Division	:	Worldwide Development
Information Type	:	Reporting and Analysis Plan (RAP)
Title	:	Reporting and Analysis Plan for A Phase I, Double-Blind, Two-Part, Sequential Study to Evaluate the Pharmacokinetics of Gepotidacin Tablets in Healthy Adult and Adolescent Participants
Compound Number	:	GSK2140944
Effective Date	:	10-DEC-2019

Description:

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report (CSR) for Protocol GSK209611.
- This RAP is intended to describe the safety, tolerability, and pharmacokinetic (PK) 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) and Interim Analysis (IA) deliverable.

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1. INTRODUCTION

The purpose of this reporting and analysis plan (RAP) is to describe the analyses to be included in the CSR for Protocol GSK209611

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

Changes to the planned statistical analysis specified in the protocol (Dated: 13-JUN-2019) are listed below.

- For adolescent serum creatinine lab data, pediatric DMID toxicity criteria will be used.
- Events associated with acetylcholinesterase inhibition will be programmatically and manually assessed as adverse events of special interest (AESIs). See analysis plan in Section 8.2 and Section 10.4.3.
- Section 7.1.1.2 of this analysis plan specifies that the accumulation ratio Ro AUC will be calculated as AUC(0-τ) after the second dose divided by AUC(0-τ) after the first dose (rather than using AUC(0-6) as stated in the protocol), to make this formula widely applicable to all dosing intervals.

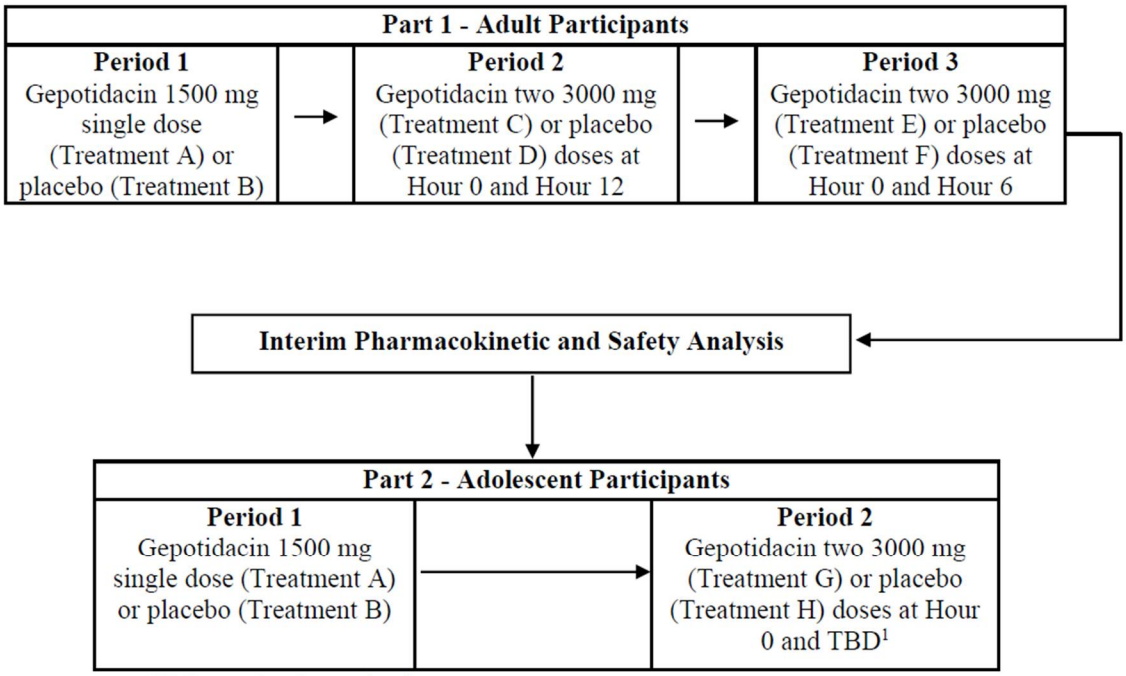
2.2. Study Objective(s) and Endpoint(s)

Objectives	Endpoints
Primary	
Part 1 • To evaluate the pharmacokinetics (PK) of a single 1500- milligrams (mg) dose and two 3000-mg doses of gepotidacin given 6 and 12 hours apart in adult participants	1500 mg single dose • Plasma gepotidacin AUC(0-t), AUC(0-∞), AUC(0-24), AUC(0-48), and Cmax, as data permit 3000 mg two doses • Plasma gepotidacin AUC(0-t), AUC(0-τ), AUC(0-24), AUC(0-48), Ro (accumulation ratio), and Cmax, as data permit

Part 2 • To evaluate the PK of a single 1500-mg dose and two 3000-mg doses of gepotidacin given at a dosing interval (to be determined) in adolescent participants	1500 mg single dose • Plasma gepotidacin AUC(0-t), AUC(0-∞), AUC(0-24), AUC(0-48), and Cmax, as data permit 3000 mg two doses • Plasma gepotidacin AUC(0-t), AUC(0-τ), AUC(0-24), AUC(0-48), Ro (accumulation ratio), and Cmax, as data permit
Parts 1 and 2 • To assess the safety of gepotidacin in adult participants and adolescent participants	• Adverse events, clinical laboratory tests, vital signs (systolic and diastolic blood pressure and heart rate), and 12-lead electrocardiogram readings
Secondary	
Part 1 • To assess the urine PK of gepotidacin following a single 1500-mg dose and two 3000-mg doses of gepotidacin given 6 and 12 hours apart in adult participants	• Urine endpoints include Ae total, Ae(t1-t2), AUC(0-τ), AUC(0-24), AUC(0-48), percentage of the given dose of drug excreted in urine (fe%), and renal clearance of drug (CLr) of gepotidacin, as data permit
Part 2 • To assess the urine PK of gepotidacin following a single 1500-mg dose and two 3000-mg doses of gepotidacin given at a dosing interval (to be determined) in adolescent participants	• Urine endpoints include Ae total, Ae(t1-t2), AUC(0-τ), AUC(0-24), AUC(0-48), fe%, and CLr of gepotidacin, as data permit
Parts 1 and 2 • To assess the plasma PK of gepotidacin	• Plasma gepotidacin Tmax, tlag, and t1/2, as data permit

2.3. Study Design

Overview of Study Design and Key Features



TBD = to be determined.

1. Exact dosing interval will be determined after interim analysis.

Note: Participants will be randomized in in a 14:3 ratio in order to obtain 12 evaluable participants on active treatment and 2 evaluable participants on placebo.

Design Features	• Phase I, double-blind, single-center, randomized, sequential, two-part study • **Part 1:** Participants will be randomly assigned to receive either all active treatment (gepotidacin) or placebo for all 3 periods. Approximately 17 participants will be randomized (in a 14:3 ratio) to receive a single dose of gepotidacin 1500 mg (Treatment A) or matching placebo (Treatment B) in Period 1, gepotidacin 3000 mg separated by 12 hours (Treatment C) or matching placebo (Treatment D) in Period 2, and gepotidacin 3000 mg separated by 6 hours (Treatment E) or matching placebo (Treatment F) in Period 3 to obtain 12 evaluable participants on active treatment and 2 evaluable participants on placebo. • **Part 2**: Participants will be randomly assigned to receive either all active treatment (gepotidacin) or placebo for both periods. Approximately 17 participants will be randomized (in a 14:3 ratio) to receive a single dose of gepotidacin 1500 mg (Treatment A) or matching placebo (Treatment B) in Period 1, and gepotidacin 3000 mg (Treatment G) or matching placebo (Treatment H) in Period 2 to obtain 12 evaluable participants on active treatment and 2 evaluable participants on placebo. • In Part 2, the interval for the two 3000-mg doses in Period 2 will be between 6 hours and 12 hours based on the PK and safety results from Part 1.

Dosing	**Part 1 – Adult Participants:** • Treatment A: Single dose 1500 mg (Period 1) • Treatment B: Matching placebo (Period 1) • Treatment C: Two 3000 mg doses given at Hour 0 and Hour 12 (Period 2) • Treatment D: Two matching placebo doses given at Hour 0 and Hour 12 (Period 2) • Treatment E: Two 3000 mg doses given at Hour 0 and Hour 6 (Period 3) • Treatment F: Two matching placebo doses given at Hour 0 and Hour 6 (Period 3) **Part 2 - Adolescent Participants** • Treatment A: Single dose 1500 mg (Period 1) • Treatment B: Matching placebo (Period 1) • Treatment G: Two 3000 mg doses (Period 2; exact dosing interval to be determined after Part 1 is complete) • Treatment H: Two matching placebo doses (Period 2; exact dosing interval to be determined after Part 1 is complete)
Time and Events	• See Appendix 1: Schedule of Activities (SoA)
Treatment Assignment	• **Part 1 – Adult Participants**: Participants will be randomly assigned to receive either all active treatment (gepotidacin, Treatment A/C/E) or placebo (Treatment B/D/F) for all 3 periods • **Part 2 – Adolescent Participants**: Participants will be randomly assigned to receive either all active treatment (gepotidacin, Treatment A/G) or placebo (Treatment B/H) for both periods.
Interim Analysis	The interim analysis will consist data management listings and WinNonLin outputs. Preliminary plasma PK and safety results from participants in Part 1 will be reviewed by the sponsor before enrolling participants into the next part of the study. The dosing interval to be used when two gepotidacin doses are given in Part 2, Period 2 will be determined after a review of the PK and safety results from Part 1. The number of PK samples and the PK sampling time points may be modified based on the adult PK data from Part 1. An ad hoc review of 12-lead electrocardiogram (ECG) data may be performed between Part 1, Period 2 and Part 1, Period 3.

