SIGNATURE INFORMATION

Document: 1302-0001--tsap

Document No.: T12-1048-01

Title Pharmacokinetics and safety of BI 695502 in healthy subjects: a randomized, single-blind, single-dose, parallel-arm, active-comparator clinical Phase I study

SIGNATURES (ELECTRONICALLY OBTAINED)

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SIGNATURE INFORMATION (continued)

Document 1302-0001--tsap

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SIGNATURES (ELECTRONICALLY OBTAINED)
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Trial Statistical Analysis Plan

T12-1048-01

BI Trial No.:	1302.1
Title:	Pharmacokinetics and safety of BI 695502 in healthy subjects: a randomized, single-blind, single-dose, parallel-arm, active-comparator clinical Phase I study
Investigational Product:	BI 695502
Responsible trial statisticians:	Phone: Fax: Phone: Fax:
Date of statistical analysis plan:	13 DEC 2012 SIGNED
Version:	Final

1. TABLE OF CONTENTS

LIST OF TABLES

2. LIST OF ABBREVIATIONS

Include a list of all abbreviations used in the TSAP

Term	Definition / description
AE	Adverse event
ADS	Analysis dataset
ANOVA	Analysis of variance
AUC_{0-tz}	Area under the concentration-time curve of the analyte in plasma over the time interval from 0 to time of the last quantifiable data point
$AUC_{0-\infty}$	Area under the concentration-time curve of the analyte in plasma from time zero to infinity
BI	Boehringer Ingelheim
BLQ	Below limit of quantification
BRPM	Blinded report planning meeting
BRPM/DBLM	Combined blinded report planning and database lock meeting
C_{max}	Maximum measured concentration of the analyte in plasma
CRF	Case Report Form
CTP	Clinical Trial Protocol
CTR	Clinical Trial Report
DM&SM	Boehringer Ingelheim Data Management and Statistics Manual
DMC	Data monitoring committee
ECG	Electrocardiogram
EMA	European Medicines Agency
ICH	International Conference on Harmonisation
MedDRA	Medical Dictionary for Regulatory Activities
N	Number of observations included in calculation
NC	Not calculated
NOA	Not analyzed
NOP	No peak detectable
NOR	No valid result
NOS	No sample available
O*C	Oracle Clinical

Term	Definition / description
PK	Pharmacokinetic(s)
PKS	Pharmacokinetic set
PV	Protocol violation
qd	Quaque die (once a day)
R/Ref	Reference treatment
RAN	Randomised set
SAS®	Statistical Analysis System
SD	Standard deviation
SDL	Subject Data Listings
T	Test treatment
TS	Treated set
TSAP	Trial statistical analysis plan
WHO-DD	World Health Organization Drug Dictionary

3. INTRODUCTION

As per 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 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, and randomization.

Study data will be stored in a trial database within the Oracle Clinical™ (O*C) system. SAS® Version 9.2 will be used for all analyses.

Pharmacokinetic (PK) parameters will be calculated using WinNonlin™ software (professional Network version 5.3, Pharsight Corporation, Mountain View, CA 94041-1530, USA).

4. CHANGES IN THE PLANNED ANALYSIS OF THE STUDY

All analyses outlined in the trial protocol are described in the TSAP. Two minor changes compared to the protocol will be made. As one referred internal SOP, namely DCP-102, was superseded by a new SOP, 001-MCS-36-472, the new SOP will be used as basis for handling PK data. Secondly, the model for the analysis of variance (ANOVA) was slightly adapted such that the slope β describing the linear trend between response and regressor was added.

5. ENDPOINTS

The PK as well as the safety endpoints are described in this section.

5.1 PRIMARY ENDPOINT

CTP: *The primary PK endpoint for assessment of PK similarity is the following:*

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

5.2 SECONDARY ENDPOINTS

5.2.1 Key secondary endpoints

As no key secondary endpoints have been specified in the protocol, this section is not applicable.

5.2.2 Other Secondary endpoints

Secondary PK parameters are:

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

The assessment of safety will secondarily be based on adverse events; see CTP Section 5.2.2.

5.5 SAFETY ENDPOINTS

Safety parameters (physical examination, vital signs, temperature, body weight, 12-lead ECG, laboratory tests); see CTP Sections 2.2.2 and 5.2.

