Division	:	Worldwide Development
Information Type	:	Reporting and Analysis Plan
Title	:	Reporting and Analysis Plan for Study 207573: a two part, randomized, open-label, cross over study in healthy elderly participants to evaluate the relative bioavailability of hydrobromide salt tablet formulations of danirixin in the fed and fasted states, and to evaluate the effect of food and gastric acid secretion suppression on danirixin pharmacokinetics following administration of hydrobromide salt tablets.
Compound Number	:	GSK1325756
Effective Date	:	06-AUG-2018

Description:

- The purpose of this Reporting and Analysis Plan is to describe the planned analyses and displays to be included in the Clinical Study Report for Protocol 207573.
- This Reporting and Analysis Plan will be provided to the study team members to convey the content of the final Statistical Analysis Complete deliverable.

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1. INTRODUCTION

The purpose of this reporting and analysis plan (RAP) is to describe the analyses to be included in the Clinical Study Report for Protocol 207573: a two part, randomized, open-label, cross over study in healthy elderly participants to evaluate the relative bioavailability of hydrobromide salt tablet formulations of danirixin in the fed and fasted states, and to evaluate the effect of food and gastric acid secretion suppression on danirixin pharmacokinetics following administration of hydrobromide salt tablets..

Revision Chronology:		
2017N316476_00	21-DEC-2017	Original
2017N316476_01	22-FEB-2018	To modify the design of Part A incorporating a fasted group for each of the 4 treatments in addition to the fed groups. Additional clarifications have been made where necessary throughout the protocol.

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

Changes from the originally planned statistical analysis specified in the protocol 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**
• All Participants population	• All Subjects population	• R&D Clinical Data Standards Board (CDSB) recommendation to use the term 'Subjects' in all displays (Tables, Figures & Listings)
• All Subjects (ALLSUB) Population includes all participants who receive at least one dose of study medication. This population will be used for the study population and safety analyses.	• All Subjects Population includes all participants who were screened and for whom a record exists on the study database. This population will be used for summaries including participants who were not randomised	• Allows summaries including participants who were not randomised and is consistent with other studies in the development program.
• No modified Intent-to-treat (mITT) population	• mITT population defined to be used for study population and safety displays	• Replaced ALLPAR population which is now defined differently as above, and is consistent with other studies in the development program.

Protocol	Reporting & Analysis Plan	
Statistical Analysis Plan	**Statistical Analysis Plan**	**Rationale for Changes**
• No exclusions from analysis were specified	• Exclusion of data from analysis is detailed in Section 7.1.4 Strategy for Intercurrent Events and Section 7.2.4 Strategy for Intercurrent Events.	• Pharmacokinetic (PK) data would be affected by incorrect meal/formulation, incomplete meals, non-compliance with OMP and inadequate PK concentration profile.

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

Objectives	Endpoints	Part
Primary Objectives	**Primary Endpoints**	
• To estimate the relative bioavailability of danirixin after single dose administration of hydrobromide (HBr) tablet (Roller Compaction [RC]), the reference treatment, relative to the test formulations of the HBr tablet (Direct Comparession [DC] 475, DC 600 and hydroxypropyl methylcellulose [HPMC] 600), in healthy elderly participants in the fed and fasted states.	• Danirixin PK parameters: area under the concentration-time curve from time zero (predose) extrapolated to infinite time (AUC[0-inf]) and maximum observed concentration (Cmax).	Part A
• To provide safety and tolerability information for oral administration of the different formulations of danirixin HBr tablets in elderly participants.	• Adverse events (AEs)/serious AEs (SAEs), vital signs, electrocardiograms (ECGs), and clinical laboratory parameters	Part A
Secondary Objectives	**Secondary Endpoints**	
• To estimate the secondary pharmacokinetic parameters of danirixin after single dose administration of HBr tablet (RC), the reference treatment, relative to the test formulations of the HBr tablet (DC 475, DC 600 and HPMC 600), in healthy elderly participants in the fed and fasted states.	• Danirixin PK parameters: area under the concentration-time curve from time zero (predose) to last time of quantifiable concentration within a participant across all treatments (AUC[0-t]), area under the concentration-time curve from time zero (predose) to 24 hours post dose (AUC[0-24]), time of occurrence of Cmax (tmax), terminal phase half-life (t1/2), time of last quantifiable concentration (tlast) and lag time before observation of drug concentrations in sampled matrix (tlag).	Part A
• To estimate the effect of food on the single dose pharmacokinetics of the danirixin HBr tablet formulation selected from Part A in healthy elderly participants.	• Danirixin PK parameters: AUC(0-inf), AUC(0-t), AUC(0-24), Cmax, tmax, t1/2, tlast and tlag.	Part B
• To estimate the effect of OMP on the single dose pharmacokinetics of the danirixin HBr tablet formulation selected from Part A in healthy elderly participants in various fed and fasted states.	• Danirixin PK parameters: AUC(0-inf), AUC(0-t), AUC(0-24), Cmax, tmax, t1/2, tlast and tlag.	Part B

Objectives	Endpoints	Part
• To estimate the relative bioavailability of danirixin after single dose administration of HBr tablet (RC), the reference treatment, relative to the test formulation of the HBr tablet (MONO), in healthy elderly participants in the fed state.	• Danirixin PK parameters: AUC(0-inf), AUC(0-t), AUC(0-24), Cmax, tmax, t1/2, tlast and tlag.	Part B
• To provide safety and tolerability information for oral administration of danirixin HBr tablets in elderly participants.	• AEs/SAEs, vital signs, ECGs, and clinical laboratory parameters	Part B

2.3. Study Design

Overview of Study Design and Key Features

Part A Group 1 and 2

Screening Period *Within 30 Days of Day* 1	Treatment Period 1	5- Day Washout	Treatment Period 2	5 Day Washout	Treatment Period 3	5 Day Washout	Treatment Period 4	Early Discontinuation/ Follow-Up Visit 3-10 days after last dose of danirixin (DNX)

Part B Group 1

Screening Period *Within 30 Days of Day* 1	Treatment Period 1	5- Day Washout	Treatment Period 2	5 Day Washout	Treatment Period 3	5 Day Washout	Treatment Period 4	Early Discontinuation Follow-Up Visit 3-10 days after last dose of DNX

Part B Group 2

Screening Period Within *30 Days of Day* 1	Day -4	Treatment Period 1	5- Day Washout	Treatment Period 2	5 Day Washout	Treatment Period 3	Early Discontinuation Follow-Up Visit 3 - 10 days after last dose of DNX
	OMP taken daily through all treatment and washout periods, ending with final assessments for Treatment period 3						

Design Features	• This is a Phase I, two part (Part A and Part B; each part contains 2 Groups), randomized, open-label, single dose, cross-over study conducted with healthy elderly participants. Part A will support the selection of the formulation and Part B will address the Proton Pump Inhibitor (PPI) effect, food effect and PK of the monohydrate.
Dosing	• On Day 1 of each treatment period, following completion of the required pre-dose measurements and procedures, the investigator or authorized study unit personnel administered a single oral dose of 50 mg danirixin to each participant in the unit. • In Part B Group 2, all participants took OMP from Day -4 relative to treatment period 1, through all periods and washouts until the final treatment period 3 PK assessment (48hr post dose).

<table>
<tr><th colspan="2">Overview of Study Design and Key Features</th></tr>
<tr><td>Time & Events</td><td>• Refer to Appendix 2: Schedule of Activities</td></tr>
<tr><td>Treatment Assignment</td><td>• In Part A, 16 participants were randomised to a treatment sequence including treatments A-D or AO-DO (Section 5.1: Study Treatment Display Descriptors). Participants randomised to a treatment sequence including treatments A-D comprised Group 1 and participants randomised to a treatment sequence including treatments AO-DO comprised Group 2. Equal numbers of participants were randomized to each of the following sequences:
<table><tr><td>ABCD</td></tr><tr><td>BDAC</td></tr><tr><td>CADB</td></tr><tr><td>DCBA</td></tr><tr><td>AOBOCODO</td></tr><tr><td>BODOAOCO</td></tr><tr><td>COAODOBO</td></tr><tr><td>DOCOBOAO</td></tr></table>• In Part B, Group 1, 12 participants were randomised to a treatment sequence including treatments E-H (Section 5.1: Study Treatment Display Descriptors). Equal numbers of participants were randomized to each of the following sequences:
<table><tr><td>EFGH</td></tr><tr><td>EGFH</td></tr><tr><td>FGEH</td></tr><tr><td>FEGH</td></tr><tr><td>GEFH</td></tr><tr><td>GFEH</td></tr></table>• In Part B, Group 2, 12 participants were randomised to a treatment sequence including treatments I-K (Section 5.1: Study Treatment Display Descriptors). Equal numbers of participants were randomized to each of the following sequences:
<table><tr><td>IJK</td></tr><tr><td>IKJ</td></tr><tr><td>JKI</td></tr><tr><td>JIK</td></tr><tr><td>KIJ</td></tr><tr><td>KJI</td></tr></table>• GSK RandAll NG was used to generate the randomisation schedules.
• Study treatment was dispensed to participants at the study visits according to the randomisation schedule.</td></tr>
<tr><td>Interim Analysis</td><td>• An interim PK analysis is planned at the end of Part A. PK parameters AUC(0-inf), AUC(0-t), AUC(0-24) and Cmax will be derived using nominal times. The formulation to be investigated in Part B will be dependent on the PK profile, relative bioavailability and between-participant variability of the test formulations (DC 475, DC 600 and HPMC 600) compared to the reference formulation (RC).</td></tr>
</table>

