Standard Operating Procedure

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Title:	Data Monitoring Committee and Trial Steering Committee		
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Author:	Mohammed Zubair	**Review Date**	August 2018
Reviewed by : Prof Deborah Symmons		**Approved By:** Prof Nalin Thakkar	
Position: Chair of Clinical Trials Management Group		**Position:** Associate Vice President for Research Integrity	
Signature: 		**Signature:** 	

Version	Date	Reason for change
1.1	**May 2014**	**Addition of version control statement for SOP**
2.0	**October 2015**	**Update of weblinks and office details**
3.0	**August 2016**	**Update of weblinks and office details**

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1.0 Background

The EU Good Clinical Practice (GCP) Directive 2001/20/EC was introduced to establish standardisation of research activity in Clinical Trials throughout the European Union. It was transposed into UK law as the Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031) which came into force on 1st May 2004. The Medicines for Human Use (Clinical Trials) Regulations together with subsequent amendments will be referred to as the Regulations in the rest of this document.

The period of time over which a clinical trial of an investigational medicinal product (CTIMP) is conducted can be lengthy. Over that period of time it is important to ensure that the CTIMP is conducted to the highest ethical and scientific standards. This means periodically reviewing the conduct and output of the trial from the perspective of patient safety in order to ensure that patients participating in the trial are not exposed to any increased risk of harm, which could have been prevented and that ,where necessary, the trial protocol be amended or the trial ended early . This oversight can be achieved through a number of different bodies. These bodies are the Ethics committees (which are mandatory for each clinical trial), a Data Monitoring Committee (which is appointed at the request of the study funder and/or Sponsor), and a Trial Steering Committee (which is required in large clinical trials and is also appointed at the request of the study funder and/or sponsor). One remit of these bodies is to ensure that patients are not exposed to any increased risk of harm which is avoidable. The final responsibility for the conduct of the clinical trial rests with the Sponsor.

Data Monitoring Committee

An independent Data Monitoring Committee (DMC) comprises a group of experts who are external to the clinical trial. The DMC reviews, in an ongoing manner, the accumulating data from the clinical trial. It mainly reviews the safety and efficacy data and may also see quality and compliance data. The DMC will usually have access to any interim data analysis resulting from the clinical trial. The DMC advises the Sponsor on the future conduct of the trial.

Trial Steering Committee

In large multicentre clinical trials a Trial Steering Committee (TSC) is usually required. The appointment of a TSC is usually required by the funder and as the Sponsor The University of Manchester may request the convening of a one. The TSC acts as a body that takes responsibility for the scientific integrity of a clinical trial. The TSC can comprise investigators, clinical experts who are not directly involved in the clinical trial and representatives of the sponsor. A TSC often takes responsibility for the scientific validity of the study protocol, assessment of study quality and conduct as well as for the scientific quality of the final study report. The TSC should not usually have access to unblinded study data.

1.1 Purpose

This SOP outlines when and how the University of Manchester, as the study sponsor, will require a DMC to be constituted. It also describes the composition and roles of a DMC.

All CTIMPs sponsored or co-sponsored by The University of Manchester will be risk assessed and a decision will be made whether a DMC is required. The University of Manchester as a potential sponsor will also consider and accept, where necessary, the terms and conditions of the funding body if these specify that a DMC be established.

1.2 Procedure

The University of Manchester, in its role as the sponsor, is responsible for the conduct of a CTIMP. The University has a nominated Person Responsible (PR) who will oversee the conduct and management of all non-commercial clinical trials sponsored/co-sponsored by The University of Manchester. The PR will chair the University's Clinical Trials Management Group (CTMG).

Data Monitoring Committee

Where the University of Manchester has been approached to consider sponsorship of a CTIMP, a risk assessment will be undertaken. The CTMG will then determine whether a DMC is required based on the results of the risk assessment where this is not a requirement of funding. Examples of situations where a DMC may be required include (i) when the aim of the CTIMP is to consider the safety and/or efficacy of an IMP; (ii) where there are limited data on whether the IMP may potentially harm the patient; and (iii) if an interim analysis is planned and a decision needed as to whether the CTIMP should be stopped early if the primary question has been answered or recruitment is low.

Composition of a DMC

The DMC members must be experts in their fields and must be independent of the conduct and management of the CTIMP. The DMC members must declare any conflicts of interest, and if there may be any major conflict of interest the DMC member must remove his/her self immediately. All the DMC members will be required to commit the necessary time needed to perform their duties. The DMC will be provided with blinded or un-blinded reports on study data and must abide by any request of confidentiality as required by the funder and the sponsor.

The DMC should have at least three members. The Chair of the DMC must have previous experience of sitting on a DMC. A DMC should have an experienced biostatistician in their membership. Any clinical members should be chosen because of their expertise in the area of medicine in which the trial is being conducted. In addition the clinical member should, ideally, have knowledge and where possible experience of potential adverse effects of the treatment being studied. The composition of the DMC should be notified to the CTMG as should any change in membership during the course of the trial.

Establishing the DMC

The DMC must be appointed as soon as possible after the trial has been funded. Ideally it should have input into the safety aspects of the protocol and the related data to be collected.

The DMC should have a preliminary meeting before any data are reviewed, in order to have a clear understanding of its responsibilities, agree the frequency with which it will meet, and to whom it will report its findings. All DMC members must maintain the confidentiality of information and other intellectual property, including both blinded and unblinded clinical trial data. The Sponsor will require that the DMC be informed of any relevant findings.

The following must be agreed with the Sponsor before a DMC can be approved:

1. Sign a confidentiality agreement, arranged through the University of Manchester Contracts Team
2. A summary of the responsibilities of the DMC
3. A list of the members of the DMC, with contact details and areas of expertise (including CVs)
4. The structure and proposed frequency of the DMC meetings and the flow of information between the DMC, sponsor, and other entities should be captured in an organisational diagram. This should also show the reporting relationship between the DMC, the Sponsor and other functional groups (e.g. Trial Steering Committee & Chief Investigator). A copy of this diagram should be kept in the Trial Master File and provided to the CTMG
5. Meetings must be minuted
6. Each member should sign a conflicts of interest declaration
7. Each member should sign a confidentiality declaration. Need for a quorum for decision making procedures for making formal recommendations to the Sponsor and/or other functional body

References:

RGF 2nd Edition
NRES Guidance Clinical Trials and DMC:
http://www.nres.nhs.uk/applications/guidance/clinical-trials/?entryid62=74624
UK Clinical Trial Regulations
http://www.ct-toolkit.ac.uk/_db/_documents/Trial_MP.pdf