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

Title	:	Reporting and Analysis Plan for study 200196 A randomised double blind (sponsor unblinded), single and repeat ascending dose First Time in Human study in healthy subjects, cold urticaria and chronic spontaneous urticarial subjects to investigate safety, tolerability, pharmacodynamics and pharmacokinetics of GSK2646264
Compound Number	:	GSK2646264
Effective Date	:	30-MAR-2015

Description :

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 200196 [2013N167482_01].
- This RAP is intended to describe the safety, pharmacokinetics and pharmacodynamics analyses required for the study for Parts A, B and C.
- An informal interim review of the data following Part A, so as to provide project team and GSK stakeholders with key data to inform internal decision making, in order to start the Part B and C (cold urticaria and spontaneous urticaria subjects) of this study will be performed.
- This RAP will be provided to the study team members to convey the content of the [Reference as Required: Statistical Analysis Complete (SAC)] deliverable.

Author's Name and Functional Area:

PPD Principal Biostatistician (PAREXEL Early Phase)	30-MAR-2015

Approved by:

PPD Manager, Clinical Statistics	30-MAR-2015

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1. REPORTING & ANALYSIS PLAN SYNPOSIS

Overview	Key Elements of the RAP
Purpose	The purpose of this RAP is to describe: • An informal interim analysis, so as to provide project team and GSK stakeholders with key data to inform internal decision making, in order to start the Part B and C (cold urticaria and spontaneous urticaria subjects) of this study. • This RAP will be provided to the study team members to convey the content of the [Reference as Required: Statistical Analysis Complete (SAC)] deliverable.
Protocol	• This RAP is based on the protocol amendment 2 [(Dated: 10/DEC/2014) of study GSK2646264 (GSK Document Number: 2013N167482_01] and eCRF Version (Version 1, 09OCT2014).
Primary Objective	• The primary objective is to investigate the safety and tolerability of topically applied GSK2646264 cream and its placebo in healthy subjects, subjects with cold urticaria (CU) and subjects with chronic spontaneous urticaria (CsU)
Primary Endpoint	• Safety and Tolerability (Number, severity and frequency of AEs and serious AEs (local and systemic), heart rate, blood pressure, 12- lead ECG, clinical laboratory safety tests, assessment of the local tolerability of the study medication
Study Design	• Randomised, double blind (sponsor unblinded), bilateral, single and repeat ascending dose First Time in Human study in healthy subjects, cold urticaria and chronic spontaneous urticaria subjects. • Approximately 18 randomised evaluable subjects in Part A, and approximately 12 randomised evaluable subjects in part B and C of study.
Planned Analyses	• Safety and Tolerability, PK, PD (Allergen challenge, UAS7, AAS), Health Outcome (DLQI)
Analysis Populations	• Primary: Safety population, • Other: PK, PD, Per-Protocol populations
Hypothesis	• There are no formal hypotheses being tested in the study; instead 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 summarized descriptively according to GSK's Integrated Data Standards Library (IDSL) standards.
Secondary Analyses	• Individual GSK2646264 plasma concentration-time profiles and median/mean (±SD) profiles will be plotted and listed. Plasma concentration time data for GSK2646264 will be analyzed by non-compartmental methods using WinNonlin and derived PK parameters (AUC, C_{max}, T_{max}, $t_{1/2}$) summarized, listed and plotted. No formal statistical analyses will be conducted.
Exploratory Analyses	• All PD endpoints will be summarized, listed and graphically presented. Where

Overview	Key Elements of the RAP
	applicable, Paired t-Tests and/or ANCOVA model will be performed. Point estimates, and 95% confidence interval will be provided.

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

The following changes or deviations to the originally planned statistical analysis specified in the protocol [(Dated: 10/DEC/2014)].

- Study endpoints were modified for Part A of the study as some of the data points mentioned in original planned protocol analyses were not feasible to obtain via method and equipment used in the study.

- After Dose escalation meeting (at the end of dose group 1), dosing of dose group 2 in Part A study was modified. In a new design, subjects will be dosed up to 4 days only and up to a maximum BSA level of 10% in order to further understand the elimination phase of the systemic drug concentration. Therefore, all analyses will be carried out using new dosing plan.

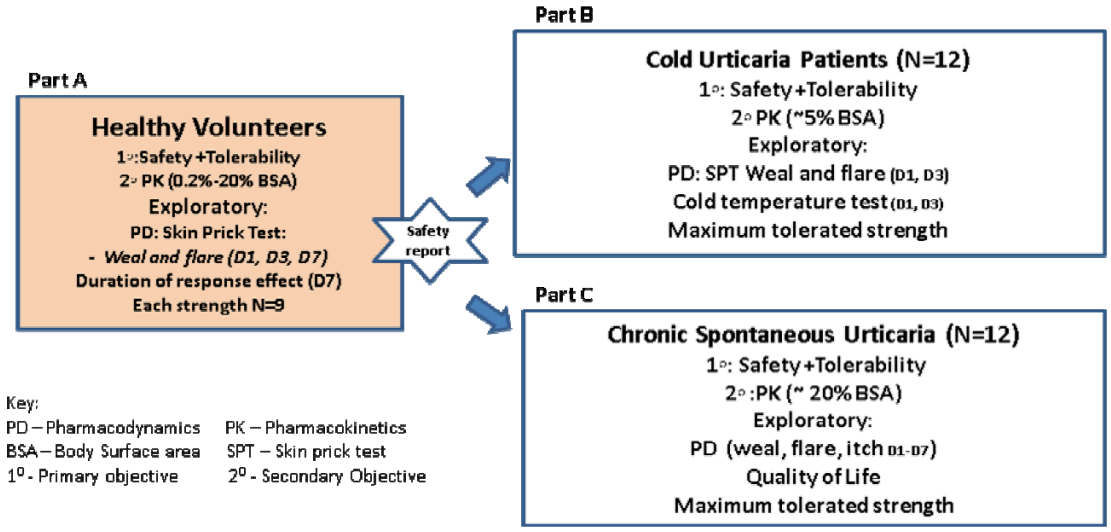
2.2. Study Objective(s) and Endpoint(s)

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
Part A, B and C	***Part A, B and C***
• To investigate the safety and tolerability of topically applied GSK2646264 cream and its placebo in healthy[1] subjects, subjects with cold urticaria (CU[1]) and subjects with chronic spontaneous urticaria (CsU).	• Number, severity and frequency of AEs and serious AEs (local and systemic) • Heart rate • Blood pressure • 12- lead ECG • Clinical laboratory safety tests • Assessment of the local tolerability of the study medication
Secondary Objectives	**Secondary Endpoints**
Part A, B and C	***Part A, B and C***
• To evaluate the plasma concentrations of GSK2646264 in Healthy, CU and CsU subjects	• Plasma concentrations of GSK2646264 and pharmacokinetic parameters, including AUC, C_{max}, T_{max}, $t_{1/2,}$ if data allows
Exploratory Objectives	**Exploratory Endpoints**
Part A: Healthy Subjects	***Part A: Healthy Subjects***
• Assess the pharmacodynamic effect of GSK2646264 on weal and flare sizes and erythema, in healthy subjects after allergen challenge (Skin Prick test, positive control (histamine) and negative control (Saline)). • Duration of response in healthy subjects	• Percent inhibition on days 1, 3, 4 and 6[6] for the longest weal diameter (measured by ruler). • Percent inhibition on days 1, 3, 4 and 6[6] for perpendicular weal length (measured by ruler). • Percent inhibition on days 1, 3, 4 and 6[6] for weal area (calculated[5]). • Percent inhibition on days 1, 3, 4 and 6[6] for Weal volume (measured by quantitative volumetric morphometry[2]) • Percent inhibition on days 1, 3, 4 and 6[6] for Flare erythema (measured by Mexameter[3]). Percent of inhibition at 48 hours post final dose, will be derived for the endpoints above

Objectives	Endpoints
Part B: Cold Urticaria Subjects	***Part B: Cold Urticaria Subjects***
• To assess the pharmacodynamic effect of GSK2646264 on weal and flare sizes and erythema, in cold urticaria subjects after allergen challenge (Skin Prick test, positive control (histamine) and negative control (Saline)).	• Percent inhibition on days 1, and 3 for the longest weal diameter (measured by ruler). • Percent inhibition on days 1, and 3 for perpendicular weal length (measured by ruler). • Percent inhibition on days 1, and 3 for weal area (calculated). • Percent inhibition on days 1, and 3 for Weal volume (measured by quantitative volumetric morphometry[1]) • Percent inhibition on days 1, and 3 for Flare erythema (measured by Mexameter[2]).
• To assess the effect of GSK2646264 on Cold Temperature Test values	• Change in Cold Temperature Test[4] values at day 1 and day 3
Part C: Chronic Spontaneous Urticaria Subjects	***Part C: Chronic Spontaneous Urticaria Subjects***
• To assess the effect of GSK2646264 on weal characterisation in CsU subjects within treated area only	• Urticaria Activity Score, a composite score using key urticaria symptoms (number of weals, Itch/Pruritus), to derive change from baseline on Day 1 through to Day 7
• To assess the Quality of Life in CsU subjects.	• Change from baseline in total Dermatology Life Quality Index (DLQI) score
• To assess the disease activity in CsU subjects.	• Change from baseline in Angioedema Activity Score (AAS)
• To investigate the relationships between (basophil histamine release) BHR test and weal characteristics	• Relationship of positive BHR test with reduction in number or size of weals

1 All Healthy subjects and the Cold Urticaria subjects should be screened for reactivity to one of the allergens used in skin prick test. (grass pollen, Dermatophagoides pteronyssinus, birch pollen and cat dander)
2 Measured using digital camera using PRIMOS 5.075D instrument software produced by GMF
3 Measures erythema and melanin index values using narrow band spectrophotometry
4 TEMPTest 4.0
5 Calculated as ellipse or oval area

2.3. Study Design

Overview of Study Design and Key Features	
	
Design Features	• This is a randomized double blind (sponsor unblinded), single, bilateral and repeat ascending dose First Time in Human study designed to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of GSK2646264 or matching placebo conducted in three parts: Part A (healthy subject cohort, inpatient), Part B (cold urticaria subject cohort, inpatient) and Part C (chronic spontaneous urticarial subject cohort, outpatient).
Dosing	• There will be a 7-28 day period from screening to admission to the clinic on Day -1. • Subjects randomised on Day -1 in Part A and B and on Day 1 in Part C of study. • Dosing will start on Day 1. The cream will be applied at 10 mg/cm2 for all doses but the dose escalation is based on both increase in cream strength (0.5 % strength for Group 1 Part A; and if data permits 1.0% strength for Group 2 Part A), and increase in surface area of the body on which the cream will be applied. The escalation based on body surface area (BSA) starts at 0.2% BSA, then 1%, then 5% BSA, then 10% BSA,. For the study, the total BSA has been chosen as 1.8 m2 and will not be measured individually, so the surface area on which the cream is applied is similar for all subjects as follows, regardless of their weight and height. All weights of cream are nominal and any one dose will not exceed 40 g.
Treatment Assignment	• Subjects will participate in the study if they fulfil the eligibility criteria at the time of screening and prior to randomisation for the relevant cohort for which they are assessed. This is the first clinical application for GSK2646264 in any formulation and therefore first exposure in each part of the study will enroll 1 sentinel subject for: o Part A dosing group1

Overview of Study Design and Key Features	
	○ Part A dosing group 2 ○ Part B ○ Part C Each sentinel subject will be dosed at least 1 day before any other subjects of their dosing group or cohort. • Subjects will be assigned to treatment in accordance with the randomization schedule using IVRS system. Randomisation will occur within each cohort of study. Each subject will be randomised to receive bilateral treatment of GSK2646264 or placebo. Randomisation will assign active and placebo to specified areas on left or right side of the body. The left or right side assignment of treatment always refers to the subject's left or right.
Interim Analysis Informal data review	• No formal interim analyses are planned. • An informal summary of the safety, tolerability, PK and PD data from Part-A will be performed once all subjects are recruited and completed all visits.

