STATISTICAL ANALYSIS PLAN

Protocol Title: A Multi-Center, Open-Label, Pharmacokinetic, and Safety Study for Reduction in Fever or Management of Pain in Pediatric Subjects Aged Birth to Six Months

Protocol No.: CPI-CL-022

Protocol Date: 01Jun2015

SAP Version: 1.0

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I hereby declare that I have reviewed the statistical analysis plan and agree to its form and content. In addition, I confirm that the outlined statistical analysis plan contains all relevant information for the data analysis to be performed in the Protocol No. **CPI-CL-022** study by the Biostatistics Department.

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TABLE OF CONTENTS

List of Abbreviations and Definition of Terms

Abbreviation	Definition
AE(s)	Adverse event(s)
AUC	Area Under the Curve
CRF	Case Report Form
CSR	Clinical Study Report
Cmax	Maximum concentration
FDA	Food and Drug Administration
IMP	Investigational Medicinal Product
IV	Intravenous
JSS India	JSS Medical Research India Private Limited
kg	Kilogram
λ	Terminal elimination rate constant
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligram
mL	Milliliter
N	Number of Subjects
NSAID	Nonsteroidal anti-inflammatory drug
OTC	Over the Counter
PEK	Pharmacokinetic-evaluable Population
PRN	pro re nata (as necessary)
PK	Pharmacokinetics
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SOC	System Organ Class
TEAE	Treatment-emergent adverse event
TLGs	Tables, Listings and Graphs
T1/2	Half-life
Tmax	Time to maximum concentration

1.0 INTRODUCTION

This Statistical Analysis Plan (SAP) describes a comprehensive and detailed description of strategy and statistical technique to be used to realize the analysis of data for Cumberland Pharmaceuticals Inc. protocol CPI-CL-022 (A Multi-Center, Open-Label, Pharmacokinetic, and Safety Study for Reduction in Fever or Management of Pain in Pediatric Subjects Aged Birth to Six Months).

This is a phase 4 study to determine the pharmacokinetics (PK) and safety of single and/or multiple doses of intravenous ibuprofen administered over 10 minutes in children less than six months of age. This study will investigate the application of intravenous ibuprofen in the treatment of pain and/or fever.

The reader of this SAP is encouraged to also read the clinical protocols for details on the conduct of this study and the operational aspects of clinical assessments and timing for completing a patient in this study.

The purpose of this SAP is to outline the planned analyses to be completed to support the completion of the Clinical Study Report (CSR) for protocol CPI-CL-022.The planned analyses identified in this SAP will be included in regulatory submissions and/or future manuscripts. In addition, exploratory analyses not necessarily identified in this SAP may be performed to support the clinical development program. Any post-hoc, or unplanned, analyses which is not identified in this SAP will be clearly identified in the respective CSR.

2.0 DESCRIPTION OF THE PROTOCOL

2.1 Protocol Number

CPI-CL-022

2.2 Protocol Title

A Multi-Center, Open-Label Pharmacokinetic and Safety Study for Reduction in Fever or Management of Pain in Pediatric Subjects Aged Birth to Six Months.

2.3 Date

01Jun2015

2.4 Amendment

Amendment 02 dated 30Sep2016

3.0 STUDY OBJECTIVES AND ENDPOINTS

3.1 Study Objectives

3.1.1 Primary Objectives

The primary objective of this study is to evaluate the PK profile of a single dose of intravenous ibuprofen administered over approximately 10 minutes.

3.1.2 Secondary Objectives

The secondary objective of this study is to evaluate the safety of single and repeated doses of intravenous ibuprofen administered to hospitalized pediatric patients by assessing treatment emergent adverse events, vital signs, and laboratory assessments.

3.2 End Points

3.2.1 Primary Pharmacokinetic Endpoints

To evaluate the primary objective of PKs, the following endpoint will be measured:

- Clearance
- Volume of distribution
- Elimination $T_{1/2}$
- $C_{max,}$
- AUC (0-∞, 0-t)

3.2.2 Secondary (Safety) Endpoints

To evaluate safety, the following endpoints will be measured:

- Treatment emergent adverse events
- Vital signs (temperature, heart rate, respiratory rate, blood pressure)
- Clinical chemistry, hematology, and coagulation assessments

4.0 STUDY METHODS

4.1 Study Design and Plan

This multi-center, open-label, single and/or multiple dose clinical study will assess the PKs (following a single dose) and safety during and after the administration of intravenous ibuprofen. A total of twenty-four subjects, between the ages of birth (> 37 weeks gestational age) to less than six months of age, will be enrolled at up to five clinical centers. The study duration will be up to 72 hours.

This 72-hour study will consist of a Screening/Baseline Period (up to 48 hours prior to the first dose of IMP), a Treatment Period (beginning with the first dose of IMP and continuing for 48 hours) and a Post-Treatment Period (beginning at the end of the Treatment Period and continuing for 24 hours).

The Screening/Baseline Period may begin up to 48 hours prior to Study Hour 0. During the Screening/Baseline Period an evaluation of the inclusion and exclusion criteria, a complete medical history, and a physical examination will be conducted. A review of the subject's pre- IMP vital signs, baseline signs and symptoms, including pain scores (if applicable), concomitant medications, and laboratory assessments will be also conducted to establish the subject's eligibility to participate in the study. The Treatment Period will begin at Hour 0 when an initial dose of investigational medicinal product will be administered over a 10-minute period. Subsequent doses of IMP will be administered, at the investigator's discretion, every 6 to 8 hours, as needed, during the 48-hour treatment period. The total daily dose should not exceed 40 mg/kg/day. Pharmacokinetic sampling will be performed utilizing a sparse sampling technique following the initial dose of IMP. Vital signs, pain scores (if applicable), laboratory assessments and concomitant medications will be monitored during the treatment period and adverse events (AEs) will be monitored during the treatment and post-treatment periods. All treatment emergent adverse events will be followed until resolution or stabilization, regardless of the assessment of severity or relationship to the study drug.

4.2 Study Initiation and Completion

The study duration will be up to 72 hours and will consist of a Screening/Baseline Period (up to 48 hours prior to the first dose of IMP), a Treatment Period (beginning with the first dose of IMP and continuing for 48 hours) and a Post-Treatment Period (beginning at the end of the Treatment Period and continuing for 24 hours).

4.3 Selection of Study Population

A total of twenty-four subjects, between the ages of birth (> 37 weeks gestational age) to less than six (6) months of age, will receive IMP.

4.3.1 Screening Population (SCREEN)

The Screening Population includes all subjects who provide informed consent and provide demographic and/or baseline screening assessments in the trail.

