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

Title	:	Reporting and Analysis Plan for Study 205893: A 2-Part Phase I, Single Dose, Crossover Relative Bioavailability Study of Both TIVICAY 10 mg Conventional Tablets and 5 mg Dispersible Tablets Compared to Conventional TIVICAY Tablets in Healthy Adult Subjects
Compound Number	:	GSK1349572
Effective Date	:	19-JUN-2017

Description :

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 205893.
- 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) deliverable.

Author's Name and Functional Area:

PPD Biostatistician II (Biostatistics, Early Development Services, PPD)	25-JUN-2017
PPD Pharmacokineticist (Biostatistics, PPD)	25-JUN-2017

Approved by:

PPD Manager (Statistics, Programming and Data Strategy, GSK)	25-JUN-2017

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1. REPORTING & ANALYSIS PLAN SYNOPSIS

Overview	Key Elements of the RAP
Purpose	• The purpose of this reporting and analysis plan (RAP) is to describe any planned analyses and output to be included in the clinical study report for Protocol 205893.
Protocol	• This RAP is based on the original protocol (Dated: 23/FEB/2017) of study 205893 (GSK Document No. 2016N302761_00).
Primary Objective	Part 1: • To evaluate the relative bioavailability (BA) of dolutegravir (DTG) conventional 10 mg tablets (5 tablets) administered direct to mouth as compared to a conventional 50 mg tablet (reference) administered direct to mouth. Part 2: • To evaluate the relative BA of DTG dispersible 5-mg tablets (5 tablets) administered as “disperse and immediately take” and of DTG dispersible 5-mg tablets (5 tablets) administered direct to mouth as compared to a conventional 25 mg tablet (reference) administered direct to mouth.
Primary Endpoint	Parts 1 and 2: • Plasma DTG AUC(0-∞), AUC(0-t), and Cmax.
Secondary Objectives	Part 1: • To compare the single dose PK of DTG conventional 10 mg tablets (5 tablets) administered direct to mouth as compared to a conventional 50 mg tablet (reference) administered direct to mouth. • To evaluate the safety and tolerability of DTG conventional 10 mg (5 tablets) administered direct to mouth as compared to the administration of a conventional 50 mg tablet (reference) administered direct to mouth. Part 2: • To compare the single dose PK of DTG dispersible 5-mg tablets (5 tablets) administered as “disperse and immediately take” and of DTG dispersible 5-mg tablets (5 tablets) administered direct to mouth as compared to a conventional 25 mg tablet (reference) administered direct to mouth. • To evaluate the safety and tolerability of DTG dispersible 5-mg tablets (5 tablets) administered as “disperse and immediately take” and of DTG dispersible 5-mg tablets (5 tablets) administered direct to mouth as compared to a conventional 25 mg tablet (reference) administered direct to mouth.
Secondary Endpoints	Parts 1 and 2: • Plasma DTG tlag, tmax, t½, λz, %AUCex, AUC0-24, CL/F and Vz/F, Ct, and C24. • Safety and tolerability parameters as assessed by change from baseline in

Overview	Key Elements of the RAP
	number of subjects with adverse events (AEs) and Division of Acquired Immune Deficiency Syndrome (DAIDS) toxicity grading for HIV-infected patients of clinical laboratory tests.
Exploratory Objective	• To evaluate the palatability of the dispersible tablets (Part 2 only).
Exploratory Endpoint	• Palatability Questionnaire (Part 2 only).
Study Design	• This study will be conducted as a 2-part, open-label, randomized, cross-over design with one group of subjects in Part 1 of the study randomized to receive each of 2 study treatments (A and B) over 2 dosing periods, and another group of subjects in Part 2 of the study randomized to receive each of 3 study treatments (C, D, and E) over 3 dosing periods. Treatments are defined below: o Treatment A: Conventional 10-mg DTG tablet (5 tablets, test) administered direct to mouth. o Treatment B: Conventional 50-mg DTG tablet (reference) administered direct to mouth. o Treatment C: 5-mg dispersible DTG tablet (5 tablets) administered as a dispersion and immediately taken (test 1). o Treatment D: 5-mg dispersible DTG tablet (5 tablets) administered as direct to mouth (test 2). o Treatment E: Conventional 25-mg DTG tablet administered as direct to mouth (reference). • Subjects will participate in only one part of the study. Parts 1 and 2 of the study may be conducted concurrently. There will be a washout of at least 7 (-4 hours) days between doses of study medication. Note: The -4 hours is an allowed tolerance window to the 7 day washout and is to allow the study site and subjects flexibility in scheduling admission and dosing for subsequent treatment periods (i.e., treatment periods 2 and/or 3). • Part 1 is a 2-period, cross-over study that will assess the relative BA of DTG conventional 10 mg tablets (5 tablets) administered direct to mouth as compared to a conventional 50 mg tablet (reference) administered direct to mouth (treatments A and B, respectively). Each subject will receive both treatments according to their assigned treatment sequence (AB or BA) • Part 2 is a 3-period, cross-over study that will assess the relative BA of DTG dispersible 5-mg tablets (5 tablets) administered as "disperse and immediately take" and of DTG dispersible 5-mg tablets (5 tablets) administered direct to mouth as compared to a conventional 25 mg tablet (reference) administered direct to mouth (treatments C, D, and E, respectively). Each subject will receive all three treatments according to their assigned treatment sequence (CDE, DEC, ECD, CED, DCE, or EDC).
Planned Analyses	• Plasma DTG concentration-time data will be analyzed by non-compartmental methods with Phoenix WinNonlin. Calculations will be based on the actual

