STU-SOP-DMS-004 – Standard Operating Procedure on Creating a Statistical Analysis Plan

1. Purpose and Definitions

To describe the procedure for preparing and finalising a statistical analysis plan (SAP) for a trial. The SAP is a comprehensive and detailed description of the methods of data analysis. Statistical analyses of Clinical Trials of Investigational Medicinal Products (CTIMPs) are required to comply with Good Clinical Practice (GCP) requirements within the Medicines for Human Use (Clinical Trials) Regulations.

Definitions	
Statistical Analysis Plan	A comprehensive description of the methods and presentation of data analysis, and expands the detail contained in the protocol.

2. Background

The SAP is the guiding document for all analysis in the trial and should carefully align with the research objectives and hypotheses stated in the trial protocol to avoid post hoc decisions that may affect the interpretation of trial findings. There should always be a pre-specified statistical methodology documented for every trial. A statistical analysis which includes a health economics analysis is called a Statistical and Health Economics Analysis Plan (SHEAP).

Further analyses of a more exploratory nature will not be bound by the SAP, although they are expected to follow the broad principles laid down within it.

Observational studies may not require a separate SAP, but the protocol must contain all necessary information on the analysis, including adjusting for multiple testing and handling missing data as required.

3. Roles and Responsibilities

The **Sponsor** has overall responsibility for confirming that a SAP has been developed prior to interim analysis, and finalised before database lock. This role will usually be delegated to the Chief Investigator, with appropriate oversight by the relevant trial committees e.g. Trial Steering Committee (TSC), etc.

The **Chief Investigator** (CI) usually has delegated responsibility for ensuring a SAP is produced that reflects the requirements of the approved protocol. The CI will involve a Statistician as early as possible, and ensure that any required amendments to the protocol are submitted for approval.

The **Trial Statistician** (TS) will be designated for each trial, and will have appropriate qualifications and experience and assume responsibility for all statistical aspects of the trial. The TS is responsible for ensuring that the SAP is written, finalised and signed off.

The **Trial Manager** (TM) supports the drafting of the SAP and ensures the document is agreed, finalised and filed in the Trial Master File before commencing the final statistical analysis of trial data.

External use of SOP: this SOP and Associated Documents (AD) may be used for research projects not adopted by STU where Swansea University (SU) staff and associated NHS organisations require guidance. In such instances, oversight responsibility for any associated tasks will not be the responsibility of STU.

4. Procedure

The SAP must be based on the trial protocol statistical section and should be version controlled, dated, written, finalised and signed off prior to data analysis and any unblinding of the data. A flow chart of the development procedure is available in Appendix 1 to this SOP.

4.1 Developing the draft

The SAP is a detailed description of the planned analyses and the statistical considerations of the trial protocol... Details of the descriptions of these items can be found in the STU SAP template.

Section 1: Administrative information for an audit trail of amendments made
Section 2: Introduction
Section 3: Study methods
Section 4: Statistical Principles
Section 5: Trial or Study Population
Section 6: Presentation of data for analysis
Section 7: Analysis
References

Differences between the methods in the protocol and SAP should be explained in the SAP and an assessment made of the need for a protocol amendment.

The SAP Template (STU-AD-TMP-009) should be used to draft the SAP. Template sections can be amended as appropriate, depending on the trial requirements.

The SAP and any updates will be circulated for review and comment to the CI and TM, and where required for an external review e.g. Data Monitoring Committee (DMC), TSC.

Any changes to the SAP during the trial must be documented, and the reasons for change noted and an assessment made of the need for a protocol amendment. Any changes made before unblinding must be fully justified and communicated in the report of the results of the trial.

4.2 Approved versions

The SAP must be ratified by the relevant trial oversight group(s) e.g. TSC, DMC.

The SAP will include sufficient details for any suitably qualified statistician to replicate the analysis.

The SAP will include a set of dummy data tables reflecting the contents of the final report(s).

5. References

- Gamble, C., et al. (2017). "Guidelines for the Content of Statistical Analysis Plans in Clinical Trials." JAMA 318(23): 2337-2343.
- Health Research Authority website (HRA) - http://www.hra.nhs.uk/
- Medicine and Healthcare products Regulatory Agency website (MHRA) - https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency/services-information
- UK policy framework for health and social care research (2017) - https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/
- UK Medicine for Human Use (Clinical Trials) Regulations 2004 - http://www.legislation.gov.uk/uksi/2004/1031/contents/made

It is assumed that by referencing the principal regulations that all subsequent amendments are included in this citation.