2.4. Statistical Analyses

No formal hypothesis will be tested. For each PK endpoint and each treatment comparison described in Section 5.1 Study Treatment Display Descriptors, point estimates and corresponding 90% confidence intervals (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. Interim Analyses

An interim PK analysis is planned at the end of Part A. PK parameters AUC(0-inf), AUC(0-t), AUC(0-24) and Cmax will be derived using nominal times (see Section 7.1.1.2: Derived Pharmacokinetic Parameters). The formulation to be investigated in Part B will be dependent on the PK profile, relative bioavailability and between-participant variability of the test formulations (DC 475, DC 600 and HPMC 600) compared to the reference formulation (RC). The analysis will be documented in a short report which will be stored in the study Trial Master File, together will the associated analysis outputs and Quality Control documentation.

3.2. Final Analyses

The final planned study population, safety and PK concentration summaries will be performed after the completion of the following sequential steps:

1. All participants have completed the study as defined in the protocol.
2. All required database cleaning activities have been completed and final Source Data Lock (SDL) has been declared by data management (DM).
3. Study is unblinded
    - Randomization schedules are released in RANDALL NG and GSK create and quality control (QC) unblinded RANDALL dataset.
    - SMS2000 data is released in HARP
4. Unblinded RANDALL dataset and SMS2000 file are released to IQVIA by GSK via secure external alliance portal (EAP)
5. Study Data Tabulation Model (SDTM) data conversion has been completed by IQVIA including unblinding activities and QC of unblinded SDTM has been completed by DM.
6. Database freeze (DBF) on unblinded study population, safety and PC SDTM datasets has been declared by DM.

Following this, the PK parameter analyses will be performed after the PP SDTM domain is available.

4. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
All Subjects (ALLSUB)	• All participants who were screened and for whom a record exist on the study database	• Participant disposition • Reasons for withdrawal prior to randomization • Inclusion/exclusion criteria deviations for non-randomized participants • AEs and SAEs for non-randomized participants
Modified Intent-to-treat (mITT)	• All randomized participants apart from those who were randomized in error (i.e. were also recorded as screen failures and did not receive a dose of study treatment). • Any participant who receives a treatment randomization number will be considered to have been randomized. • Randomized participants will be assumed to have received study medication unless definitive evidence to the contrary exists. • If a participant received an incorrect meal or formulation, by-treatment summaries will use the meal/formulation actually received.	• Study population • Safety
Pharmacokinetic (PK)	• All participants for whom a pharmacokinetic sample was obtained and analysed	• PK

Refer to Appendix 10: List of Data Displays which details the population used for each display.
If the PK and mITT populations include the same participants then the PK analysis will be run on the mITT population and data will be excluded as detailed in Section 7

4.1. Protocol Deviations

Protocol deviations (PDs) will be handled as described in Appendix 1: Protocol Deviation Management. A Per Protocol population will not be defined.

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

5.1. Study Treatment Display Descriptors

All participants will receive DNX 50mg in each treatment period. The term 'treatment' refers to the combination of formulation and meal as identified below.

Treatment Group Descriptions			
RandAll NG		Data Displays for Reporting	
Code	Description	Description	Order in TLF
A	DNX 50mg 600RC High fat Formulation 1	DNX 50mg 600RC High fat – A	1
B	DNX 50mg 475DC High fat Formulation 4	DNX 50mg 475DC High fat – B	2
C	DNX 50mg 600DC High fat Formulation 2	DNX 50mg 600DC High fat – C	3
D	DNX 50mg 600DC 5%HPMC High fat Formulation 3	DNX 50mg 600DC 5%HPMC High fat – D	4
AO	DNX 50mg 600RC Fasted Formulation 1	DNX 50mg 600RC Fasted – AO	5
BO	DNX 50mg 475DC Fasted Formulation 4	DNX 50mg 475DC Fasted – BO	6
CO	DNX 50mg 600DC Fasted Formulation 2	DNX 50mg 600DC Fasted – CO	7
DO	DNX 50mg 600DC 5%HPMC Fasted Formulation 3	DNX 50mg 600DC 5%HPMC Fasted - DO	8
E	DNX 50mg Fasted	DNX 50mg Fasted – E	9
F	DNX 50mg Normal meal	DNX 50mg Normal meal – F	10
G	DNX 50mg High fat	DNX 50mg High fat – G	11
H	DNX 50mg MONO High fat	DNX 50mg MONO High fat – H	12
I	DNX 50mg Fasted OMP	DNX 50mg Fasted OMP – I	13
J	DNX 50mg Normal meal OMP	DNX 50mg Normal meal OMP – J	14
K	DNX 50mg High fat OMP	DNX 50mg High fat OMP - K	15

Treatment comparisons will be displayed as follows using the comparison column as specified:

Part	Question	Comparison	Comparison Description
Part A Group 1	Formulation in the fed state	475mg DC tablet formulation versus 600mg RC formulation (reference)	B vs A
		600mg DC tablet formulation versus reference	C vs A
		600mg DC tablet with 5% HPMC versus reference	D vs A
Part A Group 2	Formulation in the fasted state	475mg DC tablet formulation versus 600mg RC formulation (reference)	BO vs AO
		600mg DC tablet formulation versus reference	CO vs AO

Part	Question	Comparison	Comparison Description
		600mg DC tablet with 5% HPMC versus reference	DO vs AO
Part A Group 1 & 2	Food effect	600mg RC formulation fed versus fasted	A vs AO
		475mg DC tablet formulation fed versus fasted	B vs BO
		600mg DC tablet formulation fed versus fasted	C vs CO
		600mg DC tablet with 5% HPMC fed versus fasted	D vs DO
Part B Group 1	Food effect, no OMP	High fat meal (heavy) versus fasted	G vs E
		Normal meal (light) versus fasted	F vs E
		High fat meal (heavy) versus normal meal (light)	G vs F
Part B Group 2	Food effect with OMP	High fat meal (heavy) versus fasted	K vs I
		Normal meal (light) versus fasted	J vs I
		High fat meal (heavy) versus normal meal (light)	K vs J
Part B Group 1 & 2	Drug interaction	Fasted with OMP versus fasted without OMP	I vs E
		Normal meal (light) with OMP versus normal meal (light) without OMP	J vs F
		High fat meal (heavy) with OMP versus high fat meal (heavy) without OMP	K vs G
Part B Group 1	Pharmaceutical development	Monohydrate with high fat meal versus high fat meal (heavy)	H vs G

5.2. Baseline Definitions

Any assessments made after the time of the study treatment dose will not be included in the derivation of baseline. Assessments made on the same day as dosing with a missing time are assumed to be taken prior to first dose.

If baseline data are missing, no derivation will be performed and baseline will be set to missing.

Parameter	Baseline Used in Data Display
ECG values	The average of the triplicate readings made on Day -1 of each treatment period will be calculated and used as period baseline. Any reading made after the time of dosing will not be included in the calculation.
Vital signs (pulse rate, systolic and diastolic blood pressure)	The average of the triplicate readings made pre-dose on Day 1 of each treatment period as recorded on the electronic case report form (eCRF) will be used as period baseline
Laboratory data	The assessment made on Day -1 of the first treatment period will be used as a study baseline

5.3. Multiple Comparisons and Multiplicity

No adjustments for multiplicity will be made.