Overview	Key Elements of the RAP
	sampling times recorded during the study. From the plasma concentration-time data, the following PK parameters will be determined, as data permit: AUC(0-∞), area under the plasma concentration-time curve from time of dose to last measurable concentration (AUC(0-t)), area under the plasma concentration-time curve from time of dose to 24 hr (AUC0-24), maximum observed concentration (Cmax), plasma DTG lag time for absorption (tlag), time of occurrence of Cmax (tmax), terminal elimination phase half-life (t1/2), terminal rate constant (λz), %AUCex, apparent oral clearance (CL/F) and apparent volume of distribution during terminal phase (Vz/F), Ct, and concentration at 24 hours after dose administration (C24). • Pharmacokinetic data will be listed and may be presented in graphical form and will be summarized descriptively. All PK data will be stored in the Archives, GlaxoSmithKline Research and Development (R&D) or their designee. • The PK parameters except tmax and tlag) will be ln-transformed and separately analyzed using a mixed effects model with fixed effect terms for period and treatment for each treatment comparison. Subject will be treated as a random effect in the model. Point estimates and their associated 90% confidence intervals (CIs) will be constructed for the differences in PK parameter values between test and reference treatments. The point estimates and their associated 90% CIs will then be back-transformed to provide point estimates and 90% CIs for the ratios of PK parameters between test and reference treatments. • Safety data will be presented in tabular format and summarized descriptively according to GSK's Integrated Data Standards Library (IDSL) standards. No formal statistical analysis of the safety data will be conducted. • Palatability questionnaire variables will be summarized descriptively.
Analysis Populations	• All Subjects Population: all subjects who receive at least one dose of study medication. This population will be used for all demographic and safety summaries • PK Population: subjects in the 'All Subjects' population for whom a PK sample was obtained and had evaluable PK assay results. PK samples that may be affected by protocol deviations will be reviewed by the study team to determine whether or not the sample will be excluded. This population will be used for reporting of PK data.
Hypothesis	• This study is designed to estimate the relative BA of each test treatment to the reference treatment (A vs. B; C vs. E and D vs. E) in both study parts in the fasted state. No formal hypothesis will be tested. For each pharmacokinetic endpoint (except for time of occurrence of Cmax [tmax] and tlag), point estimates and corresponding 90% CIs will be constructed for the ratio of the geometric mean of the test treatment to the geometric mean of the reference treatment, μ(test)/μ(reference).

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

The parameter "t" in the list of secondary endpoints in the protocol has been excluded as this does not represent an actual PK parameter and may be a typographical error in the protocol text. There were no other changes to or deviations from the originally planned statistical analysis specified in the protocol (Dated: 23/FEB/2017).

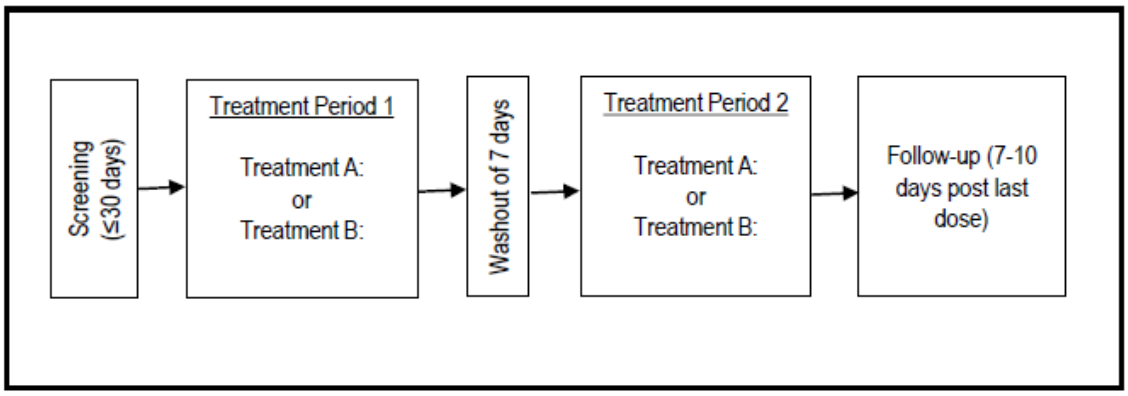
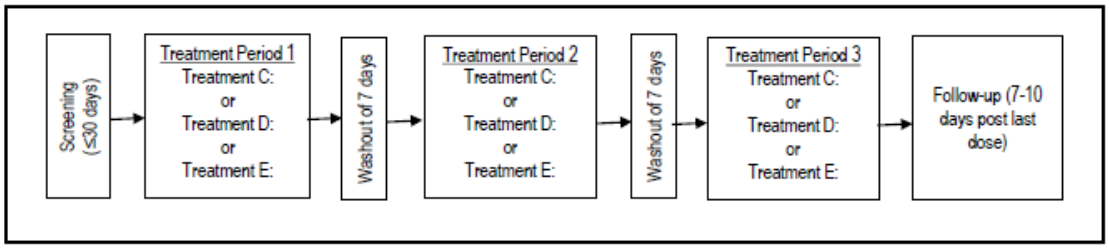
Listings of clinical laboratory data above a certain DAIDs toxicity grading are included in the outputs. Section 3.3.1 of the protocol indicated that these listings contain toxicities of grade 3 or higher; however, the listings will instead contain toxicities of grade 2 or higher.

