



TRIAL STATISTICAL ANALYSIS PLAN

c28029008-01

BI Trial No.:	1371-0021
Title:	Relative bioavailability of BI 894416 as tablet formulation following a high-fat, high-calorie breakfast compared to administration in the fasting state in healthy male subjects (an open-label, randomised, single-dose, two-period, two-sequence crossover study) (including Protocol Amendments No.1[c23506058-02] and No. 2 [c23506058-03])
Investigational Product:	BI 894416
Responsible trial statisticians:	Phone: Fax:
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Date of statistical analysis plan:	03 JUN 2019 SIGNED
Version:	Final
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2. LIST OF ABBREVIATIONS

See Medicine Glossary:

[website: glossary](#)

Term	Definition / description
ALT	Alanine transaminase
ANOVA	Analysis of variance
AST	Aspartate transaminase
AUC _{0-tz}	Area under the concentration-time curve of the analyte in plasma over the time interval from 0 to the last quantifiable data point
AUC _{0-∞}	Area under the concentration-time curve of the analyte in plasma over the time interval from 0 extrapolated to infinity
BMI	Body mass index
BWC	Bioavailability/Bioequivalence, within-subject design, time-controlled
CI	Confidence interval
C _{max}	Maximum measured concentration of the analyte in plasma
CV	Arithmetic coefficient of variation
DBLM	Database lock meeting
DILI	Drug induced liver injury
gCV	Geometric coefficient of variation
gMean	Geometric mean
LLT	Lower level term
Max	Maximum
MedDRA	Medical Dictionary for Regulatory Activities
Min	Minimum
N	Number non-missing observations
P10	10th percentile
P90	90th percentile
PKS	PK parameter set
Q1	1st quartile
Q3	3rd quartile
R / Ref	Reference treatment
RAGe	Report Appendix Generator system

Term	Definition / description
SD	Standard deviation
SOC	System organ class
T	Test treatment
TS	Treated set
ULN	Upper limit of normal
WHO-DD	World Health Organization Drug Dictionary
XPKISTAT	Library of SAS [®] Macros for PK analysis

3. INTRODUCTION

As per ICH E9 ([1](#)), the purpose of this document is to provide a more technical and detailed elaboration of the principal features of the analysis described in the protocol, and to include detailed procedures for executing the statistical analysis of the primary and secondary variables and other data.

This Trial statistical analysis plan (TSAP) assumes familiarity with the Clinical Trial Protocol (CTP). In particular, the TSAP is based on the planned analysis specification as written in CTP Section 7 “Statistical Methods and Determination of Sample Size”. Therefore, TSAP readers may consult the CTP for more background information on the study, e.g., on study objectives, study design and population, treatments, definition of measurements and variables, planning of sample size, randomisation.

Study data (including data entered in the RAVE EDC system and external data provided by suppliers) will be stored in a Clinical Data Repository (CDR).

Pharmacokinetic (PK) parameters will be calculated using Phoenix WinNonlinTM software (version 6.3 or higher, Certara USA Inc., Princeton, NJ, USA).

The statistical analyses will be performed within the validated working environment CARE, including SASTM (current Version 9.4, by SAS Institute Inc., Cary, NC, USA), and a number of SASTM-based tools (e.g., macros for the analyses of AE data or laboratory data; Report Appendix Generator system (RAGe) for compilation/formatting of the CTR appendices).

4. CHANGES IN THE PLANNED ANALYSIS OF THE STUDY

All analyses as planned in the CTP will be performed and are described in more detail in this TSAP.

5. ENDPOINTS

5.1 PRIMARY ENDPOINTS

Section 2.1.2 of the CTP: *The following pharmacokinetic parameters will be determined for BI 894416:*

- *AUC_{0-t_z} (area under the concentration-time curve of the analyte in plasma over the time interval from 0 to the last quantifiable data point)*
- *C_{max} (maximum measured concentration of the analyte in plasma)*

5.2 SECONDARY ENDPOINTS

5.2.1 Key secondary endpoints

This section is not applicable as no key secondary endpoints have been defined in the CTP.

5.2.2 Secondary endpoints

Section 2.1.3 of the CTP: *The following pharmacokinetic parameter will be determined for BI 894416:*

- *AUC_{0-∞} (area under the concentration-time curve of the analyte in plasma over the time interval from 0 extrapolated to infinity)*

6. GENERAL ANALYSIS DEFINITIONS

6.1 TREATMENTS

For basic study information on investigational products, assignment of treatment sequences and selection of doses, please see CTP, Sections 3 and 4.

