Trial Statistical Analysis Plan

c12588444-01

BI Trial No.:	1199.238
Title:	A Phase I trial to investigate the effect of nintedanib on the pharmacokinetics of a combination of ethinylestradiol and levonorgestrel in patients with non-small cell lung cancer Including revised protocol (based on global amendment 2) [c03853814-03]
Investigational Product(s):	Vargatef®, nintedanib
Responsible trial statistician(s):	Phone: Fax: Phone: Fax:
Date of statistical analysis plan:	29 JAN 2018 SIGNED
Version:	"Final"

1. TABLE OF CONTENTS

LIST OF TABLES

2. LIST OF ABBREVIATIONS

Term	Definition / description
AE	Adverse event
AESI	Adverse events of special interest
ADS	Analysis data set
BI	Boehringer Ingelheim
BLQ	Below the lower limit of quantification
BMI	Body mass index
CARE	Clinical data analysis and reporting environment
CRF	Case Report Form
CTP	Clinical Trial Protocol
CTR	Clinical Trial Report
CV	arithmetic coefficient of variation
DBLM	Database lock meeting
ECG	Electrocardiogram
eCRF	Electronic case report form
EE	Ethinylestradiol
ES	Entered set
EudraCT	European union drug regulating authorities clinical trials
gMean	Geometric mean
gCV	Geometric coefficient of variation
ICH	International Conference on Harmonisation
LE	Levonorgestrel
MedDRA	Medical Dictionary for Regulatory Activities
NOA	Not analysed
NOR	No valid result
NOS	No sample available
PK	Pharmacokinetics
PKS	Pharmacokinetic analysis set
PV	Protocol violation
R	Reference treatment
RAGe	Report appendix generator system
REP	Residual effect period

Term	Definition / description
RPM	Report planning meeting
SAE	Serious adverse event
SD	Standard deviation
T	Test treatment
TS	Treated set
TSAP	Trial statistical analysis plan

3. INTRODUCTION

As per International Conference on Harmonisation (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 Clinical Trial Protocol (CTP), 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 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 will be stored in a trial database within the Oracle Clinical™ system.

The statistical analyses will be performed within the validated working environment CARE (Clinical data Analysis and Reporting Environment), including SAS™ (current Version 9.4, by SAS Institute Inc., Cary, NC, USA), and providing SAS™-based tools (e.g., macros for the analyses of adverse event (AE) data or laboratory data; Report Appendix Generator system (RAGe) for compilation/formatting of the clinical trial report (CTR) appendices).

Pharmacokinetic (PK) parameters will be calculated using Phoenix® WinNonlin® 6.3 (or later) and/or SAS® software, version 9.4 (or later) (professional Network version 5.2, Pharsight Corporation, Mountain View, CA 94041-1530, USA).

4. CHANGES IN THE PLANNED ANALYSIS OF THE STUDY

The trial was terminated because of recruitment problems. At the time of trial termination, only two patients had been treated and completed the trial. Therefore, no statistical models can be applied for the primary and secondary endpoints. Primary and secondary PK endpoints will only be summarised with descriptive statistics.

All other analyses described in this TSAP are in accordance with the statistical methods described in the CTP.

For the display of adverse event data, the time intervals after residual effect periods of treatments have been renamed from ‘post-treatment’ to ‘follow-up’ (in contrast to Section 7.3.4 of the CTP).

5. ENDPOINTS

5.1 PRIMARY ENDPOINTS

Primary endpoints are defined in Section 5.1.1 of the CTP.

5.2 SECONDARY ENDPOINT

5.2.1 Key secondary endpoint

Not applicable, as no key secondary endpoint was specified in the CTP.

5.2.2 Secondary endpoint

The secondary endpoint is defined in Section 5.1.2 of the CTP

5.3 FURTHER ENDPOINTS

5.3.1 Safety endpoints

Safety endpoints are defined in Section 5.3 of the CTP.