5.4. Other Considerations for Data Analyses and Data Handling Conventions

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

Section	Component
10.3	Appendix 3: Assessment Windows
10.4	Appendix 4: Study Phases
10.5	Appendix 5: Data Display Standards & Handling Conventions
10.6	Appendix 6: Derived and Transformed Data
10.7	Appendix 7: Reporting Standards for Missing Data
10.8	Appendix 8: Values of Potential Clinical Importance

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Study Population Analyses

Study population analyses including analyses of participant disposition, protocol deviations, demographic and baseline characteristics, relevant medical history and concomitant medications will be based on GlaxoSmithKline (GSK) Core Data Standards. Results will generally be presented for all participants with a Part and Group, not split by treatment. Details of the split for each display are included in Section 10.10.4 Study Population Tables.

A summary of the number and percentage of participants who completed each treatment period and entered and completed each washout period, along with the reasons for withdrawal, will be displayed for each Part and Group separately. Separate study treatment compliance and exposure displays will not be produced as they would contain the same information.

Compliance with OMP will be summarized by treatment for treatments I, J and K.

Meal data will be summarized by treatment.

Details of the planned displays including the population to be used for each display are presented in Appendix 10: List of Data Displays.

7. PHARMACOKINETIC ANALYSES

7.1. Primary Pharmacokinetic Parameter Analyses

The primary PK parameter analysis is to compare the relative bioavailability of different formulations of danirixin in the fed and fasted states. The primary treatment effect to be estimated is the 'as-treated' effect of treatment (formulation and meal) in participants who consume at least 90% of the meal (in fed participants) and provided an adequate PK concentration profile to allow reliable estimation of PK parameters.

7.1.1. Endpoint / Variables

- Log-transformed AUC(0-inf) and Cmax.

The following secondary endpoints which are analysed in the same way as the primary endpoints and assess the same outcome are also included in this section:

- Log-transformed AUC(0-t), AUC(0-24) and t1/2.

The following parameters will not be log-transformed and will be included in summary tables containing untransformed values for the primary endpoint.

- tmax, tlag, tlast.

7.1.1.1. Drug Concentration Measures

Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 10.5.3 Reporting Standards for Pharmacokinetics)

7.1.1.2. Derived Pharmacokinetic Parameters

Pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using the currently supported version of WinNonlin. All calculations of non-compartmental parameters will be based on actual sampling times. Pharmacokinetic parameters listed will be determined from the blood concentration-time data, as data permits. If parameters cannot be determined, a 'Not done' or 'Not calculable' flag will be present in the data. In addition, parameters affected by the other intercurrent events identified in Section 7.1 will also be identified in the data.

Parameter	Parameter Description
AUC(0-inf)	Area under the concentration-time curve extrapolated to infinity will be calculated as: **AUC = AUC(0-t) + C(t) / lambda_z**
Cmax	Maximum observed concentration, determined directly from the concentration-time data.
AUC(0-t)	Area under the concentration-time curve from time zero to the time of the last quantifiable concentration (C(t)) will be calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid.
AUC(0-24)	Area under the concentration-time curve from time zero to 24 hours will be calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid.
Tmax	Time to reach Cmax, determined directly from the concentration-time data.
t1/2*	Apparent terminal half-life will be calculated as: **t1/2 = ln2 / lambda_z**
Tlag	Lag time before observation of drug concentrations in blood
Tlast	Time of last quantifiable concentration

* associated parameters lambda_z, lambda_z_lower, lambda_x_upper, No_points_lambda_z to be listed.

NOTES:

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

7.1.2. Summary Measure

Relative bioavailability of danirixin after single dose of three formulations of HBr tablet (DC) versus HBr tablet (RC) in fed and fasted states.

- Fed (treatment comparisons B vs A, C vs A, D vs A)
- Fasted (treatment comparisons BO vs AO, CO vs AO, DO vs AO)

7.1.3. Population of Interest

PK population.

7.1.4. Strategy for Intercurrent Events

Participants who experienced the following intercurrent events will have data from the relevant treatment period excluded from analysis:

- Received incorrect formulation or meal
- Did not consume at least 90% of the meal (in fed participants)
- Did not provide an adequate PK concentration profile to allow reliable estimation of PK parameters

Inclusion of the participant's remaining data in the analysis effectively uses a missing at random assumption to account for the excluded data.

If a participant is included in the PK population but withdrew from the study prior to a treatment period, data for that and subsequent periods will not be imputed. Inclusion of the participant's data prior to withdrawal in the analysis effectively uses a missing at random assumption to account for the missing data.

7.1.5. Statistical Analyses / Methods

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

7.1.5.1. Statistical Methodology Specification

Endpoint / Variables
• Log-transformed AUC(0-inf) and Cmax in fed and fasted states. • Log-transformed AUC(0-t), AUC(0-24) and t1/2 in fed and fasted states.
Model Specification
• Include all Part A data in the model. • Mixed effects model with fixed effect terms for period and treatment (formulation and fed/fasted state). Participant will be treated as a random effect in the model. • Point estimates on the $\log_e$ scale for the least squares (LS) mean for each treatment and the LS mean difference between treatments (for comparisons specified in Section 7.1.2: Summary Measure), and associated 90% CI for the difference will be constructed using the residual variance. The LS means, LS mean differences and associated 90% CIs will then be back-transformed to obtain geometric LS mean for each treatment, and LS treatment ratios and associated 90% CIs. • 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.
Model Checking & Diagnostics
• Model assumptions will be applied, but appropriate adjustments maybe made based on the data. • Distributional assumptions underlying the model used for analysis will be examined by obtaining a normal probability plot of the residuals and a plot of the residuals versus the fitted values (i.e. checking the normality assumption and constant variance assumption of the model respectively) to gain confidence that the model assumptions are reasonable. • If there are any departures from the distributional assumptions, alternative models will be explored using appropriate transformed data.
Model Results Presentation
• Separate outputs will be produced for fed and fasted states (although both will be analyzed using the same model) • Geometric LS means for each treatment, treatment ratios and associated 90% CIs for each parameter. • Estimates of within-participant variability (%CVw) for AUC and Cmax (%CVw represents a pooled measure of within-participant variability across treatments). • Comparative plots of individual blood PK parameters by treatment on linear and semi-logarithmic scales. • Forest plots of geometric mean treatment ratios for AUC and Cmax together with 90% CIs. • Listing of individual blood PK parameter ratios. • Supportive SAS output from statistical analysis.

7.2. Secondary Pharmacokinetic Parameter Analyses

The following analyses will be conducted to assess food effect, PPI effect and pharmaceutical development. The primary treatment effect to be estimated is the 'as-treated effect of the treatment (formulation and meal) in participants who consume at least 90% of the meal (in fed participants), are OMP compliant (in OMP participants) and provided an adequate PK concentration profile to allow reliable estimation of PK parameters.

7.2.1. Endpoint / Variables

- Log-transformed AUC(0-inf) and Cmax.
- Log-transformed AUC(0-t), AUC(0-24) and t1/2.

7.2.2. Summary Measure

Relative bioavailability of danirixin after single dose.

- Food effect in test formulation (treatment comparisons A vs AO, B vs BO, C vs CO, D vs DO)
- Food effect in selected formulation without PPI (treatment comparisons G vs E, F vs E, G vs F)
- Food effect in selected formulation with PPI (treatment comparisons K vs I, J vs I, K vs J)
- PPI effect in selected formulation (treatment comparisons I vs E, J vs F, K vs G)
- Pharmaceutical development (treatment comparison H vs G)

7.2.3. Population of Interest

PK population.

7.2.4. Strategy for Intercurrent Events

Participants who experienced the following intercurrent events will have data from the relevant treatment period excluded from analysis:

- Received incorrect formulation or meal
- Did not consume at least 90% of the meal (in fed participants)
- Missed more than one OMP dose between Days -4 and -2 or missed any other OMP dose (participants on treatments I, J, K – Section 5.1 Study Treatment Display Descriptors))
- Did not provide an adequate PK concentration profile to allow reliable estimation of PK parameters

Inclusion of the participant's remaining data in the analysis effectively uses a missing at random assumption to account for the excluded data.

If a participant is included in the PK population but withdrew from the study prior to a treatment period, data for that and subsequent periods will not be imputed. Inclusion of

the participant's data prior to withdrawal in the analysis effectively uses a missing at random assumption to account for the missing data.

7.2.5. Statistical Analyses / Methods

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

7.2.5.1. Statistical Methodology Specification

Secondary PK analyses will use the same methods as described in Section 7.1: Primary Pharmacokinetic Analysis. The data to be included in each model are described below.

Food Effect in Test Formulations
Treatment Comparisons
• A vs AO, B vs BO, C vs CO, D vs DO
Model Specification
• From model used for primary PK analysis including all Part A data.

Food Effect in Selected Formulation without PPI
Treatment Comparisons
• G vs E, F vs E, G vs F
Food Effect in Selected Formulation with PPI
Treatment Comparisons
• K vs I, J vs I, K vs J
PPI Effect in Selected Formulation
Treatment Comparisons
• I vs E, J vs F, K vs G
Model Specification
• Include all Part B data from periods 1-3.