The study will be performed as a randomised, open-label, two-way crossover trial with two treatments (T and R) and two treatment sequences (TR or RT).

In total, it was planned to assign 14 healthy male subjects to the two treatment sequences in a 1:1 ratio.

For details of dosage and formulation see Table 6.1: 1 below:

Table 6.1: 1 Treatments and labels used in the analysis

Treatment	Short label	Short label for footnote
R BI 894416, 3*10 mg tablet, qd, fasted	BI 30mg fast	BI 894416 30mg fast
T BI 894416, 3*10 mg tablet, qd, fed	BI 30mg fed	BI 894416 30mg fed

The following separate study phases will be defined for the analyses of AEs:

- **Screening** (ranging from 0:00 h on day of informed consent until first administration time of study drug)
- **On treatment** (separately for each treatment; i.e. ranging from the time of administration of the respective treatment until next drug administration or 0:00 h on the day after trial termination date)

Displays of AEs will be presented separately for the treatments described in [Table 6.1: 1](#) above

Two types of AE displays will be provided in the report:

A) Section 15.3 and Appendix 16.1.13.1.8 (for ClinicalTrials.gov and EudraCT only) of the CTR displays:

In these displays, the on treatment phase will be analysed (labelled with the name of the study treatment (short label)). Screening will not be included in this analysis.

The following total will be provided in addition (Section 15.3 only):

- a total over all on treatment phases included in this analysis ("Total on treatment")

B) Section 15.4 and Appendix 16.1.13.1.8 (except for ClinicalTrials.gov and EudraCT) of the CTR displays:

- Screening
- On treatment (labelled with the name of the study treatment (short label))

In Section 16.1.13.1.8 AE tables, the following totals will be provided in addition:

- a total over all study phases ("Total")

For detailed information on the handling of the treatments refer to Technical TSAP ADS plan and Analysis Data Reviewers guide.

6.2 IMPORTANT PROTOCOL DEVIATIONS

Data discrepancies and deviations from the CTP will be identified for all treated subjects.

Section 7.3 of the CTP: *Important protocol deviation (IPD) categories will be suggested in the Integrated Quality and Risk Management Plan (IQRMP), IPDs will be identified no later than in the Report Planning Meeting, and the IPD categories will be updated as needed.*

Consistency check listings (for identification of deviations of time windows) and a list of protocol deviations (e.g. deviations in drug administration, in blood sampling times, etc.) will be provided to be discussed at the combined report planning and database lock meeting (RPM/DBLM). At this meeting, all manual deviations identified at the sites by the CRAs and deviations too complex to program will be reviewed by the trial team to decide which are considered important. For definition of important protocol deviations (iPD), and for the process of identification of these, refer to the Boehringer Ingelheim (BI) SOP "Identify and Manage Important Protocol Deviations (iPD)" (2).

If any iPDs are identified, they are to be summarised into categories and will be captured in the RPM minutes via an accompanying Excel spreadsheet (3).

The iPDs will be summarised and listed.

6.3 SUBJECT SETS ANALYSED

Section 7.3 of the CTP:

- *Treated set (TS): The treated set includes all subjects who were treated with at least one dose of study drug. The treated set will be used for safety analyses.*
- *Pharmacokinetic parameter analysis set (PKS): This set includes all subjects in the treated set (TS) who provide at least one PK endpoint that was defined as primary and was not excluded due to a protocol deviation relevant to the evaluation of PK or due to PK non-evaluability (as specified in the following subsection 'Pharmacokinetics'). Thus, a subject will be included in the PKS, even if he contributes only one PK parameter value for one period to the statistical assessment. Descriptive and model based analyses of PK parameters will be based on the PKS.*

[...]

Plasma concentration data and parameters of a subject will be included in the statistical pharmacokinetic (PK) analyses if they are not flagged for exclusion due to a protocol deviation relevant to the evaluation of PK (to be decided no later than in the Report Planning Meeting) or due to PK non-evaluability (as revealed during data analysis, based on the criteria specified below). Exclusion of a subject's data will be documented in the CTR.