5.4 OTHER VARIABLES

5.4.1 Demographic and other baseline characteristics

At the Screening visit, the medical examination will include documentation of patient information, informed consent, demographics including height and body weight, signs and symptoms of the trial disease and concomitant therapy.

CTP: *The medical history with regard to non-small cell lung cancer shall be documented (i.e. date of first diagnosis, as well as details concerning first-line therapy with start and end dates and the reason why second-line therapy is indicated i.e. date of most recent progression) […].*

Age [years] will be determined as the difference between year of birth and year of informed consent.

Body mass index (BMI) will be calculated as weight [kg] / height $[m]^2$.

5.4.2 Treatment compliance and treatment exposure

Treatment compliance will not be analysed as a specific endpoint, cf. Section 4.3 of the CTP.

Treatment exposure is defined as the total dose of nintedanib and the total dose of Microgynon® per patient.

6. GENERAL ANALYSIS DEFINITIONS

6.1 TREATMENTS

For basic study information on the treatments to be administered and selection of dose, cf. Section 4 of the CTP. All patients were to undergo two treatment periods in a fixed sequence.

Table 6.1: 1 Treatments

Treatment description	Treatment	Period
1 x 1 tablet Microgynon®, single dose (1 tablet containing 30 microgram ethinylestradiol (EE) / 150 microgram levonorgestrel (LE))	Reference (R)	1
Day 1 - 7: 2 x 2 capsules Vargatef® continuously for at least 7 days (1 capsule containing 100 mg nintedanib); * [or in case of dose reduction: During the 7 days, switch to reduced dosing of 2 x 1 capsule Vargatef® (1 capsule containing 150 mg nintedanib) and continued intake up to Day 7;*] **Day 8:** 1 x 2 capsules Vargatef® in the morning on Day 8 of continuous Vargatef® intake (1 capsule containing 100 mg nintedanib); [or in case of dose reduction: 1 x 1 capsule Vargatef® in the morning on Day 8 of continuous Vargatef® intake (1 capsule containing 150 mg nintedanib);] 1 x 1 tablet Microgynon®, single dose in the morning on Day 8 of continuous Vargatef® intake (1 tablet containing 30 microgram EE / 150 microgram LE) 1 x 2 capsules Vargatef® in the evening on Day 8 of continuous Vargatef® intake (1 capsule containing 100 mg nintedanib); [or in case of dose reduction: 1 x 1 capsule Vargatef® in the evening on Day 8 of continuous Vargatef® intake (1 capsule containing 150 mg nintedanib);] **Day 9 - 11:** 2 x 2 capsules Vargatef® on Day 9 of continuous Vargatef® intake until end of trial visit (1 capsule containing 100 mg nintedanib); [or in case of dose reduction: 2 x 1 capsule Vargatef® on Day 9 of continuous Vargatef® intake until end of trial visit (1 capsule containing 150 mg nintedanib);]	Test (T)	2

* In case of a temporary interruption of nintedanib intake, patients can receive Microgynon® in Period 2 only if they have taken nintedanib for 7 consecutive days before intake of Microgynon®.

For statistical analysis of AEs and for listings of safety laboratory and vital signs, the study phases are defined for each patient as described in Table 6.1: 2.

Table 6.1: 2 Flow chart of analysis phases for statistical analyses of AEs, safety laboratory and vital signs

Study analysis phase	Label	Start	End
Screening	Screening	Date of informed consent or date of first laboratory assessment, whichever occurs earlier *	Date/time of first administration of study drug
On-treatment Microgynon®	**MIC**	Date/time of administration of Microgynon® in Treatment Period 1	Date/time of administration of Microgynon® in Treatment Period 1 + residual effect phase (REP, i.e. 72 h)
Follow-up Microgynon®	**FUP-MIC**	Date/time of administration of Microgynon® in Treatment Period 1 + REP (72 h)	Date/time of first administration of nintedanib in Treatment Period 2
On-treatment nintedanib loading phase	**Loading NIN**	Date/time of first administration of nintedanib in Treatment Period 2	Date/time of administration of Microgynon® in Treatment Period 2
On-treatment nintedanib plus Microgynon®	**NIN+MIC**	Date/time of administration of Microgynon® in Treatment Period 2	Date/time of administration of Microgynon® in Treatment Period 2 + REP (72 h)
On-treatment nintedanib	**NIN**	Date/time of administration of Microgynon® in Treatment Period 2 + REP (72 h)	Date/time of last administration of nintedanib in Treatment Period 2 + REP (30 days)
Follow-up nintedanib	**FUP-NIN**	Date/time of last administration of nintedanib in Treatment Period 2 + REP (30 days)	0:00 a.m. on day after trial completion date
Post study	Post-study	0:00 a.m. on day after trial completion date	Last contact with patient