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

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
Part 1 • To evaluate the relative BA of DTG conventional 10 mg tablets (5 tablets) administered direct to mouth as compared to a conventional 50 mg tablet (reference) administered direct to mouth.	**Part 1** • Plasma DTG AUC(0-∞), AUC(0-t), and Cmax.
Part 2 • To evaluate the relative BA of DTG dispersible 5-mg tablets (5 tablets) administered as "disperse and immediately take" and of DTG dispersible 5-mg tablets (5 tablets) administered direct to mouth as compared to a conventional 25 mg tablet (reference) administered direct to mouth.	**Part 2** • Plasma DTG AUC(0-∞), AUC(0-t), and Cmax.
Secondary Objectives	**Primary Objectives**
Part 1 • To compare the single dose PK of DTG conventional 10 mg tablets (5 tablets) administered direct to mouth as compared to a conventional 50 mg tablet (reference) administered direct to mouth.	**Part 1** • Plasma DTG tlag, tmax, t½, λz, %AUCex, AUC0-24, CL/F and Vz/F, Ct, and C24. • Safety and tolerability parameters as assessed by change from baseline in number of subjects with AEs and DAIDS toxicity grading for HIV-infected patients of clinical laboratory tests as described in Appendix

Objectives	Endpoints
• To evaluate the safety and tolerability of DTG conventional 10 mg (5 tablets) administered direct to mouth as compared to the administration of a conventional 50 mg tablet (reference) administered direct to mouth.	6 of the protocol.
Part 2 • To compare the single dose PK of DTG dispersible 5-mg tablets (5 tablets) administered as "disperse and immediately take" and of DTG dispersible 5 mg tablets (5 tablets) administered direct to mouth as compared to a conventional 25 mg tablet (reference) administered direct to mouth. • To evaluate the safety and tolerability of DTG dispersible 5-mg tablets (5 tablets) administered as "disperse and immediately take" and of DTG dispersible 5 mg tablets (5 tablets) administered direct to mouth as compared to a conventional 25 mg tablet (reference) administered direct to mouth.	**Part 2** • Plasma DTG tlag, tmax, t½, λz, %AUCex, AUC0-24, CL/F and Vz/F, Ct, and C24. • Safety and tolerability parameters as assessed by change from baseline in number of subjects with AEs and DAIDS toxicity grading for HIV-infected patients of clinical laboratory tests as described in Appendix 6 of the protocol.
Exploratory Objectives	**Exploratory Endpoints**
Part 2 only • To evaluate the palatability of the dispersible tablets.	**Part 2 only** • Palatability Questionnaire.

2.3. Study Design

Overview of Study Design and Key Features	
Part 1:  **Part 2:**  	
Design Features	• Phase I, 2-part, open-label, randomized, cross-over study. • **Part 1**: Approximately 14 subjects in a 2-period, cross-over study that will assess the relative BA of DTG conventional 10 mg tablets (5 tablets) administered direct to mouth (Treatment A) as compared to a conventional 50 mg tablet (reference) administered direct to mouth (Treatment B). Each subject will receive both treatments according to their assigned treatment sequence (AB or BA). Each treatment sequence will be assigned to 7 subjects. • **Part 2**: Approximately 24 subjects in a 3-period, cross-over study that will assess the relative BA of DTG dispersible 5-mg tablets (5 tablets) administered as "disperse and immediately take" (Treatment C) and of DTG dispersible 5-mg tablets (5 tablets) administered direct to mouth (Treatment D) as compared to a conventional 25 mg tablet (reference) administered direct to mouth (Treatment E). Each subject will receive all three treatments according to their assigned treatment sequence (CDE, DEC, ECD, CED, DCE, or EDC). Each sequence will be assigned to 4 subjects.
Dosing	**Part 1:** • Treatment A: Conventional 10-mg DTG tablet (5 tablets, test) administered direct to mouth. • Treatment B: Conventional 50-mg DTG tablet (reference) administered direct to mouth. **Part 2:** • Treatment C: 5-mg dispersible DTG tablet (5 tablets) administered as a dispersion and immediately taken (test 1).

Overview of Study Design and Key Features	
	• Treatment D: 5-mg dispersible DTG tablet (5 tablets) administered as direct to mouth (test 2). • Treatment E: Conventional 25-mg DTG tablet administered as direct to mouth (reference).
Treatment Assignment	**Part 1:** • On Period 1 Day 1, subjects will be randomized to one of the 2 following treatment sequences: AB or BA in accordance with the randomization schedule generated prior to the start of the study, using validated software. **Part 2:** • On Period 1 Day 1, subjects will be randomized to one of the 6 following treatment sequences: CDE, DEC, ECD, CED, DCE, or EDC in accordance with the randomization schedule generated prior to the start of the study, using validated software.
Interim Analysis	• There will be no interim analysis.

2.4. Statistical Hypotheses

This study is designed to estimate the relative BA of each test treatment to the reference treatment (A vs. B; C vs. E and D vs. E) in both study parts in the fasted state.

No formal hypothesis will be tested. For each pharmacokinetic endpoint (except for time of occurrence of Cmax [tmax] and tlag), point estimates and corresponding 90% CIs will be constructed for the ratio of the geometric mean of the test treatment to the geometric mean of the reference treatment, μ(test)/μ(reference).

3. PLANNED ANALYSES

3.1. 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.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
All Subjects	• All subjects who receive at least one dose of study medication.	• Demographic • Safety
PK	• Subjects in the "All Subjects" population for whom a PK sample was obtained and had evaluable PK assay results. PK samples that may be affected by protocol deviations will be reviewed by the study team to determine	• PK

Population	Definition / Criteria	Analyses Evaluated
	whether or not the sample will be excluded.	

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

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

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

Table 1 Overview of Appendices

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

Table 2 Overview of Planned Study Population Analyses

Display Type	Data Display's Generated		
	Figure	Table	Listing
Enrollment			
Number of Subjects Enrolled by Country and Site ID		Y	
Randomisation			
Randomisation			Y
Subject Disposition			
Subject Disposition		Y	
Reasons for Screening Failures		Y	Y
Reasons for Withdrawals			Y
Important Protocol Deviations		Y	Y
Inclusion and Exclusion Criteria Deviations			Y
Demography			
Demographics Characteristics		Y	Y
Race and Racial Combinations		Y	Y
Age Ranges		Y	
Study Populations			Y [1]
Concomitant Medications			
Concomitant Medications			Y

NOTES:

- Y = Yes display generated.

