

**This policy has been approved by Senate**

**Policy for Compliance with The Medicines for Human use (Clinical Trials) Regulations 2004 and subsequent amendments (Investigational Medicinal Products) and other Clinical Research**

**UM/10/POL/CT002**

**1.0 Background**

1.1 This policy should be read alongside The University of Manchester's Code of Good Research Conduct, by all University staff who either are working on, or are likely to work on, research projects, that are covered by the UK Clinical Trials Regulations.

1.2 The European Clinical Trials Directive 2001/20/EC ("the Directive") was introduced to establish a standardised framework for good practice in the management of Clinical Trials throughout the European Community. The Directive sets out how clinical trials investigating the safety or efficacy of a medicinal product for use in humans must be conducted, and includes clinical trials involving healthy volunteers as well as small scale or pilot studies. The Directive also requires clinical trials to be conducted in compliance with the principles of Good Clinical Practice (GCP), with detailed standards subsequently published as the European Directive 2005/28/EC (usually referred to as "the GCP Directive").

1.3 The Directive was transposed into UK law as the Medicines for Human Use (Clinical Trial) Regulations 2004, statutory instrument SI 2004/1031, which came into force on 1 May 2004. This statutory instrument and all its subsequent Amendments (including SI 2006/1928, which transposed into UK law the GCP Directive), will be referred to as "the Regulations" in the rest of the document.

1.4 The Regulations are intended to protect the rights, safety and well-being of research participants in Clinical Trials of Investigational Medicinal Products (CTIMPs) and to harmonise, and make transparent, regulatory processes relating to clinical trials of medicines for human use.

1.5 In order to be compliant with the law, organisations conducting CTIMPs must have clearly documented Standard Operating Procedures (SOPs) covering all aspects of conducting Clinical Trials.

UoM Policy on CTIMPs	Page 1
See the Intranet for the latest version	Version 2.0 Oct 2013

## **2.0 Purpose**

2.1 This policy outlines the responsibilities of the University and any of its staff involved in a CTIMP. This policy is underpinned by procedures outlined as standard operating procedures (SOPs), which provide the structure which should be applied when undertaking and managing CTIMPs.

## **3.0 Roles and Responsibilities**

3.1 The University of Manchester's lead on operational Clinical Trials matters is the Associate Vice President for Research Integrity under the auspices of the Research Conduct and Accountability Committee.

3.2 The Chair of the University Clinical Trials Management Group (CTMG) will be the Person Responsible for CTIMPs. The Chair of CTMG will be responsible for implementing overarching policies (to be ratified by the Research Compliance Committee (RCC) relating to CTIMPs (including SOPs), approve sponsorship arrangements for CTIMPs (including undertaking a risk assessment) and will receive monitoring, annual, and safety reports. CTMG will meet regularly and will involve a representative from each trial that the University sponsors.

3.3 The Research Policy Officer (Clinical Trials) is accountable to the Chair of the CTMG and will act on his/her behalf to oversee adherence to this policy.

3.4 Chief Investigators are responsible for ensuring that this policy is observed for any CTIMPs for which s/he is the Chief Investigator, and to abide by the relevant University wide and/or local standard operating procedures (SOPs). (In this policy document, the term Chief Investigator refers to the person responsible for conducting the research project).

3.5 All University members of staff working on CTIMPs are accountable to the Chief Investigator for undertaking activity in adherence with this policy.

