Statistical Analysis Plan

Protocol Number: AX-158-101

A Randomised, Double-blind, Placebo-controlled, Study of the Safety, Tolerability, and Pharmacokinetics of AX-158 Following Administration of Single and Multiple Ascending Oral Doses and Food Effect sub-study in Healthy Male Volunteers

Simbec-Orion Protocol ID: RD 675/34625

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CONFIDENTIAL

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Version: Final 1.0

The undersigned have reviewed and revised this SAP and find it to be consistent with the study requirements:

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GLOSSARY OF ABBREVIATIONS

ADaM	Analysis Data Model
AE	Adverse Event
ANCOVA	Analysis of Covariance
ANOVA	Analysis of Variance
ATC	Anatomical Therapeutic Chemical
AUC	Area Under the Concentration Curve
$AUC_{\%extrapolated}$	Residual Area
AUC_{0-inf}	Area Under the Concentration-time Curve calculated from the time of dosing to infinity
AUC_{0-t}	Area Under the Concentration-time Curve calculated from the time of dosing to the last measurable concentration
AUC_{0-tau}	Area Under the Concentration-time Curve calculated over one dosing interval at steady state
BLQ	Below Limit of Quantification
BMI	Body Mass Index
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CL	Total body clearance
CL_{ss}	Total body clearance at steady state
C_{max}	Maximum observed concentration
C_{min}	Minimum observed concentration
CRA	Clinical Research Associate
CRF	Case Report Form
CRO	Clinical Research Organisation
CS	Clinically Significant
CSR	Clinical Study Report
CV	Coefficient of Variation
DBL	Database Lock
DMP	Data Management Plan
DOB	Date of Birth
DRM	Data Review Meeting
ECG	Electrocardiogram
eTMF	Electronic Trial Master File
GM	Geometric Mean
h	Hours
ICH	International Conference on Harmonisation
IMP	Investigational Medicinal Product
K_{el}	Elimination rate constant
LLOQ	Lower Limit of Quantification
LSMean	Least Squares Mean
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligram
ml	Millilitre
N	Number of subjects in the analysis set
n	Number of subjects with non-missing observations
NCS	Not clinically significant
PD	Pharmacodynamics

PK	Pharmacokinetics
PT	Preferred Term
QC	Quality Control
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SDTM	Study Data Tabulation Model
SE	Standard Error
SOC	System Organ Class
$t_{1/2}$	Terminal phase half life
TEAE	Treatment Emergent Adverse Event
TFL	Tables, Figures and Listings
T_{max}	Time from dosing to the maximum observed concentration
TMF	Trial Master File
Vz	Apparent volume of distribution
WHO	World Health Organisation
WHODD	World Health Organisation Drug Dictionary
µg	Microgram

1 INTRODUCTION

1.1 GENERAL

This statistical analysis plan (SAP) describes the statistical methods to be used during the reporting and analyses of data collected under the AX-158-101 protocol dated 15 March 2022 and should be read in conjunction with the study protocol and electronic case report form (eCRF).

This version of the plan has been developed using protocol version 5.0 dated 15 March 2022 and annotated CRF version 4.3 dated 22AUG2022 further changes to the protocol or eCRF will be reviewed for potential impact on the SAP which will be amended if it is deemed necessary.

Draft versions of the SAP will undergo review by the Statistical Reviewer, Statistical Programmer, Project Manager, PK Analyst, Medical Writer, Principal Investigator and the Sponsor/Sponsor representative. The analysis plan will be finalised and approved by the Sponsor prior to Database Lock (DBL).

1.2 CHANGES FROM PROTOCOL

The PK Set criterion of having at least one PK sample with concentration above the lower limit of quantitation (LLOQ) has been removed to enable inclusion of subjects with all-BLQ profiles to contribute to the concentration data summaries.

For Part B the statistical analysis (ANOVA) will be performed including fixed effects for sequence, period, treatment and subject nested within sequence.

1.3 CHANGES FROM PREVIOUS VERSIONS OF THE SAP

Not applicable.

2 STUDY OBJECTIVES

Primary Objective(s):

- To assess the safety and tolerability of single and multiple ascending doses of AX-158 when administered to healthy participants (Part A and Part C)

Secondary Objective(s):

- To investigate the PK of single and multiple doses of AX-158 in healthy participants (Part A and Part C).
- To investigate any food effect on the PK of AX-158 following oral administration of a single dose to healthy participants (Part B).

3 STUDY DESIGN

3.1 OVERVIEW

This is a phase I, randomised, double-blind, placebo-controlled study to investigate the safety, tolerability, and PK of AX-158 in healthy male participants following single (Part A) and multiple (Part C) ascending doses including food effect (Part B).

The study will be conducted in three parts:

Part A

Part A (SAD) will enrol up to 8 participants per cohort randomised (3:1) to receive AX-158 or placebo. Part A will follow a single ascending dose (SAD) design with all participants receiving one dose of AX-158 (or placebo) in the fasted state.

This part will be conducted in up to 34 participants (8 participants in cohorts 1 and 5, 6 participants in cohorts 2, 3 and 4). An additional two cohorts of up to eight (8) participants each (up to 16 additional participants total) may be investigated if required.

Part B

Part B (Food Effect) will be conducted in up to 8 participants in a cross-over manner; each participant will receive AX-158 in the fed and fasted state.

This part will be conducted in up to 8 participants in a cross-over manner.

Part C

Part C (MAD) will enrol up to 8 participants per cohort randomised to (3:1) to receive AX-158 or placebo. Part C will follow a multiple ascending dose (MAD) design with participants receiving AX-158 (or placebo) once daily for 10 consecutive days, in a fed or fasted state (depending on the outcome of the Part B (Food Effect). Doses, dosing duration and dose regimen (i.e., q.i.d., b.i.d., t.i.d.) of AX-158 and matching placebo for Part C may be modified based on all available safety, tolerability, and PK data and applied to additional MAD cohorts.

This part will be conducted in up to twenty-four (24) participants (3 cohorts of up to 8 participants). An additional two cohorts of up to eight (8) participants each (up to 16 additional participants total) may be investigated if required.

Duration of study:

- Part A: approximately 6 weeks for each individual (from the screening to post-study follow-up).
- Part B: approximately 8 weeks for each individual (from the screening to post-study follow-up).
- Part C: approximately 7 weeks for each individual (from the screening to post-study follow-up).

A review of safety data and available preliminary PK data will be conducted by the DERC (Dose Escalation Review Committee). Following DERC review of data from Part A, the dose for participants in Part B will be determined. Following DERC review of data from Part B, the dose for participants in Part C will be determined, and cohorts in Part C may be administered AX-158 under fasted or fed conditions as deemed appropriate, pending DERC determination of any appreciable impact of food on the absorption, distribution, metabolism, and excretion (ADME) of AX-158.

3.2 INCLUSION AND EXCLUSION CRITERIA

To be eligible for inclusion into this study, each subject must fulfil all inclusion criteria and not violate any exclusion criteria (for the protocol under which they are entered) during screening prior to randomisation. Details of the inclusion and exclusion criteria are presented within the protocol (section 10.5).

3.3 STUDY TREATMENT

For Part A (SAD), 5 planned cohorts of 8 subjects (with an option to include up to 2 additional cohorts) will receive the following in accordance with the randomisation schedule:

- a single dose of AX-158 capsules (6 subjects)
- matching placebo (2 subjects)

The IMPs will be administered fasted with 240 ml water.

For Part B (Food Effect), 1 cohort of 8 subjects will receive a single dose of AX-158 capsules in either the fed or fasted state over 2 periods (1 per period) in accordance with the randomisation schedule.

For Part C (MAD), 3 cohorts of 8 subjects (with an option to include up to 2 additional cohorts) will receive the following in accordance with the randomisation schedule:

- AX-158 capsules for 10 days (6 subjects)
- matching placebo for 10 days (2 subjects)

The IMPs will be administered fasted with 240 ml water.

If a food effect is observed in Part B, cohorts in Part C may be dosed with a standardised meal.

For Part A (SAD) and Part C (MAD), a dose leader design will be implemented with 2 participants being dosed on the first dosing day of each cohort. Of these 2, 1 will be on active drug and 1 on placebo.

3.4 STUDY TIMEPOINTS

3.4.1 Schedule of Study Procedures

Part A

Visits[1,2]	Screening	Treatment Period																Follow up
		In-house																
Days	Day – 28 to -2	Day - 1	Day 1										Post-Treatment 1 (Day 2)		Post-Treatment 2 (Day 3)	Post-Treatment 3 (Day 4)	5-7 days from last IMP dose
Time (h)			Pre-Dose	0	0.5	0.75	1h	2h	3h	4h	6h	8h	12h	24h	36h	48h	72h	
Informed Consent	X																	
Inclusion/Exclusion[3]	X	X	X															
Demographics	X																	
Height/Weight/BMI[4]	X	X																
Medical History & Concurrent Conditions	X																	
Virology Tests (HIV, HBsAg, HCV)	X																	
Drug and Alcohol Screen[5]	X	X																
COVID-19 Test		X																
Biochemistry	X[6]	X												X			X	X
Haematology	X	X												X			X	X
Urinalysis	X	X											X	X			X	X
Coagulation[7]	X	X												X			X	X
Randomisation			X															
Adverse Events	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Vital Signs[8]	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X
Physical Examination	X	X[11]															X[11]	X[11]
12-Lead ECG[9]	X	X	X		X					X			X	X		X	X	X
Prior & Concomitant Medication	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Dose IMP[10]				X														
Blood Sampling for PK			X		X	X	X	X	X	X	X	X	X	X	X	X	X	
Exploratory PD sample			X[12]															

1. All cohorts will complete only 1 Treatment Period.
2. Participants will be in the clinical unit for their in-house period from the morning before dosing (Day -1), until the completion of all the assessments on Post-Treatment 3 (Day 4).
3. Eligibility will be determined during screening. Continued eligibility will be confirmed on Day -1, and pre-dose Day 1.
4. Height measured at Screening only.
5. A urine sample will be used to screen for drugs of abuse (including alcohol and cotinine).
6. Total serum testosterone only required at screening.
7. Coagulation testing INR, aPTT and PT.
8. Vital signs include the following assessments: supine systolic and diastolic blood pressure, supine heart rate, respiration rate and oral temperature
9. 12-lead ECG will be performed at screening, each period pre-dose and at 30 min, 4 h, 12 h, 24 h, 48 h and 72 h post-dose and at the post-study follow up visit.
10. IMP or placebo will be administered orally in a fasted state (after an overnight fast of at least 10 h) with 240 mL water. The fast will be broken 4 h post-dose with lunch.
11. Symptom directed
12. Cohort 3 onwards additional samples will be taken based on emerging data

Part B

Visits[1,2]	Screening	Treatment Periods 1 & 2 In-house															Follow up
Days	Day – 28 to -2	Day - 1	Day 1										Post-Treatment 1 (Day 2)		Post-Treatment 2 (Day 3)	Post-Treatment 3 (Day 4)	5-7 days from last IMP dose
Time (h)			Pre-Dose	0	0.5	0.75	1h	2h	3h	4h	6h	8h	12h	24h	36h	48h	72h	
Informed Consent	X																	
Inclusion/Exclusion[3]	X	X	X															
Demographics	X																	
Height/Weight/BMI[4]	X	X																
Medical History & Concurrent Conditions	X																	
Virology Tests (HIV, HBsAg, HCV)	X																	
Drug and Alcohol Screen[5]	X	X																
COVID-19 Test		X																
Biochemistry	X[6]	X	X[6]											X			X	X
Haematology	X	X												X			X	X
Urinalysis	X	X											X	X			X	X
Coagulation[7]	X	X												X			X	X
Randomisation			X															
Adverse Events	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Vital Signs[8]	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X
Physical Examination	X	X[11]															X[11]	X[11]
12-Lead ECG[9]	X	X	X		X					X			X	X		X	X	X
Prior & Concomitant Medication	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Dose IMP[10]				X														
Blood Sampling for PK			X		X	X	X	X	X	X	X	X	X	X	X	X	X	

1. All cohorts will complete Treatment Period 1 & 2.
2. For Treatment Periods 1 & 2, participants will be in the clinical unit for their in-house period from the morning before dosing (Day -1), until the completion of all the assessments on Post-Treatment 3 (Day 4).
3. Eligibility will be determined during screening. Continued eligibility will be confirmed on Day -1, and pre-dose Day 1 for Treatment Periods 1 & 2.
4. Height measured at Screening only.
5. A urine sample will be used to screen for drugs of abuse (including alcohol and cotinine).
6. Total serum testosterone required at screening and pre-dose D1 each treatment period (Biochemistry sample: pre-dose Day1 total serum testosterone only).
7. Coagulation testing INR, Aptt and PT.
8. Vital signs include the following assessments: supine systolic and diastolic blood pressure, supine heart rate, respiration rate and oral temperature
9. 12-lead ECG will be performed at screening, each period pre-dose and at 30 min, 4 h, 12 h, 24 h, 48 h and 72 h post-dose and at the post-study follow up visit.
10. Participants will receive a single dose of AX-158 following an overnight fast of at least 10 h OR following consumption of a high-fat breakfast over 2 treatment periods (1 per period). AX-158 should be administered 30 mins after the start of the meal.
11. Symptom directed

Part C

Visits[1]	Screening	In-house																Follow up
Days	Day – 28 to -2	Day – 1	Day 1-4, Day 10-13[15]														Day 5-9	5-7 days from last IMP dose
Time (h)			Pre-Dose	0	0.5	0.75	1h	2h	3h	4h	6h	8h	12h	24h	36h	48h	72h		
Informed Consent	X																		
Inclusion/Exclusion[2]	X	X	X																
Demographics	X																		
Height/Weight/BMI[3]	X	X																	
Medical History & Concurrent Conditions	X																		
Virology Tests (HIV, HbsAg, HCV)	X																		
Drug and Alcohol Screen[4]	X	X																	
COVID-19 Test		X															X[15]		
Biochemistry	X[7]	X	X[7,8]											X[7,8]			X	X[6,7,8]	X
Haematology	X	X												X			X	X[6]	X
Urinalysis	X	X											X	X			X	X[6]	X
Coagulation[5]	X	X												X			X	X[6]	X
Randomisation			X																
Adverse Events	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Vital Signs[9]	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X[6]	X
Physical Examination	X	X[13]															X[13]		X[13]
12-Lead ECG[10]	X	X	X		X					X			X	X		X	X	X[6]	X
Prior and Concomitant Medication	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Dose IMP[11]				X										X		X	X	X	
Blood Sampling for PK			X		X	X	X	X	X	X	X	X	X	X	X	X	X	X[14]	
Urine Sampling for PK			X[12]	←														→	
Exploratory PD sample			X[16]																

1. For each cohort participants will be in the clinical unit for their inpatient visit from the morning before dosing (Day -1), until the completion of all assessments on Day 13.
2. Eligibility will be determined during screening. Continued eligibility will be confirmed on Day -1, and pre-dose Day 1- 10
3. Height measured at Screening only.
4. A urine sample will be used to screen for drugs of abuse (including alcohol and cotinine)
5. Coagulation testing INR, aPTT and PT
6. Pre dose on Day 5 only
7. Total serum testosterone required at screening, fasted pre dose D1, D5 and on D11 (Biochemistry sample: pre-dose Day1 total serum testosterone only)
8. Serum LH required at pre dose D1, D5 and on D11 (Biochemistry sample: pre-dose Day1 serum LH only)
9. Vital signs include the following assessments: supine systolic and diastolic blood pressure, supine heart rate, respiration rate and oral temperature
10. 12-lead ECG will be performed at screening, pre-dose and at 30 min, 4 h, 12 h, 24 h, 48 h and 72 h post-dose Days 1 and 10 and at the post-study follow up visit.
11. For all cohorts IMP or placebo will be administered orally in a fasted state (after an overnight fast of at least 10 h) with 240 mL water. The fast will be broken 4 h post-dose with lunch on Days 1-10.
12. Urine sampling: for AX-158: pre-dose and in intervals of 0-12, 12-24, 24-48 and 48-72 h post-dose on Day 1 and Day 10
13. Symptom Directed
14. Pre-dose trough sample day 5 only
15. COVID-19 test on day 8 and prior to check out.
16. Additional samples will be taken based on emerging data

3.5 SAMPLE SIZE CONSIDERATIONS

The sample size chosen for this study is not based on a formal statistical estimation but is considered adequate to meet the objectives of the study. A sufficient number of participants will be initially screened for enrolment to ensure that the planned sample size is achieved.

3.6 RANDOMISATION

Simbec-Orion using the PROC PLAN procedure of SAS® (9.4 or higher or EG). The randomisation code will include 2 dose-leaders (1 active:1 placebo) in each cohort (for Part A and Part C only).

Part A
Format and range of randomisation numbers: 101 – 156. Replacement subjects will be assigned the same randomisation as the participant they are replacing, however, 300 will be added to the number (i.e., 401 would replace 101 etc.).

The following IMPs will be used: AX-158 capsules vs Placebo.

Part B
Format and range of randomisation numbers: 201 – 208. Replacement subjects will be assigned the same randomisation as the participant they are replacing, however, 300 will be added to the number (i.e., 501 would replace 201 etc.).

The following IMPs will be used: AX-158 capsules in fed/fasted state.

Sequence	Period 1	Period 2
1	AX-158 - Fasted	AX-158 - Fed
2	AX-158 - Fed	AX-158 - Fasted

Part C
Format and range of randomisation numbers: 301 – 340. Replacement subjects will be assigned the same randomisation as the participant they are replacing, however, 300 will be added to the number (i.e., 601 would replace 301 etc.).

The following IMPs will be used: AX-158 capsules vs Placebo.

4 STUDY VARIABLES AND COVARIATES

4.1 PRIMARY VARIABLES

The primary safety endpoints for this study are as follows:

- Adverse events
- Laboratory safety parameters (biochemistry, hematology, coagulation, urinalysis)
- Vital signs (systolic/diastolic blood pressure, heart rate, oral body temperature and respiratory rate)
- 12-Lead ECG (Heart rate, PR interval, QRS width, RR interval, QT interval and QT interval corrected using Fredericia's formula (QTcF)

4.2 SECONDARY VARIABLES

The secondary plasma pharmacokinetic (PK) endpoints for this study are as follows:

- C_{max} Maximum observed concentration

- T_{max} Time to maximum observed concentration
- T_{lag} The delay in achieving T_{max} (only in Part B)
- k_{el} Elimination rate constant
- $t_{1/2}$ Terminal elimination half-life
- AUC_{0-24} Area under the concentration-time curve (AUC) from the time of dosing to 24 hour post dose
- AUC_{0-tau} If part C dosing is not q.d.
- AUC_{0-t} Area under the concentration-time curve (AUC) from the time of dosing to the time of the last measurable concentration
- AUC_{0-inf} AUC extrapolated to infinity
- $AUC_{\% extrapolated}$ Residual area
- CL/F Apparent total body clearance
- Vz/F Apparent volume of distribution

The secondary urine PK endpoints for Part C of this study are:

- Ae Amount and cumulative amount of dose excreted in urine over each collection interval
- Ae% % and cumulative % of dose excreted in urine over each collection interval
- CL_R Renal clearance

5 DEFINITIONS AND DERIVED VARIABLES

Treatment/IMP: Treatment or IMP is taken to mean either AX-158 at all dose levels, in the fed or fasted state, or placebo.

Baseline: For Part A and Part C unless stated otherwise, baseline is defined by subject and by variable as the last non-missing value (including repeat/unscheduled assessments) before the first dose of study drug.

For Part B unless stated otherwise, baseline is defined by subject and by variable as the last non-missing value (including repeat/unscheduled assessments) before the first dose of study drug in each treatment period. This will normally be the pre-dose assessment on Day 1 of each treatment period but if this assessment is missing (or not planned) then the last assessment prior to first dose in Period 1 will be used instead, if available. Specific baselines for each endpoint are defined in Section 11, where appropriate.

Study Day: Study day is the number of days since start of treatment where the date of first dose is counted as Day 1.

Blood Sampling Time Deviation: Actual sample time – planned sample time.