2.4. Statistical Analyses

There is no formal research hypothesis that will be statistically tested in this study.

3. PLANNED ANALYSES

3.1. Interim Analyses

The interim analysis will consist data management listings and WinNonLin outputs. Preliminary plasma PK and safety results from participants in Part 1 will be reviewed by the sponsor before enrolling participants into the next part of the study. The dosing interval to be used when two gepotidacin doses are given in Part 2, Period 2 will be determined after a review of the PK and safety results from Part 1. The number of PK samples and the PK sampling time points may be modified based on the adult PK data from Part 1.

An ad hoc review of 12-lead ECG data may be performed between Part 1, Period 2 and Part 1, Period 3.

3.2. Final Analyses

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

1. All participants have completed the study as defined in the protocol
2. All required database cleaning activities have been completed and final database release and database freeze has been declared by Data Management.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Enrolled	• All participants who sign the ICF/assent.	• Study Population
Randomized	• All participants who are randomized.	• Study Population
Safety	• All participants who take at least 1 dose of study intervention.	• Study Population • Safety
PK	• Participants who receive at least 1 dose of gepotidacin and have evaluable postdose plasma concentration data for gepotidacin.	• PK Concentration
PK Parameter	• All participants in the PK population who received gepotidacin for whom valid and evaluable plasma PK parameters are derived for gepotidacin.	• PK parameter • PK statistical analysis

NOTES:

- Please refer to Appendix 10: 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, patient management or patient assessment) will be summarized and listed.

Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan.

- Data will be reviewed prior to freezing the database to ensure all important deviations and deviations which may lead to exclusion from the analysis are captured and categorized 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 electronic case report form (eCRF).

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

5.1. Baseline Definitions

For all endpoints (except as noted in baseline definitions) the baseline value will be the last available assessment prior to time of study drug administration, unless noted otherwise.

Parameter	Study Assessments Considered as Baseline				Baseline Used in Data Display
	Screening	Day -1	Day 1 (Pre-Dose) for Part 1 Period 1 and Part 2 all Periods	Day 5 (Pre-Dose) and Day 9 (Pre-Dose) for Part 1 Period 2 and 3	
	Safety				
Hematology	X	X			Day -1
Chemistry	X	X			Day -1
Routine Urinalysis	X	X			Day -1
12-Lead ECG	X	X	X	X	Day 1, Day 5 and Day 9 Pre-Dose
Vital Signs	X	X	X	X	Day 1, Day 5 and Day 9 Pre-Dose

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

If baseline data of ECG or Vital Signs is missing, substitute missing data with the Day -1 or the last non-missing baseline value, whichever date/time is closer to the reference date/time.

For any other assessment, if baseline data is missing no derivation will be performed and baseline will be set to missing, unless otherwise stated.

5.2. Other Considerations for Data Analyses and Data Handling Conventions

Other considerations for data analyses and data handling conventions are outlined in the appendices:

Section	Component
10.1	Appendix 1: Schedule of Activities
10.2	Appendix 2: Study Phases and Treatment Emergent Adverse Events
10.3	Appendix 3: Data Display Standards & Handling Conventions
10.4	Appendix 4: Derived and Transformed Data
10.5	Appendix 5: Reporting Standards for Missing Data
10.6	Appendix 6: Values of Potential Clinical Importance
10.7	Appendix 7: Division of Microbiology and Infectious Disease
10.8	Appendix 8: Multiple Comparisons and Multiplicity
10.9	Appendix 9: Abbreviations & Trade Marks
10.10	Appendix 10: List of Data Displays

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Study Population Analyses

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

Study population analyses including analyses of subjects enrolled by Country and Site ID, subject's disposition, screening failures, protocol deviations, demographic and baseline characteristics, prior and concomitant medications, and exposure and treatment compliance will be based on GSK Core Data Standards. Details of the planned displays are presented in Appendix 10: List of Data Displays.

7. PHARMACOKINETIC ANALYSES

7.1. Primary Pharmacokinetic Analyses

7.1.1. Endpoint / Variables

7.1.1.1. Drug Concentration Measures

Refer to Appendix 3: Data Display Standards & Handling Conventions (Section 10.3.3 Reporting Standards for Pharmacokinetic). Only total gepotidacin plasma PK concentrations will be measured and reported in the bioanalytical data. Therefore, unbound plasma PK concentrations will be derived by multiplying the total plasma PK concentrations by 0.67, to correct for the low plasma protein binding of gepotidacin (33%) observed in previous studies.

7.1.1.2. Derived Pharmacokinetic Parameters

Pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using the currently supported version of WinNonlin (8.0 or higher). All calculations of non-compartmental parameters will be based on actual sampling times. Pharmacokinetic parameters listed will be determined from the plasma concentration-time data, as data permit.

Parameter	Parameter Description
AUC(0-t)	Area under the plasma concentration-time curve from time 0 (predose) to the last quantifiable concentration, to 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 from time 0 (predose) extrapolated to infinite time, to be calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid. (Calculated for single dose administration)
AUC(0-24)	Area under the plasma concentration-time curve from time 0 (predose) to the concentration at 24 hours postdose (post first dose for periods where 2 doses are administered), to be calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid.
AUC(0-48)	Area under the plasma concentration-time curve from time 0 (predose) to the concentration at 48 hours postdose (post first dose for periods where 2 doses are administered), to be calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid.
AUC(0-τ)	Area under the concentration-time curve from time 0 (predose) to time tau (tau = 12 and 6 for Part 1, Periods 2 and 3, respectively; for Part 2, tau will be between 6 and 12) (Calculated for periods where 2 doses are administered)
Cmax	Maximum observed concentration, determined directly from the concentration-time data.
Ro AUC	Accumulation ratio calculated as AUC(0-τ) after the second dose, where 0 is the timepoint prior to second dose, divided by AUC(0-τ) after the first dose, where 0 is the predose timepoint prior to the first dose. (Calculated for periods where 2 doses are administered)
Ro Cmax	Accumulation ratio calculated as Cmax after the second dose divided by Cmax after the first dose. (Calculated for periods where 2 doses are administered)

NOTES:

- Additional parameters may be included as required.

7.1.2. Summary Measure

Part 1

Pharmacokinetic parameters AUC(0- t), AUC(0-∞) (Period 1), AUC(0-24), AUC(0-48), AUC(0-τ) (Part 1 Periods 2 and 3), Cmax, RO AUC (Part 1 Period 2 and 3), and RO Cmax (Part 1 Period 2 and 3) following a single 1500 mg dose of gepotidacin (Part 1 Period 1) and two 3000 mg doses of gepotidacin (Part 1 Periods 2 and 3) in healthy adult participants will be summarized by treatment. Gepotidacin PK parameter estimates will be listed by participant and treatment.

Part 2

Pharmacokinetic parameters AUC(0- t), AUC(0-∞) (Part 2 Period 1), AUC(0-24), AUC(0-48), AUC(0-τ) (Part 2 Period 2), Cmax, RO AUC (Part 2 Period 2), and RO Cmax (Part 2 Period 2) following a single 1500 mg dose of gepotidacin (Part 2 Period 1) and two 3000 mg doses of gepotidacin at a time interval determined based on data from Part 1 (Part 2 Period 2) in healthy adolescent participants will be summarized by treatment. Gepotidacin PK parameter estimates will be listed by participant and treatment.

7.1.3. Population of Interest

The primary PK analyses will be based on the PK population for plasma PK concentrations and the PK parameter population for plasma PK parameters.

7.1.4. Statistical Analyses / Methods

Details of the planned displays are provided in Section 10: List of Data Displays and will be based on GSK Data Standards and statistical principles.

Unless otherwise specified, endpoints/ variables defined in Section 7.1.1 will be summarized using descriptive statistics, graphically presented (where appropriate) and listed.

Primary plasma PK parameters AUC(0- t), AUC(0-∞) (Period 1), AUC(0-24), AUC(0-48), AUC(0-τ) (Periods 2 and 3), Cmax, RO AUC (Periods 2 and 3), and RO Cmax (Periods 2 and 3) will be estimated for gepotidacin. For each of these parameters the following summary statistics will be calculated by Study Part and treatment: median, maximum, minimum, arithmetic mean, SD, 95% confidence interval (CI) for the arithmetic mean, geometric mean, CV on geometric mean, 95% CI for the geometric mean, and SD of logarithmically transformed data.

7.1.4.1. Statistical Methodology Specification

There are no planned statistical PK analyses additional to summary statistics.