4.3.2 Safety population

The safety analysis population consists of all participants who were enrolled and received at least part of the IMP; no treated participants will be excluded from the safety analysis population. Safety analysis will be conducted on an as treated basis.

4.3.3 PK (Pharmacokinetics) -evaluable Population

Participants who received the single dose of IMP over the 10-minute infusion period and have the primary PK assessments in the 48hour study period will be eligible for inclusion in the pharmacokinetic-evaluable population (PEP).

4.4 Study Subject Group

There is only subject group: Total of twenty-four subjects, between the ages of birth (> 37 weeks gestational age) to less than six (6) months of age.

4.5 Study Background

Ibuprofen is a nonsteroidal anti-inflammatory drug (NSAID) that was first approved for marketing as a prescription drug in the United States (US) in 1974. Oral ibuprofen is currently approved for use as oral treatment for minimal to moderate pain from arthritis, surgery, sunburn, menstruation, and fever. Like aspirin and other drugs in the NSAID family, ibuprofen is believed to reduce the inflammatory response by inhibiting the formation of prostaglandins.

CALDOLOR® (ibuprofen) Injection was approved by the US Food and Drug Administration in June 2009 for adults and in May 2016 for pediatric patient greater than six months of age. CALDOLOR is indicated in adults and pediatric patients 6 months and older for the management of mild to moderate pain, management of moderate to severe pain as an adjunct to opioid analgesics and for the reduction of fever. This formulation of intravenous (IV) ibuprofen is now being studied for use in the pediatric population less than 6 months of age.

4.6 Study Rationale

For the pediatric patient population, there are multiple oral over-the-counter (OTC) ibuprofen products available for the treatment of pain in children. Motrin® (McNeil Consumer Healthcare, Fort

Washington, Pennsylvania) is one of the most commonly used oral ibuprofen products currently marketed. The recommended dose for Motrin for treatment of pain in children 6 months to 12 years of age is 10 mg/kg with the recommended maximum daily dose of 40 mg/kg. The recommended dosing for children 12 years of age and older is the same as that used for adults, 200 to 800 mg up to four times daily, with a maximum of 3200 mg per day whereas the population for this study will consist of hospitalized pediatric subjects from birth (> 37 weeks gestational age) to < 6 months of age with a clinical indication of pain and/or fever.

4.7 Schedule of Study Events

There will be three scheduled visits in the study. For an example:
Visit 1: Screening/Baseline (up to 48 hours prior to the first dose of IMP)
Visit 2: Treatment Period (beginning with the first dose of IMP and continuing for 48 hours)
Visit 3: Post-Treatment Period (beginning at the end of the Treatment Period and continuing for 24 hours)

4.8 Schedule of Visits and Procedures

Schedule of visits is shown in Table 4.8

Table 4.8 Overall schedule of time and events

Measurement/Evaluation	Study Period			
	Screening/ Baseline	Treatment		Post-Treatment
Time(s)	Hour - 48 to Hour 0	Hour 0 to Hour 24	Hour 24 to Hour 48	Hour 48 to Hour 72
Informed Consent	X			
Inclusion/Exclusion Criteria	X			
Medical History	X			
Physical Examination	X			
Demographic Data	X			
Baseline Signs & Symptoms	X			
Vital Signs	X	X	X	X#
Laboratory Assessments	X*	X$		X#
Pharmacokinetic Assessments		X¶		
Concomitant Medications	X+	X	X	
IMP Administration (Initial & PRN)		X	X	
Adverse Event Monitoring		X**	X**	X**

IMP = Investigational Medicinal Product

* Laboratory data collected within 48 hours prior to dosing may be used for Screening/Baseline Period laboratory assessments.

+ Record concomitant medication actually administered to the subject in the 8 hours prior to the first dose of IMP. ¶ PK assessment must be taken immediately following the first dose of IMP then per the sparse sampling schedule. $ Laboratory Assessment must be performed at Study Hour 24 (± 6 hours)

#Laboratory Assessment and Vital Signs must be performed at Study Hour 72 (± 6 hours) or at the time of discharge, whichever occur first.

**All treatment adverse events will be followed until resolution or stabilization, regardless of the assessment of severity or relationship to the study drug.

5.0 GENERAL CONSIDERATIONS FOR STATISTICAL ANALYSIS

5.1 Sample Size Determination

A total of 24 subjects will be enrolled in the study. No power calculations will be performed.

5.2 Method of Treatment Assignment and Randomization

All subjects who meet all the inclusion and exclusion criteria during the Screening/Baseline Period will be enrolled into the study. Only eligible subjects will be assigned to receive intravenous ibuprofen, 10 mg/kg per dose. There is no randomization; this study is open-label with respect to the treatment assignment.

5.3 Methods for Withdrawals and Missing Data

If the subject is withdrawn from the study, data collected on the subject up to the time of withdrawal must remain in the trial database (FDA 2008).

If a decision is made to withdraw the subject from the study; the investigator should clarify with the subject's parent or legal guardian if the subject is to be withdrawn from all components of the study or if the subject is withdrawn from the primary interventional component but if the subject's parent or legal guardian would be willing to allow the investigator to continue other research activities as described below and in the informed consent:

- Medical course or laboratory results obtained through non-invasive chart review
- Vital signs, as outlined in the protocol
- Adverse event monitoring, as outlined in the protocol
- Post-Treatment follow-up

If required, subjects will be replaced to ensure a total of 24 PK-evaluable subjects. The replacement criteria are given below.

Subjects who are enrolled into the study but do not receive any IMP will be replaced. Subjects who withdraw from the study after receiving IMP but who do not complete the PK portion of the study within the first 4 hours will also be replaced.

No statistical imputation will be incorporated for the missing values.

5.4 Analysis Software

All analysis will be performed using SAS® Software version 9.4 or later.

6.0 DEMOGRAPHICS AND OTHER BASELINE CHARACTERISTICS

6.1 Demographics

During the Screening/Baseline Period, the Demographic date (age, race, ethnicity, height, weight) will be captured and analyzed using descriptive statistics (mean, median, standard deviation (SD), minimum and maximum) for continuous variables and using frequency count and percentage for categorical variables.

6.2 Baseline and Screening Conditions

Descriptive statistics (mean, median, standard deviation (SD), minimum and maximum) for continuous variables and frequency count and percentage for categorical variables will be presented for all baseline characteristics such as physical examination, vital signs and laboratory parameters.

During the Screening/Baseline Period, the following evaluations will be performed to determine the subject's eligibility for this study:

- Informed consent (by parent or legal guardian)
- Inclusion and exclusion criteria
- Complete medical history
- Physical examination
- Demographic date (age, race, ethnicity, weight, sex)
- Baseline signs & symptoms
- Vital signs (temperature, heart rate, respiratory rate, and blood pressure)
- Laboratory assessment
- Concomitant medications

6.3. Baseline Medical History

The medical history should be recorded at Screening/Baseline and should include history of hepatic, renal, neurological, endocrine, cardiovascular, and pulmonary disease, operations, serious illnesses and any other condition the investigator feels is significant. Medical history should include information related to the duration, i.e. the number of months must be recorded in the case report form. Subjects reporting Medical History will be presented by using frequency (percentage) count.

