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

Title	:	Reporting and Analysis Plan for 206243, A Prospective, Longitudinal Study to Investigate the Effect of Thermal Injury on Intestinal Permeability and Systemic Inflammation (HESTIA).
Compound Number	:	No Compound
Effective Date	:	27-NOV-2018

Description:

- The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 206243.
- This RAP is intended to describe the planned safety and Biomarker 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) deliverables.

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1. SUMMARY OF KEY PROTOCOL INFORMATION

1.1. Changes to the Protocol Defined Statistical Analysis Plan

This study was terminated prior to the full sample size being achieved. As a result the initially planned sample size of 25 for the thermally injured subjects is greatly reduced to 3 . Changes from the originally planned statistical analysis specified in the protocol (Dated:26SEP2017) are outlined in Table 1.

Table 1 Changes to Protocol Defined Analysis Plan

Protocol	Reporting & Analysis Plan	
Statistical Analysis Plan	**Statistical Analysis Plan**	**Rationale for Changes**
• Co -Primary Objective 1: To determine the impact of thermal injury on the magnitude of small intestinal permeability change as soon as possible following injury compared to healthy participants.	• Summary statistics for Lactulose/Mannitol (L/M) ratio at entry will be provided. No formal stats analysis for comparing the groups.	• No stats analysis due to limited sample size.
• Exploratory objective 1: Comparison of Fractional excretion of sucralose of TI participants with Healthy participants at baseline	• Only summary will be provided. No formal stats analysis for comparing the groups.	• No stats analysis due to limited sample size.
• Exploratory objective 3: • Number of ventilator-free days, vasopressor-free days, hemofiltration-free days, episodes of confirmed infection and sepsis, surgical interventions • Total length of hospital stay • Calculate critical care and thermal injury severity scores	• None of the endpoints will be analysed for final reporting.	• Due to limited sample size, these endpoints will not be analysed. • Where relevant, these will be described using data from the SIFTI2 CRF in CSR.
• Exploratory objective 4: • Change in urine protein: creatinine and urine albumin: creatinine ratios	• This endpoint will not be analysed.	• The reason for collecting these data was to inform a pharmacokinetic model. As development of the molecule has been terminated, this model is no longer required, moreover data collected are so limited that analysis is not possible.
• Exploratory objective 5: Changes in microbiome of acute and convalescent stool samples	• This endpoint is not considered for final analysis.	• Only one stool sample has been collected from a TI patient thus no meaningful comparison is possible.
• Exploratory objective 7: Time to wound recovery	• This endpoint will not be analysis but will be listed.	• Sufficient data not available to perform the analysis.
• Exploratory objective 8: • Determine fluid input/output balance	• These endpoints are not considered for final	• Sufficient data not available to perform the analysis.

Protocol	Reporting & Analysis Plan	
Statistical Analysis Plan	**Statistical Analysis Plan**	**Rationale for Changes**
over time • Changes in serum albumin and plasma creatinine	analysis.	
• Exploratory objective 9: • Changes in intestinal microbiome • Bacterial markers of translocation	• No microbiome data analysis • Bacterial markers of translocation will be summarised.	• Insufficient stool samples have been collected for correlative analyses in TI participants.

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

1.2.1. Protocol Defined Objectives and Endpoints

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To determine the impact of thermal injury on the magnitude of small intestinal permeability change as soon as possible following injury compared to healthy participants	• Lactulose/Mannitol (L/M) ratio at entry
• To characterise the effect of thermal injury on small intestinal permeability over time and establish the clinical and demographic factors which can influence it	• Changes in L/M ratio over time
Exploratory Objectives	**Exploratory Endpoints**
• To determine the impact of thermal injury on colonic permeability as soon as possible following injury compared to healthy participants	• Fractional excretion of sucralose at entry
• To characterise the effect of thermal injury on colonic permeability over time	• Changes in the fractional excretion of sucralose over time
• To assess the relationship between severity of a participant's condition following thermal injury and changes in intestinal permeability	• Number of ventilator-free days • Number of vasopressor-free days • Number of hemofiltration-free days • Number of episodes of confirmed infection and sepsis • Number of surgical interventions • Total length of hospital stay • Calculate critical care and thermal injury severity scores
• To assess plasma and urine biomarkers of intestinal permeability, bacterial translocation and renal tubular dysfunction following thermal injury	• Change in markers of intestinal mucosal damage samples from blood • Change in urine protein: creatinine and urine albumin: creatinine ratios
• To assess the impact of thermal injury and intestinal permeability on the intestinal microbiome compared	• Changes in microbiome of acute and

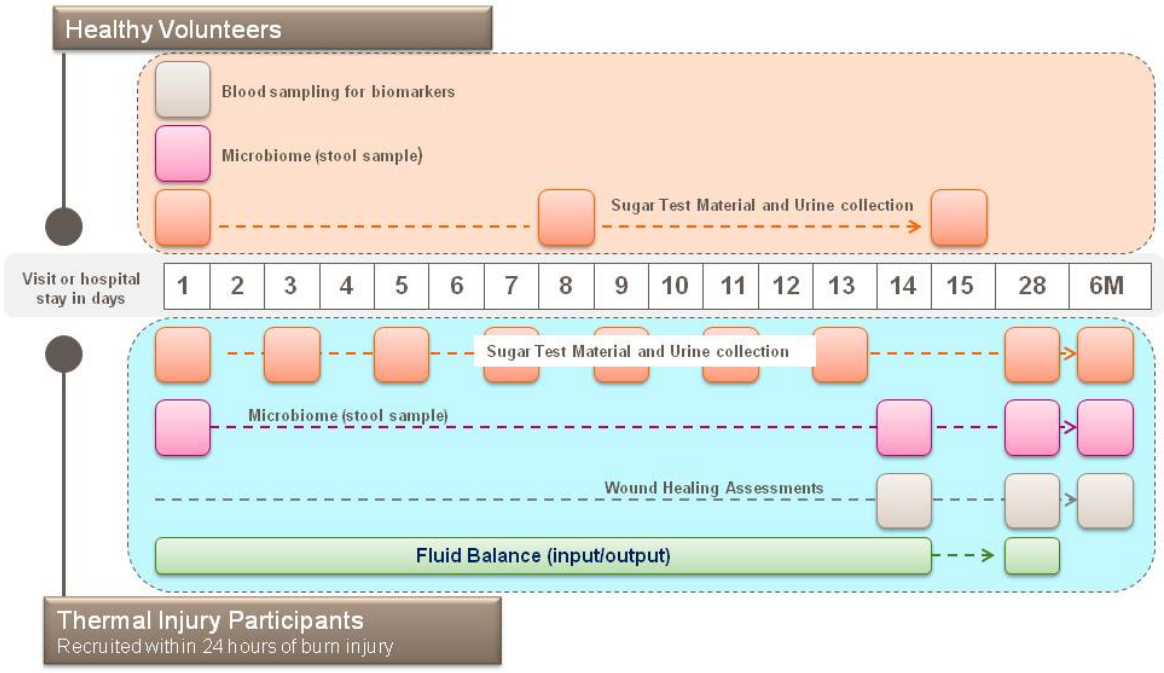
Objectives	Endpoints
to healthy participants	convalescent stool samples
• To assess the impact of pre-existing co-morbid conditions on intestinal permeability and clinical outcome following thermal injury	• Medical history and drug history at the time of admission
• To assess wound healing	• Time to wound recovery (e.g. 95%)
• To characterise parameters that may influence drug PK/PD	• Determine fluid input/output balance over time • Changes in serum albumin and plasma creatinine
• To characterise intestinal microbiota, and correlate its composition with both intestinal permeability and bacterial detection in blood	• Changes in intestinal microbiome • Bacterial markers of translocation

