Trial Statistical Analysis Plan

c08764221-02

BI Trial No.:	1270.15
Title:	A phase Ib, Open label, Single Arm, Multi-center, Dose Escalation Trial of Intravenous BI 836826 in Combination with ibrutinib in Patients with Relapsed/Refractory Chronic Lymphocytic Leukemia Including protocol amendment 1 (c03032933-02)
Investigational Product(s):	BI 836826
Responsible trial statistician(s):	Phone: Fax:
Date of statistical analysis plan:	30 JUL 2018 SIGNED
Version:	FINAL

1. TABLE OF CONTENTS

LIST OF TABLES

2. LIST OF ABBREVIATIONS

Term	Definition / description
ADS	Analysis Dataset
AE	Adverse Event
AESI	Adverse Event of Special Interest
ALKP	Alkaline Phosphatase
ALT	Alanine Amino Transferase
AST	Aspartate Amino Transferase
ATC	Anatomic Therapeutic Classification
BI	Boehringer Ingelheim
BLRM	Bayesian Logistic Regression Model
BMI	Body Mass Index
BSA	Body Surface Area
CLL	Chronic Lymphocytic Leukemia
CTCAE	Common Terminology Criteria for Adverse Events
CTh	Concomitant Therapies
CTP	Clinical Trial Protocol
CTR	Clinical Trial Report
DILI	Drug-Induced Liver Injury
DLT	Dose Limiting Toxicity
ECOG	Eastern Cooperative Oncology Group
eCRF	Electronic Case Report Form
EOT	End Of Treatment
EWOC	Escalation With Overdose Control
ICH	International Conference on Harmonisation
IPV	Important Protocol Violation
IRR	Infusion Related Reaction

Term	Definition / description
LDH	Lactate Dehydrogenase
MedDRA	Medical Dictionary for Regulatory Activities
MTD	Maximum Tolerated Dose
PT	Preferred Term
REP	Residual Effect Period
RIS	Run-in Set
RNA	Ribonucleic Acid
RP2D	Recommended Phase 2 Dose
SAE	Serious Adverse Event
SCR	Screened Set
SOC	System Organ Class
SRC	Safety Review Committee
StD	Standard deviation
TLS	Tumour Lysis Syndrome
TS	Treated Set
TSAP	Trial Statistical Analysis Plan
UDAEC	User-Defined Adverse Event Category
ULN	Upper Limit of Normal
WHO-DD	World Health Organisation Drug Dictionary

3. INTRODUCTION

As per International Conference on Harmonisation E9 (ICH E9) 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), including Protocol Amendments. 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 and definition of measurements and variables.

The study was initially planned to be a single arm, open label trial consisting of two parts: a Phase Ib dose escalation part and a Phase II part investigating one expansion cohort. Approximately 60 chronic lymphocytic leukaemia (CLL) patients who qualify for treatment with ibrutinib were to be treated with a combination of BI 836826 and ibrutinib in this trial. Approximately 20 patients were intended to be enrolled in Phase Ib and 40 patients were intended to be enrolled in the Phase II part of this study.

Dose-escalation of BI 836826 is guided by a Bayesian Logistic Regression Model (BLRM) with overdose control. The BLRM estimates the maximum tolerated dose (MTD) by updating estimates of the probability of observing a dose limiting toxicity (DLT) in the MTD evaluation period for each dose level in the study as patient information becomes available. At any time in the trial, it is not permitted to escalate to a dose which does not fulfil the escalation with overdose control (EWOC) criterion. Dose-increments are ≤100% of the previous dose level tested in the previous cohort.

Due to the strategical decision to stop the project, the Phase II part of the trial will not be conducted. Therefore, this TSAP only describes the analysis of the Phase Ib part of the trial, based on CTP amendment 1 which reflects this change in the study set-up. The decision was made that an abbreviated clinical trial report (CTR) will be written for this trial instead of a full CTR. Therefore, only analyses mandatory to be reported and additional analyses deemed necessary by the trial are described in this TSAP and will be included in the abbreviated CTR.

In the following, study medication always refers to either BI 836826 or ibrutinib.

SAS® Version 9.4 or higher will be used for all analyses.

