

DAIDS	Appendix 3	No.: DWD-POL-DM-01.00A3
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Statistical Requirements

Each clinical trial must have a senior statistician (preferably a Ph.D.) who has experience relevant to the clinical trial being conducted and who has experience with the relevant safety review process (e.g., Data and Safety Monitoring Boards (DSMBs), Safety Monitoring Committees (SMCs)).

For the clinical trial statistical requirements described below, the senior statistician may oversee the work of a junior statistician, delegate the tasks to a junior statistician, or perform the tasks him/herself.

1. Statistical Design

1.1 Trial Design

Provide input to the protocol development team regarding trial design to ensure that the trial, properly conducted, will yield statistically valid answers to the scientific question(s) posed in the protocol.

1.1.1 Design Configuration

Provide input into the design configuration of the trial (e.g., parallel group, crossover, factorial) to ensure that the scientific question(s) of the trial can be answered.

1.1.2 Type of Comparison

Provide input into the type of comparison (e.g., superiority, non-inferiority, equivalence) to support the scientific question(s) of the trial.

1.1.3 Sample Size

Calculate the sample size to ensure that it is large enough to provide a reliable answer to the scientific question(s) of the trial.

1.1.4 Interim Analyses

Provide input into the process and schedule of interim analyses, including stopping guidelines, as applicable, in order to monitor the safety and/or efficacy of the trial.

1.2 Primary and Secondary Endpoints

1.2.1 Provide input regarding the primary endpoint(s) to ensure the trial will provide the most clinically relevant and statistically valid answers directly related to the primary endpoint(s) of the trial.

1.2.2 Provide input regarding the secondary endpoint(s) to ensure that they either support measurements related to the primary study objective(s) or measure effects related to the secondary objective(s).

1.3 Other Endpoints

Provide input regarding any other endpoints to ensure that they are related to the questions to be answered in the trial.

1.4 Data Capture and Processing

Provide input into how the data are captured and processed in order to ensure that the data necessary to implement the planned analyses are captured.

1.5 Statistical Section of the Protocol

Develop the statistical section of the protocol. Include the primary and secondary endpoints; the primary and secondary objectives; the chosen sample size including rationale, power calculations, a description of the interim analyses, and the schedule of when the analyses will be performed; a description of the randomization scheme, if applicable; a description of the stratification scheme, if applicable; a description of the analysis plans for the primary and secondary objectives; and a description of monitoring committee (e.g., DSMB) reviews. Ensure that the statistical section of the protocol corresponds to the Statistical Analysis Plan.

1.6 Techniques to Avoid Bias

1.6.1 For blinded trials, develop a blinding code (either single blind or double blind) to support the trial design and develop the procedure and timing for revealing the treatment assignments.

1.6.2 For randomized trials, develop a randomization schedule to support the trial design.

2. Statistical Analysis Plan

Develop a Statistical Analysis Plan (SAP). Include an overview of the trial, a description of demographic and baseline characteristics, a description of endpoint analyses, a description of safety analyses, a description of any interim analyses, and a description of summary formats and layout. Ensure that the SAP corresponds to the statistical section of the protocol.

3. Statistical Monitoring

3.1 Protocol Changes

Provide input into any protocol changes (e.g., sample size adjustments, updates to inclusion/exclusion criteria) to ensure that any statistical consequences resulting from the changes are taken into consideration.

3.2 Study Progress and Safety Monitoring Plan

Develop a Study Progress and Safety Monitoring Plan (SPSMP) in collaboration with the Data Manager and Protocol Chair. The SPSMP must be reviewed and receive preliminary approval by DAIDS prior to trial initiation. The SPSMP should be reviewed by the DSMB/SMC prior to trial initiation if feasible or at the earliest opportunity after enrollment is initiated.

3.3 Interim Analyses

Conduct interim analyses per the process described in the protocol and maintain confidentiality of the data and results.

3.4 Data and Safety Monitoring Board (DSMB) or Safety Monitoring Committee (SMC)

3.4.1 Interface with the DSMB/SMC, as applicable, provide reports and other information as requested by the DSMB/SMC, and make presentations to the DSMB/SMC as needed.

3.4.2 Respond to all DSMB/SMC recommendations that relate to statistics and data management.

4. Statistical Analysis and Reporting

4.1 Statistical Analysis

At the end of the trial, perform the statistical analyses according to the process outlined in the statistical section of the protocol and in the Statistical Analysis Plan.

4.2 Statistical Reporting

Provide a report of the results of the analyses to the study team.