Protocol Deviation: a deviation related to study inclusion or exclusion criteria, conduct of the trial, subject management or subject assessment. This refers to any change, divergence, or departure from the study design or procedures defined in the protocol. Protocol deviations captured in the CRF will be discussed at the Data Review Meeting (DRM) before Database Lock (DBL). In addition, any deviations

identified during the DRM will be discussed and included in the database as necessary. All protocol deviations within the study database will be classified as either 'Major' or 'Minor' prior to DBL, details of which will be included within the Protocol Deviations listing.

6 ANALYSIS SETS

Membership of the analysis sets will be reviewed during the DRM and agreed prior to DBL. These will be reviewed by the Sponsor, Study Statistician, PK Analyst and Project Manager and included within the DRM minutes. Where PK data is not available at the time of DBL, subjects will be assumed to be included in the analysis set unless the PK data provide reason to exclude a subject, in which case this will be discussed with the Sponsor and documented within the Analysis Sets listing (Listing 16.2.3.1).

6.1 ALL CONSENTED SET

All subjects for whom informed consent was obtained will constitute the All Consented Set.

This analysis set will be used for the study disposition listing and summary.

6.2 SAFETY SET

All randomised subjects who receive at least 1 dose of IMP will be included in the Safety Set.

This analysis set will be used for baseline and safety summaries as well as for all study listings.

6.3 PK SET

The PK set will include subjects who receive active IMP (one dose in Part A, both doses in Part B (fed/fasted), up to 10 doses in Part C), have sufficient plasma concentration-time profiles and comply with the following criteria:

- Do not have an occurrence of vomiting (that occurs at or before 2 times median T_{max} within the appropriate cohort or treatment) or diarrhoea which renders the concentration profile unreliable. For Part C this applies to PK sampling days only.
- Do not use a concomitant medication which renders the concentration profile unreliable.
- Do not have a Day 1 pre-dose concentration that is greater than 5% of the corresponding C_{max}.
- Do not violate the protocol in such a way that may invalidate or bias the results (major protocol violators).

For Part C, a subject may be included in the PK Set if they have a valid Day 1 PK profile which meets the above criteria, as the Day 1 PK data can be included in the dose proportionality/independence assessment. For inclusion in the Day 10 dose proportionality/independence assessment, subjects must have fulfilled the above criteria and received all doses of study drug.

In order to be included in the statistical comparisons for Part B, a subject is required to be included in the PK Set for the two treatments being evaluated within the particular comparison.

All protocol deviations within the study database will be reviewed to determine whether they affect a subject's eligibility for inclusion in the PK Set. Any deviations and reasons for exclusion will be identified and documented before statistical analysis of the pharmacokinetic data is undertaken.

This analysis set will be used for PK summaries and statistical analyses.

7 SAFETY MONITORING

Following completion of each cohort, a summary of all relevant safety AEs, ECG, vital signs, laboratory assessments up to 72 h post dose) and PK data (up to 24 h post-dose for Part A & Part B and 10 days for Part C) will be produced on behalf of the Principal Investigator. Planned doses may be modified following a review of emerging data. Progression to the next SAD dose level and dose selection will be based on the available safety and PK data from at least 6 evaluable participants from the preceding dose level. Progression to the next MAD dose level and dose selection will be based on the available safety and PK data from at least 6 evaluable participants from the preceding dose level. An evaluable participant is defined as a participant who has received the planned dose (active or placebo) and has sufficient PK samples to estimate C_{max} and AUC_{0-24}. Dose escalation will be dependent upon generation of acceptable safety (and PK) data. If it is not appropriate to escalate the dose according to the proposed dose escalation schedule, then the same dose, an intermediate dose or a lower dose may be given following discussion between the Sponsor and the Principal Investigator (or deputy) if no stopping criteria are met.

Outputs for the safety review will be presented as Excel listings of the clinical database.

8 INTERIM ANALYSES

Other than data review for dose escalation purposes (see section 7), no interim PKor safety analyses are planned for this study.

9 DATA

9.1 eCRF DATA

Data captured in the eCRF will be provided by Simbec-Orion Data Management to the Statistics department as SAS datasets in a standard format. Study Data Tabulation Model (SDTM) datasets will be derived from the raw database and Analysis Data Model (ADaM) from SDTM. Both SDTM and ADaM domains will be used for programming the outputs to be included in the Clinical Study Report (CSR). Specifications of both SDTM and ADaM will be provided in a separate document. SDTM/ADaM programming will begin when populated SAS datasets are available.

9.2 EXTERNAL DATA

9.2.1 Laboratory Data

Transfers of safety laboratory data will be provided by Simbec-Orion Laboratory Services, delivered to Simbec-Orion Data Management via electronic transfer and stored within the study database and subsequently, within the appropriate SDTM and ADaM domains.. Details of laboratory data are documented in the Data Management Plan (DMP). Populated test transfers will be received before programming can start.

The following results will be included:

- **Hematology:** Hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, platelet count, red blood cell count, red blood cell distribution width, white blood cell count and WBC differential count (neutrophils, lymphocytes, monocytes, eosinophils, and basophils) (reported in absolute and percentage values).

- **Biochemistry:** Alanine transaminase, albumin, alkaline phosphatase, aspartate transaminase, bicarbonate, total bilirubin, direct bilirubin (if total bilirubin is raised), calcium, chloride, c-reactive protein, creatine kinase, creatinine, glucose (random), gamma glutamyltransferase, potassium, total protein, sodium, urea, total serum testosterone and luteinizing hormone.

- **Urinalysis:** Bilirubin, blood, glucose, ketones [or ketone bodies], leucocytes, nitrite, pH, protein, specific gravity, and urobilinogen.

- **Coagulation**: International normalized ratio, Activated partial thromboplastin time and prothrombin time.

- **Microscopy:** In the event that the urinalysis 'dipstick' test result is positive for nitrite and/or 2+ or more reported for protein, blood, and/or leucocytes, the following test parameters will be reported microscopically: bacteria, casts (non-pathogenic), casts (pathogenic), crystals, epithelial cells, red blood cells and white blood cells

- **Virology:** HBsAg, HCV Ab and HIV test (antibodies to HIV-1 and HIV-2).

- **COVID-19 Test:** A nasopharyngeal and/or oropharyngeal swab will be collected. COVID-19 testing will be routinely performed via lateral flow test (LFT) however, a RT-PCR test may be performed at the PI's discretion.

- **Drugs of Abuse Screen and Alcohol:** alcohol, amphetamines, barbiturates, benzodiazepines, cannabinoids/tetrahydrocannabinoids (THC), cocaine, cotinine, methadone, and opiates.

- **Other Parameters:** Any further parameters that are taken at the request of the Investigator that are not included as part of the above categories will be included in an 'Other Laboratory Data' listing.

9.2.2 Other non-CRF data

Pharmacokinetic Data

Plasma and urine AX-158 concentration data will be delivered to Simbec-Orion Data Management via electronic transfer from Simbec-Orion Laboratory Services and stored as a SAS dataset. This data will be stored in the appropriate SDTM domain and subsequent ADaM domain and will be used to produce the file provided to the pharmacokinetic team in order to derive the pharmacokinetic parameters using Phoenix WinNonlin v8.3 or higher. Derived PK parameters will be received from the PK Analyst as a SAS .xpt file in an agreed format and stored in the appropriate SDTM and ADaM domains.

9.3 RANDOMISATION LIST

The randomisation list (in SAS dataset format) will be released following DBL and incorporated into the relevant SDTM/ADaM domains.

9.4 PROGRAMMING AND DATA REVIEW

Programming of datasets, tables, figures and listings will be ongoing while study data management activities are in progress.

Prior to DBL, a review of the clinical database will be conducted. Outputs for the data review will be produced as Excel outputs of the clinical database. A DRM will be held to discuss the outcome of this review, any potential impact on the analyses, analysis sets and protocol deviations. Meeting minutes will be created which will include details of decisions surrounding analysis sets and protocol deviation classification. Once all data issues have been resolved, the analysis sets approved and protocol deviation classifications agreed, the database will be locked. The post-lock SDTM/ADaM datasets will be generated, the TFLs will be run and quality control (QC) will take place.

10 STATISTICAL METHODS

10.1 GENERAL PRINCIPLES

- All statistical methods will be based on the International Conference on Harmonisation (ICH) E9 document "Statistical Principles for Clinical Trials".
- All data collected will be presented within data listings.
- Generally, for Part A and Part C, data listings will be sorted by subject, visit and treatment, with the exception of baseline data listings which will be sorted by treatment, subject and visit.
- Generally, for Parts A and C, data listings will be sorted by part, cohort, treatment, subject, visit/time point. Generally, for Part B, data listings will be sorted by part, subject, visit and treatment, where appropriate.
- Generally, data will be summarised by treatment for each part separately. Where appropriate, a summary of all active treatments (Parts A and C) and treatments overall will be included. For Part B, baseline data will be summarised overall. The format of the summaries is defined in the shells at the end of this document.
- Repeated visits will be denoted with 'RPT'. Unscheduled visits will be denoted with 'UNS'.
- In summary and analysis tables of continuous variables, standard descriptive statistics (N [number within analysis set, or group, or subgroup], n [number of observations included in analysis], mean, standard deviation [SD], median, minimum and maximum) will be presented. Least squares means (LSMean) and 90/95% confidence intervals (CI) will be presented in the statistical analysis outputs as appropriate. For PK summaries, geometric mean and coefficient of variation (%CV) will also be used to summarise the data.
- Unless otherwise specified, the minimum and maximum statistics will be presented in summary tables to the same number of decimal places as the original data. The mean, median, LSMean, and CI will be presented to one more decimal place than the original data. SD will be presented to two more decimal places than the original data.
- Derived PK parameters and concentration data listings and summaries will be presented to 3 significant figures (with the exception of CV%, which will be presented to 1 decimal place). The

ratio of the geometric LSMeans (i.e. test/reference) and its associated confidence interval will be presented to 2 decimal places.

- In summary tables of categorical variables, the number of non-missing observations by category will be presented along with percentages. Unless otherwise specified, the denominator for each percentage will be the number of non-missing observations.
- All percentages will be presented to one decimal place.
- P-values will be rounded to four decimal places. P-values less than 0.0001 will be reported as <0.0001 in tables.
- All plots will use a linear time scale for the nominal times of the visits and will be labelled by time point.
- For post-dose assessments, only data obtained from scheduled visits/time points will be used in summary tables. Post-dose repeat or unscheduled assessments will be listed only. For assessments occurring prior to dosing (i.e. Screening, Day -1, Day 1 pre-dose), the last repeat assessment for each visit will be included in the summary tables and, where repeats of baseline values occur, the last assessment will be used to calculate change from baseline.
- Dates and times for all output presentations will be presented in ISO 8601 Datetime format.
- All outputs will present data in a format that complies with CDISC required terminology and codelists and the SAP will use American-English spelling in line with CDISC terminology, where appropriate (i.e. hematology).
- All statistical analysis will be performed using SAS EG 8.3 or higher.
- All hypothesis testing will be carried out at the 5% (2-sided) significance level unless stated otherwise.
- Generally, character values will be left aligned and numeric values will be decimally aligned.
- If no data is available for a specific output, the output will be produced stating an appropriate message indicating no data was present.
- If any issues arise with the planned analysis of the final data, alternative statistical methods may be used and any changes documented in the statistical methods section of the clinical study report (CSR), including the rationale for use.
- With the exception of PK data, for numeric data which includes non-numeric values (e.g. laboratory results reported as <10 or >100), results reported as $<x$ $\leq x$, $\geq x$ $>x$ will be treated as x for inclusion within the summaries/statistical analysis but will listed as reported. Refer to section 11.4 for handling of non-numeric *PK* data.

10.2 STRATIFICATION AND COVARIATE ADJUSTMENT

None.

10.3 INTERACTIONS

None.

10.4 MISSING DATA

No methods to account for missing safety data will be used.

In the instance of missing pharmacokinetic blood samples, the trapezoidal rule will be employed between the samples immediately before and after the missing sample for the AUC calculations.

10.5 POOLING OF SITES

Not applicable.

10.6 MULTIPLE COMPARISONS

No multiplicity adjustments are planned.

10.7 SUBGROUP ANALYSES

None.

10.8 STATISTICAL ISSUES

None.

11 STATISTICAL OUTPUT

General principles for layout of the statistical output are described in Section 10.1. Layout and specifications are illustrated for each unique table in the table shells in Section 14.

11.1 SUBJECT DISPOSITION

The subject disposition table will summarise the following data:

- The number of consented subjects
- The number of subjects receiving each treatment
- The number (%) of subjects who completed/withdrew from the study and the associated reasons for withdrawal
- The number (%) of subjects in each analysis set

All percentages will be calculated from the number of dosed subjects within a treatment group for Parts A and C or number of dosed subjects for Part B.

Screening and study completion/termination data (including informed consent information) will also be listed. A listing of all protocol deviations will be presented including major/minor classification. A data listing presenting subject eligibility for each analysis set and the reason for exclusion from an analysis set will also be presented.

Disposition data will be listed and summarised for the All Consented Set.

11.2 SUBJECT CHARACTERISTICS AT BASELINE

11.2.1 Demographic and Baseline Characteristics

Demographic data will be listed. Descriptive statistics (number of participants in the analysis set (N), number of participants with non-missing observations (n), mean, standard deviation (SD), minimum, median, and maximum) will be tabulated for the continuous variables age, height, weight and BMI at Screening and frequencies (number and %) for the categorical variables race and ethnicity.

Demographic data will be listed and summarised using the Safety Set.

11.3 EFFICACY ANALYSES

Not applicable.

11.4 PK ANALYSES

11.4.1 Concentration Data

Plasma PK samples will be collected for the measurement of AX-158 at the following time points:

Part A:
- Day 1 pre-dose, 30 mins, 45 mins, 1h, 2h, 3h, 4h, 6h, 8h, 12h
- Day 2: 24h, 36h
- Day 3: 48h
- Day 4: 72h

Part B: For both treatment periods
- Day 1 pre-dose, 30 mins, 45 mins, 1h, 2h, 3h, 4h, 6h, 8h, 12h
- Day 2: 24h, 36h
- Day 3: 48h
- Day 4: 72h

Part C:
- Day 1 and Day 10 pre-dose, 1h, 2h, 3h, 4h, 5h, 6h, 8h, 12h
- Day 2 and Day 11: 24h, 36h
- Day 3 and Day 12: 48h
- Day 4 and Day 13: 72h
- Day 5: pre-dose
- Day 6: Pre-dose
- Day 7: Pre-dose
- Day 8: Pre-dose

Plasma AX-158 concentrations will be listed along with blood sampling times and details of any sampling time deviations and summarised for each treatment using the descriptive statistics N, n, arithmetic mean,

geometric mean, arithmetic standard deviation (SD), coefficient of variation (CV%), minimum, median and maximum.

The individual subject plasma AX-158 concentration profiles over time will be presented graphically on both linear and semi-logarithmic scales with each subject on a separate plot. For Part C, Day 1 and Final Dosing Day (Day 10) profiles will be presented on the same plot. The geometric mean plasma AX-158 concentration profiles over time will be presented graphically on both linear and semi-logarithmic scales with all treatments on the same plot, with separate plots for Day 1 and Final Dosing Day profiles for Part C.

Urine PK samples will be collected for the measurement of AX-158 at the following time intervals: pre-dose and in intervals of 0-12, 12-24, 24-48 and 48-72 h post-dose on Day 1 and Day 10.

Urine AX-158 concentrations will be listed along with urine volumes and summarised for each treatment using the descriptive statistics N, n, arithmetic mean, geometric mean, arithmetic standard deviation (SD), coefficient of variation (CV%), minimum, median and maximum.

For inclusion within the summary tables and plots, plasma and urine concentrations below the lower limit of quantification (LLOQ) will be imputed as zero at pre-dose and as LLOQ/2 for post-dose samples. They will be listed as recorded. Data reported as not reportable or no sample/result will be handled as missing (i.e. no assumption will be made about the actual concentration).

For inclusion within the summary tables and figures, when calculating the geometric mean concentrations at pre-dose where zero values are likely to be observed, a small value (e.g. 0.001 or smaller) will be added to all individual subject pre-dose concentration values prior to calculation of the mean. This value will then be subtracted after back-transformation, i.e.

$$\textit{Geometric Mean} = exp(\frac{1}{n}\sum_{n=1}^{n}\log(x_i + 0.001)) - 0.001$$

where x_i are the individual concentration values at pre-dose.

This method is only required for pre-dose results as zero values will not occur for post-dose time points (due to the above imputation method of BLQ values). For post-dose time points, the geometric mean will be calculated using the standard formula:

$$\textit{Geometric Mean} = exp(\frac{1}{n}\sum_{n=1}^{n}\log(x_i)).$$

Concentration data listings and individual plots will be presented using the Safety Set. Concentration data summaries and mean plots will be presented using the PK Set. All concentration data included in listings and summaries will be presented to 3 significant figures.

11.4.2 Derived PK Parameters

The derived pharmacokinetic parameters of plasma AX-158 will be determined from the individual concentration versus time data using WinNonlin Phoenix v8.3 or higher. The actual time of blood sample will be used in the calculation of the derived PK parameters. Should the actual time be unavailable but a blood sample was taken, the nominal time point will be assigned.

For the purpose of calculating PK parameters, BLQ values will be imputed as zero at pre-dose and set to missing for post-dose time points. If a Day 1, pre-dose result is missing, it will be imputed as zero. The following plasma AX-158 PK parameters will be calculated using standard non-compartmental methods:

Part A:

Pharmacokinetic Parameter and Unit	Definition	Computation	WinNonlin Parameter Name
C_{max} (µg/mL)	Maximum concentration.	Maximum observed concentration, occurring at Tmax. If not unique, then the first maximum is used.	Cmax
T_{max} (h)	The time to maximum observed concentration.	Time of maximum observed concentration. If the maximum observed concentration is not unique, then the first maximum is used.	Tmax
λz (1/h)	Elimination rate constant.	First order rate constant associated with the terminal (log-linear) portion of the curve. Estimated by linear regression of time vs. log concentration; the regression analysis should contain data from at least 3 different time points in the terminal phase	lambda_z
$t_{1/2}$ (h)	Terminal elimination half-life.	$= \ln(2) / \lambda z$	HL_Lambda_z
AUC_{0-24} (h*µg/mL)	Area under the concentration-time curve (AUC) from the time of dosing to 24 h post-dose	AUC measured from the concentration at time of dosing to 24 hours post dose. The AUC is computed using the linear up-log down trapezoidal rule.	AUC0-24
AUC_{0-t} (h*µg/mL)	Area under the concentration-time curve (AUC) from the time of dosing to the time of the last measurable concentration.	AUC measured from the concentration at time of dosing to the last measurable positive concentration. The AUC is computed using the linear up-log down trapezoidal rule.	AUClast
AUC_{0-inf} (h*µg/mL)	AUC extrapolated to infinity.	AUC measured from the concentration at time of dosing extrapolated to infinity based on the last observed concentration.	AUCINF_obs

Pharmacokinetic Parameter and Unit	Definition	Computation	WinNonlin Parameter Name
		$= AUC_{0-t} + \frac{C_{lastobs}}{\lambda z}$	
$AUC_{\%extrap.}$ (%)	Percentage of $AUC_{0\text{-}inf}$ due to extrapolation from last observed concentration to infinity.	Percentage of $AUC_{0\text{-}inf}$ due to extrapolation from time of last measurable positive concentration to infinity. $= \frac{AUC_{0-inf} - AUC_{0-t}}{AUC_{0-inf}} \cdot 100$	AUC_%Extrap _obs
CL/F (L/h)	Apparent total body clearance, calculated as Dose / $AUC_{0\text{-}inf}$.	$= Dose/AUC_{0-inf}$	CL_F_obs
Vz/F (L)	Apparent Volume of Distribution during the terminal phase.	$= \frac{Dose}{\lambda z. AUC_{0-inf}}$	Vz_F_obs
λz lower (listed only)	Elimination rate constant lower limit.	Lower limit on Time for values to be included in the calculation of λz	Lambda_z_lower
λz upper (listed only)	Elimination rate constant upper limit.	Upper limit on Time for values to be included in the calculation of λz	Lambda_z_upper
No. points λz (listed only)	Number of points used for elimination rate constant.	Number of points used for elimination rate constant	No_points_ Lambda_z
R^2 adjusted (listed only)	R^2 adjusted.	Goodness of fit statistic for the terminal elimination phase, adjusted for the number of points used in the estimation of λz	Rsq_adjusted