6.4 Physical Examination

Frequency count (percentage) of subjects will be presented for each Body System.

7.0 STATISTICAL ANALYSES

The primary objective of this study is to evaluate the PK profile of a single dose of intravenous ibuprofen administered over approximately 10 minutes.

7.1 Primary Endpoint Analysis (Pharmacokinetic Parameters)

PK samples will be collected on all subjects immediately (± 5 minutes) following completion of the first dose of intravenous ibuprofen; then alternating subjects will have PK sampling performed at 30 minutes and 2 hours or at 1 hour and 4 hours following the first dose of intravenous ibuprofen (12 subjects will have samples collected immediately following the first dose, then at 30 minutes and 2 hours; and, 12 subjects will have samples collected immediately following the first dose, then at 1 hour and 4 hours). Pharmacokinetic sampling will only be performed following the first dose of IMP regardless of the total number of doses of IMP administered.

To evaluate the PKs, the following parameters will be measured:

- Clearance
- Volume of distribution
- Elimination $T_{1/2}$
- $C_{max,}$
- AUC (0-∞, 0-t)

On the basis of plasma ibuprofen concentration time data, the following PK parameters will be estimated by using a non-compartmental model:

- AUC_{0-t}, calculated by using the linear-log trapezoidal rule: linear trapezoidal rule up to time to maximum concentration, and then a log trapezoidal rule for the remainder of the curve, where t corresponds to the last measurable time point
- $AUC_{0-\infty} = AUC_{0-t} + C_t/\lambda_z$, where C_t is the last measurable ibuprofen concentration and λ_z is the terminal elimination rate constant calculated by using log linear regression of the terminal elimination phase of the plasma concentration versus time curve
- C_{max} of ibuprofen estimated by inspection of the ibuprofen concentration time curve
- T_{max} estimated by inspection of the ibuprofen concentration time curve
- Terminal $T_{1/2} = \ln(2)/\lambda_z$
- Clearance=Renal Blood Flow* extraction ratio
- Volume of distribution= Clearance/ λ_z

7.2 Secondary Endpoint Analysis

The secondary objective of this study is to evaluate the safety of single and repeated doses of intravenous ibuprofen administered to hospitalized pediatric patients by assessing treatment emergent adverse events, vital signs, and laboratory assessments. The participant population of interest for the safety analyses is the safety analysis population.

Safety will be evaluated on the basis of treatment emergent AEs. AE data will be listed individually and summarized by body system organ class and preferred terms within system organ class (MedDRA). Serious and/or unexpected AEs will also be discussed on a case by case basis. Each AE will be counted only once for a given participant. If the same AE occurs on multiple occasions, the highest severity and least favorable relationship reported will be assumed. If two or more AEs are reported as a unit, the individual terms will be reported as separate experiences.

8.0 SAFETY AND TOLERABILITY ANALYSES

The analysis of safety assessments in this study will include summaries of the following categories of safety and tolerability data collected for each subject:

- Adverse Events
- Physical examination
- Vital Signs
- Concomitant Medication
- Laboratory Parameters

8.1 Adverse Events

Adverse events will be assessed regularly during the Treatment Period. Adverse event collection will begin at the start of IMP administration and continue through Study Hour 48 or discharge, whichever comes first. Subjects do not need to remain hospitalized for the 48-hour Treatment Period. All treatment emergent adverse events will be monitored until resolution or stabilization, regardless of the assessment of severity or relationship to the study drug. All AEs, observed by, documented in the subject's medical record, or reported to the research team must be recorded in both the subject's research record and the case report form.

8.2 Vital Signs

Descriptive statistics will be presented for each test at baseline, treatment period and post-treatment period.

8.3 Concomitant Medication

Concomitant medications, during the study will be listed by subject and summarized for the enrolled population as counts and percentage.

8.4 Laboratory parameters

The summary of following laboratory parameters will be provided through descriptive statistics:

- Sodium
- Potassium

- Chloride
- Total carbon dioxide
- Glucose
- Blood urea nitrogen
- Creatinine
- Total bilirubin
- Albumin
- Total protein
- Aspartate aminotransferase
- Alanine aminotransferase
- Lactate dehydrogenase
- Hematology and coagulation include:
- White blood cellcount and differential
- Hematocrit
- Hemoglobin
- Platelets
- Prothrombin time
- Partial thromboplastin time

9.0 INTERIM ANALYSIS OR OTHER PLANNED ANALYSES

No interim analysis is planned in this study.

10.0 REPORTING CONVENTIONS

10.1 Reporting of Numeric Values

All raw data will be presented to the original number of decimal places. The mean, median and quartiles will be presented with 1 decimal place more than raw data. The standard deviation (SD), Standard Error of Mean and Confidence Interval (CI) of mean will be presented with 1 decimal place more than mean. The range (minimum and maximum) will be presented as per the raw data Percentages will be presented in xx.x% format. All categories of variables will be presented even if there is no data. Blank cells will be filled by "-"in reporting of results.
Precision of p-values will be 4 decimal places. p-values less than 0.0001 will be presented as <0.0001 and if equal to 1 then ≥ 0.9999

11.0 Output (Tables, Listings and Graphs) Considerations

The default Tables, Listings and Graphs (TLG) layout will be as follows.

Orientation	All pages should preferably be landscape.
Paper Size	Legal size
Margins	Top: 1 in Bottom: 0.75 in Left: 0.75 in

	Right: 0.75 in
Font	Font style (preferably Courier New) of the Text
Headers	**Titles of Table/Listing will be center** **Left** Sponsor: Study Name: Protocol No:
Footers	**Left** Analyst Initials: Program Name: Program Run date: time: **Right** Datasets Used: Page XXX of YYY

The margin may be reduced as necessary to allow additional rows to be presented, but not at the expense of clarity. In addition, the orientation may be changed to portrait if appropriate. The date format for all presentations will be 'DDMMMYYYY'.

