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

Title	:	Reporting and Analysis Plan for: A 2-part randomized, double-blind (sponsor-unblinded), placebo-controlled, ascending dose and parallel group study of TLR4 agonist (GSK1795091) administered to healthy subjects
Compound Number	:	GSK1795091
Effective Date	:	19-NOV-2017 (Final Version 1.0)

Description :

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 204685.
- This RAP is intended to describe the statistical analyses for safety, pharmacokinetic and pharmacodynamics analyses required for the study.
- This RAP will be provided to the study team members to convey the content of the Statistical Analysis Complete (SAC) deliverable.

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1. REPORTING & ANALYSIS PLAN SYNOPSIS

Overview	Key Elements of the RAP
Purpose	• First-time-in-human (FTIH) study to evaluate GSK1795091 for safety, pharmacokinetic (PK), and pharmacodynamic (PD) data in healthy subjects.
Protocol	• This RAP is based on the original protocol [(dated: 11-MAR-2016) of study 204685 (GSK Document No.: 2015N236402_03)], Protocol Amendment Number 03 (dated: 12-APR-2017), and ClinBase eCRF Version 4.6.07.
Primary Objective	• To evaluate the safety and tolerability of GSK1795091 when administered to healthy subjects.
Primary Endpoint	• Safety data comprising adverse events (AEs), vital signs, laboratory tests, and 12-lead electrocardiograms (ECGs).
Study Design	• The study will be conducted in two parts. • Part 1 will be a randomized, double-blind (sponsor-unblinded), placebo-controlled, single-center, single-dose escalation, sequential-group evaluation of intravenously administered GSK1795091 to evaluate the safety and tolerability in healthy subjects. • Part 2 will be an open-label, parallel-cohort evaluation of 2 doses of GSK1795091 administered, either 1 week apart (Part 2, Cohort 1) or 2 weeks apart (Part 2, Cohort 2). GSK1795091 will be administered at a dose determined by results from Part 1. • Part 2 will not begin until review/approval of Part 1 safety primary endpoints and dose selection.
Planned Analyses	• Safety, PK, PD
Analysis Populations	• All Subjects Population (Safety Population) • PK Concentration Population • PK Parameter Population • PD Population
Hypothesis	• No formal statistical hypotheses will be tested.

Overview	Key Elements of the RAP
Primary Analyses	• Safety parameters will be analysed descriptively.
Secondary Analyses	• Descriptive summaries of PK concentrations and parameters • Dose proportionality of GSK1795091 Cmax following single dose administration will be evaluated graphically and using the power model, if more than two dose cohorts are completed and if possible.
Exploratory Analyses	• Exploratory graphical PK/PD analyses may be performed to examine the relationship between GSK1795091 PK (e.g., Cmax) and response as measured by vital signs (e.g., body temperature, heart rate, etc.) or PD biomarkers (e.g., cytokines/chemokines) or other endpoints if warranted by the data (e.g., grade, onset and duration of AEs). The relationship(s) between PD endpoints and PK parameters (Cmax) initially will be explored graphically. Plots of PD endpoint versus PK parameters of GSK1795091 will be generated. • Descriptive summaries of biomarkers

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

There was a change to the originally planned statistical analysis specified in the Protocol (dated: 11-MAR-2016) and Protocol Amendment Number 03 (dated: 12-APR-2017).

The study team decided that Part 2 of the study would not be conducted following a review of data from Part 1. Therefore, all analysis planned for Part 2 per protocol will not be performed.

Study Objective(s) and Endpoint(s)

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To evaluate the safety and tolerability of GSK1795091 when administered to healthy subjects.	• Safety data comprising adverse events, vital signs, laboratory tests, and 12-lead ECGs.
Secondary Objectives	**Secondary Endpoints**
• To evaluate the systemic pharmacokinetics of GSK1795091 following administration of a single intravenous dose to healthy subjects.	• Plasma pharmacokinetic parameters such as Cmax, tmax, AUC(0-t), AUC(0-last), AUC(0-∞), CL, Vd, and t1/2.
• To evaluate the pharmacodynamic effects of GSK1795091 following administration as a single intravenous dose to healthy subjects.	• Vital signs, CRP measurements and WBC and differential.
• To evaluate the systemic pharmacokinetics of GSK1795091 following a second intravenous dose administered to healthy subjects 1 week or 2 weeks after the first dose.	• Plasma pharmacokinetic parameters such as Cmax, tmax, AUC(0-t), AUC(0-last), and AUC(0-τ), CL, Vss, t1/2, carryover, accumulation and time invariance (as possible) [1].
• To evaluate the clinical and pharmacodynamic effects of GSK1795091 following a second intravenous dose administered to healthy subjects 1 week or 2 weeks after the first dose.	• Vital signs, CRP measurements, WBC and differential, , and laboratory tests.

Objectives	Endpoints
Exploratory Objectives	**Exploratory Endpoints**
• To evaluate immune system effects following intravenous administration of GSK1795091.	• Cytokine measurements in plasma and immune cell phenotyping of leukocytes.
• To evaluate the pharmacodynamic effects of intravenous administration of GSK1795091 on gene signature analysis of Peripheral Blood Mononuclear CCells (PBMCs) from Part 2 healthy subjects.	• Gene signature analysis[2].
• To explore the relationship between pharmacokinetics, pharmacodynamic markers, and adverse events.	• Correlation between pharmacokinetics and pharmacodynamic markers, such as vital signs and CRP, and adverse events.
• To characterize the metabolic profile of GSK1795091 in plasma and urine.	• Plasma and urine may be analyzed qualitatively for GSK1795091 and other compound related metabolites and results reported under a separate GlaxoSmithKline protocol[2].

Notes:

1 AUC(0-τ), CL, Vss, t1/2, carry-over and accumulation, and time invariance are not endpoints of interest due to cancellation of Part 2 cohort expansion.

2 Will not be explored due to cancellation of Part 2 cohort expansion.

2.2. Study Design

Figure 1 **Part 1 study schematic**

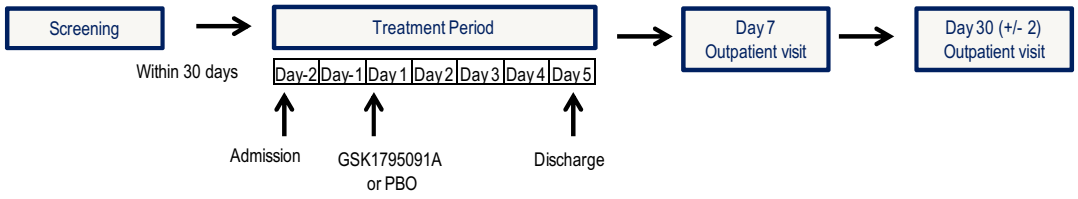
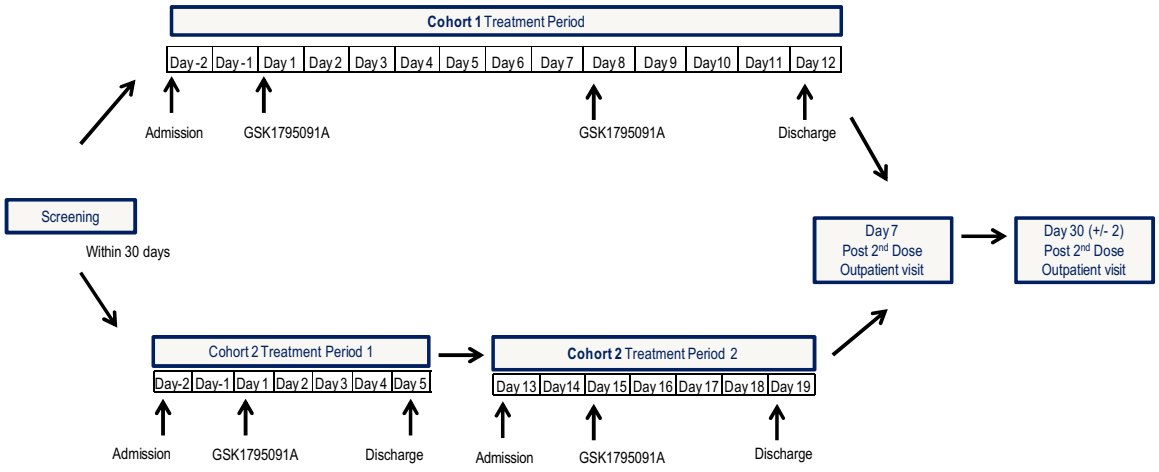


Figure 2 **Part 2 study schematic**



Design Features	• Subjects will attend the clinical unit for a screening visit and, if eligible, will attend the study within 30 days. • For both Part 1 and Part 2, subjects will be admitted to the clinical unit 2 days prior to dosing (Day -2). On Day -1, adverse events and vital signs will be recorded according to the schedule on Day 1. • In Part 1, 8 subjects in each dose cohort will be randomised to receive an intravenous dose of GSK1795091 or matching placebo in a 3:1 ratio. Subjects will then be observed as inpatients until discharge on Day 5, after assessments have been performed.

	• For Part 1, subjects will return on Day 7 for clinic visit and have a follow up contact on Day 30. • Part 2 will not begin until review/approval of Part 1 safety primary endpoints and dose selection. • In Part 2, on Day 1 subjects will receive intravenous GSK1795091 administered at a dose determined by results from Part 1. • Subjects in Part 2 Cohort 1 will be observed as inpatients until discharge on Day 12. • Subjects in Part 2 Cohort 2 will be observed as inpatients until discharge on Day 5, after assessments have been performed. They will return to the clinical unit for a second inpatient visit on Day 13 • Each subject in Part 2 will receive a second dose of GSK1795091 on Day 8 (Part 2, Cohort 1) or Day 15 (Part 2, Cohort 2) (unless AEs attributable to the first dose of GSK1795091 have not resolved, in which case the subject will not receive the second dose). • For Part 2, subjects will return to the clinical unit for a clinic visit 7 days after the second dose of GSK1795091 and have a follow up contact 30 days after their second dose of GSK1795091. Details of the assessments and procedures subjects will undergo are listed in Section 7 of the Clinical Study Protocol (CSP). The time points and visits are provided in the Time and Events table, (Appendix 1: Time & Events).
Dosing	• Part 1: The planned dose levels for GSK1795091 are: ○ Dose Level 1: 7 ng ○ Dose Level 2: 21 ng ○ Dose Level 3: 60 ng ○ Dose Level 4: 60 ng repeat ○ Dose Level 5: 100 ng ○ Dose Level 6: 150 ng ○ Dose Level 7: 210 ng ○ or Placebo. • Part 2: Actual dosing of GSK1795091 depends on the outcomes of Part 1.