2.4. Statistical Hypotheses

The primary focus of the statistical analysis is to describe safety and characterize the preliminary pharmacokinetics of GSK2646264 through estimates of parameters and their variability. Thus, an estimation approach will be taken and 95% confidence intervals will be constructed to provide a plausible range of values, where appropriate, with no formal hypothesis testing. Sample size estimations and results of succeeding sensitivity analyses are given in 9.2 of the protocol.

3. PLANNED ANALYSES

3.1. Interim Analysis (Informal Data review)

No formal interim analyses are planned.

Analysis	Definition / Criteria Analyses Evaluated
During the study	There will be ongoing data reviews conducted by the study team of the unblinded safety and pharmacodynamic data, and any available pharmacokinetic data throughout the trial progression.
Dose Escalation	Dose escalation meetings will be performed as stated in the protocol. At the end of dosing group 1 in Part A, the decision to proceed to the next higher strength and dose for dosing group 2 will be made by the SMC based on a safety report from the PI or designee, on the clinical safety, tolerability, up to and including the follow up visit, and pharmacokinetic exposure up to 24 hours after the last dose, in at least 6 subjects at the highest dose level. The GSK review team will be unblinded to the randomisation code and will usually include the GSK pharmacokineticist, GSK statistician, GSK data management, GSK medical monitor, GSK study team leader, GSK Global Clinical Safety and

Analysis	Definition / Criteria Analyses Evaluated
	Pharmacovigilance and GSK Clinical Matrix Team leader.
Part A Completion	A summary of the safety, tolerability, PK and PD data from Part-A will be performed once all subjects are recruited and completed all visits. This summary will include PK and PD data from Part-A of study cohort. All safety data including adverse events, tolerability, laboratory tests, ECGs and vital signs will be reviewed. The decision to proceed to Part B and C will be made by the investigator and the GSK SMC review team based on assessment of safety and pharmacokinetic data of the studied doses.

The Investigator or designee, study coordinators and any other unit staff who have been involved in assessing subjects will remain blinded during the study; however, they will attend the start of each review meeting to update the GSK team on safety and tolerability summary from each cohort; these team members will not be part of the unblinded dose escalation discussions. The investigator and/or designee should send the relevant data to the GSK review team prior to the meeting of the Safety Monitoring Committee (SMC). The study monitor will remain blinded.
The Safety Monitoring Committee (SMC) will consist of the GSK review team and the Investigator and/or designee. (See Section 5.5. of the protocol for further information)

3.2. Final Analyses

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

1. All subjects have completed (including for those subjects who withdrew or were withdrawn) the study as defined in the protocol.
2. All required database cleaning activities have been completed and final database released.
3. All criteria for unblinding the randomisation codes have been met.
4. Randomisation codes have been distributed according to procedure.
5. Database freeze has been declared by Data Management

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Safety Population	Comprise of subjects who receive at least one dose of study medication.	Study Population Safety
Pharmacokinetic (PK) Population	Comprise of all randomised subjects of the Safety Population for whom a pharmacokinetic sample was obtained and analysed.	PK-Analyses
Pharmacodynamic (PD) Population	Comprise of all randomised subjects of the Safety Population for whom a pharmacodynamic measurement sample was obtained and analysed. Analysis will be based on the actual treatment the subject received for the assigned area	PD -Analyses
Per-Protocol Population	• Comprise of all PD population subjects who receive at least one dose of study treatment and who comply with the protocol. • Protocol deviations that would exclude subjects from the PP population are defined in Appendix 1 (Protocol Deviation Management Plan) for Definition Per-Protocol Population).	As required for PD-Analyses

NOTES :

- Please refer to Appendix 10: 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.
- Important deviations which result in exclusion from the analysis population will also be summarised and listed. (Please refer to Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population)].
- Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviations Management Plan.
    - Data will be reviewed prior to unblinding and freezing the database to ensure all important deviations and deviations which may lead to exclusion from the analysis are captured and categorised in the protocol deviations dataset.
    - This dataset will be the basis for the summaries and listings of protocol deviations.

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

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

- There are no planned examination of covariates and subgroups.
- There are no planned adjustments made for multiple centres in this study.
- There are no planned adjustments for multiple comparisons or multiplicity.

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
11.1	Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population
11.2	Appendix 2: Time & Events
11.3	Appendix 3: Data Display Standards & Handling Conventions
11.4	Appendix 4: Derived and Transformed Data
11.5	Appendix 5: Premature Withdrawals & Handling of Missing Data
11.6	Appendix 6: Values of Potential Clinical Importance
11.7	Appendix 7: Examination of Covariates, Subgroups & Other Strata
11.8	Appendix 8: Model Checking and Diagnostics for Statistical Analyses.
11.9	Appendix 9: Abbreviations & Trade Marks
11.10	Appendix 10: List of Data Displays
11.11	Appendix 11: Example Mock Shells for 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 10: List of Data Displays.

Table 2 Overview of Planned Study Population Analyses for Part A, B and C of study

[Endpoint / Parameter / Display Type]	Data Displays Generated		
	Table	Figure	Listing
Randomisation			
Randomisation			Y
Disposition			
Subject Disposition	Y		
Investigational Product Status	Y		
Reasons for screen failure			Y
Reasons for withdrawals			Y
Important Protocol Deviations	Y		Y
Deviation leading to exclusion from PP population			Y
Inclusion and exclusion criteria deviation			Y
Study Population	Y		
Demographics			
Demographic Characteristics	Y		Y
Race and Racial Combinations	Y		Y
Medical History			
Medical History	Y		Y
Concomitant Medication			
Concomitant Medication	Y		Y

NOTES :

- Y = Yes display generated.

7. PRIMARY STATISTICAL ANALYSES

7.1. Safety Analyses

7.1.1. Overview of Planned Analyses

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

Table 3 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 10: List of Data Displays.

Table 3 Overview of Planned Safety Analyses for Part A, B and C of study

Endpoint / Parameter/ Display Type	Absolute				Change from Baseline			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
Drug Exposure								
Exposure to Study Drug	Y			Y				
Adverse Events								
Summary of All Adverse Events	Y			Y				
Drug-Related Adverse Events	Y							

Endpoint / Parameter/ Display Type	Absolute				Change from Baseline			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
Summary of All Localised Adverse Events	Y							
Serious Adverse Events	Y			Y				
AEs Leading to Discontinuation	Y			Y				
AE by Maximum Intensity	Y							
Clinical Laboratory Assessments								
Clinical Chemistry	Y			Y	Y			Y
Haematology	Y			Y	Y			Y
Urinalysis	Y			Y[1]	Y			
Electrocardiogram (ECG)								
ECG Findings	Y			Y	Y			Y
ECG Values	Y			Y	Y			Y
Vital Signs								
Vital Signs	Y			Y	Y			Y
Tolerability assessment								
Tolerability scores	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 (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.
- Tolerability analyses will be produced for Part A and B only.

1 Urinalysis will only list abnormal assessments

7.1.1.1. Dose Escalations

The principal investigator and study monitor will provide a report of findings during the last treatment for progressing to the next cohort, as defined in the protocol, but remain blinded. As required, ongoing data reviews will be conducted by the unblinded GSK study team throughout the trial progression.

8. SECONDARY STATISTICAL ANALYSES

8.1. Pharmacokinetic Analyses

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

Table 4 provides an overview of the planned analyses, with full details being presented in Appendix 10: List of Data Displays

Table 4 Overview of Planned Pharmacokinetic Analyses for Part A, B and C of study

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
Pharmacokinetics														
PK concentrations				Y	Y	Y	Y						Y	
PK parameters				Y			Y				Y			

NOTES :

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

8.1.1. Drug Concentration Measures

Refer to Appendix 4: Data Display Standards & Handling Conventions (Section 11.3.3 Reporting Process & Standards).

8.1.2. Pharmacokinetic Parameters

8.1.2.1. Deriving Pharmacokinetic Parameters

- Refer to Appendix : Data Display Standards & Handling Conventions (Section 11.3.3 Reporting Process & Standards).
- The pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using Phoenix WNL v6.3.
- All calculations of non-compartmental parameters will be based on actual sampling times.
- Pharmacokinetic parameters described in **Error! Reference source not found.** Table 5 will be determined from the plasma concentration-time data, as data permits.

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 from time zero to 24 hours after dosing
AUC(0-∞)	Area under the concentration-time curve extrapolated to infinity will be calculated as: **AUC = AUC(0-t) + C(t) / lambda_z**
%AUCex	The percentage of AUC (0-∞) obtained by extrapolation (%AUCex) will be calculated as: **[AUC(0-inf) – AUC(0-t)] / AUC(0-inf) x 100**
Cmax	Maximum observed concentration, determined directly from the concentration-time data.
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**

NOTES:

- Additional parameters may be included as required.
- Lambda z is the terminal phase rate constant.

8.1.2.2. Statistical Analysis of Pharmacokinetic Parameters

All the derived parameters described above will be listed. The first point, last point and number of points used in the determination of λ_z will be included on the listing of the derived parameters. For each of the PK parameters, except t_{max} and $\%AUC_{\infty extrap}$, the following summary statistics will be calculated for each active treatment group: median, maximum, minimum, arithmetic mean, standard deviation, coefficient of variation, geometric mean, 95% confidence interval for the geometric mean and standard deviation of logarithmically transformed data. For t_{max} and $\%AUC_{\infty\ extrap}$, median, maximum, minimum, arithmetic mean and standard deviation will be calculated. All statistical analysis results of these PK parameters will be presented in relation to the actual dose given (i.e. the BSA covered)

9. EXPLORATORY STATISTICAL ANALYSIS

9.1. Pharmacodynamic and Biomarker Analyses

9.1.1. Overview of Planned Pharmacodynamic Analyses

The pharmacodynamic analyses will be based on the 'Pharmacodynamic' and Per-protocol populations, unless otherwise specified. All summaries will be presented by treatment group and/or include total column. Figures comparing the different treatments will be displayed overlayed where possible.

- If endpoints are listed, then all data will be listed.

Table 6 provides an overview of the planned pharmacodynamic analyses, with full details of data displays being presented in Appendix 10: List of Data Displays.

Table 6 Overview of Planned Pharmacodynamic Analyses for Part A

[Endpoint / Parameter/ Display Type]	Untransformed													
	Absolute							Percent of Inhibition						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Allergen Challenge - Part A : Healthy Subjects														
Weal area (mm^2)				Y	Y		Y				Y	Y	Y	Y
Weal volume (mm^3)				Y	Y		Y				Y	Y	Y	Y
Longest Weal diameter (mm)				Y	Y		Y				Y	Y	Y	Y
Weal perpendicular length (Height) (mm)				Y	Y		Y				Y	Y	Y	Y
Flare erythema ((mm^2)				Y	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. Summary will be presented by dose strength, BSA and day (if applicable)
- Individual = Represents FL related to any displays of individual subject observed raw data.
- Weal area derived from weal longest diameter and perpendicular length; assuming elliptic shape.