Part B

Pharmacokinetic Parameter and Unit	Definition	Computation	WinNonlin Parameter Name
C_{max} (µg/mL)	Maximum concentration.	Maximum observed concentration, occurring at	Cmax

Pharmacokinetic Parameter and Unit	Definition	Computation	WinNonlin Parameter Name
		Tmax. If not unique, then the first maximum is used.	
T_{max} (h)	The time to maximum observed concentration.	Time of maximum observed concentration. If the maximum observed concentration is not unique, then the first maximum is used.	Tmax
T_{lag} (h)	The delay in achieving Tmax	Time of observation prior to the first observation with a measurable (non-zero) concentration.	Tlag
λz (1/h)	Elimination rate constant.	First order rate constant associated with the terminal (log-linear) portion of the curve. Estimated by linear regression of time vs. log concentration; the regression analysis should contain data from at least 3 different time points in the terminal phase	lambda_z
$t_{1/2}$ (h)	Terminal elimination half-life.	$= \ln(2)/\lambda z$	HL_Lambda_z
AUC_{0-24} (h*µg/mL)	Area under the concentration-time curve (AUC) from the time of dosing to 24 h post-dose	AUC measured from the concentration at time of dosing to 24 hours post dose. The AUC is computed using the linear up-log down trapezoidal rule.	AUC0-24
AUC_{0-t} (h*µg/mL)	Area under the concentration-time curve (AUC) from the time of dosing to the time of the last measurable concentration.	AUC measured from the concentration at time of dosing to the last measurable positive concentration. The AUC is computed using the linear up-log down trapezoidal rule.	AUClast
AUC_{0-inf} (h*µg/mL)	AUC extrapolated to infinity.	AUC measured from the concentration at time of dosing extrapolated to infinity based on the last observed concentration.	AUCINF_obs

Pharmacokinetic Parameter and Unit	Definition	Computation	WinNonlin Parameter Name
		$= AUC_{0-t} + \frac{C_{lastobs}}{\lambda z}$	
$AUC_{\%extrap.}$ (%)	Percentage of $AUC_{0\text{-}inf}$ due to extrapolation from last observed concentration to infinity.	Percentage of $AUC_{0\text{-}inf}$ due to extrapolation from time of last measurable positive concentration to infinity. $= \frac{AUC_{0-inf} - AUC_{0-t}}{AUC_{0-inf}} \cdot 100$	AUC_%Extrap _obs
CL/F (L/h)	Apparent total body clearance, calculated as Dose / $AUC_{0\text{-}inf}$.	$= Dose/AUC_{0-inf}$	CL_F_obs
Vz/F (L)	Apparent Volume of Distribution during the terminal phase.	$= \frac{Dose}{\lambda z. AUC_{0-inf}}$	Vz_F_obs
λz lower (listed only)	Elimination rate constant lower limit.	Lower limit on Time for values to be included in the calculation of λz	Lambda_z_lower
λz_l upper (listed only)	Elimination rate constant upper limit.	Upper limit on Time for values to be included in the calculation of λz	Lambda_z_upper
No. points λz (listed only)	Number of points used for elimination rate constant.	Number of points used for elimination rate constant	No_points_ Lambda_z
R^2 adjusted (listed only)	R^2 adjusted.	Goodness of fit statistic for the terminal elimination phase, adjusted for the number of points used in the estimation of λz	Rsq_adjusted

Part C on Day 1:

Pharmacokinetic Parameter and Unit	Definition	Computation	WinNonlin Parameter Name
C_{max} (µg/mL)	Maximum concentration.	Maximum observed concentration, occurring at Tmax. If not unique, then the first maximum is used.	Cmax
T_{max} (h)	The time to maximum observed concentration.	Time of maximum observed concentration. If the maximum observed concentration is not unique, then the first maximum is used.	Tmax
AUC_{0-24} (h*µg/mL)	Area under the concentration-time curve (AUC) from the time of dosing to 24 h post-dose	AUC measured from the concentration at time of dosing to 24 hours post dose. The AUC is computed using the linear up-log down trapezoidal rule.	AUC0-24
AUC_{0-tau} (h*µg/mL) (only required if non-q.d. dosing regimen)	Area under the plasma concentration-time curve (AUC) from the time of dosing to <X> hours (dosing interval) after the Day <X> dose.	AUC measured from the concentration at time of dosing to the concentration at <X> hours. The AUC is computed using the linear up-log down trapezoidal rule.	AUC_TAU

Part C on Final Dosing Day:

Pharmacokinetic Parameter and Unit	Definition	Computation	WinNonlin Parameter Name
C_{max} (µg/mL)	Maximum concentration.	Maximum observed concentration, occurring at Tmax. If not unique, then the first maximum is used.	Cmax
T_{max} (h)	The time to maximum observed concentration.	Time of maximum observed concentration. If the maximum observed concentration is not unique, then the first maximum is used.	Tmax

Pharmacokinetic Parameter and Unit	**Definition**	**Computation**	**WinNonlin Parameter Name**
λz (1/h)	Elimination rate constant.	First order rate constant associated with the terminal (log-linear) portion of the curve. Estimated by linear regression of time vs. log concentration; the regression analysis should contain data from at least 3 different time points in the terminal phase	lambda_z
$t_{1/2}$ (h)	Terminal elimination half-life.	$= \ln(2)/\ \lambda z$	HL_Lambda_z
$AUC_{0\text{-}24}$ (h*µg/mL)	Area under the concentration-time curve (AUC) from the time of dosing to 24 h post-dose	AUC measured from the concentration at time of dosing to 24 hours post dose. The AUC is computed using the linear up-log down trapezoidal rule.	AUC0-24
$AUC_{0\text{-}tau}$ (h*µg/mL) (only required if non-q.d. dosing regimen)	Area under the plasma concentration-time curve (AUC) from the time of dosing to 24 hours (dosing interval) after the Day 10 dose.	AUC measured from the concentration at time of dosing to the concentration at 24 hours. The AUC is computed using the linear up-log down trapezoidal rule.	AUC_TAU
$AUC_{0\text{-}t}$ (h*µg/mL)	Area under the concentration-time curve (AUC) from the time of dosing to the time of the last measurable concentration.	AUC measured from the concentration at time of dosing to the last measurable positive concentration. The AUC is computed using the linear up-log down trapezoidal rule.	AUClast
$AUC_{0\text{-}inf}$ (h*µg/mL)	AUC extrapolated to infinity.	AUC measured from the concentration at time of dosing extrapolated to infinity based on the last observed concentration. $= AUC_{0-t} + \frac{C_{lastobs}}{\lambda z}$	AUCINF_obs
$AUC_{\%extrap.}$ (%)	Percentage of $AUC_{0\text{-}inf}$ due to extrapolation from last observed	Percentage of $AUC_{0\text{-}inf}$ due to extrapolation from time of last measurable positive concentration to infinity.	AUC_%Extrap_obs

Pharmacokinetic Parameter and Unit	Definition	Computation	WinNonlin Parameter Name
	concentration to infinity.	$= \frac{AUC_{0-inf} - AUC_{0-t}}{AUC_{0-inf}} \cdot 100$	
CL/F (L/h)	Apparent total body clearance, calculated as Dose / $AUC_{0\text{-}inf}$.	$= Dose/AUC_{0-inf}$	CL_F_obs
Vz/F (L)	Apparent Volume of Distribution during the terminal phase.	$= \frac{Dose}{\lambda z. AUC_{0-inf}}$	Vz_F_obs
λz lower (listed only)	Elimination rate constant lower limit.	Lower limit on Time for values to be included in the calculation of λz	Lambda_z_lower
λz upper (listed only)	Elimination rate constant upper limit.	Upper limit on Time for values to be included in the calculation of λz	Lambda_z_upper
No. points λz (listed only)	Number of points used for elimination rate constant.	Number of points used for elimination rate constant	No_points_ Lambda_z
R^2 adjusted (listed only)	R^2 adjusted.	Goodness of fit statistic for the terminal elimination phase, adjusted for the number of points used in the estimation of λz	Rsq_adjusted

The terminal elimination rate constant (λz) will be calculated by log-linear regression of the terminal portion of the concentration-time curve only where there are sufficient data i.e. at least 3 time points excluding C_{max} and adjusted R^2 is greater than or equal to 0.85; lower adjusted R^2 values may be acceptable at the discretion of the PK analyst if the elimination phase is clearly defined by the profile, values lower than 0.85 will be flagged within the data listing. If these criteria are not fulfilled, parameters dependent on k_{el} for calculation will not be reported.

The following urine PK parameters will be calculated:

Part C on Day 1 and Final Dosing Day

Pharmacokinetic Parameter and Unit	Definition	Computation	WinNonlin Parameter Name
Ae (µg)	Cumulative amount of study drug excreted in urine during a time interval.	The sum of the individual urine volume * urine concentration of study drug. $= \Sigma\,(Concentration\,.Volume)$	N/A (calculated using SAS)
Ae% (%)	Percentage of study drug excreted in urine during a time interval.	$= 100\,.Ae/Dose$	N/A (calculated using SAS)
CL_R (L/h)	Renal clearance.	$= Ae/AUC_{0-t}$	N/A (calculated using SAS)

The derived urine pharmacokinetic parameters Ae, Ae%, CumAe, CumAe%, CLR will be determined from the individual urine concentration versus time data using SAS EG v8.3 or higher.

Derived PK parameters will be listed along with the points used to calculate λz (lower, upper, and number used) and coefficient of determination (R^2) adjusted. The derived PK parameters will also be summarised. The descriptive statistics presented will be N, n, arithmetic mean, geometric mean (with the exception of T_{max}), SD, coefficient of variation (CV%), minimum, median, and maximum.
Any $AUC_{\%\ extrap}$ values greater than 20% will be flagged within the data listing. In accordance with regulatory guidance, the associated data should not be excluded from analysis but if this is observed for >20% of the profiles, the validity of the study may be in question.

In the instance of a significant sample time deviation (≥ 5% of nominal time i.e. 72 min) for the 24 h PK sample, the $AUC_{0\text{-}24}$ values will be excluded from statistical analysis, but will be calculated, included in the derived PK data listing and flagged. Where a non-significant sample time deviation (≤72 min) for the 24 h PK sample occurs and the terminal elimination rate constant (lambda_z) is estimable, this will be used to estimate $AUC_{0\text{-}24}$. Where a non-significant sample time deviation (≤ 72 min) for the 24 h PK sample occurs and the terminal elimination rate constant (lambda_z) is not estimable, WNL is unable to estimate $AUC_{0\text{-}24}$. Therefore, in order for an $AUC_{0\text{-}24}$ value to be estimated, the actual sampling time (including bleed time deviations) at the 24 h nominal time point will be used for the partial AUC settings.

PK parameter listings will be presented using the Safety Set. PK parameter summaries will be presented using the PK Set. All PK parameter data included in listings and summaries will be presented to 3 significant figures (with the exception of CV% which will be presented to one decimal place).

11.4.3 Statistical Analysis of PK Data

Dose Proportionality

Dose proportionality will be assessed by performing a regression analysis of the log-transformed C_{max}, $AUC_{0\text{-}t}$, $AUC_{0\text{-}24}$ and $AUC_{0\text{-}inf}$ values versus the log-transformed dose using the power model with a fixed

effect for log(dose). For each parameter, point estimates for the intercept and the slope of the regression line and the 95% CI of the slope will be calculated. In addition, estimated geometric LSMeans and corresponding 95% CIs will be presented for each dose level.

The power model is defined as:

$$\log_e(C_{max}, AUC_{0\text{-}t}, AUC_{0\text{-}inf}) = \alpha + \beta\log_e(Dose) + \varepsilon,$$

where α is the intercept, β is the slope and ε is the error term.

Geometric LSMeans and associated 95% CIs along with individual subject values for the derived pharmacokinetic parameters C_{max}, $AUC_{0\text{-}t}$ and $AUC_{0\text{-}inf}$ will be presented graphically versus dose with each parameter presented on a separate plot.

Dose Independence

Dose independence will be assessed for t½ and CL/F by performing a regression analysis of the untransformed parameters versus dose with a fixed effect for dose. For each parameter, point estimates for the intercept and the slope of the regression line and the 95% CI of the slope will be calculated. In addition, estimated LSMeans and corresponding 95% CIs will be presented for each dose level.

LSmeans and associated 95% CIs along with individual subject values for the derived pharmacokinetic parameters t½ and CL/F will be presented graphically versus dose.

11.4.3.1 Part B – Food Effect

Following logarithmic transformation, C_{max}, $AUC_{0\text{-}t}$ and $AUC_{0\text{-}inf}$ values will be subjected to an analysis of variance (ANOVA) including fixed effects for sequence, period, treatment and subject nested within sequence. Point estimates and 90% confidence intervals will be constructed for the contrasts between treatments using the residual mean square error obtained from the ANOVA. The point and interval estimates will be back-transformed to give estimates of the ratios of the geometric LSMeans and corresponding 90% CIs. In addition, estimated geometric LSMeans and corresponding 95% CIs for each treatment and the within-subject CV% will be presented.

The geometric LSMean ratios and corresponding 90% CIs for C_{max} $AUC_{0\text{-}t}$ and $AUC_{0\text{-}inf}$ will be represented graphically (a plot with error bars) with all parameters on one graph. On the same graph, points indicating individual within-subject ratios for the three PK parameters will be presented. Reference lines will be included to indicate the 80.00% and 125.00% CI thresholds.

Each treatment comparison will be analysed separately and will only include data from subjects who are included in the PK Set for the two treatments being evaluated.

11.4.3.2 Part C (MAD) - Dose-Proportionality/Independence

Dose-Proportionality

For Day 1 and Final Dosing Day (Day 10), dose proportionality will be assessed by performing a regression analysis of the log-transformed C_{max}, $AUC_{0\text{-}tau}$ and $AUC_{0\text{-}inf}$ (Day 10 only) values versus the log-transformed dose using the power model with a fixed effect for log (dose). For each parameter, a point estimate and 95 % CI will be calculated for the slope of the regression line.

The power model is defined as:

$$\log_e(C_{max}, AUC_{0\text{-}t}, AUC_{0\text{-}inf}) = \alpha + \beta\log_e(Dose) + \varepsilon,$$

where α is the intercept, β is the slope and ε is the error term.

Geometric LSMeans and associated 95% CIs along with individual subject values for the derived pharmacokinetic parameters C_{max}, $AUC_{0\text{-}t}$ and $AUC_{0\text{-}inf}$ will be presented graphically versus dose with each parameter presented on a separate plot.

Dose Independence

For Final Dosing Day (Day 10), dose independence will be assessed for t½ and CL/F by performing a regression analysis of the untransformed parameters versus dose with a fixed effect for dose. For each parameter, a point estimate and corresponding 95 % CI will be calculated for the slope of the regression line.

11.4.3.3 Part C (MAD) - Steady State

For each treatment, log-transformed trough concentration levels at pre-dose on Day 5 and Final Dosing Day (Day 10) will be subjected to a mixed effects analysis of variance (ANOVA) with study day as a fixed effect and subject as a random effect in order to establish whether steady-state has been attained for each treatment. The point and interval estimates will be back-transformed to give estimates of the ratios of the geometric LSMeans and corresponding 90% CIs for the comparisons of each consecutive day (i.e. Day 10/Day 5). In addition, estimated geometric LSMeans and corresponding 95% CIs will be presented for each study day.

The geometric LSMean ratio and corresponding 90% CI for the Day 10/Day 5 comparison will be presented graphically (a plot with error bars) with all treatments on one graph. On the same graph, points indicating individual within-subject ratios for the comparison will be presented.

11.4.3.4 Part C (MAD) - Accumulation

For each dose level, log-transformed C_{max} and $AUC_{0\text{-}tau}$ (only applicable if non-q.d. dosing regimen is implemented) values on Day 1 and Final Dosing Day (Day 10) will be subjected to an ANOVA with study day as a fixed effect and subject as a random effect. For comparison, point estimates and 90% CIs for the difference between Day 10 and Day 1 will be constructed using the residual mean square error obtained from the ANOVA for each dose level. The point and interval estimates will then be back transformed to give estimates of the ratios of the geometric LSMeans and corresponding 90% CIs. In addition, estimated geometric LSMeans and corresponding 95% CIs will be presented for each study day.

The geometric LSMean ratios and corresponding 90% CIs for C_{max} and $AUC_{0\text{-}tau}$ will be represented graphically (a plot with error bars) with all dose levels on one graph, one graph per parameter. On the same graph, points indicating individual within-subject ratios will be presented.

Statistical analysis of PK parameters will be performed using the PK set.

11.5 PD ANALYSES

Not applicable.

11.6 SAFETY ANALYSES

11.6.1 Adverse Events

All adverse events (AEs) will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) dictionary version 24.1.

All AEs, including those which occurred prior to the first treatment administration, will be listed. Only treatment emergent adverse events (TEAEs), i.e., existing conditions that worsen or events that occur during the course of the study after administration of study drug, will be included within the summary tables. AEs that occur intermittently will be reported as separate events.

Part A and Part C:
An AE will be assigned to treatment if it starts on or after dosing. Where there are only partial dates/times recorded for an adverse event, the adverse event will be assigned to treatment if it cannot be ruled out based on the partial information.

Part B:
An AE will be assigned to the most recent treatment if it starts on or after the corresponding dose. Where there are only partial dates/times recorded for an adverse event, the adverse event will be assigned to every treatment where it cannot be ruled out based on the partial information.

An overall summary of AEs will be produced including the number of TEAEs; the number and % of subjects reporting at least 1 TEAE, serious TEAE (where SAE is reported as 'Yes'), TEAE leading to withdrawal from the study (Action recorded as 'Study Drug Discontinued'), TEAE leading to death (Outcome recorded as 'Fatal'); the number and % of subjects reporting TEAEs by severity and relationship to study drug. A subject with multiple occurrences of any AE is counted only once at the maximum level of severity or the strongest relationship to study drug.

The number of TEAEs and the number and % of subjects reporting at least 1 TEAE will be tabulated by system organ class (SOC) and preferred term (PT). A subject reporting multiple episodes of a particular AE within a treatment period will only contribute 1 count towards the corresponding SOC and PT.

In order to highlight the most frequently reported TEAEs, the number of TEAEs and the number and % of subjects reporting at least 1 TEAE will be tabulated by PT in order of descending frequency such that AEs reported by the greatest number of subjects are presented first. A subject reporting multiple episodes of a particular AE will only contribute 1 count towards the corresponding PT.

In addition, the number and % of subjects reporting TEAEs will be tabulated by maximum severity and strongest relationship to study drug. For the summary of TEAEs by severity, if a subject has multiple events occurring within the same SOC or PT the event with the highest severity will be counted. Similarly, for TEAEs by relationship to study drug, if a subject has multiple events occurring within the same SOC or PT, the event with the strongest relationship to study drug will be counted.

AEs will be listed by treatment. For any adverse event occuring prior to first administration of study drug, treatment will be described as 'Prior to Treatment'.

The derived variables, 'Time from Dose' and 'Duration' will be presented where full date and time are present. If partial dates are present for any parameter required in the calculation, the variable will not be populated. The following will be used to calculate the variables:

Duration (dd:hh:mm): (Date/Time of Resolution - Date/Time of Onset) + 1 minute;

Time from Dose (dd:hh:mm): (Date/Time of Onset - Date/Time of Start of Dose).

The following will be presented in listing format within the data summaries:

- Serious Adverse Events – If there are none present, the listing will be produced stating: '*No subjects experienced any serious adverse events.*'.
- Adverse Events which Led to Withdrawal – If there are none present, the listing will be produced stating: '*No subjects experienced any adverse events that led to withdrawal.*'.
- Adverse Events Leading to Death – If there are none present, the listing will be produced stating: '*No subjects experienced any adverse events that led to death.*'.

Adverse event data will be listed and summarised using the Safety Set.

11.6.2 Laboratory Data

Routine safety clinical laboratory tests (biochemistry, hematology, coagulation, urinalysis) will be carried out at:

Part A: Screening, Day -1, 24h post dose, 72h post dose and at follow-up. An additional urinalysis test will be carried out at Day 1, 12h.