7.2. Secondary Pharmacokinetic Analyses

7.2.1. Endpoint / Variables

7.2.1.1. Derived Pharmacokinetic Parameters

Pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using the currently supported version of WinNonlin (8.0 or higher) or using the currently supported version of SAS (9.4 or higher). All calculations of non-compartmental parameters will be based on actual sampling times.

Plasma/urine pharmacokinetic parameters listed below will be determined from the plasma/urine concentration-time data, as data permit.

Parameter	Parameter Description
Ae total	Total unchanged drug (total amount of drug excreted in urine), calculated by adding all the fractions of drug collected over all the allotted time intervals
Ae(t1-t2)	Amount of drug excreted in urine in time intervals of predose, 0 to 2 hours, 2 to 4 hours, 4 to 6 hours, 6 to 8 hours, 8 to 12 hours, 12 to 24 hours, 24 to 36 hours, 36 to 48 hours, and 48 to 60 hours (Part 1, Period 2 and Period 3) after dosing
AUC(0-τ)	Area under the concentration-time curve from time 0 (predose) to time tau (tau = 12 and 6 for Part 1, Periods 2 and 3, respectively; for Part 2, tau will be between 6 and 12) (urine)
AUC(0-24)	Area under the concentration-time curve from time 0 (predose) to 24 hours postdose administration following the first dose (urine)
AUC(0-48)	Area under the concentration-time curve from time 0 (predose) to 48 hours postdose administration following the first dose (urine)
fe%	Percentage of the given dose of drug excreted in urine, calculated as: fe% = (Ae total/Dose) × 100%
CLr	Renal clearance of drug, calculated as: Ae total/AUC(0-t)
Tmax	Time to reach maximum observed plasma concentration
tlag	Lag time before observation of drug concentrations in plasma
t1/2	Apparent terminal phase half-life (plasma)

NOTES:

- Additional parameters may be included as required.

7.2.2. Summary Measure

Part 1

Urine PK parameters Ae total, Ae(t1-t2), AUC(0-τ) (Periods 2 and 3), AUC(0-24), AUC(0-48), fe%, and CLr, and plasma PK parameters Tmax, Tlag, and t1/2 following a single 1500 mg dose of gepotidacin (Part 1 Period 1) and two 3000 mg doses of gepotidacin (Part 1 Periods 2 and 3) in healthy adult participants will be summarized by treatment. Gepotidacin PK parameter estimates will be listed by participant and treatment.

Part 2

Urine PK parameters Ae total, Ae(t1-t2), AUC(0-τ) (Period 2), AUC(0-24), AUC(0-48), fe%, and CLr and plasma PK parameters Tmax, Tlag, and t1/2 following a single 1500 mg dose of gepotidacin (Part 2 Period 1) and two 3000 mg doses of gepotidacin at a time interval to be determined from Part 1 (Part 2 Period 2) in healthy adolescent participants will be summarized by treatment. Gepotidacin PK parameter estimates will be listed by participant and treatment.

7.2.3. Population of Interest

The secondary PK analyses will be based on the PK population for urine/plasma PK concentrations, and the PK parameter population for urine/plasma PK parameters.

7.2.4. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 10: List of Data Displays and will be based on GSK Data Standards and statistical principles.

Unless otherwise specified, endpoints/variables defined in Section 7.2 will be summarized using descriptive statistics, graphically presented (where appropriate) and listed.

Secondary urine PK parameters Ae total, Ae(t1-t2), AUC(0-τ), AUC(0-24), AUC(0-48), fe%, and CLr, and plasma PK parameters Tmax, Tlag, and t1/2 will be estimated for gepotidacin. For each of these parameters the following summary statistics will be calculated by Study Part and treatment: median, maximum, minimum, arithmetic mean, SD, 95% CI for the arithmetic mean, geometric mean, CV on geometric mean, 95% CI for the geometric mean, and SD of logarithmically transformed data.

7.2.4.1. Statistical Methodology Specification

There are no planned statistical PK analyses additional to summary statistics.

8. SAFETY ANALYSES

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

8.1. Adverse Events Analyses

The severity of AEs and SAEs will be determined by the investigator according to the US National Institute of Allergy and Infectious Diseases Division of Microbiology and Infectious Diseases (DMID) criteria for adult toxicity assessment, with the exception of serum creatinine adolescent laboratory data, which will be assessed using pediatric toxicity criteria. All reported AEs will be coded using MedDRA and summarized by system organ class (SOC) and preferred term (PT).

Adverse event severity is classified as mild (grade = 1), moderate (grade = 2), severe (grade = 3), potentially life threatening (grade = 4) or resulting in death (grade = 5). Adverse events starting after the first dose of study treatment with a missing severity will be classified as severe. If a participant reports an AE more than once within an SOC/PT, the AE with the worst-case severity will be used in the corresponding severity summaries.

Relationship to study treatment, as indicated by the investigator, is classified as “not related” or “related”. Adverse events with a missing relationship to study treatment will be regarded as “related” to study treatment. If a participant reports the same AE more than once within an SOC/PT, the AE with the worst-case relationship to study treatment will be used in the corresponding relationship summaries.

Adverse events analyses including the analysis of AEs, SAEs and other significant AEs will be based on GSK Core Data Standards. All AEs, study drug related AEs, SAEs, and AEs leading to discontinuation of study treatment or withdrawal from study will be provided in separate listings. The relationship between SOC and PT will be listed. Summary tables will be provided by SOC, PT, and maximum grade.

In summary tables where AEs are presented by SOC, PT, and maximum grade, SOCs will be sorted in descending order of the total incidence then alphabetically, PTs will be sorted in descending order of the total incidence then alphabetically within the SOC.

For completely missing or partial missing AE start date or end date, imputation rules will be applied following Section 10.4.1.

In addition, a summary of the number and percentage of participants with common AEs, defined as AEs with ≥5% incidence in any treatment group, will be presented in descending order of total incidence by PT. The details of the planned displays are provided in Appendix 10: List of Data Displays.

8.2. Adverse Events of Special Interest Analyses

Cardiovascular, Gastrointestinal Adverse Events and events related to Acetylcholinesterase inhibition as determined by algorithm will be considered AEs of Special Interest (AESIs). AESIs except those for Acetylcholinesterase inhibition, are flagged in the eCRF and details of events are collected on special eCRF pages. Acetylcholinesterase-Inhibition AESIs will be programmatically matched with the list of AEs specified in Section 8.2.1. In addition, there will be a manual review of AE listings to ensure accuracy and completeness of AESI reporting.

8.2.1. Acetylcholinesterase-Inhibition AESIs

Any reported AE listed in the table below with a start time no later than 12 hours after the last dose administered in each treatment period, as evaluated by the investigator as per the DMID grading criteria provided in protocol Section 10.8 Appendix 8: Division of Microbiology and Infectious Disease Adult Toxicity Tables for Adverse Event Assessment, will be programmatically identified as Acetylcholinesterase inhibition related AESI.

Table 1 List of AEs for programming to be considered due to Acetylcholinesterase-Inhibition

• Respiratory
  ○ Bronchospasm (acute)
  ○ Dyspnea
  ○ Bronchorrhea

• Gastrointestinal
  ○ Nausea
  ○ Vomiting
  ○ Diarrhea
  ○ GI cramping and pain

• Cardiovascular   ○ Bradycardia

• Neurological
  ○ Seizure/Convulsions
  ○ Vasovagal syncope
  ○ Salivation
  ○ Lacrimation
  ○ Diaphoresis/sweating

AESIs will be listed and tabulated, and a Cumulative Grade will be determined, calculated by the sum of the grade of each reported AE. This enables both the number of AEs and the severity of each AE to be taken into account. For instance, if two AEs in the table above are reported, one of Grade 1 and the other of Grade 3 according to DMID, the total grade of 4 would result in a Cumulative Grade 2 per Table 2 below.

Table 2 Cumulative Grading of Acetylcholinesterase AESI

	Cumulative Grade 1	Cumulative Grade 2	Cumulative Grade 3	Cumulative Grade 4
Total Grade of Signs & Symptoms	1 to 3	4 to 6	7 to 10	≥ 11

The details of the planned displays are provided in Appendix 10: List of Data Displays.

8.3. Clinical Laboratory Analyses

Laboratory evaluations including the analyses of chemistry laboratory tests, hematology laboratory tests, urinalysis, and liver function tests will be based on GSK Core Data Standards. Division of Microbiology and Infectious Diseases (DMID) grading for all parameters as specified in the protocol will be assigned programmatically by PPD in the Laboratory Analysis Dataset. The details of the planned displays are in Appendix 10: List of Data Displays.

8.4. Other Safety Analyses

The analyses of non-laboratory safety test results including ECGs and vital signs will be based on GSK Core Data Standards, unless otherwise specified. The details of the planned displays are presented in Appendix 10: List of Data Displays.

9. REFERENCES

GlaxoSmithKline Document Numbers 2019N401436_00 (Original – 04-JUN-2019): A Phase I, Double-Blind, Two-Part, Sequential Study to Evaluate the Pharmacokinetics of Gepotidacin Tablets in Healthy Adult and Adolescent Participants (04-JUN-2019).

