing of All 12-Lead ECG Values of Potential Clinical Importance (Repeat Dose)		SAC
44.	Screened (Part B)	CP_EG3	Listing of All 12-Lead ECG Values for Subjects with any Value of Potential Clinical Importance (Repeat Dose)		SAC
45.	Screened (Part B)	CP_EG5	Listing of Abnormal 12-Lead ECG findings (Repeat Dose)		SAC
46.	Screened (Part B)	UR2a	Listing of All Urinalysis Data (Repeat Dose)		SAC

10.11.13. Non-ICH Listings: Part A (Single Dose Escalation)

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Safety Data					
47.	Screened (Part A)	AE2	Relationship between System Organ Class and Verbatim Text (Single Dose)		SAC
48.	Screened (Part A)	Other Listing 3 in /arenv/arprod/gsk2269557/pii115117/part_a/drivers/saf_l3_cp_hm7.sas	Listing of 24 Hour Holter Findings at Screening (Single Dose)		SAC
49.	Screened (Part A)	Other Listing 2 in /arenv/arprod/gsk2269557/pii115117/part_a/drivers/saf_l2_list.sas	Listing of Cardiac Telemetry ECG Findings (Single Dose)		SAC
Pharmacodynamic Data					
50.	Screened (Part A)	PFT11	Listing of %Predicted FEV1 Data at Screening (Single Dose)	To include 'Pred. Normal' and '%Pred Normal' columns. Exclude 'Pre/Post Broncho' and '%Rev' columns	SAC
51.	Screened (Part A)	PFT9	Listing of FEV1 Data (Single Dose)	Include triplicate and maximum values.	SAC

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
52.	Screened (Part A)	Listing 63 in /arenv/arprod/gsk2269557/pii116617/part_c/drivers/l_sputprep_partc.sas	Listing of Sputum Sample Preparation and Haemacytometry/Cytospin Preparation Data (Single Dose)	Include sputum weight and time to first induction at each timepoint	SAC
53.	Screened (Part A)	Listing 64 in /arenv/arprod/gsk2269557/pii116617/part_c/drivers/l_pip_partc.sas	Listing of Phospholipid Data in Sputum (Single Dose)		SAC
Pharmacokinetic Data					
54.	PK (Part A)	PKCL1x	Listing of Plasma GSK2292767 Pharmacokinetic Concentration-Time Data (Single Dose)		SAC
55.	PK (Part A)	PKUL2x	Listing of Urine GSK2292767 Excretion Data(Single Dose)	Highest dose only so will only be 1 period of data	SAC
56.	PK (Part A)	PKPL1x	Listing of Derived Plasma GSK2292767 Pharmacokinetic Data (Single Dose)	List all Part A PK parameters	SAC

10.11.14. Non-ICH Listings: Part B (Repeat Dose)

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Safety Data					
57.	Screened (Part B)	AE2	Relationship between System Organ Class and Verbatim Text (Repeat Dose)		SAC
58.	Screened (Part B)	Other Listing 3 in /arenv/arprod/gsk2269557/pii115117/part_a/drivers/saf_l3_cp_hm7.sas	Listing of 24 Hour Holter Findings at Screening (Repeat Dose)		SAC
59.	Screened (Part B)	Similar to Other Listing 2 in /arenv/arprod/gsk2269557/pii115117/part_a/drivers/saf_l2_list.sas	Listing of Cardiac Telemetry ECG Findings (Repeat Dose)	According to the protocol, cardiac telemetry might also be done in Part B depending on emerging data.	SAC
Pharmacodynamic Data					
60.	Screened (Part B)	PFT11	Listing of %Predicted FEV1 Data at Screening (Repeat Dose)	To include 'Pred. Normal' and '%Pred Normal' columns. Exclude 'Pre/Post Broncho' and '%Rev' columns	SAC
61.	Screened (Part B)	PFT8	Listing of FEV1 Data (Repeat Dose)	Include triplicate and maximum values.	SAC

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
62.	Screened (Part B)	Listing 100 in /arenv/arprod/gsk2269557/pii116617/part_b/drivers/l_sputprep_partb.sas	Listing of Sputum Sample Preparation and Haemacytometry/Cytospin Preparation Data (Repeat Dose)	Include sputum weight and time to first induction at each timepoint	SAC
63.	Screened (Part B)	Listing 102 in /arenv/arprod/gsk2269557/pii116617/part_b/drivers/l_pip_partb.sas	Listing of Phospholipid Data in Sputum (Repeat Dose)		SAC
Pharmacokinetic Data					
64.	PK (Part B)	PKCL1p	Listing of Plasma GSK2292767 Pharmacokinetic Concentration-Time Data (Repeat Dose)		SAC
65.	PK (Part B)	PKPL1p	Listing of Derived Plasma GSK2292767 Pharmacokinetic Parameters (Repeat Dose)		SAC
66.	PK (Part B)	Listing 94 in /arenv/arprod/gsk2269557/pii116617/parts_cb/drivers/l_pkaccum_partcb.sas	Listing of Peak and Trough Accumulation and GSK2292767 Peak:Trough Ratios (Repeat Dose)		SAC

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
67.	PK (Part B)	Listing 98 in /arenv/arprod/gsk2269557/pii116617/part_b/drivers/nich_l98_part_b.sas	Listing of Plasma and BAL Fluid Urea Data (Repeat Dose)	Include Dilution Factor	SAC
68.	PK (Part B)	Listing 99 in /arenv/arprod/gsk2269557/pii116617/part_b/drivers/nich_l99_partb.sas	Listing of BAL Fluid and Derived Lung ELF GSK2292767 Pharmacokinetic Concentration Data (Repeat Dose)	Include Dilution Factor and variables in Example output. Include footnote for BAL Fluid Conc LLQ and wash vol in. List corrected concentrations instead of raw concentrations.	SAC