* E.g., if a patients agrees to use laboratory data which were taken prior to informed consent.

CTR Section 15, Appendix 16.1.9.2.8.2 and Appendix 16.1.9.2.8.3 AE displays will present results for the on-treatment phases "MIC", "Loading NIN", "NIN+MIC", and "NIN" only. Screening, post-treatment and post-study periods will not be included in this analysis. CTR Section 15 AE displays (but not Appendix 16.1.9.2.8.2 and Appendix 16.1.9.2.8.3 AE displays) will additionally present the following totals:

- "**Total NIN**", defined as the total over on-treatment phases involving nintedanib, i.e. "Loading NIN" + "NIN+MIC" + "NIN".

- "**Total on-trt**", defined as the total over all on-treatment phases, i.e., "MIC" + "Loading NIN" + "NIN+MIC" + "NIN".

CTR Appendix 16.1.9.2.8.1 displays will present results for all study analysis phases defined above, and will additionally present the following totals:

- "**Total NIN**", defined as the total over on-treatment phases involving nintedanib, i.e. "Loading NIN" + "NIN+MIC" + "NIN".

- "**Total**", defined as the total over all study analysis phases.

More details on the technical implementation of these analyses are provided in the Analysis Data Set (ADS) Plan of this TSAP.

6.2 IMPORTANT PROTOCOL VIOLATIONS

Data discrepancies and deviations from the CTP will be identified for all patients in the database (i.e., treated patients). Consistency check listings (for identification of violations 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 report planning and database lock meeting (RPM/DBLM). At this meeting, it will be decided whether a discrepant data value can be used in analyses or whether it must be corrected in the clinical database. Each protocol deviation must be assessed to determine whether it is an important protocol violation (PV). For definition of important PVs, and for the process of identification of these, refer to the Boehringer Ingelheim (BI) reference document "Protocol Violation Handling Definitions" (2).

If any important PVs are identified, they are to be summarised into categories and will be captured in the RPM/DBLM minutes via an accompanying Excel spreadsheet (3). The following table contains the categories which are considered to be important PVs in this trial. If the data show other important PVs, this table will be supplemented accordingly by the time of the RPM/DBLM.

PVs will be summarised and listed.

Table 6.2: 1 Important protocol violations

Category / Code		Description	Example /Comment
A		**Entrance criteria not met**	
	A1	Patient less than 18 years old	Violation of inclusion criterion 1
B		**Informed consent**	
	B1	Informed consent not available	Violation of inclusion criterion 5
	B2	Informed consent too late	Informed consent date was after screening visit date
C		**Trial medication and randomisation**	
	C1	Incorrect trial medication taken	This will be captured manually and discussed in MQRM (check medication intake details via review listings for evidence of extreme non-compliance) or RPM
	C3	Non-compliance	This will be captured manually and discussed in MQRM (check medication compliance details via review listings for evidence of extreme non-compliance) or RPM
	C5	Incorrect intake of trial medication	This will be captured manually and discussed in MQRM (check medication intake and compliance details via review listings for evidence of extreme non-compliance) or RPM
D		**Concomitant medication**	
	D1	Prohibited medication use	This will be captured manually and discussed in MQRM (review listings of concomitant medications for prohibited medication use) or RPM
E		**Missing data**	
	E1	Certain violations of procedures used to measure primary or secondary data	This will be captured manually and discussed in MQRM (review listings for adherence to blood sampling and time points, drug administration times) or RPM
F		**Incorrect timing**	
	F1	Certain violations of time schedule used to measure primary or secondary data	This will be captured manually and discussed in MQRM (review listings for general quality of PK sampling) or RPM
G		**Other trial specific important violations**	
	G1	Incorrect intake of meal / non-adherence to dietary restrictions	This will be captured manually and discussed in MQRM (review listings of dietary restrictions) or RPM