6. GENERAL ANALYSIS DEFINITIONS

6.1 TREATMENTS

A two-stage group sequential design was planned for this trial:

- Stage 1: 90 subjects (30 per treatment group)
- Stage 2: 90 subjects (30 per treatment group)

CTP: *An interim analysis will be conducted and if the pre-specified criteria for early PK biosimilarity are achieved then the study may be stopped. It is also possible that a single arm is going to be stopped* [for proven (pairwise) biosimilarity] *based on the chosen boundaries and the interim results. This is the case if both comparisons for the specific arm show an early similarity. If any comparison does not show early similarity then the trial will proceed to Stage 2.*

This interim analysis will be performed by a DMC which will provide a recommendation whether to stop the trial for early PK biosimilarity or to continue.

Subjects are randomised to one of the three treatment arms given below.

Table 6.1: 1 Labels for treatments for use in the CTR

PKTRT	Treatment	Short label
A	BI 695502, 1.4mg/mL solution for infusion, 1mg/kg, iv, qd[1)]	BI 695502
B	Avastin(US source), 1.4mg/mL solut. for infusion, 1mg/kg, iv, qd[1)]	Avastin US
C	Avastin(EU source), 1.4mg/mL solut. for infusion, 1mg/kg, iv, qd[1)]	Avastin EU

[1)] "qd" means here a single drug administration on Day 1 of Visit 2.
Note that these labels do not necessarily reflect the actual randomised code and the DMC outputs

For detailed information on the handling of the treatments in the O*C views refer to Technical TSAP ADS plan (Chapter 2.2.1, 2.2.2). In particular, AEs and laboratory excursions will be assigned to BI 695502 or bevacizumab (Avastin ®) from both US and EU sources if they occur up to end-of-study visit.

Table 6.1: 2 Overview of treatments for inter-individual comparison

Test (T)	**Reference (R)**
A (Test 1, T1)	B (Ref 1, R1)
A (Test 1, T1)	C (Ref 2, R2)
C (Test 2, T2)	B (Ref 1, R1)

6.2 IMPORTANT PROTOCOL VIOLATIONS

Data discrepancies and deviations from the CTP will be identified for all subjects enrolled (i.e. signed informed consent available) who did not fail during screening. 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 (BRPM/DBLM). At this meeting at the latest, it will be decided whether a discrepant data point can be used or whether it must be corrected in the clinical database, and whether any identified protocol deviation is an important protocol violation (PV). A PV is in general defined as important if it affects the rights or safety of a study subject or if it can potentially influence the primary outcome measurement(s) for a subject in a way that is neither negligible nor in accordance with the study objectives. This second category of important PV forms the basis for the decision of whether a subject belongs to any analysis set.

PVs that do not influence the subjects' rights and safety or the evaluability of subject data with respect to the main study objectives are identified as non-important PVs. These are only considered to assess the overall trial quality.

Important PVs will be described narratively in the CTR (derived from Appendix 16.2). In the study report, protocol violations affecting subjects' rights will be identified separately from those affecting analysis sets.

If any important PVs have been identified, they are summarised into categories and will be captured in the BRPM/DBLM minutes via an accompanying Excel spreadsheet [001-MCS-50-413_RD-02] (1). Table 6.2: 1 contains the categories in which important PVs are classified. If other important PVs are identified at the BRPM/DBLM, this table will be supplemented accordingly.

If substantial numbers of PVs are reported at the BRPM/DBLM, a decision about summarizing the PVs in a tabular format will be made. Otherwise, only a PV listing will be provided.

Consistency checks will be prepared for identifying violations of time windows.

Table 6.2: 1 Important protocol violations

Category /Code		Description
A		**Entrance criteria not met**
	A1	Inclusion criteria not met
	A2	Exclusion criteria not met
B		**Informed consent**
	B1	Informed consent not available/not signed
	B2	Informed consent too late
C		**Trial medication and randomization**
	C1	Incorrect trial medication taken
	C2	Randomization not followed
	C3	Non-compliance
D		**Concomitant medication**
	D1	Improper medication washout
	D2	Prohibited medication use
	D3	Mandatory medication not taken
E		**Missing data (for primary and secondary endpoints)[1]**
	E4	Certain violations of procedures used to measure primary and secondary data
F		**Incorrect timing (for primary and secondary endpoints)[2]**
	F5	Certain violations of the time schedule used to measure primary and secondary data
G		**Other trial specific important violations**
	G1	Wrong dosing

[1] Missing visits, evaluations, and tests of data will be considered missing data, not protocol violations.
[2] Time deviations will only be flagged as important PV, when leading to exclusion of the entire subject from an analysis set
Source: BI DM&SM, "Handling of Protocol Violations" [001-MCS-50-413_RD-01] (2)

6.3 PATIENT SETS ANALYSED

- Randomised set (RAN):
  This subject set includes randomised subjects, whether treated or not.