10. APPENDICES

10.1. Appendix 1: Schedule of Activities

10.1.1. Protocol Defined Time and Events Table

Table 3 Part 1 Adult Participants

Procedure[1]	Check -in	Treatment Period 1 (Days)				Treatment Period 2 (Days)				Treatment Period 3 (Days)			Follow-up (7 [±3] days after last dose) or Early Termination	Notes
	–1	1	2	3	4	5	6	7	8	9	10	11		
Confined to clinic	X	X	X	X	X	X	X	X	X	X	X	X		
Inclusion and exclusion criteria	X													Recheck clinical status before study intervention
Brief physical examination[2]	X											X	X	
Pregnancy test	X												X	Urine pregnancy test (if WOCBP), as appropriate (see Table 10 in Protocol)
Drug, alcohol, and cotinine screen	X													See Table 10 in Protocol

Procedure[1]	Check -in	Treatment Period 1 (Days)				Treatment Period 2 (Days)				Treatment Period 3 (Days)			Follow-up (7 [±3] days after last dose) or Early Termination	Notes
	–1	1	2	3	4	5	6	7	8	9	10	11		
Laboratory assessments	X				X				X			X	X	Including serum chemistry, hematology, and urinalysis (see Appendix 2 in Protocol)
12-lead ECG[3]	X	X	X	X		X	X	X		X	X	X	X	See Table 4, Table 5, and Table 6 for timing of assessments
ECG Holter monitoring[4]	X	X	X		X	X	X		X	X	X			See Table 4, Table 5, and Table 6 for timing of assessments
Vital signs	X	X	X	X		X	X	X		X	X	X	X	See Table 4, Table 5, and Table 6 for timing of assessments
Study intervention		X				X				X				See Table 4, Table 5, and Table 6 for time points

Procedure[1]	Check -in	Treatment Period 1 (Days)				Treatment Period 2 (Days)				Treatment Period 3 (Days)			Follow-up (7 [±3] days after last dose) or Early Termination	Notes
	–1	1	2	3	4	5	6	7	8	9	10	11		
Blood collection for pharmacokinetics		X	X	X		X	X	X		X	X	X		See Table 4, Table 5, and Table 6 for time points
Urine collection for pharmacokinetics		X	X	X		X	X	X		X	X	X		See Table 4, Table 5, and Table 6 for time points
AE/SAE review	X	←==========→											X	
Concomitant medication review	X	←==========→											X	

AE = adverse event, ECG = electrocardiogram, SAE = serious AE; WOCBP = woman of childbearing potential.

1 When coinciding with safety and/or pharmacokinetic assessments, ECGs, vital signs, and pharmacokinetic blood collections should be performed in said order.

2 A brief physical examination will include, at a minimum, assessments of the skin, lungs, cardiovascular system, and abdomen (liver and spleen).

3 Triplicate 12-lead ECGs will be measured on Day -1.

4 ECG Holter monitoring will begin approximately 12 hours prior to first dose until 24 hours after dosing of each treatment period.

Table 3: Part 2 Adolescent Participants

Procedure[1]	Check-in	Treatment Period 1 (Days)			Check-in[2]	Treatment Period 2 (Days)			Follow-up (7 [±3] days after last dose) or Early Termination	Notes
	–1	1	2	3	–1	1	2	3		
Confined to clinic	X	X	X	X	X	X	X	X		Treatment Period 1 and Treatment Period 2 may be separated by 7 days but no more than 10 days.
Inclusion and exclusion criteria	X				X					Recheck clinical status before study intervention
Brief physical examination[3]	X				X			X	X	
Pregnancy test	X				X				X	Urine pregnancy test (if WOCBP), as appropriate (see Table 10 in Protocol)
Drug, alcohol, and cotinine screen	X				X					See Table 10 in Protocol
Laboratory assessments	X			X	X			X	X	Including serum chemistry, hematology, and urinalysis (see Appendix 2 in Protocol)
12-lead ECG[4]	X	X	X	X	X	X	X	X	X	See Table 7, Table 8, and Table 9 for timing of assessments
ECG Holter monitoring[5]	X	X	X		X	X	X			See Table 7, Table 8, and Table 9 for timing of assessments
Vital signs	X	X	X	X	X	X	X	X	X	See Table 7, Table 8, and Table 9 for timing of assessments
Study intervention		X				X				See Table 7, Table 8, and Table 9 for time points

Procedure[1]	Check-in	Treatment Period 1 (Days)			Check-in[2]	Treatment Period 2 (Days)			Follow-up (7 [±3] days after last dose) or Early Termination	Notes
	–1	1	2	3	–1	1	2	3		
Blood collection for pharmacokinetics		X	X	X		X	X	X		See Table 7, Table 8, and Table 9 for time points
Urine collection for pharmacokinetics		X	X	X		X	X	X		See Table 7, Table 8, and Table 9 for time points
AE/SAE review	X	←==========						==========→	X	
Concomitant medication review	X	←==========						==========→	X	

AE = adverse event, ECG = electrocardiogram, SAE = serious AE; WOCBP = woman of childbearing potential.

1 When coinciding with safety and/or pharmacokinetic assessments, ECGs, vital signs, and pharmacokinetic blood collections should be performed in said order.

2 Check-in procedures only necessary if participant leaves the clinic between Treatment Period 1 and Treatment Period 2.

3 A brief physical examination will include, at a minimum, assessments of the skin, lungs, cardiovascular system, and abdomen (liver and spleen).

4 Triplicate 12-lead ECGs will be measured on Day -1 (before each treatment period).

5 ECG Holter monitoring will begin approximately 12 hours prior to first dose until 24 hours after dosing of each treatment period.

10.1.2. Protocol Defined Safety and PK Assessments

Table 4 Safety and PK Assessments - Part 1, Period 1

Procedure[1]		Treatment Period 1 Time point (hours)													
	Predose	0	0.5	1	1.5	2	2.5	3	4	6	8	12	24	36	48
12-lead ECG[2]	X		X	X	X	X	X	X	X	X	X	X	X	X	X
ECG Holter monitoring	X	X													
Vital signs	X				X	X			X		X	X	X	X	X
Study intervention		X													
Blood PK sample	X		X	X	X	X	X	X	X	X	X	X	X	X	X
Urine PK collection[3]	X	X				X			X	X	X	X	X	X	X

ECG = electrocardiogram; PK = pharmacokinetic.

1 When coinciding with safety and/or PK assessments, ECGs, vital signs, and PK blood collections should be performed in said order.

2 Triplicate 12-lead ECGs will be measured at predose. Single 12-lead ECGs will be measured at all other time points.

3 Urine collection intervals include 0 (predose), 0 to 2 hours, 2 to 4 hours, 4 to 6 hours, 6 to 8 hours, 8 to 12 hours, 12 to 24 hours, 24 to 36 hours, and 36 to 48 hours.

Table 5 Safety and PK Assessments - Part 1, Period 2 (12-Hour Dose Interval)

Procedure[1]	Treatment Period 2 Time point (hours)																								
	Predose	0	0.5	1	1.5	2	2.5	3	4	6	8	12	12.5	13	13.5	14	14.5	15	16	18	20	24	36	48	60
12-lead ECG[2]	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
ECG Holter monitoring	X	X																							
Vital signs	X				X	X			X		X	X			X	X				X		X	X	X	X
Study intervention		X										X													
Blood PK sample	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Urine PK collection[3]	X	X				X			X	X	X	X				X			X	X	X	X	X	X	X

ECG = electrocardiogram; PK = pharmacokinetic.

1 When coinciding with safety and/or PK assessments, ECGs, vital signs, and PK blood collections should be performed in said order.

2 Triplicate 12-lead ECGs will be measured at predose. Single 12-lead ECGs will be measured at all other time points.

3 Urine collection intervals include 0 (predose), 0 to 2 hours, 2 to 4 hours, 4 to 6 hours, 6 to 8 hours, 8 to 12 hours, 12 to 14 hours, 14 to 16 hours, 16 to 18 hours, 18 to 20 hours, 20 to 24 hours, 24 to 36 hours, 36 to 48 hours, and 48 to 60 hours.

Table 6 Safety and PK Assessments - Part 1, Period 3 (6-Hour Dose Interval)

Procedure[1]	Treatment Period 3 Time point (hours)																							
	Predose	0	0.5	1	1.5	2	2.5	3	4	6	6.5	7	7.5	8	8.5	9	10	12	14	18	24	36	48	60
12-lead ECG[2]	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
ECG Holter monitoring	X	X																						
Vital signs	X				X	X			X				X	X			X		X	X	X	X	X	X
Study intervention		X								X														
Blood PK sample	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Urine PK collection[3]	X	X				X			X	X				X			X	X	X	X	X	X	X	X

ECG = electrocardiogram; PK = pharmacokinetic.

1 When coinciding with safety and/or PK assessments, ECGs, vital signs, and PK blood collections should be performed in said order.

2 Triplicate 12-lead ECGs will be measured at predose. Single 12-lead ECGs will be measured at all other time points.

3 Urine collection intervals include 0 (predose), 0 to 2 hours, 2 to 4 hours, 4 to 6 hours, 6 to 8 hours, 8 to 10 hours, 10 to 12 hours, 12 to 14 hours, 14 to 18 hours, 18 to 24 hours, 24 to 36 hours, 36 to 48 hours, and 48 to 60 hours.