[1] Missing visits, evaluations, and tests will be considered missing data, not PVs
[2] Time deviations will only be flagged as important PV, when leading to exclusion of the entire patient from an analysis set
Source: BI reference document 'Protocol Violation Handling Definitions' [001-MCS-50-413_RD-01] (2).

6.3 PATIENT SETS ANALYSED

All patients who received study medication will be included in the safety analysis and in the PK analysis depending on the availability of measurement values, and on their adherence to the CTP.

Analysis sets are defined in Section 7.3 of the CTP. The discussion of all exceptional cases and problems and the decisions on the allocation of patients to analysis sets will be made at latest at the RPM/DBLM.

Table 6.3: 1 Patient sets analysed

	Patient set		
Class of endpoint	Entered set (ES)	Treated set (TS)	PK analysis set (PKS)
Important PVs	X		
Disposition	X	X	
Demographic/baseline endpoints		X	
Safety endpoints		X	
PK endpoints			X

6.4 SUBGROUPS

No subgroup analyses are planned.

6.5 POOLING OF CENTRES

This section is not applicable.

6.6 HANDLING OF MISSING DATA AND OUTLIERS

CTP: *For all patients, the reason for withdrawal (e.g. adverse events) must be recorded in the electronic Case Report Form (eCRF). These data will be included in the trial database and reported.*

CTP: *With respect to safety evaluations, it is not planned to impute missing values.*

The only exception where imputation might be necessary for safety evaluation is 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). **CTP**: *Concentration data identified with NOS (no sample), NOR (no valid result), NOA (not analysed), or BLQ (below the limit of quantification) will be ignored and not replaced by zero at any time point (applies also to the lag phase).*

CTP: *In the non-compartmental analysis, concentration data identified with NOS, NOR, and NOA will not be considered. BLQ values in the lag phase will be set to zero. The lag phase is defined as the period between time zero and the first time point with a concentration above the quantification limit. All other BLQ values of the profile will be ignored.*

6.7 BASELINE, TIME WINDOWS AND CALCULATED VISITS

None of the planned analyses requires a definition of baseline.

Time windows are defined in Section 6.1 of the CTP. Adherence to time windows will be checked at the RPM/DBLM.

7. PLANNED ANALYSIS

The format of the listings and tables will follow the BI guideline "Reporting of clinical trials and project summaries" (001-MCG-159) (10).

The individual values of both patients will be listed by patient number and visit (if visit is applicable in the respective listing). Listings will also show treatment sequence, although all patients received treatments in the same sequence. AE listings will be sorted by assigned treatment (see Section 7.8.1 below for details). The listings will be contained in Appendix 16.2 of the CTR.

Descriptive data analysis of primary and secondary PK endpoints will be performed by BI and presented in Section 15.6 of the CTR.

The following standard descriptive statistical parameters will be displayed in summary tables of continuous variables:

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

For primary and secondary PK endpoints, the following descriptive statistics will additionally be calculated:

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

Moreover, the 10^{th}, 25^{th}, 75^{th} and 90^{th} percentiles will be also presented in Section 15.6.2 for the descriptive statistics of the PK parameters.

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 (%) relative to the total number of patients. Percentages will be rounded to one decimal place. The category missing will be displayed if and only if there are actually missing values. Percentages will be based on all patients in the respective patient set whether they have non-missing values or not.

7.1 DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

Only descriptive statistics are planned for this section of the CTR.

