MANCHESTER 1824

The University of Manchester

**Standard Operating Procedure**

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| **Title:** | **Data Monitoring Committee** | | |
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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. In doing so the safety of patients participating in the trial would ensure that he/she was not exposed to any increased risk of harm, which could have been prevented, and where necessary the trial be ended early where necessary. This oversight can be achieved through a number of different bodies with responsibility for the ongoing monitoring of the CTIMP. 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 sponsor, and a Trial Steering Committee which are required in large clinical trials and are also appointed at the request of the study funder and sponsor. The specific aim 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 resulting from the clinical trial. The decision as to whether a DMC is required for a clinical trial is the sponsors following a risk assessment. The DMC advises the sponsor on the future management of the trial. However, it should be noted that a DMC is not needed for all clinical trials.

### Trial Steering Committee

In large multicentre clinical trials a Trial Steering Committee (TSC) is usually required. The appointment of a TSC is a required by the funder and the sponsor because the TSC often acts as a body that takes responsibility for the scientific integrity of a clinical trial. The TSC can comprise of investigators, clinical experts who are not directly involved in the clinical trial and members of staff from 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 will not usually have access to ongoing unblended study data.

## 1.1 Purpose

This SOP outlines when and how the University as the study sponsor will require a DMC to be constituted, their composition and roles..

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 requirements of the terms and conditions of the funding body which require 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), which will consist of the Chief Investigators (CIs) and/or Trial Managers of all non-commercial clinical trials sponsored/co-sponsored by The University of Manchester.

The University of Manchester will determine when a DMC is required following a risk assessment of the proposed CTIMP.

## 1.3 Data Monitoring Committee

Where the University has been approached to consider sponsorship of a CTIMP, a risk assessment will be undertaken. In its consideration of sponsorship of the CTIMP, the sponsor may determine whether or not a DMC is required. Examples of situations where a DMC may be required is when the aim of the CTIMP is considering the safety and/or efficacy of an IMP; or where there is limited data that the IMP may potentially harm the patient; and whether it would be ethical to stop the CTIMP early when the primary question has been answered.

## 1.4 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 where 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 un-blinded reports on study data and must abide to 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 experience of sitting on a number of DMCs. A DMC should have an experienced biostatistician in their membership. Any clinical members should be chosen because of his/her expertise in the area of medicine in which the trial is being conducted. In addition

the clinical member should ideally have experience and where possible knowledge of potential adverse effects of the treatment being studied.

### 1.5 Establishing the DMC

The DMC must be appointed at the earliest time after establishment of the trial and ideally 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 is reviewed, to have a clear understanding of its responsibilities, 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 of the DMC to be directly/indirectly informed of any findings.

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

1. A summary of the responsibilities of the DMC
2. A list of the members of the DMC, with contact details and areas of expertise (including CV)
3. The structure of the DMC meetings and the flow of information between the DMC, sponsor, and other entities should be captured in an organisational diagram showing the reporting relationship among the DMC, the Sponsor and other functional groups (e.g. Steering Committee & Chief Investigator)
4. Meetings must minuted
5. A conflicts of interest declaration
6. A confidentiality declaration
7. A summary of the proposed frequency DMC meetings
8. Need for a quorum for decision making and outline of the processes for decision taking
9. Procedures for making formal recommendations to the Sponsor and/or other functional body

## 6 DMC and TSC Reports

Reports from the DMC and the TSG will be reviewed by the University Research Policy Officer (Clinical Trials). Relevant information and details from the report will be shared with the CTMG, this will enable the University as sponsor to be informed about significant issues which are likely to affect a successful completion of trial are identified in the reports e.g. insufficient funding, low recruitment, and patients likely to be harmed.

**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