Part B: Screening, Day -1, 24h post dose, 72h post dose and at follow-up. An additional biochemistry test will be carried out at Day 1 pre dose (total serum testosterone only) and an additional urinalysis test will be carried out at Day1 – 12h.

Part C: Screening, Day -1, 24h post dose, 72h post dose, pre-dose on Day 5 and at follow-up. An additional biochemistry test (total serum testosterone and LH only) will be carried out at Day 1 pre-dose, Day 5, Day 8 and Day 11 and an additional urinalysis test will be carried out at Day 1, 12h.

The laboratory parameters required for this study are listed in section 9.2.1.

Laboratory data listings will be presented in two ways:

- Out of range values - any values that fall outside of the normal/alert ranges based on the reference ranges provided by the Simbec-Orion Laboratory Services (presented in listing format within the data summaries)
- All safety laboratory data (including physician's review (Normal, Abnormal-NCS, Abnormal-CS)) with any out of range values flagged (presented within the data listings).

Descriptive statistics (N, n, mean, SD, minimum, median and maximum) of absolute and change from baseline (last assessment prior to first dose within a treatment period) values for each parameter at each protocol defined time point will be tabulated by treatment.

Microscopy, virology, COVID-19 test, urine drugs of abuse and alcohol screen and any unplanned laboratory parameters will also be listed.

If there are no further parameters databased other than those specified in section 9.2.1 then the 'Other Laboratory Data' listings should display, 'No other laboratory parameters to report'.

Laboratory data will be listed and summarised using the Safety Set.

11.6.3 Vital Signs

Vital Signs will be recorded at:

Part A: Screening, Day -1, Day 1 pre-dose, 30 mins, 45 mins, 1h, 2h, 3h, 4h, 6h, 8h, 12h, 24h post dose, 36h post dose, 48h post dose, 72h post dose and follow-up.

Part B: Screening, Day -1, Day 1 pre-dose, 30 mins, 45 mins, 1h, 2h, 3h, 4h, 6h, 8h, 12h, 24h post dose, 36h post dose, 48h post dose, 72h post dose and follow-up.

Part C: Screening, Day -1, Day 1 and Day 10 at pre-dose, 30 mins, 45 mins, 1h, 2h, 3h, 4h, 6h, 8h, 12h, 24h post dose, 36h post dose, 48h post dose, 72h post dose, pre-dose on Day 5 and follow-up.

A window of ± 10 min in relation to the nominal time-point is allowed.

Vital signs parameters (supine systolic and diasolic blood pressure and pulse rate, oral temperature and respiratory rate) will be listed with any out of normal range values (see Appendix 16.1) flagged (flag appended to relevant result). Descriptive statistics (N, n, mean, SD, minimum, median and maximum) of absolute and change from baseline (Day 1, pre-dose [of each treatment period for Part B] or last assessment prior to first dose, as applicable) values at each time point will be tabulated by treatment.

Vitals signs data will be listed and summarised using the Safety Set.

11.6.4 Electrocardiogram

12-lead ECGs will be performed at:

Part A: Screening, Day -1, Day 1 pre-dose, 30 min, 4h, 12h, 24h post dose, 48h post dose, 72h post dose, follow-up.

Part B: Screening, Day -1, Day 1 pre-dose, 30 min, 4h, 12h, 24h post dose, 48h post dose, 72h post dose, follow up.

Part C: Screening, Day -1, Day 1 and Day 10 at pre-dose, 30 min, 4h, 12h, 24h, 48h, and 72h post dose, pre-dose on Day 5 and follow-up.

A window of ± 10 min in relation to the nominal time-point is allowed.

12-lead ECG parameters (heart rate, PR interval, QRS width, QT interval and QT interval corrected using Fridericia's formula (QTcF)) will be listed with any out of normal range values (see Appendix 16.1) flagged (flag appended to relevant result). Descriptive statistics (N, n, mean, SD, minimum, median and

maximum) of absolute and change from baseline (Day 1, pre-dose [of each treatment period for Part B] or last assessment prior to first dose, as applicable) values at each time point will be summarised by treatment.
In addition, frequencies for QTcF data will be calculated and summarised according to the following categories:

For absolute values:

- QTc ≤ 450 msec
- 450 < QTc ≤ 480 msec
- 480 < QTc ≤ 500 msec
- QTc > 500 msec.

For change from baseline:

- Decreased/No Change
- QTc increase ≤ 30 msec
- 30 < QTc increase ≤ 60 msec
- QTc increase > 60 msec

ECG data will be listed and summarised using the Safety Set.

11.7 OTHER

11.7.1 Prior and Concomitant Medication

Dictionary (WHODD) coding dictionary version September 2021 and listed using the ATC Level 4 class, Preferred Term and verbatim text.

Part A and Part C:
A medication will be assigned to treatment if it starts on or after dosing. Where there are only partial dates/times recorded for a medication, the medication will be assigned to treatment if it cannot be ruled out based on the partial information.

Part B:
A medication will be assigned to the most recent treatment if it starts on or after the corresponding dose. Where there are only partial dates/times recorded for a medication, the medication will be assigned to every treatment where it cannot be ruled out based on the partial information.

A medication will be regarded as *prior* if it stops prior to first administration of IMP. The treatment phase will be presented as 'Prior to Treatment'. A medication will be regarded as *concomitant* if it starts after dosing or starts before dosing and continues after dosing. For any medication that started prior to first administration of IMP but is ongoing following administration of IMP, the treatment phase will be described as 'Prior and Ongoing'. Otherwise, treatment phase will be described as the treatment the medication started on.

Prior and concomitant medications will be listed by treatment phase using the Safety Set.

11.7.2 All Other Data

All data will be listed using the Safety Set, including the following: Substance Use History, Visit Dates, Medical History, Physical Examination, Inclusion/Exclusion Failures, PD Sampling, IMP Administration and Additional Notes.

Derivations within listings:

PK blood sampling time deviations: Calculate sample time deviation using actual time – theoretical time, display as minutes.

Analysis sets: Detail whether subject should be included within each of the analysis sets and provide reason for exclusion, as appropriate.

Inclusion/Exclusion criteria: Only failures to be presented. If there are no failures display '*All subjects passed all inclusion/exclusion criteria.*'

Protocol deviations: Major/minor classification to be assigned and confirmed by Sponsor.

12 VALIDATION

All tables, figures and listings will be subject to independent quality control and visual review and will be independently programmed. Findings will be documented in an Output Summary file quality control form and actions taken will also be documented.

The study summary sheet of the Output Summary file will be completed and signed by all persons who performed programming and QC. The final signed version of the Output Summary will be stored in the electronic Trial Master File (eTMF).

13 LITERATURE CITATIONS/REFERENCES

None.

14 LIST OF TABLES, FIGURES AND LISTINGS

List of Tables and Figures Contained in Report Section 14

14.1 Disposition and Demographic Data

14.1.1 Disposition Data

Table 14.1.1.1	Summary of Study Disposition	All Consented Set

14.1.2 Demographic Data and Baseline Characteristics

Table 14.1.2.1	Summary of Demographic Information	Safety Set

14.2 Efficacy Data

Not applicable.

14.3 Safety Data

14.3.1 Adverse Events

Table 14.3.1.1	Summary of Treatment Emergent Adverse Events	Safety Set
Table 14.3.1.2	Summary of Treatment Emergent Adverse Events by System Organ Class and Preferred Term	Safety Set
Table 14.3.1.3	Summary of Treatment Emergent Adverse Events by Preferred Term	Safety Set
Table 14.3.1.4	Summary of Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Severity	Safety Set
Table 14.3.1.5	Summary of Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Relationship to Study Drug	Safety Set
Table 14.3.1.6	Serious Adverse Events	Safety Set
Table 14.3.1.7	Adverse Events Leading to Withdrawal	Safety Set
Table 14.3.1.8	Adverse Events Leading to Death	Safety Set

14.3.2 Laboratory Safety

Table 14.3.2.1	Biochemistry Out of Normal Range Data	Safety Set
Table 14.3.2.2	Hematology Out of Normal Range Data	Safety Set
Table 14.3.2.3	Coagulation Out of Normal Range Data	Safety Set
Table 14.3.2.4	Urinalysis Out of Normal Range Data	Safety Set
Table 14.3.2.5	Summary of Absolute and Change from Baseline Biochemistry Results	Safety Set
Table 14.3.2.6	Summary of Absolute and Change from Baseline Hematology Results	Safety Set

Table 14.3.2.7	Summary of Absolute and Change from Baseline Coagulation Data	Safety Set

14.3.3 Vital Signs

Table 14.3.3.1	Summary of Absolute and Change from Baseline Vital Signs Data	Safety Set

14.3.4 ECG (

Table 14.3.4.1	Summary of Absolute and Change from Baseline 12-lead ECG Data	Safety Set
Table 14.3.4.2	Summary of 12-lead ECG QTcF Categories	Safety Set

14.4 Pharmacokinetics

14.4.1 Concentration Data

Table 14.4.1.1	Summary of Plasma AX-158 Concentration Data	PK Set
Figure 14.4.1.1	Geometric Mean Plasma AX-158 Concentration-Time Curves on a Linear Scale	PK Set
Figure 14.4.1.2	Geometric Mean Plasma AX-158 Concentration-Time Curves on a Semi-Logarithmic Scale	PK Set

14.4.2 Derived Pharmacokinetics

Table 14.4.2.1	Summary of Derived Plasma AX-158 Pharmacokinetic Parameters	PK Set
Table 14.4.2.2	Summary of Statistical Analysis of Plasma AX-158 Pharmacokinetic Data - Dose Proportionality	PK Set
Table 14.4.2.3	Summary of Statistical Analysis of Plasma AX-158 Pharmacokinetic Data - Dose Independence	PK Set
Figure 14.4.2.1	Dose Response of Plasma AX-158 Derived Pharmacokinetic Data	PK Set
Table 14.4.2.4	Summary of Statistical Analysis of Plasma AX-158 Pharmacokinetic Data - Food Effect	PK Set
Figure 14.4.2.2	Food Effect Least Squares Geometric Mean Ratios and 90% CIs of Plasma AX-158 PK Data	PK Set
Table 14.4.2.5	Summary of Statistical Analysis of Plasma AX-158 Pharmacokinetic Data - Steady State	PK Set
Figure 14.4.2.3	Steady State Least Squares Geometric Mean Ratios and 90% CIs of Plasma AX-158 Concentration Data	PK Set
Table 14.4.2.6	Summary of Statistical Analysis of Plasma AX-158 Pharmacokinetic Data - Accumulation	PK Set
Figure 14.4.2.4	Accumulation Least Squares Geometric Mean Ratios and 90% CIs of Plasma AX-158 Pharmacokinetic Data	PK Set
Table 14.4.2.7	Summary of Urine AX-158 Concentration Data	PK Set
Table 14.4.2.8	Summary of Derived Urine AX-158 Pharmacokinetic Data	PK Set

14.5 Pharmacodynamics

Not applicable.

14.6 Other

Not applicable.

Subject Data: Listings Contained in Report Appendix 16.2

16.2.1 Visit Dates, Dosing Information and Disposition		
Listing 16.2.1.1	Visit Dates	Safety Set
Listing 16.2.1.2	Study Drug Administration	Safety Set
Listing 16.2.1.3	Subject Disposition	All Consented Set
Listing 16.2.1.4	Additional Notes	Safety Set

16.2.2 Protocol Deviations		
Listing 16.2.2.1	Protocol Deviations	Safety Set

16.2.3 Analysis Sets		
Listing 16.2.3.1	Analysis Sets	All Randomised Subjects

16.2.4 Demographic Data and Other Baseline Characteristics		
Listing 16.2.4.1	Demographic Information	Safety Set
Listing 16.2.4.2	Substance Use History	Safety Set
Listing 16.2.4.3	Medical History and Concurrent Conditions	Safety Set
Listing 16.2.4.4	Virology Results	Safety Set
Listing 16.2.4.5	COVID-19 Results	Safety Set
Listing 16.2.4.6	Drugs of Abuse Results	Safety Set
Listing 16.2.4.7	Inclusion/Exclusion Criteria Failures	Safety Set

16.2.5 Drug Concentration Data and Pharmacokinetics

16.2.5 Drug Concentration Data and Pharmacokinetics		
Listing 16.2.5.1	Plasma AX-158 Concentration Data	Safety Set
Figure 16.2.5.1	Individual Plasma AX-158 Concentration-Time Curves on a Linear Scale	Safety Set
Figure 16.2.5.2	Individual Plasma AX-158 Concentration-Time Curves on a Semi-Logarithmic Scale	Safety Set

Listing 16.2.5.2	Individual Derived Plasma AX-158 Pharmacokinetic Parameters	Safety Set
Listing 16.2.5.3	Raw Statistical Analysis of Plasma AX-158 Pharmacokinetic Data - Dose Proportionality	PK Set
Listing 16.2.5.4	Raw Statistical Analysis of Plasma AX-158 Pharmacokinetic Data - Dose Independence	PK Set
Listing 16.2.5.5	Raw Statistical Analysis of Plasma AX-158 Pharmacokinetic Data – Food Effect	PK Set
Listing 16.2.5.6	Raw Statistical Analysis of Plasma AX-158 Pharmacokinetic Data - Steady State	PK Set
Listing 16.2.5.7	Raw Statistical Analysis of Plasma AX-158 Pharmacokinetic Data - Accumulation	PK Set
Listing 16.2.5.8	Urine AX-158 Concentration Data	PK Set
Listing 16.2.5.9	Derived Urine AX-158 Pharmacokinetic Data	PK Set

16.2.6 Efficacy

Not applicable.

16.2.7 Adverse Events

Listing 16.2.7.1	Adverse Events	Safety Set

16.2.8 Individual Laboratory Safety Measurements

Listing 16.2.8.1	Biochemistry Data	Safety Set
Listing 16.2.8.2	Hematology Data	Safety Set
Listing 16.2.8.3	Coagulation Data	Safety Set
Listing 16.2.8.4	Urinalysis Data	Safety Set
Listing 16.2.8.5	Microscopy Data	Safety Set
Listing 16.2.8.6	Other Laboratory Data	Safety Set

16.2.9 Vital Signs

Listing 16.2.9.1	Vital Signs Data	Safety Set

16.2.10 Physical Examination

Listing 16.2.10.1	Physical Examination Data	Safety Set

16.2.11 ECG

Listing 16.2.11.1	12-lead ECG Data	Safety Set

16.2.12 Prior and Concomitant Medication

Listing 16.2.12.1	Prior and Concomitant Medications	Safety Set

16.2.13 Pharmacodynamics

Not applicable.

16.2.14 Other

Listing 16.2.14.1	PD Sampling	Safety Set

15 SHELLS FOR TABLES, FIGURES AND LISTINGS

The intended layouts for tables, figures and listings are presented. However, it may be appropriate to change the layouts, upon review of the data available, for completeness and clarity.

QCd output will be produced as Rich Text Format (.rtf) files for convenient inclusion in the CSR.
The default tables, figures and listings (TFL) layout will be as follows:

Orientation	A4 Landscape
Margins	Top: 2.54 cm Bottom: 2.54 cm Left: 2.54 cm Right: 2.54 cm
Font	Courier New 9pt
Headers (Centre)	Sponsor Protocol Number, TFL Number, Title, Analysis Set
Footers (Left)	Source Listing, Date/Time TFL Generated, Page Number, i.e. Page x of y

Listing shells are displayed within this document without the comments field but, should there be any comments recorded for the represented data, this field will be added to the listing. In addition, at the time of programming, footnotes will be added to the listing, table or figure as needed. All footnotes will be used for purposes of clarifying the presentation.

Each table and figure will be produced for each study part (Part A, Part B or Part C) unless stated otherwise. The TFL title will include a suffix of ' – Part A' etc. Unless stated otherwise, listings will contain information from all study parts combined, with the exception of safety laboratory listings which will be created separately for each part due to file size.

Should the number of variables within a listing or table be too great to fit on one page without compromising clarity, then the variables will be split across multiple subsequent pages and key identifying variables replicated with these (i.e. subject number, visit etc). The differing pages will be identified using a sequential number which will follow the TFL title, i.e. xxxx - (1), xxxx - (2).

All final TFLs will be reported from SDTM and ADaM datasets. SDTM and ADaM details will be documented in a separate specification document.

AX-158-101
Table 14.1.1.1
Summary of Study Disposition – Part A (SAD)
All Consented Set

	Placebo* (Fasted) (N=X)	Cohort 1: AX-158 5 mg (Fasted) (N=X)	Cohort 2: AX-158 10 mg (Fasted) (N=X)	Cohort 3: AX-158 15 mg (Fasted) (N=X)	Cohort 4: AX-158 25 mg (Fasted) (N=X)	Cohort 5: AX-158 50 mg (Fasted) (N=X)	AX-158 Overall (N=X)	Overall (N=X)
Consented[a]								x
Dosed	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Completed Study	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Study Termination	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Reason for Study Termination								
ADVERSE EVENT	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
LOST TO FOLLOW-UP	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
WITHDRAWAL BY SUBJECT	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
STUDY TERMINATED BY SPONSOR	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
PHYSICIAN DECISION	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
PROTOCOL VIOLATION	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
DEATH	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
OTHER	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Safety Set	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
PK Set	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)

Source Listing: 16.2.1.2, 16.2.1.3, 16.2.3.1; Produced: yyyy-mm-ddThh:mm - Page x of y
* Placebo subjects pooled across all cohorts.
Treatment: single dose of AX-158 capsule or placebo in the fasted state.
Percentages will be calculated from the number of dosed subjects within a treatment group.
[a] Subjects for whom Informed Consent was obtained, including screening failures/non-runners.

Programming Note: Additional SAD cohorts to be added as appropriate. A similar table will be produced for Part C (MAD) – 3 cohorts, where additional MAD cohorts can be added as appropriate, with the treatment footnote

- *"Treatment: once daily dosing of AX-158 or placebo in a <fasted/fed> state for 10 days, with the final dose administered on the morning of Day 10.". This should be amended as appropriate if a once daily dosing regimen is not implemented.*

AX-158-101
Table 14.1.1.1
Summary of Study Disposition – Part B (Food Effect)
All Consented Set

	Number of Subjects (%)
Consented	X
Screening Failure/Non-Runners	x
Dosed:	
15 mg AX-158 in fed state	x (x.x)
15 mg AX-158 in fasted state	x (x.x)
Completed Study	x (x.x)
Study Termination	x (x.x)
Reason for Study Termination	
ADVERSE EVENT	x (x.x)
LOST TO FOLLOW-UP	x (x.x)
WITHDRAWAL BY SUBJECT	x (x.x)
STUDY TERMINATED BY SPONSOR	x (x.x)
PHYSICIAN DECISION	x (x.x)
PROTOCOL VIOLATION	x (x.x)
DEATH	x (x.x)
OTHER	x (x.x)
Safety Set	x (x.x)
PK Set	x (x.x)

Source Listing: 16.2.1.2, 16.2.1.3, 16.2.3.1; Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment = a single dose of 15 mg AX-158 capsules over 2 treatment periods, in the fed and fasted state.
Percentages will be calculated from the number of dosed subjects within a treatment group.

AX-158-101
Table 14.1.2.1
Summary of Demographic Information – Part A (SAD)
Safety Set

Parameter	Statistic	Placebo* (N=X)	Cohort 1: AX-158 5 mg (Fasted) (N=X)	...	Cohort 5: AX-158 50 mg (Fasted) (N=X)	AX-158 Overall (N=X)	Overall (N=X)
Age (yrs)	n	X	x	x	x	x	x
	Mean	x.x	x.x	x.x	x.x	x.x	x.x
	SD	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Min	x	x	x	x	x	x
	Median	x.x	x.x	x.x	x.x	x.x	x.x
	Max	x	x	x	x	x	x
Height (m)	n	X	x	x	x	x	x
	Mean	x.x	x.x	x.x	x.x	x.x	x.x
	SD	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Min	x	x	x	x	x	x
	Median	x.x	x.x	x.x	x.x	x.x	x.x
	Max	x	x	x	x	x	x

Source Listing: 16.2.4.1; Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: single dose of AX-158 capsule or placebo in the fasted state.
* Placebo subjects pooled across all cohorts.
Percentages calculated from the number of subjects in the Safety Set within a treatment group.