1. Listing includes only subjects excluded from any population.

7. PRIMARY STATISTICAL ANALYSES

7.1. Pharmacokinetic Analyses

7.1.1. Overview of Planned Pharmacokinetic Analyses

The PK analyses will be based on the PK Population, unless otherwise specified.

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

Table 3 Overview of Planned Pharmacokinetic Analyses

Display Type	Untransformed							Ln-Transformed						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
PK Concentrations				Y	Y[1] [2]	Y[1]	Y							
Plasma PK Parameters	Y	Y		Y	Y[1] [2]	Y	Y			Y	Y			

NOTES :

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

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

[2] Separate mean and median plots will be generated.

7.1.2. Drug Concentration Measures

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

7.1.3. Pharmacokinetic Parameters

7.1.3.1. Deriving Pharmacokinetic Parameters

- Refer to Appendix 3: Data Display Standards & Handling Conventions (Section 3 Reporting Process & Standards).
- The PK parameters will be calculated by standard non-compartmental analysis according to current working practices and using Phoenix WinNonlin Version 6.4 or higher.
- All calculations of non-compartmental parameters will be based on actual sampling times.
- Pharmacokinetic parameters described in Table 4 will be determined from the plasma concentration-time data, as data permits.

Table 4 Derived Plasma Pharmacokinetic Parameters

Parameter	Parameter Description
AUC(0-t)	Area under the concentration-time curve (AUC) from time 0 (predose) to time of 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.
AUC0-24	Area under the concentration-time curve (AUC) over time 0 (predose) to 24 hours after dose administration, 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, calculated as: $AUC(0-\infty) = AUC(0-t) + Ct / \lambda z$ where Ct is the last observed quantifiable concentration.
%AUCex	The percentage of AUC(0-∞) obtained by extrapolation (%AUCex) will be calculated as: $[AUC(0-\infty) - AUC(0-t)] / AUC(0-\infty) \times 100$
Cmax	Maximum observed concentration, determined directly from the concentration-time data.
Ct	The last observed quantifiable concentration
C24	The observed concentration at 24 hours after dose administration
tmax	Time to first occurrence of Cmax
tlag	Lag time before observation of drug concentrations in sampled matrix
t½	Terminal phase half-life will be calculated as: $t½ = \ln 2 / \lambda z$
λz	Terminal-phase rate constant
CL/F	The apparent oral clearance
Vz/F	The apparent volume of distribution during the terminal phase

NOTES:

- Additional parameters may be included as required.

7.1.3.2. Statistical Analysis of Pharmacokinetic Parameters

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

Pharmacokinetic Statistical Analyses
Endpoint(s)
• Plasma primary PK endpoints include AUC(0-∞), AUC(0-t) and Cmax of DTG, as data permit
Model Specification
• In Part 1 of this study, the ln-transformed AUC(0-∞), AUC(0-t), and Cmax values for DTG will be analyzed separately using a mixed effects model, fitting fixed effect terms for period, and

Pharmacokinetic Statistical Analyses
treatment, and treating subject as a random effect. Point estimates and 90% CIs for the differences of interest (conventional DTG 5 x 10 mg tablets administered direct to mouth [Treatment A, Test] versus conventional DTG 1 x 50 mg tablet administered direct to mouth [Treatment B, Reference]) will be constructed using the residual variance • In Part 2 of this study, the ln-transformed AUC(0-∞), AUC(0-t), and Cmax values for DTG will be analyzed separately using a mixed effects model, fitting fixed effect terms for period and treatment, and treating subject as a random effect. Point estimates and 90% CIs for the differences of interest (5 x 5 mg dispersible DTG tablets [Treatment C, Test 1] versus conventional DTG 1 x 25 mg tablet administered direct to mouth [Treatment E, Reference], and conventional DTG 5 x 5 mg tablets administered direct to mouth [Treatment D, Test 2] versus conventional DTG 1 x 50 mg tablet administered direct to mouth [Treatment E, Reference]) will be constructed using the residual variance.
Model Checking & Diagnostics
• Refer to Appendix 8: Model Checking and Diagnostics for Statistical Analyses.
Model Results Presentation
• Statistical analysis by ANOVA will be presented in tabular format with geometric mean ratios between TIVICAY™ conventional and dispersible tablets versus conventional DTG tablets, and 90% CIs for the ratios of AUC(0-∞), AUC(0-t) and Cmax for DTG. Part 1 Example SAS Code: PROC MIXED; CLASS USUBJID TRTA APERIOD; MODEL LOGPKPARM =TRTA APERIOD /DDFM=KR; RANDOM USUBJID; LSMEANS TRTA; ESTIMATE 'A VS B' TRTA 1 -1/CL ALPHA=0.1;RUN; Part 2 Example SAS Code: PROC MIXED; CLASS USUBJID TRTA APERIOD; MODEL LOGPKPARM =TRTA APERIOD /DDFM=KR; RANDOM USUBJID; LSMEANS TRTA; ESTIMATE 'C VS E' TRTA 1 0 -1/CL ALPHA=0.1; ESTIMATE 'D VS E' TRTA 0 1 -1/CL ALPHA=0.1;RUN;

7.1.4. Interim Analysis

7.1.4.1. Overview of Planned Analyses

No interim analysis is planned for this study.

8. SECONDARY STATISTICAL ANALYSES

8.1. Safety Analyses

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

Table 5 provides an overview of the planned analyses, with further details of data displays being presented in Appendix 10: List of Data Displays.