Table 7 Safety and PK Assessments - Part 2, Period 1

Procedure[1]		Treatment Period 1 Time point (hours)													
	Predose	0	0.5	1	1.5	2	2.5	3	4	6	8	12	24	36	48
12-lead ECG[2]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
ECG Holter monitoring	X	X													
Vital signs	X				X	X			X		X	X	X	X	X
Study intervention		X													
Blood PK sample	X		X	X	X	X	X	X	X	X	X	X	X	X	X
Urine PK collection[3]	X	X				X			X	X	X	X	X	X	X

ECG = electrocardiogram; PK = pharmacokinetic.

1 When coinciding with safety and/or PK assessments, ECGs, vital signs, and PK blood collections should be performed in said order.

2 Triplicate 12-lead ECGs will be measured at predose. Single 12-lead ECGs will be measured at all other time points.

3 Urine collection intervals include 0 (predose), 0 to 2 hours, 2 to 4 hours, 4 to 6 hours, 6 to 8 hours, 8 to 12 hours, 12 to 24 hours, 24 to 36 hours, and 36 to 48 hours.

Note: The number of PK samples and the PK sampling time points may be modified based on the adult PK data from Part 1.

Table 8 Safety and PK Assessments - Part 2, Period 2 (if 6-hour dose interval is selected)

Procedure[1]	Treatment Period 2 Time point (hours)																							
	Predose	0	0.5	1	1.5	2	2.5	3	4	6	6.5	7	7.5	8	8.5	9	10	12	14	18	24	36	48	60
12-lead ECG[2]	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
ECG Holter monitoring	X	X																						
Vital signs	X				X	X			X				X	X			X		X	X	X	X	X	X
Study intervention		X								X														
Blood PK sample	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Urine PK collection[3]	X	X				X			X	X				X			X	X	X	X	X	X	X	X

ECG = electrocardiogram; PK = pharmacokinetic.

1 When coinciding with safety and/or PK assessments, ECGs, vital signs, and PK blood collections should be performed in said order.

2 Triplicate 12-lead ECGs will be measured at predose. Single 12-lead ECGs will be measured at all other time points.

3 Urine collection intervals include 0 (predose), 0 to 2 hours, 2 to 4 hours, 4 to 6 hours, 6 to 8 hours, 8 to 10 hours, 10 to 12 hours, 12 to 14 hours, 14 to 18 hours, 18 to 24 hours, 24 to 36 hours, 36 to 48 hours, and 48 to 60 hours.

Note: The number of PK samples and the PK sampling time points may be modified based on the adult PK data from Part 1.

Table 9 Safety and PK Assessments - Part 2, Period 2 (if 12-hour dose interval is selected))

Procedure[1]	Treatment Period 2 Time point (hours)																								
	Predose	0	0.5	1	1.5	2	2.5	3	4	6	8	12	12.5	13	13.5	14	14.5	15	16	18	20	24	36	48	60
12-lead ECG[2]			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
ECG Holter monitoring	X	X																							
Vital signs					X	X			X		X	X			X	X				X		X	X	X	X
Study intervention		X										X													
Blood PK sample	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Urine PK collection[3]	X	X				X			X	X	X	X				X			X	X	X	X	X	X	X

ECG = electrocardiogram; PK = pharmacokinetic.

1 When coinciding with safety and/or PK assessments, ECGs, vital signs, and PK blood collections should be performed in said order.

2 Triplicate 12-lead ECGs will be measured at predose. Single 12-lead ECGs will be measured at all other time points.

3 Urine collection intervals include 0 (predose), 0 to 2 hours, 2 to 4 hours, 4 to 6 hours, 6 to 8 hours, 8 to 12 hours, 12 to 14 hours, 14 to 16 hours, 16 to 18 hours, 18 to 20 hours, 20 to 24 hours, 24 to 36 hours, 36 to 48 hours, and 48 to 60 hours.

Note: The number of PK samples and the PK sampling time points may be modified based on the adult PK data from Part 1.

10.2. Appendix 2: Study Phases and Treatment Emergent Adverse Events

10.2.1. Treatment States

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

10.2.1.1. Treatment States for Safety Data

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

NOTES:

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

10.2.1.2. Treatment States for AE Data

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

NOTES:

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

10.2.1.3. Study Phases for Concomitant Medication

Study Phase	Definition
Prior	If medication end date is not missing and is before enrollment date
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.

10.2.2. Treatment Emergent Flag for Adverse Events

Flag	Definition
Treatment Emergent	• If AE onset date/time is on or after treatment date/time & on or before the treatment stop date/time with 2 days lag time. • Study Treatment Date/Time ≤ AE Start Date/Time ≤ Study Treatment Date/Time + 2 days.

10.3. Appendix 3: Data Display Standards & Handling Conventions

10.3.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions				
Study Part	**Treatment Group**		**Data Displays for Reporting**	
	Code	**Description**	**Description**	**Order** [1]
1,2	A	Gepotidacin single dose 1500 mg (Period 1)	Single Dose 1500 mg	2
1,2	B	Matching placebo (Period 1)	Placebo	1
1	C	Gepotidacin two 3000 mg doses given at Hour 0 and Hour 12 (Period 2)	Two 3000 mg Doses 12 h Interval	3
1	D	Two matching placebo doses given at Hour 0 and Hour 12 (Period 2)	Placebo	1
1	E	Gepotidacin Two 3000 mg dose given at Hour 0 and Hour 6 (Period 3)	Two 3000 mg Dose 6 h Interval	4
1	F	Two matching placebo doses given at Hour 0 and Hour 6 (Period 3)	Placebo	1
2	G	Gepotidacin two 3000 mg doses (Period 2; exact dosing interval to be determined after Part 1 is complete)	Two 3000 mg doses 12 h Interval or 6 h Interval [2]	3
2	H	Two matching placebo doses (Period 2; exact dosing interval to be determined after Part 1 is complete)	Placebo	1

NOTES:

1. Order represents treatments being presented in TFL, as appropriate.
2. In Part 2, exact dosing interval to be determined after Part 1 is complete.

10.3.2. 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 CDISC standards (SDTM IG Version 3.2 & ADaM IG Version 1.1]. • For creation of ADaM datasets (ADCM/ADC1/ADAE), the same version of dictionary datasets will be implemented for conversion from SI to SDTM.
Generation of RTF Files
• RTF files will be generated for all reporting efforts described in the RAP.

Reporting Standards	
General	
• The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated: o 4.03 to 4.23: General Principles o 5.01 to 5.08: Principles Related to Data Listings o 6.01 to 6.11: Principles Related to Summary Tables o 7.01 to 7.13: Principles Related to Graphics	
Formats	
• All data will be reported according to the actual treatment the subject received unless otherwise stated. • GSK IDSL Statistical Principles (5.03 & 6.06.3) for decimal places (DP's) will be adopted for reporting of data based on the raw data collected. • Numeric data will be reported at the precision collected on the eCRF. • The reported precision from non eCRF sources will follow the IDSL statistical principles but may be adjusted to a clinically interpretable number of DP's.	
Planned and Actual Time	
• Reporting for tables, figures and formal statistical analyses : o Planned time relative to dosing will be used in figures (with the exception of individual PK concentration-time figures, where actual relative time will be used), summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated. o 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: o Planned and actual time relative to study drug dosing will be shown in listings (Refer to IDSL Statistical Principle 5.05.1). o Unscheduled or unplanned readings will be presented within the subject's listings. o Visits outside the protocol defined time-windows (i.e. recorded as protocol deviations) will be included in listings but omitted from figures (mean figures only for PK concentrations), summaries and statistical analyses.	
Unscheduled Visits	
• Unscheduled visits will be considered when calculating baseline and in Table 2.9 and Table 2.10, but will not be included in any other summary tables. • Unscheduled visits will not be included in figures. • All unscheduled visits will be included in listings.	
Descriptive Summary Statistics	
Continuous Data	Refer to IDSL Statistical Principle 6.06.1
Categorical Data	N, n, frequency, %
Graphical Displays	
• Refer to IDSL Statistical Principals 7.01 to 7.13.	

10.3.3. Reporting Standards for Pharmacokinetics

Pharmacokinetic Concentration Data	
PC Windows Non-Linear (WNL) File	PC WNL file (xpt format) for the non-compartmental analysis will be created according to SOP 314000(2.0). Note: Concentration values will be imputed as per GUI_51487

Descriptive Summary Statistics, Graphical Displays and Listings	Refer to IDSL PK Display Standards.
	Refer to IDSL Statistical Principle 6.06.1.
	For continuous data:
	• NQs at the beginning of a participant profile (i.e. before the first incidence of a measurable concentration) are deemed to be zero as it is assumed that in this circumstance no drug is yet measurable in the blood.
	• For NQs at the end of the participant profile (i.e. after the last incidence of a measurable concentration);
	  • for individual plots and pharmacokinetic analyses these are dropped (set to missing) as they do not provide any useful information (and can erroneously indicate that absolutely no drug is present)
	  • for summary statistics, these are set to 0 (to avoid skewing of the summary statistics)
	• Individual NQs which fall between two measurable concentrations are set to missing (individual values of this nature are assumed to be an anomaly)
	If two or more NQ values occur in succession between measurable concentrations, the profile will be deemed to have terminated at the last measurable concentration prior to these NQs. For the purpose of individual participant plots, these NQs will be set to 0, and the subsequent measurable concentrations will be retained. For the derivation of pharmacokinetic parameters, these NQs and any subsequent measurable concentrations will be omitted (set to missing).
	Note: Concentration values will be imputed as per GUI_51487 for descriptive summary statistics/analysis and summarized graphical displays only.