UoM Policy on CTIMPs	Page 2
See the Intranet for the latest version	Version 2.0 Oct 2013

## 4.0 Compliance with the UK Clinical Trials Regulations

### 4.1 Research covered by the Regulations

The EU Directive 2001/20/EC definition of a clinical trial is:

*“...any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more investigational medicinal product(s), and/or to identify any adverse reactions to one or more investigational medicinal product(s) and/or to study absorption, distribution, metabolism and excretion of one or more investigational medicinal product(s) with the object of ascertaining its (their) safety and/or efficacy”.*

The EU Directive 2001/20/EC definition of an investigational medicinal product is:

*“a pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including products already with a marketing authorisation but used or assembled (formulated or packaged) in a way different from the authorised form, or when used for an unauthorised indication, or when used to gain further information about the authorised form”.*

The EU Directive 2001/83/EC definition of an investigational medicinal product is:

*(a) Any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or*

*(b) Any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis.*

### 4.2 Determining whether a study comes under the Regulations

4.2.1 Where it is not clear whether a study is a CTIMP as defined in 4.1 above, the [MHRA algorithm](#) should be consulted and, if necessary, further clarification sought via the MHRA Helpline in accordance with the SOP Processing requests for confirmation of sponsorship for funding of CTIMPs.

### 4.3 Gaining the necessary approvals

UoM Policy on CTIMPs	Page 3
See the Intranet for the latest version	Version 2.0 Oct 2013

#### 4.3.1 Sponsorship

Sponsorship and the associated financial aspects of sponsorship, in principle must be agreed **before** any funding application is made.

The University of Manchester will only sponsor CTIMPs conducted by members of its staff.

Where the University of Manchester is requested to act as the sponsor, a risk assessment will be undertaken.

#### 4.3.2 Authorisation of the original protocol and all subsequent amendments from a National Research Ethics Service (NRES) Research Ethics Committee (REC).

The Chief Investigator **must** obtain a favourable opinion from an appropriate ethics committee.

The Chief Investigator cannot apply to any research ethics committee until the sponsor has signed the relevant documents agreeing to undertake sponsorship responsibilities.

The Chief Investigator must also ensure that the favourable opinion is registered with the Manchester Senate Committee on the Ethics on Human.

#### 4.3.3 Authorisation of the original protocol and all subsequent amendments from the MHRA–

The Chief Investigator, in liaison with the sponsor, will have to complete the Clinical Trial Authorisation (CTA) form which can be accessed via the IRAS portal.

The sponsor will submit the CTA form to the MHRA.

The Chief Investigator is not permitted to submit the CTA.

#### 4.3.4 The University of Manchester Registration –

The Chief Investigator must register with the University of Manchester any intention to submit a funding application for a CTIMP, whether or not the University of Manchester has been identified as a probable sponsor.

The Chief Investigator must keep the University informed of the funding outcome, even in cases where the application is unsuccessful or where there will be a re-submission for funding.

UoM Policy on CTIMPs	Page 4
See the Intranet for the latest version	Version 2.0 Oct 2013

For successfully funded CTIMPs, the Chief Investigator must, at all stages, keep the University informed of any intended start dates.

#### **4.4 Responsibility of the University of Manchester as the Sponsor**

4.4.1 In accordance with Regulation 3 “sponsor” means, in relation to clinical trials, the organisation which takes responsibility for the initiation, management and financing (or arranging the financing) of that trial.

4.4.2 Before it agrees to act as sponsor, and accept the responsibilities as set out in Parts 3, 4 and 5 of the UK Clinical Trial Regulations, The University of Manchester will determine whether it has adequate systems in place to undertake the responsibilities of a sponsor.

The University of Manchester will only act as the sole sponsor for a study when it is able to provide sufficient oversight of all activities detailed in the Regulations as listed below in Sections 4.43 - 4.45. This may involve the use of a UK Clinical Research Collaboration (UKCRC) registered clinical trials unit (see Appendix 1a), in which case the relevant activities will be contracted to the named clinical trials unit and detailed in a contract. In the case of First in Human (FIH) studies, the expectation is that all FIH studies will be conducted in or with the oversight of a University approved clinical research facility (CRF) (see Appendix 1b and 1c). Where an MHRA accredited Phase I CRF (see Appendix 1b) is likely to be involved, a contract will need to be agreed between the University and the CRF. Where a National Institute of Health Research (NIHR) CRF (see Appendix 1c) is likely to be involved, a contract will also need to be agreed between the University and the CRF.