12.0 REFERENCES

1. Protocol: CL022_Amendment02_30SEP2016_FINAL
2. Case Report Form (CRF), CRF - CL022_Amendment02_30SEP2016_FINAL.
3. ICH E3: Structure and content of Clinical Study Reports, November 1995, CPMP.
4. ICH E9: Statistical Principles for Clinical Trials, September 1998, CPMP

APPENDIX 1: SUMMARY OF STATISTICAL ANALYSIS

1.1 TABLES

14.1.1 Subject Disposition

Table 14.1.1.1 Summary of Inclusion/Exclusion Criteria – All Screened (N=)

Inclusion/Exclusion Criteria, n (%) [1]	All Screened (N=)
Number of Subjects Screened	
Number of Subjects meeting all Inclusion Criteria	
Number of Subjects meeting at least one exclusion criteria	
Number of eligible subjects	

Source: Listing 16.2.4
Note:
[1] Percentage will be calculated by taking respective column header count as denominator.

Table 14.1.1.2 Summary of Study Populations – All Enrolled (N=)

Category, n (%) [1]	Overall (N=)
Screened Population	
No. of Subjects in Safety Population	
No. of Subjects Completed Study	
No. of Subjects Discontinued study	
Reason for pre-mature discontinuation [2]	
Subject withdrew from the study /Consent withdrawn	
The investigator withdrew the subject from the study	
The subject was discontinued from the study secondary to an AE or SAE	
Subject non-compliance	
Enrollment Violation	
Excluded medication, Procedure, or Therapy	
Other reason	

Source: Listing 16.2.1 and Listing 16.2.3
Note:
[1] Percentage will be calculated taking respective column header group count as denominator.
[2] Percentage will be calculated using total number of discontinued subjects count as denominator.

14.1.2 Demographics and Baseline Characteristics

Table 14.1.2.1 Summary of Subject Demographics-Safety Population (N=)

Parameters	Statistic/Category, n (%) [1]	Overall (N=)
Gender		
	Male	
	Female	
Age (in days)		
	n	
	Mean	
	SD	
	Median	
	Range (Min: Max)	
Race		
	American Indian or Alaskan Native	
	Asian	
	Black or African American	
	Native Hawaiian or other Pacific Islander	
	White	
	Multi-racial	
	Other	
Ethnicity		
	Hispanic or Latino	
	Non-Hispanic or Non-Latino	
Height (cm)		
	n	
	Mean	
	SD	
	Median	
	Range (Min: Max)	
Weight (Kg)		
	n	

	Mean SD Median Range (Min:Max)

Source: Listing 16.2.5.1
Note:

[1] Percentage will be calculated taking respective column header group count as denominator.

General Note:

Days=month*30.42

14.1.3 Medical History

Table 14.1.3.1 Summary of Medical History by SOC and PT-Safety Population (N=)

System Organ Class	Preferred Term, n (%) [1]	Overall(N=)
Total (All SOC/PT)	Any	
System Organ Class 1	Any	
	Preferred term1	
	Preferred term2	
	….	
System Organ Class 2	Any	
	Preferred term1	
	Preferred term2	
	…..	

Source Data: Listing 16.2.5.2

Note:

[1] Percentages will be calculated by taking respective column header group count as denominator.

General Note:

• Medical History will be coded using MedDRA version 21.1 or later.

• NA: Not Applicable

14.1.4 Physical Examination

Table 14.1.4.1 Summary of Physical Examination--Safety Population (N=)

Parameters	Statistic/Category, n (%) [1]	Overall (N=)
Was Physical examination done? [1]		
	Yes	
	No	
General Appearance, [2]		
	Normal	
	Abnormal	
	Not Assessed	
HEENT		
	Normal	
	Abnormal	
	Not Assessed	
Cardiovascular		
	Normal	
	Abnormal	
	Not Assessed	
Respiratory		
	Normal	
	Abnormal	
	Not Assessed	
……		

Source Data: Listing 16.4.2
Note:
[1] Respective column header group counts will be used as denominator for percentage calculation.
[2] Percentages for Physical Examination will be calculated using respected 'Yes' count as denominator.
Programming Note:
The same table will be repeated for all the available visits and all the physical examination – Gastrointestinal, Hepatic, Renal, Genitourinary, Musculokeletal, Endocrine, Immune/Allegry, Central Nervous System, Dermatological, Other.

14.2 Efficacy Analysis

14.2.1 Primary Efficacy Analysis

Table 14.2.1.1 Summary of Statistics of Pharmacokinetics (PK) Parameters-PK Population(N=)

Parameters	Statistic	Overall(N=)
Clearance		
	n	
	Mean	
	Geometric Mean	
	Standard Deviation	
	Median	
	Coefficient of Variation (%)	
	Range (Min.:Max.)	
Volume of distribution		
	n	
	Mean	
	Geometric Mean	
	Standard Deviation	
	Median	
	Coefficient of Variation (%)	
	Range (Min.:Max.)	

Elimination T1/2

n

Mean

Geometric Mean

Standard Deviation

Median

Coefficient of Variation (%)

Range (Min.:Max.)

C_{max}

n

Mean

Geometric Mean

Standard Deviation

Median

Coefficient of Variation (%)

Range (Min.:Max.)

T_{max}

n

Mean

Geometric Mean

Standard Deviation

Median

Coefficient of Variation (%)

Range (Min.:Max.)

AUC(0-∞, 0-t)

n

Mean

Geometric Mean

Standard Deviation

Median

Coefficient of Variation (%)

Range (Min.:Max.)

Note:
[1] Any observation with concentration value of 0.000 will be ignored while deriving the geometric mean.
General Note:

- Any concentration below this limit of quantification is reported as 0.000.

14.2.2 Secondary Analysis (Safety Endpoint)

Table 14.2.2.1 Summary of Overall Treatment Emergent Adverse Events -Safety Population (N=)

Category	Parameter, n (%) [1]	Events (N=)	Patients (N=)	% of Patients
TOTAL				
Serious Adverse Events				
	Yes			
	No			
Intensity				
	Mild			
	Moderate			
	Serve			
Resolution				
	Resolved			
	Resolved with Sequelae			
	Chronic condition			
	Fatal			
	Unknown			
IMP Action Taken				
	None			
	IMP Interrupted			
	IMP Discontinued			

Category	Parameter, n (%) [1]	Events (N=)	Patients (N=)	% of Patients
Event Action taken				
	None			
	Concomitant Medication			
	Hospitalization (complete SAE)			
	Other			
Relationship of the event to the IMP				
	Not Related			
	Possibly Related			
	Related			

Source Data: Listing 16.2.7.1

Note:
[1] Percentages will be calculated using respective column header counts as denominator.