4. CHANGES IN THE PLANNED ANALYSIS OF THE STUDY

Clarifications:

Changes:

5. ENDPOINTS

5.1 PRIMARY ENDPOINTS

The primary endpoints of the trial are:

- Recommended Phase II dose (RP2D) of BI 836826 in combination with ibrutinib. If a MTD can be determined based on the criteria as described in Section 7 of the CTP, the RP2D will be either the MTD or a lower dose. The RP2D will be determined by the safety review committee (SRC) based on safety and efficacy considerations.

- Number of patients with DLTs during the MTD evaluation period (starting at the day of first administration of BI 836826, lasting until 14 days after the Day 15 administration of BI 836826 in the first cycle)

For definition of DLT, refer to CTP Section 5.3.6.2.

5.2 SECONDARY ENDPOINTS

5.2.1 Key secondary endpoints

Not applicable.

5.2.2 Other secondary endpoints

The secondary endpoint is the MTD. The MTD may be considered reached if the posterior probability that the true DLT rate is in the target interval [0.16, 0.33) is larger than 0.5 or if at least 15 patients have been treated in the Phase Ib part, of which at least 6 at the MTD. Patients who have been replaced are not considered evaluable for MTD determination. Only DLTs occurring in the MTD evaluation period will be considered for the determination of the MTD

6. GENERAL ANALYSIS DEFINITIONS

6.1 TREATMENTS

In this trial, treatments are not randomized (open-label, dose-escalation). Different dose levels of BI 836826 in combination with ibrutinib are being administered. All planned analyses will be presented by initial treatment group, i.e. for all dose cohorts separately and in total over all dose cohorts.

To justify the RP2D / MTD determination, DLTs occurring during the MTD evaluation period will be presented separately from those occurring during the whole on-treatment period. Patients where treatment group assignment has not been followed will be handled on a case-by-case basis and will be agreed upon latest at the report planning meeting before database lock.

For safety summaries events that start from first administration of BI 836826 and last until 30 days (residual effect period (REP)) after the last administration of BI 836826 will be considered as having occurred "on treatment". If not specified otherwise, all safety tables will be based on the on-treatment period. AEs that have an onset date during the screening, run-in, or post-study period will be displayed in separate listings from those occurred during the on-treatment period (refer to Section 7.8.1.2 for details).

Labels of each analysis treatment period, analysis numbers, the labels used for displays in the tables and listings in the CTR, as well as codes, decodes, sort order and labels for each trial medication are provided in the TSAP technical document analysis dataset (ADS) plan.

6.2 IMPORTANT PROTOCOL VIOLATIONS

No per protocol set analysis will be performed for this study, hence no patient will be excluded from the analyses. However, patients with important protocol violations (IPVs) will be documented. The following table defines the different categories of IPVs.

Table 6.2 : 1 Important protocol violations

Category / Code		Description	Example/Comment	Excluded from
A		**Entrance criteria not met**		
	A1[a]	Patient has condition that may cause additional risk from study medication	Check Inclusion/Exclusion criteria: In6, In8 Ex4, Ex9, Ex10, Ex11, Ex12, Ex13, Ex16, Ex17, Ex18, Ex19	None
	A2[a]	Patient has laboratory assessments that may cause additional risk	Check whether baseline laboratory data comply with thresholds as defined by In7 and check that In7 = "Yes"	None
	A3[a]	Patient is unable to comply with the protocol	Check Ex20	None
	A4[a+m]	Patient does not have trial diagnosis or is not part of the target population	Check Inclusion/Exclusion criteria: In1, In2, In3, In4, In9, In10 Ex1, Ex3, Ex5, Ex6, Ex7	None
B		**Informed consent**		

Table 6.2 : 1 Important protocol violations (cont.)

