UNIVERSITY OF LEICESTER, LOUGHBOROUGH UNIVERSITY
&
UNIVERSITY HOSPITALS OF LEICESTER NHS TRUST

JOINT RESEARCH SUPPORT OFFICE

STANDARD OPERATING PROCEDURES

UHL Research Support Office
SOP S-1025 UHL V5 February 2019

Standard Operating Procedure for Convening a Data Safety Monitoring Committee for Research sponsored by University Hospitals of Leicester NHS Trust (UHL)

PGC Reference No: C28/2014

OFFICE BASE

Research & Innovation
Leicester General Hospital
Gwendolen Road
Leicester
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1. **Introduction**

This Standard Operating Procedure (SOP) describes the process to be adopted when convening a Data Safety Monitoring Committee / Board for research studies sponsored by the University Hospitals of Leicester NHS Trust (UHL).

The outcome is that where required, a Data Safety Monitoring Committee / Board (DSMC/B) for research sponsored by UHL is managed and convened using a consistent process.

2. **Scope**

This SOP applies to all research studies where a DSMC/B is required.

3. **Definition**

A Data Safety Monitoring Committee (DSMC) is a group of people, independent of the trial team, who review accumulating data and advise the Sponsor (directly or indirectly) on the continuing and future management of a research study. A DSMC mainly review safety and efficacy data, but where appropriate may also be asked to review quality and compliance data.

The DSMC is usually 'unblinded' and therefore is privy to interim comparisons by arm. They often see data in a format that is not normally widely shared beyond the DSMC, or a statistical analysis team.

4. **Which research studies require Data Safety Monitoring Committees?**

The decision about whether or not a DSMC is required, will depend on a number of factors including the patient population, indication, complexity, duration and end-points of the trial. The decision will be made in collaboration with the Chief Investigator and will be considered as part of the Sponsor risk assessment. There may also be a requirement from the funding award body as a condition of funding.

UHL as Sponsor would expect that a DSMC be established for research studies involving:

- subjects with life-threatening illnesses
- vulnerable populations
- studies where there is prior knowledge or strong suspicion that a treatment under consideration has the potential to harm patients (even though being eventually more effective than treatments already available), or
- unknown or uncertain risks.

DSMCs may be appropriate for all types of research studies, including those not using Investigational Medicinal Products e.g. research studies of surgical interventions or radiotherapy.

Where a discussion about whether a DSMC is required occurs, the evidence of the discussion must always be recorded in the Trial Master File (TMF). Subsequent plans to establish a DSMC or put other formal safety monitoring arrangements in place must be described in the protocol.
5. Who sits on a Data Safety Monitoring Committee?

DSMC members are generally experienced trialists and it is recommended that at least one member of a committee has served previously on a DSMC. A formal DSMC usually consists of three (3) or more people comprising clinicians and at least one statistician.

6. How is the role of the Data Safety Monitoring Committee described?

The role and function of the DSMC should be described in writing before the DSMC reviews any trial data. This can be described in a Charter which covers the membership, roles and remit, permissible recommendations, frequency and organisation of meetings, how decisions are reached, whether they are advisory or executive and who they report to (how and when). A DSMC should be fully functional before enrolment to enable it to respond to any safety signal.

A suggested template charter is provided in Appendix 1.

7. Independence of the Data Safety Monitoring Committee

The DSMC members must ensure that any potential competing interests are declared at the outset and any new competing interests recorded in the record of each DSMC Meeting.

DSMC meetings to review unblinded data will be “closed” meetings at which the Sponsor and trial team will not be present. The DSMC may also hold “open” meetings with the Sponsor to discuss conclusions and recommendations.

8. Reporting Responsibilities

It is the role of the DSMC to make recommendations to the Sponsor on trial conduct, such as the need to amend the protocol or to terminate the trial early. This is normally done directly with the Sponsor, unless a Trial Steering Committee (TSC) has also been set up, in which case the DSMC may report to the TSC.

It is the responsibility of the Sponsor to communicate DSMC recommendations to the Competent Authority and REC in an appropriate manner. If such recommendations require implementation of an urgent safety measure it must be ensured that this is reported to the Competent Authority and REC in the required timeframe. The Sponsor should notify the REC of any recommendations made by the DSMC and provide summary reports where appropriate. It is not necessary for the REC to see minutes of DSMC meetings.

Similarly it is important that any outputs from the DSMC are clearly documented to ensure that the data used to make decisions are robust and the decisions themselves are documented and retained. It is advised that the documentation verifies who prepared and checked any reports and listings - this being particularly important if unblinded reviews are taking place to provide evidence that the trial team remained blinded.
### 9. Responsibilities

<table>
<thead>
<tr>
<th>Responsibility</th>
<th>Undertaken by</th>
<th>Activity</th>
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<tbody>
<tr>
<td>1 Sponsor</td>
<td>Head of Research Operations or their delegate</td>
<td>Discuss with CI the requirements for a DSMC</td>
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<td>2 Chief Investigator</td>
<td>Chief Investigator or their delegate</td>
<td>Coordinate with the Sponsor the set up of a DSMC</td>
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<tr>
<td>3 Chief Investigator &amp; Sponsor</td>
<td>Head of Research Operations or their delegate</td>
<td>Ensure DSMC Charter is completed and Chair appointed</td>
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<td>4 DSMC</td>
<td>DSMC Chair</td>
<td>Ensure Sponsor receives copies of open DSMC meeting minutes</td>
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<tr>
<td>5 Sponsor</td>
<td>Head of Research Operations or their delegate</td>
<td>Ensure appropriate regulatory authorities &amp; REC are notified of any changes required as a result of DSMC discussions or Urgent Safety Measures.</td>
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### 10. Legal Liability Statement

Guidelines or Procedures issued and approved by the Trust are considered to represent best practice. Staff may only exceptionally depart from any relevant Trust guidelines or Procedures and always only providing that such departure is confined to the specific needs of individual circumstances. In healthcare delivery such departure shall only be undertaken where, in the judgement of the responsible healthcare professional it is fully appropriate and justifiable – such a decision must be fully recorded in the patient’s notes and in the research site file.
This table is used to track the development and approval of the document and any changes made on revised/reviewed versions.