7.2 CONCOMITANT DISEASES AND MEDICATION

Concomitant diseases will be coded according to the most recent version of the Medical Dictionary for Regulatory Activities (MedDRA). Concomitant medication will be coded according to the most recent version of the World Health Organisation – Drug Dictionary.

Only descriptive statistics are planned for this section of the CTR.

Medications will be categorised into baseline therapies, on-treatment concomitant therapies, and post-study drug discontinuation therapies:

- Baseline therapies will be defined as treatments with a start date before first trial drug intake and a stop date after (i.e. ongoing after first trial drug intake) or on the day of the first trial drug intake.

- On-treatment concomitant therapies are defined as treatments with a start date after or on the day of first trial drug intake and before or on the day of last trial drug intake.

- Post-study drug discontinuation therapies are defined as treatments with a start date after last trial drug intake and before trial completion (as defined in Section 6.2.3 of the CTP).

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

Treatment compliance will not be analysed as a specific endpoint (cf. Section 5.4.2). Any deviations from complete intake will be addressed in the RPM/DBLM (cf. Section 6.2) and described in the CTR.

7.4 PRIMARY ENDPOINTS

Primary PK endpoints will be assessed descriptively. The analysis of standard PK parameters is performed according to BI standards (see 001-MCS-36-472_RD-01) (5).

Exclusion of PK parameters

The ADS PK6+ contains column variables KPEXC and KPEXCX indicating inclusion/exclusion (KPEXC) of a PK parameter and an analysis flag comment (KPEXCX). All analyses based on the PKS are based on PK parameters with KPEXC equal to “Included”, regardless of the analysis flag comment KPEXCX.

Exclusion of plasma concentrations

The ADS PK4+ (PK concentrations per time-point) contains column variables PKEXC and PKEXCX indicating inclusion/exclusion (PKEXC) of a plasma concentration and an analysis flag comment (PKEXCX). Exclusion of a plasma concentration depends on the analysis flag comment PKEXCX. For example, if PKEXCX is set to ‘ALL CALC’, the value will be excluded for all types of analyses based on concentrations. If PKEXCX is set to ‘DESC

STATS' the value will be excluded from descriptive evaluations per planned time point. If PKEXCX contains the addition 'TIME VIOLATION' or 'TIME DEVIATION' the value can be used for further analyses based on actual times. If PKEXCX is set to 'HALF LIFE' the value will be excluded from half-life calculation only; the value is included for all other analyses.

CTP: *However, the excluded concentration itself will be listed in the tables in section 15 of the clinical trial report associated with an appropriate flag.*

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" (6).

7.5 SECONDARY ENDPOINTS

7.5.1 Key secondary endpoint

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

7.5.2 Secondary endpoint

The secondary endpoint will be summarised with descriptive statistics.

See Section 7.4 of this TSAP for details regarding exclusion of PK parameters and plasma concentrations.

7.6 FURTHER ENDPOINTS

7.6.1 Safety endpoints

Further safety endpoints will be analysed as described in Section 7.8 of this TSAP.

7.7 EXTENT OF EXPOSURE

Only descriptive statistics are planned for this section of the CTR.

7.8 SAFETY ANALYSIS

All safety analyses will be performed on TS.

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. All analyses of AEs will be based on the number of patients with AEs and not on the number of AEs. For this purpose, AE data will be combined in a two-step procedure into AE records.

In a first step, AE occurrences, i.e., AE entries on the electronic case report form (eCRF), will be collapsed into a single AE episode provided that all of the following applies:

- The same MedDRA lowest level term was reported for the occurrences
- The occurrences were time-overlapping or time-adjacent (time-adjacency of two occurrences is given if the second occurrence started in the same hour in which the first occurrence ended)
- Treatment did not change between the onset of the occurrences OR treatment changed between the onset of the occurrences, but no deterioration was observed for the later occurrence

In a second step, AE episodes will be condensed into a single AE record per patient, treatment and dictionary level, provided that the episodes were reported with the same term on the respective MedDRA level and that the episodes are assigned to the same treatment.