Table 5 Overview of Planned Safety Analyses

Display Type	Absolute				Change from Baseline			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
Exposure								
Exposure Data				Y				
AEs								
All AEs	Y			Y				
All Drug-Related AEs	Y			Y				
Common Non-serious AEs	Y							
Serious AEs	Y			Y				
Withdrawal AEs				Y				
Laboratory Values								
Clinical Chemistry				Y [2]	Y			
Hematology				Y [2]	Y			
Urinalysis (Dipstick)	Y			Y [2]				
Electrocardiograms (ECGs)								
ECG Findings	Y			Y [3]				
ECG Values				Y [4]				
Vital Signs								
Vital Signs				Y [4]	Y			Y [4]
Liver								
Liver Events [1]				Y				

NOTES :

1. Conditional display, it will only be produced when an event has occurred.
2. Displays contain only subjects with DAIDS toxicities for HIV-infected patients of Grade 2 or higher
3. Displays contain only subjects with abnormal findings
4. Displays contain only subjects with values of potential clinical importance

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

8.2. Exploratory Analyses

The exploratory analyses will be based on the "All Subjects" population, unless otherwise specified.

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

Table 6 Overview of Planned Exploratory Analyses

Display Type	Absolute			
	Summary		Individual	
	T	F	F	L
Palatability				
Palatability Questionnaire Results	Y			Y

NOTES :

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

9. REFERENCES

GlaxoSmithKline Document Number 2016N302761_00 (Original – 23-FEB-2017): A 2-Part Phase I, Single Dose, Crossover Relative Bioavailability Study of Both TIVICAY 10 mg Conventional Tablets and 5 mg Dispersible Tablets Compared to Conventional TIVICAY Tablets in Healthy Adult Subjects (23-FEB-2017)

10. APPENDICES

Section	Appendix
RAP Section 5 : General Considerations for Data Analyses & Data Handling Conventions	
Section 10.1	Appendix 1: Time and Events
Section 10.2	Appendix 2: Treatment States & Phases
Section 10.3	Appendix 3: Data Display Standards & Handling Conventions • Study Treatment & Sub-group Display Descriptors • Baseline Definitions & Derivations • Reporting Process & Standards
Section 10.4	Appendix 4: Derived and Transformed Data • General, Study Population & Safety • Pharmacokinetic • Exploratory
Section 10.5	Appendix 5: Premature Withdrawals & Handling of Missing Data • Premature Withdrawals • Handling of Missing Data
Section 10.6	Appendix 6: Values of Potential Clinical Importance
Section 10.7	Appendix 7: Multiple Comparisons and Multiplicity
Section 10.8	Appendix 8: Model Checking and Diagnostics for Statistical Analyses
Other RAP Appendices	
Section 10.9	Appendix 9: Abbreviations & Trade Marks
Section 10.10	Appendix 10: List of Data Displays

10.1. Appendix 1: Time & Events

10.1.1. Protocol Defined Time & Events

Assessments	All Study Periods (Parts 1 and 2)							Follow-up	Notes
		Day 1			Day 2	Day 3	Day 4		• *Day -1 of Periods 2 -3 may be the same day as Day 6 of prior periods*
	Day -1	Pre-dose	0 hr	Post Dose	24 hr	48 hr	72 hr		• *At Follow-up – Male subjects with no ongoing AEs or Vital Sign/Laboratory measures of clinical concern may be followed virtually by the site via telephone contact.*
Admission to Unit	X								
Discharge							X		
Outpatient Visit								X	*Follow-up visit will occur 7 to 10 days post last dose.*
12-lead ECG (single)	X								
Vital signs	X	X			X		X	X	*Single vital sign measurements performed at all time points.*
Brief Physical Exam	X								• *Drug/Alcohol/Cotinine/pregnancy will be performed per the standard practice of the site.*
Urine Drug/Alcohol/Cotinine	X								• *Clinical laboratory tests – see Protocol Table 5, Section 9.3.4.*
Pregnancy test (urine; WCBP)	X							X	• *Clinical laboratory tests at follow-up are only necessary if subject had a previous abnormal lab value*
Clinical laboratory tests	X				X			X*	
Dosing			X						*See Protocol Section 7.1*
Palatability Assessment				Start w/in 10 min post-dose					*Complete for each dispersion treatment C (see Protocol Section 12.8, Appendix 8)*
PK Sampling		X		Collect at: 0.5, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 8, 12, 16, 24, 48 and 72 hrs post-dose.					*Pre-dose (within 15 minutes prior to dosing), Protocol Section 9.4*
Meals	Fasted from 10 hrs prior to dosing to 4 hrs post-dose			Standard for the study center					*See also Protocol Section 6.3.2 and Section 6.3.3*
Adverse Events / SAE	X	<==========X==========<						X	
Concomitant medications	X	<==========X==========<						X	

10.2. Appendix 2: Treatment States and Phases

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.

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 + 6 days
Post-Treatment	Date/Time > Study Treatment Stop Date/Time + 6 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 < Study Treatment Start Date
On-Treatment	If AE onset date is on or after treatment start date & on or before treatment stop date with 7 days lag time. Study Treatment Start Date ≤ AE Start Date ≤ Study Treatment Stop Date + 6 days
Post-Treatment	If AE onset date is after the treatment stop date with 6 days lag time. AE Start Date > Study Treatment Stop Date + 6 days
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 eCRF OR value is missing.

NOTES:

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

10.3. 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[1]	Order [2]
1	A	DTG conventional 10 mg tablets (5 tablets) administered direct to mouth (test)	Treatment A	1
1	B	DTG conventional 50 mg tablet administered direct to mouth (reference)	Treatment B	2
2	C	DTG dispersible 5-mg tablets (5 tablets) administered as a dispersion and immediately taken (test 1)	Treatment C	3
2	D	DTG dispersible 5-mg tablets (5 tablets) administered direct to mouth (test 2)	Treatment D	4
2	E	DTG conventional 25 mg tablet administered direct to mouth (reference)	Treatment E	5

NOTES:

1. The word "Treatment" may be omitted from displays in order to limit wrapping
2. Order represents treatments being presented in TFL, as appropriate.