- Treated set (TS):
  This subject set includes all randomised subjects who have received one dose of study drug.
  This is the full analysis set population in the sense of ICH-E9.

- Pharmacokinetic set (PKS):
  This subject set includes all subjects in the TS who provide at least one PK endpoint and had no important protocol violations relevant to the evaluation of PK biosimilarity.

Table 6.3: 1 Subject sets for analyses

	Subject set		
Endpoint	RAN	TS	PKS
Primary PK endpoint			X
Secondary PK endpoints			X
Secondary endpoints (safety evaluation)		X	
Demographic data/Medical history and Concomitant diagnosis, Concomitant therapy		X	
Important PVs		X	
Analysis sets assignment	X		

6.5 POOLING OF CENTRES

This section is not applicable, because centre is not included in the statistical model.

6.6 HANDLING OF MISSING DATA AND OUTLIERS

6.6.1 Safety data in general

Data of subjects randomised who were not treated will be listed only. The safety data for treated subjects who failed to complete all stages of the study (who withdraw or are removed from the trial) will be reported as far as their data are available.

It is not planned to impute missing values, with exception of missing AE start dates and times. These are imputed according to BI standards (see DM&SM "Handling of missing and incomplete AE dates" [001-MCG-156_RD-01]) (3).

All subject discontinuations will be documented and the reason for discontinuation recorded.

6.6.2 AE dates and times

Refer to TSAP Section 6.6.1 above.

6.6.3 Missing plasma concentrations and pharmacokinetic parameters

Handling of missing PK data will be performed according to the BI standard procedure "Noncompartmental Pharmacokinetic / Pharmacodynamic Analyses of Clinical Studies" [001-MCS-36-472_RD-01] (4).

Plasma concentration-time profiles and descriptive statistics of concentration data

Drug concentration data identified with NOS (no sample available), NOR (no valid result), NOA (not analyzed), BLQ (below the lower limit of quantification), or NOP (no peak detectable) will be displayed as such and not replaced by zero at any time point (this rule also applies also to the lag phase, including the pre-dose values).

Pharmacokinetic parameters and their descriptive statistics

For the noncompartmental analysis, concentration data identified with NOS, NOR or NOA will generally not be considered. Concentration values in the lag phase identified as BLQ or NOP will be set to zero. All other BLQ/NOP values of the profile will be ignored. The lag phase is defined as the period between time zero and the first time point with a concentration above the quantification limit. During the evaluation of bioanalytical data the software, e.g. WinNonlin, will automatically interpolate between the value before and the value after a "missing" value.

6.7 BASELINE, TIME WINDOWS AND CALCULATED VISITS

The baseline for all analyses will be the last measurement before trial drug administration.

CTP: *Exact times of measurements outside the permitted time windows will be documented. Time windows are permitted as follows:*

- *General medical examination: at screening (1 to 28 days prior to the first study day) and at the end-of-study evaluation (Day 99);*
- *The tolerance for vital signs and ECG will be ± 1 hour; and*
- *Study measurements and assessments scheduled to occur on Day 1 prior to drug administration have to be performed and completed within 2 hours prior to drug administration.*

For planned individual plasma concentration sampling times refer to the Flow Chart 1.1 of the CTP. *While these nominal times should be adhered to as closely as possible, the actual sampling times will be recorded and used for determination of PK parameters.*

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

7. PLANNED ANALYSIS

CTP: *The trial will be performed in a two-stage design with Pocock boundaries for early stopping. The interim analysis will be performed when approximately 50% of the subjects are evaluable for the primary endpoint. A single treatment may be stopped at interim analysis if both comparisons where the treatment is involved in show an early significance. A stop of the whole trial based on the interim analysis results for early significance is possible.*

This interim analysis will be performed by a DMC (data monitoring committee) *which will provide a recommendation whether to stop the trial for early PK biosimilarity.*

Only the final analysis will be reported in 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] (5) with the exception of those generated for PK/PD-calculations.

The individual values of all subjects will be listed, sorted by treatment, subject number and visit. The listings will be contained in Appendix 16.2 (SDL) of the CTR.

The following standard descriptive statistical parameters will be displayed in summary tables of continuous variables for non-PK parameters.