Treatment Assignment	• Part 1: In each cohort, subjects will be assigned to GSK1795091 or placebo with a ratio of 3:1. A sentinel group of 2 subjects will receive study product in a ratio of 1 GSK1795091 : 1 placebo. The remaining 6 subjects will receive study product in a ratio of 5 GSK1795091 : 1 placebo. • Part 1 will be double-blind, with both the investigator and subject blinded to study treatment. All site personnel with the exception of the pharmacy team will remain blinded to study treatment except as discussed below. The sponsor's team will be unblinded. • Part 2: All subjects will be treated with GSK1795091. • Part 2 will be open-label where the sponsor, investigator and subject will be open to study treatment.
Interim Analysis	• No formal interim analyses are planned for this study except for making dose escalation decisions (described in Section 4 of CSP).

2.3. Statistical Hypotheses

No formal statistical hypotheses will be tested. Analysis will be descriptive and exploratory. An estimation approach providing point estimates and corresponding confidence intervals will be used, where appropriate.

3. PLANNED ANALYSES

3.1. Interim Analyses

No formal interim analyses are planned for this study except as required for making dose escalation decisions or regulatory compliance. In Part 1, cohorts with next higher dose will be started sequentially after evaluation of adverse events, vital signs, laboratory tests, and 12-lead ECGs by the Principal Investigator (blinded), GSK Medical Monitor (unblinded), GSK statistician (unblinded).

3.2. Final Analyses

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

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

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Screened	• All subjects who signed the informed consent form	• Screen failure listing • Age ranges table
All Randomized	• All subjects in the Screened population who were randomized	• Exclusion of study populations listing
All Subjects Population	• All subjects enrolled into the study who have received a dose of study medication (GSK1795091 or placebo) will be included in the safety population. • This population will be based on the treatment the subject actually received.	• Safety/tolerability • Subject disposition Demography
PK Concentration Population	• All subjects in the '"All Subjects Population" for whom a pharmacokinetic blood sample was obtained and assayed.	• Listing, summarizing and plotting plasma concentration-time data
PK Parameter Population	• All subjects in the "PK Concentration Population" for whom, at least, one valid and evaluable pharmacokinetic parameter (AUC or Cmax) was derived.	• Listing, summarizing and plotting of PK parameters
PD Population	• All subjects in the "All Subjects Population" for whom valid and evaluable pharmacodynamic parameters were derived..	• Listing, summarizing and plotting of PD Parameters

NOTES :

- Please refer to Appendix 8: List of Data Displays which details the population to be used for each display being generated.

4.1. Protocol Deviations

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

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

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

- 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 Overview of Appendices

Section	Component
11.1	Appendix 1: Time & Events
11.2	Appendix 2: Treatment States and Phases
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: Abbreviations & Trade Marks
11.8	Appendix 8: List of Data Displays
11.9	Appendix 9: 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 "All Subjects 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 8: List of Data Displays.

Table 2 Overview of Planned Study Population Analyses

Endpoints	Data Displays Generated		
	Table	Figure	Listing
Randomisation			
Randomisation			Y
Subject disposition			
Subject Disposition	Y		
Study Populations	Y		
Protocol Deviations	Y		Y
Exclusion from Any populations	Y		Y
Inclusion & Exclusion Criteria Deviations			Y
Reasons for Withdrawal / Study Treatment Discontinuation			Y
Investigational Product			
Investigational Product Status	Y		Y
Demographics			
Demographics Characteristics	Y		Y
Concomitant medications			
Concomitant Medications	Y		Y
Medical History			
Medical History	Y		Y
Alcohol and Drug Screen			
Substance Use			Y

NOTES :

- Y = Yes display generated.

6.2. Disposition of Subjects

A summary of the number of subjects in each of the analysis populations described in Section 4 will be provided. A listing of subjects excluded from analysis populations will also be provided.

A summary of subject status and reason for study withdrawal will be provided. This display will show the number and percentage of subjects who withdrew from the study, including primary reasons for study withdrawal. Reasons for study withdrawal will be presented in the order they are displayed in the eCRF.

A listing of study treatment discontinuation will be generated. The listing will include cohort, last dose date, and reasons for study treatment discontinuation.

6.3. Protocol Deviations

Protocol deviations will be summarized and listed and will include inclusion/exclusion deviations.

A listing of inclusion/exclusion deviations will also be provided.

6.4. Demographic and Baseline Characteristics

The demographic characteristics (e.g., age, race, ethnicity, sex, height, and body weight) will be summarized and listed. Age, height and weight will be summarized using the mean, standard deviation, minimum, median, and maximum. In addition, age will also be categorized and summarized by <18, 18-64, 65-74 and >74. The count and percentage will be computed for age categories, sex, race and ethnicity. A separate summary table for age ranges will be provided. Race and racial combination will be summarized.

Medical conditions present at screening will be listed and will be summarized.

Substance use will be listed.

6.5. Concomitant Medications

Concomitant medications will be coded using GSK Drug coding dictionary, summarized, and listed. The summary of concomitant medications will show the number and percentage of subjects taking concomitant medications by ingredient. Multi-ingredient products will be summarized by their separate ingredients rather than as a combination of ingredients. Anatomical Therapeutic Chemical (ATC) classification Level 1 (Body System) information will be included in the dataset created, however, will not appear on the listing or summary.

In the summary of concomitant medications, each subject is counted once within each unique ingredient. For example, if a subject takes amoxicillin on two separate occasions, the subject is counted only once under the ingredient “amoxicillin”.

In the summary of concomitant medications, the ingredients will be summarized by the base only.

7. SAFETY ANALYSES

The safety analyses will be based on the "All Subjects Population", unless otherwise specified.

Table 3 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 8: List of Data Displays.

Table 3 Overview of Planned Safety Analyses

Endpoints	Absolute				Change from Baseline			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
Investigational Product Exposure								
Exposure	Y			Y				
Adverse Events								
All AEs	Y			Y				
AEs – Max Grade	Y			Y				
AEs – Drug Related	Y			Y				
AEs – Serious AE	Y			Y				
AEs – Leading to Discontinuation	Y			Y				
Laboratory Tests								
Clinical chemistry	Y		Y	Y	Y			
Hematology	Y			Y				
Coagulation	Y			Y				
Urinalysis	Y			Y				
Other Screening Tests				Y				
Vital Signs								
Vital Signs	Y			Y	Y			Y
Vital Signs by Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials	Y			Y	Y			Y
Electrocardiogram								
12-Lead ECG	Y			Y	Y			Y
ECG Findings	Y			Y				
QTcF Grades	Y			Y	Y			Y

NOTES :

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

7.1. Extent of Exposure

The number of IV bolus injections administered to study treatment will be summarised with mean, median, standard deviation, minimum, and maximum.

Dose intensity (dose delivered per bolus injection) will be summarized by cohort using mean, median, standard deviation, minimum, and maximum.

7.2. Adverse Events

An overview summary of AEs, including counts and percentages of subjects with any AE, AEs related to study treatment, AEs leading to permanent discontinuation of study treatment, SAEs, SAEs related to study treatment, fatal SAEs, and fatal SAEs related to study treatment will be produced.

A summary of non-serious AEs that occurred in strictly 5% of the subjects or above will be provided (no rounding for the percentage will be used in terms of 5% threshold, e.g., event with 4.9% incidence rate should not be included in this table). The summary will be displayed by SOC and PT.

Adverse event (AE) grading is guided by the Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials.

Additionally, adverse events will be coded to the PT level using the Medical Dictionary for Regulatory Affairs (MedDRA dictionary).

A summary of number and percentage of subjects with any adverse events by maximum grade will be produced. AEs will be sorted by PT in descending order of total incidence. The summary will use the following algorithms for counting the subject:

- **Preferred term row**: Subjects experiencing the same AE preferred term several times with different grades will only be counted once with the maximum grade.
- **Any event row**: Each subject with at least one adverse event will be counted only once at the maximum grade no matter how many events they have.

In addition, the frequency and percentage of AEs (all grades) will be summarized and displayed in descending order of total incidence by SOC and PT. In the SOC row, the number of subjects with multiple events under the same system organ class will be counted once.

A separate summary will be provided for study treatment-related AEs. A study treatment-related AE is defined as an AE for which the investigator classifies the relationship to study treatment as “Yes”. A worst case scenario approach will be taken to handle missing relatedness data, i.e. the summary table will include events with the relationship to study treatment as ‘Yes’ or missing. The summary table will be displayed in descending order of total incidence by PT only.

All AEs will be listed.

7.3. Deaths and Serious Adverse Events

In the event that a subject has withdrawn consent, no data after the withdrawal of consent date from this subject including death is supposed to appear in the database, which should be part of the data cleaning process.

All SAEs will be tabulated based on the number and percentage of subjects who experienced the event. The summary tables will be displayed in descending order of total incidence by PT only.

A study treatment-related SAE is defined as an SAE for which the investigator classifies the relationship to study treatment as "Yes". A worst case scenario approach will be taken to handle missing data, i.e. the summary table will include events with the relationship to study treatment as 'Yes'.

SAEs are included in the listing of all adverse events.

7.4. Adverse Events Leading to Discontinuation of Study Treatment and/or Withdrawal from the Study and Other Significant Adverse Events

The following categories of AEs will be summarized separately in descending order of total incidence by PT only and separate supportive listings will be generated with subject level details for those subjects:

- AEs Leading to Discontinuation of Study Treatment

7.5. Pregnancies

While pregnancy itself is not considered to be an AE or SAE, any pregnancy complication or elective termination of a pregnancy for medical reasons will be recorded as an AE or SAE as described in the protocol. If subjects become pregnant while on the study, the information will be included in the narratives and no separate table or listing will be produced.

7.6. Clinical Laboratory Evaluations

The following laboratory tests are required:

Hematology: Hemoglobin (HGB), Hematocrit (HCT), Red Blood Cell (RBC) count, White Blood Cell (WBC) count with differential (Total Neutrophils, Lymphocytes, Monocytes, Eosinophils, Basophils), Platelet count, Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH) and Mean Corpuscular Hemoglobin Concentration (MCHC).

Clinical Chemistry: Sodium, Potassium, Calcium, Glucose, Urea, Creatinine, Albumin, Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Alkaline phosphatase, C-reactive protein (CRP), Gamma Glutamyl Transferase (GGT), Ferritin, Transferrin, Triglycerides, Total Protein, Total bilirubin (total) and Direct/Indirect bilirubin.