1.2.2. Final Reporting Objectives & Endpoints Following Study Termination

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To determine the impact of thermal injury on the magnitude of small intestinal permeability change as soon as possible following injury compared to healthy participants	• Lactulose/Mannitol (L/M) ratio at entry
• To characterise the effect of thermal injury on small intestinal permeability over time and establish the clinical and demographic factors which can influence it	• Changes in L/M ratio over time
Exploratory Objectives	**Exploratory Endpoints**
• To determine the impact of thermal injury on colonic permeability as soon as possible following injury compared to healthy participants	• Fractional excretion of sucralose at entry
• To characterise the effect of thermal injury on colonic permeability over time	• Changes in the fractional excretion of sucralose over time
• To assess plasma and urine biomarkers of intestinal permeability and bacterial translocation	• Change in markers of intestinal mucosal damage samples from blood • Change in bacterial markers of translocation
• To assess the impact of pre-existing co-morbid conditions on intestinal permeability and clinical outcome following thermal injury	• Medical history and drug history at the time of admission

1.3. Study Design

Overview of Study Design and Key Features



Design Features	• Longitudinal, prospective study of healthy participants and participants who have sustained a thermal injury.
Dosing	• Not applicable
Time & Events	• Refer to Appendix 1: Schedule of Activities
Treatment Assignment	• All the participants receive STM (comprising lactulose, mannitol and sucralose).
Interim Analysis	• Not applicable
Final Analysis	• Final analysis is planned for subjects who had enrolled into the study prior to the termination of the study.

Note: The above design was prior to study termination. The study was terminated before any subjects had reached day 28. Hence, later visits are not included in the analysis.

1.4. Statistical Hypotheses / Statistical Analyses

- No formal hypothesis testing is planned.
- The key factors of interest in this study were to understand (i) the nature of any differences at entry in intestinal permeability between healthy participants and thermal injury participants (ii) to understand the trajectory of changes in intestinal permeability over time.

2. PLANNED ANALYSES

2.1. Interim Analyses

No formal interim analysis will be performed.

2.2. Final Analyses

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

1. All subjects have completed Day 28 assessments or have withdrawn from the study.
2. All required database cleaning activities have been completed and final database release and database freeze has been declared by Data Management.
3. All protocol deviations have been confirmed.
4. Analysis population exclusions have been confirmed.
5. Database freeze has been declared by Data Management.

3. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
Screened	• All participants who were screened for eligibility	• Study Population • All Listings
Safety	• Comprise of all participants who receive at least one dose of STM and have at least one post-dose safety assessment.	• Safety
Evaluable	• Comprises of all participants in the safety population excluding any healthy volunteers that received any concomitant medication or food and drink containing STM (lactulose, mannitol and sucralose), as identified by review of the protocol deviations.	• Efficacy • Biomarker • Study Population

NOTES:

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

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

Prospective approval of protocol deviations to recruitment and enrolment criteria, also known as protocol waivers or exemptions, is not permitted.

4. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

Table 2 provides an overview of appendices within the RAP for outlining general considerations for data analyses and data handling conventions.

Table 2 Overview of Appendices

Section	Component
10.1	Appendix 1: Time & Events
10.2	Appendix 2: Assessment Windows
10.3	Appendix 3: Study Phases and Treatment Emergent Adverse Events
10.4	Appendix 4: Data Display Standards & Handling Conventions
10.5	Appendix 5: Derived and Transformed Data
10.6	Appendix 6: Reporting Standards for Missing Data
10.7	Appendix 7: Abbreviations & Trade Marks
10.8	Appendix 8: List of Data Displays
10.9	Appendix 9: Example Mock Shells for Data Displays

4.1. General Considerations

- This is a longitudinal, prospective study of healthy participants and participants who have sustained thermal injury.

Unless otherwise stated, the following rules will apply:

- Summaries and displays will be presented by study group and visit (without the group information in visit).
- The following statistics will be used to summarise the data, unless otherwise specified:
    - Continuous Variables: number of observations (n), mean, standard deviation (SD), standard error (SE), median, minimum and maximum.
    - Categorical Variables: number of observations (n), frequency counts and percentages.
- Summaries by Visit: Only scheduled visits will be presented, unless otherwise stated. Unscheduled visits will be listed but will not contribute towards any summary statistics/analyses, unless otherwise stated.
- Summaries by study group: Study group (Healthy Participants and TI Participants) will be used instead of treatment group in all the tables and listing.
- No imputation will be done for missing values across visits, individual missing scores will be considered missing.

4.2. Baseline Definitions

For efficacy and biomarker endpoints, the baseline value will be Day 1 for both the groups. In case of missing Day 1 assessment, baseline would be set to missing.

Parameter	Study Assessments Considered as Baseline		Baseline Used in Data Display
	Screening [1]	Day 1 (Baseline)	
Efficacy Assessments			
L/M Ratio		X	Day 1 (Baseline)
Fractional excretion of sucralose		X	Day 1 (Baseline)
Biomarkers Assessments			
Markers of intestinal mucosal damage		X	Day 1 (Baseline)
Bacterial markers of translocation		X	Day 1 (Baseline)
Safety Assessments			
Vital Signs	X		Screening
Laboratory Assessments			
Haematology	X		Screening
Clinical Chemistry	X		Screening
Routine Urinalysis	X		Screening
[1] Screening = 1-2 Wks Prior to Day 1 (Healthy Participants).			

4.2.1. Derivations and Handling of Missing Baseline Data

For untransformed data, change from baseline at each time point is expressed as a difference (value at time point – value at baseline).

Definition	Reporting Details
Change from Baseline [1]	= Post-Baseline Visit Value – Baseline Value
% Change from Baseline [1]	= 100 x [(Post-Baseline Visit Value – Baseline Value) / Baseline Value]
[1] If the baseline value is missing the change from baseline derivations will also be missing	

5. STUDY POPULATION ANALYSES

5.1. Overview of Planned Study Population Analyses

- The Study Population analyses will be based on the Screened, Evaluable or Safety population, as appropriate unless otherwise specified.

Study population analyses including analyses of subject's disposition, 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 8: List of Data Displays.

6. EFFICACY ANALYSES

6.1. Primary Analyses

6.1.1. Endpoint / Variables

- Lactulose/mannitol ratio

6.1.2. Summary Measure

The administration of the STM is for the purpose of intestinal permeability measurement and is not therapeutic, therefore no efficacy will be assessed.

Absolute, change and % change in lactulose/mannitol ratio values will be used for analysis.

6.1.3. Population of Interest

The primary analyses will be based on the evaluable population, unless otherwise specified.

6.1.4. Statistical Analyses / Methods

Endpoints defined in Section 6.1.1 will be summarised by study group, timepoint and visit. Data will summarise mean, standard deviation, standard error, minimum, median, maximum and N.

No formal statistical analysis will be performed.

6.2. Exploratory Analyses

6.2.1. Endpoint / Variables

- Fractional excretion of sucralose

6.2.2. Summary Measure

- Absolute, Change and %Change in the fractional excretion of sucralose over

time.

6.2.3. Population of Interest

The exploratory efficacy analyses will be based on the evaluable population, unless otherwise specified.

6.2.3.1. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 9: List of Data Displays and will be based on GSK data standards and statistical principles.

Unless otherwise specified, endpoints defined in Section 6.2.1 will be summarised using descriptive statistics and listed.

6.2.3.2. Statistical Methodology Specification

There will be no planned statistical analysis.

7. SAFETY ANALYSES

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

7.1. Adverse Events Analyses

Adverse events analyses including the analysis of adverse events (AEs), Serious (SAEs) and other significant AEs will be based on GSK Core Data Standards. The details of the planned displays are provided in Appendix 8: List of Data Displays.

NOTE: As detailed in Section 9.2.1 of the protocol, only AEs deemed to be related to procedures or requirements unique to the HESTIA study will be recorded/reported for thermally injured participants. All other AEs will be recorded/reported through the SIFTI-2 study.