Pharmaceutical Development
Treatment Comparisons
• H vs G
Model Specification
• Part B non-OMP treatment arms (E-H) only. • Estimates presented for treatments G and H and difference H vs G.

8. SAFETY ANALYSES

Details of the planned displays including the population to be used for each display are presented in Appendix 10 List of Data Displays.

The estimand is the effect of actual treatment in the population of participants who were randomized and dosed. All collected data will be included in reporting as described below. If a participant received the incorrect meal or formulation, data will be reported according to the actual meal and formulation received. If a participant consumed <90% of the meal, data will still be reported according to that meal. If a participant was non-compliant with OMP dosing, data will still be reported according to the OMP-containing treatment. Non-recorded missing data following study withdrawal will not be imputed.

All safety data displays will be split by actual treatment received, except where specified below.

8.1. Adverse Events Analyses

Adverse events analyses including the analysis of AEs, SAEs and other significant AEs will be based on GSK Core Data Standards.

8.2. Clinical Laboratory Analyses

Laboratory displays including chemistry laboratory tests, hematology laboratory tests, urinalysis, and liver function tests will be based on GSK Core Data Standards. Summaries will include Screening and baseline (see Section 5.2 Baseline Definitions) values, and raw and change from baseline values at the Follow-up visit, and will be split by Part and Group.

Laboratory data from eligibility screening (follicle stimulating hormone, oestradiol, human immunodeficiency virus, hepatits B & hepatits C) will not be reported.

8.3. Other Safety Analyses

The analyses of non-laboratory safety test results including ECGs and vital signs will be based on GSK Core Data Standards, unless otherwise specified.

9. REFERENCES

None.

10. APPENDICES

10.1. Appendix 1: Protocol Deviation Management

PDs will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan (PDMP) for the study:

- PICTS database is not being used to collect protocol deviations occurring in the study. A PD spreadsheet (PD Log) is being used to collect all deviations from the protocol and is being managed by the IQVIA Clinical Research Associate.
- Every time there is a deviation, an email is sent to the GSK study team to confirm whether it should be classified as important or not, and subsequently updated in the spreadsheet.
- Participants who received an incorrect formulation or meal, consumed <90% of meal or were non-compliance with OMP will be captured as an important protocol deviation.
- The spreadsheet will be reviewed prior to SDL to ensure all important deviations are captured.
- At the end of the study, IQVIA will convert this spreadsheet into a SAS dataset which will be provided to statistics and programming along with the other datasets.
- This dataset will be the basis for the summaries and listings of PDs.
- Important PDs (including deviations related to study inclusion/exclusion criteria, conduct of the trial, participant management or participant assessment) will be summarised and listed.
- 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).
- A Per Protocol Population will not be defined.

The following PDs will lead to exclusion from the pharmacokinetic parameter analysis outputs for the specific period (tables, statistical analysis and figures). Exclusions will be programmed by statistics and programming from the SDTM data:

- incorrect meal/formulation
- non-compliance with OMP (participants on treatments I, J, K – Section 5.1 Study Treatment Display Descriptors))
- consumed <90% of meal (in fed participants)

In addition, a participant may be excluded from the pharmacokinetic parameter analysis outputs for the specific period due to having an inadequate PK concentration profile. This will be determined by the Pharmacokineticist during an initial review of the PK concentration data prior to derivation of the PK parameters. In such cases, any data identified for exclusion will be provided to statistics and programming and flagged in the relevant Analysis Data Model (ADaM) datasets. This will be documented in the ADaM Data Reviewers Guide (ADRG).

10.2. Appendix 2: Schedule of Activities

10.2.1. Protocol Defined Schedule of Events

Schedule of Activities Part A (Group 1 and Group 2) and Part B (Group 1)

Periods 1-4

Procedure	Screening (up to 30 days prior to Day 1) [1]	Study Day (Treatment Periods 1-4) [2]														Early Discontinuation /Follow-up (3 to 10 days post-last dose)
		Day -1	1													
			Pre-dose	0h	0.5h	1h	1.5h	2h	3h	4h	6h	8h	10h	12h	24h	48h	
Informed Consent	X																
Inclusion and Exclusion Criteria	X	X															
Demographics	X																
Full Physical Exam including Height and Weight	X																
Brief Physical Exam		X															X
Medical History (includes substance usage)	X	X															

Procedure	Screening (up to 30 days prior to Day 1) [1]	Study Day (Treatment Periods 1-4) [2]														Early Discontinuation /Follow-up (3 to 10 days post-last dose)
		Day -1	1													
			Pre-dose	0h	0.5h	1h	1.5h	2h	3h	4h	6h	8h	10h	12h	24h	48h	
Pregnancy Test, (WOCBP)[3]	X	X														
FSH and estradiol (if needed)	X															
HIV, Hep B and Hep C Screen	X															
Urine Drug Screen	X	X														
Alcohol Screen-Breathalyzer	X	X														
Urine Cotinine Screen	X	X														
Admission to Unit		X														
Laboratory Assessments (include liver chemistries)	X	X														X
12-lead ECG [4]	X	X						X								X

Procedure	Screening (up to 30 days prior to Day 1) [1]	Study Day (Treatment Periods 1-4) [2]														Early Discontinuation /Follow-up (3 to 10 days post-last dose)
		Day -1	1													
			Pre-dose	0h	0.5h	1h	1.5h	2h	3h	4h	6h	8h	10h	12h	24h	48h	
Vital Signs[5]	X		X												X	X	X
Randomization			X														
Meal [6]			X														
Danirixin Administration [7]				X													
Pharmacokinetic Sampling			X		X	X	X	X	X	X	X	X	X	X	X	X	
SAE Review	←==========																==========→
AE Review		X	←==========														==========→
Concomitant Medication Review		X	←==========														==========→
Discharge															X		

1. Screening must be performed within 30 days prior to receiving the dose of Danirixin on Day 1 of period 1.
2. Treatment periods 1-4 will include a minimum 5 day wash-out from day of dosing between each treatment
3. Serum pregnancy test (where applicable) will be performed at the screening visit and a urine pregnancy test at all other time points specified.

4. Triplicate ECGs at screening and on Day -1 of each treatment period only. Single ECGs at other timepoints (performed at a similar time of day as Day 1 Pre-dose), unless a reading meets the QTc stopping criteria, in which case two further measurements will be taken at the same time point and the average values captured.
5. Triplicate BP and HR at screening and pre-dose on Day 1 of each treatment period only. Single measurements at other timepoints (performed at a similar time of day as Day 1 Pre-dose). HR and BP assessments only performed at the 24 and 48 hr post dose and early discontinuation/follow-up visit timepoints.
6. Meal (where applicable) to be started and completed 30 minutes prior to of danirixin dosing. Meal to consist of 900-1000 calories and be composed of proper caloric content of protein/fat/carbohydrates per FDA guidance and participants will be required to consume at least 90% of meal.
7. When danirixin dosing occurs in the fasted state, participants will be provided with a light snack and then will fast from all food and drink (except water) from 10 hours prior to dosing until 4hrs post-dose on Day 1 in each treatment period at which time lunch will be provided. An evening meal will be provided at approximately 9 h post dose. At all other times during residency in the clinic, meals will be provided at appropriate times.