	B1[a]	Informed consent not given or too late	Check In12 Check date of IC against date of Screening visit	All
C		**Trial medication and randomisation**		
	C1[a+m]	Drug not administered according to protocol	Infusion schedule followed = "No" and medical review of associated comments	None
	C2[a]	Drug administration not according to schedule	Ibrutinib not administered continuously from start of Run-in period Cycle 1: pre-dose of 10 mg of BI836826 not administered on Day 1 and 50% of target dose on Day2 and Day 8 and 100% of target dose on Day 15. Cycles 2-4: 100% of target dose of BI836826 not administered on days 1 and 15 of each cycle Cycles 5-24: 100% of target dose of BI836826 not administered on day 1 of each cycle	None
	C3[a]	Incorrect treatment taken	Study drugs dispensing error leading to change in actual treatment	None
D		**Concomitant medication**		
	D1[a+m]	Prohibited medication	• anti-neoplastic therapy • long-term use (>7 days)of strong CYP3A inhibitor (check also Ex15) • Oral anti-coagulants (check also Ex14) ongoing systemic immunosuppressive therapy other than corticosteroids (check also Ex8)	None
	D2[a+m]	Pre-medication not administered according to protocol	Did the subject receive standard pre-medication = "No" to any standard pre-medication and medical review of associated comments – only until cycle 6, afterwards pre-medication according to investigator judgement	None

a = automated IPV; m = manual IPV; In = Inclusion criterion; Ex = Exclusion criterion

6.3 PATIENT SETS ANALYSED

The Screened Set (SCR) includes all patients who signed the informed consent form and will be used to summarize patient disposition.

The Run-In Set (RIS) includes all patients who received at least one dose of ibrutinib. The RIS will be used for the analysis of exposure to ibrutinib.

The Treated Set (TS): consists of all patients who received at least one administration of BI 836826. The TS will be used for all planned safety and efficacy analyses.

The MTD evaluation set: This patient set includes all patients who were documented to have received at least one dose of BI 836826 and were not replaced for the MTD evaluation. The MTD evaluation set will be used for the primary analyses of DLTs and MTD determination.

Rules for replacement of patients are defined in Section 3.3.4.1 of the CTP. The list of replaced patients will be provided by the Trial Clinical Monitor (TCM) no later than the last blinded report planning meeting (BRPM) and will be stored in the TMF.

6.5 POOLING OF CENTRES

This section is not applicable since there will not be any inferential statistical analysis. Thus, no statistical model in which centre or country is included as factor is applied.

6.6 HANDLING OF MISSING DATA AND OUTLIERS

Missing or incomplete AE dates are imputed according to BI standards (3).

In general, missing data not discussed in (3) will not be imputed unless required for the following analyses and definitions. Then the rules as described below apply.

1) **Change of laboratory values from baseline**

   Laboratory values at baseline: For missing laboratory data at visit 1 (before the first administration of BI 836826) the data of preceding visits will be used.

2) **Definition of on-treatment period and actual treatment**

   Date of permanent discontinuation of last study medication: All reasonable efforts should be undertaken during the study to obtain the dates of permanent discontinuation of last study medication. However, if the date of the very last administration is missing this will be imputed with:

   - If only month and year are given, the last day of the month will be used for imputation
   - If only the year is given, the 31st of December of this year will be used for imputation

   If the imputed date leads to a date that is later than the date of the end of treatment (EOT) visit, then the imputed date is the date of the EOT visit. If the imputed date leads to a date that is later than the death date, then the imputed date is the date of death.

6.7 BASELINE, TIME WINDOWS AND CALCULATED VISITS

Study days and visits will be labelled according to the flow chart of the CTP.

Unless otherwise specified, baseline is defined as the time-point closest to but prior to first administration of BI 836826. If no time is specified and the date is the same as the first administration date, then it will still be considered baseline if not specified otherwise.

Laboratory values: Baseline is defined as the latest time-point before the very first administration of BI 836826. For laboratories where not only the examination date but also time are recorded, examination time has to be taken into account when defining baseline. That is, a laboratory value on the same date as the first administration of BI 836826 is considered as baseline value if and only if the time of laboratory value is before or the same as the time of BI 836826 administration.

7. PLANNED ANALYSIS

For End-Of-Text tables, the set of summary statistics is: N / Mean / standard deviation (StD) / Min / Median / Max. For tables that are provided for endpoints with some extreme data, median, quartiles and percentiles should be preferred to mean, StD, min, and max. Efficacy data are presented by dose cohort. Displays of safety data will be presented by dose cohort and in total.

For time-to-event analysis tables, the set of statistics is: number of patients [N(%)], Number of patients with event [N(%)], <Time to event> [months] followed by P25 (25^{th} percentile), median, P75 (75^{th} percentile), Number of patients censored [N(%)]. If not specified otherwise, the duration as well as the time to event will be displayed in days.