10.3.2. Baseline Definition & Derivations

10.3.2.1. Baseline Definitions

For all endpoints (except as noted in baseline definitions) the baseline value will be the latest pre-dose assessment. Baseline definitions are applicable to each period.

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

NOTES :

Parameter	Study Assessments Considered As Baseline			Baseline Used in Data Display
	Screening	Day -1	Day 1 (Pre-Dose)	

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

10.3.2.2. Derivations and Handling of Missing Baseline Data

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

NOTES :

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

10.3.3. Reporting Process & Standards

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

Reporting Standards
General
• The current GSK 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 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 Standards	

• Reporting for tables, figures and formal statistical analyses :
  • Planned time relative to dosing will be used in figures, summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated.
  • The impact of any major deviation from the planned assessment times and/or scheduled visit days on the analyses and interpretation of the results will be assessed as appropriate.
• Reporting for Data Listings:
  • Planned and actual time relative to study drug dosing will be shown in listings (Refer to IDSL Statistical Principle 5.05.1).
  • Unscheduled or unplanned readings will be presented within the subject's listings.
  • Visits outside the protocol defined time-windows (i.e. recorded as protocol deviations) will be included in listings but omitted from figures, summaries and statistical analyses.	

Unscheduled Visits	
• Unscheduled visits will not be included in summary tables. • Unscheduled visits will not be included in figures. • All unscheduled visits will be included in listings.	
Descriptive Summary Statistics	

Continuous Data	Refer to IDSL Statistical Principle 6.06.1
	• NQs at the beginning of a subject 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 subject 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 subject 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).

Categorical Data	N (number of subjects in subgroup), n (number of subjects with evaluable data), 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	

Reporting Standards	
Descriptive Summary Statistics (Ln-Transformed)	N (number of subjects in subgroup), n (number of subjects with evaluable data), 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 ln-transformed data)
Parameters Not Being Ln-Transformed	tmax, tlag, first point, last point, and number of points used in the determination of λz, %AUCex.
Summary Tables	The following PK parameters will not be summarised: first point, last point, and number of points used in the determination of λz
Listings	Include the first point, last point and number of points used in the determination of λz.
Graphical Displays	
• Refer to IDSL Statistical Principals 7.01 to 7.13.	

10.4. Appendix 4: Derived and Transformed Data

10.4.1. General

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

• Calculated as the number of days from 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

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: o 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

ECG Parameters
RR Interval
• IF RR interval (msec) is not provided directly, then RR can be derived as : [1] If QTcB is machine read & QTcF is not provided, then : $$RR = \left[\left(\frac{QT}{QTcB}\right)^{2}\right] * 1000$$ [2] If QTcF is machine read and QTcB is not provided, then: $$RR = \left[\left(\frac{QT}{QTcF}\right)^{3}\right] * 1000$$ • If ECGs are manually read, the RR value preceding the measurement QT interval should be a collected value THEN do not derive.

ECG Parameters
• 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 Fredericia's (QTcF) formulas will be calculated, in msec, depending on the availability of other measurements. • IF RR interval (msec) is provided then missing QTcB and/or QTcF will be derived as : $QTcB = \frac{QT}{\sqrt{\frac{RR}{1000}}}$ $QTcF = \frac{QT}{\sqrt[3]{\frac{RR}{1000}}}$

AEs
AEs OF Special Interest
• Hypersensitivity reaction (HSR) and rash • Liver Events • Renal Function • Creatine Phosphokinase (CPK) elevations

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

10.5.1. Premature Withdrawals

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

10.5.2. Handling of Missing Data

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

10.5.2.1. Handling of Missing Dates

Element	Reporting Detail
General	Partial dates will be displayed as captured in subject listing displays.
AEs	• The eCRF allows for the possibility of partial dates (i.e., only month and year) to be recorded for AE start and end dates; that is, the day of the month may be missing. In such a case, the following conventions will be applied for calculating the time to onset and the duration of the event: o Missing Start Day: First of the month will be used unless this is before the start date of study treatment; in this case the study treatment start date will be used and hence the event is considered On-treatment as per Appendix 2: Treatment States and Phases. o Missing Stop Day: Last day of the month will be used, unless this is after the stop date of study treatment; in this case the study treatment stop date will be used. • Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing.

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

10.5.2.2. Handling of Partial Dates

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

Element	Reporting Detail

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	msec	> 450[1]	
		> 450[2]	≤ 479[2]
		≥ 480[2]	≤ 499[2]
		≥ 500[2]	
Absolute PR Interval	msec	< 110[1]	> 220[1]
Absolute QRS Interval	msec	< 75[1]	> 110[1]
Change from Baseline			
Increase from Baseline QTc	msec	≤ 30[2]	
	msec	> 30[2]	≤ 59[2]
	msec	≥ 60[1]	

NOTES:

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

10.6.2. Vital Signs

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

10.7. Appendix 7: Multiple Comparisons & Multiplicity

10.7.1. Handling of Multiple Comparisons & Multiplicity

No adjustments for multiplicity will be made.

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

10.8.1. Statistical Analysis Assumptions

Endpoint(s)	• PK endpoints AUC(0-∞), AUC(0-t) and Cmax
Analysis	• Mixed Effects

Assumptions:

- Model assumptions will be applied, but appropriate adjustments may be made based on the data.
- The Kenward and Roger method for approximating the denominator degrees of freedom and correcting for bias in the estimated variance-covariance of the fixed effects will be used.

