York Foundation Trust R&D Unit
Standard Operating Procedure
R&D/S72

Data Monitoring Committees for Clinical Trials

IT IS THE RESPONSIBILITY OF ALL USERS OF THIS SOP TO ENSURE THAT THE CORRECT VERSION IS BEING USED

All staff should regularly check the R&D Unit's website and/or Q-Pulse for information relating to the implementation of new or revised versions. Staff must ensure that they are adequately trained in the new procedure and must make sure that all copies of superseded versions are promptly withdrawn from use unless notified otherwise by the SOP Controller.

The definitive versions of all R&D Unit SOPs appear online. 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 R&D Unit website: www.research.yorkhospitals.nhs.uk/sops-and-guidance-/ and/or Q-Pulse

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	Date:	24th June 2019
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	Signature:	Signed copy held by R&D Unit
	Date:	24th June 2019

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

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	7th November 2011	
2.0	24th March 2014	Removal of references to the North and East Yorkshire R&D Alliance. Removal of Head of R&D and inclusion of Director of ALAR for urgent recommendations.
3.0	24th August 2017	Two year review, no changes necessary
4.0	22nd July 2019	Change of link to R&D website.

Contents

1 Introduction, Background and Purpose

A Data Monitoring Committee (DMC) — sometimes called a Data and Safety Monitoring Board (DSMB) — is an independent group of experts who monitor patient safety and treatment efficacy data while a clinical trial is ongoing.

The need to establish a Data Monitoring Committee (DMC) depends on the nature of the trial, and is not a legal requirement. Guidance on DMCs is available from a number of sources, in particular:

- The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMEA) has published guidelines at: http://www.ema.europa.eu/ema/
- Guidance from the Health research Authority (HRA) is available at: http://www.hra.nhs.uk/documents/2013/10/data-monitoring-committees-in-clinical-trials.pdf

Sponsors are strongly recommended to establish DMCs for certain kinds of clinical trial, for example those with predicted high morbidity or mortality, or double-blind trials with unknown or uncertain risks.

The DMC is a group (typically 3 to 7 members) who are independent of the sponsor of the trial. At least one DMC member will be a statistician. Clinicians knowledgeable about the disease indication should be represented, as well as clinicians knowledgeable in the fields of any major suspected safety effects (e.g. nephrology, cardiology).

The DMC will convene at predetermined intervals (three to six months typically) and may review unblinded results. The role of the DMC is to review safety and efficacy data, perform interim analyses and provide independent oversight and validation of decisions to continue with a trial. The DMC has the power to recommend termination of the study. There are typically three reasons a DMC might recommend termination of the study: safety concerns, outstanding benefit, and futility.

When the Trust is sponsor or co-sponsor for a study, an assessment will be made by the R&D Group as to whether a DMC should be established for the trial. The Clinical Trial Risk Assessment (R&D/S18) will be used to inform this decision.

2 Who Should Use This SOP

This SOP is aimed at:

- Chief Investigators (CIs), trial co-ordinators, and other professional or administrative research staff, in the investigator team or in support departments, working on clinical trials sponsored or co-sponsored by the Trust;
- R&D Unit personnel;
- Members of the R&D Group;

- Members of DMCs for Trust sponsored or co-sponsored clinical trials.

3 When this SOP Should be Used

This SOP should be used when establishing a DMC for a Trust sponsored or co-sponsored trial and throughout the conduct of that trial.

4 Procedure(s)

4.1 Requirement to establish a DMC

The R&D Group will be responsible for determining whether a DMC is required to be established for a trial sponsored or co-sponsored by the Trust. The Clinical Trial Structured Risk Assessment (R&D/S18) will help to inform this decision.

4.2 Who should establish a DMC

If a DMC is required to be established then this will be the responsibility of the appropriate Sponsor representative. The membership and terms of reference of the DMC will be informed by the nature of the trial.

4.3 Membership of the DMC

The DMC will usually be made up of 3-7 members who are independent of the trial. A minimum of 3 members should be appointed. Membership will include as a minimum (i) a statistician (ii) a clinical expert in the field of the research, and (iii) an experienced researcher. Additional individuals may be invited by the DMC Chairperson to attend to inform DMC meetings as necessary.

4.4 The Role of the Sponsor

The Sponsor will not be represented on the DMC but a Sponsor representative may attend meetings (as requested by the DMC Chairperson) to inform or assist the Committee. Sponsor representatives must not attend closed sessions where unblinded data may be reviewed or discussed.

4.5 DMC Terms of Reference

The trial DMC will 'meet' prior to participant recruitment where possible to agree Terms of Reference and to finalise membership. An example DMC Terms of Reference is available (see section 5). A Chairperson will be appointed (if not already agreed). The agreed Terms of Reference will be signed by all members of the DMC and filed in the Sponsor File.

4.6 DMC Meeting Schedule

At the initial meeting of the DMC the Committee will agree the proposed timing of meetings for the duration of the trial. The proposed schedule can be adapted as required. The trial sponsor representative may request that the DMC meets at any point during the trial as a result of any concerns it may have. Such a meeting may need to be convened immediately and the DMC members must be responsive to such a request.

4.7 DMC Meetings

The Sponsor representative will liaise with the Investigator team and DMC Chairperson to ensure that meetings are held in a timely fashion. The Sponsor representative (or delegate) will assist with organising logistical arrangements for the meeting and providing information to inform meetings as requested by the DMC. The Sponsor representative may minute meetings where he/she attends by agreement with the DMC Chairperson. Where Sponsor representative presence is not appropriate then a DMC member will be responsible for taking minutes and the DMC Chairperson is responsible for retaining these confidentially until the close of the trial whereupon they will be returned to the Sponsor.

4.8 Review of Unblinded Trial Data

Should the DMC be required to review unblinded data during the trial then the sponsor must approve the unblinding. Although the request must be made by the Sponsor on behalf of the DMC, the code break(s) must be supplied directly to the DMC Chairperson and not to the Sponsor.

4.9 Communication following DMC Meetings

The Sponsor Representative will be informed of any recommendations by the DMC in writing within 10 working days of the meeting. Recommendations received by the R&D Unit (on behalf of the Sponsor) will be communicated to the R&D Group at the next scheduled meeting (for non urgent recommendations) and to the investigators.

Any urgent recommendations following a DMC meeting must be informed within 2 working days to the Head of R&D and the Sponsor Representative. The Head of R&D (or in his/her absence the Research Adviser or Sponsor Representative) must take necessary action without delay. The DMC recommendations and remedial action taken must be communicated with the Chairperson of the R&D Group and the Investigators as soon as possible and to the R&D Group at the next scheduled meeting. All such communications must be documented and filed in the Sponsor File.

4.10 Carrying out DMC Recommendations

The R&D Group will usually take on the role of Trial Steering Committee for trials sponsored or co-sponsored by the Trust. The R&D Group will therefore, on behalf of the Sponsor, receive recommendations from the DMC and act accordingly. All recommendations and resulting actions will be fully documented in the Sponsor File.

5 Related SOPs and Documents

R&D/S18	Clinical Trial Risk Assessment
R&D/T27	DMC Terms of Reference Template