Relevant protocol deviations may be

- *Incorrect trial medication taken, i.e. the subject received at least one dose of trial medication the subject was not assigned to*
- *Incorrect dose of trial medication taken*
- *Use of restricted medications*

Plasma concentrations and/or parameters of a subject will be considered as non-evaluable, if for example

- *The subject experienced emesis at or before two times median t_{max} . Median t_{max} is to be taken either from the median t_{max} for the reference treatment or from median t_{max} for the test treatment, depending on whether the subject had experienced emesis after taken the test or the reference treatment. Median t_{max} is to be determined excluding the subjects experiencing emesis.*
- *A predose concentration of BI 894416 is $>5\% C_{max}$ value of that subject in the respective treatment period*
- *Missing samples/concentration data at important phases of PK disposition curve*

The descriptive analysis of PK concentrations will be based on the ADS ADPC as described at the beginning of [Section 7](#).

Table 6.3: 1 Subject sets analysed

Class of endpoint	Subject set	
	TS	PKS
Analyses of PK endpoints		X
Safety parameters	X	
Demographic/baseline parameters	X	
Important protocol deviations	X	
Disposition	X	

6.5 POOLING OF CENTRES

This section is not applicable, because the study was performed in only one centre.

6.6 HANDLING OF MISSING DATA AND OUTLIERS

Handling of missing data and outliers will be performed as described in the CTP, Section 7.5.

The only exceptions where imputation might be necessary for safety evaluation are AE dates. Missing or incomplete AE dates are imputed according to BI standards (see 001-MCG-156_RD-01 ([4](#))).

Missing data and outliers of PK data are handled according to BI standards (see 001-MCS-36-472_RD-01) ([5](#)).

6.7 BASELINE, TIME WINDOWS AND CALCULATED VISITS

For vital signs, the baseline is defined as the last measurement before administration of BI 894416 in each period.

For laboratory, the baseline is defined as the measurement prior to first drug administration (in Visit 2).

Section 6.1 of the CTP: *Exact times of measurements outside the permitted time windows will be documented. The acceptable time windows for screening and the end of trial examination are provided in the Flow Chart.*

Study measurements and assessments scheduled to occur 'before' trial medication administration on Day 1 are to be performed and completed within a 3 h-period prior to the trial drug administration. The acceptable deviation from the scheduled time for vital signs, ECG, and laboratory tests will be ± 1 h.

[...]

Starting from 48 hours after BI 894416 administration a time window of ± 120 min will be allowed for all study activities.

Adherence to time windows will be checked via the consistency check listings at the RPM/DBLM.

Unscheduled measurements of laboratory data and vital signs data will be assumed to be repeat measurements of the most recent scheduled measurement (e.g. for follow-up or confirmation of a particular value). Therefore, unscheduled measurements will be assigned to the planned time point of the previous scheduled measurement.

7. PLANNED ANALYSIS

Safety analysis (refer to [Section 7.8](#)) will be performed by and will be presented in Sections 15.1 to 15.4 of the CTR and in Appendix 16.2 and 16.1.13.1.

Inferential statistical analyses of PK endpoints (refer to [Section 7.4](#) and [Section 7.5.2](#)) will also be performed by and will be presented in Section 15.5 of the CTR and in Appendix 16.1.13.3.

Descriptive data analysis of PK endpoints and concentrations will be performed by the department Translational Medicine and Clinical Pharmacology (TMCP) at BI and will be presented in Section 15.6 of the CTR.

The format of the listings and tables will follow the standards defined in the BI corporate guideline “Reporting of Clinical Trials and Project Summaries” [001-MCG-159] ([6](#)) with the exception of those generated for PK-calculations ([7](#)).

The individual values of all subjects will be listed, sorted by treatment sequence, subject number, visit and actual treatment (if appropriate).

The listings will be included in Appendix 16.2 of the CTR.

For end-of-text tables, the set of summary statistics for non-PK parameters is:

N	number non-missing observations
Mean	arithmetic mean
SD	standard deviation
Min	minimum
Median	median
Max	maximum

For analyte concentrations, the following descriptive statistics will additionally be calculated:

CV	arithmetic coefficient of variation
gMean	geometric mean
gCV	geometric coefficient of variation

For PK parameters, the following descriptive statistics will additionally be calculated:

CV	arithmetic coefficient of variation
gMean	geometric mean
gCV	geometric coefficient of variation
P10	10th percentile
Q1	1st quartile
Q3	3rd quartile
P90	90th percentile

The data format for descriptive statistics of concentrations will be identical to the data format of the respective concentrations. The descriptive statistics of PK parameters will be calculated using the individual values with the number of decimal places as provided by the evaluation program. Then the individual values as well as the descriptive statistics will be reported with three significant digits in the CTR.