Pharmacokinetic Parameter Data	
PK Parameter to be Derived by Programmer	The following plasma PK parameters will be derived by the Programmer: Ro Cmax, Ro AUC The following urine PK parameters will be derived by the Programmer: Ae total, Ae(t1-t2), Fe%, CLr
Descriptive Summary Statistics, Graphical Displays and Listings	N, n, arithmetic mean, 95% CI of arithmetic mean, geometric mean, 95% CI of geometric mean, SD, SD of logged data, CV (%), and between-subject geometric coefficient of variation (CVb (%)) will be reported. CV_b (%) = $\sqrt{}$ (exp(SD^2) - 1) * 100 (SD = SD of Ln-Transformed data)
Parameters Not Being Ln-Transformed	λz, λz lower, λz upper, and λz no. of points.
Parameters Not Being Summarized	λz, λz lower, λz upper, and λz no. of points.
Listings	Include the first point, last point and number of points used in the determination of λz for listings.

10.4. Appendix 4: Derived and Transformed Data

10.4.1. General

Multiple Measurements at One Analysis Time Point
• Mean of the measurements will be calculated and used in any derivation of summary statistics but if listed, all data will be presented. • 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.
Study Day

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

Period Day

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

10.4.2. Study Population

Demographics
Age
• GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as follows: ○ Only the year of birth will be collected. The date and month will be imputed as '30th June'. • Birth date will be presented in listings as 'YYYY'.
Body Mass Index (BMI)
• Calculated as **Weight (kg) / [Height (m)^2]**

10.4.3. Safety

Adverse Events
AE'S of Special Interest
• Cardiovascular (CV) events • Gastrointestinal events • Acetylcholinesterase inhibition events
Adverse Events with Missing Relationship or Missing Serious Indicator
• If the relationship to study treatment is missing for a treatment-emergent AE, it'll be considered as related to the study treatment. • If the serious indicator "Was event serious?" is missing, the AE will be considered as SAE. • Adverse events with missing relationship or missing serious indicator will be presented as it is in listings but will be treated as related AEs or SAEs in summary tables.

Laboratory Parameters

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

ECG Parameters

RR Interval

- IF RR interval (millisecond [msec]) is not provided directly, then RR can be derived as:

  [1] If QTcB is machine read & QTcF is not provided, then:

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

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

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

- If ECGs are manually read, the RR value preceding the measurement QT interval should be a collected value THEN do not derive.
- Machine read values of RR should not be replaced with derived values.

Corrected QT Intervals

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

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

10.5. Appendix 5: Reporting Standards for Missing Data

10.5.1. Premature Withdrawals

Element	Reporting Detail
General	• Participant study completion (i.e. as specified in the protocol) was defined as completing all phases of the study including the follow-up visit. • Withdrawn participants may be replaced in the study. • All available data from participants 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. • Early termination visits will be summarized as early termination visits.

10.5.2. Handling of Missing Data

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

10.5.2.1. Handling of Missing and Partial Dates

Element	Reporting Detail
General	• Partial dates will be displayed as captured in subject listing displays.
Adverse Events	• The eCRF allows for the possibility of partial dates (i.e., only month and year) to be recorded for AE start and end dates; that is, the day of the month may be missing. In such a case, the following conventions will be applied for calculating the time to onset and the duration of the event: ○ Missing Start Day: First of the month will be used unless this is before the date of study treatment; in this case the study treatment date will be used and hence the event is considered Treatment Emergent as per Appendix 2: Study Phases and Treatment Emergent Adverse Events. ○ Missing Stop Day: Last day of the month will be used, unless this is more than 2 days after the date of study treatment; in this case the study treatment date will be used. • Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing.
Concomitant Medications/ Medical History	• Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention: ○ If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month ○ If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month. • The recorded partial date will be displayed in listings.

10.6. Appendix 6: Values of Potential Clinical Importance

10.6.1. ECG

ECG Parameter	Units	Potential Clinically Important Range	
		Lower	Upper
Absolute			
Absolute QTc Interval[3]	msec	> 450[1]	
		> 450[2]	≤ 480[2]
		> 480[2]	≤ 500[2]
		> 500[2]	
Absolute PR Interval	msec	< 110[1]	> 220[1]
Absolute QRS Interval	msec	< 75[1]	> 110[1]
Change from Baseline			
Increase from Baseline QTc[3]	msec	≤ 30[2]	
	msec	> 30[2]	≤ 60[2]
	msec	> 60[1]	

NOTES:

1. Represent standard ECG values of PCI for HV studies.
2. Represent further subdivisions of ECG values for analysis.
3. Qualifying QTc events, regardless whether QTcB or QTcF, will be captured.

10.6.2. Vital Signs

Vital Sign Parameter (Absolute)	Units	Potential Clinically Important Range	
		Lower	Upper
Systolic Blood Pressure	millimeters of mercury (mmHg)	< 85	> 160
Diastolic Blood Pressure	mmHg	< 45	> 100
Heart Rate	bpm	< 40	> 110

10.7. Appendix 7: Division of Microbiology and Infectious Diseases Adult Toxicity Tables for Adverse Events Assessments (2007)

10.7.1. Laboratory Values

Parameter values are converted to use SI units.

HEMATOLOGY				
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**
Hemoglobin	9.5 to 10.5 gm/dL	8.0 to 9.4 gm/dL	6.5 to 7.9 gm/dL	<6.5 gm/dL
Absolute Neutrophil Count	1000 to 1500 /mm^3	750 to 999 /mm^3	500 to 749 /mm^3	<500 /mm^3
Platelets	75,000 to 99,999 /mm^3	50,000 to 74,999 /mm^3	20,000 to 49,999 /mm^3	<20,000 /mm^3
White Blood Cells	11,000 to 13,000 /mm^3	13,000 to 15,000 /mm^3	15,000 to 30,000 /mm^3	>30,000 or <1000 /mm^3
% Polymorphonuclear Leukocytes + Band Cells	>80%	90 to 95%	>95%	N/A
Abnormal Fibrinogen	Low: 100 to 200 mg/dL High: 400 to 600 mg/dL	Low: <100 mg/dL High: >600 mg/dL	Low: <50 mg/dL High: N/A	Fibrinogen associated with gross bleeding or with disseminated coagulation
Fibrin Split Product	20 to 40 mcg/mL	41 to 50 mcg/mL	51 to 60 mcg/dL	>60 mcg/dL
Prothrombin Time (PT)	1.01 to 1.25 × ULN	1.26 to 1.5 × ULN	1.51 to 3.0 × ULN	>3 × ULN
Activated Partial Thromboplastin (APTT)	1.01 to 1.66 × ULN	1.67 to 2.33 × ULN	2.34 to 3 × ULN	>3 × ULN
Methemoglobin	5.0 to 9.9%	10.0 to 14.9%	15.0 to 19.9%	>20%

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

CHEMISTRIES				
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**
Hyponatremia	130 to 135 mEq/L	123 to 129 mEq/L	116 to 122 mEq/L	<116 mEq/L or abnormal sodium *with* mental status changes or seizures
Hypernatremia	146 to 150 mEq/L	151 to 157 mEq/L	158 to 165 mEq/L	>165 mEq/L or abnormal sodium *with* mental status changes or seizures
Hypokalemia	3.0 to 3.4 mEq/L	2.5 to 2.9 mEq/L	2.0 to 2.4 mEq/L or intensive replacement therapy of hospitalization required	<2.0 mEq/L or abnormal potassium *with* paresis, ileus, or life-threatening arrhythmia
Hyperkalemia	5.6 to 6.0 mEq/L	6.1 to 6.5 mEq/L	6.6 to 7.0 mEq/L	>7.0 mEq/L or abnormal potassium *with* life-threatening arrhythmia
Hypoglycemia	55 to 64 mg/dL	40 to 54 mg/dL	30 to 39 mg/dL	<30 mg/dL or abnormal glucose *with* mental status changes or coma

