York Foundation Trust R&D Unit
SOP
R&D/S85

Preparing a Statistical Analysis Plan

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SOP Reference:	R&D/S85
Version Number:	4.0
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Implementation date of current version:	15th July 2019

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	Date:	17th June 2019
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	Date:	17th June 2019

This SOP will normally be reviewed at least every 3 years unless changes to the legislation require otherwise

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Version History Log

This area should detail the version history for this document. It should detail the key elements of the changes to the versions.

Version	Date Implemented	Details of significant changes
1.0	2nd July 2012	
2.0	26th January 2015	Two year review
3.0	15th June 2017	Change of author and two year review. Minor formatting changes and update.
4.0	15th July 2019	Change of author. Change of link to R&D website and websites in Section 5. Reference to CONSORT statement added to section 1. Minor updates to section 4.

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Contents

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1 Introduction, Background and Purpose

The purpose of this SOP is to describe the purpose, content and preparation of a statistical analysis plan (SAP).

The methods to be used for statistical analysis should be outlined in the study protocol and the details provided in the protocol may be sufficient for certain studies (e.g. non CTIMPs) but, if not, a SAP should be produced. A SAP is a comprehensive and detailed description of the methods and presentation of the data analysis including both the main and any interim analyses. This is to avoid post hoc decisions that may affect the data analysis and its interpretation.

Statistical analyses of Clinical Trials of Investigational Medicinal Products (CTIMPs) should comply with the principles of Good Clinical Practice (GCP), particularly ICH E9 'Statistical Principles for Clinical Trials'.

The CONSORT 2010 Statement is a guideline for how parallel-group randomized controlled trials should be reported. Extensions of the CONSORT statement have been developed for different types of trial designs, interventions and data. These should be referred to during the development of the SAP.

2 Who Should Use This SOP

This SOP should be used by the Chief Investigator, Statistician, R&D Research Adviser and any other member of staff involved in the statistical analysis of research projects sponsored by York Teaching Hospital NHS Foundation Trust.

3 When this SOP Should be Used

This SOP applies to all research projects sponsored or co-sponsored by York Teaching Hospital NHS Foundation Trust.

4 Procedure(s)

The following procedures should be followed.

4.1 Determining the need for a Statistical Analysis Plan

The methods to be used for statistical analysis should be outlined in the study protocol and the details provided in the protocol may be sufficient for certain studies but, if not, a detailed SAP should be produced. The need for a SAP for individual studies will be decided by the R&D Unit in collaboration with the R&D Group when it considers the initial application for the Trust to act as study Sponsor. If a SAP is required, a decision about who will sign off the SAP, and when, will be taken at that time.

When a SAP is required, it should be written when the study is certain to proceed. In an unblinded trial it should be reviewed and finalised before any data analysis is begun. In a blinded trial, the SAP should be reviewed and possibly updated as

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a result of the blind review of the data but must be finalised before the blind is broken.

4.2 Content of the Statistical Analysis Plan

The plan should include:

1. The authorship of the SAP, its version number and the date it was signed off and by whom.

2. The number of subjects planned to be enrolled, the assumptions underpinning the sample size calculation and randomisation details.

3. A comprehensive and detailed description of the methods of the data analysis including both the main and any interim analyses as follows:

    - The objectives of the study

    - The hypotheses that are to be tested and /or the treatment effects that are to be estimated in order to meet the trial objectives

    - The population for analyses e.g. intention to treat, per protocol

    - All the primary and secondary outcomes for the study. If possible, one principal primary outcome should be identified

      For each outcome measure, the following information should be provided

        - How the outcome will be measured
        - How transformation of the data will be achieved if this is required
        - Which statistical tests will be used to analyse these outcome data
        - How missing data will be accounted for in the analysis

    - Level of statistical significance and whether one or two sided tests will be used (the use of one sided tests must be justified)

    - The following should also be considered / detailed where applicable:

        - Use of baseline values to improve precision or to adjust for potential baseline differences
        - Adjustment for influence of covariates
        - Methods for handling multicentre data
        - Methods for multiple comparisons
        - Methods for handling treatment interactions
        - Interim or sequential analyses and when these analyses will be performed
        - Rules for stopping the trial and allowance for this in the analysis
        - Methods for handling outliers
        - Methods for handling spurious data
        - Methods for handling withdrawals and protocol deviations
        - 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

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  - Sensitivity analyses
  - List of the tables and figures for presentation of the data

- Provision should be made for checking the statistical model and information provided about the alternative methods to be used if the test assumptions are not met.

- Any changes to the methods of analysis described originally in the study protocol and/ or a change in the sample size should be explained and justified in the SAP. Subsequent revisions to the SAP should also be justified.

- The analysis plan should be circulated for review and comment to the Chief investigator and/or the Principal Investigator and to others who may usefully comment. The SAP will be signed off in accordance with the requirements stipulated by the R&D Group.

- Links to open access articles for further guidance on what should be included in the SAP can be found in section 5.

The R&D Office have links to the University of York and could work with staff to obtain appropriate access to statistical support if required. In addition the Trust also has access to statistical software. If you wish to discuss statistical support for your research please contact the R&D Office for further details.

5 Related SOPs and Documents

Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031) and its subsequent amendments http://www.legislation.gov.uk/uksi/2004/1031/made

ICH Topic E6, Guideline for Good Clinical Practice (CPMP/ICH/135/95) July 2002, European Medicines Agency, http://www.emea.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500002874.pdf

ICH Topic E9, Statistical Principles for Clinical Trials (CPMP/ICH/363/96) September 1998, European Medicines Agency, http://www.emea.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500002928.pdf

CONSORT 2010 Statement and extension, http://www.consort-statement.org/

Guidelines for Standard Operating Procedures for Good Statistical Practice in Clinical Research, Statisticians in the Pharmaceutical Industry, June 2000.

Gamble et al. (2017) recommend a minimum set of items that should be addressed and included in Statistical Analysis Plans for clinical trials. https://jamanetwork.com/journals/jama/fullarticle/2666509

Yuan, I, Topjian, AA, Kurth, CD, et al. Guide to the statistical analysis plan. Pediatr Anesth. 2019; 29: 237– 242. https://doi.org/10.1111/pan.13576

R&D/S29 Data Management

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