UNIVERSITY OF LEICESTER

University of Leicester Research Governance Office

Standard Operating Procedures

SOP S-1028 UoL

Convening a Data Safety Monitoring Committee for Research Sponsored by the University of Leicester (UoL)

Version 4.0 November 2024

Effective Date: December 2024

This SOP will be implemented in line with this document's effective date for all UoL Sponsored research still in set up. For active clinical research that is already in the recruitment phase (or further) at the time of implementation, this SOP must be implemented within 3 months of the effective date.

Please note the appendices associated with this SOP may be subject to interim changes. Please ensure that appendices are downloaded from the RGO webpages prior to use to ensure the latest version of the document is being used. For active studies there is no requirement to update appendices to the latest version.

1.0 Introduction and Scope

This Standard Operating Procedure (SOP) defines the circumstances under which a Data Safety Monitoring Committee (DSMC) is required, and describes the process to be adopted when convening a DSMC for research studies sponsored by the University of Leicester (UoL).

2.0 Definition

Procedures must be in place to ensure that for patients participating in research there is no unavoidable increased risk for harm and to ensure that the research continues for an adequate period of time and is not stopped too early to answer its scientific questions.

The DSMC is a group of people, independent of the research team, who assess the progress, safety data and, if needed critical efficacy endpoints of a study/trial by reviewing the accumulating data and advising 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. DSMCs also go under different names like Data (Safety) Monitoring Board, Data Monitoring Committee or Data Monitoring and Ethics Committee

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. Therefore, care must be taken to ensure that blinded research staff do not inadvertently see or have access to the unblinded report(s) used by the DSMC.

The Sponsor and the investigators bear the final responsibility for the conduct of the trial. This responsibility cannot be delegated to a DSMC.

3.0 Which research studies require Data Safety Monitoring Committees?

There may be occasions when a DSMC forms part of the oversight and management of a study. The decision about whether or not a DSMC is required will depend on the complexity, duration and end-points of the research. The decision will be made in collaboration with the Chief Investigator, and will be considered as part of the Sponsor review process(S-1002) (and where applicable, the Sponsor Risk Assessment S-1003). There may also be a requirement from the funding award body as a condition of funding.

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

- Clinical Trials of Investigational Medicinal Products (CTIMPs)
- Medical Device Trials
- subjects with life-threatening illnesses
- vulnerable populations and/or with significant potential risk of harm, or
- unknown or uncertain risks

DSMCs may be appropriate for all types of randomised research studies, including those not using Investigational Medicinal Products/Medical Devices (e.g., interventional research (surgical/radiotherapy/clinical practice), and/or large multi-centre research, research with a long duration, complex endpoints, and/or certain populations (i.e., paediatric, those lacking mental capacity).

The European Medicines Agency (EMA) Guidance on Data Monitoring Committees provides an overview of when a DSMC may be required.

Where a discussion about whether a DSMC is required occurs, the evidence of the discussion must always be recorded (i.e., in the Sponsor review documentation and/or the Sponsor Risk

Assessment) and stored 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.

4.0 Who sits on a Data Safety Monitoring Committee?

DSMC work is a multidisciplinary task, therefore a DSMC needs expertise from different scientific areas. Clearly there is a need for qualified clinicians to assess the clinical aspects of safety and/or efficacy monitoring. But, as often statistical methods will be applied in the monitoring process, biostatistical expertise should also form part of a DSMC. Furthermore, as ethical aspects are important especially in safety monitoring, the inclusion of a member with expertise in ethical questions might be appropriate. A formal DSMC usually consists of three (3) or more people comprising clinicians and at least one statistician but for practical reasons the number of members of a DSMC should be limited. It is recommended that at least one member of a committee has served previously on a DSMC. Ideally, all individuals should be independent of the Sponsor, Trial Management Group (TMG)/Trial Steering Committee (TSC) and not part of the same institution as any of the applicants or members of the research team.

5.0 DSMC Charter

The role and function of the DSMC should be described in writing before the DSMC reviews any data. This should 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 suggested template charter is provided in Appendix 1 alongside a DSMC Member Signature Page (Appendix 2).

It should be clear within the Charter that only appointed members are entitled to vote and the Chair will have a casting vote.

6.0 Conflicts of Interest

The DSMC members must ensure that any possible conflicts of interests are declared at the outset (Appendix 3 – 'Conflicts of Interests Form' can be used here) and any new conflicts of interests are declared and recorded in the minutes of each DSMC Meeting.

DSMC meetings to review unblinded data will be "closed" meetings at which the Sponsor and blinded members of the research team will not be present. The DSMC may also hold "open" and/or "executive session" meetings with the Sponsor to discuss conclusions and recommendations.

7.0 Reporting Responsibilities

It is the role of the DSMC to make recommendations to the Sponsor on the continuing and future management of a research study. For example, the DSMC may recommend the need to amend the protocol and/or to terminate the research 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/or REC in an appropriate manner. If DSMC recommendations require the implementation of an Urgent Safety Measure (USM) it is important that the USM is implemented immediately and then subsequently reported to the Competent Authority and/or REC in accordance with the required timeframe and SOP S-1029. Where appropriate, the Sponsor should notify the REC of any recommendations made by the DSMC that impact participant safety and/or the conduct of the research and provide summary reports where appropriate. It is not necessary for the REC to see minutes of DSMC meetings, however meeting minutes and

recommendations letters should be provided to the Sponsor for their records and should be filed in the TMF (as appropriate e.g. at the end of the study/trial for closed reports).

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 research team remained blinded.

8.0 Responsibilities

Responsibility	Undertaken by	Activity
Sponsor	Head of Research Governance or their delegate	Discuss the requirement for a DSMC with the Chief Investigator, and where applicable, record the outcome of this discussion within the Sponsor review documentation and/or the Sponsor Risk Assessment
Chief Investigator	Chief Investigator	Coordinate with Sponsor the set-up of a DSMC
Chief Investigator and Sponsor	Chief Investigator or their delegate	Ensure DSMC charter is completed and Chair appointed
DSMC	Chair	Ensure Sponsor receives copies of open DSMC meeting minutes
Sponsor	Head of Research Governance, Chief Investigator, Principal Investigator or their delegate	Ensure that all investigators are notified of (and implement) any changes required as a result of DSMC discussions, especially if these result in an Urgent Safety Measures
Sponsor	Head of Research Governance or their delegate	Ensure that the relevant regulatory authorities are notified of any changes required as a result of DSMC discussions

9.0 Development and approval Record for this document

This table is used to track the development and approval of the document.

Author	Job title	Reviewed by	Approved by	Date approved
Cat Taylor	Head of Research Governance	UoL Research Sponsorship Management and Operation Group (RSMOG)	Professor Nigel Brunskill 	27/11/2024

10.0 Review Record

This table is used to track any changes made on revised/reviewed versions

Date	Issue Number	Reviewed By	Description Of Changes (If Any)
April 2015	2	UoL RSMOG	Minor administrative changes, including version and dates in footer. Responsibilities table added. Addition of Loughborough University to front page
Nov 2016	3	Diane Delahooke	Logo change, change of RGO address, consistency checks against UHL.
Sept 2021	3.1	Cat Taylor	Administrative changes
November 2024		Cat Taylor	• Removal of office address • Removal of distribution record • Review schedule updated to every 3 years • Administrative Changes • Updates to wording to provide clarity, particularly around when a DSMC is required and its composition. • Major Change to Appendix 1 – DSMC charter, to provide more guidance on the content of the Charter. • Addition of Appendix 2 'Charter Signature Page' and Appendix 3 'Conflicts of Interest Form'.