General Note

- Subjects may have reported more than one event per system organ class or preferred term**.** Subjects will be only counted once for each system organ class or preferred term**.**

Table 14.2.2.2. Summary of Treatment Emergent Adverse Events by System Organ Class (SOC) and Preferred Term (PT)- Safety Population (N=)

System Organ Class	Preferred Term, n(%) [1]	Events (N=)	Patients (N=)	% of Patients
TOTAL (ALL SOC/PT)	NA			
SOC 1	ANY			
	PT1			
	PT2			
SOC 2	ANY			
	PT1			
	PT2			

Source Data: Listing 16.2.7.1

Note:
[1] Percentages will be calculated using respective column header counts as denominator.
NA: Not Applicable.
General Note:

- Adverse events will be coded using MedDRA version 21.1 or later**.**
- For each SOC and preferred term the number of subjects (percent of subjects) [number of events will be presented**.**
- Subjects may have reported more than one event per system organ class or preferred term**.** Subjects will be only counted once for each system organ class or preferred term**.**
- Zero frequencies will be presented by "0 [0] (0.0%) "**.**

Table 14.2.2.3 Summary of Vital Signs – Safety Population (N=)

Parameters	Statistic/Category, n (%) [1]	Visit			
		Screening	Treatment Period (0-24 hours)	Treatment Period (24-48 hours)	Post-Treatment Period
Temperature					
	n				
	Mean				
	SD				
	Median				
	Range (Min: Max)				
Heart Rate					
	n				
	Mean				
	SD				
	Median				
	Range (Min: Max)				
Respiratory Rate					
	n				
	Mean				
	SD				
	Median				
	Range (Min: Max)				
Systolic Blood Pressure					
	n				
	Mean				
	SD				
	Median				
	Range (Min: Max)				
Diastolic Blood Pressure					
	n				

	Mean SD Median Range (Min: Max)

Source Data: Listing 16.4.3
Note:
[1] Respective column header group counts will be used as denominator for percentage calculation.

Table 14.2.2.4 Summary of Coagulation Assessments – Safety Population (N=)

Parameters	Statistic/Category, n (%) [1]	Visit			
		Screening/Baseline Study Hour -48 to Hour 0)	Treatment Period (Study Hour 0 to Hour 24) +/- 6 hrs	Treatment Period (Study Hour 24 to Hour 48) +/- 6 hrs	Post-Treatment Period (Study Hour 48 to Hour 72) +/- 6 hrs
Prothrombin time (PT)					
	n				
	Mean				
	SD				
	Median				
	Range (Min: Max)				
Clinically Significant					
	Yes				
	No				
Activated Partial Thromboplastin Time (aPTT)					
	n				
	Mean				
	SD				
	Median				
	Range (Min: Max)				
Clinically Significant					
	Yes				
	No				
International Normalized Ratio (INR)					
	n				
	Mean				
	SD				
	Median				
	Range (Min: Max)				

Clinically Significant	
	Yes
	No

Source Data: Listing 16.2.8.1
Note:
[1] Respective column header group counts will be used as denominator for percentage calculation.

Table 14.2.2.5 Summary of Haematology – Safety Population (N=)

Parameters	Statistic/Category, n (%) [1]	Visit			
		Screening/Baseline Study Hour -48 to Hour 0)	Treatment Period (Study Hour 0 to Hour 24) +/- 6 hrs	Treatment Period (Study Hour 24 to Hour 48) +/- 6 hrs	Post-Treatment Period (Study Hour 48 to Hour 72) +/- 6 hrs
Hemoglobin					
	n				
	Mean				
	SD				
	Median				
	Range (Min: Max)				
Clinically Significant					
	Yes				
	No				
Hematocrit					
	n				
	Mean				
	SD				
	Median				
	Range (Min: Max)				
Clinically Significant					
	Yes				
	No				
Platelets					
	n				
	Mean				
	SD				
	Median				
	Range (Min: Max)				
Clinically Significant					
	Yes				
	No				
White Blood Cell Count					
	n				

	Mean SD Median Range (Min: Max)
Clinically Significant	
	Yes No
Total Neutrophil Count (segmented neutrophils plus bands)	
	n Mean SD Median Range (Min: Max)
Clinically Significant	
	Yes No

Source Data: Listing 16.2.8.2
Note:
[1] Respective column header group counts will be used as denominator for percentage calculation.
Programming Note:
The same table will be repeated for all available Hematology Parameters-Lymphocytes, Monocytes, Eosinophils, Basophils.

Table 14.2.2.6 Summary of Chemistry – Safety Population (N=)

Parameters	Statistic/Category, n (%) [1]	Visit			
		Screening/Baseline Study Hour -48 to Hour 0)	Treatment Period (Study Hour 0 to Hour 24) +/- 6 hrs	Treatment Period (Study Hour 24 to Hour 48) +/- 6 hrs	Post-Treatment Period (Study Hour 48 to Hour 72) +/- 6 hrs
Sodium					
	n				
	Mean				
	SD				
	Median				
	Range (Min: Max)				
Clinically Significant					
	Yes				
	No				
Potassium					
	n				
	Mean				
	SD				
	Median				
	Range (Min: Max)				
Clinically Significant					
	Yes				
	No				
Total Carbon Dioxide/Bicarbonate					
	n				
	Mean				
	SD				
	Median				
	Range (Min: Max)				
Clinically Significant					
	Yes				
	No				

Chloride	
	n
	Mean
	SD
	Median
	Range (Min: Max)
Clinically Significant	
	Yes
	No
Glucose	
	n
	Mean
	SD
	Median
	Range (Min: Max)
Clinically Significant	
	Yes
	No

Source Data: Listing 16.2.8.3
Note:
[1] Respective column header group counts will be used as denominator for percentage calculation.
Programming Note:
The same table will be repeated for all the available Chemistry Parameters- Blood Urea Nitrogen, Creatinine, Total Bilirubin, Albumin, Total Protein, Aspartate Transaminase, Alanine Transaminase, Lactate Dehydrogenase

14.3 Safety Analysis

14.3.1 ADVERSE EVENTS

Table 14.3.1.1 Summary of Overall Adverse Events -Safety Population (N=)

Category	Parameter, n (%) [1]	Events (N=)	Patients (N=)	% of Patients
TOTAL				
Serious Adverse Events				
	Yes			
	No			
Intensity				
	Mild			
	Moderate			
	Serve			
Resolution				
	Resolved			
	Resolved with Sequelae			
	Chronic condition			
	Fatal			
	Unknown			
IMP Action Taken				
	None			
	IMP Interrupted			

Category	Parameter, n (%) [1]	Events (N=)	Patients (N=)	% of Patients
	IMP Discontinued			
Event Action taken				
	None			
	Concomitant Medication			
	Hospitalization (complete SAE)			
	Other			
Relationship of the event to the IMP				
	Not Related			
	Possibly Related			
	Related			

Source Data: Listing 16.2.7.1
Note:
[1] Percentages will be calculated using respective column header counts as denominator.
General Note
- Subjects may have reported more than one event per system organ class or preferred term**.** Subjects will be only counted once for each system organ class or preferred term**.**