For further details on summarisation of AE data, please refer to 'Handling and summarisation of adverse event data for clinical trial reports and integrated summaries' (7) [001-MCG-156 Version 5] and "Handling of missing and incomplete AE dates" (4) [001-MCG-156_RD-01].

The analysis of AEs will be based on the concept of treatment-emergent AEs. That means that all AEs will be assigned to the treatment, post-treatment, screening or post-study phases as defined in Section 6.1.

Hepatic injury and gastro-intestinal perforation are defined as protocol-specified adverse events of special interest (AESIs). For details on the definition of hepatic injury see CTP Section 5.3.6.1

Note that these events were called “Protocol specified AE of special interest” in the eCRF. The investigator had to classify all observed AEs on the eCRF whether they were of this type or not.

According to ICH E3 (9), AEs classified as ‘other significant’ need to be reported and will include those non-serious and non-significant AEs with
(i) ‘action taken = discontinuation’ or ‘action taken = reduced’, or
(ii) marked haematological and other lab abnormalities or leading to significant concomitant therapy as identified by the Clinical Monitor/Investigator at a Medical Quality Review Meeting.

An overall summary of AEs will be presented. This overall summary will comprise summary statistics for the class of other significant AEs according to ICH E3 (9).

The frequency of patients with AEs will be summarised by primary system organ class and preferred term. AEs which were considered by the investigator to be drug-related will be summarised separately. Separate tables will also be provided for patients with serious AEs

(SAEs), patients with AESIs and patients with other significant AEs (according to ICH E3 (9)). The frequency of patients with AEs will also be summarised by worst common terminology criteria grade, primary system organ class and preferred term.

The system organ classes will be sorted according to the standard sort order specified by the European Medicines Agency, preferred terms within system organ classes will be sorted by descending relative frequency.

For disclosure of AE data on ClinicalTrials.gov, the frequency of patients with non-serious AEs occurring with an incidence of greater than 5 % (in preferred terms) will be summarised by primary system organ class and preferred term. The frequency of patients with SAEs will also be summarised.

For disclosure of AE data in the European union drug regulating authorities clinical trials (EudraCT) register, the frequency of AEs, the frequency of non-serious AEs with an incidence of greater than 5 % (in preferred terms) and the frequency of SAEs will be summarised.

7.8.2 Laboratory data

Laboratory data will only be listed. The listing will be based on BI standards (8).

Possibly clinically significant abnormal laboratory values are only those identified either in the Investigator’s comments on the eCRF or at the RPM/DBLM at the latest. It is the investigator's responsibility to decide whether a lab value is clinically significant abnormal or not. Standard or project-specific rules for flagging clinically significant values will not be applied in this study.

Clinically relevant findings in laboratory data will be reported as AEs and will be analysed as part of AE analysis.

7.8.3 Vital signs

Vital signs data will only be listed.

Clinically relevant findings in vital signs data will be reported as AEs and will be analysed as part of AE analysis.

7.8.4 ECG

Clinically relevant findings in electrocardiogram (ECG) data will be reported as AEs and will be analysed as part of AE analysis.

7.8.5 Others

Physical examination findings will be reported as relevant medical history/baseline condition (i.e., a condition already existent before intake of first study drug) or as AE and will be summarised as such. No separate listing or analysis of physical examination findings will be prepared.

8. REFERENCES

1 *CPMP/ICH/363/96*: "Statistical Principles for Clinical Trials", ICH Guideline Topic E9; Note for Guidance on Statistical Principles for Clinical Trials, current version

9 *CPMP/ICH/137/95*: "Structure and Content of Clinical Study Reports", ICH Guideline Topic E3; Note For Guidance on Structure and Content of Clinical Study Reports, current version

9. ADDITIONAL SECTIONS

Not applicable as no additional information is needed.

10. HISTORY TABLE

Table 10: 1 History table

Version	Date (DD-MMM-YY)	Author	Sections changed	Brief description of change
Final	**29 JAN 2018**		None	This is the final TSAP without any modification