Routine Urinalysis (Dipstick): Specific gravity, pH, Glucose, Protein, Blood and Ketones. If urinalysis results are abnormal, the microscopic panel (leukocytes, erythrocytes, casts, crystals, bacteria, and/or epithelial cells, as appropriate) will be performed.

Coagulation: Prothrombin time or International Normalized Ratio (INR), and partial thromboplastin time (PTT).

Other Screening Tests: Human immunodeficiency virus (HIV), Hepatitis B surface antigen (HBsAg), core-antibody (anti-HBc Ab), Hepatitis C (Hep C Antibody), Follicle Stimulating Hormone

(FSH), Estradiol, Alcohol and Drug Screening (to include at minimum: amphetamines, barbiturates, cocaine, opiates, cannabinoids and benzodiazepines), serum or urine hCG pregnancy test, Lipids, Total cholesterol, HDL and LDL.

Laboratory grades will be reported using the Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials.Summary of laboratory values by scheduled visits using mean, median, standard deviation, minimum and maximum will be provided.

Other Screening Tests are only collected at screening. Therefore these tests will be only listed.

7.7. Other Safety Measures

Unless otherwise specified, the denominator in percentage calculation at each scheduled visit will be based on the number of subjects with non-missing value at each particular visit.

7.7.1. Vital Signs

Values of vital signs as well as the change from baseline will be summarized by scheduled visit using mean, median, standard deviation, minimum and maximum. At screening and pre-dose, the average of triplicated measurements will be summarized. Triplicated measurements and average will be listed.

In addition vital signs values will be categorized by Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials (Appendix 2 of the CSP) with the exception of fever and tachycardia which also require a change from time-matched baseline (per table below).

	Grade 1	Grade 2	Grade 3	Grade 4
Temperature	>0.5°C change AND >38.0°C	>1.5°C change AND >38.5°C	>3 °C change (<24 hours) AND >39.0°C	>3°C change (≥24 hours) AND >40°C
Heart rate	>15 bpm change AND >101 bpm	>30 bpm change AND >116 bpm	>45 bpm change AND >130 bpm	Emergency intervention required

Summaries of increase in vital signs from the baseline with respect to the categories defined above will be performed. These summaries will display the number and percentage of subjects with any grade increase, increase to Grade 2 and increase to Grade 3 at each scheduled assessment time and in the worst case post-baseline.

7.7.2. ECG

A summary of the number and percentage of subjects who had normal and abnormal (clinically significant and not clinically significant) ECG findings will be displayed by scheduled visits as well as for the worst case post-baseline.

The QTc values based on Fridericia formula will be rounded to the integer and the values will be categorized into the following ranges (in "msec"): Grade 0 (<450), Grade 1 (450-480), Grade 2 (481-500), and Grade 3 (≥501). Summaries of grade increase will be provided. These summaries will display the number and percentage of subjects with any grade increase, increase to Grade 2 and increase to Grade 3 at each scheduled assessment time and in the worst case post-baseline.

The changes in QTc values will be categorized into the clinical concern ranges which are specific to changes in QTc: 31-60 and >60 msec. A summary of change in QTc value will display the number and percentage of subjects with a change within each range at each scheduled assessment time point and in the worst case post-baseline. Subjects with missing baseline values will be excluded from this summary. The summaries for the QTc will use the calculated value based on Fridericia's correction formula.

In addition, ECG interval values will also be summarized. At screening, day 1 and day 4, the average of triplicated measurements will be summarized. Triplicated measurements and average will be listed.

Listings of abnormal ECG findings and a listing of ECG values will be provided.

8. PHARMACOKINETIC ANALYSES

The pharmacokinetic concentration analyses will be based on the "Pharmacokinetic Concentration" population, the PK parameter analyses will be based on the "Pharmacokinetic Parameter" population, unless otherwise specified.

Table 4 provides an overview of the planned analyses, with full details being presented in Appendix 8: List of Data Displays.

Table 4 Overview of Planned Pharmacokinetic Analyses

Endpoints	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
Pharmacokinetic Analyses														
GSK1795091 concentration				Y	Y	Y	Y							
GSK1795091 PK Parameters				Y			Y				Y			
Dose Proportionality														
GSK1795091 dose proportionality								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. Drug Concentration Measures

Refer to Appendix 3: Data Display Standards & Handling Conventions (Section 11.3.3 Reporting Process & Standards).

8.2. Pharmacokinetic Parameters

8.2.1. Deriving Pharmacokinetic Parameters

- Refer to Section 11.3: Appendix 3: 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 WinNonlin version 6.3.
- All calculations of non-compartmental parameters will be based on actual sampling times.
- Pharmacokinetic parameters described in Table 5 will be determined from the GSK1795091 concentration-time data, as data permit.

Table 5 Derived Pharmacokinetic Parameters

Parameter	Parameter Description
AUC(0-last)	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-t)	Partial area under the concentration-time curve to time (where t may be 24, 168 h or other as appropriate) will be calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid.
AUC(0-∞)	Area under the concentration-time curve extrapolated to infinity will be calculated as: **AUC = AUC(0-last) + C(last) / lambda_z**
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**
CL	Clearance **CL = Dose/AUC(0-∞)**
Vd	Volume of distribution **Vd = Dose/lambda_z * AUC(0-∞)**
Vss	Volume of distribution where **V = CL/MRTiv**

NOTES:

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

8.2.2. Statistical Analysis of Pharmacokinetic Parameters

8.2.2.1. Statistical Analysis of Pharmacokinetic Data

Except for tmax, pharmacokinetic parameters summarized descriptively to determine mean, standard deviation (SD), median, minimum. maximum, geometric mean, and the SD, CV% and 95% confidence interval of $\log_e$-transformed parameters by dose cohort in Part 1, tmax will be summarized descriptively as mean, SD, median, minimum, and maximum.

8.2.2.2. Dose-Proportionality Analysis

If data support, the PK-dose relationship initially will be examined graphically by plotting Cmax, as a function of the dose levels administered. Two plots of each PK parameter vs. dose will be produced. The first will be on a linear scale and the second will use the logarithmic scale for both axes.

If more than two dose cohorts are completed and data support, dose proportionality of GSK1795091 Cmax following single dose administration will be evaluated graphically and using the power model as described below:

$$\log_e(\text{PK parameter}) = a + b * \log_e(\text{dose})$$

where a is the intercept and b is the slope

Assessment of dose proportionality will be conducted based on the power model described above. The power model will be fitted by restricted maximum likelihood (REML) using SAS Proc Mixed. Both the intercept and slope will be fitted as fixed effects. If there is sufficient data, the model may also be fit with the intercept and/or slope as random effects depending on the ability of the model to converge and on estimation of variance-covariance matrix. An estimate of the slope with corresponding 90% confidence interval will be obtained from the power model to assess the degree of dose-proportionality (slope b around unity indicates dose-proportionality, b near zero implies the response y is independent of dose), and to describe the uncertainty (width of the CI) of the estimate.

If data support, plots will be provided showing individual subject values by treatment (dose) for each of the PK parameter Cmax, together with the predicted PK parameter value from the Power Model.

Distributional assumptions underlying the statistical analyses will be assessed by visual inspection of residual plots. Normality will be examined by normal probability plots, while homogeneity of variance will be assessed by plotting the residuals against the predicted values for the model. If the assumptions are grossly violated then alternative analyses will be performed.

Sample SAS Code for dose-proportionality analysis using power model. Programmers will need to modify as appropriate to the study:

```
proc mixed;
  by PKParameter;
  model lnPKParameter = lnDose / cl alpha=0.1 solution ddfm=kr;
run;
```

9. PHARMACOKINETIC / PHARMACODYNAMIC AND BIOMARKER ANALYSES

9.1. Pharmacodynamic Analyses

The Pharmacodynamics analyses will be based on the “PD” population, unless otherwise specified.

Pharmacodynamics endpoints / Biomarkers will be analysed numerically and graphically to explore the relationship between GSK1795091 and PD biomarkers. The PD biomarkers of interest include:

- Cytokine/Chemokine:
  - IL-6
  - TNF-alpha
  - IFN-gamma
  - IP-10
  - MCP-1
  - GM-CSF
  - IL-1Ra
  - IL-10
- Immunophenotyping:
  - Neutrophils
  - Lymphocytes
  - Monocytes

Table 6 provides an overview of the planned pharmacodynamic analyses, with full details of data displays being presented in Appendix 8: List of Data Displays.

Table 6 Overview of Planned Pharmacokinetic / Pharmacodynamic and Biomarker Analyses

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/Biomarker analyses														
Laboratory tests (CRP, Neutrophil abs., Lymphocyte abs.)				Y	Y	Y	Y				Y	Y	Y	Y
Vital Signs (HR, Body temperature, Systolic pressure, Diastolic pressure)				Y	Y	Y	Y				Y	Y	Y	Y
PD Biomarkers (Cytokine/Chemokine, Immunophenotyping)				Y	Y		Y				Y[1]			Y[1]
PK/PD analyses														
Pharmacokinetics parameters (Cmax) vs. Laboratory tests change from baseline (CRP, Neutrophil abs., Lymphocyte abs.)													Y	
Pharmacokinetics parameters (Cmax) vs. Vital signs change from baseline (HR, Body temperature, Systolic blood pressure, Diastolic blood pressure)													Y	
Pharmacokinetics concentration vs. PD Biomarkers (Cytokine/Chemokine, Immunophenotyping)						Y								

NOTES :

1 Display fold change as defined in Section 9

- 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.

The "Change from Baseline" for cytokine/chemokine biomarkers in Table 6 specifically refers to fold change, which is calculated as the ratio of the difference between a value at Time T (denote as X_T) and the baseline (predose) value X_0 over the baseline value $((X_T - X_0)/ X_0$.) If a biomarker value is below limit of quantitation limit (LOQ), then impute ½*LOQ for the calculation of fold change for tables and figures. Note imputation will not be implemented for listings.

Exploratory graphical PK/PD analyses may be performed to examine the relationship between GSK1795091 PK and response as measured by vital signs (e.g., body temperature, heart rate, etc.), PD biomarkers (e.g., cytokines, /chemokines, immunophenotyping) or other endpoints if warranted by the data (e.g., grade, onset and duration of AEs). The relationship(s) between PD endpoints and PK parameters (Cmax) initially will be explored graphically. Plots of PD endpoint versus PK parameters of GSK1795091 will be generated. In addition, PD end-points versus dose should also be explored.