Also, as given in Section 12.4 (Events NOT Meeting the AE Definition) in protocol, any clinically significant abnormal laboratory findings or other abnormal safety assessments which are associated with the underlying disease, unless judged by the investigator to be more severe than expected for the participant's condition will be considered as disease related event. Table 3 in protocol provides a list of commonly occurring AEs in participants with severe thermal injury which may meet this definition and will be entered as disease related events.

7.2. Clinical Laboratory Analyses

Laboratory evaluations including the analyses of Chemistry laboratory tests, Hematology laboratory tests and Urinalysis will be based on GSK Core Data Standards. The details of the planned displays are in Appendix 8: List of Data Displays.

Table 3 Protocol-Required Safety Laboratory Assessments for Healthy Participants:

<table>
<tr><th>Laboratory Assessments</th><th colspan="4">Parameters</th></tr>
<tr><td rowspan="4">Hematology</td><td colspan="2">Platelet Count</td><td colspan="2" rowspan="4">WBC count with Differential:
Neutrophils
Lymphocytes
Monocytes
Eosinophils
Basophils</td></tr>
<tr><td colspan="2">RBC Count</td></tr>
<tr><td colspan="2">Hemoglobin</td></tr>
<tr><td colspan="2">Hematocrit</td></tr>
<tr><td rowspan="3">Clinical Chemistry</td><td>Urea</td><td>Potassium</td><td></td><td>Total bilirubin</td></tr>
<tr><td>Creatinine</td><td>Sodium</td><td>Alanine Aminotransferase (ALT)</td><td>Total Protein</td></tr>
<tr><td>Glucose non-fasting</td><td>Calcium</td><td>Alkaline phosphatase</td><td></td></tr>
<tr><td>Routine Urinalysis</td><td colspan="4">• pH, glucose, protein, blood, ketones by dipstick
• Microscopic examination (if blood or protein is abnormal)</td></tr>
</table>

7.3. Other Safety Analyses

The analyses of non-laboratory safety test results including vital signs will be based on GSK Core Data Standards, unless otherwise specified. The details of the planned displays are presented in Appendix 8: List of Data Displays.

8. BIOMARKER ANALYSES

8.1. Exploratory Biomarker Analyses

8.1.1. Endpoint / Variables

As this is an exploratory study, a number of data presentations will be produced for a set of biomarkers to understand how they change over time. In order to simplify the investigation, the biomarkers will be grouped into biomarkers of intestinal damage and bactorial markers of translocation. All endpoints will be summarised by mean, standard deviation, standard error, median, minimum, maximum and number of subjects, by study group. These groupings of biomarkers are provided in Table 4.

Table 4 List of biomarkers considered for final analysis

Biomarker Grouping	Parameters
Markers of intestinal mucosal damage	iFABP, citrulline, Zonulin-1, Occludin
Bacterial markers of translocation	sCD14, Microbial Metabolites: (Glycodeoxycholic acid, Taurodeoxycholic acid, Taurocholic acid, Taurolithocholic acid, Oxocholic acid, Ursodeoxycholic acid)

8.1.2. Summary Measure

- Change in markers of intestinal mucosal damage samples from blood.
- Changes in Bacterial markers of translocation.

8.1.3. Population of Interest

The exploratory efficacy analyses will be based on the evaluable population, unless otherwise specified.

8.1.3.1. Statistical Analyses / Methods

Unless otherwise specified, endpoints defined in Section 8.1.1 will be summarised using descriptive statistics and listed.

Details of the planned displays are provided in Appendix 8: List of Data Displays and will be based on GSK data standards and statistical principles.

8.1.3.2. Statistical Methodology Specification

There will be no planned statistical analysis.

9. REFERENCES

GlaxoSmithKline Document Number 2016N289648_02, Study ID 206243/02, A Prospective, Longitudinal Study to Investigate the Effect of Thermal Injury on Intestinal Permeability and Systemic Inflammation (HESTIA). Effective Date: 26-SEP-2017.

10. APPENDICES

10.1. Appendix 1: Schedule of Activities

10.1.1. Protocol Defined Schedule of Events

Healthy Participants (Group 1)

Procedure	Screening	Treatment Period [Out patient days] (± 1 day)			Notes
		D1	D8	D15	
Review of inclusion/ exclusion criteria and informed consent	X				
Demography	X				
Medical history (includes substance and alcohol usage at screening) and Medication history	X				
Substance testing (urine)	X				Substances: [Recreational Drugs and Alcohol]
HIV, Hepatitis B and C screening	X				If test otherwise performed within 3 months prior to study entry, testing is not required
Laboratory assessments	X				
Pregnancy test (WOCBP only) (urine)	X	(X)			Only performed again on Day 1 if patient at risk of pregnancy at or since screening
Blood sampling for biomarkers		X			20ml of blood will be sampled in a single draw on one day, preferably Day 1
Stool sample collection		X			Participants will be given a collection container at screening to bring with them on Day 1.
Brief physical examination including measurements of height and weight Vital Signs (systolic and diastolic blood pressure and heart rate)	X	X	X	X	BMI calculated from height and weight at screening only Examinations should be conducted the day after intestinal permeability measurement.
Medical review (assessment of health status)		X	X	X	Monitor for signs and symptoms of gastro-intestinal infections and other emergent issues

Procedure	Screening	Treatment Period [Out patient days] (± 1 day)			Notes
		D1	D8	D15	
STM Training	X				Refresher training may be provided as needed
Intestinal permeability measurement: STM administration followed by a 24-hour urine collection		X	X	X	Please refer to SRM for full information Intestinal permeability measurement to be performed at home the day before the study visit.
AE/SAE and Concomitant medication reviews	(X)	←==========→			Day 1 will include concomitant medication review only

Thermal Injury Participants (Group 2)

Procedure	D1 (≤ 24 hr of admission)	Treatment Period [ICU Days] (+/4 hours)													6 mon (± 14 days)	Notes
		D2	D3	D4	D5	D6	D7	D8	D9	D 10	D 11	D 12	D 13	D 14	D28 (± 3 days)	
Review of inclusion/ exclusion criteria and informed consent	X															Participants will be co-consented to the SIFTI-2 study
Medical history (includes substance and alcohol usage) and Medication history	X															
Substance testing (urine)	X															Substances: [Recreational Drugs, Alcohol]
Pregnancy test (WOCBP only) (urine)	X														X	To be repeated at 6 months prior to final STM administration
HIV, Hepatitis B and C screening	X															If test otherwise performed within 3 months prior to study entry, testing is not required
Initial assessment of Burns	X															Calculation of %TBSA Location of thermal injury and depth
Fluid balance (total input/output)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X*	Daily (over 24 hr) *only if participant still admitted
Intestinal permeability measurement: STM administration followed by a 24-hour urine collection	X		X		X		X		X		X		X		X	X	Measurements every 48 hours from first measure. Preference: D1, 3, 5, 7, 9, 11, 13. Otherwise: D2, 4, 6, 8, 10, 12, 14. Please refer to SRM for full method.

Brief Physical Examination														X	X	Following final intestinal permeability measurement. Can be omitted if patient is still admitted to hospital.
Stool sample collection	←==========→ (A sample of the first stool produced following admission)												X	X	X	Time to first stool collection; preferably on Day 1. Then on Days 14 and 28 and 6 months
Wound Healing Assessments													X	X	X	This is to assess time to 95% wound healing
AE/SAE and Concomitant medication reviews	X	←==========→													X	AE/SAE monitoring will begin after the first administration of STM

Planned time points for all safety assessments are provided in the SoA and summarised here.

Safety Assessment	**When conducted**	
	Healthy Participants	**Thermally injured participants**
Laboratory tests	Screening. Only repeated if clinically indicated in the opinion of the investigator.	Only if clinically indicated.
Brief Physical Examination including Vital Signs Recording	Screening, Day 1, Day 8, Day 15	As a part of routine clinical care whilst admitted (not protocol specified). Following day 28 and 6-month intestinal permeability measurements (if patient not still admitted)
Detection of AEs	Day 1, Day 8, Day 15	Throughout the study
Assessment of health status	Screening, Day 1, Day 8, Day 15	Not required

10.2. Appendix 2: Assessment Windows

No visit slotting will be done.