Table 14.3.1.2. Summary of Adverse Events by System Organ Class (SOC) and Preferred Term (PT) -Safety Population(N=)

System Organ Class	Preferred Term, n(%) [1]	Events (N=)	Patients (N=)	% of Patients
TOTAL (ALL SOC/PT)	NA			
SOC 1	ANY			
	PT1			
	PT2			
SOC 2	ANY			
	PT1			
	PT2			

Source Data: Listing 16.2.7.1
Note:
[1] Percentages will be calculated using respective column header counts as denominator.
NA: Not Applicable.
Genral Note:

- Adverse events will be coded using MedDRA version 21.1 or later**.**
- For each SOC and preferred term the number of subjects (percent of subjects) [number of events will be presented**.**
- Subjects may have reported more than one event per system organ class or preferred term**.** Subjects will be only counted once for each system organ class or preferred term**.**
- Zero frequencies will be presented by "0 (0.0%) [0]"**.**

Table 14.3.1.3. Summary of Adverse Events by System Organ Class (SOC) and Preferred Term (PT) by Intensity- Safety Population (N=)

System Organ Class	Preferred Term, n (%) [1]	Intensity	Events (N=)	Patients (N=)	% of Patients
TOTAL (ALL SOC/PT)	NA				
SOC 1	ANY				
	PT1				
		Mild			
		Moderate			
		Severe			
	PT2				
		Mild			
		Moderate			
		Severe			
…….	…….	…….	…	….	….

Source Data: Listing 16.2.7.1
Note:
[1] Percentages will be calculated using respective column header counts as denominator.
General Note

- Adverse events will be coded using MedDRA version 21.1 or later**.**
- For each SOC and preferred term the number of subjects (percent of subjects) [number of events] will be presented**.**
- Subjects may have reported more than one event per system organ class or preferred term**.** Subjects will be only counted once for each system organ class or preferred term**.**
- Zero frequencies will be presented by "0 (0.0%) [0]"**.**

Table 14.3.1.4 Summary of Adverse Events by System Organ Class (SOC) and Preferred Term (PT) by Relationship - Safety Population (N=)

System Organ Class	Preferred Term	Causality	Events (N=)	Patients (N=)	% of Patients
TOTAL (ALL SOC/PT)	NA				
SOC 1	ANY				
	PT1				
		Not related			
		Possibly Related			
		Related			
	PT2				
		Not related			
		Possibly Related			
		Related			
…….	…….	…….			

Source Data: Listing 16.2.7.1
Note:
[1] Percentages will be calculated using respective column header counts as denominator.
General Note:

- Adverse events will be coded using MedDRA version 21.1 or later**.**
- For each SOC and preferred term the number of subjects (percent of subjects) [number of events] will be presented**.**
- Subjects may have reported more than one event per system organ class or preferred term**.** Subjects will be only counted once for each system organ class or preferred term**.**
- Zero frequencies will be presented by "0 (0.0%) [0]"**.**

Table 14.3.1.5 Summary of Adverse Events by System Organ Class (SOC) and Preferred Term (PT) by Action taken- Safety Population (N=)

System Organ Class	Preferred Term	Action taken	Events (N=)	Patients (N=)	% of Patients
TOTAL (ALL SOC/PT)	NA				
SOC 1	ANY				
	PT1				
		None			
		IMP Interrupted			
		IMP Discontinued			
	PT2				
		None			
		IMP Interrupted			
		IMP Discontinued			
…….	…….	…….			

Source Data: Listing 16.2.7.1
Note:

[1] Percentages will be calculated using respective column header counts as denominator.

General Note

- Adverse events will be coded using MedDRA version 21.1 or later.
- For each SOC and preferred term the number of subjects (percent of subjects) [number of events] will be presented.
- Subjects may have reported more than one event per system organ class or preferred term. Subjects will be only counted once for each system organ class or preferred term.
- Zero frequencies will be presented by "0 (0.0%) [0]".

Table 14.3.1.6 Summary of Adverse Events by System Organ Class (SOC) and Preferred Term (PT) by Event Action Taken- Safety Population (N=)

System Organ Class	Preferred Term	Outcome	Events (N=)	Patients (N=)	% of Patients
TOTAL (ALL SOC/PT)	NA				
SOC 1	ANY				
	PT1				
		None			
		Concomitant Medication			
		Hospitalization			
		Other			
	PT2				
		None			
		Concomitant Medication			
		Hospitalization			
		Other			
…….	…….	…….			

Source Data: Listing 16.2.7.1
Note:
[1] Percentages will be calculated using respective column header counts as denominator.
General Note:

- Adverse events will be coded using MedDRA version 21.1 or later**.**
- For each SOC and preferred term the number of subjects (percent of subjects) [number of events] will be presented**.**
- Subjects may have reported more than one event per system organ class or preferred term**.** Subjects will be only counted once for each system organ class or preferred term**.**
- Zero frequencies will be presented by "0 (0.0%) [0]"**.**

Table 14.3.1.7 Summary of Adverse Events by System Organ Class (SOC) and Preferred Term (PT) by Resolution- Safety Population (N=)

System Organ Class	Preferred Term	Outcome	Events (N=)	Patients (N=)	% of Patients
TOTAL (ALL SOC/PT)	NA				
SOC 1	ANY				
	PT1				
		Resolved			
		Resolved with Sequelae			
		Chronic Condition			
		Unknown			
		Fatal			
	PT2				
		Resolved			
		Resolved with Sequelae			
		Chronic Condition			
		Unknown			
		Fatal			
…….	…….	…….			

Source Data: Listing 16.2.7.1
Note:
[1] Percentages will be calculated using respective column header counts as denominator.
General Note:

- Adverse events will be coded using MedDRA version 21.1 or later.
- For each SOC and preferred term the number of subjects (percent of subjects) [number of events] will be presented.
- Subjects may have reported more than one event per system organ class or preferred term. Subjects will be only counted once for each system organ class or preferred term.
- Zero frequencies will be presented by "0 (0.0%) [0]".

