

## STATISTICAL ANALYSIS PLAN - SAP

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## STATISTICAL ANALYSIS PLAN - SAP

### SCOPE

This document defines the policy and procedures for creating, reviewing, approving, and archiving a **Statistical Analysis Plan (SAP)**. Adherence to this document ensures that the SAP accurately reflects the statistical analyses outlined in the Protocol Summary and Protocol/Protocol Amendment(s), and is sufficiently detailed to guide a lead-analyst unambiguously through the creation of the **Tables, Listings and Graphs (TLGs)** required for the final study report.

### 1.0 RESPONSIBILITIES

#### Statistician

- Produces the SAP, including TLG shells and definition of **analysis datasets (AD)**, obtaining input from Project Management (and other functions as appropriate).
- Plans and Directs the programming of the analysis planned in the SAP.

#### Statistical Programmer

- Programs all analysis datasets, analysis and outputs planned in the SAP.

#### Project Manager

- Reviews and gives input on the SAP contents.
- Reviews analysis outputs for checking data adherence.

### 2.0 PROCEDURE

#### 2.1 SAP Design and Approval

##### 2.1.1 Information Required

The basic information required to draft the SAP is the Protocol. Additional sources of information are the Protocol Amendment(s) if any, the Case Report Forms (CRFs) and the clinical database structures (annotated CRF).

##### 2.1.2 Timing

The SAP preparation should be started as soon as possible once the protocol has been approved. In any case, the Version 1.0 of the final SAP (i.e. the first approved version) should be completed at least before the Interim Analysis, if any, or Database Lock for final SAP.

Whenever a protocol amendment is required, evaluation of the impact on the currently approved version of SAP should be done and, if needed, a new version of the SAP should be created and approved.

##### 2.1.3 Format

Ideally, a SAP should be produced as a single document in Word format, comprising the following three major components:

- a description of the planned statistical analyses
- a description of the planned tables, listings and graphs (TLGs)
- a description of the analysis datasets (AD) to be used for the production of TLGs.

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It is acceptable for the three major components of the SAP to be stored as individual documents.

### 2.1.3.1 Description of Statistical Analyses

The description of the statistical analyses can be an expansion of the statistical methods section in the protocol/protocol amendment(s). It contains a detailed description of the following topics, when applicable:

- the description of the trial design
- the identification of primary efficacy and/or pharmacokinetic endpoints (if applicable)
- the identification of primary safety endpoints
- the identification of secondary efficacy endpoints
- the definition of the primary analysis population
- the description of how to handle missing data
- the safety analysis
- the analysis of the treatment compliance.

In addition the following items should also be evaluated, if applicable:

- the multiplicity adjustments for statistical testing, if applicable
- the statistical model for primary efficacy analysis
- the statistical model(s) for secondary analyses
- the pooling of centres for statistical analysis
- the sensitivity analyses for primary efficacy endpoints
- the pharmacogenomic data collection, if applicable
- the interim analysis and data monitoring plan.

### 2.1.3.2 Display Tables, Listings and Graphs Shells

This component presents a template for each display. Each shell should clearly identify the output layout and the analysis to be performed. It should indicate the header of the display, the display number, the variables to be summarized, titles and footers, patient grouping, analysis populations, and summary statistics to be presented. Multiple pages may be necessary to show all the necessary details of the table.

### 2.1.3.3 Analysis Datasets Shells

All derived variables are described in the SAP. Major details are stored in the ADs structure. It is responsibility of the Lead Analyst to define the ADs Table of Contents and develops code to create them. The table should include details for each AD with regard to algorithms for variable derivations, identified by the name and by a label, all CRF variables stored in the AD and the variable source.

## 2.1.4 Review and Approval

### 2.1.4.1 Draft SAP

The Statistician distributes the draft of the SAP to the Project Manager review and requests feedback in a timely manner.

This first draft of the SAP should contain the following components as a minimum:

- description of the statistical analyses

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- description of the relevant derived variables, i.e. the ones related to the main efficacy and safety endpoints of the study.

### 2.1.4.2 Final SAP

The Statistician distributes the final draft SAP to the Project Manager for his review, requesting feedback. If necessary, a meeting should be held to discuss and reach agreement on any outstanding issues.

Once all relevant comments have been addressed, the signature page will be signed and dated by the Project Manager and the Statistician; the SAP is saved as Version 1.0.

Depending upon the agreement reached with the PI, that may review or review and approve the SAP. The approval will be documented by e-mail.

### 2.1.4.3 SAP Amendment

No further changes to the SAP may be made after:

- the clinical database for a blinded study has been un-blinded
- or
- the clinical database for an open label study has been temporary (as for an interim analysis) or definitely locked.

However, if changes to the SAP are required, the same process described in section 3.1.4.2 should be followed. In any case the last version of the SAP should be signed before database lock.

SAP version revision number is assigned as follows:

- if minor changes are necessary, new versions of the SAP could be created, numbered as 1.1, then 1.2, etc.
- if major changes are necessary, revisions of the SAP should be created, numbered as 2.0, then 3.0, etc.

### 2.1.5 Distribution and Archiving

A paper copy of the final SAP prior to database lock should be archived in the Trial Master File by the Project Manager.

## 3.0 REFERENCES AND NOTES

- Statistical Principles for Clinical Trials (ICH E9)