10.3. Appendix 3: Study Phases and Treatment Emergent Adverse Events

10.3.1. Study Phases

10.3.1.1. Study Phases for Concomitant Medication

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

NOTES:

- Please refer to Appendix 6: 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.

10.4. Appendix 4: Data Display Standards & Handling Conventions

10.4.1. Reporting Process

Software	
• The currently supported versions of SAS software 9.4 or higher will be used.	
Reporting Area	
HARP Server	: Uk1salx00175\arprod\nocompound\mid206243
HARP Compound	: No Compound
QC Spreadsheet	: Uk1salx00175\arwork\nocompound\mid206243\Documents
Analysis Datasets	
• Analysis datasets will be created according to IDSL standards.	
Generation of RTF Files	
• RTF files will be generated for SAC.	

10.4.2. Reporting Standards

All data displays (Tables, Figures & Listings) will use the term "Subject" which reflects CDISC and GSK Data Display Standards terminology.

General

• The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated (IDSL Standards Location: https://spope.gsk.com/sites/IDSLLibrary/SitePages/Home.aspx):
  • 4.03 to 4.23: General Principles
  • 5.01 to 5.08: Principles Related to Data Listings
  • 6.01 to 6.11: Principles Related to Summary Tables
  • 7.01 to 7.13: Principles Related to Graphics
• Do not include subject level listings in the main body of the GSK Clinical Study Report. All subject level listings should be located in the modular appendices as ICH or non-ICH listings

Formats
• 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, unless otherwise stated. • Numeric data will be reported at the precision collected on the eCRF. • The reported precision from non eCRF sources will follow the IDSL statistical principles but may be adjusted to a clinically interpretable number of DP's.
Planned and Actual Time

• Reporting for tables, figures and formal statistical analyses:
  • Planned time 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 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.

Unscheduled Visits	
• Unscheduled visits will not be included in summary tables and/or 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.	

10.5. Appendix 5: Derived and Transformed Data

10.5.1. 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 First STM Dose Date:
  • Ref Date = Missing → Study Day = Missing
  • Ref Date < First STM Dose Date → Study Day = Ref Date – First STM Dose Date
  • Ref Data ≥ First STM Dose Date → Study Day = Ref Date – (First STM Dose Date) + 1

Age
• Age = Screening date – Date of Birth Date of birth will be imputed based on the assumption that all subjects were born on the 30th June (30 Jun YYYY).
Baux score
• Baux score: Age + % Total Body Surface Area (TBSA) burned

10.5.2. Efficacy

Fractional Excretion of Lactulose/Mannitol/Sucralose
Data is provided to S&P in the form of quantity of material in micrograms/litre, based on a sample of urine. Fractional excretion (FE) of lactulose or mannitol or sucralose = (urine concentration (micrograms/litre) × total urine volume excreted in litre) / probe input (micrograms). Where, • Urine concentration is provided in the BIOMARKER dataset, • Urine volumes excreted are provided in the BIOLINK dataset, • Probe input refers to the total STM taken (as per Table 7.1 of the protocol-5g Lactulose, 2g Mannitol and 2g Sucralose) Urine concentration in the BIOMARKER dataset will be provided at two timepoints per visit (0-5hr) and (0-24hr) FE will be calculated for timepoints 0-5 and 0-24 hours for Lactulose, Mannitol and Sucralose. For calculations of the 0-24 FE's, total urine volume will be based on the following: Total urine=urine excreted 0-5 hrs + urine excreted 5-24 hours. Note: If urine excreted 0-5 hrs is missing then total urine should be considered missing. Note: 1g=1000000 micrograms
L/M ratio
• L/M ratio = FE lactulose / FE mannitol
Healthy Participant – Average
• Average = Mean of all data available at all timepoint for each healthy participant.

10.5.3. Safety

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. o Example 1: 2 Decimal Points = '< x' becomes x – 0.01 o Example 2: 1 Decimal Point = '> x' becomes x + 0.1 o Example 3: 0 Decimal Points = '< x' becomes x – 1

10.6. Appendix 6: Reporting Standards for Missing Data

10.6.1. Premature Withdrawals

Element	Reporting Detail
General	• Subject study completion (i.e. as specified in the protocol) was defined as if he/she receives all planned doses of STM and completes the Day 15 in case of healthy participants and 6 months in case of participants with thermal injuries. • Withdrawn subjects 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.

10.6.2. Handling of Missing Data

Element	Reporting Detail
General	• Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument: 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.

10.6.2.1. 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: o Missing Start Day: First of the month will be used unless this is before the start date of STM; in this case the STM start date will be used. o Missing Stop Day: Last day of the month will be used, unless this is after the stop date of STM; in this case the STM 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.
Concomitant Medications/ Medical History	• Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention: o If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month o If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month. • The recorded partial date will be displayed in listings.

10.7. Appendix 7: Abbreviations & Trade Marks

10.7.1. Abbreviations

Abbreviation	Description
ACR	Albumin/creatinine ratio
ADaM	Analysis Data Model
AE/SAE	Adverse Event/ Serious Adverse Event
Anti-HBc	Anti-Hepatitis C
ART	Anti-retroviral treatment
CDISC	Clinical Data Interchange Standards Consortium
CFB	Change from Baseline
CFR	Code of Federal Regulations
CSR	Clinical Study Report
CV	Coefficient of Variation
DP	Decimal Places
eCRF	Electronic Case Record Form
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GCSP	Global Clinical Safety and Pharmacovigilance
GI	Gastrointestinal
GSK	GlaxoSmithKline
HB	Hepatitis B
HBs AG	Hepatitis B Antigen
HCV	Hepatitis C
HIV	Human Immunodeficiency Virus
ICF	Informed Consent Form
ICH	International Conference on Harmonization
ICU	Intensive Care Unit
IEC	Independent Ethics Committee
IRB	Institutional Review Board
ISS	Investigator Sponsored Study
L/M	Lactulose/mannitol ratio
MODS	Multi-organ dysfunction syndrome
NC	Nominated Consultee
NIMP	Non-investigational medicinal product
PC	Personal Consultee
PCR	Polymerase Chain Reaction
PDMP	Protocol Deviation Management Plan
RAP	Reporting and Analysis Plan
SAC	Statistical Analysis Complete
SAE	Serious Adverse Event
SIFTI-2	A Multi-centre, Prospective Study to Examine the Relationship between Neutrophil Function and Sepsis in Adults and Children with Severe Thermal Injuries
SoA	Schedule of Activities
SRM	Study Reference Manual
STM	Sugar Test Material
TBSA	Total Body Surface Area
TI	Thermally Injured
TNF	Tumour Necrosis Factor
WOCBP	Women of Child Bearing Potential

10.7.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
NONE

Trademarks not owned by the GlaxoSmithKline Group of Companies
SAS

10.8. Appendix 8: List of Data Displays

10.8.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.8	N/A
Efficacy	2.1 to 2.6	2.1 to 2.8
Safety	3.1 to 3.4	N/A
Biomarker	4.1 to 4.6	4.1 to 4.4
Section	**Listings**	
ICH Listings	1 to 23	
Other Listings	24 to 27	

10.8.2. Mock Example Shell Referencing

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

Section	Figure	Table	Listing
Efficacy	EFF_Fn	EFF_Tn	EFF_Ln
Safety	SAFE_Fn	SAFE_Tn	SAFE_Ln
Pharmacodynamic and / or Biomarker	PD_Fn	PD_Tn	PD_Ln

NOTES:

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

10.8.3. Deliverables

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

NOTES:

