Statistical analysis plan template

Author: Jonathan Jaeger

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This document is a template for a statistical analysis plan. It contains the backbone structures and instructions to fill out the sections. This template is designed to cover, at minimum, the needs for regulatory reporting. Instructions are in italic blue and hidden when document is printed out. Remove this front page before finalizing the document.

Company logo

Statistical analysis plan

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| **Protocol title:** |  |
| **Protocol number:** |  |
| **SAP Version (date):** |  |
| **Sponsor:** | Company name  Address |
| **Investigational therapy:** |  |
| **Development phase:** |  |
| **EudraCT number:** |  |
| **IND number:** |  |

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Signature page

Instructions: Update signature page as relevant.

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| **Reviewer** | | | | |
|  |  |  |  |  |
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Statistical analysis plan amendment history

Instructions: Complete the statistical analysis plan amendment history as relevant.

Document history

|  |  |
| --- | --- |
| **Protocol version** | **Date** |
| Amendment N | DD-Mmm-YYYY |
| Amendment N-1 | DD-Mmm-YYYY |
| … | DD-Mmm-YYYY |
| Amendment 1 | DD-Mmm-YYYY |
| Original | DD-Mmm-YYYY |

Amendment N (DD-Mmm-YYYY)

Amendment rationale

Changes to the previous version of the statistical analysis plan

Amendment N-1 (DD-Mmm-YYYY)

Amendment rationale

Changes to the previous version of the statistical analysis plan

Amendment 1 (DD-Mmm-YYYY)

Amendment rationale

Changes to the previous version of the statistical analysis plan

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List of tables

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List of abbreviations

Instructions: Provide list of all abbreviations used in the document. Abbreviations and acronyms are defined where first used in the document.

| **Acronym** | **Definition** |
| --- | --- |
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# Introduction

## Purpose of the statistical analysis plan

Instructions: Provide description of the purpose of the statistical analysis plan

## Objectives, estimands and statistical hypotheses

Instructions: List the objectives, the endpoints of interest, the population of interest, the desired claims and hypotheses. If needed, present it in a landscape orientation. For supplementary secondary objectives and tertiary/exploratory objectives, it is not mandatory to provide the information about the claims/hypotheses.

| **Objective** | **Endpoint** | **Population/Condition of evaluation** | **Desired claim & hypothesis** |
| --- | --- | --- | --- |
| **Primary objective(s)** |  |  |  |
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| **Key secondary objective(s)** |  |  |  |
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| **Secondary objectives** |  |  |  |
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| **Exploratory objectives** |  |  |  |
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## Study design

### Synopsis

Instructions: Provide a brief description of the study design. It is recommended copy/paste the information from the protocol. The following information should be provided: the study phase, design type (parallel, crossover, single group, ...), the control method (placebo, active comparator, historical, none) and other designs elements as required (dose-escalation, adaptation, ...).

### Treatment assignment and blinding

Instructions: Provide the method of assignment to treatment: randomization scheme (including randomization ratio, stratification, adaptation...), dose-escalation, ... Provide the blind level (open-label, single-blind, double-blind, triple-blind).

### Duration of study subject and study

Instructions: Provide information about maximal duration for each subject with sequence and definition of the study periods (screening, exposure, follow-up). Provide information about the expected duration of the study (including duration of enrolment assumptions).

### Timing of analyses, adaptations and stopping rules

Instructions: Provide list of the per-protocol planned analyses, timing of analyses, adaptations (if any) and stopping rules. If needed, subsections can be created for each analysis.

# Sample size determination

## Sample size calculation

Instructions: Provide all the information needed for the sample size calculation. Ideally, this section should be a copy/paste of the section on the sample size calculation from the protocol.

## Robustness of sample size

Instructions: Provide any relevant documentation about the robustness of the proposed sample size, including power/assurance for alternative hypothesis.

# Analysis sets and protocol deviations

## Analysis sets

Instructions: Provide the definition of each analysis set, with information at subject level. If needed, a subsection can be created for each analysis set.

## Protocol deviations

Instructions: Please refer to protocol deviation plan. If needed, please provide additional information about the conditions for major and minor programmable protocol deviations.

# Statistical analyses

## General considerations

Instructions: This section should describe general methods and definitions that do not need to be repeated in the subsequent sections. If needed, subsection can be created to streamline the general considerations. Suggested information to be provided are the following: Nominal significance levels, 1- or 2-sided tests and confidence/credibility interval probabilities; Common definitions of baseline; Handling and/or imputation of missing values (in case of detailed descriptions, e.g. for partial missing dates for exposure, medications or adverse events, creation of sections in appendix is recommended); General methods, such as handling of wrong stratification, wrong intervention assignment, handling of values below lower limit of quantification; Summary statistics for continuous and categorical variables; General choice of analysis sets for analyses; Pooling strategies for regions, centres, subpopulations, etc.

## Study population

### Disposition of subjects

Instructions: It is suggested to provide description about the summary for screened subjects and the reason for screen failure. In addition, description of the summary for study disposition including number/percentage of subjects who have completed the study versus number/percentage of subjects who have prematurely withdrawn from the study (with primary reasons for withdrawal).