The relationship between PK concentrations and PD biomarkers, i.e. cytokines and immunophenotypings, will be explored graphically.

Additional exploratory analyses may be performed to further characterize the novel biomarkers, and may be reported separately from the main clinical study report.

Further analysis may be conducted if the initial plots suggest a correlation between the PD and PK endpoints. Models to describe the relationship(s) may include linear models and/or a maximum effect models. Other more complex models may be explored if warranted by the data. Results may be included in the final study report for this study or reported separately.

10. REFERENCES

GSK Document Number 2015N236402_03: A 2-part randomized, double-blind (sponsor-unblinded), placebo-controlled, ascending dose and parallel group study of TLR4 agonist (GSK1795091) administered to healthy subjects (Protocol Amendment 03).

GUI_137354 (2.0): Information for Authors: Reporting and Analysis Plan (RAP), Global

GUI_51487 (5.0): Non-compartmental Analysis of Pharmacokinetic Data, CPMS Global

SOP_54838 (5.0): Development, Review and Approval of Reporting and Analysis Plan (RAP), Global

11. APPENDICES

Section	Appendix
RAP Section 1-5 : General Considerations for Data Analyses & Data Handling Conventions	
Section 11.1	Appendix 1: Time & Events
Section 11.2	Appendix 2: Treatment States and Phases
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
Section 11.5	Appendix 5: Premature Withdrawals & Handling of Missing Data • Premature Withdrawals • Handling of Missing Data
Other RAP Appendices	
Section 11.6	Appendix 6: Values of Potential Clinical Importance
Section 11.7	Appendix 7: Abbreviations & Trade Marks
Section 11.8	Appendix 8: List of Data Displays
Section 11.9	Appendix 9: Example Mock Shells for Data Displays

11.1. Appendix 1: Time & Events

11.1.1. Protocol Defined Time & Events

11.1.1.1. Screening

Procedure	Screening (up to 30 days prior to Day -1)
Informed consent	X
Outpatient visit	X
Inclusion and exclusion criteria	X
Demographics	X
Full physical exam including height and weight	X
Medical history[1]	X
Drug/Alcohol screen	X
Serum/urine pregnancy test (WNCBP)	X
HIV, Hep B and Hep C screen	X
Haem/Clin Chem/PT & PTT/Urinalysis	X
12-lead ECG[2]	X
Vital signs (BP and heart rate)	X
Concomitant medication review	X

1. To include substance usage, family history of premature cardiovascular disease, medication, drug/alcohol history
2. Triplicate ECGs collected 5mins apart

11.1.1.2. Part 1: In-House Assessments

Procedure	Day -2	Day -1	Treatment Period Day 1														Day 2 (24h)	Day 3 (48h)	Day 4 (72h)	Day 5 (96h)
			Pre dose	0h	5min	0.25h	0.5h	1h	2h	3h	4h	6h	8h	10h	12h	16h				
Admission to the unit	X																			
Overnight stay	X	X	←==========→																	
Serum/urine pregnancy test (WNCBP)	X																			
Full physical exam including height and weight	X																			
Inclusion and exclusion criteria	X	X																		
Haem/Clin Chem/Urinalysis /Coagulation		X	X														X		X	
WBC with differential[1]		X	X					X	X		X		X			X	X	X	X	
Drug/Alcohol test	X																			
12 lead ECG			X						X		X		X				X		X	
Vital signs (Temperature, BP and Heart rate)		X[2]	X					X	X		X	X	X		X	X	X	X	X	X
Telemetry			←==========→																	
Dosing				X																
Intravenous hydration		X	←==========→																	
PK blood sampling[3]			X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	

Procedure	Day -2	Day -1	Treatment Period Day 1													Day 2 (24h)	Day 3 (48h)	Day 4 (72h)	Day 5 (96h)
			Pre dose	0h	5min	0.25h	0.5h	1h	2h	3h	4h	6h	8h	10h	12h	16h				
Cytokine measurements[3]			X					X	X		X		X		X	X	X	X		
Leukocyte phenotyping[3]			X								X						X			
AE/SAE review[4]	X	X	←==========→																	
Concomitant medication review	X	X	←==========→																	
Discharge																				X

1. Where WBC+Differential and Haematology are scheduled for the same time, WBC+Differential may be collected as part of the Haematology assessment

2. Baseline Vital Signs to match Day 1 timepoints

3. PK and Biomarker Sampling: The pre-dose blood samples should be collected within 1 hr before administration of GSK1795091. Every attempt should be made to collect samples within ±5 min on samples up to 2 hrs, ±20 min on samples up to 12 hrs, and ±40 min on samples after 12 hrs. Actual date/time of sample collection and dosing must be recorded. Explanations are required for any deviations of >5 min from the planned time during the first 2 hrs and for deviations of more than 20 min from the planned time for samples collected at 3 hrs up to 10 hrs.

4. Blood samples may be collected to explore biomarkers at the discretion of the Investigator

11.1.1.3. Part 1 Outpatient Assessments

Procedure	Day 7	Follow-up (23 days ± 2 days post-last visit) or early withdrawal
Outpatient Visit or Contact[1]	X	X
Serum/urine pregnancy test (WNCBP)		X
Full physical exam including height and weight	X	
Haem/Clin Chem/Urinalysis/Coagulation	X	
12 lead ECG	X	
Vital signs (Temperature, BP and Heart rate)	X	
PK blood sampling[2]	X	
Cytokine measurements	X	
Leukocyte phenotyping	X	
AE/SAE review	X	X
Concomitant medication review	X	X

1. Outpatient visit at Day 7; Outpatient visit or Contact at FU. All subjects with (1) new AE or (2) unresolved AEs or abnormal labs at the Day 7 visit should return for a follow-up visit. Female subjects should return for pregnancy testing. For all other subjects a FU contact is acceptable
2. PK Sampling: Blood samples for analysis of GSK1795091 concentrations will be collected following dosing 144 hours (Day 7) after administration

11.2. Appendix 2: Treatment States and Study Phases

11.2.1. Study Phases

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

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

11.2.1.1. Study Phases for Concomitant Medication

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

NOTES:

- Please refer to Appendix 5 : Reporting Standards for Missing Data for handling of missing and partial dates for concomitant medication. Use the rules in this table if concomitant medication date is completely missing.

11.2.1.2. Treatment States for AE Data

Treatment State	Definition
Pre-Treatment	AE Start Date/Time < Study Treatment Start Date/Time
On-Treatment	Study Treatment Start Date/Time ≤ AE Start Date/Time ≤ Study Treatment Stop Date/Time
Post-Treatment	AE Start Date/Time > Study Treatment Stop Date/Time
Onset Time Since 1st Dose (Days)	If Treatment Start Date > AE Onset Date, = AE Onset Date - Treatment Start Date If Treatment Start Date ≤ AE Onset Date, = AE Onset Date - Treatment Start Date +1 Missing otherwise.
Duration (Days)	AE Resolution Date – AE Onset Date + 1
Drug-related	If relationship is marked 'YES' on Inform/CRF OR value is missing.

NOTES:

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

11.3. Appendix 3: Data Display Standards & Handling Conventions

11.3.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions – Part 1			
RandAll NG		Data Displays for Reporting	
Code	Description	Description	Order [1]
S1	7 ng single dose	GSK 7 ng	2
S2	21 ng single dose	GSK 21 ng	3
S3	60 ng single dose[2]	GSK 60 ng	4
S4NEW	60 ng single dose – redo[3]	GSK 60 ng	5
S5NEW	100 ng single dose	GSK 100 ng	6
S6NEW	150 ng single dose	GSK 150 ng	7
S7NEW	210 ng single dose	GSK 210 ng	8
P	Placebo	Placebo	1

NOTES:

1. Order represents treatments being presented in TFL, as appropriate (fewer groups possible, if dose escalation stopped).
2. Cohorts completed under Protocol Amendment 2.
3. Study restart dose following stopping criteria met under Protocol Amendment 2.

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 non-missing pre-dose assessment.

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

Parameter	Study Assessments Considered As Baseline			Baseline Used in Data Display
	Screening	Day -1	Day 1 (Pre-Dose)	
Safety Data				
Vital Signs			X	Mean of replicate assessments on Day 1
ECG			X	Mean of replicate assessments on Day 1
Laboratory tests			X	Day 1

Parameter	Study Assessments Considered As Baseline			Baseline Used in Data Display
	Screening	Day -1	Day 1 (Pre-Dose)	
Pharmacokinetic				
GSK1795091 concentration data			X	Day 1
Pharmacodynamic				
Pharmacodynamic markers			X	Day 1
Biomarkers			X	Day 1

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]
Maximum Change from Baseline	= Calculate the change from baseline at each given time point and determine the maximum change

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.
- The baseline definition will be footnoted on all change from baseline displays.

11.3.3. Reporting Process & Standards

Reporting Process
Software
• The currently supported versions of SAS and WinNonlin software will be used.
Analysis Datasets
• Analysis datasets will be created according to AdaM IG Version 1.1. • For creation of ADaM datasets (ADCM/ADAE), the same version of dictionary datasets will be implemented for conversion from SI to SDTM. • Define XML Version 2.0
Generation of RTF Files
• RTF files will be generated for Tables, Listings, and Figures, one RTF file per item.

Reporting Standards
General

• The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated:
  ○ 4.03 to 4.23: General Principles
  ○ 5.01 to 5.08: Principles Related to Data Listings
  ○ 6.01 to 6.11: Principles Related to Summary Tables
  ○ 7.01 to 7.13: Principles Related to Graphics

Formats
• All data will be reported according to the actual treatment the subject received unless otherwise stated. • GSK IDSL Statistical Principles (5.03 & 6.06.3) for decimal places (DP's) will be adopted for reporting of data based on the raw data collected. • Numeric data will be reported at the precision collected on the eCRF. • The reported precision from non eCRF sources will follow the IDSL statistical principles but may be adjusted to a clinically interpretable number of DP's. • RTF files will be generated for displays.
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, except when summarizing worst cases. • Unscheduled visits will not be included in figures. • All unscheduled visits will be included in listings.