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

10.8.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Subject Disposition					
1.1.	Evaluable	ES8	Subject Status and Reasons for Study Withdrawal	ICH E3, FDAAA, EudraCT. Include study group instead of treatment group.	SAC
1.2.	Screened	ES6	Summary of Screening Status and Reasons for Screen Failure	Journal Requirements	SAC
Protocol Deviation					
1.3.	Screened	DV1	Summary of Important Protocol Deviations	ICH E3. Include study group instead of treatment group.	SAC
Population Analysed					
1.4.	Screened	SP1	Summary of Study Populations	IDSL. Include study group instead of treatment group.	SAC
Demographic and Baseline Characteristics					
1.5.	Evaluable	DM1	Summary of Demographic Characteristics	ICH E3, FDAAA, EudraCT Add %surface area burnt, Baux score and Body mass index. Include study group instead of treatment group.	SAC
1.6.	Evaluable	DM11	Summary of Age Ranges	EudraCT Note: Include Age categories: Adult (18 – 64 years), >=65 – 84 years and >=85 years. Include study group instead of treatment group.	SAC
1.7.	Evaluable	DM5	Summary of Race and Racial Combinations	ICH E3, FDA, FDAAA, EudraCT Include study group instead of treatment group.	SAC

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable**
Medical History					
1.8.	Evaluable	MH4	Summary of Medical Conditions	ICH E3 Include study group instead of treatment group. Add the medical status (Past/Current).	SAC

10.8.5. Efficacy Tables

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
L/M ratio					
2.1.	Evaluable	EFF_T1	Summary of Absolute L/M Ratio Values	Summary by: Study group and Visit Page by: Timepoint	SAC
2.2.	Evaluable	EFF_T1	Summary of Change in L/M Ratio Values	Note: CFB, Summary by: Study group and Visit, Page by: Timepoint	SAC
2.3.	Evaluable	EFF_T1	Summary of %Change in L/M Ratio Values	Note: %CFB, Summary by: Study group and Visit, Page by: Timepoint	SAC
Fractional excretion of sucralose					
2.4.	Evaluable	EFF_T1	Summary of Fractional Excretion of Sucralose Values	Summary by: Study group and Visit, Page by: Timepoint	SAC
2.5.	Evaluable	EFF_T1	Summary of Change in Fractional Excretion of Sucralose Values	Note: CFB, Summary by: Study group and Visit, Page by: Timepoint	SAC
2.6.	Evaluable	EFF_T1	Summary of %Change in Fractional Excretion of Sucralose Values	Note: %CFB, Summary by: Study group and Visit, Page by: Timepoint	SAC

10.8.6. Efficacy Figures

Efficacy: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
L/M ratio					
2.1.	Evaluable	EFF_F1	Individual Plot of Absolute L/M Ratio Values Over Time for Healthy Subjects.	Y-axis: Absolute Values Plot by Timepoint	SAC
2.2.	Evaluable	EFF_F2	Individual Plot of Absolute L/M Ratio Values Over Time for TI Subjects.	Y-axis: Absolute Values Plot by Timepoint Average value of Healthy Subjects will be used as reference line.	SAC
2.3.	Evaluable	EFF_F2	Individual Plot of %Change L/M Ratio Values Over Time for TI Subjects.	Y-axis: %CFB Values Plot by Timepoint Average value of Healthy subjects will be used as reference.	SAC
Fractional excretion of sucralose					
2.4.	Evaluable	EFF_F1	Individual Plot of Absolute Sucralose Values Over Time for Healthy Subjects.	Y axis: Absolute Values Plot by Timepoint	SAC
2.5.	Evaluable	EFF_F2	Individual Plot of Absolute Sucralose Values Over Time for TI Subjects.	Y axis: Absolute Values, Plot by Timepoint Average value of Healthy subjects will be used as reference.	SAC
2.6.	Evaluable	EFF_F2	Individual Plot of %Change Sucralose Values Over Time for TI Subjects.	Y axis: %CFB Values Plot by Timepoint Average value of Healthy subjects will be used as reference.	SAC

L/M ratio and Fractional excretion of sucralose					
2.7.	Evaluable	EFF_F3	Individual Plot of Absolue L/M ratio and Sucralose Values Over Time for TI Subjects.	Y axis: Absolute Values Plot by Timepoint Average values of Healthy subjects will be used as reference.	SAC
2.8.	Evaluable	EFF_F3	Individual Plot of %Change L/M ratio and Sucralose Values Over Time for TI Subjects.	Y axis: %CFB Values Plot by Timepoint Average values of Healthy subjects will be used as reference.	SAC

10.8.7. Safety Tables

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events (AEs)					
3.1.	Safety	AE1CP	Summary of All Adverse Events by System Organ Class and Preferred Term	ICH E3 Include study group instead of treatment group.	SAC
3.2.	Safety	AE15	Summary of Non-Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)	FDAAA, EudraCT Include study group instead of treatment group.	SAC
3.3.	Safety	AE1CP	Summary of Diseases Related Events by Verbatim Term		SAC
Serious and Other Significant Adverse Events					
3.4.	Safety	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)	FDAAA, EudraCT	SAC

10.8.8. Biomarker Tables

Pharmacodynamic and Biomarker: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Intestinal Permeability					
4.1	Evaluable	PD_T1	Summary of Markers of Intestinal Mucosal Damage	Note: Absolute Values Summary by: Study group and Visit	SAC
4.2	Evaluable	PD_T1	Summary of Change in Markers of Intestinal Mucosal Damage	Note: CFB Values Summary by: Study group and Visit	SAC
4.3	Evaluable	PD_T1	Summary of % Change in Markers of Intestinal Mucosal Damage	Note: %CFB Values Summary by: Study group and Visit	SAC
Bacterial Translocation					
4.4	Evaluable	PD_T1	Summary of Bacterial Markers of Translocation	Note: Absolute value Summary by: Study group and Visit	SAC
4.5	Evaluable	PD_T1	Summary of Change in Bacterial Markers of Translocation	Note: CFB Values Summary by: Study group and Visit	SAC
4.6	Evaluable	PD_T1	Summary of % Change in Bacterial Markers of Translocation	Note: %CFB Values Summary by: Study group and Visit	SAC

10.8.9. Biomarker Figures

Biomarker: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Biomarkers					
4.1	Evaluable	PD_F1	Individual Plot for Markers of Intestinal Mucosal Damage (Absolute Values) Over Time	Trellis plot – One panel for each biomarker with all TI subjects. Include reference line which is average value of Healthy subjects. Note: Y axis - Absolute Values	SAC
4.2	Evaluable	PD_F1	Individual Plot for Markers of Intestinal Mucosal Damage (% Change from baseline Values) Over Time	Trellis plot – One panel for each biomarker with all TI subjects. Include reference line at Zero. Note: Y axis - %CFB Values	SAC
4.3	Evaluable	PD_F1	Individual Plot for Bacterial Translocation Associated Biomarkers (Absolute Values) Over Time	Trellis plot – One panel for each biomarker with all TI subjects. Include reference line which is average value of Healthy subjects. Note: Y axis - Absolute Values	SAC
4.4	Evaluable	PD_F1	Individual Plot for Bacterial Translocation Associated Biomarkers (% Change from baseline Values) Over Time	Trellis plot – One panel for each biomarker with all TI subjects. Include reference line at Zero Note: Y axis - %CFB Values	SAC