Programming Note: Similar tables will be presented for Part B (Food Effect) and Part C (MAD), with column headers and treatment footnotes as presented in Table 14.1.1.1.

[*Continued overleaf…*]

AX-158-101
Table 14.1.2.1
Summary of Demographic Information – Part A (SAD)
Safety Set

Parameter	Statistic	Placebo* (N=X)	Cohort 1: AX-158 5 mg (Fasted) (N=X)	...	Cohort 5: AX-158 50 mg (Fasted) (N=X)	AX-158 Overall (N=X)	Overall (N=X)
Weight (kg)	n	X	x	x	x	x	x
	Mean	x.x	x.x	x.x	x.x	x.x	x.x
	SD	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Min	x	x	x	x	x	x
	Median	x.x	x.x	x.x	x.x	x.x	x.x
	Max	x	x	x	x	x	x
BMI (kg/m^2)	n	X	x	x	x	x	x
	Mean	x.x	x.x	x.x	x.x	x.x	x.x
	SD	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Min	x	x	x	x	x	x
	Median	x.x	x.x	x.x	x.x	x.x	x.x
	Max	x	x	x	x	x	x

Source Listing: 16.2.4.1; Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: single dose of AX-158 capsule or placebo in the fasted state.
* Placebo subjects pooled across all cohorts.
Percentages calculated from the number of subjects in the Safety Set within a treatment group.

Programming Note: Similar tables will be presented for Part B (Food Effect) and Part C (MAD), with column headers and treatment footnotes as presented in Table 14.1.1.1.

[*Continued overleaf…*]

AX-158-101
Table 14.1.2.1
Summary of Demographic Information – Part A (SAD)
Safety Set

Parameter		Statistic	Placebo* (N=X)	Cohort 1: AX-158 5 mg (Fasted) (N=X)	...	Cohort 5: AX-158 50 mg (Fasted) (N=X)	AX-158 Overall (N=X)	Overall (N=X)
Gender	MALE	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
	FEMALE	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
Ethnicity	NOT HISPANIC OR LATINO	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
	HISPANIC OR LATINO	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
Race	BLACK OR AFRICAN AMERICAN	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
	AMERICAN INDIAN OR ALASKA NATIVE	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
	ASIAN	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
	NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
	WHITE	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
	MIXED	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)
	OTHER	n (%)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)	x (xx.x)

Source Listing: 16.2.4.1; Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: single dose of AX-158 capsule or placebo in the fasted state.
* Placebo subjects pooled across all cohorts.
Percentages calculated from the number of subjects in the Safety Set within a treatment group.

Programming Note: Similar tables will be presented for Part B (Food Effect) and Part C (MAD), with column headers and treatment footnotes as presented in Table 14.1.1.1.

AX-158-101
Table 14.3.1.1
Summary of Treatment Emergent Adverse Events – Part A (SAD)
Safety Set

	Placebo* (N=X)	Cohort 1: AX-158 5 mg (Fasted) (N=X)	...	AX-158 Overall (N=X)	Overall (N=X)
Number of TEAEs	x	x	...	x	x
Number (%) of subjects reporting at least one:					
TEAE	x (x.x)	x (x.x)	...	x (x.x)	x (x.x)
Serious TEAE	x (x.x)	x (x.x)		x (x.x)	x (x.x)
TEAE Leading to Withdrawal	x (x.x)	x (x.x)		x (x.x)	x (x.x)
TEAE Leading to Death	x (x.x)	x (x.x)		x (x.x)	x (x.x)
Number (%) of subjects with TEAE by severity:					
MILD	x (x.x)	x (x.x)	...	x (x.x)	x (x.x)
MODERATE	x (x.x)	x (x.x)		x (x.x)	x (x.x)
SEVERE	x (x.x)	x (x.x)		x (x.x)	x (x.x)
Number (%) of subjects with TEAE by relationship to study drug:					
REASONABLE POSSIBILITY	x (x.x)	x (x.x)	...	x (x.x)	x (x.x)
NO REASONABLE POSSIBILITY	x (x.x)	x (x.x)		x (x.x)	x (x.x)

Source Listing: 16.2.7.1; Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: single dose of AX-158 capsule or placebo in the fasted state.
A subject with multiple adverse events is counted only once at the maximum level of severity or the strongest relationship to treatment within each treatment category.
Percentages will be calculated from the number of subjects in the Safety Set within a treatment group.
* Placebo subjects pooled across all cohorts.

AX-158-101
Table 14.3.1.1
Summary of Treatment Emergent Adverse Events – Part B (Food Effect)
Safety Set

	AX-158 15 mg (Fasted) (N=X)	AX-158 15 mg (Fed) (N=X)	Overall (N=X)
Number of TEAEs	x	x	x
Number (%) of subjects reporting at least one:			
TEAE	x (x.x)	x (x.x)	x (x.x)
Serious TEAE	x (x.x)	x (x.x)	x (x.x)
TEAE Leading to Withdrawal	x (x.x)	x (x.x)	x (x.x)
TEAE Leading to Death	x (x.x)	x (x.x)	x (x.x)
Number (%) of subjects with TEAE by severity:			
MILD	x (x.x)	x (x.x)	x (x.x)
MODERATE	x (x.x)	x (x.x)	x (x.x)
SEVERE	x (x.x)	x (x.x)	x (x.x)
Number (%) of subjects with TEAE by relationship to study drug:			
REASONABLE POSSIBILITY	x (x.x)	x (x.x)	x (x.x)
NO REASONABLE POSSIBILITY	x (x.x)	x (x.x)	x (x.x)

Source Listing: 16.2.7.1; Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment= a single dose of 15 mg AX-158 capsules over 2 treatment periods, in the fed and fasted state.
A subject with multiple adverse events is counted only once at the maximum level of severity or the strongest relationship to treatment within each treatment category.
Percentages will be calculated from the number of subjects in the Safety Set within a treatment.

AX-158-101
Table 14.3.1.1
Summary of Treatment Emergent Adverse Events – Part C (MAD)
Safety Set

	Placebo* <*Fed/Fasted*>) (N=X)	Cohort 1: AX-158 5 mg (<*Fed/Fasted*>) (N=X)	Cohort 2: AX-158 <*X*> mg (<*Fed/Fasted*>) (N=X)	Cohort 3: AX-158 <*X*> mg (<*Fed/Fasted*>) (N=X)	AX-158 Overall (N=X)	Overall (N=X)
Number of TEAEs	x	x	x	x	x	x
Number (%) of subjects reporting at least one:						
TEAE	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Serious TEAE	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
TEAE Leading to Withdrawal	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
TEAE Leading to Death	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Number (%) of subjects with TEAE by severity:						
MILD	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
MODERATE	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
SEVERE	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
Number (%) of subjects with TEAE by relationship to study drug:						
REASONABLE POSSIBILITY	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
NO REASONABLE POSSIBILITY	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)

Source Listing: 16.2.7.1; Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: once daily dosing of AX-158 or placebo in a <fasted/fed> state for 10 days, with the final dose administered on the morning of Day 10.
* Placebo subjects pooled across all cohorts.
A subject with multiple adverse events is counted only once at the maximum level of severity or the strongest relationship to treatment within each treatment category.
Percentages will be calculated from the number of subjects in the Safety Set within a treatment.
Programming Note: Treatment footnote should be amended as appropriate if a once daily dosing regimen is not implemented.

AX-158-101
Table 14.3.1.2
Summary of Treatment Emergent Adverse Events by System Organ Class and Preferred Term – Part A (SAD)
Safety Set

	Number of Events / Number (%) of Subjects				
System Organ Class Preferred Term	Placebo* (N=X)	Cohort 1: AX-158 5 mg (Fasted) (N=X)	...	AX-158 Overall (N=X)	Overall (N=X)
<SYSTEM ORGAN CLASS>	x / x (x.x)	x / x (x.x)	...	x / x (x.x)	x / x (x.x)
<PREFERRED TERM>	x / x (x.x)	x / x (x.x)		x / x (x.x)	x / x (x.x)
<PREFERRED TERM>	x / x (x.x)	x / x (x.x)		x / x (x.x)	x / x (x.x)
<SYSTEM ORGAN CLASS>	x / x (x.x)	x / x (x.x)	...	x / x (x.x)	x / x (x.x)
<PREFERRED TERM>	x / x (x.x)	x / x (x.x)		x / x (x.x)	x / x (x.x)
<PREFERRED TERM>	x / x (x.x)	x / x (x.x)		x / x (x.x)	x / x (x.x)
<PREFERRED TERM>	x / x (x.x)	x / x (x.x)		x / x (x.x)	x / x (x.x)
<PREFERRED TERM>	x / x (x.x)	x / x (x.x)		x / x (x.x)	x / x (x.x)

Source Listing: 16.2.7.1; Produced: yyyy-mm-ddThh:mm – Page x of y
Treatment: single dose of AX-158 capsule or placebo in the fasted state.
* Placebo subjects pooled across all cohorts.
A subject is counted only once per SOC and PT within each treatment category.
Percentages will be calculated from the number of subjects in the Safety Set within a treatment group.
MedDRA version 24.1.

Programming note: Similar tables will be presented for Part B (Food Effect) and Part C (MAD), with column headers and treatment footnotes as presented in Table 14.3.1.1.

AX-158-101
Table 14.3.1.3
Summary of Treatment Emergent Adverse Events by Preferred Term – Part A (SAD)
Safety Set

	Number of Events / Number (%) of Subjects				
Preferred Term	Placebo* (N=X)	Cohort 1: AX-158 5 mg (Fasted) (N=X)	...	AX-158 Overall (N=X)	Overall (N=X)
<PREFERRED TERM>	x / x (x.x)	x / x (x.x)	...	x / x (x.x)	x / x (x.x)
<PREFERRED TERM>	x / x (x.x)	x / x (x.x)		x / x (x.x)	x / x (x.x)
<PREFERRED TERM>	x / x (x.x)	x / x (x.x)		x / x (x.x)	x / x (x.x)
<PREFERRED TERM>					
<PREFERRED TERM>	x / x (x.x)	x / x (x.x)	...	x / x (x.x)	x / x (x.x)
<PREFERRED TERM>	x / x (x.x)	x / x (x.x)		x / x (x.x)	x / x (x.x)
<PREFERRED TERM>	x / x (x.x)	x / x (x.x)		x / x (x.x)	x / x (x.x)
<PREFERRED TERM>	x / x (x.x)	x / x (x.x)		x / x (x.x)	x / x (x.x)
<PREFERRED TERM>	x / x (x.x)	x / x (x.x)		x / x (x.x)	x / x (x.x)

Source Listing: 16.2.7.1; Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: single dose of AX-158 capsule or placebo in the fasted state.
* Placebo subjects pooled across all cohorts.
A subject is counted only once per PT within each treatment category.
Percentages will be calculated from the number of subjects in the Safety Set within a treatment group.
MedDRA version 24.1.

Programming Note: To be sorted in descending frequency of number of subjects in Overall column.
Programming note: Similar tables will be presented for Part B (Food Effect) and Part C (MAD), with column headers and treatment footnotes as presented in Table 14.3.1.1.

AX-158-101
Table 14.3.1.4
Summary of Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Severity – Part A (SAD)
Safety Set

		Number (%) of Subjects				
System Organ Class Preferred Term	Severity	Placebo* (N=X)	Cohort 1: AX-158 5 mg (Fasted) (N=X))	...	AX-158 Overall (N=X)	Overall (N=X)
<SYSTEM ORGAN CLASS>	MILD	x (x.x)	x (x.x)	...	x (x.x)	x (x.x)
	MODERATE	x (x.x)	x (x.x)		x (x.x)	x (x.x)
	SEVERE	x (x.x)	x (x.x)		x (x.x)	x (x.x)
<PREFERRED TERM>	MILD	x (x.x)	x (x.x)		x (x.x)	x (x.x)
<PREFERRED TERM>	MILD	x (x.x)	x (x.x)		x (x.x)	x (x.x)
<PREFERRED TERM>	MILD	x (x.x)	x (x.x)		x (x.x)	x (x.x)
	MODERATE	x (x.x)	x (x.x)		x (x.x)	x (x.x)
	SEVERE	x (x.x)	x (x.x)		x (x.x)	x (x.x)

Source Listing: 16.2.7.1; Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: single dose of AX-158 capsule or placebo in the fasted state.
* Placebo subjects pooled across all cohorts.
A subject with multiple occurrences of an AE is counted only once at the maximum level of severity within a SOC, PT and treatment group.
Percentages will be calculated from the number of subjects in the Safety Set within a treatment group.
MedDRA version 24.1.

Programming note: This table will be repeated for Similar tables will be presented for Part B (Food Effect) and Part C (MAD), with column headers and treatment footnotes as presented in Table 14.3.1.1.

AX-158-101
Table 14.3.1.5
Summary of Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Relationship – Part A (SAD)
Safety Set

		Number (%) of Subjects				
System Organ Class Preferred Term	Relationship to Study Drug	Placebo* (N=X)	Cohort 1: AX-158 5 mg (Fasted) (N=X))	...	AX-158 Overall (N=X)	Overall (N=X)
<SYSTEM ORGAN CLASS TERM>	REASONABLE POSSIBILITY	x (x.x)	x (x.x)	...	x (x.x)	x (x.x)
	NO REASONABLE POSSIBILITY	x (x.x)	x (x.x)		x (x.x)	x (x.x)
<PREFERRED TERM>	REASONABLE POSSIBILITY	x (x.x)	x (x.x)		x (x.x)	x (x.x)
<PREFERRED TERM>	REASONABLE POSSIBILITY	x (x.x)	x (x.x)		x (x.x)	x (x.x)
<PREFERRED TERM>	NO REASONABLE POSSIBILITY	x (x.x)	x (x.x)		x (x.x)	x (x.x)
<PREFERRED TERM>	REASONABLE POSSIBILITY	x (x.x)	x (x.x)		x (x.x)	x (x.x)
	NO REASONABLE POSSIBILITY	x (x.x)	x (x.x)		x (x.x)	x (x.x)

Source Listing: 16.2.7.1; Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: single dose of AX-158 capsule or placebo in the fasted state.
* Placebo subjects pooled across all cohorts.
A subject with multiple occurrences of an AE is counted only once at the strongest relationship to treatment within a SOC, PT and treatment group.
Percentages will be calculated from the number of subjects in the Safety Set within a treatment group.
MedDRA version 24.1.

Programming note: Similar tables will be presented for Part B (Food Effect) and Part C (MAD), with column headers and treatment footnotes as presented in Table 14.3.1.1.

AX-158-101
Table 14.3.1.6
Serious Adverse Events – Part A (SAD) - (1)
Safety Set

<*Treatment*> OR <Cohort <X>: T*reatment*>

Subject	Event Number	System Organ Class/ Preferred Term/ Reported Term	Onset Date /Time	End Date/ Time/Ongoing	Date Reported	Duration (dd:hh:mm)	Time Post Dose (dd:hh:mm)	Severity
xxx	x	xxxxxxxxx/ xxxxxxxxx/ xxxxxxxxx	xxxxxxx Txx:xx	xxxxxxx Txx:xx	xxxxxx	xx:xx:xx	xx:xx:xx	xxxxxxx
xxx	x	xxxxxxxxx/ xxxxxxxxx/ xxxxxxxxx	xxxxxxx Txx:xx	xxxxxxx Txx:xx	xxxxxx	xx:xx:xx	xx:xx:xx	xxxxxxx
	x	xxxxxxxxx/ xxxxxxxxx/ xxxxxxxxx	xxxxxxx Txx:xx	xxxxxxx Txx:xx	xxxxxx	xx:xx:xx	xx:xx:xx	xxxxxxx
xxx	x	xxxxxxxxx/ xxxxxxxxx/ xxxxxxxxx	xxxxxxx Txx:xx	xxxxxxx Txx:xx	xxxxxx	xx:xx:xx	xx:xx:xx	xxxxxxx

Source Listing: 16.2.7.1; Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: single dose of AX-158 capsule or placebo in the fasted state.
SAE = Serious Adverse Event.
MedDRA version 24.1.

Programming note: Within a study part, AEs occurring prior to first dose of study drug and placebo AEs will be pooled across cohorts and presented first.
Programming Note: This table will be repeated for for Part B (Food Effect) and Part C (MAD), with treatment footnotes as presented in Table 14.3.1.1. Similar tables will be presented for Adverse Events Leading to Withdrawal – Parts A, B and C (Table 14.3.1.7) and Adverse Events Leading to Death – Parts A, B and C (Table 14.3.1.8).

AX-158-101
Table 14.3.1.6
Serious Adverse Events - Part A (SAD) - (2)
Safety Set

<*Treatment*> OR <Cohort <X>: T*reatment*>

Subject	Event Number	System Organ Class/ Preferred Term/ Reported Term	Relationship to Study Drug	SAE	SAE Criteria	Action	Outcome	Comment
xxx	x	xxxxxxxxx/ xxxxxxxxx/ xxxxxxxxx	xxxxxxxx	x	xxxxxxxxxxx	xxxxxx	xxxxxx	xxxxxxxxx
xxx	x	xxxxxxxxx/ xxxxxxxxx/ xxxxxxxxx	xxxxxxxx	x	xxxxxxxxxxx	xxxxxx	xxxxxx	xxxxxxxxx
	x	xxxxxxxxx/ xxxxxxxxx/ xxxxxxxxx	xxxxxxxx	x	xxxxxxxxxxx	xxxxxx	xxxxxx	xxxxxxxxx
xxx	x	xxxxxxxxx/ xxxxxxxxx/ xxxxxxxxx	xxxxxxxx	x	xxxxxxxxxxx	xxxxxx	xxxxxx	xxxxxxxxx

Source Listing: 16.2.7.1; Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: single dose of AX-158 capsule or placebo in the fasted state.
SAE = Serious Adverse Event.
MedDRA version 24.1.

Programming note: Within a study part, AEs occurring prior to first dose of study drug and placebo AEs will be pooled across cohorts and presented first.
Programming Note: This table will be repeated for for Part B (Food Effect) and Part C (MAD), with treatment footnotes as presented in Table 14.3.1.1. Similar tables will be presented for Adverse Events Leading to Withdrawal – Parts A , B and C (Table 14.3.1.7) and Adverse Events Leading to Death – Parts A , B and C (Table 14.3.1.8).

AX-158-101
Table 14.3.2.1
Biochemistry Out of Normal Range Data – Part A (SAD)
Safety Set

<*Treatment*> OR <Cohort <X>: T*reatment*>

Subject	Visit/ Time Point	Sample Date/Time	Sample ID	Parameter (Unit)	Result	Flag	Normal Range Low	Normal Range High	Alert Range Low	Alert Range High
xxx	xxxxxx	xxxxxxxxxx	xxxxx	xxxxxxx	x.xx	x	x.x	x.xx	x.x	x.xx
				xxxxxxx	x.xx	x	x.x	x.xx	x.x	x.xx
				xxxxxxx	x.xx	x	x.x	x.xx	x.x	x.xx
				xxxxxxx	x.xx	x	x.x	x.xx	x.x	x.xx
				xxxxxxx	x.xx	x	x.x	x.xx	x.x	x.xx
	xxxxxx	xxxxxxxxxx	xxxxx	xxxxxxx	x.xx	x	x.x	x.xx	x.x	x.xx
				xxxxxxx	x.xx	x	x.x	x.xx	x.x	x.xx
				xxxxxxx	x.xx	x	x.x	x.xx	x.x	x.xx
				xxxxxxx	x.xx	x	x.x	x.xx	x.x	x.xx
				xxxxxxx	x.xx	x	x.x	x.xx	x.x	x.xx

Source Listing: 16.2.8.1; Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: single dose of AX-158 capsule or placebo in the fasted state.
H* = Above Alert Range; H = Above Normal Range; Lo = Below Normal Range; L* = Below Alert Range.

Programming Note: This table will be repeated for for Part C (MAD), with treatment footnote as presented in Table 14.1.1.1. Similar tables will be produced for Hematology Out of Normal Range Data – Parts A and C (Table 14.3.2.2), Coagulation Out of Normal Range Data – Parts A and C (Table 14.3.2.3) and Urinalysis Out of Normal Range Data – Parts A and C (Table 14.3.2.4 – no alert ranges for urinalysis).