Table 7 Overview of Planned Pharmacodynamic Analyses for Part B

[Endpoint / Parameter/ Display Type]	Untransformed													
	Absolute							Percent of Inhibition/Change [1]						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Allergen Challenge - Part B: Cold Urticaria Subjects														
Weal area (mm^2)				Y	Y		Y				Y	Y	Y	Y
Weal volume (mm^3)				Y	Y		Y				Y	Y	Y	Y
Weal longest diameter (mm)				Y	Y		Y				Y	Y	Y	Y
Weal perpendicular length (Height) (mm)				Y	Y		Y				Y	Y	Y	Y
Flare erythema ((mm^2)				Y	Y		Y				Y	Y	Y	Y
Cold Temperature Test				Y	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.
- Summary will be presented by dose strength, BSA and day (if applicable)

1. Change will be produced for Cold Tem Test endpoint

Table 8 Overview of Planned Pharmacodynamic Analyses for Part C

[Endpoint / Parameter/ Display Type]	Untransformed													
	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Pharmacodynamic - Part C: Chronic Spontaneous Urticaria Subjects														
UAS7 score				Y			Y	Y			Y	Y		Y
Angioedema Activity Score (AAS				Y			Y	Y			Y	Y		Y
UAS7 components (Number of weals, Extent of Itch)				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.
- Summary will be presented by dose strength, BSA and day (if applicable)

9.1.2. Planned Pharmacodynamic Statistical Analyses

9.1.2.1. Part C: Chronic Spontaneous Urticaria Subjects

Planned Statistical Analyses
Endpoint(s)
• Change from baseline in composite total UAS7 score and components
Model Specification
• Endpoint will be analysed using paired t test and ANCOVA to compare the treatment groups. • ANCOVA model will be fitted as: Post-Pre dose as response and pre dose as covariate.
Model Checking
• Refer to Appendix 8: Model Checking and Diagnostics for Statistical Analyses.
Model Results Presentation
• Estimated treatment difference and 95% confidence intervals will be presented.
Analysis of UAS7 Components
• Analysis of UAS7 components will be performed similar to total UAS7 composite score • Summary Statistics for each component of UAS7 questionnaire will be provided by visit.
Note: • Composite score UAS7 will be derived using key urticaria symptoms (number of weal, Itch/Pruritus). The UAS7 score will be calculated using the summation of the 7 consecutive days sum. • Other questions collected as part of UAS7 questionnaire will be listed.

9.1.2.2. The Angioedema Activity Score (AAS)

Planned Statistical Analyses

Planned Statistical Analyses
Endpoint(s)
• Change from baseline in total and individual item score
Model Specification
• Endpoint will be analyzed using paired t test and ANCOVA to compare the treatment groups. • ANCOVA model will be fitted as: Post-Pre dose as response and pre dose as covariate.
Model Checking
• Refer to Appendix 8: Model Checking and Diagnostics for Statistical Analyses.
Model Results Presentation
• Estimated treatment difference and 95% confidence intervals will be presented.
Analysis of AAS Components
• Summary Statistics for each component AAS questionnaire will be provided by visit.
Note: • Details of the Angioedema Activity Score (AAS) questionnaire are provided in Appendix 7 of the protocol. Each AAS item will be scored between 0 to 3 and daily total score AAS score will range between 0 and 15. The daily AAS score will be summed up to compute 7-day total scores

9.1.2.3. Relationships between Basophil Histamine Release (BHR) Test and Weal Characteristics

Planned Statistical Analyses
Endpoint(s)
• Positive BHR Test
Model Specification
• Endpoint will be analyzed using logistic regression with weal characteristics (i.e. weal length) as covariate to establish the relationship between BHR test and weal characteristics.
Model Checking
• Refer to Appendix 8: Model Checking and Diagnostics for Statistical Analyses.
Model Results Presentation
• Odds Ratio and 95% Confidence intervals

9.1.3. Planned Health Outcome Statistical Analyses

Table 9 Overview of Planned Health Outcome Analyses for Part C

[Endpoint / Parameter/ Display Type]	Untransformed													
	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Health Outcome - Part C: Chronic Spontaneous Urticaria Subjects														
Dermatology Life Quality Index (DLQI)				Y	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.
- Summary will be presented by dose strength, BSA and day (if applicable)

9.1.3.1. Health Outcomes Analyses/ Dermatology Life Quality Index

Planned Statistical Analyses	
Endpoint(s)	
• Change from baseline in total and individual domain scores	
Model Specification	
• Endpoint will be analyzed using paired t test to compare the improvement in quality of life	
Model Checking	
• Refer to Appendix 8: Model Checking and Diagnostics for Statistical Analyses.	
Model Results Presentation	
• Estimated treatment difference and 95% confidence intervals will be presented.	
Note: The scoring of each question is as follows:	
Very much	scored 3
A lot	scored 2
A little	scored 1
Not at all	scored 0
Not relevant	scored 0
Question unanswered	scored 0
Question 7: "prevented work or studying"	scored 3
• The DLQI is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. The higher the score, the more quality of life is impaired.	
• The six subscores will be derived as follows:	

Planned Statistical Analyses		
Symptoms and feelings	Questions 1 and 2	Score maximum 6
Daily activities	Questions 3 and 4	Score maximum 6
Leisure	Questions 5 and 6	Score maximum 6
Work and School	Question 7	Score maximum 3
Personal relationships	Questions 8 and 9	Score maximum 6
Treatment	Question 10	Score maximum 3

9.1.4. Overview of Planned Biomarker Analyses

The biomarker analyses will be based on the 'Pharmacodynamic' population, unless otherwise specified.

Table 10 provides an overview of the planned pharmacodynamic analyses, with full details of data displays being presented in Appendix 10: List of Data Displays.

Table 10 Overview of Planned Biomarker Analyses

Endpoint / Parameter/ Display Type	Untransformed													
	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
Biomarker - Part A: Healthy Subjects														
Percent inhibition of CD69 biomarker				Y			Y						Y	
Biomarker - Part C: Chronic Spontaneous Urticaria Subjects														
Percent Inhibition of CD69 biomarker				Y			Y					Y		

9.2. Pharmacokinetics and Biomarker Analyses

A potential relationship between plasma exposures of GSK2646264 (C_{min}) and changes in biomarker levels and primary endpoints will be explored graphically by plotting their respective time course profiles and systemic exposure versus response profiles. The responsibility for conducting PK-PD analyses will be CPMS. These analyses will not be part of this SAP and will be reported separately.

10. REFERENCES

GlaxoSmithKline Document Number 2013N167482_01 (Protocol Amendment – 02-10-DEC-2014): A randomised double blind (sponsor unblinded), single and repeat ascending dose First Time in Human study in healthy subjects, cold urticaria and chronic spontaneous urticaria subjects to investigate safety, tolerability, pharmacodynamics and pharmacokinetics of GSK2646264 .

ICH E9, ICH HARMONISED TRIPARTITE GUIDELINE 1998
http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E9/Step4/E9_Guideline.pdf

11. APPENDICES

Section	Appendix
RAP Section 4 : Analysis Populations	
Section 11.1	Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population
RAP Section 5 : General Considerations for Data Analyses & Data Handling Conventions	
Section 11.2	Appendix 2: Time and Events
Section 11.3	Appendix 3: Data Display Standards & Handling Conventions • Study Treatment & Sub-group Display Descriptors • Baseline Definitions & Derivations • Reporting Process & Standards
Section 11.4	Appendix 4: Derived and Transformed Data • General, Study Population & Safety • Efficacy • Pharmacokinetic • Pharmacodynamic and or Biomarkers
Section 11.5	Appendix 5: Premature Withdrawals & Handling of Missing Data • Premature Withdrawals • Handling of Missing Data
Section 11.6	Appendix 6: Values of Potential Clinical Importance
Section 11.7	Appendix 7: Examination of Covariates and Subgroups
Section 11.8	Appendix 8: Model Checking and Diagnostics for Statistical Analyses
Other RAP Appendices	
Section 11.9	Appendix 9: Abbreviations & Trade Marks
Section 11.10	Appendix 10: List of Data Displays
Section 11.11	Appendix 11: Example Mock Shells for Data Displays

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

11.1.1. Protocol Deviation Definitions for Exclusion from predefined Populations

- Exclusions from the Study Populations should be defined prior to unblinding and should be summarized and listed [ICH E9, 1998, Section 5.2.2.] This will be included in Section 6.1 – Study Populations.
    - Exclusions from study populations may be defined as a subset of the Important Deviations as appropriate. These details should be documented in the Plan for Managing Protocol Deviations and in the RAP.
    - Any planned exclusions from study populations which are not considered to be deviations, should be defined in the RAP with rationale and any programming details as appropriate.

11.1.2. Exclusions from Per Protocol Population

A subject meeting any of the following criteria will be excluded from the Per Protocol population:

Number	Exclusion Description
01	• Failure of any inclusion/exclusion criteria
02	• Subjects who developed the withdrawal criteria but were not withdrawn
03	• Any deviation that impact the safety of subjects
04	• Failed to provide scheduled assessment
05	• Major deviation from the conduct of trial

Protocol deviation definition criteria and resulting exclusion from analysis populations will be agreed and summarized in a separate protocol deviation definition document that has to be updated and reviewed on a regular basis.

11.2. Appendix 2: Time & Events

11.2.1. Protocol Defined Time & Events

11.2.1.1. Part A, Dose Group 1 (Healthy Volunteers)

Day:	Screening	-1	1	2	3	4	Follow-up	Notes
Visit Window (relative to Day 1)	-28 to -7						Day 5 to Day 7	
Admission to Unit		X						
Informed Consent	X							
Demographics	X							
Complete physical	X						X	
Body weight (kg)	X							
Height (cm) without shoes	X							
Brief physical		X						
Medical/medication/drug/ alcohol history	X							
12-lead ECG[1]	X	X				X	X	1. Triplicate ECG at screening and CV risk factors questionnaire
Vital signs	X	X	X	X	X	X	X	
Urine drug/alcohol screen	X	X						
HIV, Hep B and Hep C screen	X							
Clinical Laboratory Tests	X	X				X	X	

Day:	Screening	-1	1	2	3	4	Follow-up	Notes
Visit Window (relative to Day 1)	-28 to -7						Day 5 to Day 7	
Allergen Challenge- Skin Prick Test	X[3,4]		X[3, 5]		X[3,5]	X[7]		3. SPT- Skin Prick Test analysis will be performed at ~15-20mins post challenge. 4. SPT with all 4 specified allergens 5. SPT using one allergen will be performed 6 hours post dose (see Clinical Trial Protocol Section 6.4.1) 7. SPT using one allergen will be performed 24 hrs after the last dose
TSH[2]	X							2. TSH test only at screening only
Randomisation		X						
Tolerability Assessment			X[9] ←----------→					9. Tolerability assessment at pre – and ~6 hours post-dose Note: No tolerability assessment on day 4.
AE assessment		X	←----------→				X	
Concomitant Medication		X	←----------→				X	
Pharmacokinetic Blood Sample[6]			X	X	X	X[8]		6.PK blood sample taken at pre dose, 1 ,2, 4, 8, 12 and 24hr post dose 8.PK refers to sample 24 hours post dose
Study Treatment Dosing			X	X	X			
Discharge from unit						X		
Outpatient visit	X						X	