10.8.10. ICH Listings

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.	Screened	ES7	Listing of Reasons for Screen Failure	Journal Guidelines	SAC
2.	Screened	ES2	Listing of Reasons for Study Withdrawal	ICH E3	SAC
3.	Screened	SD2	Listing of Reasons for STM Discontinuation	ICH E3 Mention study group instead of Treatment group.	SAC
4.	Screened	AG1	Listing of STM administration		SAC
Protocol Deviations					
5.	Screened	DV2	Listing of Important Protocol Deviations	ICH E3 Mention study group instead of Treatment group.	SAC
6.	Screened	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations	ICH E3 Include study group instead of treatment group.	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Populations Analysed					
7.	Screened	SP3	Listing of Subjects Excluded from Any Population	ICH E3 Mention Evaluable population instead of ITT and per protocol population and study group instead of Treatment group	SAC
Demographic and Baseline Characteristics					
8.	Screened	DM2	Listing of Demographic Characteristics	ICH E3 Include study group instead of treatment group. Include Baux score, % surface area burnt and Body mass index.	SAC
9.	Screened	DM9	Listing of Race	ICH E3 Include study group instead of treatment group.	SAC
Concomitant Medications and Medical History					
10.	Screened	CM3	Listing of Concomitant Medications	IDSL Mention study group instead of Treatment group.	SAC
11.	Screened	SU3	Listing of Substance Use	Include study group instead of treatment group.	SAC
12.	Screened	SP1	Listing of Subjects Who Had Surgery/Procedure	IDSL Include study group instead of treatment group.	SAC
Adverse Events					
13.	Screened	AE8	Listing of All Adverse Events	ICH E3 Mention study group instead of Treatment group.	SAC
14.	Screened	AE7	Listing of Subject Numbers for Individual Adverse Events	ICH E3 Include study group instead of treatment group.	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
15.	Screened	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text	IDSL	SAC
Serious and Other Significant Adverse Events					
16.	Screened	AE8	Listing of Fatal Serious Adverse Events	ICH E3 Mention study group instead of Treatment group.	SAC
17.	Screened	AE8	Listing of Disease Related Outcomes/Events.	Only for TI participants.	
18.	Screened	AE14	Listing of Reasons for Considering as a Serious Adverse Event	ICH E3 Mention study group instead of Treatment group.	SAC
19.	Screened	AE8	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment	ICH E3 Mention study group instead of Treatment group.	SAC
All Laboratory					
20.	Screened	LB5	Listing of All Laboratory Data for all Subjects	ICH E3, Mention study group instead of Treatment group.	SAC
21.	Screened	LB14	Listing of Laboratory Data with Character Results for all Subjects	ICH E3, Mention study group instead of Treatment group.	SAC
22.	Screened	UR2A	Listing of Urinalysis Data for all Subjects	ICH E3, Include study group instead of treatment group.	SAC
Vital Signs					
23.	Screened	VS4	Listing of All Vital Signs Data for all Subjects	IDSL Include study group instead of treatment group.	SAC

10.8.11. Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Efficacy					
24.	Screened	EFF_L1	Listing of Lactulose, Mannitol, L/M Ratio and Sucralose Data	Note: Numeric Score, CFB & %CFB	SAC
Biomarkers					
25.	Screened	PD_L1	Listing of Biomarker Data	Note: Include Character result, Numeric score, CFB & %CFB.	SAC
Time to wound recovery					
26.	Screened	TW_L1	Listing of Time to Wound Recovery Data for All TI Subjects		SAC
Subject Characteristics					
27.	Screened	SC1	Listing of Subject Characteristics		SAC

10.9. Appendix 9: Example Mock Shells for Data Displays

Example SP1
Protocol: 206243
Population: Screened

Table 1.5
Summary of Study Populations

Population	Healthy Subjects (N=200)	TI Subjects (N=250)	Total (N=500)
Screened	200 (100%)	250 (100%)	500 (100%)
Safety	195 (98%)	245 (98%)	440 (88%)
Evaluable	200 (100%)	250 (100%)	460 (92%)

Example EFF_T1
Protocol: 206243
Population: Evaluable

Timepoint: 0-5 hours/0-24 hours

Table 2.1
Summary of Lactulose:Mannitol (L/M) ratio / Change in Lactulose:Mannitol (L/M) Ratio

Study Group	N	Visit	n	Mean	SD	SE	Median	Min.	Max.
Healthy Subjects	200	Day 1	200	91.6	11.32	0.80	90.0	68	140
		Day 8	190	92.4	9.83	0.71	90.0	70	122
		Day 15	186	92.6	10.87	0.80	89.0	72	125
		Average	186	92.2	10.33	0.75	90.0	70	140
TI Subjects	200	Day 1	200	91.6	11.32	0.80	90.0	68	140
		Day 3	190	92.4	9.83	0.71	90.0	70	122
		...	195	92.1	10.80	0.77	89.0	72	120
		Day 28	186	92.6	10.87	0.80	89.0	69	125
		6 months	195	92.1	10.80	0.77	89.0	72	120

Note: Day 1 is considered as baseline for both the study groups.

Programming note:
Include all study visits for TI Subjects.
Produce same table for %Change from baseline values.
Produce similar tables for parameter Fractional excretion of sucralose.
Produce table for both the timepoints by page.

Example PD_T1
Protocol: 206243
Population: Evaluable

Table 3.1
Summary of Intestinal Permeability/ Bacterial Translocation Associated Biomarkers

Biomarkers(Unit)	Study Group	N	Visit	n	Mean	SD	SE	Median	Min.	Max.
Claudin 3	Healthy Subjects	200	Day 1	200	91.6	11.32	0.80	90.0	68	140
	TI Subjects	200	Day 1	200	91.6	11.32	0.80	90.0	68	140
			Day 3	190	92.4	9.83	0.71	90.0	70	122
			...	195	92.1	10.80	0.77	89.0	72	120
			Day 28	186	92.6	10.87	0.80	89.0	69	125
			6 months	195	92.1	10.80	0.77	89.0	72	120
Citrulline	Healthy Subjects	200	Day 1	200	91.6	11.32	0.80	90.0	68	140
	TI Subjects	200	Day 1	200	91.6	11.32	0.80	90.0	68	140
			Day 3	190	92.4	9.83	0.71	90.0	70	122
			...	195	92.1	10.80	0.77	89.0	72	120
			Day 28	186	92.6	10.87	0.80	89.0	69	125
			6 months	195	92.1	10.80	0.77	89.0	72	120

Note: Day 1 is considered as baseline for both the study groups.

Programming note:
Include all study visits for TI Subjects.
Produce same table for absolute, Change from baseline and % Change from baseline values for all biomarkers.

Example: EFF_L1
Protocol: 206243
Population: Screened

Study Group: Healthy Subjects

Listing of Lactulose, Mannitol, L/M Ratio and Sucralose Data

Site ID./ Subj.	Age(Y)/ Sex/ Race Detail	Visit	Time-point	Date/ Study Day	Total Volume of Urine (Unit)	Concentration in urine (Unit)			Fractional excretion			L/M ratio	Change from baseline		% Change from baseline	
						Lactulose	Mannitol	Sucralose	Lactulose	Mannitol	Sucralose		L/M ratio	Sucralose	L/M ratio	Sucralose
PPD	57/ M/ Asian - Central /South Asian Heritage	Day 1	0-5 hours													
			0-24 hours													
		Day 8	0-5 hours													
			0-24 hours													
		Day 15	0-5 hours													
			0-24 hours													

Example: PD_L1
Protocol: 206243
Population: Screened

Listing of Biomarker Data

Study Group	Site ID./ Subj.	Age(Y)/ Sex/ Race Detail	Biomarker (Unit)	Visit	Date/ Study Day	Character result [optional]	Numeric Score	Change from Baseline
	XXX/ XXX	57/ M/ Asian - Central/South Asian Heritage		Day 1				
	XXX/ XXX							

Example: TW_L1
Protocol: 206243
Population: Screened

Listing of Time to Wound Recovery Data

Study Group	Centre ID./ Subj.	Age(Y)/ Sex/ Race Detail	Visit	Screening Date	Wound recovery Date	Time to wound recovery (in days)
	XXX/ XXX	57/ M/ Asian - Central/South Asian Heritage	Day 1			
	XXX/ XXX					

Example: AG1
Protocol: 206243
Population: Screened

Listing of STM Administration

Study Group	Site ID./ Subj.	Age(YEARS)/ Sex/ Race Detail	Visit	Start date of STM	Start time of STM
	XXX/ XXX	57/ M/ Asian - Central/ South Asian Heritage	Day 1		
	XXX/ XXX				

