Standard Operating Procedure for Design of Trials

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Revision Chronology:

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<td>JBRU/SPON/S03/01</td>
<td>22/01/2010</td>
<td>New SOP</td>
<td>Rumana Omar Julie Barber Gareth Ambler</td>
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ACRONYMS:

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<th>Acronym</th>
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<tr>
<td>JBRU</td>
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<td>GCP</td>
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Standard Operating Procedure for the Design of Trials

1. PURPOSE

This Standard Operating Procedure (SOP) has been written to describe the procedure for statistical design aspects of a trial involving statisticians of the JBRU Biostatistics Group. This document is intended for use by statisticians in the JBRU Biostatistics Group.

2. JOINT UCLH/UCL BIOMEDICAL RESEARCH UNIT POLICY

All SOPs produced from the JBRU must be used in conjunction with local NHS Trust and UCL policies and procedures.

The JBRU acts as the representative of the Sponsor and will be the official name used on all SOPs.

3. BACKGROUND

At the planning stage of the trial, the trial statistician will work within the trial team to develop the design and protocol.

4. SCOPE OF THIS SOP

This SOP applies to the statistical aspects involved in the design of a trial and should be followed for design of all trials where Biostatistics group members are the main trial statistician.

5. RESPONSIBLE PERSONNEL

The trial statistician should follow this SOP.

6. PROCEDURE

6.1. Overview of responsibility

The trial statistician takes overall responsibility for all statistical aspects of the trial design. They will be actively involved in methodological decisions and will take responsibility for drafting the statistical sections of the protocol (see SOP for Protocol writing). In particular the trial statistician will help choose an appropriate study design and will provide: a detailed sample size calculation (see SOP for calculating Sample Size); plans for creating randomisation lists (see SOP for producing randomisation lists); plans for interim analyses; and plans for final analysis (see SOP for Writing a Statistical Analysis Plan).

6.2. Areas for statistical consideration

The following describes areas where statistical input may be provided. The list is not intended to be exhaustive.

Study Design (see SOP for Protocol writing)

- Research question(s)
- Type of study design (e.g. parallel group, cross-over, cluster randomised, equivalence) and phase of study (I, II, III, pilot) according to the research question.
- Choice and definition of primary and secondary endpoints / outcomes
• Choice of comparison group (e.g. active control / placebo) if appropriate
• Use of method of randomisation
• Use of blinding

Data
• Source of the data (e.g. subject questionnaires, patient medical notes, electronic data, procedure)
• Time point(s) for collection (baseline, during treatment, at follow up point)
• Reasons for data collection (e.g. baseline comparisons, main outcome, important prognostic / explanatory variables)
• The form of the data (e.g. binary, continuous (numeric), time to event)
• Consideration of approaches to limit loss to follow-up / drop out, missing data and non compliance

Sample size calculation (see SOP for calculating Sample Size)
• Generally trials will be powered based on the analysis of the primary outcome(s) as defined in the trial protocol

Randomisation (see SOP for Producing Randomisation lists)
• The type (e.g. simple, block, stratified, minimisation) and implementation of randomisation
• Concealed allocation (e.g. sealed envelopes, telephone central allocation office, computerised randomisation)

Interim analysis and data monitoring
• Stopping guidelines for efficacy, safety and futility based on statistical analysis
• Adjustments to sample size calculation

Final statistical analysis (see SOP for Writing a Statistical Analysis Plan)
• The final analysis plan provided in the trial protocol will also be developed into a detailed Statistical Analysis Plan

Additional considerations
Cross over trials
  o Carry over and washout period
  o Within patient variation
  o Period effects and treatment by period interaction
Cluster randomised trials
  o Definition of cluster
  o Intraclass correlation
Equivalence / non inferiority trials
  o Definition of equivalence
Factorial trials
  o Treatment interaction (if investigating two interventions for the same disease simultaneously)

7. REFERENCES

8. APPENDICES

9. TEMPLATES/LOGS ASSOCIATED TO THIS SOP
10. SOP DISSEMINATION AND TRAINING

This SOP will be provided to all statisticians of the Biostatistics group by the SOP authors. BSG staff will be requested to read the SOP and will be given an opportunity to ask specific questions. BSG statisticians will then sign the SOP training log in section 12.

11. SIGNATURE PAGE

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<tr>
<th>Author and Job Title:</th>
<th>Rumana Omar, Julie Barber, Gareth Ambler</th>
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# 12. SOP TRAINING LOG

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