Where The University of Manchester is being asked to co-sponsor a study, it will need to be satisfied that it can provide sufficient oversight of the activities specified in a sponsorship agreement. The University of Manchester as a sponsor will also need to be satisfied that the co-sponsor has adequate systems in place to take on the responsibilities delegated to it in the sponsorship agreement.

#### **4.4.3 Where The University of Manchester takes on the responsibilities of the sponsor as outlined in Part 3 of the regulations, “Authorisation and Ethics Committee Opinion” The University will:**

1. Take responsibility for ensuring that all necessary approvals are in place before allowing the trial to commence. The University will submit the request for a Clinical

UoM Policy on CTIMPs	Page 5
See the Intranet for the latest version	Version 2.0 Oct 2013

Trials Authorisation (CTA) to the MHRA. The University will not grant approval for a clinical trial to commence until it has received a favourable opinion from an appropriate ethics committee and the clinical trial has been authorised by the competent authority (MHRA).

2. Undertake to allow inspection of its premises by the Regulator.
3. Give notice to the MHRA of amendments to the CTA and make representations to the MHRA in relation to amendments.
4. Give notice of amendments to the protocol to the MHRA and ethics committee.
5. Give notice to the MHRA and ethics committee that a trial has ended.

**4.4.4 Where the University of Manchester takes on the responsibilities of the sponsor outlined in Part 4 of the regulations “Good Clinical Practice and Conduct”, the University will:**

1. Put and keep in place arrangements to adhere to Good Clinical Practice in accordance with its SOP for Good Clinical Practice\*
2. Ensure Investigational Medicinal Products are made available to subjects free of charge.
3. Take appropriate urgent safety measures (if no other person is specified to do so) in accordance with its SOP on Urgent Safety Measures.

**4.4.5 Where the University of Manchester takes on the responsibilities of the sponsor outlined in Part 5 of the regulations “Pharmacovigilance”, the University will adhere to these responsibilities in accordance with its SOP on Pharmacovigilance, which includes:**

1. Keeping records of all adverse events reported by investigators.
2. Ensuring the recording and prompt reporting of Suspected Unexpected Serious Adverse Reactions (SUSARs) to the MHRA.
3. Ensuring investigators are informed of SUSARs.
4. Ensuring all SUSARs, including those in third countries, are entered into a European database.
5. Providing an annual list of suspected adverse reactions and a safety report to the MHRA.

**4.5 Responsibility and requirements of the Chief Investigator where the University of Manchester is acting as sponsor.**

UoM Policy on CTIMPs	Page 6
See the Intranet for the latest version	Version 2.0 Oct 2013

4.5.1 The Chief Investigator is responsible for making an application for an ethics committee opinion from an appropriate NHS REC.

4.5.2 The Chief Investigator cannot commence the clinical trial until the University has given its approval for the trial to start (a formal green light letter issued by the University of Manchester). This will not be until the relevant Faculty has given its approval, a favourable opinion has been received from the ethics committee and the clinical trial has been authorised by the licensing authority (MHRA).

4.5.3 The Chief Investigator will be required to sign and adhere to an Investigator Agreement which sets out the responsibilities delegated to Investigators by The University of Manchester.

4.5.4 The Chief Investigator must abide by the relevant University wide and/or local Standard Operating Procedures (SOPs) as detailed in the Investigator Agreement.

4.5.5 Co-sponsor - Chief Investigator will adhere to his/her responsibilities as delegated in the division of responsibilities as agreed collaboratively between the University of Manchester and the co-sponsor(s).

4.5.6 The Chief Investigator will be expected to comply with the reporting requirements of the regulator (MHRA) and Research Ethics Committee and provide the University with any such reports including annual reports. The University also requires Chief Investigators to complete an annual self-assessment questionnaire for CTIMPs. The Chief Investigator is expected to provide these reports in a timely manner.