Example: SC1
Protocol: 206243
Population: Screened

Listing of Subject Characteristics

Study Group	Site ID./ Subj. id	Age(YEARS)/ Sex/ Race Detail	Subject characteristic	Result
			Subject ID for Non GSK Study	A-021
	XXX/ XXX	57/ M/ Asian - Central/South Asian Heritage	Recruited Within 24 Hr Sustaining Injury	N
			Date and Time of Enrollment	21FEB2018T16:35
			Date and Time of Injury	20FEB2018T16:00
	XXX/ XXX			

Example: SU3
Protocol: 206243
Population: Screened

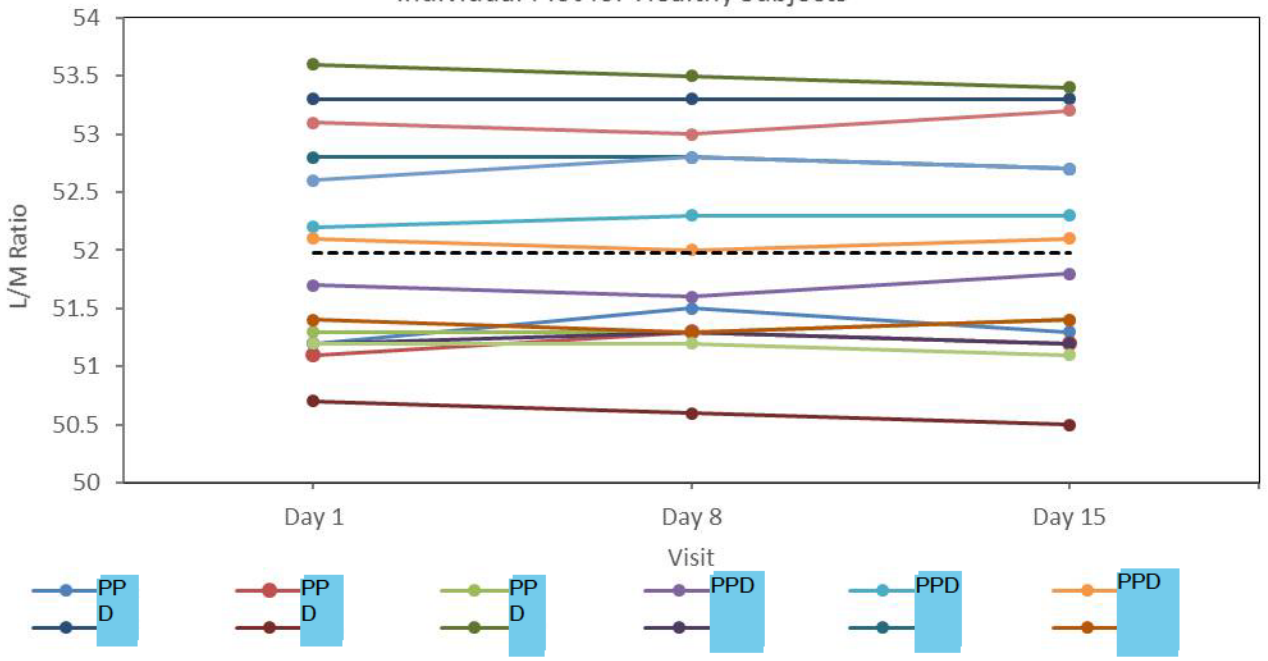
Listing X
Listing of Substance Use

Study Group	Centre id./ Subj.	Visit	Smoking History	Last smoked	Smokeless Tobacco History	Last used Smokeless Tobacco	Drink Alcohol	Units per Week	Drink Alcohol Prior Study
Healthy Subjects	PPD	Visit 1	Never		Never		Yes	20	
		Visit 1	Current		Current		No		
TI Subjects		Visit 1	Former	23JAN2016	Never		Yes	15	Yes, 21FEB2018 16:28

Example: EFF_F1
Protocol: 206243
Population: Evaluable

Timepoint: 0-5 hours

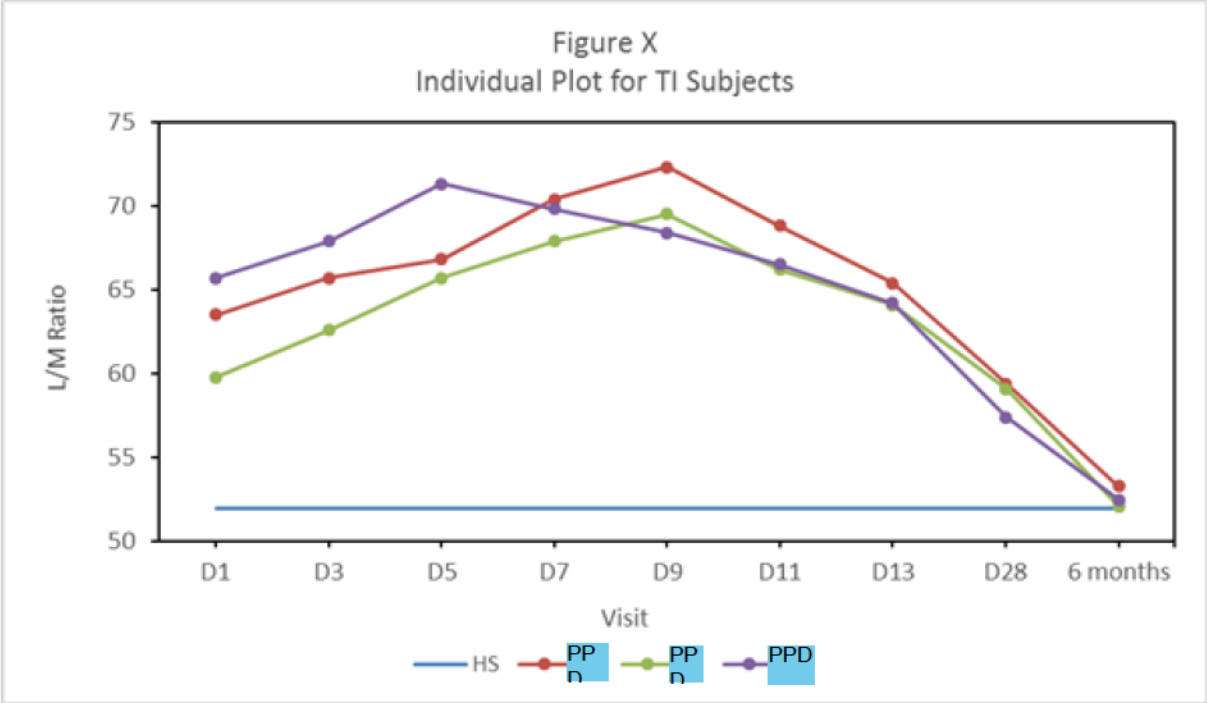
Figure X
Individual Plot for Healthy Subjects



Note: Above plot is based on healthy subjects.
Note: Reference line represents average over whole data for Healthy subjects which will be used as reference value for thermally injured Subjects.
Programming note: Include all the available Healthy Subjects in the plot. Produce this plot for endpoint L/M ratio and Sucralose. Produce similar graph for timepoint 0 – 24 hours.