AX-158-101
Table 14.3.2.1
Biochemistry Out of Normal Range Data – Part B (Food Effect)
Safety Set

Subject	Study Period	Treatment	Visit	Sample Date/Time	Sample ID	Parameter (Unit)	Result	Flag	Normal Range Low	Normal Range High	Alert Range Low	Alert Range High
xxx	x	xxxxxxxx	xxxx	xxxxxxxxxx	xxxxx	xxxxxxx	x.xx	x	x.x	x.xx	x.x	x.xx
						xxxxxxx	x.xx	x	x.x	x.xx	x.x	x.xx
						xxxxxxx	x.xx	x	x.x	x.xx	x.x	x.xx
						xxxxxxx	x.xx	x	x.x	x.xx	x.x	x.xx
						xxxxxxx	x.xx	x	x.x	x.xx	x.x	x.xx
	x	xxxxxxxx	xxxx	xxxxxxxxxx	xxxxx	xxxxxxx	x.xx	x	x.x	x.xx	x.x	x.xx
						xxxxxxx	x.xx	x	x.x	x.xx	x.x	x.xx
						xxxxxxx	x.xx	x	x.x	x.xx	x.x	x.xx
						xxxxxxx	x.xx	x	x.x	x.xx	x.x	x.xx
						xxxxxxx	x.xx	x	x.x	x.xx	x.x	x.xx

Source Listing: 16.2.8.1; Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment= a single dose of 15 mg AX-158 capsules over 2 treatment periods, in the fed and fasted state.
H* = Above Alert Range; H = Above Normal Range; Lo = Below Normal Range; L* = Below Alert Range.

Programming Note: Similar tables will be produced for Hematology Out of Normal Range Data – Part B (Table 14.3.2.2), Coagulation Out of Normal Range Data – Part B (Table 14.3.2.3) and Urinalysis Out of Normal Range Data – Part B (Table 14.3.2.4 – no alert ranges for urinalysis).

AX-158-101
Table 14.3.2.5
Summary of Absolute and Change from Baseline Biochemistry Results – Part A (SAD)
Safety Set

<Parameter (<units>)>

		Absolute						Change from Baseline					
Treatment	Visit/ Time Point	n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Placebo / Cohort *<X>*: *<X>* mg AX-158 (Fasted) (N=x)	*<VISIT>*	x	x.xx	x.xxx	x.x	x.xx	x.x						
	<VISIT>	x	x.xx	x.xxx	x.x	x.xx	x.x						
	<VISIT>	x	x.xx	x.xxx	x.x	x.xx	x.x						
	<VISIT>	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	<VISIT>	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x
	<VISIT>	x	x.xx	x.xxx	x.x	x.xx	x.x	x	x.xx	x.xxx	x.x	x.xx	x.x

Source Listing: Listing 16.2.8.1; Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: single dose of AX-158 capsule or placebo in the fasted state.
Baseline defined per subject as the last available assessment prior to dosing.

Programming Note: This table will be repeated for Part B and Part C, with visit/time points as appropriate and treatment footnotes as per Table 14.1.1.1. Similar tables will be produced for Summary of Absolute and Change from Baseline Hematology Results – Parts A, B and C (Table 14.3.2.6) and Summary of Absolute and Change from Baseline Coagulation Results – Parts A, B and C (Table 14.3.2.7).

AX-158-101
Table 14.3.3.1
Summary of Absolute and Change from Baseline Vital Signs Data – Part A (SAD)
Safety Set

<Parameter (<units>)>

		Absolute						Change from Baseline					
Treatment	Visit/ Time Point	n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
Placebo /	*<VISIT>*	x	x.x	x.xx	x	x.x	x						
Cohort <*X*>:	*<VISIT>*	x	x.x	x.xx	x	x.x	x						
<*X*> mg AX-158	*<VISIT>*	x	x.x	x.xx	x	x.x	x						
(Fasted)	*<VISIT>*	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
(N=x)	*<VISIT>*	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	<VISIT>	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	<VISIT>	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	<VISIT>	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	<VISIT>	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	<VISIT>	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	<VISIT>	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	<VISIT>	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x

Source Listing: 16.2.9.1; Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: single dose of AX-158 capsule or placebo in the fasted state.
Baseline defined per subject as the last available pre-dose result at each treatment period.

Programming Note: This table will be repeated for Part B and Part C, with visit/time points as appropriate and treatment footnotes as per Table 14.1.1.1.

AX-158-101
Table 14.3.4.1
Summary of Absolute and Change from Baseline 12-Lead ECG Data – Part A (SAD)
Safety Set

<*Parameter* (<*units*>)>

		Absolute						Change from Baseline					
Treatment	Visit/ Time Point	n	Mean	SD	Min	Median	Max	n	Mean	SD	Min	Median	Max
	<*VISIT*>	x	x.x	x.xx	x	x.x	x						
Placebo /	<*VISIT*>	x	x.x	x.xx	x	x.x	x						
Cohort <*X*>:	<*VISIT*>	x	x.x	x.xx	x	x.x	x						
<*X*> mg AX-158	<*VISIT*>	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
(Fasted)(N=x)	<*VISIT*>	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	<*VISIT*>	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	<*VISIT*>	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	<*VISIT*>	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x
	<*VISIT*>	x	x.x	x.xx	x	x.x	x	x	x.x	x.xx	x	x.x	x

Source Listing: 16.2.11.1; Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: single dose of AX-158 capsule or placebo in the fasted state.
Baseline defined per subject as the last available assessment prior to dosing.

Programming Note: This table will be repeated for Part B and Part C, with visit/time points as appropriate and treatment footnotes as per Table 14.1.1.1.

AX-158-101
Table 14.3.4.2
Summary of 12-Lead ECG QTcF Categories – Part A (SAD)
Safety Set

		Number of Subjects (%)							
Treatment	Visit/Time Point	QTcF<= 450 mSec	451<= QTcF <=480 mSec	481<= QTcF <=500 mSec	QTcF > 500 mSec	QTcF Decreased/ No Change	QTcF Increase <=30 mSec	30< QTcF Increase <=60 mSec	QTcF Increase >60 mSec
Placebo / Cohort *<X>*: *<X>* mg AX-158 (Fasted) (N=x)	*<VISIT>*	x (x.x)	x (x.x)	x (x.x)	x (x.x)				
	<VISIT>	x (x.x)	x (x.x)	x (x.x)	x (x.x)				
	<VISIT>	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	<VISIT>	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	<VISIT>	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	<VISIT>	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	<VISIT>	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	<VISIT>	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	<VISIT>	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	<VISIT>	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	<VISIT>	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)
	<VISIT>	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)	x (x.x)

Source Listing: Listing 16.2.11.1; Produced: yyyy-mm-ddThh:mm; Page x of y
Treatment: single dose of AX-158 capsule or placebo in the fasted state.
Baseline defined per subject as the last available assessment prior to dosing.
Percentages calculated from the number of non-missing observations.

Programming Note: This table will be repeated for Part B and Part C, with visit/time points as appropriate and treatment footnotes as per Table 14.1.1.1.

AX-158-101
Table 14.4.1.1
Summary of Plasma AX-158 Concentration Data – Part A (SAD)
PK Set

Treatment	Visit/ Time Point	AX-158 Concentration (<*units*>) n	Mean	Geometric Mean	SD	%CV	Minimum	Median	Maximum
Placebo / Cohort <*X*>: <*X*> mg AX-158 (Fasted) (N=x)	*<VISIT>/<TIME POINT>*	x	x.xx	x.xx	x.xxx	x.x	x.x	x.xx	x.x
	<VISIT>/<TIME POINT>	x	x.xx	x.xx	x.xxx	x.x	x.x	x.xx	x.x
	<VISIT>/<TIME POINT>	x	x.xx	x.xx	x.xxx	x.x	x.x	x.xx	x.x
	<VISIT>/<TIME POINT>	x	x.xx	x.xx	x.xxx	x.x	x.x	x.xx	x.x
	<VISIT>/<TIME POINT>	x	x.xx	x.xx	x.xxx	x.x	x.x	x.xx	x.x
	<VISIT>/<TIME POINT>	x	x.xx	x.xx	x.xxx	x.x	x.x	x.xx	x.x
	<VISIT>/<TIME POINT>	x	x.xx	x.xx	x.xxx	x.x	x.x	x.xx	x.x
	<VISIT>/<TIME POINT>	x	x.xx	x.xx	x.xxx	x.x	x.x	x.xx	x.x
	<VISIT>/<TIME POINT>	x	x.xx	x.xx	x.xxx	x.x	x.x	x.xx	x.x
	<VISIT>/<TIME POINT>	x	x.xx	x.xx	x.xxx	x.x	x.x	x.xx	x.x
	<VISIT>/<TIME POINT>	x	x.xx	x.xx	x.xxx	x.x	x.x	x.xx	x.x
	<VISIT>/<TIME POINT>	x	x.xx	x.xx	x.xxx	x.x	x.x	x.xx	x.x
	<VISIT>/<TIME POINT>	x	x.xx	x.xx	x.xxx	x.x	x.x	x.xx	x.x

Source Listing: 16.2.5.1; Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: single dose of AX-158 capsule or placebo in the fasted state.
Lower Limit of Quantitation – xx.xx <*units*>. BLQ values set to 0 at pre-dose and LLOQ/2 for post-dose samples.
In order to capture the zero values within the calculation of the geometric mean, a value of 0.001 was added to all pre-dose values prior to log-transformation. The geometric means were then calculated and 0.001 subtracted from the estimate, i.e. geometric mean = exp(mean of log(concentration+0.001)) – 0.001.

Programming note: This table will be repeated for Part B and Part C, with visit/time points as appropriate and treatment footnotes as per Table 14.1.1.1.

AX-158-101
Figure 14.4.1.1
Geometric Mean Plasma AX-158 Concentration-Time Curves on a Linear Scale – Part A (SAD)
PK Set

Figure Specifications

By: Treatment, with all treatments on one plot

x axis: Time
x axis: Label: Time (h)
x axis: values: Day 1, Pre-dose, 30 min, 45 min, 1h, 2h, 3h, 4h, 6h, 8h, 12h, 24h, 36h, 48h, 72h (x-axis should present sampling time points only)

Y axis: Geometric mean concentration
Y axis Label: Geo. Mean AX-158 Conc. (<*units*>)
Y axis values: As appropriate

Legend (different line style/colour/symbol for each treatment):

Cohort <X>: AX-158 <X> mg (Fasted) (N=X)

Source Listing: 16.2.5.1; Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: single dose of AX-158 capsule or placebo in the fasted state.
Lower Limit of Quantification = xx.xx <*units*>. BLQ values set to zero at pre-dose and LLOQ/2 for post-dose samples.
In order to capture the zero values within the calculation of the geometric mean, a value of 0.001 was added to all pre-dose values prior to log-transformation. The geometric means were then calculated and 0.001 subtracted from the estimate, i.e. geometric mean = exp(mean of log(concentration+0.001)) – 0.001.

Programming note: This figure will be repeated for Part B (Food Effect) and Part C by Day (MAD), with treatment footnotes as per Table 14.1.1.1. Similar figures will be produced for Geometric Mean Plasma AX-158 Concentration-Time Curves on a Semi-Logarithmic Scale (Figure 14.4.1.2).

AX-158-101
Table 14.4.2.1
Summary of Derived Plasma AX-158 Pharmacokinetic Parameters – Part A (SAD)
PK Set

Treatment	Summary Statistic	C_{max} (<*units*>)	T_{max} (<units>)	AUC_{0-t} (<units>)	AUC_{0-24} (<units>)	AUC_{0-inf} (<*units*>)	$AUC_{\%extrap}$ (<*units*>)	$t_{1/2}$ (<*units*>)	λ_z (1/h)	CL/F (<*units*>)	Vz/F (<*units*>)
Cohort <*X*>:	n	x	x	x	x	x	x	x	x	x	x
AX-158 <*X*> mg	Mean	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
(N=x)	Geo. Mean	x.xx	N/A	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	SD	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx	x.xxx
	CV%	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Min	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Median	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Max	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x

Source Listing: 16.2.5.2; Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: single dose of AX-158 capsule or placebo in the fasted state.
Lower Limit of Quantification = xx.xx <*units*>. For the purposes of PK parameter calculation, BLQ values were set to zero at pre-dose and missing for post-dose time points.
N/A = Not applicable.

Programming note: This table will be repeated for Part B (Food Effect) and Part C (MAD) (for Day 1 and Day 10), with treatment footnotes as per Table 14.1.1.1.
Programming note: A similar table will be presented for Table 14.4.2.8 Summary of Derived Urine AX-158 Pharmacokinetic Data.

AX-158-101
Table 14.4.2.2
Summary of Statistical Analysis of Plasma AX-158 Dose Proportionality – Part A (SAD)
PK Set

	Geometric LSMeans (95% CI)					
Parameter	Cohort 1: AX-158 5 mg (N=X)	Cohort 2: AX-158 10 mg (N=X)	...	Cohort 5: AX-158 50 mg (N=X)	Intercept	Slope (95% CI)
C_{max} (<*units*>)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	...	x.xx (x.xx, x.xx)	x.xxx	x.xxx (x.xxx, x.xxx)
AUC_{0-t} (<*units*>)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	...	x.xx (x.xx, x.xx)	x.xxx	x.xxx (x.xxx, x.xxx)
AUC_{0-inf} (<*units*>)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	...	x.xx (x.xx, x.xx)	x.xxx	x.xxx (x.xxx, x.xxx)
AUC_{0-24} (<*units*>)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	...	x.xx (x.xx, x.xx)	x.xxx	x.xxx (x.xxx, x.xxx)

Source Listing: 16.2.5.2; Produced: yyyy-mm-ddThh:mm Page x of y
Treatment: single dose of AX-158 capsule or placebo in the fasted state.
Results obtained using a regression analysis on log-transformed values versus log-transformed dose using the power model.

Programming Note: A similar table will be presented for Part C (MAD), including C_{max} and AUC_{0-tau} results for Day 1 and Day 10 and AUC_{0-inf} results for Day 10, with treatment footnote as presented in Table 14.3.1.1.

AX-158-101
Table 14.4.2.3
Summary of Statistical Analysis of Plasma AX-158 Dose Independence – Part A (SAD)
PK Set

	LSMeans (95% CI)					
Parameter	Cohort 1: AX-158 5 mg (N=X)	Cohort 2: AX-158 10 mg (N=X)	...	Cohort 5: AX-158 50 mg (N=X)	Intercept	Slope (95% C.I.)
$t_{1/2}$ (*<units>*)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	...	...	x.xxx	x.xxx (x.xxx, x.xxx)
CL/F (*<units>*)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	...	...	x.xxx	x.xxx (x.xxx, x.xxx)

Source Listing: 16.2.5.2; Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: single dose of AX-158 capsule or placebo in the fasted state.
Results obtained using a fixed effects ANOVA on non-transformed data with a fixed effect of dose.

Programming Note: A similar table will be presented for Part C (MAD), including results for final dosing day (Day 10), with treatment footnote as presented in Table 14.3.1.1.

AX-158-101
Figure 14.4.2.1
Dose Response of Derived Plasma AX-158 Pharmacokinetic Parameters – Part A (SAD)
PK Set

< parameter (<units>) >

Figure Specifications

Procedure: SGPLOT

By: Parameter, one parameter per page

x axis: Dose
x axis: Label: AX-158 Dose (mg)
x axis: values: All dose levels

Y axis Geometric LSMeans and 95% CI for C_{max}, AUC_{0-t} and AUC_{0-inf}; LSMeans and 95% CI for and $t_{1/2}$ and CL/F – overlaid with individual subject values
Y axis Label: Geo. LSMeans (95% CI) for C_{max} , AUC_{0-t} and AUC_{0-inf}
LSMeans (95% CI) for and $t_{1/2}$ and CL/F
Y axis values: As Appropriate

Legend: Not Applicable

Source Listing: 16.2.5.2; Produced: yyyy-mm-ddThh:mm Page x of y
Treatment: single dose of AX-158 capsule or placebo in the fasted state.
Results for C_{max}, AUC_{0-t} and AUC_{0-inf} obtained using a regression analysis on log-transformed values versus log-transformed dose using the power model. Results for CL/F and $t_{1/2}$ obtained using a fixed effects ANOVA on non-transformed data with a fixed effect of dose.

Programming Note: A similar figure will be presented for Part C (MAD), including C_{max} and AUC_{0-tau} results for Day 1 and Day 10 and AUC_{0-inf}, *$t_{1/2}$ and CL/F for Day 10, with treatment footnote as presented in Table 14.3.1.1.*

AX-158-101
Table 14.4.2.4
Summary of Statistical Analysis of Plasma AX-158 Food Effect – Part B
PK Set

	Geometric LSMeans (95% CI)		Geometric LSMean Ratio (%) (90% CI) [Within-Subject CV%]
Parameter	15 mg AX-158 - Fed (N=x)	15 mg AX-158 - Fasted (N=x)	Fed / Fasted
C_{max} (*<units>*)	xx.x (xx.x – xx.x)	xx.x (xx.x – xx.x)	xx.x (xx.x – xx.x) [xx.x]
AUC_{0-t} (*<units>*)	xx.x (xx.x – xx.x)	xx.x (xx.x – xx.x)	xx.x (xx.x – xx.x) [xx.x]
AUC_{0-inf} (*<units>*)	xx.x (xx.x – xx.x)	xx.x (xx.x – xx.x)	xx.x (xx.x – xx.x) [xx.x]

Source Listing: 16.2.5.2 Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment = a single dose of 15 mg AX-158 capsules over 2 treatment periods, in the fed and fasted state.
Results obtained using an ANOVA with fixed effects of treatment, period, sequence and subject nested within sequence.

AX-158-101
Figure 14.4.2.2
Food Effect Least Squares Geometric Mean Ratios and 90% CI of Plasma AX-158 PK Data – Part B (Food Effect)
PK Set

Figure Specifications

Plot type: Least squares geometric mean ratios (with 90% CI) overlaid with individual subject ratios.

By: Parameter - C_{max}, AUC_{0-t} and AUC_{0-inf} displayed on one plot.

x axis: Parameter
x axis: Label: Label each parameter including units
x axis: values: 3 PK parameters (C_{max}, AUC_{0-t}, AUC_{0-inf})

Y axis: Least squares geometric mean ratio and 90% CI, with individual subject ratios
Y axis Label: Ratio (90% CI) (%)
Y axis values: As appropriate

Legend:
15 mg AX-158 - Fed / 15 mg AX-158 – Fasted

Source Listing: 16.2.5.2; Produced: yyyy-mm-ddThh:mm – Page x of y
Treatment = = a single dose of 15 mg AX-158 capsules over 2 treatment periods, in the fed and fasted state.
Results obtained using an ANOVA with fixed effects for fed/fasted state and subject.

AX-158-101
Table 14.4.2.5
Summary of Statistical Analysis of Plasma AX-158 Steady State – Part C (MAD)
PK Set

	AX-158 Trough Concentration (<*units*>)		
	Geometric LSMeans (95% CI)		Geometric LSMean Ratio (90% CI)
Treatment	Day 5	Day 10	Day 10/Day 5
Cohort <*X*>: AX-158<*X*> mg (N=x)	xxx (xx.xx, xx.xx)	xxx (xx.xx – xx.xx)	x.xx (x.xx – x.xx)
Cohort <*X*>: AX-158<*X*> mg (N=x)	xxx (xx.xx, xx.xx)	xxx (xx.xx – xx.xx)	x.xx (x.xx – x.xx)

Source Listing: 16.2.5.1; Produced: yyyy-mm-ddThh:mm Page x of y
Treatment: once daily dosing of AX-158 or placebo in a <fasted/fed> state for 10 days, with the final dose administered on the morning of Day 10.
Results obtained using a mixed effects ANOVA on log-transformed data with a fixed effect of study day and a random effect of subject.

AX-158-101
Figure 14.4.2.3
Steady State Least Squares Geometric Mean Ratios and 90% CIs of Plasma AX-158 Concentration Data – Part C (MAD)
PK Set

<Treatment>

Figure Specifications

Plot type: Least squares geometric mean ratios (with 90% CI) overlaid with individual subject ratios.