If not otherwise specified, the abbreviation Pxx should be used for displaying the xx^{th} percentile.

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 (%) relative to the respective treatment group (unless otherwise specified, all patients in the respective patient set whether they have non-missing values or not). Percentages will be rounded to one decimal place. The category missing will be displayed only if there are actually missing values. The denominator of the main categories is defined by the number of patients in the used patient set. The main categories define the denominators of the subcategories. Subcategories should be intended and "[N(%)]" will be displayed only for the main category. If a table includes only categorical data, "[N(%)]" is to be displayed in the column header.

Abbreviations (e.g. Wors.) should not be displayed without any explanations. They will be either spelled out in the table or explained in footnotes (whatever is more reasonable from the programming point of view).

If applicable, conversion from days to weeks, months and years will be as follows:

- Weeks = Days/7
- Months = (Days ×12)/365.25
- Years = Days/365.25

7.1 DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

Descriptive statistics are planned for this section.

7.1.1 Disposition of patients

For patient disposition the standard descriptive table will be populated. Additionally, patients with discontinuations by initial treatment and the reasons will be listed. An overview table with respect to analysis sets (as defined in Section 6.3) will be provided.

7.1.2 Important protocol violations

The number of patients with important protocol violations will be displayed.

7.1.3 Demographic and other baseline characteristics

Standard descriptive analysis and summary tables for all patients treated by initial treatment will be created for demography, oncology history, virology, physical examination (including constitutional symptoms), eastern cooperative oncology group (ECOG) performance score, tumour size, previous therapies and previous stem cell transplantations.

7.2 CONCOMITANT DISEASES AND MEDICATION

Descriptive statistics are planned for this section of the report.

Concomitant diseases will be coded similarly as adverse events based on the most current MedDRA version. Concomitant therapies (CTh) will be coded according to the World Health Organisation Drug Dictionary (WHO DD). They will be classified according to the Anatomical, Therapeutic, Chemical (ATC) classification system. The third ATC level will be used to categorise CThs by therapy type. In situations where a medical product may be used for more than one equally important indication, there are often several classification alternatives. As appropriate, patients receiving CThs with more than one possible ATC level-three category will be counted more than once; footnotes will clarify this possible double counting in tables.

Summaries will be presented for previous and concomitant medications started at baseline and for concomitant therapies started after first administration of BI 836826. Transfusions will be displayed separately.

7.3 TREATMENT COMPLIANCE

Compliance will be evaluated by whether or not the medication was always administered according to protocol for BI 836826.

For patients where the infusion schedule was not followed a listing with comments will be presented.

Furthermore, a listing will show all administrations of BI 836826 including also the administration of premedication Analgesic/Antipyretic, Glucocorticoid and Antihistamine as well as the dose changes and interruptions of ibrutinib.

7.4 PRIMARY ENDPOINTS

The primary endpoints are the RP2D and the number of patients with DLTs in the MTD evaluation period. The number of patients with DLTs at each dose level will be presented for the MTD evaluation period for the MTD evaluation set and for the whole on-treatment period for the treated set separately.

The RP2D will either be the MTD or any lower dose, examined based on safety and efficacy criteria. The analysis of the MTD is based on a BLRM guided by the EWOC principle. Estimation of the MTD during the dose escalation phase of the study will be based upon the estimation of the posterior probability of the incidence of DLT in toxicity categories during the MTD evaluation period for all evaluable patients. The model to be used is specified in CTP Section 7.

The posterior probabilities that the toxicity rates of each dose level fall into the categories specified in CTP Section 7 estimated from the BLRM will be displayed graphically as well as in a table. This will be done for the MTD evaluation period as well as for the complete on-treatment period.

7.5 SECONDARY ENDPOINTS

7.5.1 Key secondary endpoints

Not applicable.

7.5.2 Other Secondary endpoints

The secondary endpoint is the MTD. This will analysed analogously to the primary endpoint RP2D. Only patients evaluable for MTD determination will be used for the analysis of the MTD, i.e. patients, if any, who were replaced during the MTD evaluation period will be excluded from the analysis of the MTD.