Example: EFF_F2
Protocol: 206243 Page 1 of x
Population: Evaluable

Timepoint: 0-5 hours

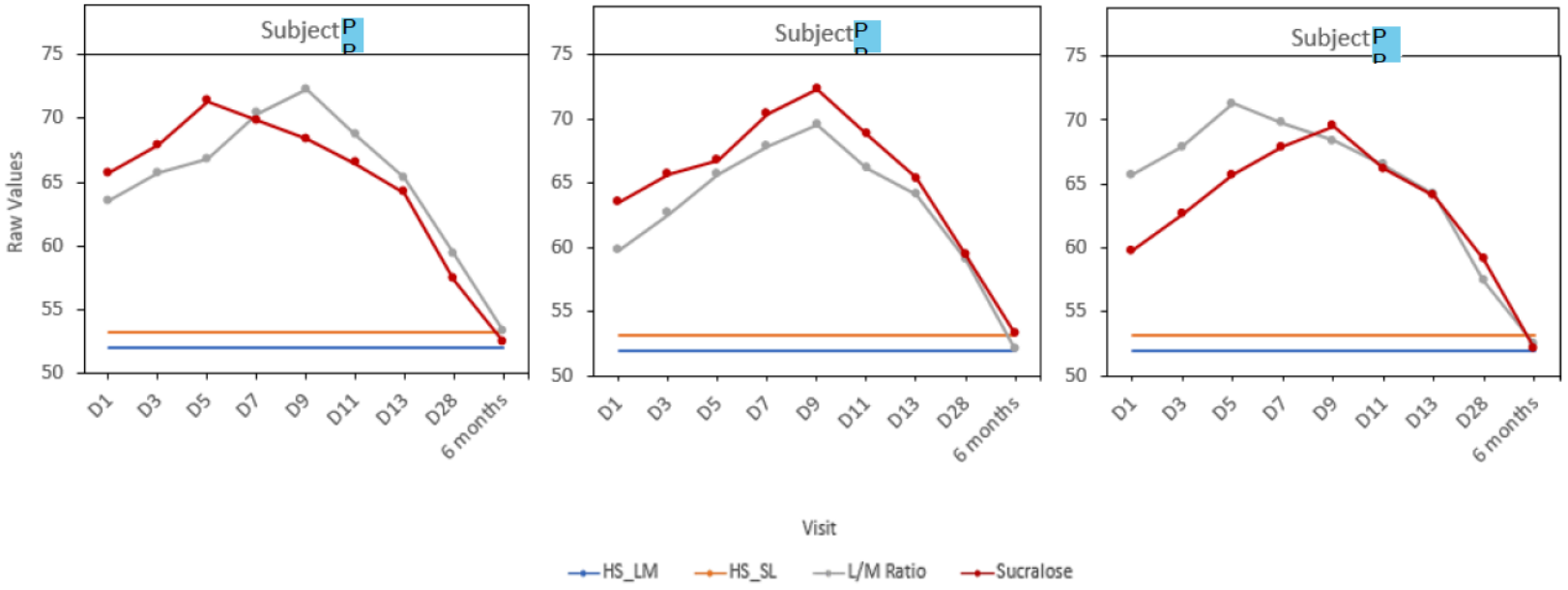


Note: Above plot is based on thermally injured subjects.
Note: The reference line (HSA) is based on average value of Healthy subjects.
Note: TI= thermally injured, HS=Healthy Subjects, S= thermally injured subject.
Programming note: Change HS to HSA in the legend in above graph. Include all the available TI subjects in the plot.
Produce similar plot for endpoint Sucralose. Also, produce graph for timepoint 0-24 hours.
The reference line for %CFB graph will be either 0 or average of %change in healthy subjects which will be decided based on the data.

Example: EFF_F3
Protocol: 206243
Population: Evaluable

Timepoint: 0-5 hours

Figure x
Individual Plot of L/M Ratio and Sucralose Over Time for TI subjects

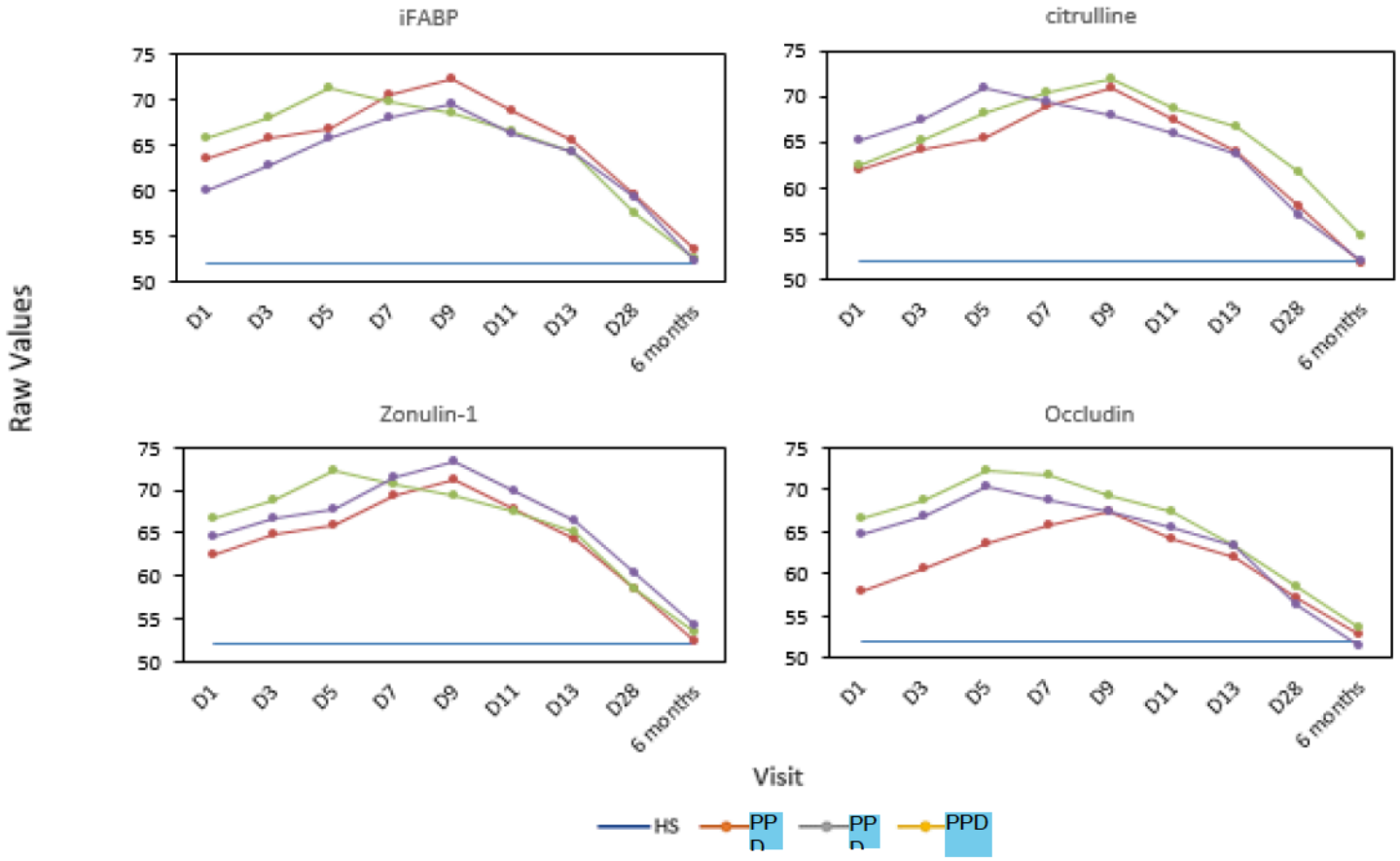


Note: D=Day, HS_LM=Average value of L/M ratio based on healthy subjects, HS_SL=Average value of Sucralose based on healthy subjects.
Note: L/M Ratio and Sucralose raw values are based on thermal injured subjects.

Programming note: Produce similar graph for %CFB. Also, produce graph for timepoint 0-24 hours.
The reference line for %CFB graph will be either 0 or average of %change in healthy subjects which will be decided based on the data.

Example: PD_F1
Protocol: 206243
Population: Evaluable

Subject Profile plot for Intestinal Permeability/ Bacterial Translocation Biomarkers



Note: Above plot is based on thermally injured subjects.
Note: The reference line (HSA: Healthy Subject's Average value) is based on average value of Healthy Subjects at day 1.
Note: HS= Healthy Subjects, S= thermally injured subjects.

Programming note: Include all the available thermally injured subjects in the plot.
Produce plot for all the biomarker groups.
Produce similar graph for %CFB.
The reference line for %CFB graph should be plot at 0.
Change HS to HSA in the legend in above graph.