11.2.1.2. Part A: Healthy Volunteer Time and Event Table Dose group 2

Day:	Screening	-1	1	2	3	4	5	6	7	8	Follow-up	Notes
Visit Window (relative to Day 1)	-28 to -7										Day 9 – Day 11	
Admission to Unit		X										
Informed Consent	X											
Demographics	X											
Complete physical	X										X	
Body weight (kg)	X											
Height (cm) without shoes	X											
Brief physical		X										
Medical/medication/drug /alcohol history	X											
12-lead ECG[1]	X	X								X	X	1. Triplicate ECG at screening and CV risk factors questionnaire
Vital signs	X	X	X	X	X	X	X	X	X	X	X	
Urine drug/alcohol screen	X	X										
Urine for metabolite analysis			X[10]			X[22]						10. Pre dose and pool samples taken 0-12 and 12-24 hours post dose 22. Pool samples taken 0-12 and 12-24 hours post
HIV, Hep B and Hep C screen	X											
Clinical Laboratory Tests	X[17]	X[17]		X[9]		X[9]	X[17]		X[17]		X[17]	9. Pre-dose AST, ALT, Alkaline Phosphatase, Total Bilirubin Only- : results to be communicated to the GSK Medical monitor on the same day 17.Clinical lab test as per Section 6.3.4 of the protocol

Day:	Screening	-1	1	2	3	4	5	6	7	8	Follow-up	Notes
Visit Window (relative to Day 1)	-28 to -7										Day 9 – Day 11	
Allergen Challenge- Skin Prick Test	X[3,4]		X[3,5]		X[3,5]	X[3, 5]		X [3,7]				3. SPT- Skin Prick Test measurements will be performed ~15-20 mins post challenge. 4. SPT with all 4 specified allergens 5. SPT will be performed 6 hours post dose 7. SPT will be performed 48 hours post dose of Day 4 (on the morning of Day 6)
TSH[2]	X											2. TSH test only at screening only
Randomisation		X										
Tolerability Assessment			X[11] ←----------→ only on dosing days 1 to 4									11. Tolerability assessment at pre – and ~6 hours post-dose on dosing days
AE assessment		X	←----------→								X	
Concomitant Medication		X	←----------→								X	
Pharmacokinetic Blood Sample			X[6]	X[6]	X[6]	X[6]	X[18]	X[19]	X[20]	X[21]		6. PK blood sample taken at pre dose, 1, 2, 4, 8, 12 and 24hours post previous dose 18. PK blood sample taken at 30, 36, 48 hours, post dose of Day 4 19. PK blood sample taken at 54, 60, 72 hours, post dose of Day 4 20. PK blood sample taken at 78, 84 hours post dose of Day 4 21. PK blood sample taken at 96 hours post dose of Day 4

Day:	Screening	-1	1	2	3	4	5	6	7	8	Follow-up	Notes
Visit Window (relative to Day 1)	-28 to -7										Day 9 – Day 11	
Blood Sample for CD69 expression			X[12]			X[13]	X[14]		X[15]	X[16]		12. Predose 13. 4 hours post dose of Day 4 14. 24 hours post dose of Day 4 (sample taken in the morning of day 5) 15. 72 hours post dose of Day 4 16. 96 hours post dose of Day 4
Study Treatment Dosing[8]			X	X	X	X						8. This will be once daily dosing using fresh bottles at 1% strength in the morning
Discharge from unit										X		
Outpatient visit	X										X	

11.2.1.3. Part B (Cold Urticaria Subjects)

Day:	Screening	-1	1	2	3	4	Follow-up	Notes
Visit Window (relative to Day 1)	-28 to -7 days						Day 5 to Day 7 after last dose	
Admission to Unit		X						
Informed Consent	X							
Demographics	X							
Complete physical	X						X	
Body weight (kg)	X							
Height (cm) without shoes	X							
Brief physical		X						
Medical/medication/ drug/alcohol history	X							

Day:	Screening	-1	1	2	3	4	Follow-up	Notes
Visit Window (relative to Day 1)	-28 to -7 days						Day 5 to Day 7 after last dose	
12-lead ECG[1]	X	X			X		X	1. Triplicate ECG at screening and CV risk factors questionnaire
Vital signs	X	X	X	X	X		X	
Urine drug/alcohol screen	X	X						
Pregnancy Test (women)[2]	X(S)		X(S/U)				X(S)	2. Pregnancy test will be performed 3 times during screening, serum on day -28, day -7 to -4, and a serum or urine pregnancy test the day of the start of the study prior to dosing and a serum pregnancy test at the follow up visit
HIV, Hep B and Hep C screen	X							
Clinical Laboratory Tests	X	X			X		X	
Allergen Challenge- SPT	X[4,5]		X[4,6]		X[4,6]			4. SPT- Skin Prick Test measurements will be performed ~15-20mins post challenge 5. SPT using all 4 specified allergens 6. SPT will be performed at 6 hours post dose (see Clinical Trial Protocol Section 6.4.1)
TSH[3]	X							3. TSH test only at screening only
Cold Temp Test (Temp Test 4.0)	X		X		X	X[7]		7. 24 hours after last dose
Review of eligibility criteria and medication prior to randomisation		X						
Randomisation		X						
Tolerability Assessment			X[10] ←----------→					10. Tolerability assessment at pre – and ~6 hours post-dose
AE assessment		X	←----------→				X	
Concomitant Medication		X	←----------→				X	

Day:	Screening	-1	1	2	3	4	Follow-up	Notes
Visit Window (relative to Day 1)	-28 to -7 days						Day 5 to Day 7 after last dose	
Pharmacokinetic Blood Sample[8]			X		X	X[9]		8. PK blood sample taken at pre dose,1,2,4, 8, 12hr post dose 9. If only once daily dosing then a PK sample will be taken at 24h post dose
Study Treatment Dosing			X	X	X			
Discharge from unit						X		
Outpatient visit	X						X	

11.2.1.4. Part C (Chronic Spontaneous Urticaria Cohort)

Day:	Screening	1	2	3	4	5	6	7	Follow-up	Notes
Visit Window (relative to Day 1)	-28 to -7 days								9-14 days after last dose	
Informed Consent	X									
Demographics	X									
Complete physical	X								X	
Body weight (kg)	X									
Height (cm) without shoes	X									
Brief physical		X							X	
Medical/medication/ drug/alcohol history	X									
12-lead ECG[1]	X	X						X	X	1. Triplicate ECG at screening and CV risk factors questionnaire
Vital signs	X	X			X			X	X	
Urine drug/alcohol screen	X	X								

Day:	Screening	1	2	3	4	5	6	7	Follow-up	Notes
Visit Window (relative to Day 1)	-28 to -7 days								9-14 days after last dose	
Pregnancy Test (women)[2]	X(S)	X (S/U)							X(S)	2. Pregnancy test will be performed 3 times during screening, serum (S) on day -28, day -7 to -4, and a serum or urine (U) pregnancy test the day of the start of the study prior to dosing and a serum pregnancy test at the follow up visit
HIV, Hep B and Hep C screen	X									
Clinical Laboratory Tests	X	X						X	X	
TSH[3]	X									3. TSH test only at screening only
Blood Sample for CD69 expression[11]		X[9]						X[10]		9. Predose 10. 4 hours post dose 11 A decision will be made after Part A on whether samples are taken in Part C
Randomisation		X								
UAS-7 Diary[4]	X	X	X	X	X	X	X	X		4. Screening UAS7 diary will be completed using 7 successive days before randomisation (day 1). If there is a lapse in any day prior to day 1 the subject must complete the full 7 days worth of diary entries again during the screening period.
QOL (DLQI)	X	X						X		
AAS	X	X	X	X	X	X	X	X		
AE assessment		X[8] ←----------→							X	8. Tolerability assessment at pre – and post-dose

Day:	Screening	1	2	3	4	5	6	7	Follow-up	Notes
Visit Window (relative to Day 1)	-28 to -7 days								9-14 days after last dose	
BHR- Basophil Histamine Release Test		X[5]								5. Sample taken predose
Pharmacokinetic Blood Sample[6]		X			X			X		6. PK blood sample taken at pre-dose sample and 2 and 4hr post dose
Study Treatment Dosing		X	X[7]	X[7]	X	X[7]	X[7]	X		7. The nurse will visit the subject at home to apply the dose
Outpatient visit	X	X			X			X	X	

11.3. Appendix 3: Data Display Standards & Handling Conventions

11.3.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions			
RandAll NG		Data Displays for Reporting	
Code	Description	Description	Order [1]
A	GSK2646264 X.X mg	GSKX.X mg	2
P	Placebo	Placebo	1

NOTES:

1. Order represents treatments being presented in TFL. Placebo is to be presented at start in Tables, Figures and Listings. Dosing of GSK treatment will be displayed in ascending order, where appropriate.

In accordance with the body surface area (BSA) to be used Arm, Leg and Front Torso of the subjects had to be treated on the different body sides with either GSK2646264 or matching placebo treatment as displayed below:

Table 11 Overview of Treatments Doses and Analyses.

Part	Dose	BSA treated per body side (left/right)	Day of Treatment (Tests performed)	Comment
A	0.5% (Group 1)	0.2% 1% 5%	D1 (PK/PD) D2 (PK) D3 (PK/PD)	qd
A	1.0% (Group 2)	5% 5% 10% 10%	D1 (PK/PD) D2 (PK) D3 (PK/PD) D4 (PK)	qd
B	.0.5 or 1%	0.2%+5% 0.2%+5% 0.2%+5%	D1(PK/PD) D2 D3(PK/PD)	qd or bid (D3 morning dose only)
C	.0.5 or 1%	X.X2%	D1 (PK/PD) D2 (PD) D3 (PD) D4 (PK/PD) D5 (PD) D6 (PD) D7 (PK/PD)	Qd or bid

[1] maximum tolerated dose (taken from Part A)
[2] maximum BSA treated (taken from Part A)

The following changes to treatment dosing were made to dose group 2 (Part A) in light of dose escalation review meeting at the end of dose group 1:

Table 12 Treatment applied to specified areas per day on Part A; healthy subjects, n=9, dose group 2

	Day 1-2	Day 3-4	Day 5 to 7
Area	**AM[a]**	**AM[a]**	
Left Arm	0.36g of 1.0%[b] GSK2646264 or placebo cream applied to 36cm^2 (~0.2% BSA)		NO DOSING
Right Arm	0.36g of 1.0%[b] GSK2646264 or placebo cream applied to 36cm^2 (~0.2% BSA)		NO DOSING
Left Front Torso	9g of 1.0% [b] GSK2646264 or placebo cream applied to 900cm^2 (~5% BSA)	18g of 1.0% [b] GSK2646264 or placebo applied to 1800cm^2 (~10% BSA)	NO DOSING
Right Front Torso	9g of 1.0% [b] GSK2646264 or placebo applied to 900cm^2 (~5% BSA)	18g of 1.0% [b] GSK2646264 or placebo applied to 1800cm^2 (~10% BSA)	NO DOSING

a. AM dosing only
b. 0.5% strength may be used if data for Part A and/or group 2 supports

11.3.2. Baseline Definition & Derivations

11.3.2.1. Baseline Definitions

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

Parameter	Study Assessments Considered As Baseline			Baseline Used in Data Display
	Screening	Day -1	Day 1 (Pre-Dose)	
Safety Assessment				
Laboratory	X	X[2]		Day -1, (Part A & B) Screening (Part C)
Vital Signs	X		X	Day 1 (pre)
ECG	X	X		Screening[1]
Pharmacodynamics				
Allergen Challenge SPT (Part A & B)				No baseline
Cold Temp test (Part B)				No baseline
UAS7 (Part C)	X			Screening
AAS (Part C)	X			Screening

Parameter	Study Assessments Considered As Baseline			Baseline Used in Data Display
	Screening	Day -1	Day 1 (Pre-Dose)	
Health Outcome				
DLQI (Part C)	X			Screening

NOTES :

1. Use the mean of replicate assessments at any given time point as the value for that time point in all summaries, figures and statistical analyses.
2. Not in Part C

11.3.2.2. 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]
% inhibition	=[(control – treatment)/control]x100

NOTES :

- Unless otherwise specified, the baseline definitions specified in Section 11.3.2.1 Baseline Definitions will be used for derivations for endpoints / parameters and indicated on summaries and listings.
- Unless otherwise stated, if baseline data is missing no derivation will be performed and will be set to missing.
- As only one baseline will be defined for all parameters (i.e. at the start of the study), there will only be one baseline on all summaries (i.e. not a separate baseline for each subsequent repeat dose).
- The baseline definition will be footnoted on all change from baseline outputs, where applicable.
- If baseline value for (day -1) is missing, screening value will be used as baseline. If both assessments are missing then no derivation will be performed and will be set to missing..