7.7 EXTENT OF EXPOSURE

Standard descriptive analyses over all treatment courses will be performed. This will include a summary of the variables already described in Section 5.4.2. This descriptive analysis will comprise a mixture of frequencies and percentages, as well as summary statistics.

7.8 SAFETY ANALYSIS

If not specified otherwise, all safety analyses will be performed on the treated set.

7.8.1 Adverse events

7.8.1.1 Maximum tolerated dose / RP2D and dose limiting toxicity

A summary of the number of patients with DLTs within the MTD evaluation period will be displayed for the MTD evaluation set. This table will also be created for all treatment courses of the on-treatment period by initial treatment for the treated set.

Patients who were replaced within the MTD evaluation period will be excluded from the determination of the MTD but will be considered for all other safety evaluations. A listing of replaced patients will be provided.

Refer to Section 7.4 for more details on the analysis of the MTD and the RP2D.

7.8.1.2 Adverse events

Unless otherwise specified, adverse events analyses will be performed for the on-treatment period. Selected analyses will be repeated for the MTD evaluation period and for the run-in period.

The analyses of AEs will be descriptive in nature and will follow the standard procedure laid down in (4). All analyses of AEs will be based on the number of patients with AEs and NOT on the number of AEs.

AEs will be coded with the most recent version of MedDRA. The version number will be displayed as a footnote in the respective tables and listings. The severity of AEs will be scaled according to CTCAE version 4.0.

The system organ classes (SOCs) will be sorted alphabetically. In tables displaying AEs by dose cohort, preferred terms (PTs) will be sorted by descending frequency of adverse events in the "Total" BI 836826 group.

Each patient can be observed during the trial under several doses. Analysing the AEs of all treatment courses will be carried out under the initial treatment. No formal statistical analysis is planned for the safety comparison.

The analysis of AEs will be based on the concept of treatment emergent AEs. That means that all AEs occurring from the first administration of BI 836826 until 30 days after last administration of BI 836826 will be assigned to the on-treatment period. All AEs occurring before first administration of any trial medication will be assigned to "Screening", all AEs occurring after the first administration of ibrutinib and before the first administration of BI 836826 will be assigned to "Run-in" and all AEs occurring after last administration of BI 836826 + 30 days will be assigned to "Post-study" (for listings only). The actual planned dosage of BI 836826 and ibrutinib administered on the day each AE starts will also be derived and will be included in the listing. Listings of screening events will not be sorted by initial treatment. Post-study listings will be sorted by initial treatment. For details on the treatment definition please refer to Section 6.1.

According to the BI standards, multiple recordings of AEs will be collapsed to episodes on the lowest level term and multiple episodes will be condensed to records on the PT and SOC level. CTCAE grade will be an additional criterion for collapsing and condensing AEs. The maximum CTCAE grade will be assigned to episodes and records. CTCAE grade and DLT information will be displayed in AE listings. MedDRA levels for condensing will be SOC and PT.

An overall summary of adverse events will be presented.

Reporting of CTCAE grades:

CTCAE grading within AE tables in Section 15 of the CTR is displayed as "all Grades", "missing Grade", "Grade 1", "Grade 2", "Grade 3", "Grade 4" and "Grade 5", but the "missing grade" column should only be displayed in case AEs with a missing CTCAE grade occurred. A separate table will show AEs leading to death. In this table no CTCAE grades will be shown.

Frequencies of patients with AEs will be summarised by treatment, highest CTCAE grade, primary SOC and PT. Tables will be provided for patients with drug-related AEs, with serious AEs (SAEs), with drug-related SAEs, with AEs leading to discontinuation of last study medication (i.e. leading to discontinuation of the last administered study medication), with AEs leading to discontinuation of BI 836826, with AEs leading to discontinuation of ibrutinib, with AEs leading to dose reduction of BI 836826, with AEs leading to dose reduction of inbrutinib, with protocol-specified AEs of special interest (AESI), and with AEs leading to death.

7.8.2 Laboratory data

The analyses of laboratory data will be descriptive in nature and will follow the standard procedure laid down in (2). Patients will be counted under the initial treatment. The analysis of laboratory data will use the same 'analysing treatments' as described for the AEs, except for that the baseline laboratory value (as defined in Section 6.7) will be included in the 'on treatment' period. Patients having at least one post-baseline laboratory value will be displayed in the descriptive analyses. Patients with missing CTCAE grade at baseline or no baseline value but with post-baseline laboratory values will be displayed in the category "Missing CTCAE grade at baseline".