4.5.7 The Chief Investigator is required to maintain a Trial Master File (TMF) for each CTIMP. The contents of the TMF should conform to the requirements set out in The University of Manchester SOP on creating and maintaining a TMF. The TMF must include the quality management documentation required by CTMG as specified in the same SOP.

4.5.8 The Chief Investigator must co-operate with audits that the University will undertake of a CTIMP at a frequency detailed in the Investigator Agreement.

4.5.9 The Chief Investigator will co-operate with University preparations for an inspection by the MHRA and make him/herself available during the dates specified for the inspection.

4.5.10 The Chief Investigator will be expected to attend an annual meeting of the University's Clinical Trials Management Group.

4.5.11 The Chief Investigator is required to undertake GCP training every two years and to ensure that all persons involved in a CTIMP are also GCP trained and that the training is taken every 2 years. Training records should be documented in the TMF, and where required copies should be sent to the relevant Faculty Research Office.

UoM Policy on CTIMPs	Page 7
See the Intranet for the latest version	Version 2.0 Oct 2013

4.5.12 The Chief Investigator is responsible for ensuring that any adverse events are reported to The University in adherence to the its SOP on Pharmacovigilance and that annual safety reports are completed and returned to the main REC and MHRA and copied to the University as detailed in the Investigator Agreement.

4.5.13 The Chief Investigator cannot negotiate his/her own agreements/ contracts. All agreements/contracts with an external organisation or body must be negotiated via the University Contracts Team in the University Research and Business Engagement Support Services Office. The University Contracts team must be informed of any proposed protocol amendment, to assess and review the impact of the proposed change on any contract.

4.5.14 The Chief Investigator must ensure that all data is collected, stored, verified and analysed in a secure and appropriate manner and in accordance with the ethically approved protocol and University SOP for Data Management. Personal data must be handled in accordance with the UK Data Protection Act and in line with the University of Manchester Good Research Practice Guide.

4.5.15 Arrangements for the archiving of essential documents and research data must be in place before the CTIMP commences and these arrangements must be adhered to by the Chief Investigator. Where records are to be stored at The University of Manchester this must be in accordance with The University of Manchester SOP on Archiving which requires that records must be maintained in appropriate conditions and all appropriate documentation is available and transferred for archiving at the appropriate and agreed time.

#### **4.6 Expectations of an organisation that enters into a co-sponsorship arrangement with the University of Manchester**

4.6.1 Where The University of Manchester is being asked to co-sponsor a study, it will need to be satisfied that the co-sponsor has adequate systems in place to take on the responsibilities delegated to it in the sponsorship agreement.

4.6.2 The University will assess the suitability of the co-sponsor in accordance with its SOP on Assessing the Suitability of a co-Sponsor, checking that the standards and expectations are at least equivalent to the standards and expectations of the University as set out in this Policy and supporting SOPs.

#### **4.7 The role of the University of Manchester where an external organization undertakes sponsorship of a CTIMP**

UoM Policy on CTIMPs	Page 8
See the Intranet for the latest version	Version 2.0 Oct 2013

4.7.1 Where an external organization agrees to be a sponsor for a CTIMP, (irrespective of whether the research is commercial or non-commercial research), The University of Manchester requires that the Chief Investigator inform and negotiate all contracts in co-operation with the University Contracts Team.

Where a favourable ethical opinion has been received for the proposed research, the opinion must be registered with the University Research Ethics Office for insurance purposes.

Where there is a breach of GCP involving the PI or any other member of staff employed by the University, that this be reported both to the sponsor and the University immediately to the Research Policy Officer (Clinical Trials).

## **5 Consultation, Approval and Ratification Process**

### **5.1 Consultation and Communication with Stakeholders**

5.1.1 All University of Manchester-wide Clinical Trials documents are written by members of staff with relevant expertise and experience. Additional advice is sought from members of the research community within the University or external advisors, as necessary.

### **5.2 Document Approval Process**

5.2.1 All Standard Operating Procedures related to the conduct and management of Clinical Trials of Investigational Medicinal Products are approved by the CTMG and the Associate Vice President for Research Integrity.