Tabulations of frequencies for categorical data will include all possible categories and will display the number of observations in a category, as well as the percentage (%) for each treatment sequence/group. Percentages will be rounded to one decimal place and will be based on all subjects in the respective subject set whether they have non-missing values or not. The category 'missing' will be displayed only if there are actually missing values.

Units of variables should be given in the titles or column/row descriptors in square brackets (e.g. [mg]).

Exclusion of PK parameters

The ADS ADPP (PK parameters) contains column variables indicating inclusion/exclusion (APEXC) of a PK parameter and an analysis flag comment (APEXCO). All analyses based on the PKS will include parameters if they are not flagged for exclusion, that is APEXCO is equal to "Included".

Exclusion of PK concentrations

The ADS ADPC (PK concentrations per time-point or per time-interval) contains column variables ACEXC and ACEXCO indicating inclusion/exclusion (ACEXC) of a concentration and an analysis flag comment (ACEXCO). Exclusion of a concentration depends on the analysis flag comment ACEXCO. For example, if ACEXCO is set to 'ALL CALC', the value will be excluded for all types of analyses based on concentrations. If ACEXCO is set to 'DESC STATS' the value will be excluded from descriptive evaluations per planned time point/time interval. If ACEXCO contains the addition 'TIME VIOLATION' or 'TIME DEVIATION' the value can be used for further analyses based on actual times. If ACEXCO is set to 'HALF LIFE', the value will be excluded from half-life calculation (and, as a consequence, any calculation that relies on λ_z) only; the value is included for all other analyses.

Further details are given in 001-MCS-36-472_RD-01 "Noncompartmental Pharmacokinetic / Pharmacodynamic Analyses of Clinical Studies" ([5](#)) and 001-MCS-36-472_RD-03 "Description of Analytical Transfer Files and PK/PD Data Files" ([11](#)).

7.1 DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

Only descriptive statistics are planned for this section of the report, based on the TS.

The data will be summarised by treatment sequence and in total.

7.2 CONCOMITANT DISEASES AND MEDICATION

Frequency tables are planned for this section of the report, based on the TS.

Concomitant diseases will be coded using the coding system of the Medical Dictionary for Drug Regulatory Activities (MedDRA). Medications will be coded using the World Health Organization Drug Dictionary (WHO-DD). The coding version number will be displayed as a footnote in the respective output.

The diagnoses and medications will be listed. Subjects without any concomitant diagnoses or concomitant therapies should be marked with a “No” in the respective column.

The relevance of the concomitant therapies to the evaluation of PK will be decided no later than at the RPM/DBLM.

7.3 TREATMENT COMPLIANCE

Section 4.3 of the CTP: *Compliance will be assured by administration of all trial medication in the study centre under supervision of the investigating physician or a designee. The measured plasma concentrations of trial medication will provide additional confirmation of compliance.*

It is not intended to list the compliance separately. Any deviations from complete intake will be addressed in the RPM/DBLM (cf. TSAP [Section 6.2](#)) and described in the CTR.

7.4 PRIMARY ENDPOINTS

Relative bioavailability is to be determined on the basis of the primary pharmacokinetic endpoints (see [Section 5.1](#)).

7.4.1 Primary analysis of the primary endpoints

Section 7.3.1 of the CTP: *The statistical model used for the analysis of the primary (AUC_{0-tz} and C_{max}) and secondary ($AUC_{0-\infty}$) endpoints will be an analysis of variance (ANOVA) model on the logarithmic scale. This model will include effects accounting for sources of variation: ‘sequence’, ‘subjects within sequences’, ‘period’ and ‘treatment’. The effect ‘subjects within sequences’ will be considered as random, whereas the other effects will be considered as fixed. For tests on subject, period, and treatment effects, the denominator sum of squares will be the sum of squares for error; while for tests on sequence effects, the denominator will be the sum of squares for subjects. The model is described by the following equation:*

$y_{ijkm} = \mu + \zeta_i + s_{im} + \pi_j + \tau_k + e_{ijkm}$, where

y_{ijkm} = logarithm of response (AUC_{0-tz} , C_{max} and $AUC_{0-\infty}$) measured on subject m in sequence i receiving treatment k in period j ,

μ = the overall mean,

ζ_i = the i^{th} sequence effect, $i = 1, 2$

s_{im} = the effect associated with the m^{th} subject in the i^{th} sequence,
 $m = 1, 2, \dots, n_i$

π_j = the j^{th} period effect, $j = 1, 2$

τ_k = the k^{th} treatment effect, $k = 1, 2$

e_{ijkm} = the random error associated with the m^{th} subject in sequence i who received treatment k in period j .