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

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. Percentages will be rounded to one decimal place. The category 'missing' will be displayed only if there are current missing values. Percentages will be based on all subjects in the each subject set.

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

CTP: *The following descriptive statistics will be calculated for plasma concentrations as well as for all primary and secondary PK parameters: N (sample size), arithmetic mean, standard deviation, minimum, median, maximum, arithmetic coefficient of variation, geometric mean, and geometric coefficient of variation. The data format for descriptive statistics of concentrations will be identical with 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. The individual values as well as the descriptive statistics will be reported with three significant digits in the CTR.*

The format of the listings and tables will follow the standards defined in this TSAP.

7.1 DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

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

The following variables will be displayed: gender, race, age, height, weight, body mass index, smoking status and alcohol status.

The data will be summarised by treatment and in total.

7.2 CONCOMITANT DISEASES AND MEDICATION

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

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.

7.3 TREATMENT COMPLIANCE

CTP: *Compliance will be assured by administration of all study medication under supervision of the investigating physician or a designee at the investigational sites in New Zealand. The measured plasma concentrations will provide additional information about compliance.*

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

7.4 PRIMARY ENDPOINT

CTP: *The objective of the current study is to establish the PK biosimilarity of BI 695502 compared to bevacizumab (Avastin®) US and EU source […], respectively, following one iv administration. A three-fold comparison will be performed (BI 695502 vs bevacizumab (Avastin®), US source, BI 695502 vs bevacizumab (Avastin ®), EU source, and bevacizumab (Avastin®), US source vs bevacizumab (Avastin ®), EU source).*

Similarity of BI 695502 and bevacizumab (Avastin ®) will be investigated on the primary PK parameter ($AUC_{0-\infty}$).

Statistical model

CTP: *The statistical model used for the analysis of the primary PK parameter ($AUC_{0-\infty}$) will be an analysis of variance (ANOVA) model on the logarithmic scale. This model will include*

effects accounting for the following sources of variation: 'treatment' and 'weight at baseline'. All effects will be considered as fixed. The model is described by the following equation:

$$y_{ij} = \mu + \tau_i + \beta \cdot \xi_j + e_{ij}$$

where

y_{ij} *= logarithm of response measured on subject j receiving treatment i;*

μ *= the overall mean;*

τ_i *= i^th treatment effect, i = 1, 2, 3;*

ξ_j *= weight of j^th subject;*

β = regression coefficient; *and*

e_{ij} *= the random error associated with the j^th subject who received treatment i.*

and $e_{ij} \sim N(0, \sigma_i^2)$ are independent random variables.

This analysis will be accomplished by using the repeated measures model (MIXED procedure with unstructured covariance structure; for the approximation of the degrees of freedom the Kenward and Roger method will be used). The analysis will be based on the PKS and performed using the following (dummy) SAS code:

```
PROC MIXED DATA=indata;
    CLASS treatment;
    MODEL logkp = treatment weight / DDFM=KR HTYPE=2;
    REPEATED / TYPE=UN(1) GROUP=treatment;
    LSMEANS treatment / PDIFF CL ALPHA=0.0607;
RUN;
```

The α-level for the significance testing will be adjusted based on Pocock boundaries due to the two stage group sequential design. Hence the confidence intervals considering at each analysis (interim and final) are 93.93 % confidence intervals.

CTP: *The primary PK parameter (see Section 7.1.3* of the CTP*) will be log transformed (natural logarithm) prior to fitting the ANOVA model described in Section 7.1.4* of the CTP*. The difference between the expected means for log(Test)-log(Reference) will be estimated by the difference in the corresponding least-squares means (point estimate), and two-sided 93.93% 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 and interval estimates for the inter-subject ratio of the geometric means for treatments.*

A claim of PK similarity will be made if the 93.93% confidence interval(s) of the ratio of the geometric means are contained in the pre-defined acceptance range for all three comparisons.

As additional sensitivity analysis, the combined data from the two stages will be analysed including a term for stage in the ANOVA model.

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 Other Secondary endpoints

CTP: For the final analysis, *the PK parameters $AUC_{0\text{-}tz}$ and C_{max} will be statistically assessed using the same statistical model as described for the primary endpoint. For these endpoints ($AUC_{0\text{-}tz}$ and C_{max}) the 90% confidence intervals will be computed.*

For the safety endpoints refer to Section 7.8 for detailed description.