11.3.3. Reporting Process & Standards

Reporting Process	
Software	
• The currently supported versions of SAS software will be used to perform all data analyses and generation of displays (tables, figures, and listings).	
Reporting Area	
HARP Server	PHU058
HARP Area	: \ARWORK\GSK2646264\final or \ARWORK\GSK2646264\final
QC Spreadsheet	: Not applicable]
Analysis Datasets	
• Analysis datasets will be created according to CDISC / ADaM Standards Library standards. For creation of ADaM datasets (ADCM/ADAE), the same version of dictionary datasets will be implemented for conversion from SI to SDTM.	
Generation of Files	
• PDF files will be generated.	

Reporting Standards	
General	
• The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated: o 4.03 to 4.23: General Principles o 5.01 to 5.08: Principles Related to Data Listings o 6.01 to 6.11: Principles Related to Summary Tables o 7.01 to 7.13: Principles Related to Graphics	
Formats	
• All data will be reported according to the actual treatment the subject received unless otherwise stated. • GSK IDSL Statistical Principles (5.03 & 6.06.3) for decimal places (DP's) will be adopted for reporting of data based on the raw data collected. • Numeric data will be reported at the precision collected on the eCRF. • The reported precision from non eCRF sources will follow the IDSL statistical principles but may be adjusted to a clinically interpretable number of DP's.	
Planned and Actual Time	
• Reporting for tables, figures and formal statistical analyses : • Planned time relative to dosing will be used in figures, summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated. • The impact of any major deviation from the planned assessment times and/or scheduled visit days on the analyses and interpretation of the results will be assessed as appropriate. • Reporting for Data Listings: • Planned and actual time relative to study drug dosing will be shown in listings (Refer to IDSL Statistical Principle 5.05.1). • Unscheduled or unplanned readings will be presented within the subject's listings. • Visits outside the protocol defined time-windows (i.e. recorded as protocol deviations) will be included in listings but omitted from figures, summaries and statistical analyses.	
Unscheduled Visits	
• Unscheduled visits will not be included in summary tables. • Unscheduled visits will not be included in figures. • All unscheduled visits will be included in listings.	
Descriptive Summary Statistics	
Continuous Data	Refer to IDSL Statistical Principle 6.06.1 ➢ N, n, mean, 95% CI of the mean, standard deviation (SD), median, minimum (min) and maximum (max).
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	N, n, geometric mean, 95% CI of geometric mean, standard deviation (SD) of logged data and [between and or within] geometric coefficient of variation

Reporting Standards	
(Log Transformed)	(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).
Graphical Displays	
• Refer to IDSL Statistical Principals 7.01 to 7.13.	

11.4. Appendix 4: Derived and Transformed Data

11.4.1. General

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

• Calculated as the number of days from randomisation date :
  • Ref Date = Missing → Study Day = Missing
  • Randomisation 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

11.4.2. Study Population

Demographics
Age

• GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as follows:
  ○ Any subject with a missing day will have this imputed as day '15'.
  ○ Any subject with a missing date and month will have this imputed as '30th June'.
• Birth date will be presented in listings as 'YYYY'.

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

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

11.4.3. Safety

ECG Parameters

RR Interval

- IF RR interval (msec) is not provided directly, then RR can be derived as :
  [1] If QTcB is machine read & QTcF is not provided, then :

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

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

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

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

Corrected QT Intervals

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

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

Adverse Events

AE Type	Derivations
AE Onset Time Since First 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
AE Duration (Days)	➢ **AE Resolution Date – AE Onset Date + 1**
AE = On Treatment	➢ If AE onset date is on or after the treatment start date and on or before the treatment stop date.
AE = Post Treatment	➢ If AE onset date is after the treatment stop date.
AE = Drug-related	➢ If relationship is marked 'YES' on eCRF OR value is missing.

Current update MedRA version 17.1 will be used

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

Tolerability Assessments

Tolerability will be assessed with the skin irritation scoring system for Part A and B of study, where the score consists of a numeric score according to the dermal response scoring i), and a letter according to the other effects scoring ii), as follows
0 = no evidence of irritation
1 = minimal erythema, barely perceptible (pink)
2 = moderate erythema (definite redness), readily visible; minimal edema or minimal papular response
3 = strong erythema (intense redness), or erythema and papules
4 = definite edema
5 = erythema, edema, and papules
6 = vesicular eruption
7 = strong reaction spreading beyond test site
ii) Other effects:
Z = no other effect
A = slight glazed appearance
B = marked glazing
C = glazing with peeling and cracking
F = glazing with fissures
G = film of dried serous exudate covering all or part of the patch site
H = small petechial erosions and/or scabs

For each skin assessment, letter grade will be converted to numeric values as below: A=0,Z=0, B=1, C=2, F=3, G=3, H=3. A combined score for each subject will be calculated by adding all numeric and letter scores. A maximum score of 3 is allowed. Mean irritation score for each subject will be computed through the study period. Mean score will be analyzed.

11.5. Appendix 5: Premature Withdrawals & Handling of Missing Data

11.5.1. Premature Withdrawals

Element	Reporting Detail
General	• Subject study completion (i.e. as specified in the protocol) was defined as subjects who completed all visits of the study including the follow-up visit. • Withdrawn subjects were not 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.

11.5.2. Handling of Missing Data

Element	Reporting Detail
General	• Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument : o These data will be indicated by the use of a “blank” in subject listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table. o Answers such as “Not applicable” and “Not evaluable” are not considered to be missing data and should be displayed as such.
Outliers	• Any subjects excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report.
UAS7 score	In presence of one or more missing daily UAS7 scores, the following algorithm will be applied: • If a patient has at least 4 non-missing daily UAS7 scores within the 7 days, the UAS7 score will be calculated as the sum of the available eDiary UAS7 scores in that week, divided by the number of days that have a non-missing diary UAS7 score, multiplied by 7. • If there are less than 4 non-missing daily UAS7 scores, then the UAS7 score will be missing.
AAS	Missing values will not be imputed
DLQI	1. If one question is left unanswered this is scored 0 and the scores are summed and expressed as usual out of a maximum of 30. 2. If two or more questions are left unanswered the questionnaire is not scored. 3. If question 7 is answered 'yes' this is scored 3. If question 7 is answered 'no' or 'not relevant' but then either 'a lot' or 'a little' is ticked this is then scored 2 or 1. If it is answered 'no', but the second half is left incomplete, the score will remain 0. 4. If two or more response options are ticked, the response option with the highest score should be recorded. 5. If there is a response between two tick boxes, the lower of the two score options

Element	Reporting Detail
	should be recorded. 6. When using sub-scales, if the answer to one question in a sub-scale is missing, that sub-scale should not be scored.

11.5.2.1. Handling of Missing Dates

Element	Reporting Detail
General	Partial dates will be displayed as captured in subject listing displays.
Adverse Events	• The eCRF allows for the possibility of partial dates (i.e., only month and year) to be recorded for AE start and end dates; that is, the day of the month may be missing. In such a case, the following conventions will be applied for calculating the time to onset and the duration of the event: o Missing Start Day: First of the month will be used unless this is before the start date of study treatment; in this case the study treatment start date will be used and hence the event is considered On-treatment. o Missing Stop Day: Last day of the month will be used, unless this is after the stop date of study treatment; in this case the study treatment stop date will be used. • Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing. • Start or end dates which are completely missing (i.e. no year specified) will remain missing, with no imputation applied.

11.5.2.2. Handling of Partial Dates

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

11.6. Appendix 6: Values of Potential Clinical Importance

11.6.1. 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
Red Blood Cell Count (RBC)	$x10^6$ cells/µL		4.2	5.9
Mean Corpuscular Volume (MCV)	fL		80	100
Mean Corpuscular Hemoglobin (MCH)	pg		28	32
Mean Corpuscular Hemoglobin Concentration (MCHC)	g/L		32	36
Monocytes	$x10^9$/ L			0.208
Eosinophils	$x10^9$/ L			0.44
Basophils	$x10^9$/ L			0.01

Clinical Chemistry				
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (>x)**
Albumin	g/L		30	
Calcium	mmol/L		2	2.75
Creatinine	mmol/L			1.3*ULN
	µmol/L			159
	µmol/L	Δ from BL		44
Glucose	mmol/L		3	11.1
Potassium	mmol/L		3	5.5
Sodium	mmol/L		130	150

Liver Function			
Test Analyte	**Units**	**Category**	**Clinical Concern Range**

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	≥ 1.5x ULN
T Bilirubin	µmol/L	High	≥ 1.5xULN
T. Bilirubin + ALT	µmol/L U/L	High	1.5xULN T. Bilirubin + ≥ 2x ULN ALT
Urea Nitrogen (BUN)	mmol/L	Low	<2.9
Urea Nitrogen (BUN)	mmol/L	High	>7.1
Chloride	mmol/L	Low	<98
	mmol/L	High	>106
Gamma-glutamyl Transpeptidase (GGT)	U/L	Low	<8
	U/L	High	>78
Direct Bilirubin	µmol/L	High	>5.1
Total Protein	g/L	Low	<60
	g/L	High	>78

11.6.2. ECG

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

11.6.3. 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

Vital Sign Parameter (Change from Baseline)	Units	Clinical Concern Range			
		Decrease		Increase	
		Lower	Upper	Lower	Upper
Systolic Blood Pressure	mmHg	≥ 20	≥ 40	≥ 20	≥ 40
Diastolic Blood Pressure	mmHg	≥ 10	≥ 20	≥ 10	≥ 20
Heart Rate	bpm	≥ 15	≥ 30	≥ 15	≥ 30

11.7. Appendix 7: Examination of Covariates, Subgroups & Other Strata

11.7.1. Handling of Covariates, Subgroups & Other Strata

- Not applicable.