[...]

The pharmacokinetic parameters (AUC_{0-tz} and C_{max} and $AUC_{0-\infty}$) will then be log transformed (natural logarithm) prior to fitting the ANOVA model. The difference between the expected means for test treatments and reference treatment $\log(T)-\log(R)$, will be estimated by the difference in the corresponding Least Square Means (point estimate) and two-sided 90% confidence intervals based on the t -distribution will be computed. These quantities will then be back transformed to the original scale to give the point estimator (geometric mean) and interval estimates for the ratio between response under test/fed condition and response under reference/faasted condition.

The implementation for this analysis will be accomplished by using the XPKISTAT macro, based on PKS, and option BWC (Bioavailability/Bioequivalence, within-subject design, time-controlled).

Note, that the computed CIs must be interpreted in the context exploratory character, i.e. confidence intervals are considered as interval estimates for effects.

Since the main focus is on estimation and not testing, an acceptance range was not specified, that is, no hypothesis will be tested.

7.5 SECONDARY ENDPOINTS

7.5.1 Key secondary endpoints

This section is not applicable as no key secondary endpoint has been specified in the protocol.

7.5.2 Secondary endpoints

The secondary PK parameter $AUC_{0-\infty}$ (AUCINF_pred) will be assessed using the same methods as described for the primary endpoints.

7.7 EXTENT OF EXPOSURE

Descriptive statistics are planned for this section of the report based on the TS. The date and time of drug administration will be listed for each subject.

7.8 SAFETY ANALYSIS

All safety analyses will be performed on the TS.

The safety data for treated subjects who failed to complete the study (dropouts or withdrawals) will be reported as far as their data are available. All withdrawals will be documented and the reason for withdrawal recorded.

7.8.1 Adverse Events

AEs will be coded with the most recent version of MedDRA.

The analyses of AEs will be descriptive in nature and will be based on BI standards as presented in the corporate guideline: “Analysis and Presentation of Adverse Event Data from Clinical Trials” [001-MCG-156] ([8](#)).

The standard AE analyses will be based on the number of subjects with AEs (and not on the number of AEs).

For analysis, multiple AE occurrence data on the case report form (CRF) will be collapsed into one AE provided that all of the following applies:

- All AE attributes are identical (lower level term (LLT), intensity, action taken, therapy required, seriousness, reason for seriousness, relationship, outcome, AE of special interest)
- The occurrences were time-overlapping or time-adjacent (time-adjacency of two occurrences is given if the second occurrence started within one hour after end of the first occurrence).

For further details on summarization of AE data, please refer to [001-MCG-156] ([8](#)).

Section 5.2.6.1.4 of the CTP: The following are considered as AESIs:

- Hepatic injury
A hepatic injury is defined by the following alterations of hepatic laboratory parameters:
 - *An elevation of AST (aspartate transaminase) and/or ALT (alanine transaminase) ≥ 3 -fold ULN combined with an elevation of total bilirubin ≥ 2 -fold ULN measured in the same blood sample, or*
 - *Aminotransferase (ALT, and/or AST) elevations ≥ 10 fold ULN*

These lab findings constitute a hepatic injury alert and the subjects showing these lab abnormalities need to be followed up according to the 'DILI checklist' provided in the ISF. In case of clinical symptoms of hepatic injury (icterus, unexplained

encephalopathy, unexplained coagulopathy, right upper quadrant abdominal pain, etc.) without lab results (ALT, AST, total bilirubin) available, the Investigator should make sure that these parameters are analysed, if necessary in an unscheduled blood test. Should the results meet the criteria of hepatic injury alert, the procedures described in the DILI checklist should be followed.

The analysis of adverse events will be based on the concept of treatment emergent adverse events.

Section 1.2.1 of the CTP: The Residual Effect Period (REP, i.e., the period after the last dose with measurable drug levels and/or pharmacodynamic effects still likely to be present) of BI 894416 has not been defined yet. [...]

Therefore, all AEs reported until the end of trial examination (last per protocol contact) will be considered as on treatment.

Section 7.3.4 of the CTP: Note that AEs occurring after the last per protocol contact but entered before final database lock will be reported to Pharmacovigilance only and will not be captured in the trial database.

For more detail see the TSAP ADS plan.