Reporting Standards	
Descriptive Summary Statistics	
Continuous Data	Refer to IDSL Statistical Principle 6.06.1
Categorical Data	N, n, frequency, %
Reporting of Pharmacokinetic Concentration Data	
Descriptive Summary Statistics	Refer to IDSL Statistical Principle 6.06.1 Assign zero to NQ values (Refer to GUI_51487 for further details)
Reporting of Pharmacokinetic Parameters	
Descriptive Summary Statistics (Log Transformed)	N, n, geometric mean, 95% CI of geometric mean, standard deviation (SD) of logged data and [between] geometric coefficient of variation (CVb (%)) will be reported. CV_b (%) = $\sqrt{}$ (exp(SD^2) - 1) * 100 (SD = SD of log transformed data)
Parameters Not Being Log Transformed	tmax
Listings	Additionally, include the first point, last point and number of points used in the determination of lambda_z for listings. Also, list %AUCextrap.
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
  • 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
Body Mass Index (BMI)
• Calculated as **Weight (kg) / [Height (m)]^2**

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 phases of the study including the follow-up visit or contact. • Withdrawn subjects may be replaced in the study. • All available data from subjects who were withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified.

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 : ○ These data will be indicated by the use of a “blank” in subject listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table. ○ Answers such as “Not applicable” and “Not evaluable” are not considered to be missing data and should be displayed as such.
Outliers	• Any subjects excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report.

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	• Imputation will not be implemented for partial dates or missing dates. Consequently, time to onset and duration of such events will be missing. • The recorded partial date will be displayed in listings.

11.5.2.2. Handling of Partial Dates

Element	Reporting Detail
Concomitant Medications	• Imputation will not be implemented for partial dates or missing dates. Consequently, time to onset and duration of such events will be missing. • The recorded partial date will be displayed in listings.

11.6. Appendix 6: Values of Potential Clinical Importance

11.6.1. Laboratory Values

Clinical laboratory test results within potential clinical importance range will be flagged in the listings. Note: a high flagged or low flagged laboratory value is not necessarily of clinical concern. Reference ranges included are taken from CSP, Chapter 12.2 (with a Grading of 3 or worse).

Haematology				
Laboratory Parameter	**Units**	**Category**	**Potential Clinical Importance Range**	
			Low Flag (< x)	**High Flag (>x)**
Haemoglobin	g/dL	Male	10.5	
		Female	9.5	
		Δ from BL	-	2.0
Lymphocytes decrease	cell / mm³		500	
Neutrophils decrease	cell / mm³		1000	
Eosinophils	cell / mm³			5000
Platelets decreased	cell / mm³		100000	
White Blood Cell Count (WBC) increase	cell / mm³			20000
White Blood Cell Count (WBC) decrease	cell / mm³		1500	

Clinical Chemistry				
Laboratory Parameter	**Units**	**Category**	**Potential Clinical Importance Range**	
			Low Flag (< x)	**High Flag (>x)**
Albumin	g/dL		2.5	
Calcium	mg/dL		7.5	11.5
Creatinine	mg/dL			2.0
Glucose	mg/dL		55	125 (fasting) 200 (random)
Magnesium	mg/dL		1.1	
Phosphorus	mg/dL		2.0	
Potassium	mEq/L		3.3	5.4
Sodium	mEq/L		130	147
Blood Urea Nitrogen	mg/dL			31
CPK	mg/dL			3*ULN
Total Protein	g/dL		5.0	
Cholesterol	mg/dL			225

Clinical Chemistry				
Laboratory Parameter	**Units**	**Category**	**Potential Clinical Importance Range**	
			Low Flag (< x)	**High Flag (>x)**
Amylase				2xULN
Lipase				2xULN

Liver Function			
Test Analyte	**Units**	**Category**	**Potential Clinical Importance Range**
ALT/SGPT	U/L	High	> 5x ULN
AST/SGOT	U/L	High	> 5x ULN
AlkPhos	U/L	High	> 3x ULN
Total Bilirubin when Liver Function Test is normal; increase by factor	µmol/L	High	> 2xULN
Total Bilirubin + increase in Liver function test	µmol/L U/L	High	1.51xULN T. Bilirubin + ≥ 2x ULN Liver function test

Coagulation				
Laboratory Parameter	**Units**	**Category**	**Potential Clinical Importance Range**	
			Low Flag (< x)	**High Flag (>x)**
PT – increase by factor	sec			1.20*ULN
PTT – increase by factor	sec			1.40*ULN
Fibrinogen increase	mg/dL			600
Fibrinogen decrease	mg/dL		125	

Urine				
Laboratory Parameter	**Units**	**Category**	**Potential Clinical Importance Range**	
			Low Flag (< x)	**High Flag (>x)**
Protein				1+
Glucose				1+
Blood (microscopic) – red blood cells per high power field (rbc/hpf)				50

11.6.2. ECG

ECG Parameter	Units	Potential Clinical Importance Range	
		Lower	Upper
Absolute			
Absolute QTc Interval	msec		
		> 450	≤ 480
		≥ 481	≤ 500
		≥ 501	
Absolute PR Interval	msec	< 110	> 220
Absolute QRS Interval	msec	< 75	> 110
Increase from Baseline QTc	msec		
	msec	> 30	≤ 60
	msec	≥ 61	

11.6.3. Vital Signs

Vital Sign Parameter (Absolute)	Units	Potential Clinical Importance Range	
		Lower (<x)	Upper (>x)
Systolic Blood Pressure	mmHg	80	155
Diastolic Blood Pressure	mmHg	45	100
Heart Rate	bpm	45	130
Body temperature	°C		38.9
Respiratory rate	breaths/min		25

Vital Sign Parameter (Change from Baseline)	Units	Potential Clinical Importance 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: Abbreviations & Trade Marks

11.7.1. Abbreviations

Abbreviation	Description
A&R	Analysis and Reporting
ADaM	Analysis Data Model
AE	Adverse Event
ANOVA	Analysis of Variance
AUC	Area-under-the-curve
$AUC_{(0-\infty)}$	Area under the concentration-time curve extrapolated to infinity
$AUC_{(0\text{-last})}$	Area under the concentration-time curve from time zero to the time of the last quantifiable concentration
$AUC_{(0-t)}$	Partial area under the concentration-time curve to time
BP	Blood Pressure
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CL	Clearance
C_{max}	Maximum observed concentration, determined directly from the concentration-time data.
CPMS	Clinical Pharmacology Modelling & Simulation
CS	Clinical Statistics
CSP	Clinical Study Protocol
CSR	Clinical Study Report
CTR	Clinical Trial Register
CV_b / CV_w	Coefficient of Variation (Between) / Coefficient of Variation (Within)
DLT	Dose-limiting Toxicity
DP	Decimal Places
ECG	Electrocardiogram
eCRF	Electronic Case Record Form
FSH	Follicle Stimulating Hormone
FTIH	First-time-in-human
GSK	GlaxoSmithKline
GUI	Guidance
HIV	Human Immunodeficiency Virus
IA	Interim Analysis
ICH	International Conference on Harmonisation
IDMC	Independent Data Monitoring Committee
IDSL	Integrated Data Standards Library
IMMS	International Modules Management System
INR	International Normalized Ratio
IP	Investigational Product
ITT	Intent-To-Treat
Lambda_z	Terminal Phase Rate Constant
LOCF	Last Observation Carries Forward

Abbreviation	Description
MMRM	Mixed Model Repeated Measures
PCI	Potential Clinical Importance
PD	Pharmacodynamic
PDMP	Protocol Deviation Management Plan
PK	Pharmacokinetic
PP	Per Protocol
PT	Prothrombin Time or Preferred Term
PTT	Partial Thromboplastin Time
QC	Quality Control
LOQ	Limit of Quatitation
QTcF	Frederica's QT Interval Corrected for Heart Rate
RAMOS	Randomization & Medication Ordering System
RAP	Reporting & Analysis Plan
Ro	Accumulation ratio
SAC	Statistical Analysis Complete
SAE	Serious Adverse Event
SDTM	Study Data Tabulation Model
SOC	System Organ Class
SOP	Standard Operation Procedure
$t_{½}$	Apparent terminal half-life
TA	Therapeutic Area
TFL	Tables, Figures & Listings
t_{max}	Time to reach Cmax, determined directly from the concentration-time data.
VD	Volume of distribution
VSS	Volume of distribution where $V=CL/MRT_{iv}$

11.7.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
NONE

Trademarks not owned by the GlaxoSmithKline Group of Companies
SAS
WinNonlin

11.8. Appendix 8: List of Data Displays

11.8.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.10	Not applicable
Efficacy	Not applicable	Not applicable
Safety	3.1 to 3.24	Not applicable
Pharmacokinetic	4.1 to 4.4	4.1 to 4.3
Pharmacodynamic and / or Biomarker	5.1 to 5.24	5.1 to 5.39
Pharmacokinetic / Pharmacodynamic	Not applicable	6.1 to 6.14
Section	**Listings**	
ICH Listings	1 to 29	
Other Listings	30 to 56	

11.8.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required an example mock-up displays provided in Appendix 9: Example Mock Shells for Data Displays.

Section	Figure	Table	Listing
Study Population	POP_Fn	POP_Tn	POP_Ln
Efficacy	EFF_Fn	EFF_Tn	EFF_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
Pharmacokinetic / Pharmacodynamic	PKPD_Fn	PKPD_Tn	PK/PD_Ln

NOTES:

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

11.8.3. Deliverable [Priority]

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

NOTES:

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

11.8.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.1.	All Subjects	ES8	Summary of Subject Status and Reason for Study Withdrawal	Programmer to update primary reason for withdrawal to be study specific. ICH E3, GSK CTR, FDAAA, EudraCT	SAC [1]
Protocol Deviations					
1.2.	All Subjects	DV1	Summary of Protocol Deviations	Generated, if data permits. As required, refer to PDMP. ICH E3	SAC [1]
Study Populations					
1.3.	All Subjects	SP1	Summary of Study Populations	IDSL	SAC [1]
1.4.	All Subjects	SP2	Summary of Exclusions from Any Population	IDSL	SAC [1]
Demographic and Baseline characteristics					
1.5.	All Subjects	DM1	Summary of Demographic Characteristics	ICH E3, GSK CTR, FDAAA, EudraCT	SAC [1]
1.6.	Screened	DM11	Summary of Age Ranges	EudraCT	SAC [1]
1.7.	All Subjects	DM5	Summary of Race and Racial Combinations	ICH E3, FDA, FDAAA, EudraCT	SAC [1]
Prior and Concomitant Medications					
1.8.	All Subjects	MH4	Summary of Medical Conditions	ICH E3	SAC [1]
1.9.	All Subjects	CM1	Summary of Concomitant Medications	ICH E3	SAC [1]
Exposure and Treatment Compliance					
1.10.	All Subjects	EX1	Summary of Exposure to Study Treatment	ICH E3	SAC [1]

11.8.5. Efficacy Tables

Not applicable.