7.7 EXTENT OF EXPOSURE

Descriptive statistics are planned for this section of the report based on the TS.

7.8 SAFETY ANALYSIS

All safety analyses will be performed on the TS.

If not stated otherwise, the safety results will be sorted by treatment.

7.8.1 Adverse events

The analyses of AEs will be descriptive in nature and will be based on BI standards as presented in the corporate guideline: "Handling and summarisation of adverse event data for clinical trial reports and integrated summaries" [001-MCG-156] (7).

AEs will be coded with the most recent available version number of MedDRA referred to in the footnote of tables and listings.

All analyses of AEs will be based on the number of subjects with AEs (and not on the number of AEs). For this purpose, AEs data will be combined in a 2-step procedure into AEs records.

In a first step, AEs occurrences, i.e. AEs entries on the CRF (case report form), will be collapsed into AEs episodes provided that all of the following applies:

- the same lowest level term was reported for the occurrences;
- the occurrences were time-overlapping or time-adjacent (time-adjacency of 2 occurrences was given if the second occurrence started on the same day or on the day following the end date of the first occurrence);
- 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, AEs episodes will be condensed into AEs records provided that the episodes are 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 AEs data are available in the guideline "Handling and summarization of adverse event data for clinical trial reports and integrated summaries" [001-MCG-156] (7).

The analysis of adverse events will be based on the concept of treatment emergent adverse events. All adverse events occurring before drug intake will be assigned to 'screening'. All AEs occurring up to end-of-study visit will be assigned to the treatment period and all AEs occurring after the end-of-study visit will be assigned to 'post study'. For more detail see TSAP ADS plan (Chapter 2.2.3).

According to ICH E3 (8), AEs classified as 'other significant' 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 lead to significant concomitant therapy as identified by the Clinical Monitor/Investigator at a Report Planning Meeting.

An overall summary of adverse events will be presented for each part.

Frequency of subjects with adverse events will be summarised by treatment, primary system organ class and preferred term. Separate tables will be provided for subjects with other significant adverse events according to ICH E3 (8), for subjects with serious adverse events

as well as for subjects with drug related AEs. The system organ classes will be sorted according to the standard sort order specified by EMA (European Medicines Agency). Preferred terms will be sorted by frequency (within system organ class).

In addition, frequency of subjects with non-serious adverse events that exceed 5%-threshold will be summarised by treatment, primary system organ class and preferred term.

7.8.2 Laboratory data

The analyses of laboratory data will be descriptive in nature and will be based on BI standards (see DM&SM: "Display and Analysis of Laboratory Data" [001-MCG-157]) (9). Descriptive statistics will be calculated over time and for the difference from baseline including post examination values. Baseline is understood as the last available measurement before the start of trial medication 'Last value on treatment' is understood as the last measurement.

CTP: *Frequency tables of changes with respect to the reference range between baseline and last value on treatment will also be presented.*

7.8.3 Vital signs

Only descriptive statistics 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. Baseline is understood as the last available measurement before start of trial medication.

In addition, descriptive statistics for body weight as well as for body temperature will be performed on the TS.

7.8.4 ECG

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 adverse events (when they occurred during treatment).

7.8.5 Others

A frequency table of local tolerability will be provided on the TS.

8. REFERENCES

1 *001-MCS-50-413_RD-02*: Reference Document, "Important Manual Protocol Violations Spreadsheet"; IDEA for CON.

2 *001-MCS-50-413_RD-01*: Reference Document, "Handling of Protocol Violations", current version; IDEA for CON.

3 *001-MCG-156_RD-01*: Reference Document, "Handling of missing and incomplete AE dates", current version; IDEA for CON.

4 *001-MCS-36-472_RD-01*: Reference Document, "Noncompartmental Pharmacokinetic / Pharmacodynamic Analyses of Clinical Studies", current version; IDEA for CON.

5 *001-MCG-159*: Corp Guideline, “Reporting of clinical trials and project summaries”, current version; IDEA for CON.

6 *001-MCS-36-472*: Corp SOP, "Standards and processes for analyses performed within Clinical Pharmacokinetics/Pharmacodynamics", current version; IDEA for CON.

7 *001-MCG-156*: Corp Guideline, “Handling and summarization of adverse event data for clinical trial reports and integrated summaries”, current version; IDEA for CON.

8 *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 *001-MCG-157*: "Display and Analysis of Laboratory Data", 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	**13-Dec-12**		None	This is the final TSAP without any modification