Part B – Group 2

Periods 1-3

Procedure		Study Day (Treatment Periods -1-3) [2]																Early Discontinuation /Follow-up (3 to 10 days post-last dose)
	Screening (Up to 30 days prior to Day 1) [1]	Qualification Visit Day -4[9]	Day -1	1														
				Pre-dose	0h	0.5h	1h	1.5h	2h	3h	4h	6h	8h	10h	12h	24h	48h	
Informed Consent	X																	
Inclusion and Exclusion	X		X															
Demographics	X																	
Full Physical Exam including Height and Weight	X																	
Brief Physical Exam			X															X
Medical History (includes	X		X															

Procedure		Study Day (Treatment Periods -1-3) [2]																Early Discontinuation /Follow-up (3 to 10 days post-last dose)
	Screening (Up to 30 days prior to Day 1) [1]	Qualification Visit Day -4[9]	Day -1	1														
				Pre-dose	0h	0.5h	1h	1.5h	2h	3h	4h	6h	8h	10h	12h	24h	48h	
substance usage)																		
Pregnancy Test,[3] (WOCBP)	X	X	X															
FSH and estradiol (if needed)	X																	
HIV, Hep B and Hep C Screen	X																	
Urine Drug Screen	X	X	X															
Alcohol Screen-Breathalyzer	X	X	X															
Urine Cotinine Screen	X	X	X															
Admission to Unit			X															
Laboratory Assessments	X		X															X

Procedure		**Study Day (Treatment Periods -1-3)** [2]																**Early Discontinuation /Follow-up (3 to 10 days post-last dose)**
	Screening (Up to 30 days prior to Day 1) [1]	**Qualification Visit Day -4**[9]	**Day -1**	**1**														
				Pre-dose	**0h**	**0.5h**	**1h**	**1.5h**	**2h**	**3h**	**4h**	**6h**	**8h**	**10h**	**12h**	**24h**	**48h**	
(include liver chemistries)																		
12-lead ECG [4]	X		X						X									X
Vital Signs [5]	X			X												X	X	X
Randomization				X														
Meal[6]				X														
Danirixin Administration[7]					X													
Omeprazole Administration [8]		X	X		X											X	X	
Diary Card completion for Omeprazole Dosing		←==========→																
Pharmacokinetic Sampling				X		X	X	X	X	X	X	X	X	X	X	X	X	

Procedure		Study Day (Treatment Periods -1-3) [2]															Early Discontinuation /Follow-up (3 to 10 days post-last dose)
	Screening (Up to 30 days prior to Day 1) [1]	Qualification Visit Day -4[9]	Day -1	1													
				Pre-dose	0h	0.5h	1h	1.5h	2h	3h	4h	6h	8h	10h	12h	24h	48h	
SAE Review	←==========→																	
AE Review			X	←==========→														
Concomitant Medication Review			X	←==========→														
Discharge																X		

1. Screening must be performed within 30 days prior to receiving the dose of Danirixin on Day 1 of period 1.
2. Treatment periods 1-3 will include a minimum 5 day wash-out from day of dose between each treatment.
3. Serum pregnancy test (where applicable) will be performed at the screening visit and a urine pregnancy test at all other time points specified.
4. Triplicate ECGs at screening and on Day -1 of each treatment period only. Single ECGs at other timepoints (performed at a similar time of day as Day 1 Pre-dose), unless a reading meets the QTc stopping criteria, in which case two further measurements will be taken at the same time point and the average values captured.
5. Triplicate BP and HR assessments at screening and pre-dose on Day 1 of each treatment period only. Single measurements at other timepoints (performed at a similar time of day as Day 1 Pre-dose). HR and BP assessments only performed at the 24 and 48 hr post dose and early discontinuation/follow-up visit timepoints.
6. Meal (where applicable) to be started and completed within 30 minutes prior to danirixin dosing. Normal and high fat meal will be described in the SRM.
7. When danirixin dosing occurs in the fasted state, participants will be provided with a light snack and then will fast from all food and drink (except water) from 10 hours prior to dose until 4 hr post-dose on Day 1 in each treatment period at which time lunch will be provided. An evening meal will be provided at approximately 9 h post dose. At all other times during residency in the clinic, meals will be provided at appropriate times.
8. OMP will be taken starting on Day -4 continuing daily through all treatment and washout periods until the day of the Period 3, 48hour PK assessment. The Day -4 Qualification visit only applies to period 1.

10.3. Appendix 3: Assessment Windows

Data will be reported according to the nominal time of clinic visits and assessments as specified in the protocol.

10.4. Appendix 4: Study Phases

Assessments and events collected outside scheduled study visits will be classified into study phases according to the time of occurrence relative to the start and/or stop date of study treatment.

10.4.1. Study Phases for Treatment Period

A treatment period will be considered complete if study treatment was administered. The washout period will start the day after dosing and stop the day before dosing in the next period.

10.4.2. Study Phases for Adverse Event Data

Classification of an AE/SAE as having onset on-treatment will be made with reference to the study treatment dates and the event onset date. If the event onset date is missing, then the event will be considered on-treatment. Events with onset up to 1 day after the date of a treatment will be considered on-treatment.

Study Phase	Definition
Pre-treatment	Events with onset before the first treatment defined as: (onset date < first study treatment dose date or no study treatment dose date)
On-treatment	Events with onset on the day of each treatment and up to 1 day afterwards, defined as: (study treatment dose date <= onset date <= study treatment dose date + 1 or onset date missing)

Events that are not pre- or on-treatment will be presented in listings only

10.4.3. Study Phases for Concomitant Medication

No study phases will be defined for concomitant medications; all concomitant medications taken will be summarized together.

10.5. Appendix 5: Data Display Standards & Handling Conventions

10.5.1. Reporting Process

Software	
• The currently supported versions of SAS software will be used.	
Reporting Area	
HARP Server	: uk1salx00175
HARP Compound	: GSK1325756
Analysis Datasets	
• Analysis datasets will be created according to CDISC standards (SDTM IG Version 3.2 & ADaM IG Version 1.1).	
Generation of RTF Files	
• RTF files will be generated for all tables in the final reporting effort.	

10.5.2. Reporting Standards

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 4.24: General Principles • 5.01 to 5.08: Principles Related to Data Listings • 6.01 to 6.11: Principles Related to Summary Tables • 7.01 to 7.13: Principles Related to Graphics
Formats
○ GSK IDSL Statistical Principle 4.24 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. ○ Summaries of continuous data will include number of participants, mean, standard deviation (SD), median, minimum and maximum. ○ Percentages between 1% and 99%, inclusive, will be rounded to integers. Percentages greater than 0%, but less than 1%, will be reported as <1%, and percentages greater than 99%, but less than 100%, will be reported as >99%. ○ Actual time will be reported as HH:MM. Seconds will not be presented.
Planned and Actual Time
○ Reporting for tables, figures and formal statistical analyses: • Planned time relative to dosing will be used in figures, summaries and statistical analyses. Calculation of derived PK parameters will use actual time. • 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 participant's listings.
Unscheduled Visits
o Unscheduled visits will not be included in summary tables or figures. o 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
o Refer to IDSL Statistical Principals 7.01 to 7.13.

10.5.3. Reporting Standards for Pharmacokinetics

Pharmacokinetic Concentration Data	
PC Windows Non-Linear (WNL) File	PC WNL file (CSV format) for the non compartmental analysis by Clinical Pharmacology Modelling and Simulation function will be created according to Standards for the Transfer and Reporting of PK Data document. Note: Concentration values will be imputed as per GUI_51487
Descriptive Summary Statistics, Graphical Displays and Listings	Refer to IDSL PK Display Standards. Refer to IDSL Statistical Principle 6.06.1. Note: Concentration values will be imputed as per GUI_51487 for descriptive summary statistics/analysis and summarized graphical displays only.
Pharmacokinetic Parameter Derivation	
PK Parameter to be Derived by Programmer	None
Pharmacokinetic Parameter Data	
Is Not Quantifiable (NQ) impacted PK Parameters Rule Being Followed	No (PK parameter derivation is not expected to be affected by NQs.)
Descriptive Summary Statistics (Log Transformed parameters AUCs, Cmax, t1/2)	Refer to IDSL PK Display Standards. N, n, geometric mean, 95% CI of geometric mean, SD of logged data and [between or within] geometric coefficient of variation (CVb/w (%)) will be reported. [1] CV_b (%) = $\sqrt{}$ (exp(SD^2) - 1) * 100 (SD = SD of log transformed data) [2] CV_w (%) = $\sqrt{}$ (exp(MSE) - 1) * 100 (MSE = mean square error from mixed effect model of log-transformed data).
Untransformed Parameters	Tmax, tlag, and tlast
PK Parameters listed only	lambda_z, lambda_z_lower, lambda_x_upper, No_points_lambda_z

10.6. Appendix 6: Derived and Transformed Data

10.6.1. General

Multiple Measurements at One Analysis Time Point
○ The mean of the triplicate vital sign assessments as recorded on the eCRF will be reported; all individual assessments will be listed. ○ The mean of the triplicate ECG assessments will be calculated and reported; all individual assessments will be listed. The baseline ECG assessment will be calculated as described in Section 5.2 Baseline Definitions. ○ For any other parameter with multiple measurements at one time point, the mean of the measurements will be calculated and used in any derivation of summary statistics but if listed, all data will be presented.
Study Day
○ Calculated as the number of days from first study treatment dose date: • Ref date = missing → study day = missing • Ref date < first study treatment dose date → study day = ref date – first study treatment dose date • Ref date ≥ first study treatment dose date → study day = ref ate – (first study treatment dose date) + 1
Period Study Day
○ Period day refers to the study day within a period. ○ For period 1, period day will be the same as study day. ○ For period 2, period day will be calculated as (ref date – 2nd treatment dose date + 1). ○ For period 3, period day will be calculated as (ref date – 3rd treatment dose date + 1). ○ For period 4, period day will be calculated as (ref date – 4th treatment dose date + 1).
Study Completion Definition
○ A participant is considered to have completed the study if they have not withdrawn and were dosed in their last scheduled treatment period.