11.8.6. Efficacy Figures

Not applicable.

11.8.7. Safety Tables

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events					
3.1.	All Subjects	AE1	Summary of All Adverse Events by System Organ Class and Preferred Term	ICH E3 Sort Preferred Terms by highest incidence rate Please summarize safety tables by dose group (placebo, 7ng, 21 ng, 60ng, 120ng) and include a column for total drug-treated (7, 21, 60, 100)	SAC [1]
3.2.	All Subjects	AE5B	Summary of Adverse Events by Maximum Grade by System Organ Class and Preferred Term	ICH E3 For each SOC, sort Preferred Terms by highest incidence rate	SAC [1]
3.3.	All Subjects	AE1	Summary of Drug-Related Adverse Events by System Organ Class and Preferred Term	ICH E3 For each SOC, sort Preferred Terms by highest incidence rate	SAC [1]
3.4.	All Subjects	AE15	Summary of Common (≥5%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Participant and Occurrences)	FDAAA, EudraCT For each SOC, sort Preferred Terms by highest incidence rate	SAC [1]

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Serious and Other Significant Adverse Events					
3.5.	All Subjects	AE3	Summary of Serious Adverse Events by Overall Frequency	GSK CTR	SAC [1]
3.6.	All Subjects	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Participants and Occurrences)	FDAAA, EudraCT For each SOC, sort Preferred Terms by highest incidence rate	SAC [1]
3.7.	All Subjects	AE3	Summary of Drug-Related Serious Adverse Events by Overall Frequency	GSK CTR	SAC [1]
3.8.	All Subjects	AE1	Summary of Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study by Preferred Term	IDSL	SAC [1]
Laboratory: Clinical Chemistry					
3.9.	All Subjects	LB1	Summary of Clinical Chemistry	ICH E3 Order Parameters alphabetically Includes pre-specified parameters repeated in conventional units.	SAC [1]
3.10.	All Subjects	LB2	Summary of Clinical Chemistry data outside reference range	Order Parameters alphabetically Includes pre-specified parameters repeated in conventional units	SAC [1]
Laboratory: Hematology					
3.11.	All Subjects	LB1	Summary of Hematology	ICH E3 Order Parameters alphabetically Includes pre-specified parameters repeated in conventional units.	SAC [1]

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.12.	All Subjects	LB2	Summary of Hematology data outside reference range	Order Parameters alphabetically Includes pre-specified parameters repeated in conventional units	SAC [1]
Laboratory: Coagulation					
3.13.	All Subjects	LB1	Summary of Coagulation	ICH E3 Order Parameters alphabetically Includes pre-specified parameters repeated in conventional units.	SAC [1]
3.14.	All Subjects	LB2	Summary of Coagulation data outside reference range	Order Parameters alphabetically Includes pre-specified parameters repeated in conventional units	SAC [1]
Laboratory: Urinalysis					
3.15.	All Subjects	LB1	Summary of Urinalysis Results	ICH E3 Order Parameters alphabetically	SAC [1]
ECG					
3.16.	All Subjects	EG1	Summary of ECG Findings	IDSL Use ECG findings categories (and change from baseline categories, if applicable).	SAC [1]
3.17.	All Subjects	EG1	Summary of ECG Findings worst case post-baseline	IDSL	SAC [1]
3.18.	All Subjects	EG2	Summary of ECG Values by Visit	IDSL	SAC [1]
3.19.	All Subjects	EG2	Summary of Change from Baseline in ECG Values by Visit	IDSL Includes Baseline values.	SAC [1]
3.20.	All Subjects	EG10	Summary of QTcF Grades by Visit	IDSL	SAC [1]

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.21.	All Subjects	EG11	Summary of Change from Baseline and worst case post-baseline QTcF Grades by Visit	IDSL Includes Baseline values.	SAC [1]
Vital Signs					
3.22.	All Subjects	VS1	Summary of Vital Signs by Visit	IDSL	SAC [1]
3.23.	All Subjects	VS1	Summary of Change from Baseline in Vital Signs by Visit	IDSL Includes Baseline values	SAC [1]
3.24.	All Subjects	VS6	Summary of Vital Signs by Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials	IDSL	SAC [1]

11.8.8. Safety Figures

Not applicable.

11.8.9. Pharmacokinetic Tables

Pharmacokinetic : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Pharmacokinetic					
4.1.	PK Concen-tration	PK01	Summary statistics of GSK1795091 concentration data		SAC [1]
4.2.	PK Parameter	PK04	Summary statistics of GSK1795091 PK Parameters		SAC [1]
4.3.	PK Parameter	PK13	Listing of GSK1795091 PK Parameters	Standard listing format; include as table in table section	SAC [1]
Dose proportionality					
4.4.	PK Parameter	Non-Standard	Summary of Results of Dose Proportionality Assessment for Cmax Using Power Model Single dose		SAC [1]

11.8.10. Pharmacokinetic Figures

Pharmacokinetic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Pharmacokinetic					
4.1.	PK Concen-tration	PK17	Mean (95% CI) PK Concentration of GSK1795091	Linear and Log Scale	SAC [1]
4.2.	PK Concen-tration	LB11	Individual subject plots of PK Concentration for GSK1795091	Linear and Log Scale	SAC [1]
Dose proportionality					
4.3.	PK Parameter	PK29	Individual and Box Plot of Dose-Normalized GSK1795091 PK Parameter by Dose following Single Dose	Cmax only, Linear and Log Scale	SAC [1]

11.8.11. Pharmacodynamic/Biomarker Tables

Pharmacodynamic/Biomarker : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Cytokines/Chemokines					
5.1.	PD	PD1	Summary of Concentration of IL-6	Summarize by visit for each dose level, and group all placebos together	SAC [1]
5.2.	PD	PD1	Summary of Concentration of TNF-alpha	Summarize by visit for each cohort. Exclude subjects administered placebo from each cohort, and group all placebos together	SAC [1]
5.3.	PD	PD1	Summary of Concentration of IFN-gamma	Summarize by visit for each dose level, and group all placebos together	SAC [1]
5.4.	PD	PD1	Summary of Concentration of IP-10	Summarize by visit for each dose level, and group all placebos together	SAC [1]
5.5.	PD	PD1	Summary of Concentration of MCP-1	Summarize by visit for each dose level, and group all placebos together	SAC [1]
5.6.	PD	PD1	Summary of Concentration of GM-CSF	Summarize by visit for each dose level, and group all placebos together	SAC [1]
5.7.	PD	PD1	Summary of Concentration of IL-1Ra	Summarize by visit for each dose level, and group all placebos together	SAC [1]
5.8.	PD	PD1	Summary of Concentration of IL-10	Summarize by visit for each dose level, and group all placebos together	SAC [1]
5.9.	PD	PD3	Summary of Fold Change of Concentration of IL-6 from Baseline	Summarize by visit for each dose level, and group all placebos togetherImpute 0.5LOQ if a value is below LOQ.	SAC [1]

Pharmacodynamic/Biomarker : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.10.	PD	PD3	Summary of Fold Change of Concentration of TNF-alpha from Baseline	Summarize by visit for each dose level, and group all placebos together. Impute 0.5LOQ if a value is below LOQ.	SAC [1]
5.11.	PD	PD3	Summary of Fold Change of Concentration of IFN-gamma from Baseline	Summarize by visit for each dose level, and group all placebos together. Impute 0.5LOQ if a value is below LOQ.	SAC [1]
5.12.	PD	PD3	Summary of Fold Change of Concentration of IP-10 from Baseline	Summarize by visit for each dose level, and group all placebos together. Impute 0.5LOQ if a value is below LOQ	SAC [1]
5.13.	PD	PD3	Summary of Fold Change of Concentration of MCP-1 from Baseline	Summarize by visit for each dose level, and group all placebos together. Impute 0.5LOQ if a value is below LOQ	SAC [1]
5.14.	PD	PD3	Summary of Fold Change of Concentration of GM-CSF from Baseline	Summarize by visit for each dose level, and group all placebos together.Impute 0.5LOQ if a value is below LOQ	SAC [1]
5.15.	PD	PD3	Summary of Fold Change of Concentration of IL-1Ra from Baseline	Summarize by visit for each dose level, and group all placebos together. Impute 0.5LOQ if a value is below LOQ	SAC [1]
5.16.	PD	PD3	Summary of Fold Change of Concentration of IL-10 from Baseline	Summarize by visit for each dose level, and group all placebos together. Impute 0.5LOQ if a value is below LOQ	SAC [1]
Immunophenotyping					
5.17.	All Subjects	PD4	Summary of Neutrophils	Summarize abs. only. Summarize by visit for each dose level, and group all placebos together.	SAC [1]

Pharmacodynamic/Biomarker : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.18.	All Subjects	PD4	Summary of Lymphocytes	Summarize abs. only. Summarize by visit for each dose level, and group all placebos together	SAC [1]
5.19.	All Subjects	PD4	Summary of Monocytes	Summarize abs. only. Summarize by visit for each dose level, and group all placebos together	SAC [1]
5.20.	All Subjects	PD3	Summary of Neutrophils Change from Baseline	Summarize abs. only. Summarize by visit for each dose level, and group all placebos together. Impute 0.5LOQ if a value is below LOQ.	SAC [1]
5.21.	All Subjects	PD3	Summary of Lymphocytes Change from Baseline	Summarize abs. only. Summarize by visit for each dose level, and group all placebos together. Impute 0.5LOQ if a value is below LOQ.	SAC [1]
5.22.	All Subjects	PD3	Summary of Monocytes Change from Baseline	Summarize abs. only. Summarize by visit for each dose level, and group all placebos together. Impute 0.5LOQ if a value is below LOQ.	SAC [1]
Laboratory Tests					
5.23.	All Subjects	PD4	Summary of CRP	Summarize by visit for each dose level, and group all placebos together.	SAC [1]
5.24.	All Subjects	PD3	Summary of CRP Change from Baseline	Summarize by visit for each dose level, and group all placebos together.	SAC [1]