By: Treatment and comparison – Day 10/Day 5 displayed on one plot, one plot per treatment.

x axis: Parameter
x axis: Label: Comparison
x axis: values: Day 10/Day 5

Y axis: Least squares geometric mean ratio and 90% CI, with individual subject ratios
Y axis Label: Ratio (90% CI)
Y axis values: As appropriate

Legend: N/a

Source Listing: 16.2.5.1; Produced: yyyy-mm-ddThh:mm – Page x of y
Treatment: once daily dosing of AX-158 or placebo in a *<fasted/fed>* state for 10 days, with the final dose administered on the morning of Day 10.
Results obtained using a mixed effects ANOVA on log-transformed data with a fixed effect of study day and a random effect of subject.

AX-158-101
Table 14.4.2.6
Summary of Statistical Analysis of Plasma AX-158 Accumulation – Part C (MAD)
PK Set

Dose Level	Parameter	n	Geometric LSMeans (95% CI) Day 1	Geometric LSMeans (95% CI) Day 10	Geometric LSMean Ratio (90% C.I.) Day 10 / Day 1
Cohort <*X*>: AX-158 <*X*> mg (N=x)	C_{max} (<*units*>)	x	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
	AUC_{0-tau} (<*units*>)	x	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Cohort <*X*>: AX-158 <*X*> mg (N=x)	C_{max} (<*units*>)	x	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
	AUC_{0-tau} (<*units*>)	x	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)

Source Listing: 16.2.5.7; Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: once daily dosing of AX-158 or placebo in a <*fasted/fed*> state for 10 days, with the final dose administered on the morning of Day 10.
Results obtained using a mixed effects ANOVA on log-transformed data with a fixed effect of study day and a random effect of subject.

AX-158-101
Figure 14.4.2.4
Accumulation Least Squares Geometric Mean Ratios and 90% CIs of Plasma AX-158 Pharmacokinetic Data – Part C (MAD)
PK Set

Day 10 / Day 1

Figure Specifications

Plot type: Least squares geometric mean ratios (with 90% CI) overlaid with individual subject ratios.

By: Parameter and treatment - C_{max} and AUC_{0-tau} displayed on separate plots.

x axis: Parameter
x axis: Label: AX-158 Dose (mg)
x axis: values: AX-158 dose levels

Y axis: Least squares geometric mean ratio and 90% CI, with individual subject dose-normalised values
Y axis Label: Ratio (90% CI)
Y axis values: As appropriate

Source Listing: 16.2.5.7; Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: once daily dosing of AX-158 or placebo in a <fasted/fed> state for 10 days, with the final dose administered on the morning of Day 10.
Results obtained using a mixed effects ANOVA on log-transformed data with a fixed effect of study day and a random effect of subject.

AX-158-101
Table 14.4.2.7
Summary of Urine AX-158 Concentration Data – Part C (MAD)
PK Set

Treatment	Study Day	Time Interval	AX-158 Concentration (<*units*>) n	Mean	Geometric Mean	SD	%CV	Minimum	Median	Maximum
Cohort <*X*>:	x	PRE-DOSE	x	x.xx	x.xx	x.xxx	x.x	x.x	x.xx	x.x
AX-158 <*X*> mg		0 H – 12 H	x	x.xx	x.xx	x.xxx	x.x	x.x	x.xx	x.x
(N=x)		12 H – 24 H	x	x.xx	x.xx	x.xxx	x.x	x.x	x.xx	x.x
		24 H – 48 H	X	x.xx	x.xx	x.xxx	x.x	x.x	x.xx	x.x
		48 H – 72 H	x	x.xx	x.xx	x.xxx	x.x	x.x	x.xx	x.x
Cohort <*X*>:	x	PRE-DOSE	x	x.xx	x.xx	x.xxx	x.x	x.x	x.xx	x.x
AX-158 <*X*> mg		0 H – 12 H	x	x.xx	x.xx	x.xxx	x.x	x.x	x.xx	x.x
(N=x)		12 H – 24 H	x	x.xx	x.xx	x.xxx	x.x	x.x	x.xx	x.x
		24 H – 48 H	X	x.xx	x.xx	x.xxx	x.x	x.x	x.xx	x.x
		48 H – 72 H	x	x.xx	x.xx	x.xxx	x.x	x.x	x.xx	x.x

Source Listing: 16.2.5.8; Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: once daily dosing of AX-158 or placebo in a <fasted/fed> state for 10 days, with the final dose administered on the morning of Day 10.
Lower Limit of Quantitation – xx.xx <*units*>. BLQ values set to 0 at pre-dose and LLOQ/2 for post-dose samples.
In order to capture the zero values within the calculation of the geometric mean, a value of 0.001 was added to all pre-dose values prior to log-transformation. The geometric means were then calculated and 0.001 subtracted from the estimate, i.e. geometric mean = exp(mean of log(concentration+0.001)) – 0.001.

AX-158-101
Listing 16.2.1.1
Visit Dates
Safety Set

Part <*X*> (<SAD/Food Effect/MAD - Cohort <*X*>: <*Treatment*>)

Subject	Visit	Start Date
xxx	xxxxxxx	xxxxxx
	xxxxxxx	xxxxxx
	xxxxxxx	xxxxxx
	xxxxxxx	xxxxxx
	xxxxxxx	xxxxxx
xxx	xxxxxxx	xxxxxx
	xxxxxxx	xxxxxx
	xxxxxxx	xxxxxx
	xxxxxxx	xxxxxx
	xxxxxxx	xxxxxx
xxx	xxxxxxx	xxxxxx
	xxxxxxx	xxxxxx
	xxxxxxx	xxxxxx
	xxxxxxx	xxxxxx
	xxxxxxx	xxxxxx

Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: <*appropriate treatment footnote for study part*>

Programming Note: Cohort and treatment will not be included in the sub-header for Part B. For Part B, treatment will be included as a column within the listing.

Programming note: Listings will be repeated within an output for each part with the appropriate treatment footnote for each part.

AX-158-101
Listing 16.2.1.2
Study Drug Administration - (1)
Safety Set

Part <*X*> (<SAD/Food Effect/MAD - Cohort <*X*>: <*Treatment*>)

Subject	Visit	Pre-Dose Assessments Performed	Fasted for 10h	Consumed Meal 30 min Prior to Dosing	Fluid Withheld for 1h	Satisfy Inclusion/ Exclusion Criteria	Still Eligible for Dosing
xxx	xxxxxx	x	x	x	x	x	x
xxx	xxxxxx	x	x	x	x	x	x
xxx	xxxxxx	x	x	x	x	x	x
xxx	xxxxxx	x	x	x	x	x	x
xxx	xxxxxx	x	x	x	x	x	x
xxx	xxxxxx	x	x	x	x	x	x
xxx	xxxxxx	x	x	x	x	x	x
xxx	xxxxxx	x	x	x	x	x	x
xxx	xxxxxx	x	x	x	x	x	x
xxx	xxxxxx	x	x	x	x	x	x
xxx	xxxxxx	x	x	x	x	x	x
xxx	xxxxxx	x	x	x	x	x	x
xxx	xxxxxx	x	x	x	x	x	x

Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: <*appropriate treatment footnote for study part*>

Programming Note: Cohort and treatment will not be included in the sub-header for part B. For Part B, treatment will be included as a column within the listing.

AX-158-101
Listing 16.2.1.2
Study Drug Administration - (2)
Safety Set

Part *<X>* (<SAD/Food Effect/MAD - Cohort *<X>*: *<Treatment>)*

Subject	Visit	Dosing Date/Time	Dose Admin-istered (mg)	Frequency	Consume 240 ml of water with dose? If not specify.	Hand/ Mouth Check	Remained Seated for 1h	Avoided Fluid Until 1h Post-Dose
xxx	xxxxxx	xxxxxxTxx:xx	xxx	xxxxxx	x	x	xxx	x
	xxxxxx	xxxxxxTxx:xx	xxx	xxxxxx	x	x	xxx	x
	xxxxxx	xxxxxxTxx:xx	xxx	xxxxxx	x	x	xxx	x
	xxxxxx	xxxxxxTxx:xx	xxx	xxxxxx	x	x	xxx	x
	xxxxxx	xxxxxxTxx:xx	xxx	xxxxxx	x	x	xxx	x
	xxxxxx	xxxxxxTxx:xx	xxx	xxxxxx	x	x	xxx	x
	xxxxxx	xxxxxxTxx:xx	xxx	xxxxxx	x	x	xxx	x
	xxxxxx	xxxxxxTxx:xx	xxx	xxxxxx	x	x	xxx	x
	xxxxxx	xxxxxxTxx:xx	xxx	xxxxxx	x	x	xxx	x
	xxxxxx	xxxxxxTxx:xx	xxx	xxxxxx	x	x	xxx	x
	xxxxxx	xxxxxxTxx:xx	xxx	xxxxxx	x	x	xxx	x
	xxxxxx	xxxxxxTxx:xx	xxx	xxxxxx	x	x	xxx	x
	xxxxxx	xxxxxxTxx:xx	xxx	xxxxxx	x	x	xxx	x

Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: *<appropriate treatment footnote for study part>*

Programming Note: Cohort and treatment will not be included in the sub-header for part B. For Part B, treatment will be included as a column within the listing.

AX-158-101
Listing 16.2.1.3
Subject Disposition
All Consented Set

Part <*X*> (<SAD/Food Effect/MAD - Cohort <*X*>: <*Treatment*>)

	Informed Consent		Screening Completion		Study Completion/Termination			
Subject/ Screening Number	Date/ Time	Version	Screening Failure/ Non-Runner	Date Randomised	Study Completed	Date of Completion/ Withdrawal	Reason for Withdrawal	Comments
xxx	xxxxxTxx:xx	xxxx	x	xxxxxxx	x	xxxx	xxxx	xxxxxxx
xxx	xxxxxTxx:xx	xxxx	x	xxxxxxx	x	xxxx	xxxx	xxxxxxx
xxx	xxxxxTxx:xx	xxxx	x	xxxxxxx	x	xxxx	xxxx	xxxxxxx
xxx	xxxxxTxx:xx	xxxx	x	xxxxxxx	x	xxxx	xxxx	xxxxxxx
xxx	xxxxxTxx:xx	xxxx	x	xxxxxxx	x	xxxx	xxxx	xxxxxxx
xxx	xxxxxTxx:xx	xxxx	x	xxxxxxx	x	xxxx	xxxx	xxxxxxx
xxx	xxxxxTxx:xx	xxxx	x	xxxxxxx	x	xxxx	xxxx	xxxxxxx
xxx	xxxxxTxx:xx	xxxx	x	xxxxxxx	x	xxxx	xxxx	xxxxxxx

Produced: yyyy-mm-ddThh:mm - Page x of y

Programming Note: randomised subjects should be presented before screening failures/non-runners and Subject Number will be presented for randomised subjects and Screening number for screening failures/non-runners.
For Part B, Cohort and treatment will not be included in the sub-header.

AX-158-101
Listing 16.2.1.4
Additional Notes
Safety Set

Part <*X*> (<SAD/Food Effect/MAD - Cohort <*X*>: <*Treatment*>)

Subject	Comment Number	Date	Form/Visit	Comment
xxx	x	xxxxxx	xxxxx-xxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
	x	xxxxxx	xxxxx-xxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
	x	xxxxxx	xxxxx-xxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
	x	xxxxxx	xxxxx-xxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
xxx	x	xxxxxx	xxxxx-xxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
	x	xxxxxx	xxxxx-xxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
	x	xxxxxx	xxxxx-xxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
xxx	x	xxxxxx	xxxxx-xxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
	x	xxxxxx	xxxxx-xxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
	x	xxxxxx	xxxxx-xxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
	x	xxxxxx	xxxxx-xxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx

Produced: yyyy-mm-ddThh:mm - Page x of y

Programming Note: For Part B, cohort and treatment will not be included in the sub-header.

AX-158-101
Listing 16.2.2.1
Protocol Deviations
Safety Set

Part <*X*> (<SAD/Food Effect/MAD - Cohort <*X*>: <*Treatment*>)

Subject	Deviation Number	Date of Deviation	Deviation Type	Deviation	Classification
xxx	x	xxxxxx	xxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	<Major/Minor>
	x	xxxxxx	xxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	<Major/Minor>
	x	xxxxxx	xxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	<Major/Minor>
	x	xxxxxx	xxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	<Major/Minor>
xxx	x	xxxxxx	xxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	<Major/Minor>
	x	xxxxxx	xxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	Major/Minor>
	x	xxxxxx	xxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	<Major/Minor>
xxx	x	xxxxxx	xxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	<Major/Minor>
	x	xxxxxx	xxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	Major/Minor>
	x	xxxxxx	xxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	<Major/Minor>
	x	xxxxxx	xxxxxxxx	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	<Major/Minor>

Produced: yyyy-mm-ddThh:mm - Page x of y

Programming Note: For Part B, cohort and treatment will not be included in the sub-header.

AX-158-101
Listing 16.2.3.1
Analysis Sets
All Consented Set

Part <*X*> (<SAD/Food Effect/MAD - Cohort <*X*>: <*Treatment*>)

Subject/ Screening Number	All Consented Set	Safety Set	Reason for Exclusion from Safety Set	PK Set	Reason for Exclusion from PK Set
xxx	x	x		x	
xxx	x	x		x	
xxx	x	x		x	
xxx	x	x		x	
xxx	x	x		x	
xxx	x	x		x	xxxxxxxxxxxxxxxxxxxx
xxx	x	x		x	
xxx	x	x	xxxxxxxxxxxxxxxxxx	x	xxxxxxxxxxxxxxxxxxxx

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AX-158-101
Listing 16.2.4.1
Demographic Information
Safety Set

Part *<X>* (<SAD/Food Effect/MAD - Cohort *<X>*: *<Treatment>)*

Subject	Screening Number	Year of Birth	Age (Yrs)	Gender	Ethnicity	Race	Height (m)	Weight (kg)	BMI (kg/m^2)
xxx	xxx	xxxxx	xxx	x	xxxxxxx	xxxxxxx	xxx	xxx	xxx
xxx	xxx	xxxxx	xxx	x	xxxxxxx	xxxxxxx	xxx	xxx	xxx
xxx	xxx	xxxxx	xxx	x	xxxxxxx	xxxxxxx	xxx	xxx	xxx
xxx	xxx	xxxxx	xxx	x	xxxxxxx	xxxxxxx	xxx	xxx	xxx
xxx	xxx	xxxxx	xxx	x	xxxxxxx	xxxxxxx	xxx	xxx	xxx
xxx	xxx	xxxxx	xxx	x	xxxxxxx	xxxxxxx	xxx	xxx	xxx
xxx	xxx	xxxxx	xxx	x	xxxxxxx	xxxxxxx	xxx	xxx	xxx
xxx	xxx	xxxxx	xxx	x	xxxxxxx	xxxxxxx	xxx	xxx	xxx
xxx	xxx	xxxxx	xxx	x	xxxxxxx	xxxxxxx	xxx	xxx	xxx
xxx	xxx	xxxxx	xxx	x	xxxxxxx	xxxxxxx	xxx	xxx	xxx
xxx	xxx	xxxxx	xxx	x	xxxxxxx	xxxxxxx	xxx	xxx	xxx
xxx	xxx	xxxxx	xxx	x	xxxxxxx	xxxxxxx	xxx	xxx	xxx

Produced: yyyy-mm-ddThh:mm - Page x of y

Programming Note: For Part B, cohort and treatment will not be included in the sub-header.

AX-158-101
Listing 16.2.4.2
Substance Use History
Safety Set

Part <*X*> (<SAD/Food Effect/MAD - Cohort <*X*>: <*Treatment*>)

Subject	Smoking Status	Average number of cigarettes per day	Date Stopped Smoking	Smoking Comments
xxx	xxxxxxxxxx	xxxxxxxxxx	xxxxxxx	xxxxxxxxxx
xxx	xxxxxxxxxx	xxxxxxxxxx	xxxxxxx	xxxxxxxxxx
xxx	xxxxxxxxxx	xxxxxxxxxx	xxxxxxx	
xxx	xxxxxxxxxx	xxxxxxxxxx	xxxxxxx	
xxx	xxxxxxxxxx	xxxxxxxxxx	xxxxxxx	
xxx	xxxxxxxxxx	xxxxxxxxxx	xxxxxxx	
xxx	xxxxxxxxxx	xxxxxxxxxx	xxxxxxx	
xxx	xxxxxxxxxx	xxxxxxxxxx	xxxxxxx	
xxx	xxxxxxxxxx	xxxxxxxxxx	xxxxxxx	xxxxxxxxxx
xxx	xxxxxxxxxx	xxxxxxxxxx	xxxxxxx	
xxx	xxxxxxxxxx	xxxxxxxxxx	xxxxxxx	

Produced: yyyy-mm-ddThh:mm - Page x of y

Programming Note: For Part B, cohort and treatment will not be included in the sub-header.

AX-158-101
Listing 16.2.4.3
Medical History and Concurrent Conditions
Safety Set

Part <*X*> (<SAD/Food Effect/MAD - Cohort <*X*>: <*Treatment*>)

Subject	Medical History Number	System Organ Class/ Preferred Term/ Reported Term	Date of Onset	Date Resolved/ Ongoing	Medication Taken/Treatment Currently Given?	Clinically Significant
xxx	x	xxxxxxxxxx/ xxxxxxxxxx/ xxxxxxxxxx	xxxxxxx	xxxxxxx	x	x
	x	xxxxxxxxxx/ xxxxxxxxxx/ xxxxxxxxxx	xxxxxxx	xxxxxxx	x	x
	x	xxxxxxxxxx/ xxxxxxxxxx/ xxxxxxxxxx	xxxxxxx	xxxxxxx	x	x

Produced: yyyy-mm-ddThh:mm - Page x of y
MedDRA version <*x.x*>.

Programming Note: For Part B, cohort and treatment will not be included in the sub-header.

AX-158-101
Listing 16.2.4.4
Virology Results
Safety Set

Part <*X*> (<SAD/Food Effect/MAD - Cohort <*X*>: <*Treatment*>)

Subject	Visit	Sample Date/Time	Sample ID	Source	Parameter	Result	Repeat Required
xxx	xxxxxx	xxxxxx	xxxxxx	<*CRF/Lab*	xxxxxx	xxxxxx	x
		Txx:xx		*Transfer*>	xxxxxx	xxxxxx	x
					xxxxxx	xxxxxx	x
				<*CRF/Lab*	xxxxxx	xxxxxx	x
				Transfer>	xxxxxx	xxxxxx	x
					xxxxxx	xxxxxx	x
xxx	xxxxxx	xxxxxx	xxxxxx	<*CRF/Lab*	xxxxxx	xxxxxx	x
		Txx:xx		*Transfer*>	xxxxxx	xxxxxx	x
					xxxxxx	xxxxxx	x
				<*CRF/Lab*	xxxxxx	xxxxxx	x
				Transfer>	xxxxxx	xxxxxx	x
					xxxxxx	xxxxxx	x

Produced: yyyy-mm-ddThh:mm - Page x of y

Programming Note: For Part B, cohort and treatment will not be included in the sub-header.

AX-158-101
Listing 16.2.4.5
COVID-19 Results
Safety Set

Part <*X*> (<SAD/Food Effect/MAD - Cohort <*X*>: <*Treatment*>)

Subject	Visit	Date/Time	Sample ID	Source	Parameter	Result	Repeat Required
xxx	xxxxxx	xxxxxxTxx:xx	xxxxxxxx	<*CRF/ Lab Transfer*>	xxxxxxxxxxx	xxxxxxx	x
xxx	xxxxxx	xxxxxxTxx:xx	xxxxxxxx	<*CRF/ Lab Transfer*>	xxxxxxxxxxx	xxxxxxx	x
xxx	xxxxxx	xxxxxxTxx:xx	xxxxxxxx	<*CRF/ Lab Transfer*>	xxxxxxxxxxx	xxxxxxx	x
xxx	xxxxxx	xxxxxxTxx:xx	xxxxxxxx	<*CRF/ Lab Transfer*>	xxxxxxxxxxx	xxxxxxx	x
xxx	xxxxxx	xxxxxxTxx:xx	xxxxxxxx	<*CRF/ Lab Transfer*>	xxxxxxxxxxx	xxxxxxx	x

Produced: yyyy-mm-ddThh:mm - Page x of y

Programming Note: For Part B, cohort and treatment will not be included in the sub-header.