Hyperglycemia (nonfasting and no prior diabetes)	116 to 160 mg/dL	161 to 250 mg/dL	251 to 500 mg/dL	>500 mg/dL or abnormal glucose *with* ketoacidosis or seizures
Hypocalcemia (corrected for albumin)	8.4 to 7.8 mg/dL	7.7 to 7.0 mg/dL	6.9 to 6.1 mg/dL	<6.1 mg/dL or abnormal calcium *with* life-threatening arrhythmia or tetany
Hypercalcemia (corrected for albumin)	10.6 to 11.5 mg/dL	11.6 to 12.5 mg/dL	12.6 to 13.5 mg/dL	>13.5 mg/dL or abnormal calcium *with* life-threatening arrhythmia
Hypomagnesemia	1.4 to 1.2 mEq/L	1.1 to 0.9 mEq/L	0.8 to 0.6 mEq/L	<0.6 mEq/L or abnormal magnesium *with* life-threatening arrhythmia
Hypophosphatemia	2.0 to 2.4 mg/dL	1.5 to 1.9 mg/dL or replacement Rx required	1.0 to 1.4 mg/dL intensive therapy or hospitalization required	<1.0 mg/dL or abnormal phosphate *with* life-threatening arrhythmia
Hyperbilirubinemia (when accompanied by any increase in other liver function test)	1.1 to <1.25 × ULN	1.25 to <1.5 × ULN	1.5 to 1.75 × ULN	>1.75 × ULN
Hyperbilirubinemia (when other liver function tests are in the normal range)	1.1 to <1.5 × ULN	1.5 to <2.0 × ULN	2.0 to 3.0 × ULN	>3.0 × ULN
Blood urea nitrogen	1.25 to 2.5 × ULN	2.6 to 5 × ULN	5.1 to 10 × ULN	>10 × ULN
Hyperuricemia (uric acid)	7.5 to 10.0 mg/dL	10.1 to 12.0 mg/dL	12.1 to 15.0 mg/dL	>15.0 mg/dL
Creatinine	1.1 to 1.5 × ULN	1.6 to 3.0 × ULN	3.1 to 6.0 × ULN	>6 × ULN or dialysis required

Rx=therapy; ULN=upper limit of normal.

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

ULN=upper limit of normal.

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

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

10.8. Appendix 8: Multiple Comparisons & Multiplicity

10.8.1. Handling of Multiple Comparisons & Multiplicity

No adjustments for multiplicity will be made.

10.9. Appendix 9: Abbreviations & Trade Marks

10.9.1. Abbreviations

λz	terminal-phase rate constant
ADaM	Analysis Data Model
AE	adverse event
AESI	adverse event of special interest
Ae total	total unchanged drug
Ae (t1-t2)	amount of drug excreted in urine in a time interval
AUC	area under the concentration-time curve
AUC(0-∞)	area under the concentration-time curve from time 0 (predose) extrapolated to infinite time
AUC(0-24)	area under the concentration-time curve from time 0 (predose) to 24 hours post dose administration following the first dose (plasma or urine)
AUC(0-48)	area under the concentration-time curve from time 0 (predose) to 48 hours post dose administration following the first dose (plasma or urine)
AUC(0-t)	area under the concentration-time curve from time 0 to the time of the last quantifiable concentration ((plasma or urine)
AUC(0-τ)	area under the concentration-time curve from time 0 (predose) to time tau (plasma or urine)
BMI	body mass index
CI	confidence interval
CLr	renal clearance of drug
Cmax	maximum observed concentration
CSR	Clinical Study Report
DMID	Division of Microbiology and Infectious Diseases
ECG	electrocardiogram
eCRF	electronic case report form
fe%	percentage of the given dose of drug excreted in urine
GSK	GlaxoSmithKline
ICF	informed consent form
IDSL	Integrated Data Standards Library
MedDRA	Medical Dictionary for Regulatory Activities
MIC	minimum inhibitory concentration
mg	milligrams
mmHg	millimeters of mercury
msec	millisecond
PK	pharmacokinetic
QTc	corrected QT interval; the measure of time between the start of the Q wave and the end of the T wave
QTcB	corrected QT interval using the Bazett formula
QTcF	corrected QT interval using the Fridericia formula
RAP	Reporting and Analysis Plan
SAE	serious adverse event
SAS	Statistical Analysis Software
SD	Standard Deviation
SoA	schedule of activities
$t_{1/2}$	terminal phase half life
t_{lag}	lag time before observation of drug concentrations

T_{max}	time to reach maximum observed plasma concentration
WOCBP	women of childbearing potential

10.9.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
GSKDrug

Trademarks not owned by the GlaxoSmithKline Group of Companies
MedDRA
WHODrug
WinNonlin
SAS

10.10. Appendix 10: List of Data Displays

10.10.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.10	NA
Safety	2.1 to 2.17	2.1 to 2.3
Pharmacokinetic	3.1 to 3.4	3.1 to 3.11
Section	**Listings**	
ICH Listings	1 to 48	
Other Listings	49 to 52	

10.10.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated.

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

NOTES:

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

10.10.3. Deliverables

Delivery	Description
SAC	Final Statistical Analysis Complete

10.10.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition and Analysis Sets					
1.1	Safety	NS1	Summary of Number of Subjects Enrolled by Country and Site ID		SAC [1]
1.2	Safety	ES1	Summary of Subject Disposition		SAC [1]
1.3	Safety	ES4	Summary of Subject Disposition at Each Study Epoch		SAC [1]
1.4	Screened	ES6	Summary of Reasons for Screening Failures		SAC [1]
1.5	Safety	SD1	Summary of Treatment Status and Reasons for Discontinuation of Study Treatment		SAC [1]
1.6	Enrolled	DV1	Summary of Important Protocol Deviations		SAC [1]
Demographics and Baseline Characteristics					
1.7	Safety	DM3	Summary of Demographic Characteristics		SAC [1]
1.8	Safety	DM5	Summary of Race and Racial Combinations		SAC [1]
1.9	Safety	DM11	Summary of Age Ranges		SAC [1]
1.10	Safety	MH4	Summary of Current Cardiovascular and Liver Disease Related Medical Conditions		SAC [1]

10.10.5. Safety Tables

Safety Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events					
2.1	Safety	AE5B	Summary of Adverse Events by System Organ Class and Preferred Term and Maximum Grade		SAC [1]
2.2	Safety	AE5B	Summary of Drug- Related Adverse Events by System Organ Class and Preferred Term and Maximum Grade		SAC [1]
2.3	Safety	AE15	Summary of Common (>=5%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)		SAC [1]
2.4	Safety	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)		SAC [1]
2.5	Safety	AE5B	Summary of Acetylcholinesterase-Inhibition Adverse Events of Special Interest by System Organ Class and Preferred Term and Maximum Grade		SAC[1]
2.6	Safety	SAFE_T1	Summary of Cumulative Grades of Acetylcholinesterase-Inhibition Adverse Events of Special Interest		SAC [1]
Laboratory Measurements					
2.7	Safety	LB1	Summary of Chemistry Change from Baseline		SAC [1]
2.8	Safety	LB1	Summary of Hematology Change from Baseline		SAC [1]
2.9	Safety	UR3	Summary of Urinalysis Dipstick Results		SAC [1]
2.10	Safety	LIVER1	Summary of Liver Monitoring/Stopping Event Reporting		SAC [1]
Electrocardiograms					
2.11	Safety	EG1	Summary of ECG Findings		SAC [1]

2.12	Safety	SAFE_T2	Summary of Frequency of Maximum Post-Dose ECG Parameter Corrected QTc Interval		SAC [1]
2.13	Safety	SAFE_T3	Summary of Frequency of Maximum Change from Baseline for ECG Parameter Corrected QTc Interval		SAC [1]
2.14	Safety	EG2	Summary of Change from Baseline in ECG Values		SAC [1]
Vital Signs					
2.15	Safety	VS1	Summary of Change from Baseline in Vital Signs		SAC [1]
Cardiovascular Risk Factors					
2.16	Safety	FH1	Summary of Family History of Cardiovascular Risk Factors		SAC [1]
2.17	Safety	SU1	Summary of Substance Use		SAC [1]

10.10.6. Safety Figures

Safety Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events					
2.1	Safety	AE10	Gastrointestinal Adverse Events of Special Interest Adverse Events	Part 1, Part 2, and combined	SAC [1]
2.2	Safety	SAFE_F1	Plot of Distribution of Cumulative Grades of Acetylcholinesterase-Inhibition Adverse Events of Special Interest	Combine Part 1 and Part 2 in one page	SAC [1]
2.3	Safety	SAFE_F2	Plot of duration and severity of Adverse Events for Individual Participants	Part1 and Part 2	SAC [1]

10.10.7. Pharmacokinetic Tables

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK Concentration Data					
3.1.	PK	PKCT1	Summary of Gepotidacin Plasma Pharmacokinetic Concentration-Time Data (units) by Treatment	Paginate by study part	SAC [1]
3.2.	PK	PKCT1	Summary of Gepotidacin Urine Pharmacokinetic Concentration-Time Data (units) by Treatment	Paginate by study part	SAC [1]
PK Derived Parameters					
3.3.	PK Parameter	PKPT4	Summary Statistics of Derived Gepotidacin Plasma Pharmacokinetic Parameters by Treatment	Parameters with units. Do not ln-transform Tmax or Tlag. Paginate by study part	SAC [1]
3.4.	PK Parameter	PKPT4	Summary Statistics of Derived Gepotidacin Urine Pharmacokinetic Parameters by Treatment	Parameters with units, Paginate by study part	SAC [1]