5.2.2 All policies related to the conduct and management of Clinical Trials of Investigational Medicinal Products are ratified by the Research Conduct and Accountability Committee.

## **6 Dissemination and Implementation**

### **6.1 Dissemination**

UoM Policy on CTIMPs	Page 9
See the Intranet for the latest version	Version 2.0 Oct 2013

6.1.1 When approved, this document will be posted on the Clinical Trials pages of the University's Research Office website. Only the current version will be available.

6.1.2 All Chief Investigators will be notified by email when the latest version of the document is available.

## **6.2 Implementation of Procedural Documents**

6.2.1 Training covering the content of this document will be included in any in-house Clinical Trial training delivered by the Research Policy Officer (Clinical Trials) and the Research and Business Engagement Support Services Office.

6.2.2 Support and advice on the implementation of this document can be obtained via the Research Policy Officer (Clinical Trials) or Chair of the Clinical Trials Management Group.

## **7 Review, Monitoring Compliance with and the Effectiveness of Procedural Documents**

### **7.1 Process for Monitoring Compliance and Effectiveness**

7.1.1 The Chair of the Clinical Trials Management Group/Research Policy Officer (Clinical Trials) will monitor compliance through regular audits and monitoring visits, as well as self-assessment questionnaires.

7.1.2 Document content will be reviewed against any changes to the applicable GCP guidelines and UK Clinical Trials Regulations and taking into account any feedback received from the Chief Investigator.

7.1.3 The outcome of any review, and any resulting amendments, will be reported to the Research Conduct and Accountability Committee.

### **7.2 Standards and Key Performance Indicators 'KPIs'**

7.2.1 This document will be available on the University intranet.

7.2.2 This document will be reviewed by the CTMG at least every two years or when there are significant changes. All changes will require ratification by the RCAC.

UoM Policy on CTIMPs	Page 10
See the Intranet for the latest version	Version 2.0 Oct 2013

## Appendix 1

### Appendix 1a – UKCRC registered clinical trials unit in Manchester

[www.ukcrc-ctu.org.uk](http://www.ukcrc-ctu.org.uk)

**Manchester Academic Health Science Centre - Trials Coordination Unit (MAHSC-CTU)**

### Appendix 1b - MHRA accredited Phase I clinical research facility (CRF) in Manchester

**Medicines Evaluation Unit (MEU)**

**Manchester**

**ICON**

**Manchester**

### Appendix 1c - National Institute of Health Research (NIHR) CRF

<http://www.nihr.ac.uk/infrastructure/Pages/CRFs.aspx>

**NIHR/Wellcome Trust Manchester CRF**

**Central Manchester University Hospitals NHS Foundation Trust**

**NIHR/Cancer Research UK Christie CRF**

**The Christie NHS Foundation Trust**

**NIHR/South Manchester Respiratory and Allergy CRF**

**University Hospital of South Manchester NHS Foundation Trust**

UoM Policy on CTIMPs	Page 11
See the Intranet for the latest version	Version 2.0 Oct 2013

Document control box	
Policy title:	Policy on Compliance with The Medicines for Human use (Clinical Trials) Regulations 2004 and subsequent amendments (Investigational Medicinal Products) and other Clinical Research
Date approved:	2nd October
Approving body:	Senate
Version:	2.0
Supersedes:	N/A
Previous review dates:	
Next review date:	2 years (proposed)
Related Statutes, Ordinances, General Regulations:	Medicines for Human Use (Clinical Trial) Regulations 2004, statutory instrument SI 2004/1031; subsequent Amendments including SI 2006/1928;
Equality relevance outcome:	Medium (provisional assessment)
Related policies:	
Related procedures:	All CTIMP related SOPs
Related guidance and or codes of practice:	European Directives 2001/20/EC & 2005/28/EC
Related information:	See 'References' section of policy
Policy owner and lead contact	Professor Deborah Symmons