10.9. Appendix 9 – Abbreviations & Trade Marks

10.9.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
AUC(0-t)	Area under the concentration-time curve (AUC) from time 0 (predose) to time of the last quantifiable concentration
AUC0-24	Area under the concentration-time curve (AUC) over time 0 (predose) to 24 hours after dose administration
AUC(0-∞)	Area under the concentration-time curve from time 0 (predose) extrapolated to infinite time
%AUCex	The percentage of AUC(0-∞) obtained by extrapolation
BA	Bioavailability
BMI	Body Mass Index
C24	The observed concentration at 24 hours after dose administration
CDISC	Clinical Data Interchange Standards Consortium
CL/F	The apparent oral clearance
Cmax	Maximum observed concentration
CI	Confidence Interval
CPK	Creatine Phosphokinase
Ct	The last observed quantifiable concentration
CV_b	Coefficient of Variation (Between)
DAIDS	Division of Acquired Immune Deficiency Syndrome
DTG	Dolutegravir
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
GSK	GlaxoSmithKline
HSR	Hypersensitivity reaction
ICH	International Conference on Harmonisation
IDSL	Integrated Data Standards Library
kg	Kilograms
m	Meters
mg	Milligrams
msec	Milliseconds
PK	Pharmacokinetic
QTcF	Fridericia's QT Interval Corrected for Heart Rate
QTcB	Bazett's QT Interval Corrected for Heart Rate
R&D	Research and Development
RAP	Reporting & Analysis Plan
SAC	Statistical Analysis Complete
SAS	Statistical Analysis Software
SD	Standard deviation
SDTM	Study Data Tabulation Model
TFL	Tables, Figures & Listings

Abbreviation	Description
t½	Terminal phase half-life
tlag	Lag time before observation of drug concentrations in sampled matrix
tmax	Time to first occurrence of Cmax
Vz/F	The apparent volume of distribution during the terminal phase
λz	Terminal-phase rate constant

10.9.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
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Phoenix WinNonlin
SAS

10.10. Appendix 10: List of Data Displays

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.8	NA
Safety	2.1 to 2.9	NA
Pharmacokinetic	3.1 to 3.5	3.1 to 3.7
Exploratory (Palatability)	4.1	NA
Section	**Listings**	
ICH Listings	1 to 38	

10.10.1. 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
Exploratory (Palatability)	EXP_Fn	EXP_Tn	EXP_Ln

NOTES:

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

10.10.2. Deliverable [Priority]

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

NOTES:

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

10.10.3. 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	All Subjects	NS1	Summary of Number of Subjects Enrolled by Country and Site ID		SAC [1]
1.2	All Subjects	ES1	Summary of Subject Disposition		SAC [1]
1.3	Screened	ES6	Summary of Reasons for Screening Failures		SAC [1]
1.4	Screened	DV1	Summary of Important Protocol Deviations		SAC [1]
Demographics					
1.5	All Subjects	DM1	Summary of Demographic Characteristics		SAC [1]
1.6	All Subjects	DM5	Summary of Race and Racial Combinations		SAC [1]
1.7	All Subjects	DM6	Summary of Race and Racial Combinations Details		SAC [1]
1.8	All Subjects	DM11	Summary of Age Ranges		SAC[1]

10.10.4. Safety Tables

Safety : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
AEs					
2.1	All Subjects	AE1	Summary of All Adverse Events		SAC [1]
2.2	All Subjects	AE1	Summary of All Drug-Related Adverse Events		SAC [1]
2.3	All Subjects	AE15	Summary of Common (>=5%) Non-serious Adverse Events by System Organ Class and Preferred Term		SAC [1]
2.4	All Subjects	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term		SAC[1]
Laboratory Values					
2.5	All Subjects	LB1	Summary of Clinical Chemistry Values Change from Baseline		SAC [1]
2.6	All Subjects	LB1	Summary of Haematology Values Change from Baseline		SAC [1]
2.7	All Subjects	UR3	Summary of Urinalysis Dipstick Results		SAC [1]
Electrocardiograms					
2.8	All Subjects	EG1	Summary of ECG Findings		SAC [1]
Vital Signs					
2.9	All Subjects	VS1	Summary of Change from Baseline in Vital Signs		SAC[1]

10.10.5. Pharmacokinetic Tables

Pharmacokinetic : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK Concentration Data					
3.1	PK	PKCT1	Summary of DTG Plasma Pharmacokinetic Concentration-Time Data by Study Part and Treatment		SAC [1]
PK Derived Parameters					
3.2	PK	PKPT4	Summary of Derived DTG Plasma Pharmacokinetic Parameters (Non-Transformed) by Study Part and Treatment	Parameters with units	SAC [1]
3.3	PK	PKPT4	Summary of Derived DTG Plasma Pharmacokinetic Parameters (Ln-Transformed) by Study Part and Treatment	Parameters with units	SAC [1]
PK Analysis Tables					
3.4	PK	PKPT3	Statistical Analysis of DTG Plasma Pharmacokinetic Parameters, Study Part 1	AUC(0-t), AUC(0-∞), and Cmax only by Treatment. Part 1 only.	SAC [1]
3.5	PK	PKPT3	Statistical Analysis of DTG Plasma Pharmacokinetic Parameters, Study Part 2	AUC(0-t), AUC(0-∞), and Cmax only by Treatment. Part 2 only.	SAC [1]