10.6.2. Study Population

Demographic Characteristics
Age
○ GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as follows: ○ Any participant with a missing day will have this imputed as day '15'. ○ Any participant with a missing date and month will have this imputed as '30th June'. ○ Birth date will be presented in listings as 'YYYY'. ○ Age will be calculated based on the Screening visit date.
Body Mass Index (BMI)
○ Calculated as Weight (kg) / [Height $(m)^2$]

Compliance
Compliance with OMP
○ An OMP dose scheduled to be taken in the clinic will be counted if the answer to 'Did the subject receive the correct treatment' in the OMP dosing section of the eCRF is 'Yes'. ○ The total number of OMP doses taken will be calculated as the sum of each dose taken in the clinic on Days -4, -1, 1, 2, and 3 and the actual number of doses taken at home between Day -4 and Day -1 (as recorded in the eCRF). ○ Compliance with OMP will be calculated as: Total doses taken*100/(number of days between Day -4 and Day 3) ○ Compliance with OMP will be summarized as a continuous variable and also in the categories: ○ <80% ○ 80-<120% ○ ≥120%

Meals
○ The duration of the meal (in minutes) will be calculated and summarized as a continuous variable. ○ The proportion of the meal consumed will be summarized as a continuous variable and also in the categories: ○ <90% ○ 90-<95% ○ ≥95% ○ The actual time between the start of the meal and the time of dosing will be summarized as a continuous variable and also in the categories: ○ <20 min ○ 20-<40min ○ ≥40 min

10.6.3. Safety

ECG		
ECG Categories		
QTcB and QTcF values at each time point will be reported in categories as below		
ECG Parameter	**Units**	**Category**
Absolute		
Absolute QTcF Interval	msec	No Change or Decrease to <=450
		Increase To >450 to <=480
		Increase To >480 to <=500
		Increase To >500
Change from Baseline		
Change from Baseline QTcF	msec	Increase of <=30 ms
		Increase of 31-60 msec
		Increase of >60 msec

10.7. Appendix 7: Reporting Standards for Missing Data

10.7.1. Premature Withdrawals

Element	Reporting Detail
General	• Participant study completion was defined in the protocol as completion of all phases of the study including the final follow-up visit for the Part for which the participant was enrolled. • For the purposes of reporting, a participant is considered to have completed the study if they have not withdrawn and have completed their last scheduled treatment period. • If participants prematurely discontinue the study, additional replacement participants may be recruited and assigned to the same treatment sequence at the discretion of the Sponsor in consultation with the investigator. • AE and concomitant medication data from participants who were withdrawn from the study will be listed and included in summary tables. • Laboratory, vital sign and ECG data from an Early Discontinuation visit will not be included in any summaries but will be listed.

10.7.2. Handling of Missing Data

Element	Reporting Detail

General	• Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument:
	  ○ These data will be indicated by the use of a “blank” in participant listing displays. If all data for a specific visit is missing the data is excluded from the table/participant listing.
	  ○ Answers such as “Not applicable” and “Not evaluable” are not considered to be missing data and should be displayed as such.

Outliers	• If outliers are identified, analyses may be repeated excluding the outlying data. • Any participants excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report.

10.7.2.1. Handling of Missing and Partial Dates

Element	Reporting Detail
General	• Partial dates will be displayed as captured in participant listing displays.
Adverse Events	• The eCRF allows for the possibility of partial dates (i.e., only month and year) to be recorded for AE start and end dates; that is, the day of the month may be missing. In such a case, the following conventions will be applied for calculating the time to onset and the duration of the event: ○ Missing Start Day: First of the month will be used unless this is before the 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 4: Study Phases. ○ 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.
Concomitant Medications	• Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention: ○ If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month ○ If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month. • The recorded partial date will be displayed in listings.

10.8. Appendix 8: Values of Potential Clinical Importance

10.8.1. Laboratory Values

Hematology Analyte (units)			
		Low	**High**
Platelet Count (x10^9/L)		0.90x	1.10x
Red Blood Cell Count (x10^{12}/L)		0.93x	1.07x
White Blood Cell Count (x10^9/L)		0.70x	1.60x
Reticulocyte Count (%)			>4%
Hemoglobin (g/L)	Males	0.85x	1.05x
	Females	0.85x	1.15x
Hematocrit (Ratio of 1)	Males	0.80x	1.02x
	Females	0.80x	1.15x
Mean Corpuscular Volume (fL)		0.80x	1.20x
Mean Corpuscular Hemoglobin (pg)		0.90x	1.10x
Neutrophils (%)		0.85x	1.50x
Lymphocytes (%)		0.85x	1.50x
Monocytes (%)		0.50x	2.00x
Eosinophils (%)			2.00x
Basophils (%)			5.00x

Chemistry Analyte (units)		
	Low	**High**
Blood Urea Nitrogen (mmol/L)	0.70x	1.60x
Creatinine (μmol/L)		1.30x (or >27 μmol/L increase from baseline)
Glucose (mmol/L)	0.85x	1.20x
Sodium (mmol/L)	0.95x	1.05x
Potassium (mmol/L)	0.85x	1.10x
Calcium (mmol/L)	0.90x	1.05x
Albumin (mmol/L)	0.90x	1.20x
Total Protein (mg/dL)		1.20x

Note: Multipliers are identified by "x", otherwise actual comparison values are provided with units.

Liver Function Test Analyte (units)	
	High
Alanine aminotransferase (ALT)/SGPT (U/L)	2x
Aspartate amintransferase/SGOT (U/L)	2x
Alkaline Phosphatase (U/L)	2x
Total Bilirubin (μmol/L)	1.5x
Direct Bilirubin (μmol/L)	1.5x
Total Bilirubin (μmol/L) + ALT (U/L)	≥ 1.5x ULN Total Billirubin + ≥ 2x ULN ALT

10.8.2. ECG

ECG Parameter (units)		
	Low	**High**
Absolute QTc Interval (QTcB, QTcF) (msec)		>450
PR Interval (msec)	<110	>220
QRS Interval (msec)	<75	>110
Change from Baseline QTcF, QTcB		>60

10.8.3. Vital Signs

Vital Sign Parameter (units)		
	Low	**High**
Systolic Blood Pressure (mmHg)	<85	>160
Diastolic Blood Pressure (mmHg)	<50	>100
Heart Rate (bpm)	<50	>110

10.9. Appendix 9: Abbreviations & Trade Marks

10.9.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
ADRG	ADaM Data Reviewers Guide
AE	Adverse Event
ALLSUB	All Subjects
ALT	Alanine aminotransferase
AUC(0-24)	Area under the concentration-time curve from time zero (predose) to 24 hours post dose
AUC(0-inf)	Area under the concentration-time curve from time zero (predose) extrapolated to infinite time
AUC(0-t)	Area under the concentration-time curve from time zero (predose) to time of last quantifiable concentration within a participant across all treatments
BMI	Body Mass Index
BP	Blood pressure
CDISC	Clinical Data Interchange Standards Consortium
CDSB	Clinical Data Standards Board
CI	Confidence Interval
Cmax	Maximum observed concentration
$\%CV_B$	Coefficient of Variation (Between)
$\%CV_w$	Coefficient of Variation (Within)
DBF	Database freeze
DC	Direct Compression
DM	Data Management
DNX	Danirixin
DP	Decimal Places
EAP	External alliance portal
ECG	Electrocardiogram
eCRF	Electronic Case Record Form
GSK	GlaxoSmithKline
HBr	Hydrobromide
HPMC	Hydroxypropyl methylcellulose
HR	Heart rate
IDSL	Integrated Data Standards Library
LS	Least squares
mITT	Modified Intent-to-treat
MSE	Mean squared error
NQ	Non-quantifiable
OMP	Omeprazole
PD	Protocol deviation
PDMP	Protocol Deviation Management Plan
PK	Pharmacokinetic
PPI	Proton pump inhibitor

Abbreviation	Description
QC	Quality control
RAP	Reporting & Analysis Plan
RC	Roller Compaction
SAE	Serious adverse event
SD	Standard deviation
SDL	Source Data Lock
SDTM	Study Data Tabulation Model
t1/2	Terminal phase half-life
tlag	Lab time before observation of drug concentrations in sampled matrix
tlast	Time of last quantifiable concentration
tmax	Time of occurrence of Cmax
WNL	Windows Non Linear

10.9.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
NONE

Trademarks not owned by the GlaxoSmithKline Group of Companies
NONMEM
SAS
WinNonlin

10.10. Appendix 10: List of Data Displays

10.10.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.16	-
Pharmacokinetic	2.1 to 2.10	2.1 to 2.18
Safety	3.1 to 3.20	-
Section	**Listings**	
ICH Listings	1 to 32	
Other Listings	33 to 38	

10.10.2. Mock Example Shell Referencing

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

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

NOTES:

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

10.10.3. Deliverables

In all displays the term "Subjects" is used to refer to "Participants".