11.8.12. Pharmacodynamic/Biomarker Figures

Pharmacodynamic/Biomarker: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Cytokines					
5.1.	PD	EG9	Mean Concentration of IL-6 with 95% CI over Time by Dose	Time course Each dose as single figure, placebo pooled	SAC [1]
5.2.	PD	EG9	Mean Concentration of TNF-alpha with 95% CI over Time by Dose	Time course Each dose as single figure, placebo pooled	SAC [1]
5.3.	PD	EG9	Mean Concentration of IFN-gamma with 95% CI over Time by Dose	Time course Each dose as single figure, placebo pooled	SAC [1]
5.4.	PD	EG9	Mean Concentration of IP-10 with 95% CI over Time by Dose	Time course Each dose as single figure, placebo pooled	SAC [1]
5.5.	PD	EG9	Mean Concentration of MCP-1 with 95% CI over Time by Dose	Time course. Each dose as single figure, placebo pooled	SAC [1]
5.6.	PD	EG9	Mean Concentration of GM-CSF with 95% CI over Time by Dose	Time course. Each dose as single figure, placebo pooled	SAC [1]
5.7.	PD	EG9	Mean Concentration of IL-1Ra with 95% CI over Time by Dose	Time course Each dose as single figure, placebo pooled	SAC [1]
5.8.	PD	EG9	Mean Concentration of IL-10 with 95% CI over Time by Dose	Time course Each dose as single figure, placebo pooled	SAC [1]

Pharmacodynamic/Biomarker: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Immunophenotyping					
5.9.	All Subjects	EG9	Mean Neutrophils abs. with 95% CI over Time by Dose	Time course Each dose as single figure, placebo pooled	SAC [1]
5.10.	All Subjects	EG9	Mean Change from Baseline in Neutrophils abs. with 95% CI over Time by Dose	Time course Each dose as single figure, placebo pooled	SAC [1]
5.11.	All Subjects	LB11	Individual Neutrophils abs. over Time	Spaghetti plot of individual values, Each dose as single figure, placebo as pooled cohort	SAC [1]
5.12.	All Subjects	LB11	Individual Change from Baseline in Neutrophils abs. over Time	Spaghetti plot of individual values, Each dose as single figure, placebo as pooled cohort	SAC [1]
5.13.	All Subjects	EG9	Mean Lymphocytes abs. with 95% CI over Time by Dose	Time course Each dose as single figure, placebo pooled	SAC [1]
5.14.	All Subjects	EG9	Mean Change from Baseline in Lymphocytes abs. with 95% CI over Time by Dose	Time course Each dose as single figure, placebo pooled	SAC [1]
5.15.	All Subjects	LB11	Individual Lymphocytes abs. over Time	Spaghetti plot of individual values, Each dose as single figure, placebo as pooled cohort	SAC [1]
5.16.	All Subjects	LB11	Individual Change from Baseline in Lymphocytes abs. over Time	Spaghetti plot of individual values, Each dose as single figure, placebo as pooled cohort	SAC [1]

Pharmacodynamic/Biomarker: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.17.	All Subjects	EG9	Mean Change from Baseline in Monocytes abs. with 95% CI over Time by Dose	Time course Each dose as single figure, placebo pooled	SAC [1]
5.18.	All Subjects	LB11	Individual Monocytes abs. over Time	Spaghetti plot of individual values, Each dose as single figure, placebo as pooled cohort	SAC [1]
5.19.	All Subjects	LB11	Individual Change from Baseline in Monocytes abs. over Time	Spaghetti plot of individual values, Each dose as single figure, placebo as pooled cohort	SAC [1]
Vital signs					
5.20.	All Subjects	EG9	Mean Body Temperature values with 95% CI over Time	Time course Each dose as single figure, placebo pooled	SAC [1]
5.21.	All Subjects	EG9	Mean Change from Baseline in Body Temperature values with 95% CI over Time	Time course Each dose as single figure, placebo pooled	SAC [1]
5.22.	All Subjects	LB11	Individual Body Temperature values over Time	Spaghetti plot of individual values, each dose as single figure, placebo as pooled cohort	SAC [1]
5.23.	All Subjects	LB11	Individual Change from Baseline in Body Temperature values over Time	Spaghetti plot of individual values, Each dose as single figure, placebo as pooled cohort	SAC [1]
5.24.	All Subjects	EG9	Mean Heart Rate values with 95% CI over Time	Time course Each dose as single figure, placebo pooled	SAC [1]

Pharmacodynamic/Biomarker: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.25.	All Subjects	EG9	Mean Change from Baseline in Heart Rate values with 95% CI over Time	Time course All doses on a single graph, placebo pooled	SAC [1]
5.26.	All Subjects	LB11	Individual Heart Rate values over Time	Spaghetti plot of individual values, each cohort as single figure, placebo as pooled cohort	SAC [1]
5.27.	All Subjects	LB11	Individual Change from Baseline in Heart Rate values over Time	Spaghetti plot of individual values, Each dose as single figure, placebo as pooled cohort	SAC [1]
5.28.	All Subjects	EG9	Mean Systolic Blood Pressure values with 95% CI over Time	Time course All doses on a single graph, placebo pooled	SAC [1]
5.29.	All Subjects	EG9	Mean Change from Baseline in Systolic Blood Pressure values with 95% CI over Time	Time course Each dose as single figure, placebo pooled	SAC [1]
5.30.	All Subjects	LB11	Individual Systolic Blood Pressure values over Time	Spaghetti plot of individual values, each dose as single figure, placebo as pooled cohort	SAC [1]
5.31.	All Subjects	LB11	Individual Change from Baseline in Systolic Blood Pressure values over Time	Spaghetti plot of individual values, Each dose as single figure, placebo as pooled cohort	SAC [1]
5.32.	All Subjects	EG9	Mean Diastolic Blood Pressure values with 95% CI over Time	Time course Each dose as single figure, placebo pooled	SAC [1]

Pharmacodynamic/Biomarker: Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
5.33.	All Subjects	EG9	Mean Change from Baseline in Diastolic Blood Pressure values with 95% CI over Time	Time course Each dose as single figure, placebo pooled	SAC [1]
5.34.	All Subjects	LB11	Individual Diastolic Blood Pressure values over Time	Spaghetti plot of individual values, each dose as single figure, placebo as pooled cohort	SAC [1]
5.35.	All Subjects	LB11	Individual Change from Baseline in Diastolic Blood Pressure values over Time	Spaghetti plot of individual values, Each dose as single figure, placebo as pooled cohort	SAC [1]
Laboratory Tests					
5.36.	All Subjects	EG9	Mean CRP values with 95%CI over Time	Time course Each dose as single figure, placebo pooled	SAC [1]
5.37.	All Subjects	EG9	Mean Change from Baseline in CRP values with 95%CI over Time	Time course Each dose as single figure, placebo pooled	SAC [1]
5.38.	All Subjects	LB11	Individual CRP values over Time	Spaghetti plot of individual values, Each dose as single figure, placebo as pooled cohort	SAC [1]
5.39.	All Subjects	LB11	Individual Change from Baseline in CRP values over Time	Spaghetti plot of individual values, Each dose as single figure, placebo as pooled cohort	SAC [1]

11.8.13. Pharmacokinetic / Pharmacodynamic Tables

Not applicable.

11.8.14. Pharmacokinetic / Pharmacodynamic Figures

Pharmacokinetic / Pharmacodynamic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.1.	All Subjects	Non-Standard2	Relationship of GSK1795091 PK Parameters and Vital Signs Maximum Changes from Baseline	Scatterplot (X-axis: PK parameter, Y-axis: Maximum change, pair X and Y by SubjID) Individual figure. Use different colors or symbols to distinguish dose levels. Draw linear trending line for each dose level. Exclude subjects administered placebo from each cohort, and group all placebos together. X: Cmax only. Y: HR, Body temperature, Systolic blood pressure, Diastolic blood pressure	SAC [1]
6.2.	All Subjects	Non-Standard2	Relationship of GSK1795091 PK Parameters and WBC incl. differential Maximum Changes from Baseline	Scatterplot (for each subject, X-axis: PK parameter, Y-axis: Maximum change, pair X and Y by SubjID) Individual figure. Use different colors or symbols to distinguish dose levels. Draw linear trending line for each dose level. Exclude subjects administered placebo from each cohort, and group all placebos together. X: Cmax only.	SAC [1]

Pharmacokinetic / Pharmacodynamic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.3.	All Subjects	Non-Standard2	Relationship of GSK1795091 PK Parameters and Laboratory Tests Maximum Changes from Baseline	Scatterplot (for each subject, X-axis: PK parameter, Y-axis: Maximum change, pair X and Y by SubjID) Individual figure. Use different colors or symbols to distinguish dose levels. Draw linear trending line for each dose level. Exclude subjects administered placebo from each cohort, and group all placebos together. X: Cmax only Y: Laboratory tests (CRP, Neutrophil abs., Lymphocyte abs.)	SAC [1]
6.4.	PD	Non-Standard2	Relationship of GSK1795091 PK Concentrations and IL-6	Scatterplot with trending lines (X-axis: PK concentration, Y-axis: Biomarker, pair X and Y by SubjID and Time) Use distinct colors or symbols to distinguish dose levels. Exclude subjects administered placebo from each cohort, and group all placebos together. Draw linear trending line for each dose level	SAC [1]

Pharmacokinetic / Pharmacodynamic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.5.	PD	Non-Standard2	Relationship of GSK1795091 PK Concentrations and TNF-alpha	Scatterplot with trending lines (X-axis: PK concentration, Y-axis: Biomarker, pair X and Y by SubjID and Time) Use distinct colors or symbols to distinguish dose levels. Exclude subjects administered placebo from each cohort, and group all placebos together. Draw linear trending line for each dose level	SAC [1]
6.6.	PD	Non-Standard2	Relationship of GSK1795091 PK Concentrations and IFN-gamma	Scatterplot with trending lines (X-axis: PK concentration, Y-axis: Biomarker, pair X and Y by SubjID and Time) Use distinct colors or symbols to distinguish dose levels. Exclude subjects administered placebo from each cohort, and group all placebos together. Draw linear trending line for each dose level	SAC [1]

Pharmacokinetic / Pharmacodynamic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.7.	PD	Non-Standard2	Relationship of GSK1795091 PK Concentrations and IP-10	Scatterplot with trending lines (X-axis: PK concentration, Y-axis: Biomarker, pair X and Y by SubjID and Time) Use distinct colors or symbols to distinguish dose levels. Exclude subjects administered placebo from each cohort, and group all placebos together. Draw linear trending line for each dose level	SAC [1]
6.8.	PD	Non-Standard2	Relationship of GSK1795091 PK Concentrations and MCP-1	Scatterplot with trending lines (X-axis: PK concentration, Y-axis: Biomarker, pair X and Y by SubjID and Time) Use distinct colors or symbols to distinguish dose levels. Exclude subjects administered placebo from each cohort, and group all placebos together. Draw linear trending line for each dose level	SAC [1]