### Protocol deviations

Instructions: Provide information on which type of protocol deviations will be summarized and how those summary information will be provided.

### Subjects by analysis sets

Instructions: Provide information on how summary of subjects per analysis set will be provided, including information about primary reasons for subjects being excluded from an analysis set.

### Demographics and other baseline characteristics

Instructions: Provide information about the demographics and baseline characteristics that will have to be summarized. In case of complex derivation for a demographic variable or baseline characteristics, provide the information to compute it in appendix.

### Medical history and concomitant diseases

Instructions: Provide information about the medical history and concomitant diseases, including definition and dictionary version. In case of medical history and/or concomitant diseases coded using multiple dictionary version (DSUR, ISS, ...), provide information about harmonization of the dictionary versions.

### Prior and concomitant medications

Instructions: Provide information about prior and concomitant medications, including definition of prior and concomitant medications and dictionary version. In case of medications coded using multiple dictionary version (DSUR, ISS, ...), provide information about harmonization of the dictionary versions.

## Primary evaluations

Instructions: Section aligned to structure outlined in ICH E9 (R1). In case of multiple primary endpoints, it is recommended to have one subsection per endpoint and to repeat all the below subsections.

### Definition of the endpoint

Instructions: If not sufficiently clear from the section on objectives, estimands and statistical analysis, state how the endpoint is defined, calculated and derived.

### Main analytical approach

Instructions: In case of regulatory agencies specific estimand, describe the main analysis for each estimand and indicate which estimands are required by with regulatory agency. Describe how intercurrent events are handled (events and censoring rules for time to event endpoints). If applicable, refer to the statistical hypothesis. Describe the main analytical approach, including how missing data will be handled. Describe how summary information (including missing pattern) and analysis results will be presented.

### Sensitivity analyses

Instructions: Describe the planned sensitivity analyses, i.e., the analyses intended to explore the robustness of inference from the main analytical approach.

### Supplementary analyses

Instructions: Describe any supplementary analyses.

## Secondary evaluation

Instructions: For key/confirmatory secondary endpoints, if applicable, document false positive rate control. Repeat all the subsections from the primary endpoint analysis. Less details can be provided for supportive secondary endpoints.

## Exploratory evaluation

Instructions: Describe analyses of exploratory endpoints to the same level of detail as for the supportive secondary endpoints.

## Safety evaluation

Instructions: This is a standard section for safety evaluation, aligned with Section 12 of ICH E3. In case one of the subsections is already covered withing the previous section, it is not needed to repeat the information withing the safety evaluation section.

### Extent of exposure and treatment compliance

Instructions: Describe the summaries that will be provided for extent of exposure to study intervention, which may include the number of subjects exposed, the duration of exposure, the dose(s) to which they were exposed and dose modifications. If applicable, describe how to calculate the exposure endpoints. If applicable, duration of exposure to any treatment can be summarized with descriptive statistics by period.

### Adverse events

Instructions: Provide definition of treatment-emergent adverse events. Provide information about summaries information that will be presented including but not limited to overall, by drug relationship, grade, by special interest, by temporary study drug discontinuation status. If relevant, provide summary information by period. Specify whether counts, proportions of subjects and/or counts (rates) of events will be summarized. Specify which level term will be summarized (system organ class and preferred terms or alternatives).

### Death, other serious adverse events and other significant adverse events

Instructions: Provide information about reporting (summary and listing) on deaths, other serious adverse events and significant adverse events that occurred during the clinical trial. Significant events would be any events that led to an intervention, including withdrawal of test drug/investigational product treatment, dose reduction, or significant additional concomitant therapy.

### Clinical laboratory evaluation

Instructions: Provide description on how clinical laboratory evaluation will be summarized, analysed and reported, including standard summary information, shift outputs (grade and/or normal range), ...

### Vital signs, physical findings, and other observations related to safety

Instructions: Provide description on how vital signs, physical findings and other observations related to safety will be summarized, analysed and reported.

# Appendix

## Changes to protocol-planned analyses

Instructions: Provide list of all the changes to the protocol-planned analyses. Please note that in case of modification of the primary or key secondary main analytical approach and sensitivity analysis, it is recommended to proceed with a protocol amendment.

## Study procedures and flowchart

Instructions: This section is not mandatory and can be deleted if not required. If section kept, copy/paste information from the protocol for the study procedure and flowchart.

## Index of tables, figures, and listings

Instructions: If not in a specific document, provide the numbering, title and analysis set for the out-text clinical study report tables, figures and listing.

## Programming considerations

Instructions: If not in a specific document, provide description for the programming considerations for the analysis datasets and the conventions to be used for the tables, figures and listings.

### Analysis datasets

### Tables, figures, and listings conventions

# References

Instructions: Provide full details of all references mentioned in the document (papers, guidance, guidelines, ...).

# Appendices

Instructions: Add appendices as relevant.