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

11.8.1. Statistical Analysis Assumptions

Endpoint(s)	• PD Parameters
Analysis	• ANOVA to estimate the effect of GSK2646264 relative to Placebo as comparison of interest. Point estimates and corresponding 95% confidence intervals will be constructed.
Analysis	• ANCOVA.
	• 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.
Analysis	• Logistic Regression
	• Model fit will be assesses by o plotting observed probability vs predictive probability o Chi-square test for goodness fit test

11.9. Appendix 9: Abbreviations & Trade Marks

11.9.1. Abbreviations

Abbreviation	Description
AAS	Angioedema Activity Score
AE	Adverse Event
ALT	Alanine aminotransferase (SGPT)
AST	Aspartate aminotransferase (SGOT)
AUC	Area under concentration-time curve
AUC(0-∞)	Area under the concentration-time curve from time zero (pre-dose) extrapolated to infinite time
AUC(0-t)	Area under the concentration-time curve from time zero (pre-dose) to last time of quantifiable concentration
AUC(0-τ)	Area under the concentration-time curve over the dosing interval
BHR	Basophil Histamine Release
BMI	Body mass index
BP	Blood pressure
BPM	Beat Per Minute
BQL	Below the quantification limit
BUN	Blood urea nitrogen
CI	Confidence Interval
Cmax	Maximum observed concentration
CPDS	Clinical Pharmacology Data Sciences
CPK	Creatine phosphokinase
CPMS	Clinical Pharmacology Modelling & Simulation
CPSR	Clinical Pharmacology Study Report
CsU	Chronic spontaneous Urticaria
CU	Cold Urticaria
CV	Coefficient of variance
DBP	Diastolic blood pressure
ECG	Electrocardiogram
FTIH	First time in humans
GGT	Gamma glutamyltransferase
GSK	GlaxoSmithKline
hCG	Human chorionic gonadotropin
HIV	Human Immunodeficiency Virus
h/hr	Hour(s)
HR	Heart rate
IP	Investigational Product
IU	International Unit
Kg	Kilogram
λz	Terminal phase rate constant
L	Liter
ln	Naperian (natural) logarithm

Abbreviation	Description
LOQ	Limit of quantification
LLQ	Lower limit of quantification
MedDRA	Medical Dictionary for Regulatory Activities
Mg	Milligrams
mL	Milliliter
msec	Milliseconds
NQ	Non-quantifiable concentration measured as below LLQ
PD	Pharmacodynamic
PK	Pharmacokinetic
QD	Once daily
RAP	Reporting and Analysis Plan
RBC	Red blood cells
SAE	Serious adverse event(s)
SAS	Statistical Analysis Software
SD	Standard deviation
SUSAR	Suspected, Unexpected, Serious Adverse drug Reaction
t½	Terminal phase half-life
τ	Dosing interval
tmax	Time of occurrence of Cmax
ULN	Upper limit of normal
WBC	White blood cells
GSK	GlaxoSmithKline

11.9.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
NONE

Trademarks not owned by the GlaxoSmithKline Group of Companies
SAS
SAS/STAT

11.10. Appendix 10: List of Data Displays

11.10.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.8	Not applicable
Safety	3.1 to 3.18	Not applicable
Pharmacokinetic	4.1 to 4.3	4.1 to 4.3
Pharmacodynamic and / or Biomarker	5.1 to 5.15	5.1 to 5.14
Section	**Listings**	
ICH Listings	1 to 28	
Other Listings	29 to 35	

11.10.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required an example mock-up displays provided in Appendix 11: Example Mock Shells for Data Displays.

Section	Figure	Table	Listing
Study Population	POP_Fn	POP_Tn	POP_Ln
Safety	SAFE_Fn	SAFE_Tn	SAFE_Ln
Pharmacokinetic	PK_Fn	PK_Tn	PK_Ln
Pharmacodynamic and / or Biomarker	PD_Fn	PD_Tn	PD_Ln
Other Listings			OTHER_Ln

NOTES:

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

11.10.3. Deliverable [Priority]

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

NOTES:

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

11.10.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Disposition					
1.1.	Safety	CP_ES1	Summary of Subject Disposition	Programmer to update primary reason for withdrawal to be study specific. Please only include Total column (not treatment columns)	IA[1], SAC [1]
1.2.	Safety	SA1	Summary of Study Populations		IA[1],SAC [1]
1.3.	Safety	DVA1	Summary of Important Protocol Deviations	Generated, if data permits. As required, refer to PDMP. Please only include Total column (not treatment columns)	IA[1],SAC [1]
1.4.	Safety	SD1	Summary of Investigational Product Status	Please only include Total column (not treatment columns)	IA[1],SAC [1]
Demographics					
1.5.	Safety	DM1	Summary of Demographic Characteristics	Please only include Total column (not treatment columns)	IA[1],SAC [1]
1.6.	Safety	DM5	Summary of Race and Racial Combinations	Please only include Total column (not treatment columns)	IA[1],SAC [1]
Medical History					
1.7.	Safety	MH4	Summary of Medical History	Please only include Total column (not treatment columns)	IA[1],SAC [1]
Concomitant Medication					

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
1.8.	Safety	CP_CM1	Summary of Concomitant Medications by Generic Term	Please only include Total column (not treatment columns)	IA[1],SAC [1]

11.10.5. Efficacy Tables

Not applicable.

11.10.6. Safety Tables

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Drug Exposure					
3.1.	Safety	EX1	Summary of Exposure to Study Drug	Please only include Total column (not treatment columns)	IA[1],SAC [1]
Adverse Events					
3.2.	Safety	CP_AE1p	Summary of All Adverse Events	Please only include Total column (not treatment columns)	IA[1],SAC [1]
3.3.	Safety	CP_AE1p	Summary of Drug-Related Adverse Events	Please only include Total column (not treatment columns)	IA[1],SAC [1]
3.4.	Safety	CP_AE1p	Summary of All Localised Adverse Events		IA[1],SAC [1]
3.5.	Safety	CP_AE1p	Summary of Serious Adverse Events	Please only include Total column (not treatment columns)	IA[1],SAC [1]
3.6.	Safety	CP_AE1p	Summary of AEs Leading to Permanent Discontinuation of Study Drug or Withdrawal from Study	Please only include Total column (not treatment columns)	IA[1],SAC [1]
3.7.	Safety	AE5	Summary of Adverse Events by Maximum Intensity/Grade	Please only include Total column (not treatment columns)	IA[1],SAC [1]
3.8.	Safety	AE2	Relationship between System Organ Class and Verbatim Text		IA[1],SAC [1]
Clinical Laboratory Assessments					
3.9.	Safety	LB1	Summary (Absolute and Change from Baseline) of Clinical Chemistry Laboratory Values	Please only include Total column (not treatment columns). Order parameters alphabetically	IA[1],SAC [1]

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.10.	Safety	LB2	Summary of Clinical Chemistry Data Outside the Reference Range	Order parameters alphabetically	IA[1],SAC [1]
3.11.	Safety	LB1	Summary (Absolute and Change from Baseline) of Haematology Laboratory Values	Please only include Total column (not treatment columns).Order parameters alphabetically	IA[1],SAC [1]
3.12.	Safety	LB2	Summary of Haematology Data Outside the Reference Range	Order parameters alphabetically	IA[1],SAC [1]
3.13.	Safety	UR3	Summary of Urinalysis Dipstick Results	Please only include Total column (not treatment columns).Order parameters alphabetically	IA[1],SAC [1]
Electrocardiogram (ECG)					
3.14.	Safety	EG1	Summary (Absolute and Change from Baseline) of ECG Findings	Please only include Total column (not treatment columns).Order parameters alphabetically	IA[1],SAC [1]
3.15.	Safety	EG2	Summary (Absolute and Change from Baseline) of ECG Values	Please only include Total column (not treatment columns).Order parameters alphabetically	IA[1],SAC [1]
Vital Signs					
3.16.	Safety	VS1	Summary (Absolute and Change from Baseline) of Vital Signs	Please only include Total column (not treatment columns).Order parameters alphabetically	IA[1],SAC [1]
Tolerability assessment					
3.17.	Safety	Non- Standard SAFE_T1	Summary (Absolute and Change from Baseline) of Mean irritation score assessment		IA[1],SAC [1]

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.18.	Safety	Non- Standard SAFE_T2	Assessment of Maximum Dermal Reactions and Response		IA[1],SAC [1]

11.10.7. Safety Figures

Not applicable.

11.10.8. Pharmacokinetic Tables

Pharmacokinetic : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Pharmacokinetics					
4.1.	PK	PKCT1	Summary of Serum GSK2646264 Pharmacokinetic Concentrations versus time by actual dose		IA[1],SAC [1]
4.2.	PK	PKPT1	Summary of Derived Serum GSK2646264 Pharmacokinetic Parameters by actual dose		IA[1],SAC [1]
4.3.	PK	PKPT3	Summary of Log-Transformed Derived Serum GSK2646264 Pharmacokinetic Parameters by actual dose		IA[1],SAC [1]

11.10.9. Pharmacokinetic Figures

Pharmacokinetic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Pharmacokinetics					
4.1.	PK	PKCF1	Individual Serum GSK2646264 Concentration-Time Plot (Linear and Semi-log)	1. x-axis should display Actual relative time 2. Include line for LLQ along with footnote defining LLQ value. 3. Include values below LLQ	IA[1],SAC [1]
4.2.	PK	PKCF3	Median Serum GSK2646264 Concentration-Time Plot (Linear and Semi-log)	1. X-axis should display Planned relative time 2. Include line for LLQ along with footnote defining LLQ value. 3. Include values below LLQ Use different symbols for treatments	IA[1],SAC [1]
4.3.	PK	PKCF4	Mean and SD of Serum GSK2646264 Concentration-Time Plot (Liner and Semi-log)	1. X-axis should display Planned relative time 2. Include line for LLQ along with footnote defining LLQ value. 3. Include values below LLQ Use different symbols for treatments	IA[1],SAC [1]

11.10.10. Pharmacodynamic and Biomarker Tables

Pharmacodynamic and Biomarker: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Pharmacodynamics					
5.1.	PD	Non-Standard_PDT 1	Allergen Challenge, Weal Area - Summary Statistics (Absolute and Percent of Inhibition)	Absolute and Percent of Inhibition Part A + B	IA[1],SAC [1]
5.2.	PD	Example Non-Standard_PDT 1 modified based on endpoint.	Allergen Challenge, Weal Volume – Summary Statistics (Absolute and Percent of Inhibition)	Absolute and Percent of Inhibition Part A + B	IA[1],SAC [1]
5.3.	PD	Example Non-Standard_PDT 1 modified based on endpoint.	Allergen Challenge, Longest Weal Diameter- Summary Statistics (Absolute and Percent of Inhibition)	Absolute and Percent of Inhibition Part A + B	IA[1],SAC [1]
5.4.	PD	Example Non-Standard_PDT 1 modified based on endpoint.	Allergen Challenge, Weal perpendicular length - Summary Statistics (Absolute and Percent of Inhibition)	Absolute and Percent of Inhibition Part A + B	IA[1],SAC [1]
5.5.	PD	Example Non-Standard_PDT 1 modified based on endpoint.	Allergen Challenge, Flare Erythema - Summary Statistics (Absolute and Percent of Inhibition)	Absolute and Percent of Inhibition Part A + B	IA[1],SAC [1]

Pharmacodynamic and Biomarker: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.6.	PD	Example Non-Standard_PDT 1 modified based on endpoint.	Cold Temp Test, Change in critical temperature thresholds	Absolute Part B only	SAC [1]
5.7.	PD	Example Non-Standard_PDT 1 modified based on endpoint.	UAS7 Scores – Summary Statistics (Absolute and Change from Baseline**)**	Absolute and Change from Baseline Part C only	SAC [1]
5.8.	PD	Example Non-Standard_PDT 2	Change from baseline in composite total UAS7 Scores – Treatment Comparison	Paired t-Test (95%CI) and ANCOVA to compare treatments groups. Pre-Dose Value as Covariate Part C only	SAC [1]
5.9.	PD	Example Non-Standard_PDT 1 modified based on endpoint.	UAS7 Components – Summary Statistics (Absolute and Change from Baseline)	Absolute and Change from Baseline Part C only	SAC [1]
5.10.	PD	Example Non-Standard_PDT 2 modified based on endpoint.	Change from baseline in composite total UAS7 Components – Treatment Comparison	Paired t-Test (95%CI) and ANCOVA to compare treatments groups. Pre-Dose Value as Covariate Part C only	SAC [1]