According to ICH E3 (9), AEs classified as 'other significant' need to be reported and will include those non-serious and non-significant adverse events with
(i) 'action taken = discontinuation' or 'action taken = reduced', or
(ii) marked haematological and other lab abnormalities or lead to significant concomitant therapy as identified by the Clinical Monitor/Investigator at the Report Planning Meeting.

An overall summary of AEs (including AESIs) will be presented.

The frequency of subjects with AEs will be summarised by treatment, primary system organ class (SOC) and preferred term (PT). Separate tables will be provided for subjects with other significant AEs according to ICH E3 (9), for subjects with serious AEs, for subjects with drug-related AEs, for subjects with drug related serious adverse events and for subjects with AESIs.

The SOCs and PTs will be sorted by frequency (within SOC). The MedDRA version number will be displayed as a footnote in the respective output.

In addition, frequencies of subjects with non-serious AEs that had an incidence of > 5% for at least one treatment will be summarised by treatment, primary SOC and PT.

For disclosure of adverse events on EudraCT, additional information not included in a standard AE analysis will be performed. The following three entries will be created:

- Adverse Events per arm for disclosure on EudraCT
- Non-serious Adverse Events for disclosure on EudraCT
- Serious Adverse Events for disclosure on EudraCT

7.8.2 Laboratory data

The analyses of laboratory data will be descriptive in nature and will be based on BI standards [001-MCG-157] ([10](#)).

Laboratory data will be analysed qualitatively via comparison of laboratory data to their reference ranges. Values outside the reference range as well as values defined as possibly clinically significant will be flagged in the data listings.

It is the investigator's responsibility to decide whether a lab value is clinically significantly abnormal or not (at the RPM/DBLM at the latest).

Descriptive statistics of laboratory data will be calculated by planned time point based on the worst value of the subject at that planned time point (or assigned to that planned time point).

7.8.3 Vital signs

Descriptive statistics over time including change from baseline will be performed for vital signs (blood pressure and pulse rate). In the listing the difference from baseline will also be displayed.

For vital signs, descriptive statistics will be calculated by planned time point based on the last value of the subject at that planned time point (or assigned to that planned time point).

Clinically relevant findings in vital signs will be reported as AEs.

7.8.4 ECG

ECG recordings will be checked by the investigator for pathological results. Clinically relevant abnormal findings for ECG will be listed under 'Relevant Medical History / Baseline Conditions' (when they occurred during screening) or will be reported as AEs (when they occurred during treatment).

7.8.5 Others

This section is not applicable as no other variables have been specified in the protocol.

8. REFERENCES

1.	<i>CPMP/ICH/363/96</i> : "Statistical Principles for Clinical Trials", ICH Guideline Topic E9, Note For Guidance on Statistical Principles for Clinical Trials, current version.
2.	<i>001-MCS-40-413</i> : "Identify and Manage Important Protocol Deviations (iPD) ", current version, IDEA for CON.
3.	<i>BI-KMED-COPS-TMP-0001</i> : "iPD log", current version; IDEA for GEN.
4.	<i>001-MCG-156_RD-01</i> : "Handling of Missing and Incomplete AE Dates", current version; IDEA for CON.
5.	<i>001-MCS-36-472_RD-01</i> : "Noncompartmental Pharmacokinetic/Pharmacodynamic Analyses of Clinical Studies", current version; IDEA for CON.
6.	<i>001-MCG-159</i> : "Reporting of Clinical Trials and Project Summaries", current version; IDEA for CON.
7.	<i>001-MCS-36-472</i> : "Standards and processes for analyses performed within Clinical Pharmacokinetics/Pharmacodynamics", current version; IDEA for CON.
8.	<i>001-MCG-156</i> : "Analysis and Presentation of Adverse Event Data from Clinical Trials", current version; IDEA for CON.
9.	<i>CPMP/ICH/137/95</i> : "Structure and Content of Clinical Study Reports", ICH Guideline Topic E3; Note For Guidance on Structure and Content of Clinical Study Reports, current version.
10.	<i>001-MCG-157</i> : "Handling, Display and Analysis of Laboratory Data", current version; IDEA for CON.
11.	<i>001-MCS-36-472_RD-03</i> : "Description of Analytical Transfer Files and PK/PD Data Files", current version; IDEA for CON.

10. HISTORY TABLE

Table 10: 1 History table

Version	Date (DD-MMM-YY)	Author	Sections changed	Brief description of change
Final	03-JUN-2019		None	This is the final TSAP without any modification