Pharmacokinetic / Pharmacodynamic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.9.	PD	Non-Standard2	Relationship of GSK1795091 PK Concentrations and GM-CSF	Scatterplot with trending lines (X-axis: PK concentration, Y-axis: Biomarker, pair X and Y by SubjID and Time) Use distinct colors or symbols to distinguish dose levels. Exclude subjects administered placebo from each cohort, and group all placebos together. Draw linear trending line for each dose level	SAC [1]
6.10.	PD	Non-Standard2	Relationship of GSK1795091 PK Concentrations and IL-1Ra	Scatterplot with trending lines (X-axis: PK concentration, Y-axis: Biomarker, pair X and Y by SubjID and Time) Use distinct colors or symbols to distinguish dose levels. Exclude subjects administered placebo from each cohort, and group all placebos together. Draw linear trending line for each dose level	SAC [1]

Pharmacokinetic / Pharmacodynamic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.11.	PD	Non-Standard2	Relationship of GSK1795091 PK Concentrations and IL-10	Scatterplot with trending lines (X-axis: PK concentration, Y-axis: Biomarker, pair X and Y by SubjID and Time) Use distinct colors or symbols to distinguish dose levels. Exclude subjects administered placebo from each cohort, and group all placebos together. Draw linear trending line for each dose level	SAC [1]
6.12.	All Subjects	Non-Standard2	Relationship of GSK1795091 PK Concentrations and Neutrophils abs.	Scatterplot with trending lines (X-axis: PK concentration, Y-axis: Biomarker, pair X and Y by SubjID and Time) Use distinct colors or symbols to distinguish dose levels. Exclude subjects administered placebo from each cohort, and group all placebos together. Draw linear trending line for each dose level	SAC [1]

Pharmacokinetic / Pharmacodynamic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
6.13.	All Subjects	Non-Standard2	Relationship of GSK1795091 PK Concentrations and Lymphocytes abs.	Scatterplot with trending lines (X-axis: PK concentration, Y-axis: Biomarker, pair X and Y by SubjID and Time) Use distinct colors or symbols to distinguish dose levels. Exclude subjects administered placebo from each cohort, and group all placebos together. Draw linear trending line for each dose level	SAC [1]
6.14.	All Subjects	Non-Standard2	Relationship of GSK1795091 PK Concentrations and Monoocytes abs.	Scatterplot with trending lines (X-axis: PK concentration, Y-axis: Biomarker, pair X and Y by SubjID and Time) Use distinct colors or symbols to distinguish dose levels. Exclude subjects administered placebo from each cohort, and group all placebos together. Draw linear trending line for each dose level	SAC [1]

11.8.15. ICH Listings

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.	Screened	ES7	Listing of Reason for Screening Failure	Journal Guidelines	SAC [1]
2.	All Subjects	ES2	Listing of Reasons for Withdrawal	ICH E3	SAC [1]
3.	All Subjects	SD2	Listing of Reasons for Study Treatment Discontinuation	ICH E3	SAC [1]
4.	All Subjects	BL1	Listing of Subjects for Whom the Treatment Blind was Broken	ICH E3	SAC [1]
5.	All Subjects	TA1	Listing of Planned and Actual Treatments	IDSL	SAC [1]
Protocol Deviation					
6.	All Subjects	DV2	Listing of Protocol Deviations	ICH E3 Listing also includes analysis population exclusions.	SAC [1]
7.	All Subjects	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations	ICH E3	SAC [1]
Populations Analysed					
8.	All randomised	SP3	Listing of Subjects Excluded from Any Population	ICH E3	SAC [1]
Demographics and Baseline Characteristics					
9.	All Subjects	DM2	Listing of Demographics Characteristics	ICH E3	SAC [1]
Prior and Concomitant Medication					
10.	All Subjects	CM3	Listing of Concomitant Medications	IDSL	SAC [1]
Exposure and Treatment Compliance					
11.	All Subjects	EX3	Listing of Exposure Data	ICH E3	SAC [1]

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Medical History					
12.	All Subjects	MH2	Listing of Medical History	IDSL	SAC [1]
13.	All Subjects	SU2	Listing of Substance Use	IDSL	SAC [1]
Adverse Events					
14.	All Subjects	AE8	Listing of All Adverse Events	ICH E3	SAC [1]
15.	All Subjects	AE7	Listing of Subject Numbers for Individual Adverse Events	ICH E3	SAC [1]
16.	All Subjects	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text	IDSL	SAC [1]
17.	All Subjects	AE8	Listing of Serious Adverse Events	ICH E3	SAC [1]
18.	All Subjects	AE14	Listing of Reasons for Considering as a Serious Adverse Event	ICH E3	SAC [1]
19.	All Subjects	AE8	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment	ICH E3	SAC [1]
All Laboratory					
20.	All Subjects	LB5	Listing of Clinical Chemistry for Subjects with Any Value of Potential Clinical Importance	ICH E3 Include a normal range column in the listing	SAC [1]
21.	All Subjects	LB5	Listing of Hematology for Subjects with Any Value of Potential Clinical Importance	ICH E3	SAC [1]
22.	All Subjects	LB5	Listing of Coagulation for Subjects with Any Value of Potential Clinical Importance	ICH E3	SAC [1]
23.	All Subjects	UR2A	Listing of Urinalysis for Subjects with Any Value of Potential Clinical Importance	ICH E3	SAC [1]
24.	All Subjects	LB5	Listing of Laboratory Values of Potential Clinical Importance	ICH E3	SAC [1]

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
ECG					
25.	All Subjects	EG3	Listing of All ECG Data for Subjects with Any Value of Potential Clinical Importance	IDSL	SAC [1]
26.	All Subjects	EG3	Listing of ECG Values of Potential Clinical Importance	IDSL	SAC [1]
27.	All Subjects	EG5	Listing of Abnormal ECG Findings	IDSL	SAC [1]
Vital Signs					
28.	All Subjects	VS4	Listing of All Vital Signs Data for Subjects with Any Value of Potential Clinical Importance	IDSL	SAC [1]
29.	All Subjects	VS4	Listing of Vital Signs of Potential Clinical Importance	IDSL	SAC [1]

11.8.16. Non-ICH Listings

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Pharmacokinetic					
30.	PK Concen-tration	PK07	Listing of GSK1795091 Concentration-Time data	Sort by subject, treatment, day, and time	SAC [1]
Laboratory Tests					
31.	All Subjects	OLB7	Listing of Selected Laboratory Tests	IDSL CRP, Neutrophils abs., Lymphocytes abs.	SAC [1]
32.	All Subjects	OLB7	Listing of Change from Baseline in Selected Laboratory Tests	IDSL CRP, Neutrophils abs., Lymphocytes abs.	SAC [1]
Vital Signs					
33.	All Subjects	OVT7A	Listing of Selected Vital Signs with Values Potential Clinical Importance	IDSL HR, Body temperature, Sys BP, Dias BP	SAC [1]
34.	All Subjects	OVT7A	Listing of Vital Signs Change from Baseline with Values Potential Clinical Importance	IDSL HR, Body temperature, Sys BP, Dias BP	SAC [1]
Pharmacodynamic					
35.	PD	PD16	Listing of Concentration of IL-6	Sort by subject, treatment, day, and time	SAC [1]
36.	PD	PD16	Listing of Concentration of TNF-alpha	Sort by subject, treatment, day, and time	SAC [1]

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
37.	PD	PD16	Listing of Concentration of IFN-gamma	Sort by subject, treatment, day, and time	SAC [1]
38.	PD	PD16	Listing of Concentration of IP-10	Sort by subject, treatment, day, and time	SAC [1]
39.	PD	PD16	Listing of Concentration of MCP-1	Sort by subject, treatment, day, and time	SAC [1]
40.	PD	PD16	Listing of Concentration of GM-CSF	Sort by subject, treatment, day, and time	SAC [1]
41.	PD	PD16	Listing of Concentration of IL-1Ra	Sort by subject, treatment, day, and time	SAC [1]
42.	PD	PD16	Listing of Concentration of IL-10	Sort by subject, treatment, day, and time	SAC [1]
43.	PD	PD16	Listing of Fold Change of Concentration of IL-6 from Baseline	Sort by subject, treatment, day, and time	SAC [1]
44.	PD	PD16	Listing of Fold Change of Concentration of TNF-alpha from Baseline	Sort by subject, treatment, day, and time	SAC [1]
45.	PD	PD16	Listing of Fold Change of Concentration of IFN-gamma from Baseline	Sort by subject, treatment, day, and time	SAC [1]
46.	PD	PD16	Listing of Fold Change of Concentration of IP-10 from Baseline	Sort by subject, treatment, day, and time	SAC [1]
47.	PD	PD16	Listing of Fold Change of Concentration of MCP-1 from Baseline	Sort by subject, treatment, day, and time	SAC [1]
48.	PD	PD16	Listing of Fold Change of Concentration of GM-CSF from Baseline	Sort by subject, treatment, day, and time	SAC [1]

Non-ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
49.	PD	PD16	Listing of Fold Change of Concentration of IL-1Ra from Baseline	Sort by subject, treatment, day, and time	SAC [1]
50.	PD	PD16	Listing of Fold Change of Concentration of IL-10 from Baseline	Sort by subject, treatment, day, and time	SAC [1]
51.	PD	PD16	Listing of Neutrophils	List both % and abs.. Sort by subject, treatment, day, and time	SAC [1]
52.	PD	PD16	Listing of Lymphocytes	List both % and abs.. Sort by subject, treatment, day, and time	SAC [1]
53.	PD	PD16	Listing of Monocytes	List both % and abs.. Sort by subject, treatment, day, and time	SAC [1]
54.	PD	PD16	Listing of Neutrophils abs. Change from Baseline	List abs. only. Sort by subject, treatment, day, and time	SAC [1]
55.	PD	PD16	Listing of Lymphocytes abs. Change from Baseline	List abs. only. Sort by subject, treatment, day, and time	SAC [1]
56.	PD	PD16	Listing of Monocytes abs. Change from Baseline	List abs. only. Sort by subject, treatment, day, and time	SAC [1]

11.9. Appendix 9: Example Mock Shells for Data Displays

Example : Non-Standard 2

Protocol : 204685

Population : All Subjects

Figure 6.16

Relationship of GSK1795091 PK Parameters and Vital Signs Maximum Changes from Baseline