### DEVELOPMENT AND APPROVAL RECORD FOR THIS DOCUMENT

<table>
<thead>
<tr>
<th>Author / Lead Officer</th>
<th>Job Title: Medical Writer, Clear Clinical Research Ltd / UHL</th>
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<tbody>
<tr>
<td>Joanne Thompson / Carolyn Maloney</td>
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<tr>
<td>Reviewed by:</td>
<td>UHL R&amp;I Management Meeting</td>
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<tr>
<td>Approved by:</td>
<td>Professor Nigel Brunskill</td>
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<td>Date Approved:</td>
<td>11-03-19</td>
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### REVIEW RECORD

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<th>Issue No</th>
<th>Reviewed By</th>
<th>Description Of Changes (If Any)</th>
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<tr>
<td>April 2015</td>
<td>2</td>
<td>Carolyn Maloney</td>
<td>Addition of Responsibilities table, changes to name and Logo.</td>
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<tr>
<td>September 2016</td>
<td>3</td>
<td>CM, LW, JJ</td>
<td>Checks for consistency adding HRA process.</td>
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<tr>
<td>February 2017</td>
<td>4</td>
<td>Carolyn Maloney</td>
<td>Update to logo.</td>
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<tr>
<td>February 2019</td>
<td>5</td>
<td>CM / Clear Clinical</td>
<td>Consistency checks. Rewording to mirror national phrases.</td>
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### DISTRIBUTION RECORD:

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Appendix 1
Data Safety Monitoring Committee Charter for University Hospitals of Leicester NHS Trust
Sponsored Research (Suggested Template)

1. INTRODUCTION
1.1 Name (& Sponsor's ID) of trial
1.2 Objectives of trial, including interventions being investigated
1.3 Outline of scope of charter

2. ROLES AND RESPONSIBILITIES
2.1 A broad statement of the aims of the committee
2.2 Terms of reference
2.3 Specific roles of DSMC

3. BEFORE OR EARLY IN THE TRIAL
3.1 Whether the DSMC will have input into the protocol
3.2 Whether the DSMC will meet before the start of the trial
3.3 Any issues specific to the disease under study
3.4 Any specific regulatory issues
3.5 Any other issues specific to the treatment under study
3.6 Whether members of the DSMC will have a contract

4. COMPOSITION
4.1 Membership and size of the DSMC The Chair, how they are chosen, and the chair's role (Likewise, if relevant for the vice-Chairman)
4.2 The responsibilities of the DSMC statistician
4.3 The responsibilities of the trial statistician
4.4 The responsibilities of the trials unit team
4.5 The responsibilities of the Chief Investigator and other members of the Trial Management Group (TMG)

5. RELATIONSHIPS
5.1 Relationships with Chief Investigators, other trial committees (e.g. Trial Steering Committee)
5.2 Clarification of whether the DSMC is advisory (make recommendations) or executive (make decisions)
5.3 Payments to DSMC members
5.4 The need for DSMC members to disclose information about any competing interests
6. **ORGANISATION OF MEETINGS**
6.1 Expected frequency of DSMC meetings
6.2 Whether meetings will be face-to-face or by teleconference
6.3 How DSMC meetings will be organised, especially regarding open and closed sessions, including who will be present in each session

7. **TRIAL DOCUMENTATION AND PROCEDURES TO ENSURE CONFIDENTIALITY AND PROPER COMMUNICATION**
7.1 Intended content of material to be available in open sessions
7.2 Intended content of material to be available in closed sessions
7.3 Whether or not the DSMC will be blinded to the treatment allocation
7.4 The people who will see the accumulating data and interim analysis
7.5 Responsibility for identifying and circulating external evidence (e.g. from other trials/ systematic reviews)
7.6 To whom the DSMC will communicate the decisions/ recommendations that are reached
7.7 Whether reports to the DSMC be available before the meeting or only at/during the meeting
7.8 What will happen to the confidential papers after the meeting?

8. **DECISION MAKING**
8.1 What decisions/recommendations will be open to the DSMC
8.2 The role of formal statistical methods, specifically which methods will be used and whether they will be used as guidelines or rules
8.3 How decisions or recommendations will be reached within the DSMC
8.4 When the DSMC is quorate for decision-making
8.5 Can DSMC members who cannot attend the meeting input
8.6 What happens to members who do not attend meetings
8.7 Whether different weight will be given to different end points (e.g. Safety/efficacy)
8.8 Any specific issues relating to the trial design that might influence the proceedings e.g. cluster trials, equivalence trials, multi-arm trials

9. **REPORTING**
9.1 To whom will the DSMC report their recommendations/decisions, and in what form
9.2 Whether minutes of the meetings be made, if so by whom, and where will they be kept
9.3 What will be done if there is a disagreement between the DSMC and the body to which it reports

10. **AFTER THE TRIAL - Publication of results**
10.1 The information about the DSMC that will be included in published reports
10.2 Whether the DSMC will have the opportunity to approve publications especially with respect to reporting of any DSMC recommendations regarding termination of a trial
10.3 Any constraints on DSMC members divulging information about their delivery after the trial has been published