Delivery	Description
SAC	Final Statistical Analysis Complete

10.10.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.1.	mITT	CP_ES1	Summary of Participant Disposition	ICH E3, FDAAA, EudraCT	SAC
1.2.	ALLSUB	NS1	Summary of Number of Subjects Enrolled by Country and Site ID	Split by Part and Group, not split by treatment	SAC
1.3.	mITT	ES4	Summary of Subject Disposition at Each Study Epoch	ICH E3 For treatment periods, only 'completed' row is required. For washouts use all 3 options as in shell	SAC
1.4.	ALLSUB	ES6	Summary of Screening Status and Reasons for Screen Failure	Journal Requirements	SAC
Protocol Deviation					
1.5.	mITT	DV1	Summary of Important Protocol Deviations	ICH E3 Split by Part and Group, not split by treatment	SAC
1.6.	ALLSUB	IE2	Summary of Inclusion/ Exclusion Criteria Deviations for Screen Failures	Add a row "Number of Screen Failures" above "any criteria deviations". Percentage will be based on number of screen failures	SAC
1.7.	mITT	IE2	Summary of Inclusion/ Exclusion Criteria Deviations for the Modified Intent-to-treat Population	Split by Part and Group, not split by treatment	SAC

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Population Analysed					
1.8.	ALLSUB	SP1	Summary of Study Populations	IDSL Number of participants who were randomized and number in the mITT population. Of those the number and percentage of participants in the PK population Split by Part and Group, not split by treatment	SAC
1.9.	PK	SP2A	Summary of Exclusions from the Pharmacokinetic Parameter Analysis	Split by treatment	SAC
Demographic and Baseline Characteristics					
1.10.	mITT	DM3	Summary of Demographic Characteristics	ICH E3, FDAAA, EudraCT Include BMI Split by Part and Group, not split by treatment	SAC
1.11.	ALLSUB	DM11	Summary of Age Ranges	EudraCT Include total column Split by Part and Group, not split by treatment	SAC
1.12.	mITT	DM5	Summary of Race and Racial Combinations	ICH E3, FDA, FDAAA, EudraCT Split by Part and Group, not split by treatment	SAC
Medical Conditions					
1.13.	mITT	MH1	Summary of Relevant Medical Conditions	Split by Part and Group, not split by treatment	SAC

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Prior and Concomitant Medications					
1.14.	mITT	CP_CM1	Summary of Concomitant Medications by Generic Term	ICH E3 Medications will be sorted in descending order of total incidence across treatment groups for generic term. If the total incidence for any two or more generic terms is equal, the events will be presented in alphabetical order. Split by Part and Group, not split by treatment	SAC
1.15.	mITT	POP_T1	Summary of Compliance with Omeprazole Therapy	Split by treatment Includes treatment I-K only	SAC
1.16.	mITT	POP_T2	Summary of Meal Data	Split by treatment	SAC

10.10.5. Pharmacokinetic Tables

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.1.	PK	PK01	Summary of Danirixin Blood Pharmacokinetic Concentration-Time Data	Split by Part, Group and by treatment	SAC
2.2.	PK	PK03	Summary Statistics of Untransformed Derived Danirixin Blood Pharmacokinetic Parameters	Split by Part, Group and by treatment	SAC
2.3.	PK	PK05	Summary Statistics of Log-transformed Derived Danirixin Blood Pharmacokinetic Parameters	Split by Part, Group and by treatment	SAC
2.4.	PK	201037 Table 3.6	Summary of Statistical Analysis of Log-transformed Danirixin Blood Pharmacokinetic Parameters: Fed State	Part A	SAC
2.5.	PK	201037 Table 3.6	Summary of Statistical Analysis of Log-transformed Danirixin Blood Pharmacokinetic Parameters: Fasted State	Part A	SAC
2.6.	PK	201037 Table 3.6	Summary of Statistical Analysis of Log-transformed Danirixin Blood Pharmacokinetic Parameters: Food Effect in Test Formulations	Part A	SAC
2.7.	PK	201037 Table 3.6	Summary of Statistical Analysis of Log-transformed Danirixin Blood Pharmacokinetic Parameters: Food Effect in Selected Formulation without Proton Pump Inhibitor	Part B	SAC
2.8.	PK	201037 Table 3.6	Summary of Statistical Analysis of Log-transformed Danirixin Blood Pharmacokinetic Parameters: Food Effect in Selected Formulation with Proton Pump Inhibitor	Part B	SAC
2.9.	PK	201037 Table 3.6	Summary of Statistical Analysis of Log-transformed Danirixin Blood Pharmacokinetic Parameters: Proton Pump Inhibitor Effect in Selected Formulation	Part B	SAC

Pharmacokinetic: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.10.	PK	201037 Table 3.6	Summary of Statistical Analysis of Log-transformed Danirixin Blood Pharmacokinetic Parameters: Pharmaceutical Development	Part B	SAC

10.10.6. Pharmacokinetic Figures

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.1.	PK	PK16b	Individual Subject Danirixin Blood Concentration-Time Plot (Linear and Semi-log) by Subject	All treatments for one participant on same panel	SAC
2.2.	PK	PK24	Individual Subject Danirixin Blood Concentration-Time Plot (Linear and Semi-log) by Treatment	All participants for one treatment on same panel	SAC
2.3.	PK	PK19	Arithmetic Mean (+SD) Danirixin Blood Concentration-Time Plot (Linear and Semi-log)		SAC
2.4.	PK	PK20	Median (Range) Danirixin Blood Concentration-Time Plot (Linear and Semi-log)		SAC
2.5.	PK	PK25	Comparative Plot of Individual Subject Danirixin Blood Concentration-Time Parameters vs. Treatment: Fed State	Treatments A-D	SAC
2.6.	PK	PK25	Comparative Plot of Individual Subject Danirixin Blood Concentration-Time Parameters vs. Treatment: Fasted State	Treatments AO-DO	SAC
2.7.	PK	PK25	Comparative Plot of Individual Subject Danirixin Blood Concentration-Time Parameters vs. Treatment: Food Effect in Test Formulations	Treatments A, AO, B, BO, C, CO, D, DO	SAC

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.8.	PK	PK25	Comparative Plot of Individual Subject Danirixin Blood Concentration-Time Parameters vs. Treatment: Food Effect in Selected Formulation without Proton Pump Inhibitor	Treatments E-G	SAC
2.9.	PK	PK25	Comparative Plot of Individual Subject Danirixin Blood Concentration-Time Parameters vs. Treatment: Food Effect in Selected Formulation with Proton Pump Inhibitor	Treatments I-K	SAC
2.10.	PK	PK25	Comparative Plot of Individual Subject Danirixin Blood Concentration-Time Parameters vs. Treatment: Proton Pump Inhibitor Effect in Selected Formulation	Treatments E, I, F, J, G, K	SAC
2.11.	PK	PK25	Comparative Plot of Individual Subject Danirixin Blood Concentration-Time Parameters vs. Treatment: Pharmaceutical Development	Treatments G-H	SAC
2.12.	PK	201037 Figure 3.7	Geometric Mean (90% CI) Treatment Ratios of Danirixin Blood Pharmacokinetic Parameters: Fed State	Treatment comparisons B vs A, C vs A, D vs A	SAC
2.13.	PK	201037 Figure 3.7	Geometric Mean (90% CI) Treatment Ratios of Danirixin Blood Pharmacokinetic Parameters: Relative Bioavailability in Fasted State	Treatment comparisons BO vs AO, CO vs AO, DO vs AO	SAC
2.14.	PK	201037 Figure 3.7	Geometric Mean (90% CI) Treatment Ratios of Danirixin Blood Pharmacokinetic Parameters Food Effect in Test Formulations	Treatment comparisons A vs AO, B vs BO, C vs CO, D vs DO	SAC
2.15.	PK	201037 Figure 3.7	Geometric Mean (90% CI) Treatment Ratios of Danirixin Blood Pharmacokinetic Parameters Food Effect in Selected Formulation without Proton Pump Inhibitor	Treatment comparisons G vs E, F vs E, G vs F	SAC
2.16.	PK	201037 Figure 3.7	Geometric Mean (90% CI) Treatment Ratios of Danirixin Blood Pharmacokinetic Parameters: Food Effect in Selected Formulation with Proton Pump Inhibitor	treatment comparisons K vs I, J vs I, K vs J	SAC