10.10.6. Pharmacokinetic Figures

Pharmacokinetic : Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Individual Concentration Plots					
3.1	PK	PKCF1X	Individual DTG Plasma Concentration-Time Plots by Subject (Linear and Semi-Logarithmic)	Paginate by Subject	SAC [1]
Mean / Median Concentration Plots					
3.2	PK	PKCF2	Mean DTG Plasma Concentration-Time Plots by Treatment (Linear and Semi-Logarithmic)	All treatments for each Part on one page	SAC [1]
3.3	PK	PKCF3	Median DTG Plasma Concentration-Time Plots by Treatment (Linear and Semi-Logarithmic)	All treatments for each Part on one page	SAC [1]
PK Analysis Plots					
3.4	PK	PKPF3	Comparative Plot of Individual DTG Plasma Cmax by Treatment (Linear and Semi-Logarithmic)	All treatments for each Part on one page	SAC [1]
3.5	PK	PKPF3	Comparative Plot of Individual DTG Plasma AUC(0-t) by Treatment (Linear and Semi-Logarithmic)	All treatments for each Part on one page	SAC [1]
3.6	PK	PKPF3	Comparative Plot of Individual DTG Plasma AUC(0-∞) by Treatment (Linear and Semi-Logarithmic)	All treatments for each Part on one page	SAC [1]
3.7	PK	PKPF3	Comparative Plot of Individual DTG Plasma C24 by Treatment (Linear and Semi-Logarithmic)	All treatments for each Part on one page	SAC [1]

10.10.7. Exploratory Tables

Exploratory : Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Palatability					
4.1	All Subjects	EXP_T1	Summary of Palatability Questionnaire Results (Part 2, Treatment C Only)		SAC[1]

10.10.8. ICH Listings

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Randomisation					
1	All Subjects	CP_TA1	Listing of Randomised and Actual Treatment		SAC [1]
Subject Disposition					
2	All Subjects	ES2	Listing of Reasons for Study Withdrawal		SAC [1]
3	Screened	ES7	Listing of Reasons for Screening Failure		SAC [1]
4	Screened	DV2	Listing of Important Protocol Deviations		SAC [1]
5	All Subjects	IE4	Listing of Subjects with Inclusion/Exclusion Criteria Deviations		SAC[1]
6	Screened	SP3	Listing of Subjects Excluded from Any Population		SAC [1]
Demographics					
7	All Subjects	DM4	Listing of Demographic Characteristics		SAC [1]
8	All Subjects	DM10	Listing of Race		SAC [1]

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Concomitant Medications					
9	All Subjects	CM4	Listing of Concomitant Medications		SAC[1]
Exposure					
10	All Subjects	SAFE_L1	Listing of Exposure Data		SAC[1]
AEs					
11	All Subjects	AE2	Listing of Relationship Between System Organ Class and Verbatim Text		SAC[1]
12	All Subjects	AE7	Listing of Subject Numbers for Individual Adverse Events		SAC[1]
13	All Subjects	AE9CP	Listing of All Adverse Events		SAC[1]
14	All Subjects	AE9CP	Listing of Study Drug Related Adverse Events		SAC[1]
15	All Subjects	SAFE_L2	Listing of Serious Adverse Events		SAC[1]
16	All Subjects	AE9CP	Listing of Adverse Events Leading to Withdrawal from Study Drug		SAC[1]
17	All Subjects	SAFE_L3	Listing of Liver Adverse Events		SAC[1]

ICH : Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Laboratory Values					
18	All Subjects	LB6	Listing of Clinical Chemistry Toxicities of Grade 2 or Higher		SAC [1]
19	All Subjects	LB6	Listing of All Clinical Chemistry Data for Subjects with Toxicities of Grade 2 or Higher		SAC [1]
20	All Subjects	LB6	Listing of Haematology Toxicities of Grade 2 or Higher		SAC [1]
21	All Subjects	LB6	Listing of All Haematology Data for Subjects with Toxicities of Grade 2 or Higher		SAC [1]
22	All Subjects	LB6	Listing of Urinalysis Toxicities of Grade 2 or Higher		SAC [1]
23	All Subjects	LB6	Listing of All Urinalysis Data for Subjects with Toxicities of Grade 2 or Higher		SAC [1]
Electrocardiograms					
24	All Subjects	EG6	Listing of Abnormal ECG Findings		SAC [1]
25	All Subjects	EG6	Listing of All ECG Findings for Subjects with an Abnormal Finding		SAC [1]
26	All Subjects	EG4	Listing of ECG Values of Potential Clinical Importance		SAC [1]
27	All Subjects	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					
28	All Subjects	VS5	Listing of Vital Signs of Potential Clinical Importance		SAC [1]
29	All Subjects	VS5	Listing of All Vital Signs for Subjects with Potential Clinical Importance Values		SAC [1]
Liver Event					
30	All Subjects	LIVER5	Listing of Liver Monitoring/Stopping Event Reporting		SAC[1]
31	All Subjects	MH3	Listing of Medical Conditions for Subjects with Liver Stopping Events		SAC[1]
32	All Subjects	SAFE_L5	Listing of Alcohol Intake at Onset of Liver Event		SAC[1]
33	All Subjects	PKCL1X	Listing of Plasma Concentration Data for Subjects with Liver Stopping Events		SAC[1]
34	All Subjects	LIVER7	Listing of Liver Biopsy Details		SAC[1]
35	All Subjects	LIVER8	Listing of Liver Imaging Details		SAC[1]
Pharmacokinetic					
36	PK	PKCL1X	Listing of DTG Plasma Pharmacokinetic Concentration-Time Data by Treatment	Please list all the concentration data including unscheduled. Repeat for all treatments and Parts.	SAC [1]
37	PK	PKPL1X	Listing of Derived DTG Plasma Pharmacokinetic Parameters by Treatment	Repeat for all treatments and Parts.	SAC [1]
Exploratory					
38	All Subjects	EXP_L1	Listing of Palatability Questionnaire Results (Part 2, Treatment C Only)		SAC[1]