Pharmacodynamic and Biomarker: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.11.	PD	Example Non-Standard_PDT 1 modified based on endpoint.	Angioedema Activity Score (AAS) – Summary Statistics (Absolute and Change from Baseline)	Absolute and Change from Baseline Part C only	SAC [1]
5.12.	PD	Example Non-Standard_PDT 2 modified based on endpoint.	Change from baseline in total Angioedema Activity Score (AAS) – Treatment Comparison	Paired t-Test (95%CI) and ANCOVA to compare treatments groups. Pre-Dose Value as Covariate Part C only	SAC [1]
5.13.	PD	Example Non-Standard_PDT 1 modified based on endpoint.	Dermatology Life Quality Index (DLQI) – Summary Statistics (Absolute and Change from Baseline)	Absolute and Change from Baseline Part C only Sum-Score and Analysis of Subscores	SAC [1]
5.14.	PD	Example Non-Standard_PDT 2 modified based on endpoint.	Change from baseline in total Dermatology Life Quality Index (DLQI) – Comparison Improvement from baseline	Paired t-Test (95%CI) Part C only No treatment comparison involved. Improvement from baseline in Quality Index	SAC [1]

Pharmacodynamic and Biomarker: Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Biomarker					
5.15.	PD	Example Non-Standard_PDT 1 modified based on endpoint.	Inhibition of CD69 biomarker by strength, BSA and day – Summary Statistics	Part A + C	IA[1],SAC [2]
5.16.	PD	Example Non-Standard_PDT 1 modified based on endpoint.	Relationship between Basophil Histamine (BHR) test and Weal Characteristics	Part C only No treatment comparison involved.	SAC[2]

11.10.11. Pharmacodynamic Figures

Pharmacodynamic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Pharmacodynamics					
5.1.	PD	Non-Standard _PD_F1	Allergen Challenge, Weal Area (Percent of Inhibition) - Individual Subject Plot	Part A + B Page by : Treatment X-Axis : Continuous scale for visit (days) Y-Axis : Scaled accordingly to Parameter and include parameter name Legend : Subject	SAC [1]
5.2.	PD	Non-Standard _PD_F2	Allergen Challenge, Weal Area (Percent of Inhibition, absolute value) - Box Plot	Part A + B X-Axis : Days Y-Axis : Result Legend : Treatment	SAC [1]

Pharmacodynamic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.3.	PD	Example Non-Standard _PD_F1	Allergen Challenge, Weal Volume (Percent of Inhibition) - Individual Subject Plot	Part A + B Page by : Treatment X-Axis : Continuous scale for visit (days) Y-Axis : Scaled accordingly to Parameter and include parameter name Legend : Subject	SAC [1]

Pharmacodynamic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.4.	PD	Example Non-Standard _PD_F2	Allergen Challenge, Weal Volume (Percent of Inhibition, absolute value) - Box Plot	Part A + B X-Axis : Days Y-Axis : Result Legend : Treatment	SAC [1]
5.5.	PD	Example Non-Standard _PD_F1	Allergen Challenge, longest weal Diameter (Percent of Inhibition) - Individual Subject Plot	Part A + B Page by : Treatment X-Axis : Continuous scale for visit (days) Y-Axis : Scaled accordingly to Parameter and include parameter name Legend : Subject	IA[1],SAC [1]
5.6.	PD	Example Non-Standard _PD_F2	Allergen Challenge, longest Weal Diameter (Percent of Inhibition, absolute value) - Box Plot	Part A + B X-Axis : Days Y-Axis : Result Legend : Treatment	IA[1],SAC [1]

Pharmacodynamic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.7.	PD	Example Non-Standard _PD_F1	Allergen Challenge, Weal perpendicular length (Percent of Inhibition) - Individual Subject Plot	Part A + B Page by : Treatment X-Axis : Continuous scale for visit (days) Y-Axis : Scaled accordingly to Parameter and include parameter name Legend : Subject	IA[1],SAC [1]
5.8.	PD	Example Non-Standard _PD_F2	Allergen Challenge, Weal perpendicular length (Percent of Inhibition, absolute value) - Box Plot	Part A + B X-Axis : Days Y-Axis : Result Legend : Treatment	IA[1],SAC [1]
5.9.	PD	Example Non-Standard _PD_F1	Allergen Challenge, Flare Erythema (Percent of Inhibition) - Individual Subject Plot	Part A + B Page by : Treatment X-Axis : Continuous scale for visit (days) Y-Axis : Scaled accordingly to Parameter and include parameter name Legend : Subject	IA[1],SAC [1]

Pharmacodynamic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.10.	PD	Example Non-Standard _PD_F2	Allergen Challenge, Flare Erythema (Percent of Inhibition, absolute value) - Box Plot	Part A + B X-Axis : Days Y-Axis : Result Legend : Treatment	IA[1],SAC [1]
5.11.	PD	Example Non-Standard _PD_F1	Cold Temp Test (Change) - Individual Subject Plot	Part B only Page by : Treatment X-Axis : Continuous scale for visit (days) Y-Axis : Scaled accordingly to Parameter and include parameter name Legend : Subject	SAC [1]
5.12.	PD	Example Non-Standard _PD_F2	Cold Temp Test (Change) - Mean (95% CI) Plot	Part B only X-Axis : Days Y-Axis : Mean (± 95% CI) Result Legend : Treatment	SAC [1]
5.13.	PD	Example Non-Standard _PD_F2	UAS7 Score (Change from Baseline) - Mean (95% CI) Plot	Part C only X-Axis : Days Y-Axis : Mean (± 95% CI) Result Legend : Treatment	,SAC [1]

Pharmacodynamic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.14.	PD	Example Non-Standard _PD_F2	Angiodema Activity ScoreScore (AAS) (Change from Baseline) - Mean (95% CI) Plot	Part C only X-Axis : Days Y-Axis : Mean (± 95% CI) Result Legend : Treatment	SAC [1]
5.15.	PD	Example Non-Standard _PD_F2	Dermatology Life Quality Index (DLQI) - Box Plot	Part C only X-Axis : Days Y-Axis : Result Legend : Treatment	SAC [1]

11.10.12. ICH Listings

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Randomisation					
1.	Safety	CP_TA1	Listing of Randomised and Actual Treatments		IA [1], SAC [1]
Subject Disposition					
2.	Safety	ES7	Listing of Reasons for Screen Failure		IA [1], SAC [1]
3.	Safety	ES2	Listing of Reasons for Withdrawal		IA [1], SAC [1]
4.	Safety	DV2	Listing of Important Protocol Deviations		IA (SAC)
5.	Safety	ES2	Listing of Exclusions from Per Protocol Population		IA (SAC)
Inclusion and Exclusion Criteria					
6.	Safety	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations		IA [1], SAC [1]
Demograhics					
7.	Safety	DM2	Listing of Demographic Characteristics		IA [1], SAC [1]
8.	Safety	DM9	Listing of Race		IA [1], SAC [1]
Medical History					
9.	Safety	MH2	Listing of Medical History		IA [1], SAC [1]
Concomitant Medication					
10.	Safety	CP_CM3	Listing of Concomitant Medication by Generic Term		IA [1], SAC [1]
Study Drug Exposure					
11.	Safety	EX3	Listing of Exposure Data	If applicable adapt to study data	IA [1], SAC [1]

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events					
12.	Safety	AE7	Listing of All Adverse Events		IA [1], SAC [1]
13.	Safety	CP_AE8	Listing of Subject Numbers for Individual Adverse Events		IA [1], SAC [1]
14.	Safety	CP_AE8a	Listing of Serious Adverse Events		IA [1], SAC [1]
15.	Safety	CP_AE8	Listing of Adverse Events Leading to Withdrawal from Study		IA [1], SAC [1]
Clinical Laboratory Assessments					
16.	Safety	CP_LB5	Listing of Haematology Abnormalities of Potential Clinical Importance		IA [1], SAC [1]
17.	Safety	CP_LB5	Listing of All Haematology Laboratory Data for Subjects with Abnormalities of Potential Clinical Importance	Including change from Baseline	IA [1], SAC [1]
18.	Safety	CP_LB5	Listing of Clinical Chemistry Abnormalities of Potential Clinical Importance		IA [1], SAC [1]
19.	Safety	CP_LB5	Listing of Clinical Chemistry Laboratory Data for Subjects with Abnormalities of Potential Clinical Importance	Including change from Baseline	IA [1], SAC [1]
20.	Safety	CP_LB5	Listing of All Hematology Laboratory Data for Subjects with Adverse Events of Interest		IA [1], SAC [1]
21.	Safety	UR2b	Listing of Urinalysis Data for Subjects with Abnormalities of Potential Clinical Concern		IA [1], SAC [1]
Electrocardiogram (ECG)					
22.	Safety	CP_EG3	Listing of ECG Values of Potential Clinical Importance		IA [1], SAC [1]

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
23.	Safety	CP_EG3	Listing of All ECG Values for Subjects with a Value of Potential Clinical Importance	Including change from Baseline	IA [1], SAC [1]
24.	Safety	CP_EG5	Listing of Abnormal ECG Findings		IA [1], SAC [1]
Vital Signs					
25.	Safety	CP_VS4	Listing of Vital Signs of Potential Clinical Importance		IA [1], SAC [1]
26.	Safety	CP_EG3	Listing of All Vital Sign for Subjects with a Value of Potential Clinical Importance	Including change from Baseline	IA [1], SAC [1]
27.	Safety	CP_VS4	Listing of All Vital Signs for Subjects with Values of Potential Clinical Importance		IA [1], SAC [1]

11.10.13. Non-ICH Listings

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Tolerability assessment					
28.	Safety	Non-Standard_Other_L1	Listing of irritation score assessment		IA [1], SAC [1]
Pharmacokinetics					
29.	PD	pkcl1p	Listing of GSK2646264 plasma PK Concentration-Time Data		IA[1],SAC [1]
30.	PD	pkpl1p	Listing of derived GSK2646264 plasma PK parameters		IA[1],SAC [1]
Pharmacodynamics					
31.	PD	Non-Standard _Other_L2	Listing of Allergen Challenge Parameters	Absolute and percent of inhibition to be presented. Part A + B	IA[1],SAC [1]
32.	PD	Example Non-Standard _Other_L2 modified based on endpoint.	Listing of Critical Temperature Thresholds	Absolute and change from baseline result to be presented. Part B only	SAC [1]
33.	PD	Example Non-Standard _Other_L2 modified based on endpoint.	Listing of UAS7 Scores and Subscores	Absolute and change from baseline result to be presented. Part C only	SAC [1]

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
34.	PD	Example Non-Standard _Other_L2 modified based on endpoint.	Listing of Angioedema Activity Score(AAS)	Absolute and change from baseline result to be presented. Part C only	SAC [1]
35.	PD	Example Non-Standard _Other_L2 modified based on endpoint.	Listing of Dermatology Life Quality Index (DLQI)	Absolute and change from baseline result to be presented. Total score and Subscores Part C only	SAC [1]