Pharmacokinetic: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.17.	PK	201037 Figure 3.7	Geometric Mean (90% CI) Treatment Ratios of Danirixin Blood Pharmacokinetic Parameters: Proton Pump Inhibitor Effect in Selected Formulation	Treatment comparisons I vs E, J vs F, K vs G	SAC
2.18.	PK	201037 Figure 3.7	Geometric Mean (90% CI) Treatment Ratios of Danirixin Blood Pharmacokinetic Parameters: Pharmaceutical Development	Treatment comparison H vs G	SAC

10.10.7. Safety Tables

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events (AEs)					
3.1.	mITT	CP_AE1x	Summary of On-treatment Adverse Events by System Organ Class and Preferred Term	ICH E3	SAC
3.2.	mITT	CP_AE1x	Summary All Drug-Related Adverse Events by System Organ Class and Preferred Term	ICH E3	SAC
3.3.	mITT	AE15	Summary of Common (>=5%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Subject and Occurrences)	FDAAA, EudraCT Use TD_AE4VCTR macro	SAC
Serious and Other Significant Adverse Events					
3.4.	mITT	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)	FDAAA, EudraCT Use TD_AE4VCTR macro	SAC
3.5.	mITT	CP_AE1x	Summary of On-treatment Serious Adverse Events by System Organ Class and Preferred Term		SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.6.	mITT	CP_AE1x	Summary of Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study by System Organ Class and Preferred Term	IDSL	SAC
Laboratory: Chemistry					
3.7.	mITT	LB1	Summary of Pre-dose Clinical Chemistry Laboratory Values	ICH E3	SAC
Laboratory: Hematology					
3.8.	mITT	LB1	Summary of Pre-dose Haematology Laboratory Values	ICH E3	SAC
Laboratory: Urinalysis					
3.9.	mITT	200163 Table 2.17	Summary of Urinalysis Dipstick Data	ICH E3	SAC
Laboratory: Hepatobiliary (Liver)					
3.10.	mITT	MH2	Listing of Medical Conditions for Subjects with Liver Stopping Events	Only create if there is a liver event	SAC
3.11.	mITT	SU2	Listing of Substance Use for Subjects with Liver Stopping Events	Only create if there is a liver event	SAC
3.12.	mITT	LIVER5	Listing of Liver Monitoring/Stopping Event Reporting	Only create if there is a liver event	SAC
3.13.	mITT	LIVER6	Listing of Liver Stopping Event Information for RUCAM Score	Only create if there is a liver event	SAC
3.14.	mITT	LIVER7	Listing of Liver Biopsy Details	Only create if there is a liver event	SAC
3.15.	mITT	LIVER8	Listing of Liver Imaging Details	Only create if there is a liver event	SAC
3.16.	mITT	LIVER13	Listing of Subjects Meeting Hepatobiliary Laboratory Criteria	Only create if there is a liver event	SAC
ECG					
3.17.	mITT	CP_EG9	Summary of Change from Baseline in 2h Post-dose ECG Values	IDSL Include all parameters collected	SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.18.	mITT	CP_EG11	Frequency of QTc Values at 2h Post-dose by Pre-specified Categories	IDSL Include QTcF, QTcB	SAC
3.19.	mITT	CP_EG12	Frequency of Change from Baseline in QTc Values at 2h Post-dose by Pre-specified Categories	IDSL Include QTcF, QTcB	SAC
Vital Signs					
3.20.	mITT	VS1	Summary of Vital Signs	ICH E3	SAC

10.10.8. ICH Listings

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.	ALLSUB	ES7	Listing of Reasons for Screen Failure	Journal Guidelines	SAC
2.	mITT	CP_ES10x	Listing of Reasons for Study Withdrawal	ICH E3	SAC
3.	mITT	TA2	Listing of Planned and Actual Treatments	IDSL	SAC
Protocol Deviations					
4.	mITT	DV2	Listing of Important Protocol Deviations	ICH E3	SAC
5.	ALLSUB	IE4	Listing of Screen Failure Subjects with Inclusion/Exclusion Criteria Deviations		SAC
6.	mITT	IE4	Listing of Subjects with Inclusion/Exclusion Criteria Deviations	ICH E3	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Populations Analysed					
7.	PK	SP3	Listing of Exclusions from the Pharmacokinetic Analysis	ICH E3	SAC
Demographic and Baseline Characteristics					
8.	mITT	DM4	Listing of Demographic Characteristics	ICH E3	SAC
9.	mITT	DM10	Listing of Race	ICH E3	SAC
Prior and Concomitant Medications					
10.	mITT	CP_CM4	Listing of Concomitant Medications using Generic Term	IDSL	SAC
11.	PK	POP_L1	Listing of Omeprazole Dosing Times		SAC
Pharmacokinetic					
12.	PK	PK08	Listing of Danirixin Blood Concentration-Time Data		SAC
13.	PK	PK14	Listing of Danirixin Blood Pharmacokinetic Parameters		SAC
14.	PK	PK15	Listing of Danirixin Blood Pharmacokinetic Parameter Ratios		SAC
Adverse Events					
15.	ALLSUB	AE9	Listing of All Adverse Events	ICH E3	SAC
16.	ALLSUB	AE7	Listing of Subject Numbers for Individual Adverse Events	ICH E3	SAC
17.	ALLSUB	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text	IDSL	SAC
Serious and Other Significant Adverse Events					
18.	ALLSUB	AE9a	Listing of Serious Adverse Events	ICH E3 Include fatal and non-fatal SAEs Add identification of treatment phase and treatment	SAC
19.	ALLSUB	AE14	Listing of Reasons for Considering as a Serious Adverse Event	ICH E3	SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
20.	ALLSUB	AE9	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment	ICH E3	SAC
21.	ALLSUB	AE9	Listing of Drug-Related Adverse Events	ICH E3	SAC
All Laboratory					
22.	mITT	CP_LB6	Listing of All Clinical Chemistry Laboratory Data for Subjects with Any Value of Potential Clinical Importance	ICH E3	SAC
23.	mITT	CP_LB6	Listing of All Haematology Laboratory Data for Subjects with Any Value of Potential Clinical Importance	ICH E3	SAC
24.	mITT	CP_LB6	Listing of Clinical Chemistry Abnormalities of Potential Clinical Importance		SAC
25.	mITT	CP_LB6	Listing of Haematology Abnormalities of Potential Clinical Importance		SAC
26.	mITT	UR2A/UR2B	Listing of Urinalysis Data	ICH E3	SAC
ECG					
27.	mITT	CP_EG4	Listing of All ECG Values for Subjects with Any Value of Potential Clinical Importance	IDSL	SAC
28.	mITT	CP_EG4	Listing of ECG Values of Potential Clinical Importance	IDSL	SAC
29.	mITT	CP_EG6	Listing of All ECG Findings for Subjects with an Abnormal ECG Finding	IDSL	SAC
30.	mITT	CP_EG6	Listing of Abnormal ECG Findings	IDSL	SAC
Vital Signs					
31.	mITT	CP_VS5	Listing of All Vital Signs Data for Subjects with Any Value of Potential Clinical Importance	IDSL	SAC
32.	mITT	CP_VS5	Listing of Vital Signs of Potential Clinical Importance	IDSL	SAC

10.10.9. Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
33.	ALLSUB	POP_L2	Listing of Study Treatment Misallocations		SAC
Past and Current Medical History					
34.	mITT	MH3	Listing of Medical Conditions		SAC
Pharmacokinetics					
35.	PK	No shell (SAS output)	Supportive SAS Output from Statistical Analysis of Log-Transformed Danirixin Pharmacokinetic Parameters: Relative Bioavailability, Fed and Fasted States and Food Effect in Test Formulations		SAC
36.	PK	No shell (SAS output)	Supportive SAS Output from Statistical Analysis of Log-Transformed Danirixin Pharmacokinetic Parameters: Food Effect in Selected Formulation with and without PPI, and PPI Effect in Selected Formulation		SAC
37.	PK	No shell (SAS output)	Supportive SAS Output from Statistical Analysis of Log-Transformed Danirixin Pharmacokinetic Parameters:Pharmaceutical Development		SAC
38.	PK	CP_MP1x	Listing of Dosing Times, Meal Start and End Times	Include proportion of meal eaten	SAC

10.11. Appendix 11: Example Mock Shells for Data Displays

Mock shells will be created in a separate document.