10.10.8. Pharmacokinetic Figures

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Individual Concentration Plots					
3.1.	PK	PKCF1P	Individual Gepotidacin Plasma Concentration-Time Plots by Treatment (Linear and Semi-Logarithmic)	Paginate by Study Part and Treatment Dashed line represents the LLQ Participants Overlaid	SAC [1]
3.2.	PK	PKCF1P	Individual Gepotidacin Urine Concentration-Time Plots (Linear and Semi Logarithmic)	Paginate by Study Part and Treatment Dashed line represents the LLQ Participants Overlaid	SAC [1]
Mean / Median Concentration Plots					
3.3.	PK	PKCF2	Mean (± Standard Deviation) Gepotidacin Plasma Concentration-Time Plots by Treatment (Linear and Semi-Logarithmic)	Treatments Overlaid; All part 1 and part 2 treatments on same page	SAC [1]
3.4.	PK	PKCF2	Mean (± Standard Deviation) Gepotidacin Urine Concentration-Time Plots by Treatment (Linear and Semi-Logarithmic)	Treatments Overlaid; all part 1 and part 2 treatments on the same page	SAC [1]
3.5.	PK	PKCF3	Median (Range) Gepotidacin Plasma Concentration-Time Plots by Treatment (Linear and Semi-Logarithmic)	Treatments Overlaid: all part 1 and part 2 treatments on the same page	SAC [1]

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.6.	PK	PKCF3	Median (Range) Gepotidacin Urine Concentration-Time Plots by Treatment for Study Part 1 (Linear and Semi-Logarithmic)	Treatments Overlaid; all part 1 and part 2 treatments on the same page	SAC [1]
3.7.	PK	PKPF1	Scatter plot of Gepotidacin Plasma Pharmacokinetic Parameters for 1500 mg dose against Body Weight	Part 1 & Part 2, adults and adolescents shown on the same page with different symbols, with a regression line and the equation; PK Parameters: Cmax, AUC (0-∞)	SAC [1]
3.8.	PK	PKPF1	Scatter plot of Gepotidacin Body-Weight Adjusted Plasma Pharmacokinetic Parameters for 1500 mg Dose against Body Weight	If significant correlation between body weight and PK parameters, then generate an additional figure of body-weight-adjusted PK parameters versus body weight	SAC [1]
3.9.	PK	PKPF1	Scatter plot of Gepotidacin Plasma Pharmacokinetic Parameters for Two 3000 mg Doses against Body Weight	PK Parameters: Cmax and AUC(0-48); by treatment; For adults and adolescents receiving the same treatment intervals, shown them on the same page with different symbols, with a regression line and the equation;	SAC [1]

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.10.	PK	PKPF1	Scatter plot of Gepotidacin Body-Weight Adjusted Plasma Pharmacokinetic Parameters for Two 3000 mg Doses against Body Weight	If significant correlation between body weight and PK parameters, then generate an additional figure of body-weight-adjusted PK parameters versus body weight	SAC [1]
3.11.	PK	PKPF2	BOX-Whisker plots of PK Parameters for Adults and Adolescents	PK Parameters: Cmax and AUC (0-∞) for 1500mg; Cmax and AUC (0-48) for 3000 mg two doses; 1500mg and 3000mg (various intervals) on different pages; adults and adolescents on the same page	SAC [1]

10.10.9. ICH Listings

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Randomization					
1	Randomized	CP_TA1	Listing of Randomised and Actual Treatment		SAC [1]
Subject Disposition					
2	Safety	ES3	Listing of Reasons for Study Withdrawal		SAC [1]
3	Safety	SD3	Listing of Reasons for Study Treatment Discontinuation		SAC [1]
4	Randomized	BL1	Listing of Subjects for Whom the Treatment Blind was Broken During the Study		SAC [1]
5	Screened	ES7	Listing of Reasons for Screening Failure		SAC [1]
6	Enrolled	DV2	Listing of Important Protocol Deviations		SAC [1]
7	Screened	IE4	Listing of Subjects with Inclusion/Exclusion Criteria Deviations		SAC [1]
8	Safety	SP3	Listing of Subjects Excluded from Any Population		SAC [1]
9	Safety	SAFE_L1	Listing of Subjects in Previous Clinical Trial		SAC [1]
Demographics					
10	Safety	DM4	Listing of Demographic Characteristics	Include height, weight and BMI	SAC [1]
11	Safety	DM10	Listing of Race		SAC [1]
Medical Conditions and Concomitant Medications					
12	Safety	MH3	Listing of Medical Conditions		SAC [1]
13	Safety	CM4	Listing of Concomitant Medications		SAC [1]

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Exposure					
14	Safety	SAFE_L2	Listing of Exposure Data		SAC [1]
Safety					
15	Safety	AE2	Listing of Relationship Between System Organ Class and Verbatim Text		SAC[1]
16	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events		SAC [1]
17	Safety	AE9CP	Listing of All Adverse Events		SAC [1]
18	Safety	AE9CP	Listing of Study Drug Related Adverse Events		SAC [1]
19	Safety	AE9CPA	Listing of Serious Adverse Events		SAC [1]
20	Safety	AE9CP	Listing of Adverse Events Leading to Withdrawal from Study		SAC [1]
21	Safety	SAFE_L3	Listing of Cardiovascular Adverse Events of Special Interest	Conditional display	SAC [1]
22	Safety	SAFE_L4	Listing of Gastrointestinal Adverse Events of Special Interest	Conditional display	SAC [1]
23	Safety	SAFE_L5	Listing of Acetylcholinesterase-Inhibition Adverse Events of Special Interest	Conditional display, Flag events with onset time of 0-6hr post last dose	SAC [1]
24	Safety	SAFE_L6	Listing of Non-Gastrointestinal Acetylcholinesterase-Inhibition Adverse Events of Special Interest.	Conditional display, Flag events with onset time of 0-6hr post last dose	SAC[1]
25	Safety	SAFE_L7	Summary of Acetylcholinesterase-Inhibition Adverse Events of Special Interest by Treatment and by Maximum Grade of Each Participant	Conditional display	SAC[1]

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
26	Safety	SAFE_L8	Listing of Liver Adverse Events	Conditional display	SAC [1]
27	Safety	SAFE_L9	Listing of Clostridium Difficile Testing	Conditional display	SAC [1]
Laboratory Measurements					
28	Safety	LB6	Listing of Chemistry Toxicities of Grade 3 or Higher		SAC [1]
29	Safety	LB6	Listing of All Chemistry Data for Subjects with Toxicities of Grade 3 or Higher		SAC [1]
30	Safety	LB6	Listing of Hematology Toxicities of Grade 3 or Higher		SAC [1]
31	Safety	LB6	Listing of All Hematology Data for Subjects with Toxicities of Grade 3 or Higher		SAC [1]
32	Safety	UR2b	Listing of Urinalysis Toxicities of Grade 3 or Higher		SAC [1]
33	Safety	UR2b	Listing of All Urinalysis Data for Subjects with Toxicities of Grade 3 or Higher		SAC [1]
ECGs					
34	Safety	EG6	Listing of Abnormal ECG Findings		SAC [1]
35	Safety	EG6	Listing of All ECG Findings for Subjects with an Abnormal Finding		SAC [1]
36	Safety	HM10	Listing of Holter Abnormalities		SAC [1]
37	Safety	EG4	Listing of ECG Values of Potential Clinical Importance		SAC [1]
38	Safety	EG4	Listing of ECG Change from Baseline of Potential Clinical Importance		SAC [1]
39	Safety	EG4	Listing of All ECG Values for Subjects with Any Value of Potential Clinical Importance		SAC [1]

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Vital Signs					
40	Safety	VS5	Listing of Vital Signs of Potential Clinical Importance		SAC [1]
41	Safety	VS5	Listing of All Vital Signs for Subjects with Potential Clinical Importance Values		SAC [1]
Liver Events					
42	Safety	LIVER5	Listing of Liver Monitoring/Stopping Event Reporting	Conditional display	SAC [1]
43	Safety	LIVER10	Listing of Hepatobiliary Laboratory Abnormalities	Conditional display	SAC [1]
44	Safety	MH3	Listing of Medical Conditions for Subjects with Liver Stopping Events	Conditional display	SAC [1]
45	Safety	MH3	Listing of Plasma Concentration Data for Subjects with Liver Stopping Events	Conditional display	SAC [1]
46	Safety	SAFE_L10	Listing of Alcohol Intake at Onset of Liver Event	Conditional display	SAC [1]
47	Safety	LIVER7	Listing of Liver Biopsy Details	Conditional display	SAC [1]
48	Safety	LIVER8	Listing of Liver Imaging Details	Conditional display	SAC [1]

10.10.10. Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Pharmacokinetics					
49	PK	PKCL1P	Listing of Gepotidacin Plasma Concentrations (units) by Treatment	Parts 1 and 2 combined.	SAC [1]
50	PK	PKUL1P	Listing of Gepotidacin Urine Concentrations (units) by Treatment	Parts 1 and 2 combined.	SAC [1]
51	PK Parameter	PKPL1P	Listing of Gepotidacin Plasma Pharmacokinetic Parameters by Treatment	Parts 1 and 2 combined.	SAC [1]
52	PK Parameter	PKPL1P	Listing of Gepotidacin Urine Pharmacokinetic Parameters by Treatment	Parts 1 and 2 combined.	SAC [1]