11.11. Appendix 11: Example Mock Shells for Data Displays

Example : Non- Standard_SAFE_T1 Page x of y

Protocol : 2013N167482_01
Population : Safety

Table 3.17

Summary (Absolute and Change from Baseline) of Mean irritation score assessment

Treatment	Visit	Mean Irritation Score	Mean of change from baseline Irritation Score
GSK2646264 0.5%	XX	XX	XX
XXXX	XX	XX	XX
--	--	--	--
Placebo	XX	XX	XX

Programming Notes :	[1] As required to be modified based on data and any applicable IDSL standard principals for listings

Example : Non- Standard_SAFE_T2

Protocol : 2013N167482_01
Population : Safety

Table 3.18
Assessment of Maximum Dermal Reactions and Response

Assessment	Reaction Grade	Statistic	GSK2646264 (0.5%) (N = XX)	GSK2646264 (1.0%) (N = XX)	Placebo (N = XX)
Dermal Response	1	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
	2	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
	-	-	-	-	-
	-				
	7	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Any Dermal Reaction		n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Grade 3 reaction (the mean time to get Grade 3) score ≥3 on the dermal response grading scale or a letter score of F, G, or H for other effects		n (%)(mean time (days))	XX (XX.XX) (XX.XX)	XX (XX.XX) (XX.XX)	XX (XX.XX) (XX.XX)
		n (%)(mean time (days))	XX (XX.XX) (XX.XX)	XX (XX.XX) (XX.XX)	XX (XX.XX) (XX.XX)

N: Number of subjects dosed with each treatment; n: Number of subjects with adverse event with particular reaction grade;
%: Calculated using the number of subjects treated with each treatment as the denominator (n/N*100);

Programming Notes : [1] As required to be modified based on data and any applicable IDSL standard principals for listings

Example : Non-Standard_PD_T1
Protocol : 2013N167482_01
Population : PD

Table 5.1
Allergen challenge, Weal Area- Summary Statistics (Absolute and Percent of Inhibition)

Summary: Absolute

Treatment	Time	N	Mean	CI 95% Lower	CI 95% Upper	S.D	Min	Median	Max
Placebo	X	x	xxx.x	xxx.x	xxx.x	xx.xx	xxx	xxx	xxx
	X	x	xxx.x	xxx.x	xxx.x	xx.xx	xxx	xxx	xxx
	X	x	xxx.x	xxx.x	xxx.x	xx.xx	xxx	xxx	xxx
	.	.	.	.	.	.	.	.	.
GSK2646264 (0.5%)	X	x	xxx.x	xxx.x	xxx.x	xx.xx	xxx	xxx	xxx
	X	x	xxx.x	xxx.x	xxx.x	xx.xx	xxx	xxx	xxx
	X	x	xxx.x	xxx.x	xxx.x	xx.xx	xxx	xxx	xxx
	.	.	.	.	.	.	.	.	.
GSK2646264 (1.0%)	X	x	xxx.x	xxx.x	xxx.x	xx.xx	xxx	xxx	xxx
	X	x	xxx.x	xxx.x	xxx.x	xx.xx	xxx	xxx	xxx
	X	x	xxx.x	xxx.x	xxx.x	xx.xx	xxx	xxx	xxx
	.	.	.	.	.	.	.	.	.
ETC									

Programming Notes :	[1] For applicable endpoints, include parameter as either a BY parameter or as first column in the table [²] If absolute and percent inhibition fit in one table results can be unified in one table.

Example : Non-Standard_PD_T1 **(Continued)**
Protocol : 2013N167482_01
Population : PD

Table 5.1
Allergen challenge, Weal Area- Summary Statistics (Absolute and Percent of Inhibition)

Summary: Percent of Inhibition

Treatment	Time	N	Mean	CI 95% Lower	CI 95% Upper	S.D	Min	Median	Max
Placebo	X	x	xxx.x						
	X	x	xxx.x						
	X	x	xxx.x						
	.	.	.	.	.	.	.	.	.
GSK2646264 (0.5%)	X	x	xxx.x	xxx.x	xxx.x	xx.xx	xxx	xxx	xxx
	X	x	xxx.x	xxx.x	xxx.x	xx.xx	xxx	xxx	xxx
	X	x	xxx.x	xxx.x	xxx.x	xx.xx	xxx	xxx	xxx
	.	.	.	.	.	.	.	.	.
GSK2646264 (1.0%)	X	x	xxx.x	xxx.x	xxx.x	xx.xx	xxx	xxx	xxx
	X	x	xxx.x	xxx.x	xxx.x	xx.xx	xxx	xxx	xxx
	X	x	xxx.x	xxx.x	xxx.x	xx.xx	xxx	xxx	xxx
	.	.	.	.	.	.	.	.	.
ETC									

Programming Notes :	[1] For applicable endpoints, include parameter as either a BY parameter or as first column in the table [²] If absolute and percent inhibition fit in one table results can be unified in one table.

Example : Non-Standard _PD_T2
Protocol : 2013N167482_01
Population : PD

Table 3.17
Change from baseline in composite total UAS7 Scores – Comparison

Treatment	N	Mean	Mean Difference vs. Placebo and CI 95% of mean difference
Placebo	x	xxx.x	
GSK2646264 (0.5%)	x	xxx.x	xx.x (xx.x, xx.x)
GSK2646264 (1.0%)	x	xxx.x	xx.x (xx.x, xx.x)
	.	.	.

Programming Notes : [1] As required to be modified based on data and any applicable IDSL standard principals for listings

Example : Non-Standard _Other_L1
Protocol : 2013N167482_01
Population : Safety

Listing 28
Listing of irritation score assessment

Subject	Treatment	Visit	Irritation Score assessment
XXX	GSK2646264 (0.5%)	XX	XX
		XX	XX
	--	--	--
	XXX	XX	XX

Programming Notes : [1] As required to be modified based on data and any applicable IDSL standard principals for listings

Example : Non-Standard _Other_L2
Protocol : 2013N167482_01
Population : PD

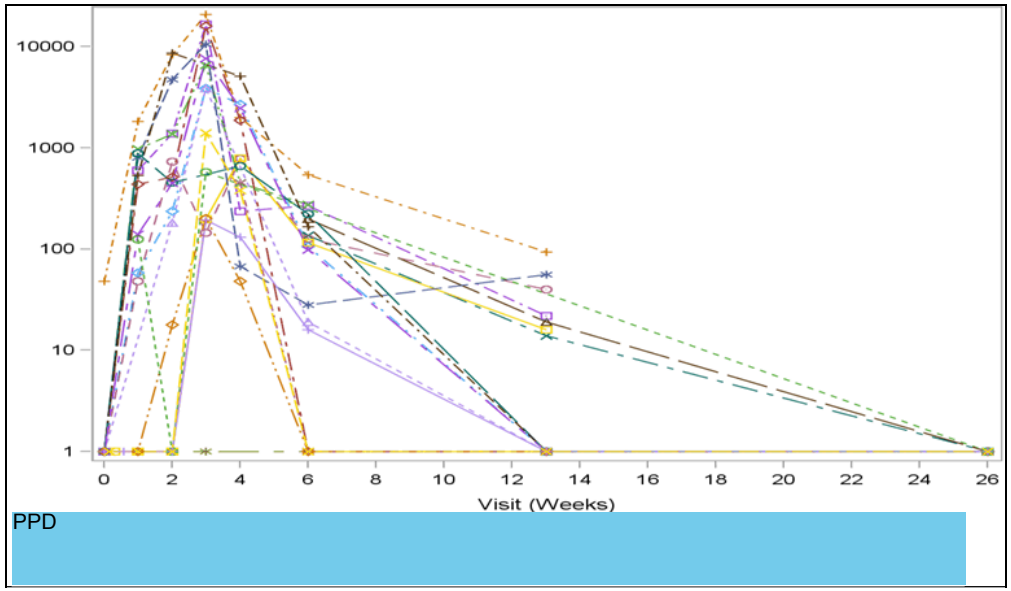
Listing 31
Listing of Allergen Challenge Parameters

Treatment	Inv./ Subj.	Visit	Parameter (Unit)	Result	Percent of Inhibition
XXXXX	XXXXX/ XXX	XXXX	XXXXX	XXX.XX	XXX.XX
			XXXXX	XXX.XX	XXX.XX
			XXXXX	XXX.XX	XXX.XX
			XXXXX	XXX.XX	XXX.XX
			XXXXX	XXX.XX	XXX.XX
		XXXX	XXXXX	XXX.XX	XXX.XX
			XXXXX	XXX.XX	XXX.XX
			XXXXX	XXX.XX	XXX.XX

Programming Notes : [1] As required to be modified based on data and any applicable IDSL standard principals for listings

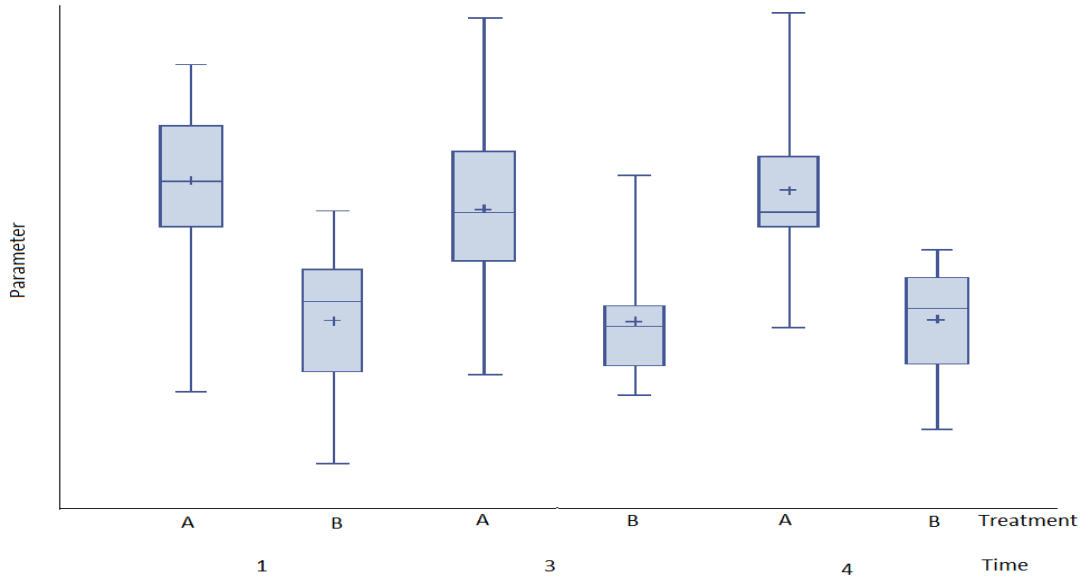
Example : Non-Standard _PD_F1
Protocol : 2013N167482_01
Population : PD

Figure 5.1
Allergen Challenge, Weal Area (Percent of Inhibition) - Individual Subject Plot



Programming Notes :	[1] Plot adapted accordingly based on study data (overlayed by treatment) [2] Subject will have two values one for treatment and another for placebo. Therefore use one colour for the subject id and two symbols for treatment (e.g. o=placebo, +=Treatment). Adapt the graph correspondingly.

Figure 5.2
Allergen Challenge, Weal Area (Percent of Inhibition) - Mean (95% CI) Plot



Treatment: A= Verum, B=Placebo

Programming Notes :	[1] Plot adapted accordingly based on study data. [2] Replicate this box plot to other similar plots, eg. for absolute values..