14.3.2 SERIOUS ADVERSE EVENTS

Table 14.3.2.1 Summary of Overall Serious Adverse Events -Safety Population (N=)

Category	Parameter, n (%) [1]	Events (N=)	Patients (N=)	% of Patients
TOTAL Event Occurred				
	Hospital			
	Home			
	Rehabilitation Facility			
	Outpatient Diagnostic Facility			
	Ambulatory Surgical Facility			
	Outpatient Treatment Facility			
	Other			
Outcome				
	Death			
	Life-threatening			
	Hospitalization - Initial or Prolonged			
	Other Serious (important Medical Condition)			
	Disability or Permanent Damage			
	Congenital Anomaly/Birth Defect			
subject discontinued				

Category	Parameter, n (%) [1]	Events (N=)	Patients (N=)	% of Patients
	Yes			
	No			
	Not Applicable			
Event Abated after the IMP was stopped?				
	Yes			
	No			
	Not Applicable			
Event reappeared after IMP reintroduction?				
	Yes			
	No			
	Not Applicable			
Was the event expected?				
	Expected			
	Unexpected			

Source Data: Listing 16.2.7.1
Note:
[1] Percentages will be calculated using respective column header counts as denominator.
General Note

- Adverse events will be coded using MedDRA version 21.1 or later**.**
- For each SOC and preferred term the number of subjects (percent of subjects) [number of events] will be presented**.**
- Subjects may have reported more than one event per system organ class or preferred term**.** Subjects will be only counted once for each system organ class or preferred term**.**
- Zero frequencies will be presented by "0 (0.0%) [0]"**.**

Table 14.3.2.2. Summary of Serious Adverse Events by System Organ Class (SOC) and Preferred Term (PT) -Safety Population (N=)

System Organ Class	Preferred Term, n(%) [1]	Events (N=)	Patients (N=)	% of Patients
TOTAL (ALL SOC/PT)	NA			
SOC 1	ANY			
	PT1			
	PT2			
SOC 2	ANY			
	PT1			
	PT2			

Source Data: Listing 16.2.7.1
Note:
[1] Percentages will be calculated using respective column header counts as denominator.
NA: Not Applicable.
General Note:

- Adverse events will be coded using MedDRA version 21.1 or later**.**
- For each SOC and preferred term the number of subjects (percent of subjects) [number of events will be presented**.**
- Subjects may have reported more than one event per system organ class or preferred term**.** Subjects will be only counted once for each system organ class or preferred term**.**
- Zero frequencies will be presented by "0(0.0%) [0]"**.**
- SAE's: Serious Adverse Events

14.3.3 CONCOMITANT MEDICATION

Table 14.3.3.1 Summary of Concomitant Medication -Safety Population (N=)

Therapeutic Class	Generic name, n (%) [1]	Overall(N=)
Therapeutic Class 1	Any	
	Generic Name 1	
	Generic Name 2	
	….	
Therapeutic Class 1	Any	
	Generic Name 1	
	Generic Name 2	
	….	

Source Data: Listing 16.4.4

Note:

[1] Percentages will be calculated by taking respective column header group count as denominator.

General Note:

• All Concomitant medications were coded and summarized according to their generic drug names using the WHO Drug classifications version 1st September 2018 or later. One patient may have taken more than one medication.

• NA: Not Applicable

1.2 LISTINGS

16.2 PATIENT DATA LISTINGS

Listing 16.2.1 Listing of Patient Study Completion Status

Site No./ Subject No.	Age/Gender	Subject Completed the Study	If Yes, date of study completion/pre-mature discontinuation	Primary reason for pre-mature discontinuation	Other Specify
XX/NNN	NN/XX	Yes/No	DDMMMYYYY	XX	XX
XX/NNN	NN/XX	Yes/No	DDMMMYYYY	XX	XX
XX/NNN	NN/XX	Yes/No	DDMMMYYYY	XX	XX
…	…	…	…	…	…

Did the subject experience any adverse events during the post-treatment period?	Subject's Clinical outcome at the time of the final follow-up	If deceased, date of death	If deceased, cause of death	Did the subject receive NSAIDs or acetaminophen from 4 hours prior to IMP through Study Hour 48?	If Yes, date of restricted Medication	If Yes, Time of restricted Medication
Yes/No	NN/XX	DDMMMYYYY	XX	Yes/No	DDMMMYYYY	XX
Yes/No	NN/XX	DDMMMYYYY	XX	Yes/No	DDMMMYYYY	XX
Yes/No	NN/XX	DDMMMYYYY	XX	Yes/No	DDMMMYYYY	XX
…	…	…	…	…	…	…

Listing 16.2.2 Listing of Protocol Deviation

Site No./ Subject No.	Age/Gender	Visit	Date	Deviation	Comments
XX/NNN	NN/XX	XXX	DDMMMYYYY	XX	XX
XX/NNN	NN/XX	XXX	DDMMMYYYY	XX	XX
XX/NNN	NN/XX	XXX	DDMMMYYYY	XX	XX
…	…	…	…	…	…

Listing 16.2.3 Listing of Informed Consent

Site ID/ Subject No.	Age/Gender	Screening Number	Randomization Number	Date of Screening	Date Informed Consent Signed	Time Informed Consent Signed
XXX/NNN	NN/XXX	NNN	NNN	DDMMMYYYY	DDMMMYYYY	HH:MM
XXX/NNN	NN/XXX	NNN	NNN	DDMMMYYYY	DDMMMYYYY	HH:MM
XXX/NNN	NN/XXX	NNN	NNN	DDMMMYYYY	DDMMMYYYY	HH:MM
…	…	…	…	…	…	…

Listing 16.2.4 Listing of Inclusion/Exclusion Criteria

Site ID/Subject No.	Age/Gender	All Inclusion Criteria Met	If No, Inclusion Criteria Number(s)	Exclusion Criteria Met	If Yes, Exclusion Criteria Number(s)	Subject is eligible for the study
XX/NNN	NN/XX	Yes/No	NN	Yes/No	NN	Yes/No
XX/NNN	NN/XX	Yes/No	NN	Yes/No	NN	Yes/No
XX/NNN	NN/XX	Yes/No	NN	Yes/No	NN	Yes/No
…	…	…	…	…	…	…

16.2.5 LISTING OF DEMOGRAPHICS

Listing 16.2.5.1 Listing of Demographics at Screening

Site ID/Subject No.	Age/Gender	Date of birth	Ethnicity	Race	If race is Multi-racial	Weight (Kg)
XX/NNN	NN/XX	DDMMMYYYY	XX	XX	XX	XX
XX/NNN	NN/XX	DDMMMYYYY	XX	XX	XX	XX
XX/NNN	NN/XX	DDMMMYYYY	XX	XX	XX	XX
…	…	…	…..	…..	…..	…..