Single time courses by initial treatment will be used to display normalized laboratory values over time by dose cohort. The graphs may be truncated if sufficient data is not available. These graphs will be displayed in Section 16.1.13.1 of the CTR for the following parameters, using the BI normalised values for haematology and differentials, and the multiples of the ULN for enzymes.

Haematology: haemoglobin, white blood cell count

Differentials: absolute lymphocyte count

Enzymes: LDH

Descriptive statistics, including change from baseline, frequency of patients with transitions relative to the references range, will be provided. No post-study laboratory values will be considered. CTCAE grade for applicable laboratory parameters will be calculated according to CTCAE v4.0. The following outputs will be presented:

- Worst CTCAE grade experienced during the on-treatment period
- Transitions of the CTCAE grade from baseline to the worst lab values, from baseline to the last lab values, and from the worst to last values during the on-treatment period
- Possible clinically significant laboratory values

Note: For calculating the change in CTCAE grade from baseline, patients with a CTCAE grade of -9 (no CTCAE grade defined) will be treated as a CTCAE grade 0 for all analyses. In laboratory listings, the CTCAE grade is displayed as -9.

For Uric Acid and Hypokalemia, the CTCAE grade cannot always be assigned by the laboratory parameter itself as two different CTCAE grades have the same laboratory constellation, but are distinguished by additional clinical parameter. In this case a CTCAE grade of -1 will be assigned initially. Patients with a CTCAE grade of -1 will be treated as

- Grade 1 for Uric Acid
- Grade 1 for Hypokalemia

for all analyses. In laboratory listings, the CTCAE grade will be displayed as -1.

The prioritized laboratory values (see Section 5.4.5) will be displayed in Section 15 of the final CTR while all other laboratory parameters will be displayed in the Appendix of the CTR.

Patients with hepatic enzyme elevation will be tabulated (drug-induced liver injury (DILI) supporting table). In addition, a separate listing will be presented giving patients with missing parameter in the given time frame.

For potential Hy's law cases, possible clinically significant abnormal laboratory values and cases of TLS frequency tables will be provided.

7.8.3 Vital signs

A summary table and a listing of vital signs at each planned time will be provided for the treated set.

7.8.4 ECG

No separate analyses are planned. Newly emergent abnormalities will be recorded and analysed as AEs.

7.8.5 Others

Not applicable

8. REFERENCES

1	*001-MCS-36-472_RD-01*: "Noncompartmental Pharmacokinetic / Pharmacodynamic Analyses of Clinical Studies", current version; IDEA for CON.
2	*001-MCG-157*: "Handling, Display and Analysis of Laboratory Data", current version; IDEA for CON.
3	*001-MCG-156_RD-01:* "Handling of missing and incomplete AE dates", current version; IDEA for CON.
4	*001-MCG-156*: "Handling and summarization of adverse event data for clinical trial reports and integrated summaries", current version; IDEA for CON.
R10-4429	Hallek M., Cheson BD, Catovsky D, Caligaris-Cappio F, Dighiero G, Doehner H, Hillmen P, Keating MJ, Montserrat E, Rai KR, Kipps TJ. Guidelines for the diagnosis and treatment of chronic lymphocytic leukemia: a report from the International Workshop on Chronic Lymphocytic Leukemia updating the National Cancer Institute-Working Group 1996 guidelines. Blood 111 (12), 5446 - 5456 (2008)
R10-4848	Common terminology criteria for adverse events (CTCAE): version 4.0 (NIH publication no.09-5410, published: May 28, 2009 (v4.03: June 14, 2010), revised June 2010, reprinted June 2010). htts://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03_2010-06-14_QuickReference_8.5x11.pdf2010

10. HISTORY TABLE

Table 10: 1 History table

Version	Date (DD-MMM-YY)	Author	Sections changed	Brief description of change
Initial version	**19-JUL-16**		None	This is the initial version of the TSAP with necessary information for the trial conduct
Final	**30-JUL-18**		1-9	This is the final TSAP