6. Associated Documents

Number	Title	Location
STU-AD-TMP-009	SAP Template	Q-Pulse

7. Abbreviations

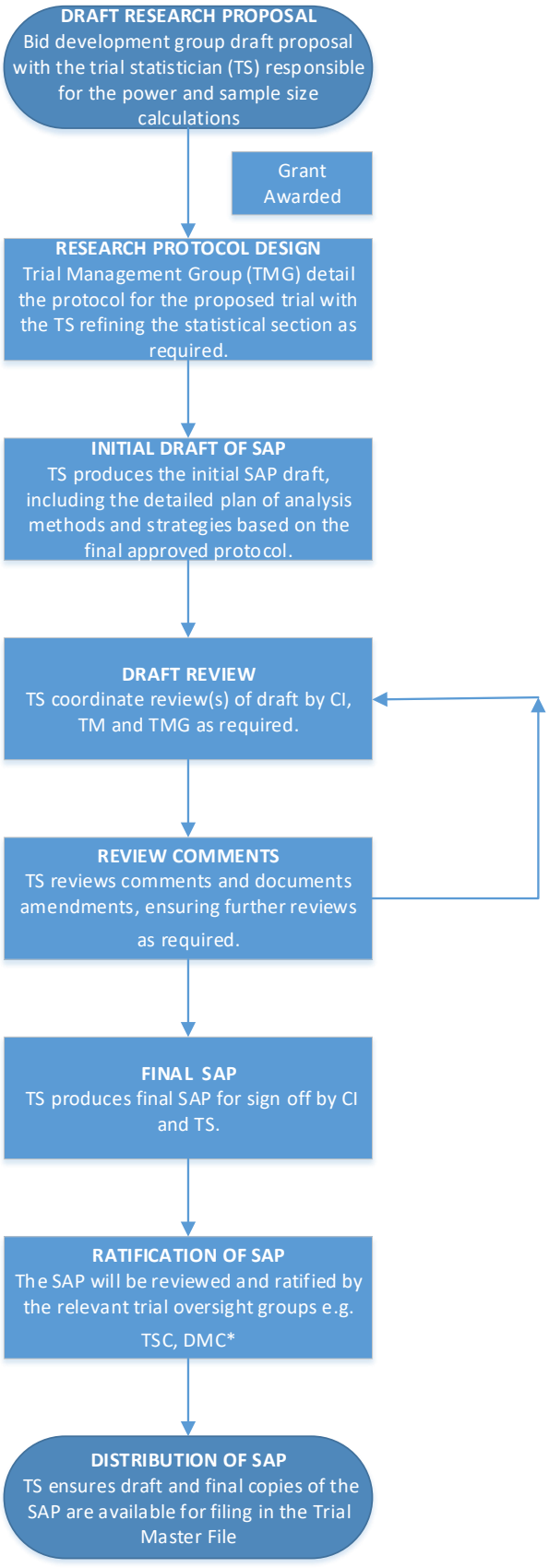
List of Abbreviations	
CI	Chief Investigator
CRF	Case Report Forms
CTIMP	Clinical Trial of an Investigational Medicinal Product
DMEC	Data Monitoring and Ethics Committee
GCP	Good Clinical Practice
MHRA	Medicines and Healthcare products Regulatory Agency
PI	Principal Investigator
SOP	Standard Operating Procedure
STU	Swansea Trials Unit
TM	Trial Manager
TMF	Trial Master File
TS	Trial Statistician
TSC	Trial Steering Committee
SAP	Statistical Analysis Plan
SHEAP	Statistical and Health Economics Analysis Plan

8. Appendices

Appendix 1: Document History

Version No:	3	**Effective Date:**	22-Apr-2024
Description of changes:	Update to Template v5		

Appendix 2: SAP Development Process Flowchart



* DMC emergency reviews of safety data may result in an amendment to the protocol and subsequently to the SAP. Any SAP amendments will follow the same development procedure as above.