Listing 16.2.5.2 Listing of Medical History

Site ID/Subject No.	Age/Gender	Condition/ Surgery	Generic Name	Therapeutic Class	Onset Date	End Date	Comment	Allergies or reaction
XX/NNN	NN/XX	Yes/No	XX	XX	DDMMMYYYY	DDMMMYYYY	XX	XX
XX/NNN	NN/XX	Yes/No	XX	XX	DDMMMYYYY	DDMMMYYYY	XX	XX
XX/NNN	NN/XX	Yes/No	XX	XX	DDMMMYYYY	DDMMMYYYY	XX	XX
…	…	…..	…	…	…	…	…	…

16.2.6 LISTING OF SAFETY ANALYSIS

Listing 16.2.7.1 Listing of Adverse Event

Site No./ Subject No.	Age/Gender	AE Term	System Organ Class	Preferred Term	Stop Date	Intensity	Serious AE	Resolution: Is the event going?	Resolution Date	Resolution	IMP Action	Event Action	Other specify	Relationship of the event to the IMP
XX/NNN	NN/XX	XXX	XX	XXX	DDMMMYYYY	XX	XX	Yes/No	DDMMMYYYY	XX	XXX	XXX	XXX	XXX
XX/NNN	NN/XX	XXX	XX	XXX	DDMMMYYYY	XX	XX	Yes/No	DDMMMYYYY	XX	XXX	XXX	XXX	XXX
XX/NNN	NN/XX	XXX	XX	XXX	DDMMMYYYY	XX	XX	Yes/No	DDMMMYYYY	XX	XXX	XXX	XXX	XXX
…	…	…	…	…	…	…	…	…	…	…	…	…	…	…

16.2.8 LABORATORY TEST

Listing 16.2.8.1 Listing of Coagulation Assessment

Site No./ Subject No.	Age/ Gender	Visit	If Yes, Date Sample Collected	Time Sample Collected	Lab Test	Result	Result is CS/NCS
XX/ NNN	NN/ XX	XX	DDMMMYYYY	HH:MM	XX	XX	XX
XX/ NNN	NN/ XX	XX	DDMMMYYYY	HH:MM	XX	XX	XX
XX/ NNN	NN/ XX	XX	DDMMMYYYY	HH:MM	XX	XX	XX
…	…	…	…	…	…	…	…

Listing 16.2.8.2 Listing of Haematology

Site No./ Subject No.	Age/ Gender	Visit	If Yes, Date Sample Collected	Time Sample Collected	Lab Test	Result	Result is CS/NCS
XX/ NNN	NN/ XX	XX	DDMMMYYYY	HH:MM	XX	XX	XX
XX/ NNN	NN/ XX	XX	DDMMMYYYY	HH:MM	XX	XX	XX
XX/ NNN	NN/ XX	XX	DDMMMYYYY	HH:MM	XX	XX	XX
…	…	…	…	…	…	…	…

Listing 16.2.8.3 Listing of Chemistry

Site No./ Subject No.	Age/ Gender	Visit	If Yes, Date Sample Collected	Time Sample Collected	Lab Test	Result	Result is CS/NCS
XX/ NNN	NN/ XX	XX	DDMMMYYYY	HH:MM	XX	XX	XX
XX/ NNN	NN/ XX	XX	DDMMMYYYY	HH:MM	XX	XX	XX
XX/ NNN	NN/ XX	XX	DDMMMYYYY	HH:MM	XX	XX	XX
…	…	…	…	…	…	…	…

16.4 INDIVIDUAL PATIENT DATA LISTINGS

Listing 16.4.1 Listing of Treatment Period IMP Dose 1 and Assessments

Site No./ Subject No.	Age/ Gender	Dose Date	Dose Time	IMP/ PRN	Location	Dose administered	If No, Specify	Did the subject receive any PRN Dose of the study drug during the Treatment Period?
XX/ NNN	NN/ XX	DDMMMYYYY	HH:MM		NN	Yes/No	XXX	NN
XX/ NNN	NN/ XX	DDMMMYYYY	HH:MM		NN	Yes/No	XXX	NN
XX/ NNN	NN/ XX	DDMMMYYYY	HH:MM		NN	Yes/No	XXX	NN
…	…	…	…		…	…	…	…

Listing 16.4.2 Listing of Physical Examination

Site No./ Subject No.	Age/ Gender	Date of Examination	Time of Examination	Body System	Normal/Abnormal	Specify, If abnormal
XX/ NNN	NN/ XX	DDMMMYYYY	HH:MM	XXX	Yes/No	XXX
XX/ NNN	NN/ XX	DDMMMYYYY	HH:MM	XXX	Yes/No	XXX
XX/ NNN	NN/ XX	DDMMMYYYY	HH:MM	XXX	Yes/No	XXX
…	…	…	…	…	…	…

Listing 16.4.3 Listing of Vital Signs

Site No./ Subject No.	Age/ Gender	Visit	Date Performed	Time Performed	Temperature	Route of Temperature Measurement	Heart Rate	Respiratory Rate	Blood Pressure (Systolic /Diastolic)
XX/ NNN	NN/ XX	XXX	DDMMMYYYY	HH:MM	NN	XXX	NN	NN	NN/NN
XX/ NNN	NN/ XX	XXX	DDMMMYYYY	HH:MM	NN	XXX	NN	NN	NN/NN
XX/ NNN	NN/ XX	XXX	DDMMMYYYY	HH:MM	NN	XXX	NN	NN	NN/NN
…	…	…	…	…	…	…	….	…	…

Listing 16.4.4 Listing of Concomitant Medication

Site No./ Subject No.	Age/Gender	Name of Medication	Generic Name	Therapeutic Class	Dose	Dose (Units)	If Other, specify	Dose Frequency	If Other, specify	Route	If Other, specify	Was concomitant medication prescribed to treat an Adverse Event?	Start Date	Start time	Ongoing	End Date	End Time
XX/NNN	NN/XX	XXX	XXX	XXX	N	XX	XX	XXX	XX	XX	XX	Yes/No	DDMMMYYYY	HH:MM	XXX	DDMMMYYYY	HH:MM
XX/NNN	NN/XX	XXX	XXX	XXX	N	XX	XX	XXX	XX	XX	XX	Yes/No	DDMMMYYYY	HH:MM	XXX	DDMMMYYYY	HH:MM
XX/NNN	NN/XX	XXX	XXX	XXX	N	XX	XX	XXX	XX	XX	XX	Yes/No	DDMMMYYYY	HH:MM	XXX	DDMMMYYYY	HH:MM
…	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…

Listing 16.4.5 Listing of Pharmacokinetic Sampling

Site No./ Subject No.	Age/Gender	Time of PK Collection	Date of PK Collection	Collected by means	Date and time the sample spun	Date and time the sample frozen	Number of Aliquot Tubes
XX/NNN	NN/XX	HH:MM	DDMMMYYYY	XXX	YYYYMMDD/HH:MM	YYYYMMDD/HH:MM	XXX
XX/NNN	NN/XX	HH:MM	DDMMMYYYY	XXX	YYYYMMDD/HH:MM	YYYYMMDD/HH:MM	XXX
XX/NNN	NN/XX	HH:MM	DDMMMYYYY	XXX	YYYYMMDD/HH:MM	YYYYMMDD/HH:MM	XXX
…	….	….	….	…..	….	…..	….