AX-158-101
Listing 16.2.4.6
Drugs of Abuse Results
Safety Set

Part <*X*> (<SAD/Food Effect/MAD - Cohort <*X*>: <*Treatment*>)

Subject	Visit	Sample Date/Time	Sample ID	Source	Parameter	Result	Repeat Required
xxx	xxxxxx	xxxxxx Txx:xx	xxxxxx	<*CRF/Lab Transfer*>	xxxxxx	xxxxxx	x
					xxxxxx	xxxxxx	
					xxxxxx	xxxxxx	
					xxxxxx	xxxxxx	
					xxxxxx	xxxxxx	
					xxxxxx	xxxxxx	
				<*CRF/Lab Transfer*>	xxxxxx	xxxxxx	x
					xxxxxx	xxxxxx	
					xxxxxx	xxxxxx	
					xxxxxx	xxxxxx	
					xxxxxx	xxxxxx	
					xxxxxx	xxxxxx	

Produced: yyyy-mm-ddThh:mm - Page x of y

Programming Note: For Part B, cohort and treatment will not be included in the sub-header.

AX-158-101
Listing 16.2.4.7
Inclusion/Exclusion Criteria Failures
Safety Set

Part <*X*> (<SAD/Food Effect/MAD - Cohort <*X*>: <*Treatment*>)

Subject	Visit	Inclusion/ Exclusion	Criteria Number	Result
xxx	xxxxxx	xxxxxx	xx	xxxxxx
xxx	xxxxxx	xxxxxx	xx	xxxxxx
xxx	xxxxxx	xxxxxx	xx	xxxxxx

Produced: yyyy-mm-ddThh:mm - Page x of y

Programming note: If there are no inclusion/exclusion criteria failures, display 'All subjects complied with the inclusion/exclusion criteria'.

Programming Note: For Part B, cohort and treatment will not be included in the sub-header.

AX-158-101
Listing 16.2.5.1
Plasma AX-158 Concentration Data
Safety Set

Part <*X*> (<SAD/Food Effect/MAD - Cohort <*X*>: <*Treatment*>)

Subject	Visit	Time Point	Theoretical Date/Time of Sample	Actual Date/Time of Sample	Deviation (min)	AX-158 Conc. (<*units*>)	Comment
xxx	xxxxxxxxx	xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xx	xxx	
		xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xx	xxx	
		xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xx	xxx	xxxxxxxx
		xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xx	xxx	
		xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xx	xxx	
		xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xx	xxx	
		xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xx	xxx	xxxxxxxx
		xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xx	xxx	
		xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xx	xxx	
		xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xx	xxx	
		xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xx	xxx	

Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: <*appropriate treatment footnote for study part*>
Lower Limit of Quantitation – XX.XX <*units*>.

Programming Note: For Part B, treatment will be included as a column within the listing.

AX-158-101
Figure 16.2.5.1
Individual Plasma AX-158 Concentration-Time Curves on a Linear Scale
Safety Set

Part <*X*> (<SAD/Food Effect/MAD - Cohort <*X*>: <*Treatment*>

Figure Specifications
.
By: Treatment with all subjects on one plot, and also study day for Part C, with a separate plot for each PK profile day. For Part B, one plot per subject presenting all treatments.

x axis: Time
x axis: Label: Time (h)
x axis: values: 0 to last sampling time point (present sampling time points only)

Y axis: AX-158 concentration
Y axis Label: AX-158 Conc. (<*units*>)
Y axis values: As appropriate

Legend N/A

Source Listing: 16.2.5.1; Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: <*appropriate treatment footnote for study part*>
Lower Limit of Quantification = xx.xx <*units*>. BLQ values set to zero at pre-dose and LLOQ/2 for post-dose samples.
In order to capture the zero values within the calculation of the geometric mean, a value of 0.001 was added to all Day 1 pre-dose values prior to log-transformation. The geometric means were then calculated and 0.001 subtracted from the estimate, i.e. geometric mean = exp(mean of log(concentration+0.001)) – 0.001.

Programming note: Similar figures will be produced for Individual Plasma AX-158 Concentration-Time Curves on a Semi-Logarithmic Scale (Figure 16.2.5.2).

AX-158-101
Listing 16.2.5.2
Individual Derived Plasma AX-158 Pharmacokinetic Parameters
Safety Set

Part <*X*> (<SAD/Food Effect/MAD - Cohort <*X*>: <*Treatment*>)

Subject	Visit	Parameter	Value	Unit
xxx	xxxxxxxx	xxxxxxxxxx	x.x	xxxx
		xxxxxxxxxx	x.x	xxxx
		xxxxxxxxxx	x.x	xxxx
		xxxxxxxxxx	x.x	xxxx
		xxxxxxxxxx	x.x	xxxx
		xxxxxxxxxx	x.x	xxxx
xxx	xxxxxxxx	xxxxxxxxxx	x.x	xxxx
		xxxxxxxxxx	x.x	xxxx
		xxxxxxxxxx	x.x	xxxx
		xxxxxxxxxx	x.x	xxxx
		xxxxxxxxxx	x.x *	xxxx
		xxxxxxxxxx	x.x	xxxx

Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: <*appropriate treatment footnote for study part*>
Lower Limit of Quantification = xx.xx <*units*>. For the purposes of PK parameter calculation, BLQ values were set to zero at pre-dose and missing for post-dose time points.
* $AUC_{\%extrap}$ value greater than 20%.

Programming note: A similar listing will be produced for Listing 16.2.5.9 Individual Derived Urine AX-158 Pharmacokinetic Data.

AX-158-101
Listing 16.2.5.3
Raw Statistical Analysis of Plasma AX-158 Pharmacokinetic Data - Dose Proportionality
PK Set

To be populated with raw ANOVA output.

Source Listing: 16.2.5.2 Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: <*appropriate treatment footnote for study part*>
Results obtained using a regression analysis on log-transformed values versus log-transformed dose using the power model.

Programming Note: Similar listings will be presented for:
Listing 16.2.5.4 Raw Statistical Analysis of Plasma AX-158 Pharmacokinetic Data - Dose Independence
Listing 16.2.5.5 Raw Statistical Analysis of Plasma AX-158 Pharmacokinetic Data - Food Effect
Listing 16.2.5.6 Raw Statistical Analysis of Plasma AX-158 Pharmacokinetic Data - Steady State
Listing 16.2.5.7 Raw Statistical Analysis of Plasma AX-158 Pharmacokinetic Data - Accumulation

AX-158-101
Listing 16.2.5.8
Urine AX-158 Concentration Data
Safety Set

Part C (MAD) - Cohort <*X*>: <*Treatment*>)

Subject	Visit	Time Interval	Theoretical Start Date/Time of Sample	Theoretical End Date/Time of Sample	Actual Start Date/Time of Sample	Actual End Date/Time of Sample	Urine Weight (g)	Repeat Taken
xxx	xxxxxxx	xx - xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xx	xxx
		xx - xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xx	xxx
		xx - xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xx	xxx
		xx - xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xx	xxx
		xx - xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xx	xxx
		xx - xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xx	xxx
		xx - xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xx	xxx
		xx - xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xx	xxx
		xx - xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xx	xxx
		xx - xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xx	xxx
		xx - xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xxxxxxTxx:xx	xx	xxx

Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: <*appropriate treatment footnote for study part*>
Lower Limit of Quantitation – XX.XX <*units*>.

AX-158-101
Listing 16.2.7.1
Adverse Events – (1)
Safety Set

Part <*X*> (<SAD/Food Effect/MAD – Cohort <*X*>: <*Treatment*>)

Subject	Event Number	System Organ Class/ Preferred Term/ Reported Term	Onset Date/ Time	End Date/ Time/Ongoing	Date Reported	Duration (dd:hh:mm)	Time Post Dose (dd:hh:mm)	Severity
xxx	x	xxxxxxxxx/ xxxxxxxxx/ xxxxxxxxx	xxxxxxx Txx:xx	xxxxxxx Txx:xx	xxxxxx	xx:xx:xx	xx:xx:xx	xxxxxxx
xxx	x	xxxxxxxxx/ xxxxxxxxx/ xxxxxxxxx	xxxxxxx Txx:xx	xxxxxxx Txx:xx	xxxxxx	xx:xx:xx	xx:xx:xx	xxxxxxx
	x	xxxxxxxxx/ xxxxxxxxx/ xxxxxxxxx	xxxxxxx Txx:xx	xxxxxxx Txx:xx	xxxxxx	xx:xx:xx	xx:xx:xx	xxxxxxx
xxx	x	xxxxxxxxx/ xxxxxxxxx/ xxxxxxxxx	xxxxxxx Txx:xx	xxxxxxx Txx:xx	xxxxxx	xx:xx:xx	xx:xx:xx	xxxxxxx

Produced: yyyy-mm-ddThh:mm – Page x of y
Treatment: <*appropriate treatment footnote for study part*>
SAE = Serious Adverse Event.
MedDRA version <*x.x*>.

Programming Note: Within a study part, AEs occurring prior to first dose of study drug and placebo AEs will be pooled across cohorts and presented first.

AX-158-101
Listing 16.2.7.1
Adverse Events – (2)
Safety Set

Part <*X*> (<SAD/Food Effect/MAD - Cohort <*X*>: <*Treatment*>)

Subject	Event Number	System Organ Class/ Preferred Term/ Reported Term	Relationship to Study Drug	SAE	SAE Criteria	Action	Outcome	Comment
xxx	x	xxxxxxxxx/ xxxxxxxxx/ xxxxxxxxx	xxxxxxxx	x	xxxxxxxxxxx	xxxxxx	xxxxxx	xxxxxxxxx
xxx	x	xxxxxxxxx/ xxxxxxxxx/ xxxxxxxxx	xxxxxxxx	x	xxxxxxxxxxx	xxxxxx	xxxxxx	xxxxxxxxx
	x	xxxxxxxxx/ xxxxxxxxx/ xxxxxxxxx	xxxxxxxx	x	xxxxxxxxxxx	xxxxxx	xxxxxx	xxxxxxxxx
xxx	x	xxxxxxxxx/ xxxxxxxxx/ xxxxxxxxx	xxxxxxxx	x	xxxxxxxxxxx	xxxxxx	xxxxxx	xxxxxxxxx

Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: <*appropriate treatment footnote for study part*>
SAE = Serious Adverse Event.
MedDRA version <*x.x*>.

Programming Note: Within a study part, AEs occurring prior to first dose of study drug and placebo AEs will be pooled across cohorts and presented first.

AX-158-101
Listing 16.2.8.1
Biochemistry Data
Safety Set

Part <*X*> (<SAD/Food Effect/MAD - Cohort <*X*>: <*Treatment*>)

							Normal Range		Alert Range		
Subject	Visit	Sample Date/Time	Sample ID	Parameter (Unit)	Result	Flag	Lower	Upper	Lower	Upper	Repeat Req.
xxx	xxxxxxx	xxxxxxxx	xxxxxxx	xxxxxxxx	x.xx	H	x.x	x.xx	x.x	x.x	x
		Txx:xx		xxxxxxxx	x.xx		x.x	x.xx	x.x	x.x	
				xxxxxxxx	x.xx		x.x	x.xx	x.x	x.x	
				xxxxxxxx	x.xx		x.x	x.xx	x.x	x.x	
				xxxxxxxx	x.xx	Lo	x.x	x.xx	x.x	x.x	
				xxxxxxxx	x.xx	H*	x.x	x.xx	x.x	x.x	
				xxxxxxxx	x.xx		x.x	x.xx	x.x	x.x	
				xxxxxxxx	x.xx		x.x	x.xx	x.x	x.x	
				xxxxxxxx	x.xx		x.x	x.xx	x.x	x.x	
				xxxxxxxx	x.xx		x.x	x.xx	x.x	x.x	
				xxxxxxxx	x.xx	L*	x.x	x.xx	x.x	x.x	
				xxxxxxxx	x.xx		x.x	x.xx	x.x	x.x	
				Interpretation	xxxxxx						

Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: <*appropriate treatment footnote for study part*>
H* = Above alert range; H = Above normal range; Lo = Below normal range; L* = Below alert range.

Programming Note: For Part B, treatment will be included as a column within the listing.

Programming note: Similar Listings will be produced for hematology (Listing 16.2.8.2), coagulation (Listing 16.2.8.3), urinalysis [without alert ranges] (Listing 16.2.8.4), microscopy [without alert ranges] (Listing 16.2.8.5) and other laboratory data (Listing 16.2.8.6).

AX-158-101
Listing 16.2.9.1
Vital Signs Data
Safety Set

Part <*X*> (<SAD/Food Effect/MAD - Cohort <*X*>: <*Treatment*>)

Subject	Visit/ Time Point	Date/Time	Systolic Blood Pressure (mmHg)	Diastolic Blood Pressure (mmHg)	Pulse Rate (beats/ min)	Oral Temp. (C)	Respiration Rate (resps/min)	Review	Repeat Taken
xxx	xxxxxxxx	xxxxxxTxx:xx	xxx	xxx	xxx	xxx	xxx	xxxxx	x
	xxxxxxxx	xxxxxxTxx:xx	xxx	xxx	xxx	xxx	xxx	xxxxx	x
	xxxxxxxx	xxxxxxTxx:xx	xxx	xxx	xxx	xxx	xxx	xxxxx	x
	xxxxxxxx	xxxxxxTxx:xx	xxx	xxx	xxx	xxx	xxx	xxxxx	
	xxxxxxxx	xxxxxxTxx:xx	xxx	xxx	xxx H	xxx	xxx	xxxxx	x
	xxxxxxxx	xxxxxxTxx:xx	xxx	xxx	xxx	xxx	xxx	xxxxx	x
	xxxxxxxx	xxxxxxTxx:xx	xxx	xxx	xxx	xxx	xxx	xxxxx	x
	xxxxxxxx	xxxxxxTxx:xx	xxx	xxx	xxx	xxx	xxx	xxxxx	
	xxxxxxxx	xxxxxxTxx:xx	xxx	xxx	xxx	xxx	xxx	xxxxx	x
	xxxxxxxx	xxxxxxTxx:xx	xxx	xxx	xxx	xxx L	xxx	xxxxx	x
									x

Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: <*appropriate treatment footnote for study part*>
H = Above normal range; L = Below normal range.

Programming Note: Cohort and treatment will not be included in the sub-header for part B. For Part B, treatment will be included as a column within the listing.

AX-158-101
Listing 16.2.10.1
Physical Examination
Safety Set

Part <*X*> (<SAD/Food Effect/MAD - Cohort <*X*>: <*Treatment*>)

Subject	Visit	Performed	Date	Time
xxx	xxxxxxx	x	xxxxxx	xx:xx
xxx	xxxxxxx	x	xxxxxx	xx:xx
xxx	xxxxxxx	x	xxxxxx	xx:xx
xxx	xxxxxxx	x	xxxxxx	xx:xx
xxx	xxxxxxx	x	xxxxxx	xx:xx
xxx	xxxxxxx	x	xxxxxx	xx:xx
xxx	xxxxxxx	x	xxxxxx	xx:xx
xxx	xxxxxxx	x	xxxxxx	xx:xx
xxx	xxxxxxx	x	xxxxxx	xx:xx

Produced: yyyy-mm-ddThh:mm - Page x of y

Programming Note: Cohort and treatment will not be included in the sub-header for part B.

AX-158-101
Listing 16.2.11.1
12-Lead ECG Data
Safety Set

Part <*X*> (<SAD/Food Effect/MAD - Cohort <*X*>: <*Treatment*>)

Subject	Visit/ Time Point	Seq. No.	Date/Time	Heart Rate (beats/min)	RR Interval (msec)	PR Interval (msec)	QRS Width (msec)	QT Interval (msec)	QTcF Interval (msec)	Review	Repeat Taken
xxx	xxxxxxxx	x	xxxxxxTxx:xx	xxx	xxx	xxx	xxx	xxx	xxx	xxxxxx	x
		x	xxxxxxTxx:xx	xxx	xxx	xxx	xxx	xxx	xxx	xxxxxx	x
		x	xxxxxxTxx:xx	xxx	xxx	xxx	xxx	xxx	xxx	xxxxxx	x
	xxxxxxxx	x	xxxxxxTxx:xx	xxx	xxx	xxx	xxx	xxx	xxx	xxxxxx	x
		x	xxxxxxTxx:xx	xxx	xxx	xxx	xxx	xxx	xxx	xxxxxx	x
		x	xxxxxxTxx:xx	xxx	xxx	xxx	xxx	xxx	xxx	xxxxxx	x
	xxxxxxxx	x	xxxxxxTxx:xx	xxx	xxx	xxx	xxx	xxx	xxx	xxxxxx	x
		x	xxxxxxTxx:xx	xxx	xxx	xxx	xxx	xxx	xxx	xxxxxx	x
		x	xxxxxxTxx:xx	xxx	xxx	xxx	xxx	xxx	xxx	xxxxxx	x

Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: <*appropriate treatment footnote for study part*>
H = Above Normal Range; L = Below Normal Range.

Programming Note: Cohort and treatment will not be included in the sub-header for part B. For Part B, treatment will be included as a column within the listing.

AX-158-101
Listing 16.2.12.1
Prior and Concomitant Medications
Safety Set

Part <*X*> (<SAD/Food Effect/MAD - Cohort <*X*>: <*Treatment*>)

Subject	Medication Number	ATC Level 4/ Preferred Term/ Medication	Dose	Dose Unit	Frequency	Indication/ AE Number	Route	Start Date /Time	Stop Date/ Time/ Ongoing	Admin-istered by
xxx	x	xxxxxxxx/ xxxxxxxx/ xxxxxxxx	xxx	xx	xxxxxx	xxxxxxxx	xxxx	xxxxxxTxx:xx	xxxxxxTxx:xx	xxx
xxx	x	xxxxxxxx/ xxxxxxxx/ xxxxxxxx	xxx	xx	xxxxxx	xxxxxxxx	xxxx	xxxxxxTxx:xx	xxxxxxTxx:xx	xxx
xxx	x	xxxxxxxx/ xxxxxxxx/ xxxxxxxx	xxx	xx	xxxxxx	xxxxxxxx	xxxx	xxxxxxTxx:xx	xxxxxxTxx:xx	xxx

Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: <*appropriate treatment footnote for study part*>
WHO DDE version <*XXXXXX*>.

Programming note: Within a study part, medications taken prior to first dose of study drug, prior and ongoing medications and medications taken by placebo subjects will be pooled across cohorts and presented first.

AX-158-101
Listing 16.2.14.1
PD Sampling
Safety Set

Part <*X*> (<SAD/Food Effect/MAD - Cohort <*X*>: <*Treatment*>)

Subject	Visit	Were the PD Blood Samples taken at this Visit?	Date of Sample	Time of Sample	Timepoint	Comment
xxx	xxx	xxx	xxx	xx	xxxxxx	xxxxxxxx
xxx	xxx	xxx	xxx	xx	xxxxxx	xxxxxxxx
xxx	xxx	xxx	xxx	xx	xxxxxx	xxxxxxxx

Produced: yyyy-mm-ddThh:mm - Page x of y
Treatment: <*appropriate treatment footnote for study part*>
WHO DDE version <*XXXXXX*>.

Programming note: Within a study part, medications taken prior to first dose of study drug, prior and ongoing medications and medications taken by placebo subjects will be pooled across cohorts and presented first.

16 APPENDICES

16.1 NORMAL RANGES

Vital Sign Parameters		
Parameter	**Normal Range**	**Units**
Pulse Rate	40-100	beat(s) per minute (bpm)
Systolic Blood pressure	90-140	millimetre(s) of mercury (mmHg)
Diastolic Blood pressure	50-90	millimetre(s) of mercury (mmHg)
Respiratory Rate	12-18	breath(s) per minute
Oral Temperature	35.0-37.5	degrees Celsius (°C)

ECG Parameters		
Parameter	**Normal Range**	**Units**
Heart Rate (HR)	40-100	beat(s) per minute (bpm)
PR Interval	120-220	millisecond(s) (ms)
QRS Width	70-120	millisecond(s) (ms)
QT Interval	N/A	N/A
QTc Interval (Fridericia's Formula)	Male: 350-450	millisecond(s) (ms)