RD&I	NHS University Hospitals Plymouth NHS Trust **STANDARD OPERATING PROCEDURE**

DO NOT USE THIS SOP IN PRINTED FORM WITHOUT FIRST CHECKING IT IS THE LATEST VERSION

The definitive versions of all UHPNT RD&I Dept SOPs appear online, not in printed form, to ensure that up to date versions are used. If you are reading this in printed form check that the version number and date below is the most recent one as shown on the Trust's website: https://www.plymouthhospitals.nhs.uk/research-sops

Statistical Analysis Plans (SAPs)

SOP No: P17

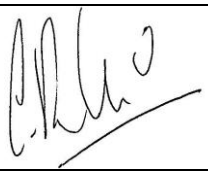
Version No: 2.1

Effective Date: Jan 2019

Supersedes: Version 2.0, Sep 2017

Page: **1** of **6**

Last Review Date: Jan 2019 Next review date: Sep 2022

	APPROVED BY
Name:	Chris Rollinson
Job Title:	Research Governance Manager
Signature:	
Date:	21st Jan 2019

1 Purpose and Scope

To define the content of the statistical analysis plan for research studies.

The statistical analysis plan should be a comprehensive and detailed description of the methods and presentation of data analyses proposed for a clinical trial, to avoid post hoc decisions that may affect the interpretation of the statistical analysis. The statistical analysis plan will be determined for individual research studies by discussion between the statistician and the principal investigator.

The definition of the statistical analysis plan will include all those procedures that are required to write a statistical analysis plan in accordance with the protocol, the principles of Good Clinical Practice (GCP) and the applicable statutory and regulatory requirements.

In scope: research sponsored by University Hospitals Plymouth NHS Trust (UHPNT). Statistical analysis plan responsibilities may be transferred in writing to other groups outside UHPNT.

Definitions

PI	Principal Investigators
CI	Chief Investigator
GCP	Good Clinical Practice
RD&I	Research Development & Innovation
SOP	Standard Operating Procedure
UHPNT	University Hospitals Plymouth NHS Trust

2 Who should read this document?

All staff involved in setting up and analysis of research e.g. Chief Investigators (CI), Principal Investigators (PI), Research Nurses & Midwives and RD&I Managers.

3 Procedure to Follow

The statistical methods to be used for the analysis of the trial data should be included in the protocol.

The details provided in the protocol may be sufficient, but if not, a separate statistical analysis plan document that provides full details should be written (See SAP Template at http://staffnet.plymouth.nhs.uk/Departments/ResearchandDevelopment/Documents.aspx?folderId=6999&view=gridview&pageSize=10.

The statistical analysis plan should be finalised prior to data analysis and before any treatment unblinding. It should to provide full details, if necessary including templates of tables, listings and figures of what will be presented in the statistical report. Any changes between methods in the protocol and analysis plan should be explained in the analysis plan.

The study statistician should review the data collection forms to ensure that primary and secondary outcome measures are collected appropriately to satisfy analyses described in the statistical analysis plan, and will update the statistical analysis plan to reflect changes to the forms and protocol during the conduct of the trial.

The statistical authorship of the analysis plan, version and date should be clear.

The statistical analysis plan should define the populations (e.g., intention-to-treat, as randomised, efficacy evaluable, etc.) to be used, and the analyses that these populations will be used in.

All primary and secondary outcomes should be clearly identified in the statistical analysis plan. If possible, a single primary measure of efficacy should be identified.

The statistical analysis plan should specify the hypotheses to be tested and any parameters that are to be estimated in order to meet trial objectives.

The statistical analysis plan should include, at a minimum, for each primary and secondary outcome measure:

- how the outcome will be measured
- any transformations on the data likely to be required before analysis
- appropriate statistical tests which will be used to analyse the data
- how missing data will be accounted for in the analyses
- methods for handling more than two treatment groups and multiple comparison methods
- any analysis subgroups

Consideration should be given to the following:

- methods for handling multiple observations
- rules for calculation of derived variables including definitions that can be programmed from the data
- use of baseline values and covariate data
- methods for handling multi-centre data
- treatment interactions, particularly with centre

- interim or sequential analyses
- rules for stopping the trial, and allowance for them in the analysis
- levels of statistical significance (one-tailed or two-tailed) and clinical relevance
- methods for handling outliers
- methods for point and interval estimation
- approach to handling concomitant medications
- definition of the safety population
- specification of computer systems and packages to be used for statistical analysis
- any sensitivity analyses

Provision should be made within the statistical analysis plan for checking the statistical model and then for alternative methods to be used if the test assumptions are not met.

The analysis plan should be compliant with the principles of GCP, particularly E9 (Statistical Principles for Clinical Trials) and E3 (Structure and Content of Clinical Study Reports).

The analysis plan should be circulated for review and comment to the Chief Investigator (CI) and or the Principal Investigator (PI), and any others who may usefully comment.

The statistical analysis plan should be reviewed / updated immediately before the blinded code is broken (or before analysis begins in an unblinded trial).

Changes in the statistical analysis plan should be justified and fully documented in the statistical report.

4 Document Ratification Process

The review period for this document is set as ***default of three*** years from the date it was last ratified, or earlier if developments within or external to the Trust indicate the need for a significant revision to the procedures described.

This document will be approved by the ***RD&I Manager or their Deputy***.

Non-significant amendments to this document may be made, under delegated authority from ***a Senior RD&I manager***, by the nominated author. These must be ratified by ***a Senior RD&I manager***.

Significant reviews and revisions to this document will include a consultation with ***appropriately knowledgeable staff***. For non-significant amendments, informal consultation will be restricted to ***staff*** who are directly affected by the proposed changes.

Dissemination and implementation

4.1. Dissemination of this SOP

4.1.1. New SOPs and new versions of existing SOPs: The Research Governance Manager will be responsible for ensuring authorised SOPs are uploaded on the RD&I intranet site. Internal Trust Staff are expected to use the RD&I intranet site to access latest versions of SOPs and to check the website regularly for updates.

Notice of new or amended procedural documents that have undergone a major amendment will be given *via* the following routes:

- Inclusion in the Trust weekly e-bulletin Vital Signs
- Direct email to Trust Researchers and or teams

4.2. Training in this SOP

4.2.1. All staff whose activities are subject to this SOP should ensure that they read and understand the content of the SOP.

5 Reference material

"Guidelines for Standard Operating Procedures for Good Statistical Practice in Clinical Research", written by the PSI Professional Standards Working Party

ICH Harmonised Tripartite Guideline for Statistical Principles for Clinical Trials E9, current step 4 version, dated 5 February 1998

ICH Topic E3, Structure and Content of Clinical Study Reports, Step 5 "Note for Guidance on Structure and Content of Clinical of Clinical Study Reports" (CPMP/ICH/137/95)

6 Amendment History

Version Number:	2.1
Date Of Amendment:	Jan 2019
Details Of Amendment:	Updated Trust and Dept. name; Reduce signature requirement to single senior RD&I Manager.

Version Number:	2.0
Date Of Amendment:	Aug 2017
Details Of Amendment:	Updated SOP template and numbering system. Reviewed and updated SOP.

Version Number:	1.1 (minor amendment)

Date of Amendment: Mar 2012

Details of Amendment: Cover page - Change of SOP location address.